Ex-post evaluation: EU competition enforcement and acquisitions of innovative competitors in the pharma sector leading to the discontinuation of overlapping drug research and development projects

Final Report

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Ex-post evaluation: EU competition enforcement and acquisitions of innovative competitors in the pharma sector leading to the discontinuation of overlapping drug research and development projects

Final report and Appendices

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The study report was finalised in May 2024. A targeted update to the report was made in November 2024 to reflect the findings of the European Court of Justice in its judgment of 3 September 2024 in the Illumina / GRAIL case.

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Abstract

In recent years, concerns about transactions in the pharmaceutical sector harming innovation and competition through the discontinuation of overlapping drug R&D projects, so-called "killer acquisitions", have prompted regulatory action and research.

The objective of this study is twofold. First, the "fact-finding" challenge aims at assessing the pervasiveness and characteristics of the phenomenon of killer acquisitions. Second, the "evaluation" challenge aims to conduct an ex-post evaluation of cases that may have involved killer acquisitions.

Under the fact-finding challenge, the study collects publicly available evidence on a large sample of transactions occurring in the period 2014-2018, seeking to determine whether any may have led to a potential killer acquisition. The study is novel in that it assesses not only mergers and acquisitions, but also other types of transactions such as licensing deals and R&D cooperation agreements. In addition, the fact finding assessment goes beyond a statistical assessment of the probability of killer acquisitions by applying the following 2-stage approach: i) a large-scale and automated analysis to detect transactions followed by discontinuations of overlapping drug R&D projects not seemingly justified by technical or commercial reasons and ii) a qualitative, case-by-case examination to evaluate the key elements of a killer acquisition hypothesis in some of the most relevant discontinuations identified through the large-scale analysis.

Out of a total of 6,315 transactions that were identified in the pharmaceutical sector in the period 2014-2018, information on the remit of the deal was available for 3,193 transactions. Out of these, 240 transactions involved the acquisition of potentially substitutable drug R&D projects, conservatively based on a narrow definition of competitive overlap. A significant proportion thereof (89 out of 240, or 37% of transactions) were followed by the discontinuation of one of the overlapping drug R&D projects *and* warranting further scrutiny, in the sense that – based on publicly available data – there was no clearly identifiable technical or safety reason explaining the discontinuation in question. The study further finds that public information sources alone do not typically suffice to conclusively assess the existence of a killer acquisition theory of harm, or the absence thereof. Any further scrutiny has to largely rely on *non-public* (company internal) information.

Under the evaluation challenge, the study examines the Commission's past efforts to address potential killer acquisitions, and the legal framework guiding the Commission's actions. The study first analyses how well the Commission's substantive merger assessment dealt with five notified concentrations in the pharmaceutical sector. It finds that the Commission correctly assessed the killer acquisition theories of harm in these cases, with a suggestion for potential improvement in the remedy design. Then, it analyses the suitability of the merger and antitrust tools to deal with killer acquisitions which are not notified to the Commission, by simulating Art. 22 EUMR and Art. 101/102 TFEU assessments in two case studies. Past experience and a legal assessment suggest that Art. 22 EUMR (for concentrations) and Art. 101/102 TFEU (for non-concentrations) are valuable tools (albeit with limitations) to address such killer acquisitions, with potential for improvement in the establishment of a registry or notice system to identify potentially harmful transactions.

Executive summary

In recent years, there has been mounting concern among antitrust authorities that mergers and acquisitions (M&As) involving highly innovative firms in concentrated industries may have substantial effects not only on prices but also on innovation. Existing studies have shown that mergers may encourage or discourage research efforts and, in turn, innovation output, depending on factors such as the level of competition, efficiencies resulting from consolidation, and changes in the appropriability of innovation (Gilbert, 2022; Haucap & Stiebale, 2023).

There is also a specific concern about a 'loss of potential competition' which is commonly related to the "killer acquisition" theory of harm. This is generally understood as incumbents buying a start-up to pre-empt the threat of future product market competition or even a replacement of their core-business by eliminating a specific rival's overlapping pipeline. Crawford et al. (2020)[1] argue that acquisitions may also deter innovation competition, i.e., be an opportunity of "'buying' instead of expending effort in rival innovation",[2] with the risk of jeopardizing competitive dynamism from the outset, even before R&D efforts shape specific product development.

The pharmaceutical sector is one of the industries with the highest levels of research and development (R&D) investment, where innovation plays a pivotal role in contributing to advances in both economic prosperity and health outcomes (Bokhari, et al., 2021). A consistent finding of existing studies is that market consolidation in the pharmaceutical industry leads to substantial reductions in research spending and patent output among the consolidated firms (Ornaghi, 2009a; Haucap, et al., 2019), as well as a significant decline in the productivity of inventors from the target firms (Ornaghi & Cassi, 2023). However, empirical research on alliances between smaller biotech firms and larger pharmaceutical entities, considered as potential substitutes or complements to mergers, offers a more optimistic perspective, as there is evidence of a positive correlation between a larger firm's clinical development expertise and the likelihood of successful outcomes for small firms (Grabowski & Kyle, 2008).

Concerns about the detrimental effects of mergers on innovation have intensified following the publication of the "Killer Acquisitions" paper by Cunningham et al. (2021), which shows that acquired drug projects are less likely to be developed when they overlap with the acquirer's existing product portfolio, especially when the acquirer's market power is large because of weak competition or distant patent expiration. According to the authors, these acquisitions disproportionately occur just below the relevant thresholds for antitrust scrutiny. This latter finding is reminiscent of the analysis by Wollmann (2019), which finds that following the increase in the pre-notification exemption threshold for mergers in the U.S., pharmaceuticals were among the top five industries with the highest number of horizontal exempt mergers in the post-amendment period. It is also in line with the Commission's internal assessment of mergers that did not meet the turnover thresholds of the EU Merger Regulation (EUMR).[3]

[1] 'How tech rolls': Potential competition and 'reverse' killer acquisitions, Gregory Crawford, Tommaso Valletti, and Cristina Caffarra, VoxEU, 11 May 2020, https://cepr.org/voxeu/blogs-and-reviews/how-tech-rolls-potential-competition-and-reverse-killer-acquisitions.

[2] Ibidem.

[3] Commission Staff Working Document (2021), "Evaluation of procedural and jurisdictional aspects of EU merger control", SWD (2021) 66 final, 26 March.

This assessment showed that in the pharmaceutical sector there were mergers involving overlapping drug projects which failed to meet the turnover thresholds even though acquirers appeared ready to pay a high price for the acquisition of low-turnover innovative targets. Finally, the findings in Cunningham et al. (2021) are also consistent with the work on mergers and acquisitions in the pharmaceutical industry commissioned by the European Commission and carried out by Informa Pharma Consulting and Szücs (2020), which shows that the probability of a drug project being discontinued increases if it overlaps with another drug project of the acquiring company for the same indication. In addition, the study shows no acceleration in the pace of drug development following an acquisition, contrary to industry claims that acquisitions speed up the R&D process.

As part of its continuing commitment to preserving innovation in the pharmaceutical industry, in 2022 the Commission launched a new project – of which this study presents the results – to assess the pervasiveness and characteristics of the phenomenon of killer acquisitions, focusing on a large sample of transactions (both M&A and non-M&A), that occurred in the pharmaceutical sector in the period 2014-2018.

The Technical Specifications define killer acquisitions in the pharmaceutical sector as transactions that are likely to have as their object or effect the discontinuation of overlapping drug research and development projects ("drug R&D projects") to the detriment of future competition and ultimately of consumers. [4] This is the definition adopted in this study.

The objective of the study is twofold. First, it provides fresh evidence on the phenomenon, through an analysis of a large sample of transactions occurring in the period 2014-2018, with the aim of ascertaining, with the benefit of hindsight, whether they have likely caused a discontinuation of overlapping projects *and* have altered competition in the market ("fact-finding challenge"). As a novelty, the study examines *all* types of transactions (not only mergers and acquisitions, but also asset purchases, licensing agreements, R&D agreements and others). Another important novelty relates to the methodology required by this study, as it collects factual evidence that would support a killer acquisition narrative at the deal level, whereas existing research only provides theoretical or statistical evidence of the existence or magnitude of the phenomenon.

Second, this study evaluates (i) the Commission's past efforts to tackle the phenomenon of killer acquisitions and (ii) the legal framework within which the Commission operates, in the light of evidence that killer acquisitions may also occur below merger regulation thresholds or may not be structured as concentrations in the first place ("evaluation challenge"). In particular, the second chapter assesses the current rules and recent practice under the EUMR, as well as the merits of (and issues arising from) the application of Articles 101 and 102 of the Treaty on the Functioning of the European Union (TFEU) to address transactions that the EUMR regulatory grid may fail to detect.

Fact-finding challenge

The first chapter relates to the *fact-finding* challenge and illustrates an analysis of a large sample of transactions that occurred in the pharmaceutical sector between 2014 and 2018. The analysis was conducted with the benefit of hindsight, but it relied on *publicly available* data: for this reason, it faced several limitations that are discussed

[4] Technical Specifications, footnote 2, reference this definition.

below. On the basis of factual evidence, it sought to determine whether any of these transactions may have led to the discontinuation of overlapping projects (including both pipeline-to-pipeline overlaps and marketed-to-pipeline overlaps) *and* altered the competitive landscape in the relevant product market.

For the fact-finding analysis, the study has developed a four-step methodology that identifies publicly available data sources and provides tools that can be used to help determine whether a given transaction has led to the discontinuation of competing drug R&D projects in a pattern consistent with a killer acquisition theory of harm:

- Identification of narrow overlaps. In line with the Commission practice and the existing literature, the study uses therapeutic indications (TIs) and mechanisms of action (MoAs) to determine whether drug R&D projects are direct substitutes. We refer to this type of overlap as "narrow overlap", in contrast to "broad overlap" based only on TI. The study has developed proxies to identify potential competition between drug R&D projects that may present different TIs and MoAs at different stages of their development. In particular, this study suggests that Medical Subject Headings (MeSH) terms that are associated with clinical trials in the relevant US registry (ClinicalTrials.gov), which is the most comprehensive database publicly available,[5] provide a numerical and hierarchical structure that clarifies the relationship (if any) between two apparently different TIs. Furthermore, when two drugs' MoAs are not identical – as may be the case if they are not yet well-established – potential substitutability between them can still be assessed by reference to joint citations in articles from medical journals that are published and searchable online in PubMed Central® (PMC), a public archive maintained by the US National Library of Medicine.
- Identification and classification of discontinuations. There are numerous ways an overlapping drug R&D project may be discontinued following an acquisition. In some cases, ClinicalTrials.gov clearly indicates that a trial has been terminated or withdrawn (and sometimes indicates the reason). In other cases, there is no evidence, other than inactivity in the clinical trials process, that could be used to infer whether a trial, or the further development of a drug in a given TI, has been abandoned. Finally, drug R&D projects may be discontinued in one therapeutic indication, to be reoriented in a different one. In the absence of any information on termination or withdrawal, the study assumes that when at least two years of inactivity are observed in the development of a drug R&D project in a given TI and no further development has occurred thereafter, the project has been discontinued. By relying on the numerical structure of MeSH terms, the study also detects cases where an apparent competitive overlap has been eliminated through a reorientation of one of the overlapping drug R&D projects to a different TI.[6] The reasons of termination in the clinical trials registry (when available), the period of inactivity, the nature of the sponsors (whether it is a private or public entity) and the evolution

[5] We performed a comparative analysis and found that the vast majority of trials reported in the European Clinical Trial Register ("EUCTR") are also included in ClinicalTrials.gov (that on the other hand, offers larger coverage and more information). In addition, we rely on EUCTR for completeness when performing manual screening (see point 4).

[6] For the purpose of this study, delays shorter than two years are, by contrast, not taken into account; even longer delays, if a development event occurs still before the end of the observational period available to the study, are not considered relevant in this study (even if they may cause harm for the time of the delay). In these cases, however, it cannot be excluded that there was competitive harm in the form of delayed development of a competing drug, which is not captured by the study.

of the TI over time for both overlapping drugs contribute to filter, out of all the observed discontinuations, those that appear unrelated to the deal and seemingly related to technical and clinical reasons (e.g. poor experimental design, low accrual). The discontinuations that remain at the end of this filtering process are referred to as *prima facie* relevant for a killer acquisition assessment.

- The study relies on a machine learning algorithm (Least Absolute Shrinkage and Selection Operator, known as "LASSO") with the aim of characterising ex-ante transactions that would deserve further scrutiny. We start with an initial list of observable characteristics, suggested by the literature and pre-selected by our group of business experts, which may indicate that the parties involved in a given transaction had either the incentive or the ability to kill competition in a relevant market. The LASSO specification includes variables capturing the strength of future product market competition. We rely on LASSO to select which of these initial features may best help to identify drug projects that more likely would not have been discontinued in the absence of the deal *and* whose discontinuation potentially lessened competition in the assessed markets.[7] Thus, LASSO is intended to separate, out of the transactions leading to *prima facie* relevant discontinuations, those that are more likely to reflect a killer acquisition narrative. The analytical steps described so far are part of a "large-scale" analysis, since they aim at detecting potentially anticompetitive discontinuations based on an automated analysis of a large number of observations, with a set of predefined rules.
- Finally, the study conducts a "manual screening" of the *prima facie* relevant discontinuations displaying the LASSO validated features ("LASSO-KA") and of a subset of the (remaining) *prima facie* relevant discontinuations, to test the reliability of the LASSO results. The manual screening consists, for a subgroup of deals, in a case-by-case verification and a reasoned assessment of the facts. The discontinuation of an overlapping drug R&D project, even if caused by a deal, is a necessary but not sufficient condition to conclude that the acquisition has stifled (or likely will stifle) competition and innovation. In our study, the notion of killer acquisition refers to a theory of harm in which a transaction causes the discontinuation of an R&D project ***and*** (is likely to) result in a negative effect on competition. In other words, the notion of killer acquisition theory of harm that we adopt in our study excludes cases where the acquiror terminates the development of a drug without, however, altering the competitive dynamics prevailing in the relevant market. This approach requires a full understanding of the pattern of substitutability between the overlapping drugs, their clinical relevance and the level of competition in the relevant market, especially when the overlap in TI is not perfect and potential substitutability needs to be carefully evaluated, as well as an assessment of the parties' commercial incentives and funding constraints. The ultimate objective of the manual screening is to gather evidence that would fully endorse (or the opposite, not endorse) a killer acquisition theory of harm underlying the transactions, taking into account the above aspects as far as possible with the information available in the public domain. In the manual screening, we have relied on public information sources and types of data beyond those that could possibly inform the large-scale analysis, such as a review of companies' reports, company

[7] *LASSO is trained based on sample restricted to those prima facie relevant discontinuations more likely relatable to strategic or business motives, that are then compared to a control group consisting of overlapping drug projects where we find either no discontinuation right after the deal, or whose discontinuation appears more seemingly related to technical and clinical reasons.*

announcements relating to the transaction, articles in the specialised press commenting on the deal; as well as on a tailored assessment by the team of experts of the technical and commercial viability of the discontinued drug R&D projects, in light of public technical reports on the parties' and their competitors' R&D activities (referenced on ClinicalTrials.gov or accessible via PMC).

While relying on a complex methodology, the fact-finding challenge bears the following important caveats:

- the study focuses on competition from ongoing pipeline products at clinical trial stage and, thus, does not allow to fully assess the impact of a deal on innovation competition. For instance, the large-scale analysis does not cover either pre-clinical trials or future intentions of the parties to pursue a new therapeutic indication;
- the study relies on public sources and does not have access to company internal documents and presentations, that could help understanding whether the deal has changed the commercial incentives of the parties when pursuing the development of a drug. Further, publicly available information does often not allow for a clear reconstruction of the competitive landscape and of the competitive pressure exerted by each competitor or other firms in the market;
- when assessing licensing deals or R&D agreements, identifying the deal's "object" and "perimeter" (i.e., respectively, the drugs and therapeutic indications targeted by the deal, and the other relevant overlapping drugs affected by the deal) and determining the party benefiting from the exchange of rights becomes complex.[8] By necessity, this implies that the study may not well capture the extent and character of potential killer acquisitions in these two categories of transactions; in addition, incentives of the parties depend on the allocation of marketing and distribution rights for the joint innovation: the notion of killer acquisition theory of harm, as endorsed by this study, involves a transaction that enables a party to gain control rights[9] over a substitutable drug R&D project. Such details about R&D agreements are not public, so it is not possible to understand whether they can create exclusive rights, even when manually screening them;
- the study takes a relatively comprehensive approach in assessing potential substitutability between drug R&D projects, but it does not take into account deals that bring under common control drug R&D projects that share only the same therapeutic indication or therapeutic class. Broad (rather than narrow) overlaps fall

[8] For a large number of deals, a deal object or target could not be identified. The main reason for this was that one of the companies involved was not present in our clinical trials dataset, which typically occurs when companies do not have R&D projects in their portfolio (e.g. because they are active in platforms, technologies and devices rather than drug development, or their drug R&D projects are at the preclinical stage and they have not yet registered clinical trials).

[9] This study intends control rights as those that would suffice to provide an entity with the legal ability – should it also have the incentives – to eliminate one of two overlapping drug R&D projects that, absent the deal, would be rival, thus potentially affecting future product market competition. In acquisitions and asset purchases, the nature of the transactions implies a transfer of property rights to the acquirer, usually enough to safely assume that the latter can dispose at its convenience of both overlapping drug R&D projects. In licensing deals, what is relevant is the scope of the licensing: in this respect, in addition to the specific therapeutic indications targeted by the deal, we try to detect exclusivity and to control for the geographic scope of the licensing, to make such an assumption robust. In R&D agreements, as already discussed, whether the deal can modify the ability and incentives of either of the parties to discontinue one of two overlapping drug R&D projects depends on how marketing and distribution rights for the joint innovation set out by the agreement are allocated to the partners, something that, however, neither the deal type itself nor public information help us being conclusive about.

outside the scope of this study – further research may help to shed light on the extent to which these could also generate relevant discontinuations;
- while the study considers a relatively extended period of inactivity as an indication that a project may have been discontinued, this conclusion is not applicable if further development, such as the registration of a new trial, is observed even after a long period of inactivity. Accordingly, although competitively significant, development delays are not addressed in this study; and
- while the study considers the interests of the parent and subsidiaries of the companies directly involved in the deal, it does not take into account cases in which minority shareholdings may give rise to incentives and an ability to cause a killer acquisition.

Despite the aforementioned limitations, the study originally contributes to the growing literature striving to characterise the phenomenon of killer acquisitions.

Fact finding results

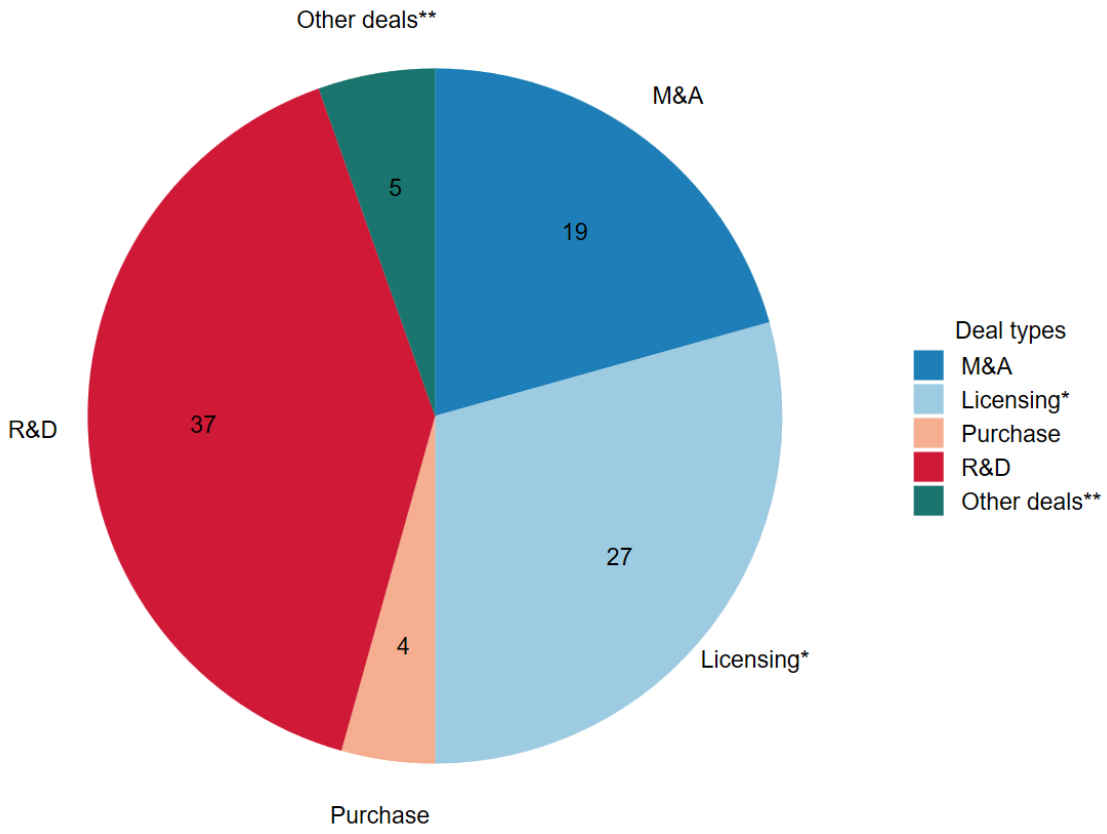
Out of a total of 6,315 transactions that were identified in the pharmaceutical sector in the period 2014-2018, information on the remit of the deal was available for 3,193 transactions.[10] Out of these, 240 entailed the acquisition of potentially substitutable drug R&D projects, conservatively based on a narrow definition of competitive overlap (with overlapping TI and MoA). In the vast majority of these deals (183), at least one narrowly overlapping drug was discontinued after the transaction. This striking result raises the question of what the reason for the discontinuation was and whether it could be consistent with a killer acquisition theory of harm. We find that 92 (or 38%) of the deals with a narrow overlap were followed by a discontinuation of at least one of those projects that appear *prima facie* relevant for a killer acquisition assessment.

The figure below shows the distribution of *prima facie* relevant discontinuations by deal type:[11]

[10] The deals that informed the analysis are those, among the ones listed in the initial dataset, for which we have sufficient information to identify the parties' marketed drugs and drug R&D projects affected by the transaction.

[11] The large-scale analysis has been designed and run separately by deal type, to take into account the specificities of each deal type.

The distribution of *prima facie* relevant discontinuations by deal type



*Source: Lear analysis. Notes: *There are 12 "exclusive" licensing agreements, identified using search text tools on the descriptions in our deal dataset, which exhibit prima facie relevant discontinuations.**For the group Other deals, prima facie relevant discontinuations are in the following deal types: Equity investment (2 deals), Joint venture (1 deal), Joint venture R&D (1 deal), Marketing agreement (1 deal); no discontinuation of narrow overlaps is found in Partnerships and Cross-Licensing agreements*

Prima facie relevant discontinuations are detected in around 40% of the deals with overlapping drug R&D projects in our analysis. In more detail, they represent 54% of the deals with narrow overlaps in M&As, 27% in licensing agreements, 33% in Purchases and 43% in R&D agreements. They are also distributed across equity investments (with 2 deals), followed then by joint ventures (JV), JV R&Ds and marketing agreements (one deal in each of these deal types), while in partnerships and cross-licensing agreements no *prima facie* relevant discontinuation has been detected. These findings suggest that a large proportion of deals involving overlapping R&D projects, in particular mergers and acquisitions as well as licensing and R&D agreements, are *prima facie* relevant for a killer acquisition assessment.

To detect transactions where a killer acquisition theory of harm could have potentially been present or anticipated, exploiting relevant data collected for all narrow overlaps, this study set out to explore the LASSO approach, followed by a manual screening to validate the LASSO results. When applied to M&A, licensing and R&D agreements, the LASSO led to select 53 *prima facie* relevant discontinuations as "LASSO-KAs", distributed over 19 different deals.

The manual screening then covered: all *prima facie* relevant discontinuations in M&As (including 6 LASSO-KAs) and in exclusive licensing deals (including 9 LASSO-KAs);[12] 5% in R&D agreements (22% in terms of deals, including 4 LASSO-KAs);[13] all *prima facie* relevant discontinuations in all other deal types (Partnerships, JV R&D agreements and JV, Equity investments, Marketing agreements, Cross-licensing, grouped together under the label "Other deals"), where the LASSO approach could not be applied because of the small sample size.

The manual screening highlighted that *prima facie* relevant discontinuations are of diverse nature, even within each deal type and when they share similar "LASSO features" (i.e., the conditions defined by the LASSO model solution, on the basis of which we identify LASSO-KAs),[14] showing that these are not sufficient to grasp the specificities of these deals. Notably, despite the presence of LASSO features, the available evidence (publicly available information) is not conclusive on the killer acquisition narrative or its absence, thus making these deals subject to the same degree of uncertainty as transactions leading to *prima facie* relevant discontinuations but not having the same features. This hinders the ability of the LASSO solution to assist competition authorities to ex-ante identify transactions that would deserve further scrutiny.

Moreover, without access to the firms' internal documents, drawing conclusions about the extent to which the transaction has altered the commercial incentives of the parties proved challenging, even during the manual screening conducted on a case-by-case basis. Public evidence generally does not provide a solid basis for determining whether or not the *prima facie* relevant discontinuations fully reflect a killer acquisition theory of harm, preventing us from making a conclusive assessment. This is even more true for some deal types, especially R&D agreements, and in the miscellaneous of Other deals.[15]

As already discussed, the notion of killer acquisition theory of harm, as endorsed by this study, involves a transaction that enables a party to gain control rights over a substitutable drug R&D project, causes the discontinuation of a pipeline in a given TI or the termination of a molecule, and ultimately is likely to lessen competition and innovation. For most of *prima facie* relevant discontinuations that have been manually investigated, publicly available information could not provide compelling evidence that firmly suggests: (i) the degree of substitutability (or closeness of competition, which is key in a killer acquisition theory of harm) between overlapping drug projects, and most notably, that the drugs can similarly treat the same disease, rather than being apt for different patient segments, parallel or sequential treatment, or combined therapies; (ii) that the discontinuation lacks a valid clinical or other technical justification; or can be

[12] As to licensing, a non-exclusive licensing agreement would hardly provide the ability and incentives to discontinue a drug project. Therefore, the manual screening has focused on exclusive licensing deals. Exclusive licensing transactions are identified applying search text tools to the description of the deals.

[13] Public information available is typically little informative for R&D agreements, where not even the focal exchange of rights between the parties over the relevant drugs is known. Such limits consistently constrain the analysis and findings, discouraging more extended screening.

[14] As the LASSO models were run by deal type, they led to different solutions (and thus different features) depending on the deal type. In our first estimation of the model in the sample of M&A deals, the LASSO selects only one regressor, i.e. the interaction between: one of the overlapping molecules in Phase 4 (i.e. marketed), one of the overlapping molecules in Phase 2, and the maximum number of competitors in the market equal to three.

[15] See footnote 13.

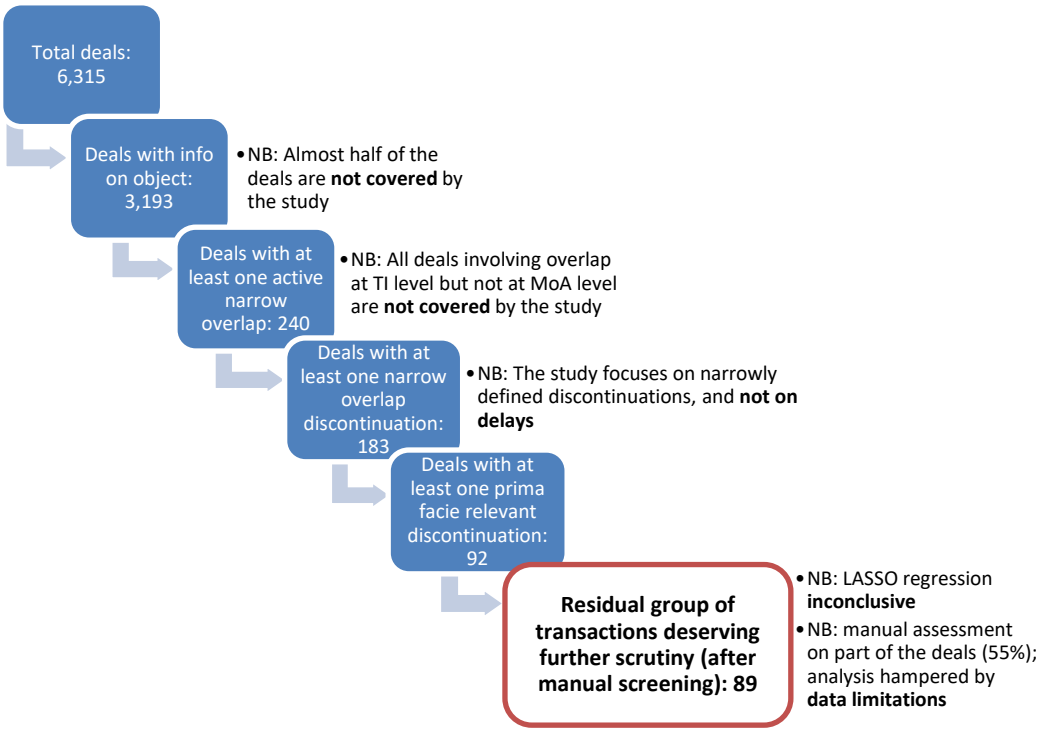
justified by a commercial assessment that would have emerged even in the absence of the transaction; (iii) that competition in the relevant market was adversely affected by the discontinuation (a more in depth assessment of the degree of substitutability with the parties' overlapping drugs is required also for 'competing' drugs). In addition, for R&D agreements we cannot draw conclusions in general because of the opacity of the legal rights exchanged by the parties.

At the same time, there are only a few instances where the publicly available evidence more clearly suggests that a killer acquisition narrative can be confidently discarded. These are mainly cases where we find that, contrary to the large-scale analysis findings, the discontinued drug is still in development (two deals in the M&A group and one in the licensing group, resulting respectively, in five and three discontinuations at the overlap level).

In summary, the study shows that a significant proportion (89 out of 240, 37%) of the deals in which there was a narrow overlap was followed by a discontinuation that would deserve further scrutiny, in the sense that based on publicly available data there was no clearly identifiable technical or safety reason explaining the discontinuation in question. The study further finds that public information sources do not typically suffice to conclusively assess the existence of a killer acquisition theory of harm, or the absence thereof. Any further scrutiny would have to largely rely on *non-public* (company internal) information, to conclusively assess the existence of a killer acquisition theory of harm in the case at hand.

The below chart summarises the main findings:

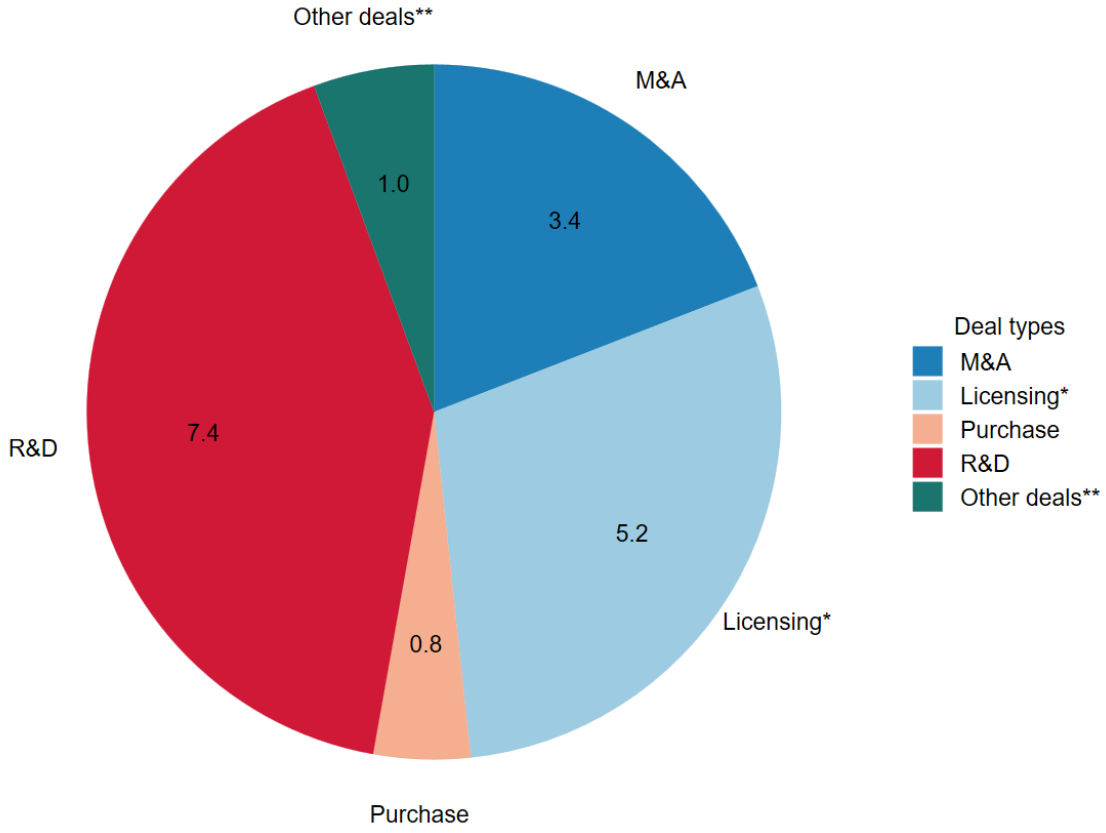
Results of the fact-finding challenge



Source: Lear analysis

To better illustrate the magnitude of the phenomenon of deals deserving further scrutiny, the figure below shows their average annual number by deal type over the period analysed:

Annual average number of deals deserving further scrutiny (2014-2018)



*Source: Lear analysis. Notes: *Over the years 2014-2018, there are 12 "exclusive" licensing agreements, identified using search text tools on the descriptions in our deal dataset, among those deserving further scrutiny.**For the group Other deals, over the years 2014-2018, deals deserving further scrutiny are in the following deal types: Equity investment (2 deals), Joint venture (1 deal), Joint venture R&D (1 deal), Marketing agreement (1 deal); no discontinuation of narrow overlaps is found in Partnerships and Cross-Licensing agreements*

For the period 2014-2018, the study finds an average of 3.4 M&A deals deserving further scrutiny per year, 5.2 licensing deals, 0.8 purchase deals, 7.4 R&D agreements and 1 deal in the residual category.

The findings are further supported by the analysis of the characteristics of this residual group of transactions for M&A deals, which reveals distinct features compared to transactions not followed by discontinuations or followed by seemingly benign ones. Specifically, discontinuations deserving further scrutiny and related transactions often involve overlapping drugs in advanced development stages, potentially indicating a significant competitive threat that may drive a "killer acquisition" strategy. Additionally, they tend to occur in highly concentrated markets where actual competitors are scarce, further incentivising such actions.

The *fact-finding* challenge suggests that the phenomenon of killer acquisitions should continue to be of concern for competition agencies.

While comparing the quantitative results of the study with those by Cunningham et. al (2021) requires formulating assumptions and caveats, the overall conclusions align: Cunningham et al. (2021) suggest "caution against interpreting acquisitions of nascent technologies solely as incumbents' efforts to integrate and foster entrepreneurial innovation".[16]

Fact-finding challenge: policy recommendations

In conclusion, the fact-finding challenge underscores the growing concerns of competition agencies regarding the anticompetitive object and effects of acquisitions involving overlapping drug R&D projects. The study emphasises the importance of a case-by-case assessment, rather than broad-scale or probabilistic evaluations, to grasp the incentives of the involved parties and the impact of the transaction on competitive dynamics. Specific information about the deals is crucial for understanding factors such as drug substitutability, their technical and commercial viability, and the competitive threat posed by other drugs in the market. Publicly available information can aid in the preliminary screening of such acquisitions, especially for merger and acquisitions. However, it is insufficient to draw definitive conclusions about their implications on future market competition.

We recommend that the Commission maintains its proactive approach in monitoring concentrations within the pharmaceutical sector, as evidenced by its past activity in promptly identifying potential concentrations for ex-ante review under the EUMR utilising referrals under Article 22 as also further described below. However, analysing deals structured outside of concentrations, such as R&D agreements and other collaborations, presents greater complexity. Publicly available information often falls short in elucidating how these deals modify the entitlement to the disposal of targeted innovations and, consequently, how it can affect the commercial incentives of the parties toward either overlapping drugs' development projects.

Despite the caveats outlined in our analysis, the report reveals that the phenomenon of "killer acquisitions" may impact R&D agreements as significantly as M&A transactions. Approximately half of the transactions with narrow overlaps, for both deal types, are followed by discontinuations that warrant further scrutiny. Further research is thus essential to better categorise them, understand their implications, and assess their susceptibility to a "killer acquisition" narrative.

Evaluation challenge

The second chapter of the report aims to assess the application and, where appropriate, to uncover the limitations of the current EUMR as well as to assess the merits of the application of antitrust rules where relevant.

Firstly, an evaluation of the Commission's past efforts to tackle killer acquisitions under the EU merger regulation is provided, by examining *ex post* the assessment that the Commission conducted for five notified concentrations. Subsequently, the general legal framework within which the Commission operates is evaluated, and the applicability of Article 22 EUMR and Articles 101 and 102 TFEU are simulated in two apposite case studies. Both elements of the study are based on extensive desk-research of publicly

[16] Cunningham et al. (2021), p. 696.

available information. The assessment of the legal framework relies on legal and economic literature, with a strong focus on legal precedents and court decisions.

It is important to note that since the time of writing of this study (May 2024), the European Court of Justice has ruled on Illumina's and GRAIL's jurisdictional appeals in Joined Cases C-611/22 P and C-625/22 P. In its judgment, the Court of Justice clarified that a Member State is required to be competent under its national merger control rules, or have no merger control rules in place, to be able to refer a concentration to the Commission under Article 22 EUMR[17]. Following that ruling, the Commission has thus moved away from its revised approach to Article 22, which consisted of accepting, in certain circumstances, the referral of cases where the referring Member State did not have competence under national rules, but which were likely to affect trade and competition within the EU. Going forward, and in line with the Court's findings, the Commission has indicated that it will only accept referrals from Member States that are themselves competent to review the concentration concerned[18], or that have no domestic merger control regime (like Luxemburg) (see also Section II.2.3 for further details). Subject to these limitations, Article 22 EUMR remains a valuable enforcement tool for the Commission to be able to review mergers that seem likely to raise competition concerns despite falling below the EUMR thresholds.

In assessing individual transactions, we relied on the following sources of information:

- Springer Nature's AdisInsight database on drugs in commercial development worldwide;[19]
- ClinicalTrials.gov, a comprehensive registry of clinical trials worldwide;[20]
- online resources for medical professionals, including journal articles regarding the results of clinical trials and R&D trends/challenges that were accessible free of charge through the PubMed database,[21] treatment guidelines of various medical associations (e.g. ESMO) that were in force (and often amended) over the period covered in this study, and information published by the EMA and FDA on their official websites;
- representations made by transaction parties (in, e.g. their press releases, annual reports, SEC filings, published pipelines, management interviews, and the like), which were assembled from the parties' websites and other online archives; and

[17] Judgment of 3 September 2024, Illumina, Inc. v European Commission, Joined Cases C-611/22 P and C-625/22 P, EU:C:2024:677.

[18] This may include circumstances in which a transaction meets applicable merger control thresholds set in national law, as well as cases where national competition authorities exercise their power, based on national law, to "call in" a transaction giving rise to competition concerns without meeting applicable domestic thresholds (at the time of writing, eight EU Member States – Denmark, Hungary, Ireland, Italy, Latvia, Lithuania, Slovenia and Sweden – and two EFTA Member States – Norway and Iceland – have provided for such "call-in" powers in their national laws). EU Member States are competent to initiate Article 22 referral requests, whereas the EFTA Member States may not initiate but may join in a pending referral request.

[19] A full description of this database is provided in section I.1.2 of this Report.

[20] A full description of this registry is provided in section I.1.3 of this Report.

[21] PubMed (https://pubnmed.ncbi.nlm.nih.gov) is a searchable database of citations and abstracts of medical research literature, maintained by the U.S. National Library of Medicine, that provides links to other websites carrying the relevant, full-text material.

- news reports and analyses by specialists in the pharmaceuticals sector (e.g. Scrip[22] and Fierce Pharma[23]), as well as more general, business-oriented news publications online.

Where these public sources were not sufficiently clear, we drew on the knowledge and experience of pharmaceutical industry experts in the Team to assess, e.g. the scope for competition between different molecules, technical trial results and their commercial ramifications, pipeline prospects for success, and the various incentives that might have shaped firms' strategic decisions.

Evaluation challenge results

The *evaluation challenge* chapter begins by examining how well the Commission's substantive merger assessment addressed transactions notified to it in the pharmaceutical sector involving overlapping R&D projects. This study includes an *ex-post* evaluation of five selected pharmaceutical acquisitions that were notified to the Commission and cleared (sometimes with remedies).[24] These cases represent, among those investigated in the relevant timeframe of this study,[25] those involving human drug R&D projects (as opposed to R&D for medical devices) and market-to-pipeline overlaps or pipeline-to-pipeline overlaps. These include one deal that was flagged in the *fact-finding* challenge as deserving further scrutiny and in particular one narrow overlap that has not raised concerns in the Commission investigation, because they have been able to access non-public information that this study could not take into account. The *ex-post* evaluation aimed at assessing whether the acquisitions were followed by a discontinuation of overlapping R&D projects that might have eliminated competition and harmed consumers. This includes an assessment of remedies, and how pipelines evolved after the implementation of those remedies.

The study shows that the Commission has generally correctly identified possible killer acquisitions. While, as indicated above, in one of the cases examined, the analysis based on publicly available evidence suggests a potential area of concern that could have merited further scrutiny, the authors of the study understand that the Commission had access to confidential data that would lead to dismiss any possible concern. Out of the five cases assessed in this study, two were cleared by the Commission unconditionally and three were cleared subject to remedies. The ex-post evaluation conducted by the Team revealed that in all five cases at least one of the molecules in overlap at the time of the deal was subsequently discontinued in the relevant therapeutic indication. This does not mean that the Commission intervention was not adequate: in fact, our evaluation reinforced the Commission's action (specifically, the need to introduce remedies in three cases and the appropriateness of clearing the remaining two

[22] Scrip (https://scrip.citeline.com) is a subscription-based source of global commercial pharmaceutical news and analysis that was part of Informa PLC for most of the period covered by this study and, in 2022, was divested and merged with Norstella.

[23] Fierce Pharma (https://fiercepharma.com) is a free (advertiser-supported) daily news service providing general coverage of pharmaceutical companies and developments worldwide that is owned and operated by Questex, LLC.

[24] M.8401 J&J/Actelion; M.7275 Novartis/GlaxoSmithKline Oncology Business; M.7872 Novartis/GSK (Ofatumumab Autoimmune Indications); M.9294 BMS/Celgene; M.9461 AbbVie/ Allergan.

[25] Although the period considered in the fact-finding challenge analysis goes from 2014 to 2018, we considered cases notified to the Commission also in 2019, because two very relevant cases for the ex-post evaluation were notified in such year (BMS/ Celgene and AbbVie/ Allergan).

unconditionally). We note that the mere fact that a divested pipeline has been discontinued does not mean that the remedies were ill-designed, as it can simply reflect the fact that the successful development of pipeline drugs is by nature uncertain. In the cases examined, we could not exclude that the divested pipelines might have been discontinued for technical reasons unrelated to the remedies, but in one case, J&J/Actelion, also suggested that under more stringent remedies the relevant pipeline would have been more likely to reach the market. In that case, it appears that the remedy could have been better designed. In particular, it seems that the remedy design may not have prevented the discontinuation of a pipeline as a result of actions of third parties (as the remedy was partly based on the active participation of a partner which decided to end the collaboration).

Killer acquisitions, however, may fall below merger thresholds or may not be structured as concentrations. Our *prima facie* relevant discontinuations – which are possible candidates for a killer acquisition assessment – also involve deal types different from M&A.

Competition regulators worldwide have struggled to identify systematic means of addressing acquisitions of competitively important but relatively small innovators in fast-moving sectors without adopting reforms of their merger control programmes that would likely disrupt a constructive balance (reflected in their general notification thresholds) between the burdens of notification and the benefits of *ex ante* review. In situations where one or more Member States have competence over a transaction, including potentially due to "call-in" powers (or in the absence of any merger control regime of their own), the referral mechanism foreseen under Article 22 EUMR may effectively provide a basis to facilitate the Commission's review of this type of transaction. The Commission's application of Article 22 in certain cases confirms that it can play a role to address the enforcement gap that has been identified in highly innovative sectors with small but competitively significant operators (as shown in *J&J/TachoSil*). Besides the limitations of its scope of application which was clarified by the Court of Justice in the Joined Cases C-611/22 P and C-625/22 P, an additional potential shortcoming of Article 22 is that while it provides a means of asserting jurisdiction over transactions that do not trigger the normal pre-notification thresholds, it provides no assurance that problematic transactions will come to the Commission's or Member States' attention in the first place.[26] We understand that the Commission already does actively monitor pharmaceutical transactions to identify candidate cases for the application of Article 22.[27] The monitoring procedure is developed along the same lines of the four-step methodology developed in the fact-finding challenge and is already pretty comprehensive. Nevertheless, it may be possible to envisage a "light touch" registry of deals and post-deal developments to provide an even greater ability to identify relevant deals *ex ante*, as well as providing notice of planned discontinuations

[26] As noted above, the European Court of Justice has also clarified that the Commission may accept referrals under Article 22 EUMR only from Member States that are themselves competent to review the transaction or have no national rules on merger control (like Luxemburg). Accordingly, the referral mechanism set out in Article 22 may not be available for some transactions that do not meet any EU or national merger control thresholds, unless one or more Member States lawfully request a reference after exercising their "call-in" powers (or the transaction presents a sufficient nexus with Luxemburg).

[27] This is indicated, for example, in European Commission, Directorate-General for Competition, Update on competition enforcement in the pharmaceutical sector (2018-2022) – European competition authorities working together for affordable and innovative medicines – Report from the Commission to the Council and the European Parliament, Publications Office of the European Union, 2024, https://data.europa.eu/doi/10.2763/427709

ex post. Such a registry might be applicable to companies of sufficient size that an EU nexus is assured. A cost/benefits analysis by the Commission is nonetheless warranted.

This chapter also discusses that Articles 101 and 102 TFEU are valuable tools to address killer acquisitions that are not structured as concentrations. Taking as a starting point the facts of two deals that effectively took place and would deserve further scrutiny according to the fact-finding challenge, we developed two hypothetical case studies that allowed us to conduct assessments under Article 22 EUMR and Articles 101 and 102 TFEU. In particular, one of the case studies focuses on a concentration below threshold and includes the assessment under Article 22 EUMR tailored to the specific, hypothetical, facts assumed in that case. The other case study allows to formulate two distinct hypothetical scenarios: one where the transaction can be seen as a concentration - and hence the Article 22 EUMR assessment is conducted - and one where it can be seen as a license agreement - and hence the Article 101 and 102 TFEU assessments are carried out.

Evaluation challenge: Policy recommendations

In conclusion, the evaluation challenge highlighted that, where killer acquisitions are structured as concentrations and involve companies of sufficient size to trigger the EUMR notification thresholds, the Commission review is typically apt to prevent the anti-competitive effects of such deals and ultimately consumer harm.

Moreover, the study concluded that also when killer acquisitions are structured as concentrations below threshold or differently from concentrations, legal tools exist in certain situations to tackle such transactions. Article 22 EUMR is a valuable and effective means to capture potential killer acquisitions taking the form of concentrations below applicable EU merger control thresholds, provided the referring Member States are competent to refer under their national rules or have no merger control regime of their own. For deals not structured as concentrations, the general antitrust provisions are important available tools. Additionally, to ensure that problematic transactions come to the Commission's attention, the study recommends considering the introduction of a registry or notification system of relevant deals and planned discontinuations: this will be especially valuable to capture potentially harmful transactions taking the form of exclusive licenses (which, as such, are not subject to any *ex-ante* review under the EUMR).

Abstrakt

In den letzten Jahren haben Bedenken hinsichtlich Transaktionen im Pharmasektor, die Innovation und Wettbewerb durch die Einstellung überlappender Arzneimittelforschungs- und Entwicklungsprojekte beeinträchtigen könnten, zu regulatorischen Maßnahmen und Untersuchungen über die sogenannte Killer-Akquisitionen geführt.

Das Ziel dieser Studie ist zweifach. Erstens soll die „Tatsachenfeststellung" (*fact-finding challenge*) die Verbreitung und die Merkmale des Phänomens im Zeitraum 2014-2018 bewerten. Zweitens soll die „Evaluierungherausforderung" (*evaluation challenge*) eine ex-post Bewertung von Fällen durchführen, die möglicherweise Killer-Akquisitionen beinhalten

Im Rahmen der Faktenfindung sammelt die Studie öffentlich verfügbare Beweise für eine große Anzahl von Transaktionen, die im Zeitraum von 2014 bis 2018 stattgefunden haben, um zu bestimmen, ob einige davon zu einer potenziellen Killer-Akquisitionen geführt haben könnte.

Die Studie ist neuartig, da sie nicht nur Fusionen und Übernahmen, sondern auch andere Arten von Transaktionen wie Lizenzvereinbarungen und F&E-Kooperationsvereinbarungen bewertet. Darüber hinaus geht die Tatsachenfeststellung über eine statistische Bewertung der Wahrscheinlichkeit von Killer-Akquisitionen hinaus, indem der folgende zweistufige Ansatz angewendet wird: i) eine umfangreiche und automatisierte Analyse um Transaktionen zu erkennen, denen Einstellungen überlappender Arzneimittel-F&E-Projekte gefolgt sind, die nicht durch technische oder kommerzielle Gründe gerechtfertigt scheinen, und ii) eine qualitative, fallweise Untersuchung, um die Schlüsselelemente von Killer-Akquisitionen zu identifizieren und zu bewerten.

Von den 3.193 untersuchten Transaktionen betrafen 240 den Erwerb potenziell austauschbarer Arzneimittel-F&E-Projekte. Einem signifikanten Anteil (89 von 240, 37 %) dieser Transaktionen folgten Einstellungen, die eine weitere Überprüfung aufgrund nicht-öffentlicher (firmeninterner) Informationen rechtfertigen, um letztendlich die Theorie eines schädlichen Effekts durch Killer-Akquisitionen zu bestätigen. Die bisherigen Anstrengungen und rechtlichen Bewertungen lassen darauf schließen, dass Art. 22 FKVO und Art. 101/102 AEUV effektive Werkzeuge zur Bekämpfung von Killer-Akquisitionen darstellen, wobei Potenzial für Verbesserungen in der Gestaltung von Abhilfemaßnahmen und der Einrichtung eines Registers oder Benachrichtigungssystems besteht, um potenziell schädliche Transaktionen zu identifizieren.

Unter der Evaluierungsherausforderung prüft die Studie die bisherigen Bemühungen der Kommission, potenzielle Killer-Akquisitionen zu adressieren, und den rechtlichen Rahmen, der die Handlungsmöglicheiten der Kommission begrenzt. Die Studie kommt zu dem Schluss, dass die Kommission die Killer-Akquisitionstheorien in diesen Fällen korrekt bewertet hat, und gibt Empfehlungen zur möglichen Verbesserung der Gestaltung der Abhilfemaßnahmen. Zunächst analysiert die Studie, wie effektiv die Kommission die materielle Fusionskontrolle bei fünf angemeldeten Zusammenschlüssen im Pharmasektor gehandhabt hat. Anschließend wird die Angemessenheit der fusions- und kartellrechtlichen Instrumente zur Bewältigung von Killer-Akquisitionen beurteilt, indem die Anwendung von Art. 22 EUMR und Art. 101/102 AEUV in zwei Fallstudien simuliert wird. Anschließend wird die Eignung der Fusions- und Kartellrechtsinstrumente zur Bewältigung von Killer-Akquisitionen, die nicht der Kommission gemeldet werden, analysiert, indem die Bewertungen nach Art. 22 EUMR und Art. 101/102 AEUV in zwei Fallstudien simuliert werden. Vergangene Erfahrungen und eine rechtliche Bewertung

legen nahe, dass Art. 22 EUMR (für Zusammenschlüsse) und Art. 101/102 AEUV (für Nicht-Zusammenschlüsse) wertvolle Instrumente zur Bekämpfung solcher Killer-Akquisitionen sind, wobei ein Potenzial zur Verbesserung in der Einrichtung eines Registers oder eines Benachrichtigungssystems zur Identifizierung potenziell schädlicher Transaktionen besteht.

Zusammenfassung

In den letzten Jahren haben Kartellbehörden zunehmend Bedenken geäußert, dass Fusionen und Übernahmen (M&A) von hochinnovativen Unternehmen in konzentrierten Branchen nicht nur erhebliche Auswirkungen auf die Preise, sondern auch auf die Innovationstätigkeit haben könnten. Bestehende Studien haben gezeigt, dass Fusionen die Forschungsbemühungen und damit die Innovationsausgaben sowohl fördern als auch hemmen können, abhängig von Faktoren wie Wettbewerbsniveau, Effizienzsteigerungen durch Konsolidierung und Veränderungen bei der Aneignung von Innovationen (Gilbert, 2022; Haucap & Stiebale, 2023).

Besonders besorgniserregend ist der 'Verlust potenzieller Konkurrenz', der oft mit der Theorie der sogenannten "Killer-Akquisitionen" in Verbindung gebracht wird. Dies wird üblicherweise so verstanden, dass etablierte Unternehmen ein Start-up kaufen, um drohenden Produktmarktwettbewerb abzuwehren oder ihr Kerngeschäft durch Ausschalten einer spezifischen, konkurrierenden Produktlinie zu schützen. Crawford et al. (2020)[28] argumentieren, dass solche Übernahmen auch den Innovationswettbewerb untergraben können, also eine Möglichkeit darstellen, „Innovation zu kaufen, statt in konkurrierende Innovation zu investieren",[29] mit dem Risiko, die Wettbewerbsdynamik von Beginn an zu gefährden, noch bevor Forschungs- und Entwicklungsanstrengungen zu spezifischen Produktentwicklungen führen.

Der Pharmasektor ist einer der Industriezweige mit den höchsten Forschungs- und Entwicklungsausgaben, in dem Innovation eine entscheidende Rolle bei der Förderung sowohl des wirtschaftlichen Wohlstands als auch der Gesundheit spielt. Eine konstante Erkenntnis bisheriger Studien ist, dass die Marktkonsolidierung in der pharmazeutischen Industrie zu erheblichen Reduktionen bei den Forschungsausgaben und der Patentproduktion der fusionierten Unternehmen führt, sowie zu einem signifikanten Rückgang der Produktivität von Erfindern aus den Zielunternehmen (Ornaghi, 2009a; Haucap et al., 2019; Ornaghi & Cassi, 2023). Empirische Forschungen zu Allianzen zwischen kleineren Biotech-Firmen und größeren pharmazeutischen Unternehmen, als potenzielle Alternativen oder Ergänzungen zu Fusionen bieten jedoch eine optimistischere Sichtweise, da sie eine positive Korrelation zwischen der klinischen Entwicklungskompetenz eines größeren Unternehmens und dem Erfolg kleiner Firmen aufzeigen (Grabowski & Kyle, 2008).

Die Besorgnis über die nachteiligen Auswirkungen von Fusionen auf die Innovation hat sich nach der Veröffentlichung der Studie zu "Killer-Akquisitionen" von Cunningham et al. (2021) verstärkt, welche aufzeigt, dass erworbene Arzneimittelprojekte weniger wahrscheinlich weiterentwickelt werden, wenn sie mit dem bestehenden Produktportfolio des Erwerbers überlappen, insbesondere wenn die Marktmacht des Erwerbers aufgrund schwachen Wettbewerbs oder weit entferntem Patentablauf groß ist. Laut den Autoren finden solche Übernahmen unverhältnismäßig oft knapp unter den relevanten Schwellenwerten für kartellrechtliche Überprüfungen statt. Dies steht im Einklang mit einer Analyse von Wollmann (2019), die feststellt, dass nach der Anhebung der Schwelle für die Anmeldepflicht von Zusammenschlussvorhaben in den USA die Pharmaindustrie zu den fünf Branchen mit der höchsten Zahl an horizontalen, von der

[28] 'How tech rolls': Potential competition and 'reverse' killer acquisitions, Gregory Crawford, Tommaso Valletti, and Cristina Caffarra, VoxEU, 11 May 2020, https://cepr.org/voxeu/blogs-and-reviews/how-tech-rolls-potential-competition-and-reverse-killer-acquisitions.

[29] Ibidem.

Anmeldung befreiten Fusionen in der Zeit nach der Änderung gehört. Dies steht auch im Einklang mit der internen Bewertung von Fusionen durch die Europäische Kommission, die die Umsatzschwellen der EU-Fusionskontrollverordnung (FKVO) nicht erreicht haben.[30]Diese Bewertung ergab, dass es im Pharmasektor Fusionen zwischen Unternehmen mit sich überschneidenden Arzneimittelprojekten gab, die die Umsatzschwellen nicht erreichten, obwohl die Käufer bereit waren, einen hohen Preis für den Erwerb von innovativen Unternehmen mit niedrigem Umsatz zu zahlen.

Die Ergebnisse von Cunningham et al. (2021) decken sich auch mit den von der Europäischen Kommission in Auftrag gegebenen und von Informa Pharma Consulting und Szücs (2020) durchgeführten Studien zu Fusionen und Übernahmen in der Pharmaindustrie. Diese zeigen, dass die Wahrscheinlichkeit einer Einstellung eines Arzneimittelprojekts steigt, wenn es mit einem anderen Projekt des erwerbenden Unternehmens für dieselbe Indikation überlappt. Zudem zeigt die Studie, dass nach einer Übernahme keine Beschleunigung in der Entwicklung von Arzneimitteln gibt, entgegen den Behauptungen der Industrie, dass Übernahmen den F&E-Prozess beschleunigen.

Im Rahmen ihres fortlaufenden Engagements zur Förderung von Innovationen in der Pharmaindustrie hat die Kommission im Jahr 2022 ein neues Projekt gestartet, dessen Ergebnisse diese Studie präsentiert. Es untersucht die Verbreitung und Merkmale des Phänomens der sogenannten Killer-Akquisitionen, mit einem Fokus auf eine große Anzahl von Transaktionen (sowohl M&A als auch Nicht-M&A), die im Zeitraum 2014-2018 im Pharmasektor stattfanden.

Die technischen Spezifikationen definieren Killer- Akquisitionen im Pharmasektor als Transaktionen, die wahrscheinlich das Ziel oder den Effekt haben, sich überschneidende Forschungs- und Entwicklungsprojekte für Arzneimittel ("Arzneimittel-F&E-Projekte") zum Nachteil des zukünftigen Wettbewerbs und letztendlich der Verbraucher einzustellen.[31] Dies ist die in dieser Studie angewandte Definition.

Das Ziel der Studie ist zweifach. Erstens bietet sie neue Erkenntnisse über das Phänomen durch die Analyse einer großen Anzahl von Transaktionen, die im Zeitraum 2014-2018 stattfanden, um retrospektiv zu beurteilen, ob diese Transaktionen wahrscheinlich zu einer Einstellung überlappender Projekte geführt und den Wettbewerb im Markt beeinflusst haben ("Fact-Finding-Herausforderung"). Als Neuheit untersucht die Studie alle Arten von Transaktionen, nicht nur Fusionen und Übernahmen, sondern auch Vermögenskäufe, Lizenzvereinbarungen, F&E-Vereinbarungen und andere. Eine weitere wichtige Neuerung betrifft die Methodik dieser Studie, die faktische Beweise sammelt, die eine Beurteilung von Killer-Akquisitionen auf der Ebene einzelner Deals unterstützen könnten, während die bisherige Forschung nur theoretische oder statistische Beweise für die Existenz oder das Ausmaß des Phänomens liefert.

Zweitens evaluiert diese Studie (i) die bisherigen Bemühungen der Kommission zur Bekämpfung des Phänomens der Killer- Akquisitionen und (ii) den rechtlichen Rahmen, in dem die Kommission operiert, im Licht der Beweise dafür, dass Killer- Akquisitionen auch unterhalb der Schwellenwerte der Fusionsregulierung stattfinden können oder nicht als Zusammenschlüsse strukturiert sind ("Evaluations-Herausforderung"). Im

[30] Commission Staff Working Document (2021), "Evaluation of procedural and jurisdictional aspects of EU merger control", SWD (2021) 66 final, 26 March.

[31] Technische Spezifikationen, Fußnote 2, beziehen sich auf diese Definition.

speziellen werden im zweiten Kapitel die aktuellen Regeln und Praktiken unter der EU-Fusionskontrollverordnung sowie die Vorzüge und Probleme der Anwendung der Artikel 101 und 102 des Vertrags über die Arbeitsweise der Europäischen Union (AEUV) zur Erfassung von Transaktionen, die möglicherweise vom EU-Regulierungsnetz nicht erfasst werden, bewertet.

Fact-Finding-Herausforderung

Das erste Kapitel thematisiert die Herausforderungen der Faktenermittlung und präsentiert eine Analyse einer umfangreichen Stichprobe von Transaktionen, die zwischen 2014 und 2018 im Pharmasektor stattfanden. Die Analyse, durchgeführt mit dem Vorteil der Rückschau, stützte sich auf öffentlich zugängliche Daten. Aus diesem Grund stieß sie auf mehrere Einschränkungen, die nachfolgend diskutiert werden. Auf Basis der Faktenlage wurde versucht zu ermitteln, ob diese Transaktionen zur Einstellung sich überlappender Projekte geführt haben könnten (einschließlich Pipeline-zu-Pipeline-Überlappungen und Überlappungen zwischen vermarkteten und Pipelineprodukten) und ob sie die Wettbewerbslandschaft im relevanten Produktmarkt verändert haben.

Für die Faktenermittlungsanalyse entwickelte die Studie eine vierstufige Methodik, die öffentlich zugängliche Datenquellen identifiziert und Werkzeuge bereitstellt, um zu bestimmen, ob eine bestimmte Transaktion zur Einstellung konkurrierender Arzneimittel-F&E-Projekte in einer Art geführt hat, die der Theorie des Schadens durch "Killer-Akquisitionen" entspricht:

- Identifikation enger Überlappungen. In Übereinstimmung mit der Praxis der Kommission und der existierenden Literatur nutzt die Studie therapeutische Indikationen (TIs) und Wirkmechanismen (MoAs), um zu bestimmen, ob Arzneimittel-F&E-Projekte direkte Substitute sind. Diese Art der Überlappung wird als "enge Überlappung" bezeichnet, im Gegensatz zur "breiten Überlappung", die nur auf TI basiert. Die Studie entwickelte zudem Proxies, um potenziellen Wettbewerb zwischen Arzneimittel-F&E-Projekten zu identifizieren, die unterschiedliche TIs und MoAs in verschiedenen Entwicklungsstadien aufweisen könnten. Insbesondere legt diese Studie nahe, dass die Medical Subject Headings (MeSH), die in klinischen Studien im relevanten US-Register (ClinicalTrials.gov) gebraucht werden,[32] eine numerische und hierarchische Struktur bieten, die die Beziehung zwischen zwei scheinbar unterschiedlichen TIs klärt. Darüber hinaus kann, wenn die MoAs zweier Arzneimittel nicht identisch sind – wie es der Fall sein kann, wenn sie noch nicht gut etabliert sind – die potenzielle Austauschbarkeit zwischen ihnen dennoch durch Bezugnahme auf gemeinsame Zitate in Artikeln aus medizinischen Fachzeitschriften beurteilt werden, die online in PubMed Central® (PMC), einem öffentlichen Archiv der US-amerikanischen Nationalbibliothek der Medizin, veröffentlicht und durchsuchbar sind.
- Identifikation und Klassifizierung von Projektbeendigungen. Es gibt zahlreiche Gründe, warum sich überschneidende Arzneimittel-F&E-Projekte nach einer Akquisition eingestellt werden können. Manchmal zeigt ClinicalTrials.gov klar an,

[32] Wir führten eine vergleichende Analyse durch und stellten fest, dass die überwiegende Mehrheit der in dem Europäischen Klinischen Studienregister („EUCTR") gemeldeten Studien ebenfalls in ClinicalTrials.gov aufgeführt sind, welches andererseits eine größere Abdeckung und mehr Informationen bietet. Zudem stützen wir uns auf das EUCTR hinsichtlich der Vollständigkeit bei der Durchführung manueller Überprüfungen (siehe Punkt 4).

dass eine Studie beendet oder zurückgezogen wurde (manchmal sogar unter Angabe des Grundes). In anderen Fällen gibt es keine Hinweise außer Inaktivität, die darauf hindeuten könnten, dass eine Studie oder die weitere Entwicklung eines Medikaments in einer bestimmten TI eingestellt wurde. Schließlich können F&E-Projekte in einer therapeutischen Indikation beendet und in einer anderen neu ausgerichtet werden. Wenn keine Informationen über Beendigung oder Rückzug vorliegen, geht die Studie davon aus, dass ein Projekt eingestellt wurde, wenn mindestens zwei Jahre lang Inaktivität bei der Entwicklung eines F&E-Projekts in einer bestimmten TI beobachtet wurde und danach keine Weiterentwicklung erfolgte. Mit Hilfe der numerischen Struktur der MeSH-Begriffe erkennt die Studie auch Fälle, in denen eine offensichtliche Wettbewerbsüberschneidung durch eine Neuausrichtung eines der überlappenden Arzneimittel-F&E-Projekte auf eine andere TI beseitigt wurde.33 Die Gründe für die Beendigung im Register für klinische Studien (wenn verfügbar), der Zeitraum der Inaktivität, die Art der Sponsoren (ob privat oder öffentlich) und die Entwicklung der TI über die Zeit für beide sich überschneidenden Medikamente helfen dabei, aus allen beobachteten Abbrüchen diejenigen herauszufiltern, die anscheinend nicht mit dem Deal zusammenhängen und scheinbar aus technischen und klinischen Gründen resultieren (z.B. schlechtes Versuchsdesign, niedrige Teilnehmerzahl). Die Abbrüche, die am Ende dieses Filterprozesses verbleiben, werden als prima facie relevant für eine Bewertung im Rahmen einer Killer-Akquisitionsanalyse angesehen.

- Die Studie basiert auf einem maschinellen Lernalgorithmus (Least Absolute Shrinkage and Selection Operator, bekannt als „LASSO"), mit dem Ziel, ex-ante Transaktionen zu charakterisieren, die einer weiteren Überprüfung bedürfen. Wir beginnen mit einer Ausgangsliste von Merkmalen, die von der Literatur vorgeschlagen und von unserem Expertenteam im Voraus ausgewählt wurden. Diese Merkmale können darauf hindeuten, dass die an einer Transaktion beteiligten Parteien entweder den Anreiz oder die Möglichkeit hatten, den Wettbewerb auf einem relevanten Markt zu unterbinden. Die LASSO-Spezifikation umfasst Variablen, die die Intensität des zukünftigen Produktmarktwettbewerbs erfassen. LASSO hilft uns zu bestimmen, welche dieser ursprünglichen Merkmale am besten geeignet sind, Arzneimittelprojekte zu identifizieren, die wahrscheinlich ohne die Transaktion nicht eingestellt worden wären und deren Einstellung den Wettbewerb auf den bewerteten Märkten verringert hat.[34] LASSO zielt darauf ab, aus den Transaktionen, die zu *prima facie* relevanten Einstellungen führen, jene herauszufiltern, die am ehesten „Killer-Akquisitionen" darstellen. Die beschriebenen analytischen Schritte sind Teil einer großangelegten Analyse, die darauf abzielt, potenziell wettbewerbswidrige Einstellungen durch eine automatisierte Untersuchung einer großen Anzahl von Beobachtungen mit einem Satz vordefinierter Regeln zu erkennen.

[33] Für die Zwecke dieser Studie werden Verzögerungen unter zwei Jahren nicht berücksichtigt; selbst längere Verzögerungen, wenn ein Entwicklungsereignis noch vor dem Ende des Beobachtungszeitraums eintritt, werden nicht als relevant erachtet (auch wenn sie zeitweise Schaden verursachen können). In diesen Fällen kann nicht jedoch ausgeschlossen werden, dass ein wettbewerblicher Schaden in Form einer verzögerten Entwicklung eines konkurrierenden Arzneimittels entstanden ist, der von der Studie nicht erfasst wurde.

[34] LASSO wird anhand einer Stichprobe trainiert, die auf solche auf den ersten Blick relevanten Einstellungen beschränkt ist, die wahrscheinlich mit strategischen oder geschäftlichen Motiven in Verbindung stehen. Diese werden dann mit einer Kontrollgruppe verglichen, die aus überlappenden Arzneimittelprojekten besteht, bei denen wir entweder unmittelbar nach dem Geschäftsabschluss keine Einstellung feststellen oder deren Einstellung eher aus technischen und klinischen Gründen zu erfolgen scheint.

- Abschließend führt die Studie ein „manuelles Screening" der *prima facie* relevanten Einstellungen durch, die die von LASSO bestätigten Merkmale ("LASSO-KA") aufweisen, sowie eine Untersuchung einer Teilmenge der verbleibenden prima facie relevanten Einstellungen, um die Zuverlässigkeit der LASSO-Ergebnisse zu testen. Das manuelle Screening besteht bei einer Untergruppe von Transaktionen in einer Einzelfallprüfung und einer fundierten Bewertung der Fakten. Die Einstellung eines sich überschneidenden F&E-Projekts für ein Medikament, selbst wenn sie durch eine Übernahme verursacht wurde, ist eine notwendige, aber nicht hinreichende Bedingung, um zu dem Schluss zu kommen, dass die Übernahme den Wettbewerb und die Innovation behindert hat (oder wahrscheinlich behindern wird). In unserer Studie bezieht sich der Begriff „Killer-Akquisition" auf eine Schadenshypothese, bei der eine Transaktion zur Einstellung eines F&E-Projekts führt und wahrscheinlich negative Auswirkungen auf den Wettbewerb hat. Mit anderen Worten, das Konzept der "Killer-Akquisition", das wir in unserer Studie verwenden, schließt Fälle aus, in denen der Erwerber die Entwicklung eines Medikaments beendet, ohne jedoch die Wettbewerbsdynamik auf dem relevanten Markt zu verändern. Dieser Ansatz erfordert ein umfassendes Verständnis der Austauschbarkeit zwischen den sich überschneidenden Arzneimitteln, ihrer klinischen Bedeutung und dem Wettbewerbsniveau auf dem relevanten Markt, insbesondere wenn die Überschneidung bei den therapeutischen Indikationen nicht perfekt ist und die potenzielle Austauschbarkeit sorgfältig bewertet werden muss, sowie eine Beurteilung der kommerziellen Anreize und finanziellen Beschränkungen der beteiligten Parteien. Das ultimative Ziel des „manuellen Screenings" ist es, Beweise zu sammeln, um zu bewerten, ob eine Transaktion eine Killer-Akquisition darstellt oder nicht, wobei die oben genannten Aspekte so weit wie möglich mit den öffentlich verfügbaren Informationen berücksichtigt werden. Bei der manuellen Überprüfung haben wir uns auf öffentliche Informationsquellen und Datentypen gestützt, die über das hinausgehen, was die großangelegte Analyse leisten kann, einschließlich der Überprüfung von Unternehmensberichten, Unternehmensankündigungen im Zusammenhang mit der Transaktion, Artikeln in der Fachpresse, die den Deal kommentieren, sowie einer maßgeschneiderten Bewertung durch unser Expertenteam bezüglich der technischen und kommerziellen Machbarkeit der eingestellten Arzneimittel-F&E-Projekte, gestützt auf öffentliche technische Berichte über die F&E-Aktivitäten der beteiligten Parteien und ihrer Wettbewerber (verwiesen auf ClinicalTrials.gov oder zugänglich über PMC).

Obwohl sie auf einer komplexen Methodologie basiert, ist die Herausforderung der Datenerhebung durch folgende wichtige Einschränkungen gekennzeichnet:

- Die Studie konzentriert sich auf den Wettbewerb durch derzeit in der Entwicklung befindlichen Produkte, die sich in der klinischen Testphase befinden, und erlaubt es daher nicht, die Auswirkungen einer Übernahme auf den Innovationswettbewerb vollständig zu erfassen. Beispielsweise berücksichtigt die umfangreiche Analyse weder präklinische Versuche noch zukünftige Absichten der Parteien, eine neue therapeutische Anwendung zu verfolgen;
- Die Studie stützt sich auf öffentlich zugängliche Quellen und hat keinen Zugang zu internen Unternehmensdokumenten und Präsentationen, die aufschlussreich sein könnten, ob der Deal die kommerziellen Anreize der Parteien bei der Medikamentenentwicklung verändert hat. Zudem erlauben öffentlich verfügbare Informationen oft keine eindeutige Darstellung der Wettbewerbslandschaft und des von den Wettbewerbern oder anderen Firmen im Markt ausgeübten Wettbewerbsdrucks;

- Bei der Bewertung von Lizenzvereinbarungen oder F&E-Verträgen ist die Identifizierung des "Gegenstands" und des "Umfangs" der Vereinbarung (d.h. der von der Vereinbarung betroffenen Arzneimittel und therapeutischen Indikationen sowie anderer relevanter überlappender Arzneimittel) und die Bestimmung der Partei, die von dem Rechteaustausch profitiert, komplex.[35] Dies bedeutet notwendigerweise, dass die Studie das Ausmaß und die Eigenschaften möglicher Killer-Akquisitionen in diesen Transaktionskategorien nicht vollständig erfassen kann; zudem hängen die Anreize der Parteien von der Zuweisung der Marketing- und Vertriebsrechte für die gemeinsame Innovation ab: Der Begriff der "Killer-Akquisition" im Sinne dieser Studie umfasst eine Transaktion, die es einer Partei ermöglicht, Kontrollrechte[36] über ein substituierbares F&E-Projekt für ein Medikament zu erlangen. Solche Details über F&E-Vereinbarungen sind nicht öffentlich, sodass selbst bei manueller Überprüfung nicht ermittelbar ist, ob sie exklusive Rechte schaffen könnten;
- Die Studie nimmt einen relativ umfassenden Ansatz bei der Bewertung der möglichen Substituierbarkeit zwischen Arzneimittel-F&E-Projekten an, berücksichtigt jedoch keine Vereinbarungen, die Arzneimittel-F&E-Projekte unter gemeinsame Kontrolle bringen, die lediglich dieselbe therapeutische Indikation oder therapeutische Klasse teilen. Breite (anstatt enge) Überlappungen sind nicht Gegenstand dieser Studie – weitere Forschung könnte dazu beitragen, das Ausmaß, in dem diese auch zu signifikanten Unterbrechungen führen könnten, zu erhellen;
- Während die Studie einen relativ langen Zeitraum der Inaktivität als Indikator dafür sieht, dass ein Projekt möglicherweise eingestellt wurde, ist diese Schlussfolgerung nicht anwendbar, wenn weitere Entwicklungen, wie die Registrierung einer neuen Studie, auch nach einem langen Zeitraum der Inaktivität beobachtet werden. Folglich werden, obwohl wettbewerbsrelevant, Verzögerungen in der Entwicklung in dieser Studie nicht behandelt; und
- Obwohl die Studie die Interessen der Muttergesellschaft und der Tochtergesellschaften der direkt am Deal beteiligten Unternehmen berücksichtigt, nimmt sie keine Rücksicht auf Fälle, in denen Minderheitsbeteiligungen Anreize

[35] Für eine große Anzahl von Transaktionen konnte kein Transaktionsobjekt oder -ziel identifiziert werden. Der Hauptgrund dafür war, dass eines der beteiligten Unternehmen nicht in unserem Datensatz zu klinischen Studien enthalten war, was typischerweise auftritt, wenn Unternehmen keine F&E-Projekte in ihrem Portfolio haben (z.B. weil sie in Plattformen, Technologien und Geräten tätig sind anstatt in der Medikamentenentwicklung, oder ihre F&E-Projekte für Medikamente sich im präklinischen Stadium befinden und sie noch keine klinischen Studien registriert haben).

[36] Diese Studie versteht Kontrollrechte als solche, die ausreichen würden, um einer Einheit die rechtliche Fähigkeit zu verleihen – sollten auch die Anreize vorhanden sein –, eines von zwei sich überschneidenden F&E-Projekten für Medikamente zu eliminieren, die ohne die Transaktion Rivalen wären und somit potenziell den zukünftigen Wettbewerb auf dem Produktmarkt beeinflussen könnten. Bei Übernahmen und Asset-Käufen impliziert die Natur der Transaktionen eine Übertragung von Eigentumsrechten auf den Erwerber, was normalerweise ausreicht, um sicher anzunehmen, dass Letzterer nach Belieben über beide sich überschneidenden F&E-Projekte für Medikamente verfügen kann. Bei Lizenzgeschäften ist der Umfang der Lizenzierung relevant: In dieser Hinsicht versuchen wir neben den spezifischen therapeutischen Indikationen, die durch die Transaktion abgedeckt werden, Exklusivität zu erkennen und den geografischen Umfang der Lizenzierung zu berücksichtigen, um diese Annahme robust zu machen. Bei F&E-Vereinbarungen hängt es, wie bereits diskutiert, davon ab, ob die Transaktion die Fähigkeit und Anreize einer der Parteien, eines von zwei sich überschneidenden F&E-Projekten für Medikamente einzustellen, verändern kann, davon ab, wie die Marketing- und Vertriebsrechte für die durch die Vereinbarung festgelegte gemeinsame Innovation unter den Partnern verteilt werden – etwas, worüber jedoch weder der Transaktionstyp selbst noch öffentliche Informationen uns eine endgültige Aussage ermöglichen.

schaffen und die Fähigkeit besitzen könnten, eine Killer-Akquisitionen zu verursachen.

Trotz der genannten Einschränkungen leistet die Studie einen originären Beitrag zur wachsenden Literatur, die das Phänomen der Killer-Akquisitionen zu charakterisieren versucht.

Ergebnisse der Fact-Finding-Herausforderung

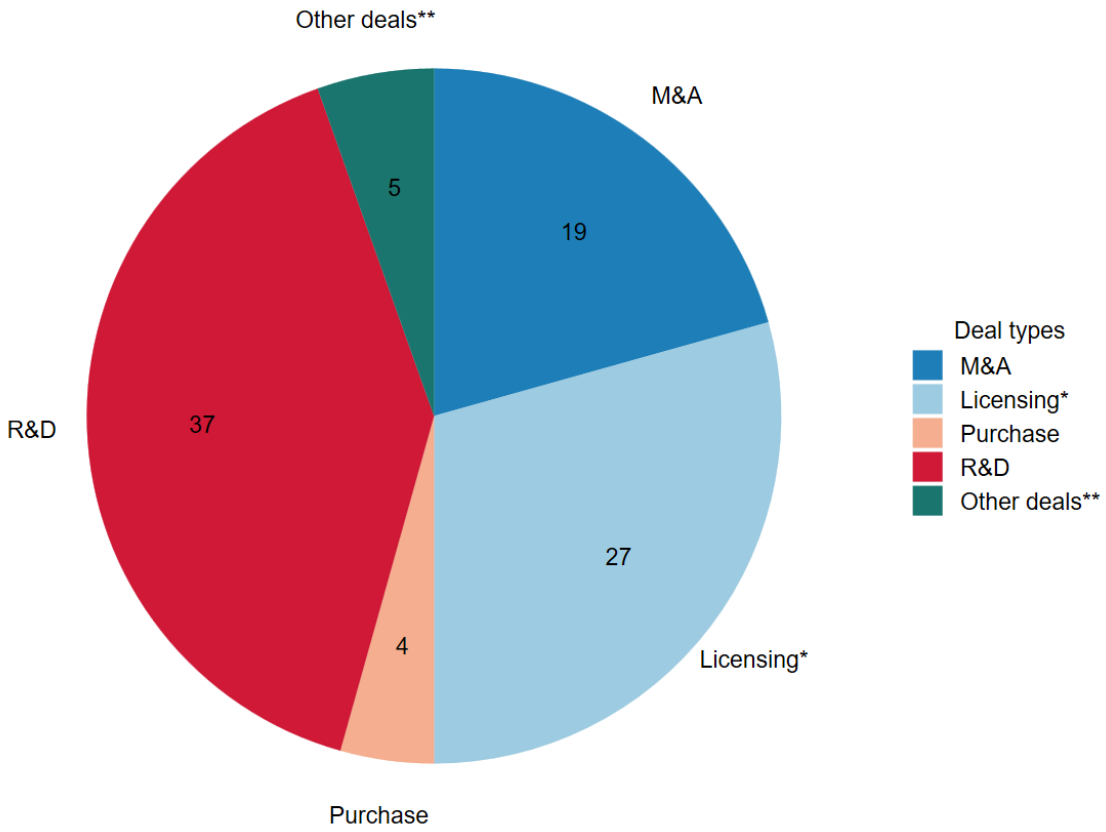
Von insgesamt 6.315 Transaktionen, die im Zeitraum 2014-2018 im Pharmasektor identifiziert wurden, waren für 3.193 Transaktionen Informationen über den Umfang der Transaktion verfügbar.[37] Out of these, 240 entailed the acquisition of potentially substitutable drug R&D projects, conservatively based on a narrow definition of competitive overlap (with overlapping TI and MoA). In der überwiegenden Mehrheit dieser Transaktionen (183) wurde mindestens ein eng überlappendes Arzneimittel-F&E-Projekt nach der Transaktion eingestellt. Dieses bemerkenswerte Ergebnis wirft Fragen nach den Gründen für die Einstellung auf und ob dies durch die Theorie der 'Killer-Akquisitionen' erklärt werden könnte. Wir haben festgestellt, dass in 92 (oder 38%) der Transaktionen mit engen Überlappungen mindestens eines der Projekte eingestellt wurde, was *prima facie* für die Bewertung einer Killer-Akquisition relevant ist.[38]

Die nachfolgende Abbildung veranschaulicht die Verteilung der *prima facie* relevanten Einstellungen nach Art des Deals:

[37] Die Geschäfte, die die Analyse informierten, sind jene aus dem anfänglichen Datensatz, für die wir ausreichend Informationen haben, um die von der Transaktion betroffenen, vermarkteten Arzneimittel und die Arzneimittel- F&E-projekte der beteiligten Parteien zu identifizieren.

[38] Die großangelegte Analyse wurde nach Geschäftsart getrennt entworfen und durchgeführt, um die Besonderheiten jeder Geschäftsart zu berücksichtigen.

Die Verteilung der *prima facie* relevante Abkündigungen nach Deal-Art



*Quelle: Lear-Analyse. Anmerkungen: *Es gibt 12 „exklusive" Lizenzvereinbarungen, die mit Hilfe von Suchtextwerkzeugen in den Beschreibungen in unserem Deal-Datensatz identifiziert wurden und prima facie relevante Abkündigungen aufweisen.**Für die Gruppe Sonstige Deals gibt es prima facie relevante Abkündigungen in den folgenden Deal-Typen: Kapitalbeteiligung (2 Deals), Joint Venture (1 Deal), Joint Venture F&E (1 Deal), Marketingvereinbarung (1 Deal); keine Abschaffung enger Überschneidungen in Partnerschaften und Cross-Licensing-Vereinbarungen*

Prima facie relevante Einstellungen werden in etwa 40% der Transaktionen mit sich überschneidenden Arzneimittel-F&E-Projekten in unserer Analyse festgestellt. Im Detail stellen sie 54% der Transaktionen mit engem Überlappen bei M&A, 27% bei Lizenzvereinbarungen, 33% bei Käufen und 43% bei F&E-Vereinbarungen. Sie verteilen sich auch auf Eigenkapitalbeteiligungen (mit 2 Deals), gefolgt von Joint Ventures (JV), F&E-Joint-Ventures und Marketingvereinbarungen (jeweils ein Deal in diesen Deal-Typen), während in Partnerschaften und Cross-Licensing-Vereinbarungen keine prima facie relevanten Einstellungen festgestellt wurden. Diese Ergebnisse deuten darauf hin, dass ein großer Teil der Transaktionen mit sich überschneidenden F&E-Projekten, insbesondere Fusionen und Übernahmen sowie Lizenz- und F&E-Vereinbarungen, prima facie relevant für eine Beurteilung als "Killer-Akquisition" sind.

Um Transaktionen zu identifizieren, bei denen eine Theorie des Schadens durch "Killer-Akquisition" potenziell vorhanden oder absehbar gewesen sein könnte, und unter Ausnutzung relevanter Daten, die für alle engen Überschneidungen gesammelt wurden, hat dieser Studie den LASSO-Ansatz untersucht, gefolgt von einer manuellen Überprüfung zur Bestätigung der LASSO-Ergebnisse. Bei Anwendung auf M&A-, Lizenz-

und F&E-Vereinbarungen wählte das LASSO 53 *prima facie* relevante Einstellungen als „LASSO-KAs" aus, verteilt über 19 verschiedene Deals.

Das manuelle Screening umfasste folgende Bereiche: Alle auf den ersten Blick relevanten Einstellungen bei Fusionen und Übernahmen (einschließlich 6 LASSO-KAs) sowie bei exklusiven Lizenzierungsvereinbarungen (einschließlich 9 LASSO-KAs);[39] 5 % der F&E-Vereinbarungen (22 % im Hinblick auf die Anzahl der Deals, einschließlich 4 LASSO-KAs);[40] alle *prima facie* relevanten Beendigungen bei anderen Geschäftstypen (Partnerschaften, F&E-Joint-Venture-Vereinbarungen und JVs, Eigenkapitalbeteiligungen, Marketingvereinbarungen, Cross-Licensing, zusammengefasst unter der Bezeichnung "Sonstige Geschäfte"), bei denen der LASSO-Ansatz aufgrund der kleinen Stichprobengröße nicht anwendbar war.

Das manuelle Screening verdeutlichte, dass die auf den ersten Blick relevanten Einstellungen vielfältiger Natur sind, selbst innerhalb einzelner Transaktionstypen und auch wenn sie ähnliche „LASSO-Eigenschaften" teilen (d.h. die Bedingungen, die durch die Lösung des LASSO-Modells definiert werden, auf deren Basis wir LASSO-KAs identifizieren),[41] was zeigt, dass diese Eigenschaften nicht ausreichen, um die Spezifika dieser Transaktionen vollständig zu erfassen. Bemerkenswert ist, dass trotz der Präsenz von LASSO-Merkmalen die verfügbaren Beweise (öffentlich zugängliche Informationen) keine schlüssigen Aussagen über das Vorhandensein oder Fehlen von "Killer-Akquisitionen" zulassen. Dies führt dazu, dass diese Transaktionen dem gleichen Grad an Unsicherheit unterliegen wie Transaktionen, die zu *prima facie* relevanten Einstellungen führen, aber nicht die gleichen Merkmale aufweisen. Dies beeinträchtigt die Fähigkeit der LASSO-Lösung, Wettbewerbsbehörden im Vorfeld dabei zu unterstützen, Transaktionen zu identifizieren, die eine genauere Prüfung verdienen würden.

Zudem war es ohne Zugriff auf interne Unternehmensdokumente selbst bei der manuellen Überprüfung auf Einzelfallbasis schwierig, Schlussfolgerungen darüber zu ziehen, in welchem Ausmaß die Transaktion die kommerziellen Anreize der beteiligten Parteien verändert hat. Öffentliche Beweise bieten generell keine ausreichend solide Grundlage, um zu bestimmen, ob die *prima facie* relevanten Einstellungen die Theorie der Killer-Akquisitionen vollständig widerspiegeln, was uns daran hindert, eine endgültige Bewertung vorzunehmen. Dies trifft insbesondere auf bestimmte Transaktionsarten zu, vor allem auf F&E-Vereinbarungen und die Mischung bei den sonstigen Geschäften.[42]

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[39] Was die Lizenzierung betrifft, so würde ein nicht-exklusiver Lizenzvertrag kaum die Möglichkeit und Anreize bieten, ein Arzneimittelprojekt einzustellen. Daher konzentrierte sich das manuelle Screening auf exklusive Lizenzgeschäfte. Exklusive Lizenztransaktionen werden durch die Anwendung von Textsuchwerkzeugen auf die Beschreibung der Geschäfte identifiziert.

[40] Die öffentlich verfügbaren Informationen sind für F&E-Vereinbarungen typischerweise wenig aufschlussreich, bei denen nicht einmal der zentrale Austausch von Rechten zwischen den Parteien über die relevanten Arzneimittel bekannt ist. Solche Einschränkungen behindern die Analyse und die Ergebnisse konsequent und entmutigen eine umfassendere Überprüfung.

[41] Da die LASSO-Modelle nach Geschäftsart durchgeführt wurden, führten sie je nach Art des Geschäfts zu verschiedenen Lösungen (und damit zu unterschiedlichen Merkmalen). Bei unserer ersten Schätzung des Modells in der Stichprobe von M&A-Geschäften wählt das LASSO nur einen Regressor aus, nämlich die Interaktion zwischen: einer der sich überschneidenden Moleküle in Phase 4 (d.h. vermarktet), einem der sich überschneidenden Moleküle in Phase 2 und der maximalen Anzahl von Wettbewerbern auf dem Markt, die drei beträgt.

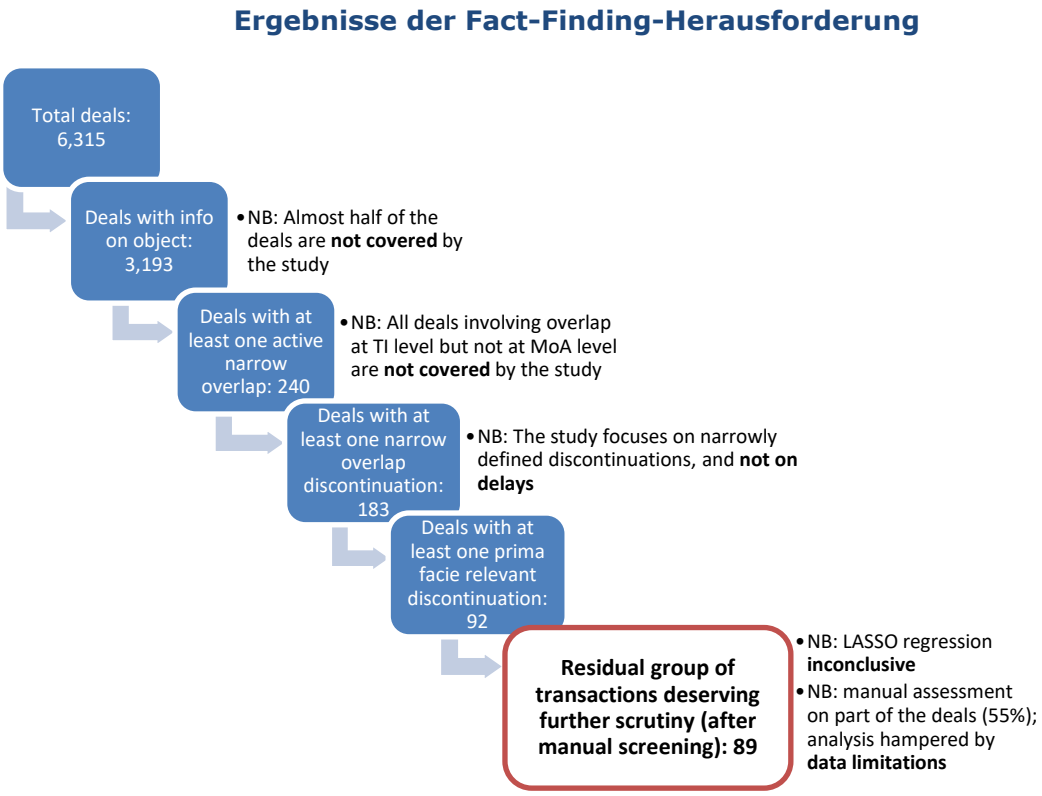
[42] Siehe Fußnote 41.

Wie bereits diskutiert, bezieht sich die Theorie des Schadens durch 'Killer-Akquisitionen', wie sie dieser Studie zugrunde liegt, auf eine Transaktion, die es einer Partei ermöglicht, Kontrollrechte über ein austauschbares Arzneimittel-F&E-Projekt zu erlangen. Dies führt zur Einstellung einer Pipeline in einem bestimmten therapeutischen Bereich oder zur Beendigung der Entwicklung eines Moleküls und verringert letztendlich wahrscheinlich den Wettbewerb und die Innovation. Für die meisten auf den ersten Blick relevanten Einstellungen, die manuell untersucht wurden, konnten öffentlich zugängliche Informationen keine ausreichend überzeugenden Beweise für folgende Aspekte liefern: (i) das Maß an Substituierbarkeit (oder Wettbewerbsnähe, was in der der Killer-Akquisitionen Theorie entscheidend ist) zwischen sich überschneidenden Arzneimittelprojekten, insbesondere ob die Medikamente dieselbe Krankheit auf ähnliche Weise behandeln können, statt für verschiedene Patientensegmente, parallele oder sequenzielle Behandlungen oder kombinierte Therapien geeignet zu sein; (ii) das Fehlen einer gültigen klinischen oder sonstigen technischen Rechtfertigung für die Einstellung; oder dass sie durch eine kommerzielle Bewertung gerechtfertigt werden könnte, die auch ohne die Transaktion entstanden wäre; (iii) dass der Wettbewerb im relevanten Markt durch die Einstellung beeinträchtigt wurde (eine tiefere Bewertung der Substituierbarkeit mit den sich überschneidenden Arzneimitteln der Parteien ist auch für „konkurrierende" Medikamente erforderlich).

Gleichzeitig gibt es nur wenige Fälle, in denen die öffentlich zugänglichen Beweise eindeutiger darauf hindeuten, dass das Vorliegen einer Killer-Akquisitionen sicher verworfen werden kann. Dies sind vor allem Fälle, in denen entgegen den Ergebnissen umfangreicher Analysen das eingestellte Medikament weiterhin entwickelt wird (zwei Transaktionen in der M&A-Gruppe und eine in der Lizenzierungsgruppe, die jeweils zu fünf bzw. drei Einstellungen auf der Überschneidungsebene geführt haben).

Zusammenfassend zeigt die Studie, dass ein signifikanter Anteil (89 von 240, 37%) der Transaktionen mit engen Überschneidungen von einer Einstellung gefolgt war, die eine genauere Prüfung verdient, insofern als auf Grundlage öffentlich zugänglicher Daten kein eindeutig identifizierbarer technischer oder sicherheitsrelevanter Grund für die betreffende Einstellung erkennbar war. Die Studie stellt zudem fest, dass öffentliche Informationsquellen in der Regel nicht ausreichen, um das Vorhandensein oder Fehlen einer Theorie des Schadens durch "Killer-Akquisition" abschließend zu bewerten. Eine weitere Prüfung müsste größtenteils auf nicht-öffentlichen (unternehmensinternen) Informationen basieren, um das Vorhandensein einer solchen Theorie des Schadens im konkreten Fall abschließend zu beurteilen.

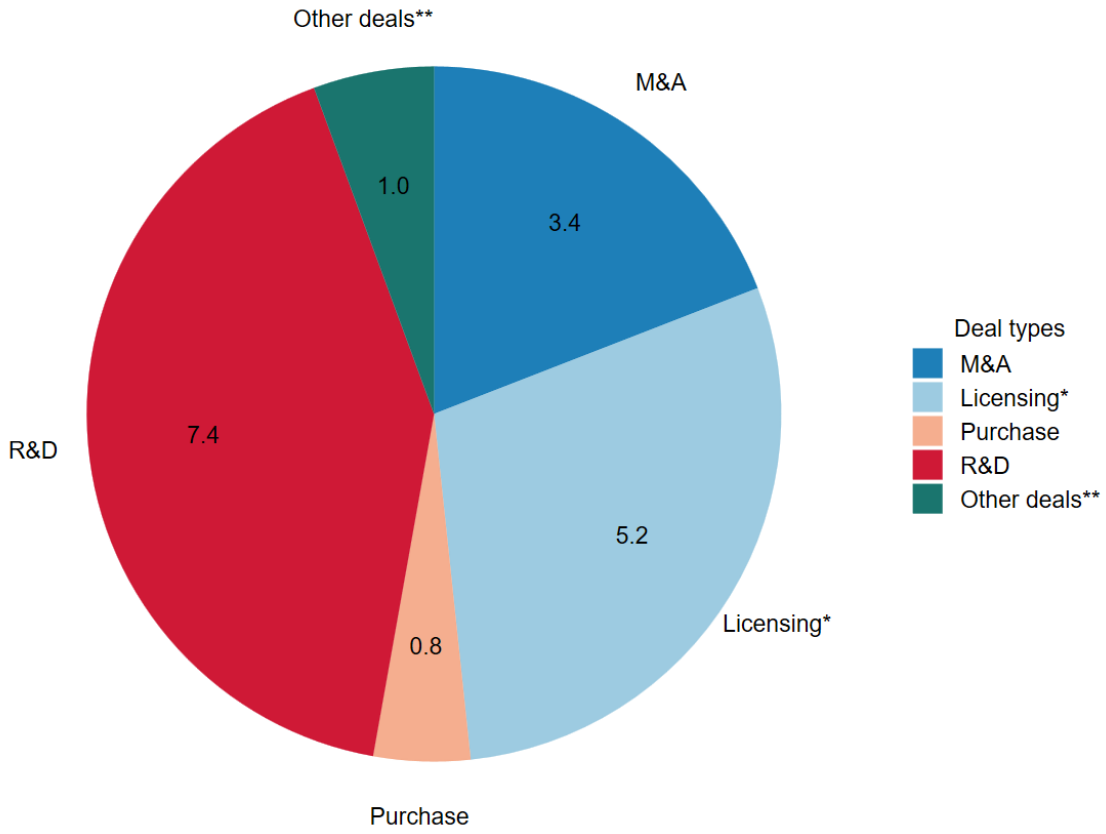
Die nachstehende Grafik fasst die Hauptergebnisse zusammen:



Quelle: Lear-Analyse

Um das Ausmaß des Phänomens der näher zu betrachtenden Transaktionen besser zu veranschaulichen, zeigt die folgende Abbildung die durchschnittliche jährliche Anzahl der Transaktionen nach Transaktionsart im Untersuchungszeitraum:

Jährliche durchschnittliche Anzahl von Vorgängen, die einer eingehenderen Prüfung bedürfen (2014-2018)



*Quelle: Lear-Analyse. Anmerkungen: *In den Jahren 2014-2018 gehören 12 „exklusive" Lizenzvereinbarungen, die mit Hilfe von Suchtexttools anhand der Beschreibungen in unserem Transaktionsdatensatz identifiziert wurden, zu den Transaktionen, die eine genauere Untersuchung verdienen. **Für die Gruppe Sonstige Transaktionen wurden in den Jahren 2014-2018 Transaktionen, die eine genauere Untersuchung verdienen, in den folgenden Transaktionstypen identifiziert: Kapitalbeteiligung (2 Transaktionen), Joint Venture (1 Transaktion), Joint Venture F&E (1 Transaktion), Marketingvereinbarung (1 Transaktion); in den Bereichen Partnerschaften und Kreuzlizenzvereinbarungen wurden keine engen Überschneidungen festgestellt*

Für den Zeitraum 2014-2018 identifiziert die Studie durchschnittlich 3,4 M&A-Deals pro Jahr, die eine nähere Betrachtung verdienen, 5,2 Lizenzdeals, 0,8 Kaufdeals, 7,4 F&E-Deals und 1 Deal in der Restkategorie.

Die Ergebnisse werden weiterhin durch die Analyse der Merkmale dieser speziellen Gruppe von Transaktionen bei M&A-Deals unterstützt, welche sich durch distinkte Eigenschaften von Transaktionen ohne Folgeabbrüche oder mit scheinbar harmlosen Abbrüchen abheben. Insbesondere Abbrüche, die einer genaueren Untersuchung bedürfen und die dazugehörigen Transaktionen betreffen oft Medikamente in fortgeschrittenen Entwicklungsphasen, was auf eine erhebliche Wettbewerbsbedrohung hindeutet und eine „Killer-Akquisitionsstrategie" motivieren könnte. Zudem treten sie häufig in stark konzentrierten Märkten auf, wo echte Wettbewerber rar sind, was solche Strategien weiterhin begünstigt.

Die Fact-Finding-Herausforderung legt nahe, dass das Phänomen der Killer-Akquisitionen weiterhin eine Besorgnis für Wettbewerbsbehörden darstellen sollte.

Während ein Vergleich der quantitativen Studienergebnisse mit denen von Cunningham et al. (2021) die Formulierung von Annahmen und Einschränkungen erfordert, stimmen die übergeordneten Schlussfolgerungen überein: Cunningham et al. (2021) raten davon ab, „Akquisitionen von aufkommenden Technologien allein als Bestreben etablierter Unternehmen zu deuten, unternehmerische Innovation zu integrieren und zu fördern".[43]

Fact-Finding-Herausforderung: Politische Empfehlungen

Zusammenfassend bestätigen die Ergebnisse der Herausforderung der Faktenermittlung die zunehmende Besorgnis der Wettbewerbsbehörden bezüglich des wettbewerbswidrigen Charakters und der Auswirkungen von Übernahmen, die sich überschneidende Arzneimittel-F&E-projekte involvieren. Die Studie hebt die Notwendigkeit einer fallbezogenen Bewertung hervor, statt pauschaler oder probabilistischer Ansätze, um die Anreize der beteiligten Akteure und die Auswirkungen der Transaktion auf die Wettbewerbsdynamik zu erfassen. Spezifische Informationen zu den Transaktionen sind entscheidend, um Faktoren wie die Austauschbarkeit von Arzneimitteln, deren technische und kommerzielle Tragfähigkeit sowie die Wettbewerbsbedrohung durch andere Marktteilnehmer zu verstehen. Öffentlich zugängliche Informationen können bei der ersten Überprüfung solcher Übernahmen hilfreich sein, besonders bei Fusionen und Übernahmen, reichen jedoch nicht aus, um endgültige Schlussfolgerungen über deren Auswirkungen auf den zukünftigen Marktwettbewerb zu ziehen.

Es ist wichtig hervorzuheben, dass seit Fertigstellung dieser Studie (im Mai 2024) der Gerichtshof der Europäischen Union sein Urteil über die Berufungen seitens Illumina und GRAIL in den verbundenen Rechtssachen C-611/22 und C-625/22 P erlassen hat.[44] In diesem Urteil stellt der Gerichtshof der Europäischen Union klar, dass nur Mitgliedstaaten, die nach ihrem nationalen Fusionskontrollregime zuständig sind oder über kein nationales Fusionskontrollregime verfügen, einen Zusammenschluss nach Artikel 22 der Fusionskontrollverordnung an die Kommission verweisen können. In der Folge hat die Kommission von ihrer rekalibrierten Anwendungsweise von Artikel 22 der Fusionskontrolle Abstand genommen, welche darin bestand, Verweisungsanträgen von Zusammenschlüssen anzunehmen, die zwar nicht der nationalen Fusionskontrolle unterworfen waren, aber dennoch drohten, den Wettbewerb und den Handel innerhalb der der EU zu beeinträchtigen. Die Kommission hat angezeigt, dass sie in der Zukunft im Einklang mit den Schlussfolgerungen des Gerichtshofes, Verweisungen nach Artikel 22 der Fusionskontrollverordnung annehmen wird, wenn diese von Mitgliedstaaten beantragt werden, die entweder nach ihrem nationalen Recht zuständig sind[45], oder keine nationales Fusionskontrollregime haben (namentlich Luxemburg). Unter

[43] Cunningham et al. (2021), p. 696.

[44] Urteil vom 3. September 2024, Illumina, Inc. v Europäische Kommission, Verbundene Rechtsachen C-611/22 P and C-625/22 P, EU:C:2024:677.

[45] Dies umfasst Umstände, in welchen ein Zusammenschluss die Zuständigkeitschwellenwerte der nationalen Fusionskontrolle erreicht oder wenn nationale Behörden ihre Befugnisse nach nationalem Recht ausgeübt haben, einen Zusammenschluss der Fusionskontrolle zu unterwerfen, welcher nicht einer Anmeldepficht unterliegt, aber Wettbewerbsbedenken hervoruft - sogenannte "Call-in" Befugnisse (zum Zeitpunkt des Verfassens dieser Studie haben acht Migliedstaaten solche Call-in Befugnisse: Dänemark, Ungarn, Irland, Italien, Lettland, Litauen Slovenien and Schweden – und zwei EFTA Mitgliedstaaten – Norwegen und Island. EU-Mitgliedstaaten sind befugt, Verweisungsanträge nach Artikel 22 FKVO zu stellen, während die EFTA-Mitgliedstaaten zwar keine Verweisungsanträge stellen, sich aber einem anhängigen Verweisungsantrag anschließen können.

Berücksichtigung dieser Limitierungen bleibt Artikel 22 der Fusionskontrollverordnung ein nützliches Werkzeug, das es der Kommission erlaubt, wettbewerblich bedenkliche Zusammenschlüsse zu überprüfen, welche die Aufgreifschwellenwerte der Fusionskontrollverordnung nicht erreichen.

Trotz der in unserer Analyse aufgeführten Einschränkungen zeigt der Bericht, dass das Phänomen der „Killer-Akquisitionen" bei Forschungs- und Entwicklungsvereinbarungen ebenso gravierende Auswirkungen haben kann wie bei M&A-Transaktionen. Etwa die Hälfte der Transaktionen mit engen Überschneidungen bei beiden Geschäftsarten führt zu Einstellungen, die eine weitere Überprüfung erfordern. Weitere Forschungen sind daher essenziell, um diese besser zu klassifizieren, ihre Implikationen zu verstehen und ihre Anfälligkeit für eine „Killer-Acquisitions" -Erzählung zu bewerten.

Herausforderung der Evaluierung

Das zweite Kapitel der Studie hat zum Ziel, die Anwendung und, wo angebracht, die Grenzen der aktuellen EU-Fusionskontrollverordnung zu bewerten und aufzudecken sowie die Vorteile der Anwendung von Wettbewerbsregeln, wo relevant, zu beurteilen.

Zunächst wird eine Bewertung der bisherigen Bemühungen der Kommission unternommen, sogenannte „Killer-Akquisitionen" gemäß der EU-Fusionskontrollverordnung zu bekämpfen, indem rückblickend die Beurteilung der Kommission von fünf angemeldeten Zusammenschlüssen untersucht wird. Anschließend wird der allgemeine rechtliche Rahmen, in dem die Kommission agiert, evaluiert und die Anwendbarkeit von Artikel 22 der EU-Fusionskontrollverordnung sowie der Artikel 101 und 102 des AEUV in zwei passenden Fallstudien simuliert. Beide Studienaspekte wurden auf Basis umfangreicher Recherchen zu öffentlich zugänglichen Informationen durchgeführt. Die Beurteilung des rechtlichen Rahmens stützt sich auf juristische und ökonomische Fachliteratur, mit einem starken Fokus auf rechtliche Präzedenzfälle und Gerichtsentscheidungen.

Wir weisen darauf hin, dass zum Zeitpunkt der Abfassung dieser Studie (Mai 2024) das Urteil des Europäischen Gerichtshofs über die Zuständigkeitsbeschwerden von Illumina und GRAIL in den verbundenen Rechtssachen C-611/22 P und C-625/22 P noch aussteht. Es ist daher zum Zeitpunkt der Abfassung ungewiss, ob der Europäische Gerichtshof das Urteil des Gerichts bestätigen und die Auslegung der Kommission zu Artikel 22 EUMR bestätigen wird (siehe auch Abschnitt II.2.3 für weitere Einzelheiten).

Bei der Bewertung einzelner Transaktionen stützten wir uns auf folgende Informationsquellen:

- Springer Nature's AdisInsight-Datenbank über weltweit kommerziell entwickelte Medikamente;[46]
- ClinicalTrials.gov, ein umfassendes Register klinischer Studien weltweit;[47]
- Online-Ressourcen für medizinisches Fachpersonal, einschließlich Fachartikeln über Ergebnisse klinischer Studien und F&E-Trends/Herausforderungen, die kostenlos

[46] Eine vollständige Beschreibung dieser Datenbank finden Sie in Abschnitt I.1.2 dieses Berichts.

[47] Eine vollständige Beschreibung dieser Datenbank finden Sie in Abschnitt I.1.3 dieses Berichts.

über die PubMed-Datenbank[48] zugänglich waren, Behandlungsrichtlinien verschiedener medizinischer Verbände (z. B. ESMO), die während des Untersuchungszeitraums gültig waren (und oft angepasst wurden), sowie Informationen, die von der EMA und der FDA auf ihren offiziellen Websites veröffentlicht wurden;
- Zusicherungen der Transaktionsparteien (z. B. in ihren Pressemitteilungen, Geschäftsberichten, SEC-Einreichungen, veröffentlichten Pipelines, Managementinterviews und Ähnlichem), die von den Websites der Parteien und anderen Online-Archiven zusammengestellt wurden;
- Nachrichtenberichte und Analysen von Spezialisten aus dem Pharmasektor (z. B. Scrip[49] und Fierce Pharma[50]) sowie allgemeinere geschäftsorientierte Online-Nachrichtenpublikationen.

Wo diese öffentlichen Quellen nicht ausreichend klar waren, zogen wir das Wissen und die Erfahrung von Experten aus der pharmazeutischen Industrie im Team heran, um beispielsweise den Wettbewerbsspielraum zwischen verschiedenen Molekülen, die Ergebnisse technischer Versuche und deren kommerzielle Auswirkungen, die Erfolgsaussichten der Pipeline und die verschiedenen Anreize, die möglicherweise die strategischen Entscheidungen der Firmen beeinflusst haben, zu bewerten.

Ergebnisse der Herausforderung der Evaluierung

Das Kapitel „Evaluation challenge" beginnt mit der Untersuchung, wie gut die inhaltliche Fusionskontrollbewertung der Kommission Transaktionen im Pharmasektor, die sich überschneidende F&E-Projekte betreffen, behandelt hat. Diese Studie beinhaltet eine Ex-post-Bewertung von fünf ausgewählten Pharmaübernahmen, die bei der Kommission angemeldet und freigegeben wurden, teilweise unter Auflagen.[51] Diese Fälle repräsentieren innerhalb des relevanten Zeitrahmens der Studie[52] jene, die F&E-Projekte für Humanarzneimittel betreffen (im Gegensatz zu Medizinprodukten) und Überschneidungen zwischen bestehenden und geplanten Produktlinien (Market-to-Pipeline oder Pipeline-to-Pipeline) aufweisen. Eine Transaktion wurde während der Faktenerhebung als besonders prüfungsbedürftig hervorgehoben, insbesondere wegen einer Überschneidung, die in der Untersuchung der Kommission keine Bedenken begründete, da die Kommission Zugang zu nicht-öffentlichen Informationen hatte, die diese Studie nicht berücksichtigen konnte. Die Ex-post-Bewertung zielte darauf

[48] PubMed (https://pubmed.ncbi.nlm.nih.gov) ist eine durchsuchbare Datenbank mit Zitaten und Abstracts aus der medizinischen Forschungsliteratur, die von der US-amerikanischen Nationalbibliothek für Medizin gepflegt wird. Sie bietet Verlinkungen zu anderen Webseiten, die die entsprechenden Volltextmaterialien bereitstellen.

[49] Scrip (https://scrip.citeline.com) ist eine abonnementbasierte Quelle für globale kommerzielle pharmazeutische Nachrichten und Analysen, die für den größten Teil des in dieser Studie abgedeckten Zeitraums Teil von Informa PLC war und im Jahr 2022 abgestoßen und mit Norstella fusioniert wurde.

[50] Fierce Pharma (https://fiercepharma.com) ist ein kostenloser (durch Werbung unterstützter) täglicher Nachrichtendienst, der allgemeine Berichterstattung über pharmazeutische Unternehmen und Entwicklungen weltweit bietet und von Questex, LLC betrieben wird.

[51] M.8401 J&J/Actelion; M.7275 Novartis/GlaxoSmithKline Oncology Business; M.7872 Novartis/GSK (Ofatumumab Autoimmune Indications); M.9294 BMS/Celgene; M.9461 AbbVvie/ Allergan.

[52] Obwohl der in der Analyse der Sachverhaltsermittlung betrachtete Zeitraum von 2014 bis 2018 reicht, haben wir auch Fälle berücksichtigt, die der Kommission im Jahr 2019 gemeldet wurden, da zwei sehr relevante Fälle für die Ex-post Bewertung in diesem Jahr gemeldet wurden (BMS/Celgene und AbbVie/Allergan).

abzubeurteilen, ob die Transaktionen zu einer Einstellung von sich überschneidenden F&E-Projekten führten, was den Wettbewerb hätte verringern und den Verbrauchern schaden können. Dies umfasst eine Bewertung der Abhilfemaßnahmen und die Entwicklung der Pipelines nach Implementierung dieser Maßnahmen.

Die Studie zeigt, dass die Kommission im Allgemeinen sogenannte Killer-Akquisitionen korrekt identifiziert hat. Obwohl die Analyse eines der Fälle, basierend auf öffentlich zugänglichen Beweisen, einen potenziell besorgniserregenden Bereich aufzeigt, der weitere Untersuchungen gerechtfertigt hätte, verstehen die Autoren der Studie, dass die Kommission Zugang zu vertraulichen Daten hatte, die jegliche Bedenken ausräumen konnten. Von den fünf in dieser Studie bewerteten Fällen wurden zwei von der Kommission bedingungslos freigegeben und drei unter Auflagen freigegeben. Die nachträgliche Bewertung durch das Team ergab, dass in allen fünf Fällen mindestens eine der zum Zeitpunkt der Transaktion sich überschneidenden Moleküle in der relevanten therapeutischen Indikation anschließend eingestellt wurde. Dies bedeutet nicht, dass das Eingreifen der Kommission unangemessen war: Tatsächlich verstärkte unsere Bewertung die Maßnahmen der Kommission (insbesondere die Notwendigkeit, in drei Fällen Auflagen einzuführen und die Angemessenheit, die übrigen zwei bedingungslos freizugeben).

Wir heben jedoch hervor, dass die Tatsache, dass eine veräußerte Pipeline eingestellt wurde, nicht notwendigerweise bedeutet, dass die Abhilfemaßnahmen schlecht konzipiert waren, da solche Einstellungen auch Ausdruck der Unsicherheit in der Entwicklung von Pipeline-Medikamenten sein können. In den untersuchten Fällen konnten wir nicht ausschließen, dass die veräußerten Pipelines aus technischen Gründen, die nicht mit den Abhilfemaßnahmen zusammenhängen, eingestellt worden sein könnten. In einem Fall, J&J/Actelion, wurde jedoch auch vorgeschlagen, dass unter strengeren Abhilfemaßnahmen die betreffenden Pipelines wahrscheinlicher den Markt erreicht hätten. In diesem Fall scheint es, dass die Abhilfemaßnahme besser hätte gestaltet werden können. Insbesondere scheint die Gestaltung der Abhilfemaßnahme die Einstellung einer Pipeline infolge von Handlungen Dritter möglicherweise nicht verhindert zu haben (da die Maßnahme teilweise auf der aktiven Teilnahme eines Partners basierte, der sich entschied, die Zusammenarbeit zu beenden).

Killer-Akquisitionen können jedoch unter die Fusionskontrollschwellen fallen oder nicht als Konzentrationen strukturiert sein. Unsere *prima facie* relevanten Einstellungen – mögliche Kandidaten für eine Bewertung als Killer-Akquisitionen – betreffen auch Deal-Typen, die von M&A abweichen.

Weltweit ringen Wettbewerbsbehörden damit, systematische Mittel zur Regulierung von Übernahmen wettbewerbskritischer, jedoch relativ kleiner Innovatoren in schnelllebigen Branchen zu finden, ohne dass durchgreifende Reformen ihrer Fusionskontrollverfahren erforderlich werden. Diese Reformen könnten das ausgewogene Verhältnis zwischen den Belastungen einer Anmeldepflichtigkeit und den Vorteilen einer ex ante Prüfung beeinträchtigen. In Situationen, in denen eine oder mehrere nationale Wettbewerbsbehörden nach nationalem Recht zuständig sind, einen Zusammenschluss zu überprüfen, inklusive Situationen, in denen diese Zuständigkeit durch die Ausübung sogenannter Call-in Befugnisse begründet wird, oder ein Mitgliedstaat über keinerlei Fusionskontrollregime verfügt, kann der im Artikel 22 FKVO vorgesehene Verweisungsmechanismus effektiv eine Grundlage bieten, auf welcher Kommission diese Art von Transaktionen überprüfen kann. , Die Anwendung von Artikel 22 durch die Kommission in bestimmten Fällen zeigt, dass dieser einen Beitrag zur Schließung der Durchsetzungslücke in hochinnovativen Sektoren mit kleinen, aber wettbewerbsentscheidenden Akteuren leisten kann (wie durch J&J/TachoSil illustriert).

Jedoch über die Limitierungen des Anwendungsbereichs, welche durch den Gerichtshof in den Verbundenen Rechtssachen C-611/22 P und C-625/22 P klargestellt wurden, bestehen ein potenzieller Nachteil von Artikel 22 darin, dass er zwar ein Mittel zur wettbewerblichen Prüfung von Transaktionen bietet, die die normalen Vorabmeldeschwellen nicht erreichen, aber keine Sicherheit besteht, dass problematische Transaktionen überhaupt die Aufmerksamkeit der Kommission oder der Mitgliedstaaten erregen.[53] Wir wissen, dass die Kommission bereits aktiv pharmazeutische Transaktionen überwacht, um mögliche Fälle für die Anwendung von Artikel 22 zu identifizieren.[54] Das Überwachungsverfahren orientiert sich an der vierstufigen Methodik der Sachverhaltsermittlung und ist bereits sehr umfassend. Es könnte jedoch möglich sein, ein „Light-Touch"-Register von Transaktionen und Entwicklungen nach dem Geschäftsabschluss zu erwägen, um die Identifizierung relevanter Geschäfte ex ante zu verbessern und ex-post über geplante Einstellungen zu informieren. Ein solches Register könnte auf Unternehmen anwendbar sein, die groß genug sind, um eine EU-Relevanz zu sichern. Eine Kosten-Nutzen-Analyse durch die Kommission ist dennoch angebracht.

Dieses Kapitel diskutiert weiterhin, dass die Artikel 101 und 102 AEUV wertvolle Instrumente darstellen, um gefährliche Übernahmen zu adressieren, die nicht als Fusionen strukturiert sind. Ausgehend von den Fakten zweier tatsächlich stattgefundener Transaktionen, die einer weiteren Untersuchung laut der Sachverhaltsermittlung bedürfen, entwickelten wir zwei hypothetische Fallstudien. Diese ermöglichten es uns, Bewertungen nach Artikel 22 FKVO sowie nach Artikel 101 und 102 AEUV vorzunehmen. Eine der Fallstudien konzentriert sich auf eine Fusion unterhalb der Schwellenwerte und beinhaltet eine auf spezifische, hypothetische Fakten zugeschnittene Prüfung nach Artikel 22 FKVO. Die andere Fallstudie ermöglicht die Formulierung zweier verschiedener hypothetischer Szenarien: eines, in dem das Vorhaben als Fusion angesehen wird – und somit die Prüfung nach Artikel 22 FKVO erfolgt – und eines, in dem es als Lizenzvereinbarung betrachtet wird – und somit die Bewertungen nach Artikel 101 und 102 AEUV durchgeführt werden.

Herausforderung der Evaluierung: Politische Empfehlungen

Zusammenfassend betont die Evaluierungsstudie, dass die Überprüfung der Kommission in Fällen von Killer-Akquisitionen, die als Fusionen strukturiert sind und Unternehmen betreffen, die groß genug sind, um die Meldegrenzen der EU-Fusionskontrollverordnung (FKVO) zu erreichen, in der Regel geeignet ist, wettbewerbswidrige Auswirkungen solcher Vereinbarungen zu verhindern und somit Verbraucherschäden abzuwenden.

Weiterhin ergab die Studie, dass auch wenn Killer-Akquisitionen als Konzentrationen unterhalb der Schwellenwerte oder in anderer Form als Fusionen strukturiert sind, rechtliche Mechanismen existieren, um solche Transaktionen zu adressieren. Artikel 22 der EU-Fusionskontrollverordnung in bestimmten Konstellationen ist ein wertvolles und

[53] Wir stellen fest, dass zum Zeitpunkt der Erstellung dieser Studie (Mai 2024) das Urteil des EuGH (in den verbundenen Rechtssachen C-611/22 P und C-625/22 P) darüber, ob Zusammenschlüsse, die auf nationaler Ebene nicht meldepflichtig sind, Gegenstand einer Verweisung nach Artikel 22 EUMR sein können, noch aussteht.

[54] Dies wird beispielsweise in folgendem Dokument angegeben: Europäische Kommission, Generaldirektion Wettbewerb, Update on competition enforcement in the pharmaceutical sector (2018-2022) – European competition authorities working together for affordable and innovative medicines – Report from the Commission to the Council and the European Parliament, Publications Office of the European Union, 2024, https://data.europa.eu/doi/10.2763/427709.

effektives Instrument, um potenzielle Killer-Akquisitionen in Form von Konzentrationen unterhalb der Schwellenwerte zu erfassen - vorausgesetzt, dass die verweisenden Mitgliedstaaten nach nationalem Recht zuständig sind, eine Verweisung zu beantragen, oder über keinerlei Fusionskontrollregime verfügen. Für Geschäfte, die nicht als Fusionen strukturiert sind, spielen die allgemeinen wettbewerbsrechtlichen Bestimmungen eine wichtige Rolle. Zudem empfiehlt die Studie zur Sicherstellung, dass problematische Transaktionen der Kommission gemeldet werden, die Erwägung der Einführung eines Registers oder eines Benachrichtigungssystems für relevante Geschäfte und geplante Einstellungen: Dies wird besonders wichtig sein, um potenziell schädliche Transaktionen in Form von exklusiven Lizenzen zu identifizieren, die per se keiner vorgängigen Überprüfung nach der EU-Fusionskontrollverordnung unterliegen.

Abstrait

Au cours des dernières années, les inquiétudes liées aux opérations de concentration dans le secteur pharmaceutique, qui nuisent à l'innovation et la concurrence par l'arrêt de projets de R&D de médicaments concurrents - dites "acquisitions tueuses" -, ont conduit à des actions réglementaires et à des recherches sur ce type d'acquisitions.

L'objectif de cette étude est double. Premièrement, le «défi d'enquête» vise à évaluer la prévalence et les caractéristiques du phénomène des acquisitions tueuses. Deuxièmement, le « défi d'évaluation » vise à réaliser une analyse ex post des cas impliquant potentiellement des acquisitions tueuses. Dans le cadre de l'enquête, l'étude recueille des renseignements publics sur un large éventail d'opérations réalisées entre 2014 et 2018, pour déterminer si certaines pourraient constituer des acquisitions potentiellement tueuses. L'étude est novatrice en ce sens qu'elle évalue non seulement les fusions et acquisitions, mais également d'autres types de transactions telles que les accords de licence et les accords de coopération en matière de R&D. De plus, l'évaluation de l'enquête va au-delà d'une analyse statistique de la probabilité des acquisitions tueuses en appliquant une approche en deux étapes: i) une analyse automatisée à grande échelle pour repérer les opérations entraînant l'arrêt de projets de R&D sans justifications techniques ou commerciales apparentes sur des médicaments se chevauchant et ii) une évaluation qualitative, au cas par cas, pour analyser les éléments clés d'une hypothèse d'acquisition tueuse dans certaines interruptions les plus pertinentes identifiées lors de l'analyse à grande échelle.

Sur un total de 6 315 transactions identifiées dans le secteur pharmaceutique entre 2014 et 2018, des informations sur l'objet de l'opération étaient disponibles pour 3 193 transactions. Parmi celles-ci, 240 transactions concernaient l'acquisition de projets de R&D de médicaments potentiellement substituables, sur la base d'une définition restreinte de chevauchement concurrentiel. Une proportion significative d'entre elles (89 sur 240, soit 37% des transactions) a été suivie de l'interruption d'un des projets de R&D de médicaments se chevauchant, nécessitant un examen plus approfondi, dans la mesure où – sur la base des données disponibles publiquement – aucune raison technique ou de sécurité clairement identifiable n'expliquait la l'interruption en question. L'étude conclut en outre que les seules sources d'information publiques ne suffisent généralement pas pour évaluer de manière concluante l'existence ou l'absence d'un effet anticoncurrentiel du fait de l'acquisition tueuse. Tout examen plus approfondi doit en grande partie s'appuyer sur des informations non publiques (internes à l'entreprise).

Concernant le défi d'évaluation, l'étude examine les efforts antérieurs de la Commission pour aborder les acquisitions potentiellement tueuses et le cadre juridique orientant les actions de la Commission. L'étude évalue en premier lieu l'efficacité avec laquelle l'évaluation substantielle des fusions de la Commission a traité cinq concentrations notifiées dans le secteur pharmaceutique. Elle évalue ensuite la pertinence des outils à disposition pour les cas de fusion et d'antitrust pour traiter les acquisitions tueuses non notifié à la Commission, en simulant des évaluations selon l'Article 22 du Règlement européen sur les concentrations et les Articles 101/102 du TFUE dans deux études de cas. L'expérience passée et une évaluation juridique suggèrent que l'article 22 du Règlement européen sur les concentrations (pour les concentrations) et les articles 101/102 du TFUE (pour les ententes et autres accords restrictifs et l'abus de position dominante respectivement) sont des outils précieux pour traiter de telles acquisitions tueuses, avec un potentiel d'amélioration dans l'établissement d'un registre ou d'un système de notification pour identifier les transactions potentiellement nuisibles.

Résumé exécutif

Au cours des dernières années, les autorités de la concurrence ont exprimé leurs préoccupations croissantes concernant les effets notables que les fusions et acquisitions (F&A) impliquant des entreprises très innovantes dans des secteurs concentrés peuvent entrainer non seulement sur les prix mais également sur l'innovation. Des études préexistantes ont démontré que les fusions peuvent soit stimuler soit inhiber les efforts de recherche et, par conséquent, le rendement en matière d'innovation, en fonction de facteurs tels que le niveau de concurrence, les gains d'efficacité découlant de l'opération, et les modifications de l'appropriabilité des innovations (Gilbert, 2022 ; Haucap & Stiebale, 2023).

Il existe également une inquiétude spécifique s'agissant de la « perte de concurrence potentielle », souvent associée aux effets anticoncurrentiels des « acquisitions tueuses ». Cela se traduit généralement par des entreprises établies rachetant une start-up concurrente pour prévenir une menace concurrentielle future, ou qui remplacent leur cœur de métier en éliminant les activités communes avec les leurs d'un concurrent spécifique. Crawford et al. (2020) [55] avancent que les acquisitions peuvent aussi entraver la concurrence en matière d'innovation, c'est-à-dire qu'elles peuvent représenter une stratégie d'« achat » évitant de « déployer des efforts dans l'innovation du concurrent », [56] avec le risque de compromettre dès le départ la dynamique concurrentielle, et ce avant même que les efforts de R&D ne façonnent le développement des produits.

Le secteur pharmaceutique, où les investissements en recherche et développement (R&D) sont parmi les plus élevés, voit l'innovation jouer un rôle essentiel en favorisant la croissance économique et l'essor de progrès techniques dans le domaine de la santé (Bokhari, et al., 2021). L'une des conclusions constantes des études existantes est que la concentration du marché du secteur pharmaceutique conduit à des réductions considérables des dépenses de recherche et de production de brevets de la part des entreprises fusionnées, ainsi qu'à un déclin significatif de la productivité des inventeurs des entreprises cibles (Ornaghi, 2009a; Haucap, et al., 2019; Ornaghi & Cassi, 2023). Toutefois, la recherche empirique sur les alliances entre les petites entreprises de biotechnologie et les grandes entités pharmaceutiques, envisagées comme des substituts ou des compléments aux fusions, révèle une perspective plus optimiste, montrant une corrélation positive entre l'expertise en développement clinique d'une grande entreprise et la probabilité de succès des projets des petites entreprises (Grabowski & Kyle, 2008).

Les inquiétudes concernant les impacts négatifs des fusions sur l'innovation se sont intensifiées suite à la publication de l'étude sur les « Killer Acquisitions » par Cunningham et al. (2021), révélant que les projets de médicaments acquis sont moins susceptibles d'être développés lorsqu'ils se superposent au portefeuille de produits existant de l'acquéreur, en particulier quand le pouvoir de marché de ce dernier est important, en raison d'une faible concurrence ou d'une expiration éloignée des brevets. Selon les auteurs, ces acquisitions surviennent fréquemment juste en dessous des seuils requis pour l'ouverture d'une procédure de contrôle par les autorités de la concurrence.

[55] 'How tech rolls': Potential competition and 'reverse' killer acquisitions, Gregory Crawford, Tommaso Valletti, and Cristina Caffarra, VoxEU, 11 Mai 2020, https://cepr.org/voxeu/blogs-and-reviews/how-tech-rolls-potential-competition-and-reverse-killer-acquisitions.

[56] Idem.

Cette observation fait écho à l'analyse de Wollmann (2019), qui note qu'après l'augmentation du niveau du seuil d'exemption pré-notification des fusions américaines, l'industrie pharmaceutique figurait parmi les cinq industries avec le plus grand nombre de fusions horizontales exemptées durant la période post-amendement. Ceci est également conforme à l'évaluation interne des fusions par la Commission, qui n'ont pas atteint les seuils de chiffre d'affaires du Règlement européen sur les concentrations. [57]

Cette évaluation a révélé que dans le secteur pharmaceutique, certaines fusions impliquant des projets de médicaments concurrents n'atteignaient pas les seuils de chiffre d'affaires, bien que les acquéreurs semblassent disposés à payer un prix élevé pour acquérir des cibles innovantes réalisant de faibles chiffres d'affaires. Finalement, les conclusions de Cunningham et al. (2021) concordent également avec les études sur les fusions et acquisitions dans l'industrie pharmaceutique commandées par la Commission européenne et réalisées par Informa Pharma Consulting et Szücs (2020), montrant que la probabilité d'abandon d'un projet pharmaceutique augmente lorsqu'il se chevauche avec un autre projet du même type chez l'acquéreur. De plus, l'étude ne révèle aucune accélération du rythme de développement des médicaments suite à une acquisition, contrairement aux affirmations de l'industrie prétendant que les acquisitions accélèrent le processus de R&D.

Dans le cadre de son engagement continu pour la préservation de l'innovation dans le secteur pharmaceutique, la Commission a lancé en 2022 un nouveau projet – dont cette étude présente les résultats – pour évaluer la prévalence et les caractéristiques des acquisitions dites "tueuses", en se concentrant sur un large éventail d'opérations (fusions-acquisitions et autres) survenues dans le secteur pharmaceutique entre 2014 et 2018.

Les spécifications techniques définissent les acquisitions tueuses dans le secteur pharmaceutique comme des opérations susceptibles d'avoir pour objectif ou effet l'interruption des projets de R&D de médicaments substituables, au détriment d'une concurrence future et donc des consommateurs. [58] Cette définition est adoptée dans cette étude.

L'objectif de l'étude est double. D'une part, elle apporte de nouvelles preuves sur ce phénomène grâce à l'analyse d'un large échantillon d'opérations ayant eu lieu entre 2014 et 2018, afin de déterminer, avec le temps, si ces transactions ont conduit à l'abandon de projets en concurrence et modifié la concurrence sur le marché ("l'enquête"). La particularité de l'étude étant que l'étude examine tous types d'opérations (pas seulement les fusions et acquisitions, mais également les achats d'actifs, les accords de licence, les accords de R&D, etc.). Une autre particularité importante porte sur sa méthodologie, qui vise à collecter des preuves factuelles soutenant un scénario d'acquisition tueuse au moment de l'accord entre les parties, alors que les recherches existantes fournissent uniquement des preuves théoriques ou statistiques de l'existence ou de l'ampleur du phénomène.

D'autre part, cette étude évalue (i) les efforts passés de la Commission pour combattre le phénomène des acquisitions tueuses et (ii) le cadre juridique dans lequel la Commission opère, en sachant que les acquisitions tueuses peuvent également se

[57] Document de travail des services de la Commission (2021), "Evaluation des aspects procéduraux et juridictionnels du contrôle des concentrations de l'UE", SWD (2021) 66 final, 26 Mars.

[58] Les spécifications techniques, note de bas de page 2, font référence à cette définition.

produire en dessous des seuils de régulation des concentrations ou même ne pas être considérées comme des concentrations au départ ("l'évaluation"). En particulier, le deuxième chapitre examine les règles en vigueur et pratiques récentes au titre du Règlement européen sur les concentrations, ainsi que les bénéfices (mais aussi les problèmes qui en découlent) de l'application des articles 101 et 102 du Traité sur le Fonctionnement de l'Union Européenne (TFUE) pour aborder les opérations que les dispositions du Règlement européen sur les concentrations ne permettent pas de détecter.

Défi d'enquête

Le premier chapitre aborde l'enquête et présente l'analyse d'un large échantillon d'opérations survenues dans le secteur pharmaceutique entre 2014 et 2018. Bien que rétrospective, cette analyse repose cependant sur des données publiques, ce qui lui confère certaines limites discutées ultérieurement. Sur la base de preuves factuelles, elle vise à déterminer si certaines de ces opérations ont pu entraîner l'abandon de projets concurrents (que ce soit entre produits substituables en développement ou déjà commercialisés) et ainsi modifier le paysage concurrentiel sur le marché du produit concerné.

Cette analyse factuelle se base sur une méthodologie en quatre étapes permettant d'identifier les sources de données publiques et de fournir des outils utiles pour déterminer si une opération spécifique a conduit à l'abandon de projets de R&D concurrents, en accord avec la théorie du préjudice lié à une "acquisition tueuse" :

- Identification des chevauchements étroits. En accord avec les pratiques de la Commission et les publications existantes, l'étude utilise les indications thérapeutiques (IT) et les mécanismes d'action (MoA) pour évaluer si les projets de R&D pharmaceutique sont des substituts directs. Ce type de chevauchement est désigné par « chevauchement étroit », par opposition à un « chevauchement large » qui repose uniquement sur les IT. L'étude a développé des proxies pour identifier la compétition potentielle entre projets de R&D pharmaceutique présentant différents IT et MoA à divers stades de développement. En particulier, cette étude propose que les termes des Medical Subject Headings (MeSH) associés aux essais cliniques dans le registre américain compétent (ClinicalTrials.gov), qui constitue la base de données publique la plus complète,[59] fournissent une structure numérique et hiérarchique clarifiant la relation entre deux IT apparemment différents. De plus, même lorsque les MoA de deux médicaments ne sont pas identiques – comme cela peut être le cas s'ils ne sont pas encore bien établis – la substituabilité potentielle peut encore être évaluée par les citations croisées dans les articles de revues médicales accessibles sur PubMed Central® (PMC), une archive publique gérée par la Bibliothèque Nationale de Médecine des États-Unis.
- Identification et classification des interruptions. Il existe de nombreuses façons pour un projet de R&D pharmaceutique de s'interrompre suite à une acquisition. Parfois, ClinicalTrials.gov indique clairement qu'un essai a été terminé ou retiré (mentionnant parfois la raison). Dans d'autres cas, seule l'inactivité du processus d'essais cliniques peut servir d'indice pour déduire qu'un essai ou le développement

[59] Nous avons effectué une analyse comparative et constaté que la grande majorité des essais signalés dans le registre européen des essais cliniques ("EUCTR") sont également inclus dans ClinicalTrials.gov (qui, par ailleurs, offre une couverture plus large et davantage d'informations). En outre, nous nous appuyons sur l'EUCTR pour assurer l'exhaustivité lors de la sélection manuelle (voir point 4).

ultérieur d'un médicament dans une IT donnée a été abandonné. Par ailleurs, les projets de R&D peuvent être arrêtés dans une IT pour être redirigés vers une autre. En l'absence d'informations sur l'arrêt ou le retrait, l'étude présume que, lorsqu'une inactivité de deux ans est observée dans le développement d'un projet de R&D sur un médicament dans une IT et qu'aucun développement supplémentaire n'a lieu par la suite, le projet est considéré comme interrompu. Grâce à la structure numérique des termes MeSH, l'étude prend également en compte les cas où un chevauchement concurrentiel apparemment évident a été éliminé par la réorientation d'un des projets vers une autre IT.[60] Les motifs d'interruption mentionnées dans le registre des essais cliniques (lorsqu'elles sont disponibles), la période d'inactivité, la nature des promoteurs (privé ou public) et l'évolution de l'IT au fil du temps pour les deux médicaments concernés permettent de filtrer, parmi toutes les interruptions observées, celles qui semblent sans lien avec la transaction et plutôt liées à des raisons techniques et cliniques (par exemple, un mauvais design expérimental, une faible participation). Les interruptions restantes à l'issue de ce processus de filtrage sont alors considérées à première vue comme pertinentes pour une analyse d'acquisition tueuse.

- L'étude s'appuie sur un algorithme d'apprentissage automatique (Least Absolute Shrinkage and Selection Operator, ou « LASSO ») pour caractériser les opérations ex-ante qui nécessiteraient un examen plus approfondi. Nous débutons avec une liste initiale de caractéristiques observables, suggérées par la littérature et présélectionnées par notre groupe d'experts en affaires, pouvant indiquer que les parties d'une opération donnée avaient soit la motivation, soit la capacité d'éliminer la concurrence sur un marché pertinent. La méthode LASSO inclut des variables qui capturent l'intensité de la concurrence future sur le marché. LASSO nous aide à déterminer les caractéristiques initiales les plus aptes à identifier les projets pharmaceutiques qui auraient probablement continué sans accord de transaction et dont l'abandon a potentiellement réduit la concurrence sur les marchés évalués. [61] Ainsi, LASSO vise à distinguer, parmi les opérations menant à des abandons à première vue pertinentes, celles qui qui sont plus susceptibles de refléter un scénario d'acquisition tueuse. Les étapes analytiques jusqu'ici décrites font partie d'une analyse « de grande envergure », visant à détecter les abandons potentiellement anticoncurrentiels à partir d'une analyse automatisée d'un vaste ensemble d'observations, suivant des règles prédéfinies.
- Enfin, l'étude procède à une « sélection manuelle » des interruptions à première vue pertinentes qui présentent les caractéristiques validées par LASSO (« LASSO-KA ») et du sous-ensemble des autres interruptions à première vue pertinentes, afin de tester la fiabilité des résultats de LASSO. Cette sélection manuelle implique, pour un sous-groupe d'opérations, une vérification individuelle et une évaluation rationnelle des faits. L'abandon d'un projet de R&D sur des médicaments concurrents, bien

[60] Pour cette étude, les reports inférieurs à deux ans ne sont pas considérés ; de même que les reports plus longs, où un développement survient avant la fin de la période d'observation, ne sont pas jugés pertinents (bien qu'ils puissent être préjudiciables durant cette période de report). Cependant, dans de tels cas, il ne peut être exclu qu'il y ait eu un préjudice concurrentiel sous la forme d'un retard dans le développement d'un médicament concurrent qui n'est pas pris en compte par l'étude.

[61] *LASSO est entraîné sur la base d'un échantillon restreint d'interruptions à première vue pertinentes, plus probablement liées à des motifs stratégiques ou commerciaux, qui sont ensuite comparées à un groupe de contrôle composé de projets de médicaments qui se chevauchent et pour lesquels nous ne constatons pas d'interruption juste après la transaction, ou dont l'interruption semble plus vraisemblablement liée à des raisons techniques et cliniques.*

qu'induit par une transaction, est une condition nécessaire mais non suffisante pour conclure que l'acquisition a entravé (ou est susceptible d'entraver) la concurrence et l'innovation. Dans notre étude, le concept d'acquisition tueuse se réfère à une théorie du préjudice dans laquelle une transaction entraîne l'arrêt d'un projet de R&D et est susceptible de produire un effet négatif sur la concurrence. En d'autres termes, la notion d'effet anticoncurrentiel d'une acquisition tueuse retenue dans notre étude exclut les cas où l'acquéreur met fin au développement d'un médicament sans pour autant modifier la dynamique concurrentielle qui prévaut sur le marché concerné. Cette approche exige une compréhension approfondie du modèle de substituabilité entre les médicaments concurrents, de leur pertinence clinique, et du niveau de concurrence dans le marché concerné, surtout lorsque la superposition n'est pas parfaite et que la substituabilité potentielle doit être minutieusement évaluée, ainsi qu'une analyse des motivations commerciales et des contraintes de financement des parties. L'objectif final de la sélection manuelle est de rassembler des preuves qui confirmeraient (ou non) la thèse d'un acquisition tueuse qui sous-tend ces opérations, en tenant compte au maximum des aspects susmentionnés à l'aide des informations disponibles dans le domaine public. Durant la sélection manuelle, nous nous sommes appuyés sur des sources publiques d'informations et des types de données qui vont au-delà de ceux pouvant éclairer l'analyse à grande échelle, comme l'examen des rapports d'entreprises, des annonces liées aux opérations, des articles de presse spécialisée commentant l'opération, ainsi que sur une évaluation personnalisée par notre équipe d'experts de la viabilité technique et commerciale des projets de R&D interrompus, basée sur des rapports techniques publics concernant les activités de R&D des parties et de leurs concurrents (référencés sur ClinicalTrials.gov ou accessibles via PMC).

Bien qu'elle repose sur une méthodologie complexe, l'étude présente cependant certaines limitations :

- L'étude se concentre sur la concurrence des produits en développement au stade des essais cliniques, ce qui ne permet pas d'évaluer pleinement l'impact d'une fusion ou acquisition sur la concurrence en matière d'innovation. Par exemple, l'analyse à grande échelle n'englobe ni les essais précliniques ni les intentions futures des parties de développer de nouvelles indications thérapeutiques;
- L'étude repose sur des sources publiques et n'a donc pas accès aux documents et présentations internes des entreprises, pouvant aider à comprendre comment l'accord a modifié les incitations commerciales des parties à poursuivre le développement d'un médicament. De plus, les informations disponibles publiquement ne permettent souvent pas de reconstruire clairement le paysage concurrentiel ni la pression concurrentielle exercée par chaque concurrent ou d'autres firmes sur le marché;
- Lors de l'évaluation des accords de licence ou des accords de R&D, il est complexe d'identifier l'« objet » et le « périmètre » de l'accord (respectivement, les médicaments et les indications thérapeutiques ciblés par l'accord, et les autres médicaments concernés par des chevauchements). De plus, il est difficile de

déterminer quelle partie bénéficie de l'échange de droits[62]. En conséquence, l'étude ne peut pas saisir pleinement l'ampleur et la nature des acquisitions dites "tueuses"; de plus, les motivations des parties dépendent de l'allocation des droits de commercialisation et de distribution pour l'innovation conjointe : la notion d'effet anticoncurrentiel d'une acquisition meurtrière, telle qu'elle est soutenue par la présente étude, implique une transaction qui permet à une partie d'acquérir des droits de contrôle[63] sur un projet de recherche et développement de médicaments substituables. Ces détails sur les accords de R&D n'étant pas publics, il est impossible de savoir s'ils peuvent conférer des droits exclusifs, même en les examinant manuellement;

- L'étude adopte une approche relativement complète pour évaluer la substituabilité potentielle entre les projets de R&D pharmaceutique, mais elle ne prend pas en compte les accords qui placent sous contrôle commun des projets de R&D partageant seulement la même indication ou classe thérapeutique. Les chevauchements larges, plutôt que étroits, ne sont pas couverts par cette étude. Des recherches supplémentaires pourraient éclairer dans quelle mesure ces chevauchements pourraient également entraîner des abandons;
- Bien que l'étude prenne en compte une période prolongée d'inactivité comme indice d'un possible abandon du projet, cette conclusion n'est pas valable si le développement reprend, comme l'enregistrement d'un nouvel essai, même après une longue période d'inactivité. Ainsi, bien que significatifs du point de vue concurrentiel, les retards de développement ne sont pas traités dans cette étude;
- L'étude prend en compte les intérêts de la société mère et des filiales des entreprises directement impliquées dans l'accord, mais elle ne prend pas en considération les cas où les participations minoritaires peuvent créer des incitations et une capacité à réaliser une acquisition tueuse.

Malgré les limites mentionnées, l'étude contribue de manière originale à la littérature croissante en cherchant à caractériser le phénomène des acquisitions tueuses.

[62] Pour un grand nombre d'accords, un objet ou une cible de l'accord n'a pas pu être identifié. La raison principale en était qu'une des entreprises impliquées n'était pas présente dans notre ensemble de données d'essais cliniques, ce qui se produit généralement lorsque les entreprises n'ont pas de projets de R&D dans leur portefeuille (par exemple, parce qu'elles sont actives dans les plateformes, technologies et équipements plutôt que dans le développement de médicaments, ou que leurs projets de R&D de médicaments sont au stade préclinique et qu'elles n'ont pas encore enregistré d'essais cliniques).

[63] Cette étude considère les droits de contrôle comme ceux qui suffiraient à fournir à une entité la capacité juridique – si elle avait également les incitations – d'éliminer l'un des deux projets de R&D de médicaments qui se chevauchent et qui, en l'absence de l'accord, seraient concurrents, affectant ainsi potentiellement la concurrence future sur le marché des produits. Dans les acquisitions et les achats d'actifs, la nature des transactions implique un transfert de droits de propriété à l'acquéreur, ce qui suffit généralement à supposer que ce dernier peut disposer à sa convenance des deux projets de R&D de médicaments qui se chevauchent. Dans les accords de licence, ce qui est pertinent est la portée de la licence : à cet égard, en plus des indications thérapeutiques spécifiques visées par l'accord, nous essayons de détecter l'exclusivité et de contrôler la portée géographique de la licence, afin de rendre cette hypothèse robuste. Dans les accords de R&D, comme déjà discuté, la capacité de l'accord à modifier la capacité et les incitations de l'une ou l'autre des parties à interrompre l'un des deux projets de R&D de médicaments qui se chevauchent dépend de la manière dont les droits de commercialisation et de distribution pour l'innovation conjointe définis par l'accord sont attribués aux partenaires, ce qui, cependant, ne peut être conclu ni par le type d'accord lui-même ni par les informations publiques.

Résultats de l'enquête

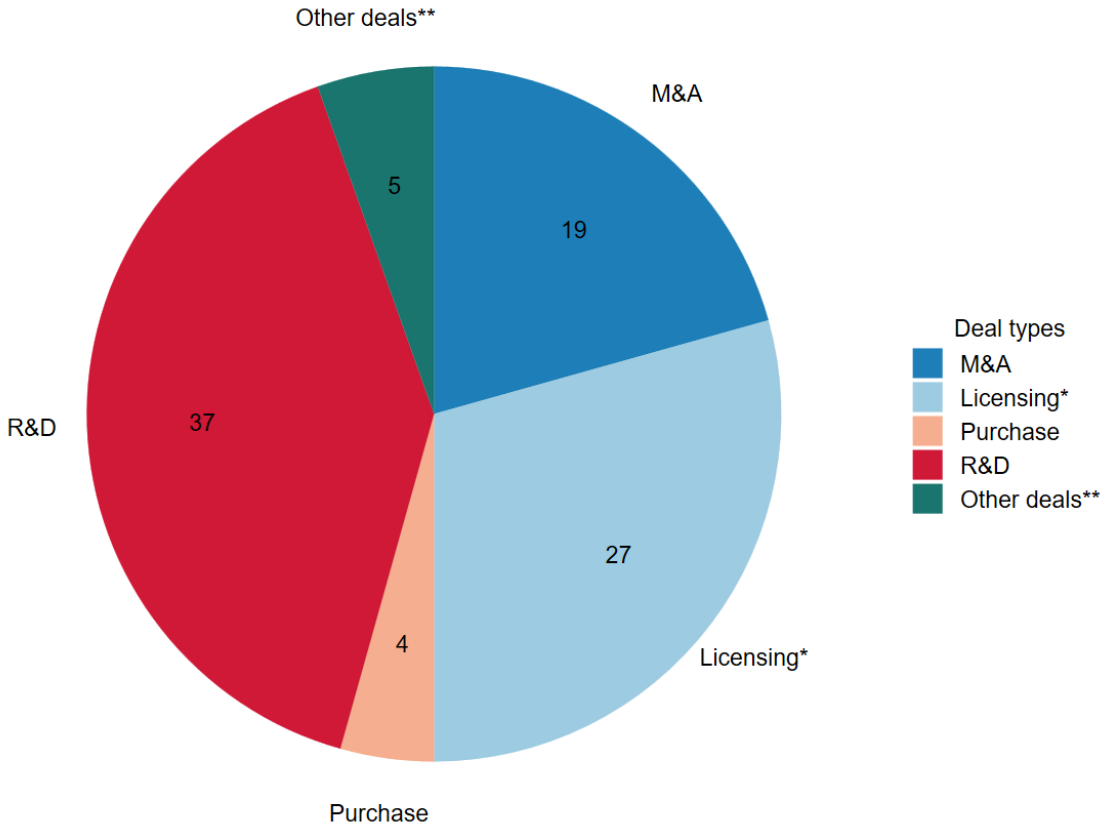
Sur un total de 6 315 transactions identifiées dans le secteur pharmaceutique au cours de la période 2014-2018, des informations sur l'objectif de l'opération étaient disponibles pour 3 193 transactions. [64] dont parmi ceux-ci, 240 concernaient l'acquisition de projets de R&D pour des médicaments potentiellement substituables sur la base d'une définition restreinte du chevauchement concurrentiel (avec chevauchement des technologies de l'information et des protocoles d'accord). Dans la grande majorité de ces opérations (183), au moins un médicament avec un chevauchement étroit a été abandonné suite à la transaction. Ce résultat frappant soulève la question des raisons de ces abandons et si elles pourraient correspondre à une acquisition "tueuse". Nous avons constaté que dans 92 (soit 38%) des opérations avec un chevauchement étroit, l'arrêt d'au moins un des projets semblait, à première vue, pertinent pour évaluer une possible acquisition tueuse.

Le graphique suivant illustre la répartition des abandons jugés pertinents à première vue par type d'opération : [65]

[64] Les opérations qui ont servi de base à l'analyse sont celles, figurant dans l'ensemble de données initial, pour lesquelles nous disposons de suffisamment d'informations pour identifier les médicaments commercialisés par les parties et les projets de recherche et de développement de médicaments concernés par l'opération.

[65] L'analyse à grande échelle a été conçue et réalisée selon chaque type d'opération, afin de prendre en compte leurs spécificités.

La distribution des interruptions à première vue pertinentes par type d'opération



*Source : Analyse de Lear. Remarques : *Il existe 12 accords de licence « exclusifs », identifiés à l'aide d'outils de recherche textuels sur les descriptions de notre ensemble de données, qui présentent des interruptions à première vue pertinentes.**Pour le groupe Autres accords, les interruptions à première vue pertinentes concernent les types d'accords suivants : Prise de participation (2 accords), Entreprise commune (1 accord), Entreprise commune R&D (1 accord), Accord de marketing (1 accord) ; aucune interruption de chevauchement étroit n'est constaté dans les accords de partenariat et de licences croisées*

Des interruptions à première vue pertinentes ont été détectés dans environ 40 % des transactions impliquant des projets de R&D pour des médicaments avec chevauchements. Plus précisément, ces abandons représentent 54 % des transactions avec des chevauchements étroits dans les fusions-acquisitions, 27 % dans les accords de licence, 33 % dans les achats, et 43 % dans les accords de R&D. Ils sont également observés dans les prises de participation (2 transactions), les entreprises communes (EC), les EC en R&D et les accords de marketing (une transaction pour chaque type), tandis qu'aucun abandon à première vue pertinent n'a été détecté dans les partenariats et les accords de licence croisée. Ces résultats suggèrent qu'une grande partie des transactions impliquant des projets de R&D se chevauchant, en particulier les fusions et les acquisitions ainsi que les accords de licence et de R&D, sont à première vue pertinentes pour l'évaluation d'une acquisition tueuse.

Afin d'identifier les transactions où une acquisition tueuse aurait pu être présente ou anticipée, en exploitant les données pertinentes recueillies pour tous les chevauchements étroits, l'étude a adopté l'approche LASSO, complétée par un examen manuel pour confirmer les résultats du LASSO. Appliqué aux fusions-acquisitions, aux

accords de licence et de R&D, l'approche LASSO a permis de sélectionner 53 interruptions jugées à première vue pertinentes comme des « LASSO-KA », répartis sur 19 transactions différentes.

L'examen manuel a ensuite inclus : toutes les interruptions jugées à première vue pertinentes dans les fusions-acquisitions (incluant 6 LASSO-KA) et les accords de licence exclusive (incluant 9 LASSO-KA); [66] 5 % des accords de R&D (représentant 22 % des transactions, incluant 4 LASSO-KA); [67] toutes les interruptions à première vue pertinentes pour tous les autres types de transactions (partenariats, accords de R&D en entreprise commune, prise de participation, accords de marketing, licences croisées, regroupés sous le terme « autres transactions »), là où l'approche LASSO était inapplicable en raison de la taille réduite de l'échantillon.

L'examen manuel a révélé que les interruptions à première vue pertinentes varient considérablement, même au sein d'un même type de transaction et lorsqu'elles présentent des caractéristiques LASSO similaires (c'est-à-dire, les conditions définies dans le modèle LASSO qui nous permettent d'identifier les LASSO-KA), [68] démontrant ainsi que ces caractéristiques ne suffisent pas à capturer les spécificités de ces accords. En particulier, malgré la présence de caractéristiques LASSO, les preuves disponibles (informations publiques) ne permettent pas de conclure à l'existence ou à l'absence d'un scénario d'acquisition tueuse., rendant ces transactions aussi incertaines que celles conduisant à des interruptions à première vue pertinentes sans ces caractéristiques. Cela limite la capacité de la méthode LASSO à aider les autorités de la concurrence à identifier ex ante les transactions méritant une analyse plus approfondie.

De plus, en l'absence d'accès aux documents internes des entreprises, il a été difficile de conclure sur la manière dont la transaction a modifié les incitations commerciales des parties, même lors de l'examen manuel effectué au cas par cas. Les données publiques ne fournissent généralement pas une base solide pour déterminer ou non si les interruptions à première vue pertinentes correspondent entièrement à une acquisition tueuse, empêchant ainsi une évaluation définitive. Ceci est d'autant plus vrai pour certains types de transactions, notamment les accords de R&D et pour les diverses « autres transactions ». [69]

Comme déjà discuté, la notion d' acquisition tueuse, telle que reconnue par cette étude, concerne une transaction permettant à une partie d'acquérir des droits de contrôle sur un projet de R&D pour un médicament substituable, entraînant l'interruption d'un processus de développement dans un domaine thérapeutique spécifique ou l'abandon

[66] En ce qui concerne les licences, un accord de licence non exclusif ne permet pas de mettre un terme à un projet de développement médicament et ne donnerait également aucune incitation à le faire. C'est pourquoi la sélection manuelle s'est concentrée sur les accords de licence exclusive. Les transactions de licences exclusives sont identifiées en appliquant des outils de recherche textuelle à la description des transactions.

[67] Les informations publiques disponibles sont généralement peu instructives sur les accords de R&D, où l'on ne connaît pas le détail de l'échange des droits entre les parties sur les médicaments concernés. Ces limites restreignent considérablement l'analyse et les résultats, empêchant ainsi un examen plus approfondi.

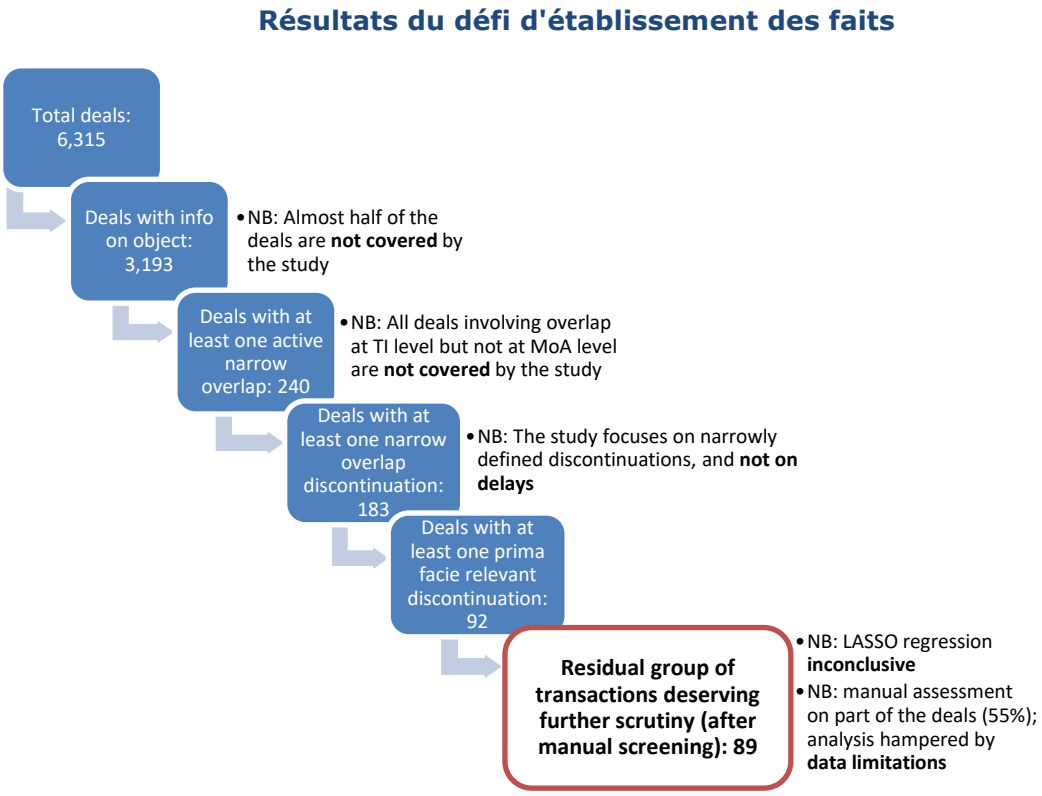
[68] Comme le modèle LASSO a été exécuté par type d'opération, il a donné lieu à des solutions différentes (et donc à des caractéristiques différentes) en fonction du type d'opération. Dans notre première estimation du modèle dans l'échantillon de fusions-acquisitions, le modèle LASSO ne sélectionne qu'un seul régresseur, à savoir l'interaction entre : l'une des molécules se chevauchant dans la phase 4 (c'est-à-dire la commercialisation), l'une des molécules se chevauchant dans la phase 2, et le nombre maximum de concurrents sur le marché fixé à trois.

[69] Voir note de bas de page n° 64.

d’une molécule, et susceptible de diminuer la concurrence et l'innovation. Pour la plupart des interruptions à première vue pertinentes qui ont été examinés manuellement, les informations disponibles publiquement n'ont pas fourni de preuves convaincantes attestant : (i) le degré de substituabilité (ou la proximité concurrentielle, qui est cruciale dans la théorie du préjudice d'une acquisition tueuse) entre les projets de médicaments concurrents, et plus particulièrement, le fait que les médicaments peuvent traiter la même maladie de manière similaire, plutôt que d'être adaptés à différents segments de patients, à un traitement parallèle ou séquentiel, ou à des thérapies combinées ; (ii) l'absence de justification clinique ou technique valable pour l’interruption ; ou justifiable par une évaluation commerciale qui serait survenue même en l'absence de la transaction; (iii) que la concurrence sur le marché concerné a été négativement affectée par l’interruption (une évaluation plus approfondie du degré de substituabilité avec les médicaments concurrents des parties est également nécessaire pour les médicaments « concurrents »). En outre, pour les accords de R&D, nous ne pouvons pas tirer de conclusions générales en raison de l'opacité des droits légaux échangés entre les parties.

Dans le même temps, il n'existe que quelques cas où les preuves publiquement disponibles indiquent plus clairement que l'hypothèse d’une acquisition tueuse peut être écartée avec assurance. Ces cas concernent principalement des situations où, contrairement aux résultats de l’analyse à grande échelle, le médicament interrompu est encore en développement (deux transactions dans le groupe des fusions et acquisitions et une dans le groupe des licences, aboutissant respectivement à cinq et trois interruptions au niveau du chevauchement).

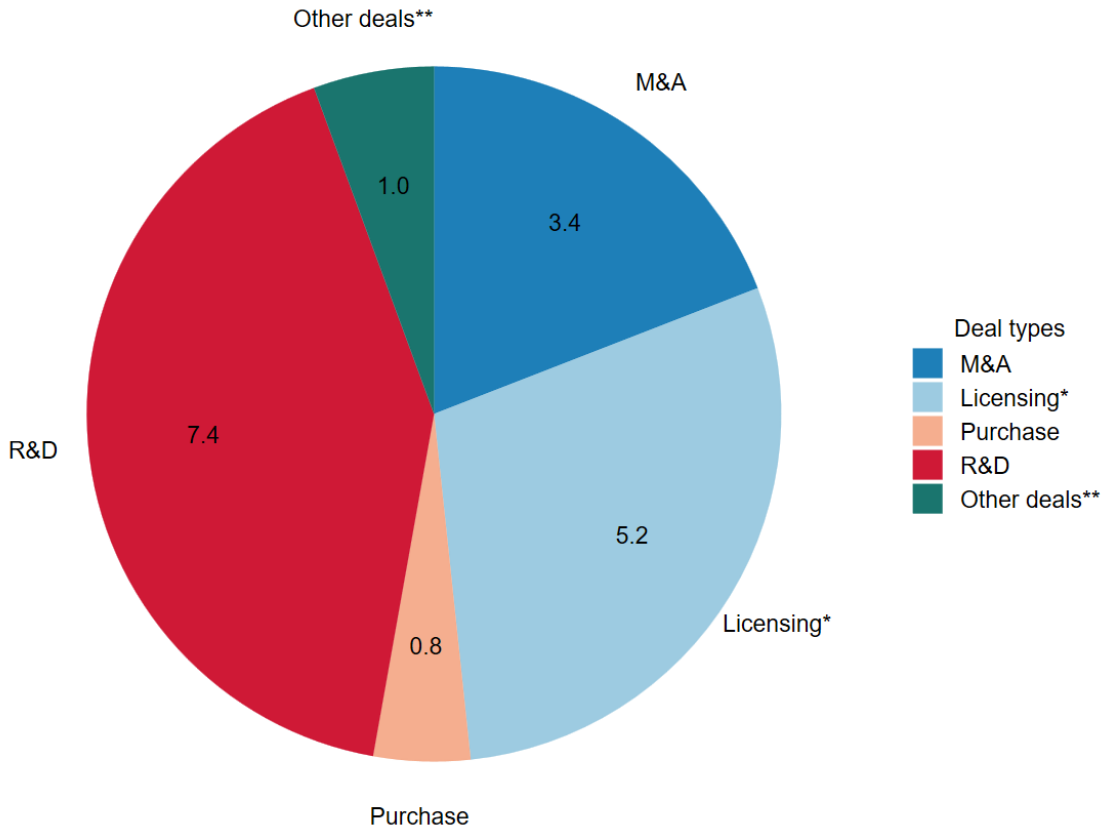
En résumé, l'étude révèle qu'une proportion significative (89 sur 240, soit 37 %) des transactions présentant un chevauchement étroit a été suivie d'une interruption méritant un examen plus approfondi, en ce sens que, sur la base des données accessibles publiquement, il n'y avait pas de raison technique ou sécuritaire clairement identifiable expliquant l'interruption en question. L'étude montre en outre que les sources d'information publiques ne suffisent généralement pas à évaluer de manière concluante l'existence ou l'absence d'une théorie du préjudice fondée sur l'acquisition d'un produit meurtrier. Tout examen plus approfondi devrait s'appuyer en grande partie sur des informations non publiques (internes à l'entreprise), afin d'évaluer de manière concluante l'existence d'une acquisition tueuse dans le cas d'espèce. Le graphique ci-dessous résume les principales découvertes :



Source: Analyse de Lear

Pour mieux illustrer l'ampleur du phénomène des opérations méritant un examen plus approfondi, la figure ci-dessous montre leur nombre annuel moyen par type d'opération au cours de la période analysée:

Nombre moyen annuel d'opérations méritant un examen plus approfondi (2014-2018)



*Source: Analyse de Lear. Notes : *Sur la période 2014-2018, 12 accords de licence « exclusifs » ont été identifiés à l'aide d'outils de recherche textuelle sur les descriptions dans notre ensemble de données d'accords, parmi ceux qui méritent un examen plus approfondi.**Pour le groupe Autres accords, sur la période 2014-2018, les accords qui méritent un examen plus approfondi se situent dans les types d'accords suivants : Prise de participation (2 accords), Entreprise commune (1 accord), Entreprise commune R&D (1 accord), Accord de marketing (1 accord), aucun chevauchement étroit n'est constaté dans les accords de partenariats et de licences croisées*

Pour la période 2014-2018, l'étude révèle une moyenne de 3,4 fusions-acquisitions méritant un examen plus approfondi par an, 5,2 accords de licence, 0,8 accord d'achat, 7,4 accords de R&D et 1 accord dans la catégorie résiduelle.

Les résultats sont également étayés par l'analyse des caractéristiques de ce groupe résiduel de transactions pour les accords de fusion et d'acquisition, qui révèle des traits distinctifs par rapport aux transactions qui ne sont pas suivies d'interruptions ou qui sont suivies d'interruptions apparemment bénignes. En particulier, les interruptions nécessitant une enquête approfondie et les transactions associées impliquent souvent des médicaments en stades avancés de développement, pouvant signaler une menace concurrentielle importante qui pourrait favoriser une stratégie d'acquisition tueuse. De plus, ces transactions ont tendance à se produire dans des marchés hautement concentrés où les concurrents réels sont rares, incitant encore plus à de telles stratégies.

L'enquête suggère que le phénomène des acquisitions tueuses devrait continuer à être un sujet de préoccupation pour les autorités de la concurrence. Bien que la comparaison des résultats quantitatifs de cette étude avec ceux de Cunningham et al. (2021) exige

de formuler des suppositions et des réserves, les conclusions sont concordantes : Cunningham et al. (2021) recommandent « de faire preuve de prudence dans l'interprétation des acquisitions de technologies émergentes comme étant simplement des tentatives des entreprises établies pour intégrer et stimuler l'innovation entrepreneuriale ». [70]

Défi d'enquête : recommandations politiques

En conclusion, le défi d'enquête souligne les préoccupations croissantes des autorités de concurrence vis-à-vis des objectifs et des effets anticoncurrentiels des acquisitions impliquant des projets de R&D de médicaments concurrents. L'étude met en avant l'importance d'une évaluation individualisée, plutôt que des analyses généralisées ou probabilistes, afin de comprendre les motivations des parties concernées et l'impact de la transaction sur la dynamique concurrentielle. Des informations précises sur les accords sont essentielles pour appréhender des aspects tels que la substituabilité des médicaments, leur faisabilité technique et commerciale, ainsi que la menace concurrentielle posée par d'autres médicaments présents sur le marché. Les informations publiques peuvent servir à un examen préliminaire de ces acquisitions, notamment dans le cadre de fusions et acquisitions. Cependant, elles sont insuffisantes pour conclure définitivement sur leurs répercussions futures sur la concurrence.

Nous recommandons que la Commission continue de faire preuve de proactivité dans la surveillance des concentrations dans le secteur pharmaceutique, comme le démontre son activité antérieure dans l'identification rapide des concentrations susceptibles de faire l'objet d'une revue préalable en vertu du Règlement européen sur les concentrations, en utilisant les renvois en vertu de l'Article 22 comme décrit plus en détail ci-dessous. Toutefois, l'analyse des transactions réalisées en dehors du cadre des concentrations, tels que les partenariats de R&D et autres collaborations, est nettement plus complexe. Les informations publiques sont souvent insuffisantes pour détailler comment ces accords modifient les droits liés à l'exploitation des innovations ciblées et, en conséquence, comment ils peuvent influencer les incitations commerciales des parties à l'égard des projets de développement de médicaments concurrents.

Malgré les réserves exprimées dans notre analyse, le rapport indique que le phénomène des 'acquisitions tueuses' pourrait impacter les accords de R&D autant que les opérations de fusion et acquisition. Environ la moitié des transactions avec des chevauchements étroits, pour les deux types de transactions, se concluent par des abandons qui nécessitent une attention supplémentaire. Des recherches plus poussées sont donc indispensables pour mieux les classifier, comprendre leurs conséquences et caractériser comme une 'acquisition tueuse'.

Défi d'évaluation

Le deuxième chapitre du rapport a pour objectif d'évaluer l'application et, le cas échéant, de mettre en lumière les limites de l'actuel Règlement européen sur les concentrations ainsi que d'apprécier les bénéfices de l'application des règles antitrust si nécessaire.

Tout d'abord, ce rapport présente une évaluation des efforts passés de la Commission pour lutter contre les acquisitions tueuses sous le régime du Règlement européen sur les concentrations, à travers l'analyse ex-post des évaluations menées par la

[70] Cunningham et al. (2021), p. 696.

Commission sur cinq concentrations notifiées. Ensuite, le cadre juridique général dans lequel la Commission opère est examiné, et l'applicabilité de l'Article 22 du Règlement européen sur les concentrations ainsi que des Articles 101 et 102 du TFUE sont évaluées à travers deux études de cas spécifiques. Ces éléments de l'études reposent sur des recherches documentaires approfondies d'informations publiques. L'évaluation du cadre juridique s'appuie sur des ouvrages de droit et d'économie, en mettant un accent particulier sur la jurisprudence et les décisions de justice.

Il importe de relever que depuis la rédaction de cette étude (mai 2024), la Cour de Justice de l'Union européenne a statué sur les recours d'Illumina et GRAIL dans les affaires jointes C-611/22 P et C-625/22 P. Dans son arrêt, la Cour de justice a clarifié qu'un État membre doit être compétent en vertu de ses règles nationales en matière de contrôle des concentrations, ou ne pas disposer de règles en la matière, pour pouvoir renvoyer une concentration à la Commission au titre de l'article 22 du Règlement européen sur les concentrations.[71] À la suite de cet arrêt, la Commission s'est donc écartée de son approche révisée de l'article 22, qui consistait à accepter, dans certaines circonstances, le renvoi d'opérations de concentration pour lesquelles l'État Membre de renvoi n'était pas compétent au titre de ses règles de droit nationales, mais qui étaient susceptibles d'affecter les échanges et la concurrence au sein de l'UE. À l'avenir, et conformément aux conclusions de la Cour, la Commission a indiqué qu'elle n'accepterait que les renvois émanant d'États membres qui sont eux-mêmes compétents pour examiner la concentration concernée[72], ou qui n'ont pas de régime national de contrôle des concentrations (comme le Luxembourg) (voir également la section II.2.3 pour plus de détails). Sous réserve de ces limitations, l'article 22 du Règlement européen sur les concentrations reste un outil utile dans la mesure où il permet à la Commission – dans certaines circonstances – d'examiner des concentrations susceptibles de poser des problèmes de concurrence mais qui tombent en deçà des seuils fixés par le Règlement européen sur les concentrations.

Afin d'évaluer les opérations individuelles, nous nous sommes basés sur les sources d'information suivantes :

- La base de données AdisInsight de Springer Nature sur les médicaments en développement commercial à l'échelle mondiale;[73]
- ClinicalTrials.gov, un registre exhaustif d'essais cliniques internationaux; [74]
- Des ressources en ligne destinées aux professionnels de santé, incluant des articles de revues sur les résultats d'essais cliniques et les tendances/défis de la R&D

[71] Arrêt de la Cour de Justice du 3 septembre 2024, Illumina c. Commission, Affaires Jointes C-611/22 P et C-625/22 P, EU:C:2024:677.

[72] Cela peut inclure les cas dans lesquels une opération de concentration atteint les seuils applicables en matière de contrôle des concentrations fixés par le droit national, mais aussi les cas dans lesquels les autorités nationales de la concurrence exercent leur prérogative, sur base du droit national, de requérir la notification d'une opération suscitant des problèmes de concurrence sans atteindre les seuils applicables au niveau national (à la date de la rédaction du présent rapport, huit États Membres de l'UE - le Danemark, la Hongrie, l'Irlande, l'Italie, la Lettonie, la Lituanie, la Slovénie et la Suède - et deux États membres de l'AELE - la Norvège et l'Islande – accordent de telles prérogatives à leurs autorités de concurrence dans leurs droits nationaux). Les États Membres de l'UE peuvent initier des demandes de renvoi au titre de l'article 22, tandis que les États Membres de l'AELE ne peuvent initier de telles demandes, mais peuvent se joindre à une demande de renvoi pendante.

[73] Une description complète est fournie à la section I.1.2 du présent rapport.

[74] Une description complète de ce registre est fournie à la section I.1.3 du présent rapport.

accessibles gratuitement via la base de données PubMed, [75] les recommandations de traitement de diverses associations médicales (telles que l'ESMO) en vigueur (et souvent révisées) durant la période étudiée, ainsi que les informations diffusées par l'EMA et la FDA sur leurs sites officiels;

- Les déclarations des parties prenantes aux opérations (comme dans leurs communiqués de presse, leurs rapports annuels, leurs documents déposés auprès de la SEC, leurs projets publiés, leurs entretiens de gestion, etc.), collectées à partir des sites web des parties et d'autres archives en ligne;
- Des reportages et des analyses de spécialistes du secteur pharmaceutique (par exemple, Scrip[76] et Fierce Pharma[77]), ainsi que des publications plus générales disponibles en ligne, axées sur l'actualité économique et commerciale. Lorsque ces sources publiques n'étaient pas suffisamment précises, nous avons fait appel à l'expertise et à l'expérience des spécialistes de l'industrie pharmaceutique de notre équipe pour évaluer, par exemple, le degré de concurrence entre différentes molécules, les résultats des essais techniques et leurs implications commerciales, les perspectives de réussite des projets, et les diverses incitations qui auraient pu influencer les décisions stratégiques des firmes.

Résultats de l'évaluation

Le chapitre consacré au défi d'évaluation débute par l'examen de l'appréciation matérielle de la Commission en matière de concentrations sur les opérations qui lui ont été notifiées dans le secteur pharmaceutique et impliquant des projets de R&D qui se chevauchent. Cette étude inclut une évaluation ex post de cinq acquisitions pharmaceutiques sélectionnées, notifiées à la Commission et approuvées (parfois sous conditions). [78] Ces cas illustrent, pendant la période étudiée,[79] les acquisitions impliquant des projets de R&D sur les médicaments à usage humain (par opposition à ceux pour les appareils médicaux), et présentant des chevauchements de marchés-à-pipelines ou de pipeline-à-pipeline. Cette étude comprend notamment une transaction identifiée comme nécessitant une analyse approfondie lors de l'enquête préliminaire, ainsi qu'un chevauchement étroit n'ayant pas soulevé de préoccupations lors de l'enquête de la Commission, grâce à l'accès à des informations confidentielles non disponibles pour cette étude. L'évaluation ex post a cherché à vérifier si les acquisitions entraînaient l'arrêt de projets de R&D concurrentiels, éliminant potentiellement la concurrence et nuisant aux consommateurs. Cela inclut une évaluation des mesures correctives et de l'évolution des projets suite à l'application de ces mesures.

[75] PubMed (https://pubnmed.ncbi.nlm.nih.gov) est une base de données consultable de références et de synthèses de la littérature de recherche médicale, gérée par la National Library of Medicine des États-Unis, qui fournit des liens vers d'autres sites web contenant les documents correspondants dans leur intégralité.

[76] Scrip (https://scrip.citeline.com) est une source d'actualité et d'analyses sur les marchés pharmaceutiques mondiaux, accessible par abonnement, qui a fait partie d'Informa PLC pendant la majeure partie de la période couverte par cette étude et qui, en 2022, a été cédée et a fusionné avec Norstella.

[77] Fierce Pharma (https://fiercepharma.com) est un service d'information quotidien gratuit (financé par la publicité) qui fournit une couverture générale des sociétés pharmaceutiques et des développements dans le monde entier. Il est détenu et exploité par Questex, LLC.

[78] M.8401 J&J/Actelion; M.7275 Novartis/GlaxoSmithKline Oncology Business; M.7872 Novartis/GSK (Ofatumumab Autoimmune Indications); M.9294 BMS/Celgene; M.9461 AbbVvie/ Allergan.

[79] Bien que la période considérée pour l'enquête couvre les années 2014 à 2018, nous avons pris en compte les affaires notifiées à la Commission également en 2019, car deux affaires très pertinentes pour l'évaluation ex post ont été notifiées cette année-là (BMS/Celgene et AbbVie/Angergan).

L'étude révèle que la Commission a généralement bien identifié les acquisitions potentiellement préjudiciables. Toutefois, comme indiqué ci-dessus, dans l'un des cas examinés, l'analyse basée sur les preuves publiques soulève des problèmes qui aurait mérité un examen plus approfondi, les auteurs reconnaissent que la Commission disposait de données confidentielles justifiant de ne pas poursuivre l'analyse. Sur les cinq cas évalués dans cette étude, deux ont été approuvés sans conditions par la Commission et trois ont été approuvés sous réserve de remèdes. L'évaluation ex-post menée par l'équipe a révélé que, dans les cinq cas, au moins une des molécules en chevauchement au moment de l'accord a été par la suite abandonnée dans l'indication thérapeutique pertinente. Cela ne signifie pas que l'intervention de la Commission n'était pas adéquate : en fait, notre évaluation a renforcé l'action de la Commission (en particulier, la nécessité d'introduire des remèdes dans trois cas et la pertinence d'approuver les deux autres sans condition).

Il est important de noter que l'arrêt d'un projet cédé ne signifie pas nécessairement que les remèdes étaient inadéquats, car cela peut simplement refléter l'incertitude inhérente au processus de développement de médicaments. Nous ne pouvons donc exclure que les projets cédés aient été abandonnés pour des raisons techniques indépendantes des mesures correctives, mais dans un cas, J&J/Actelion, il a également été suggéré que des remèdes plus stricts auraient augmenté les chances que le projet pertinent sorte sur le marché. Dans ce cas, il semble que le remède aurait pu être mieux conçu. En particulier, il semble que la conception du remède n'a pas pu empêcher l'abandon d'un projet de recherche à la suite d'actions de tiers (car le remède reposait en partie sur la participation active d'un partenaire qui a décidé de mettre fin à la collaboration). Certaines acquisitions tueuses peuvent ne pas atteindre les seuils de notification des concentrations ou ne pas être structurées comme des concentrations. Les interruptions à première vue pertinentes sélectionnées, candidates potentielles à l'évaluation des acquisitions tueuses, incluent également des types de transactions autres que les fusions et acquisitions traditionnelles.

Les autorités de la concurrence du monde entier ont rencontré des difficultés pour déterminer des méthodes systématiques permettant de traiter les acquisitions de petites entreprises innovantes mais stratégiquement importantes dans des secteurs dynamiques, sans pour autant réformer leurs régimes de contrôle des concentrations, ce qui risquerait de perturber un équilibre constructif (représenté par les seuils de notification habituels) entre les contraintes de la notification et les avantages d'une revue préalable. Dans les cas où un ou plusieurs États membres sont compétents pour examiner une opération de concentration, y compris potentiellement au titre de pouvoirs d'appel (ou en l'absence d'un régime national de contrôle des concentrations), le mécanisme de renvoi prévu par l'article 22 du Règlement européen sur les concentrations peut fournir une base permettant l'examen par la Commission de ce type d'opération. L'application de l'article 22 par la Commission dans certaines affaires confirme qu'il peut jouer un rôle pour combler les lacunes constatées en matière d'application de la législation dans des secteurs hautement innovants comptant des acteurs de petite taille mais significatifs sur le plan de la concurrence (comme illustré par les affaires J&J/TachoSil). Outre les limites de son champ d'application, qui ont été clarifiées par la Cour de Justice dans les affaires jointes C-611/22 P et C-625/22 P, l'une des faiblesses potentielles de l'article 22 réside dans le fait que, bien qu'il permette d'analyser des transactions ne franchissant pas les seuils habituels de pré-notification, il ne garantit pas que les transactions problématiques seront portées à l'attention de la

Commission ou des États Membres[80]. Nous comprenons que la Commission surveille déjà activement les transactions pharmaceutiques pour identifier les cas potentiels d'application de l'article 22. [81] Le processus de surveillance suit les mêmes lignes que la méthodologie en quatre étapes développées lors de l'enquête et est déjà assez complet. Cependant, il pourrait être envisageable de mettre en place un registre "allégé" des transactions et des développements post-transaction afin de renforcer encore la capacité d'identifier préventivement les accords pertinents, ainsi que de notifier les interruptions planifiées après coup. Un tel registre serait pertinent pour les entreprises d'une taille suffisante pour qu'un lien avec l'UE soit assuré. Une analyse coût-bénéfice par la Commission est cependant nécessaire.

Ce chapitre aborde également l'utilité des articles 101 et 102 du TFUE pour lutter contre les acquisitions tueuses qui ne sont pas structurées comme des concentrations. Prenant comme point de départ les faits de deux transactions réellement effectuées, qui mériteraient une analyse approfondie selon l'enquête, nous avons développé deux études de cas hypothétiques permettant de réaliser des évaluations en vertu de l'article 22 du Règlement européen sur les concentrations et des articles 101 et 102 du TFUE. Notamment, une des études de cas porte sur une concentration inférieure aux seuils requis et inclut une évaluation selon l'article 22 du Règlement européen sur les concentrations, adaptée aux faits hypothétiques spécifiques de ce cas. L'autre étude de cas permet d'élaborer deux scénarios hypothétiques distincts : un où la transaction est considérée comme une concentration - et donc l'évaluation de l'article 22 est appliquée - et un où elle est vue comme un accord de licence - et donc les évaluations des articles 101 et 102 sont menées.

Défi d'évaluation : recommandations stratégiques

En conclusion, l'évaluation a mis en évidence que, lorsque les acquisitions dites "tueuses" sont structurées sous forme de concentrations et impliquent des entreprises de taille suffisante pour dépasser les seuils de notification du Règlement européen sur les concentrations, l'examen par la Commission est généralement à même de prévenir les effets anticoncurrentiels de telles opérations et, par conséquent, de protéger les consommateurs.

De plus, l'étude a démontré que même lorsque les acquisitions "tueuses" sont structurées en tant que concentrations tombant en deçà des seuils de notification, ou structurées de manière différente, des outils juridiques existent pour examiner de telles opérations. Dans certaines circonstances, l'article 22 du Règlement européen sur les concentrations offre un moyen efficace et précieux pour appréhender les acquisitions

[80] Comme indiqué ci-dessus, la Cour de Justice de l'UE a également clarifié que la Commission ne peut accepter de renvois au titre de l'article 22 du Règlement européen sur les concentrations que de la part d'États Membres qui sont eux-mêmes compétents pour examiner l'opération faisant l'objet du renvoi, ou qui n'ont pas de règles nationales en matière de contrôle des concentrations (comme le Luxembourg). Par conséquent, le mécanisme de renvoi prévu à l'article 22 est susceptible de n'être pas disponible pour certaines opérations qui n'atteignent pas les seuils de notification européens et nationaux, à moins qu'un ou plusieurs États membres soient en mesure d'exercer des pouvoirs d'appel, c'est-à-dire de requérir la notification d'une concentration échappant aux seuils nationaux mais susceptible de poser des problèmes de concurrence (ou que l'opération présente un lien suffisant avec le Luxembourg).

[81] Cela est indiqué, par exemple, dans: Commission européenne, Direction générale de la concurrence, Mise à jour sur l'application des règles de concurrence dans le secteur pharmaceutique (2018-2022) - Les autorités européennes de la concurrence travaillent ensemble pour des médicaments abordables et innovants - Rapport de la Commission au Conseil et au Parlement européen, Office des publications de l'Union européenne, 2024, https://data.europa.eu/doi/10.2763/427709

potentiellement "tueuses" se présentant sous forme de concentrations tombant en deçà des seuils de notification, pour autant que les États Membres de renvoi soient compétents au titre de leurs règles nationales or n’aient aucun régime de contrôle des concentrations. Pour les transactions non structurées en concentrations, les règles de concurrence classiques restent des outils essentiels. En outre, afin de garantir que les transactions problématiques soient signalées à la Commission, l'étude recommande d'envisager la mise en place d'un registre ou d'un système de notification des transactions pertinentes et des interruptions d'activité planifiées : cela s'avérera particulièrement précieux pour identifier les transactions potentiellement néfastes prenant la forme de licences exclusives, et qui, en tant que telles, ne sont pas soumises à un examen préalable en vertu du Règlement européen sur les concentrations.

Abstract

Negli ultimi anni, le transazioni nel settore farmaceutico hanno fatto sorgere preoccupazioni riguardo i possibili effetti negativi su innovazione e concorrenza causati dall'interruzione dello sviluppo di progetti di ricerca attinenti a farmaci tra loro potenzialmente sostituibili; tali, cosiddette "killer acquisition" hanno spinto all'azione regolatoria e hanno motivato la ricerca accademica.

Questo studio ha un duplice obiettivo, riflesso in due diverse fasi di analisi: la prima, la "fact-finding challenge", mira a valutare la pervasività e le caratteristiche del fenomeno delle *killer acquisition*; la seconda, l'"evaluation challenge", mira a condurre una valutazione ex-post di un insieme di transazioni che potrebbero aver coinvolto una *killer acquisition*.

Nell'ambito della *fact-finding challenge*, lo studio usa dati pubblicamente disponibili riguardanti un ampio campione di transazioni avvenute nel periodo 2014-2018, con la finalità di determinare quali di queste possano essere qualificate come potenziali *killer acquisition*. Lo studio è innovativo in quanto non si limita a esaminare operazioni di fusione e acquisizione, ma anche altri tipi di transazioni, come accordi di licenza e di ricerca e sviluppo (R&S). Inoltre, la *fact-finding challenge* non si limita a una valutazione statistica della probabilità di *killer acquisition*, ma applica il seguente approccio in due fasi: i) un'analisi automatizzata su larga scala con l'obiettivo di individuare le transazioni seguite dall'interruzione dello sviluppo di farmaci potenzialmente sostituibili (i.e., con effetti terapeutici simili), non apparentemente giustificata da motivi tecnici o commerciali; e ii) un esame qualitativo, approfondito, per alcune delle interruzioni più rilevanti identificate attraverso l'analisi su larga scala, volto a valutare la sussistenza degli elementi caratterizzanti un'ipotesi di *killer acquisition*.

Delle 6.315 transazioni avvenute nel settore farmaceutico nel periodo 2014-2018, informazioni sull'oggetto dell'accordo sono disponibili per 3.193 transazioni. Di queste, 240 riguardano l'acquisizione di progetti di ricerca e sviluppo di farmaci che possono potenzialmente essere considerati sostituibili. Per una percentuale significativa di queste operazioni (89 su 240, 37%) si è osservata una interruzione dello sviluppo di almeno un trattamento in sovrapposizione con quello dell'altra parte che richiederebbe un esame più approfondito, nel senso che - sulla base di informazioni pubbliche - non sono state individuate ragioni tecniche che possano spiegare l'interruzione. Inoltre, un altro risultato di questo studio è che le sole informazioni nel dominio pubblico non sono di solito sufficienti per concludere se l'ipotesi di una *killer acquisition* sia verificata o meno. Qualunque ulteriore analisi deve necessariamente basarsi anche su informazioni non pubbliche (interne all'impresa).

Nella parte di "evaluation", lo studio esamina sia gli sforzi compiuti in passato dalla Commissione per affrontare potenziali *killer acquisitions*, che l'idoneità degli strumenti giuridici a disposizione della Commissione per perseguire le *killer acquisitions*. Questa seconda parte inizia con l'analisi di cinque operazioni di concentrazione notificate alla Commissione nel settore farmaceutico, per valutare *ex post* l'appropriatezza delle decisioni della Commissione in ciascun caso. L'analisi suggerisce che la Commissione in questi casi ha identificato correttamente i rischi di *killer acquisitions*, e si offre in un caso un suggerimento relativo alla definizione dei rimedi. A seguito, si analizza l'idoneità della normativa antitrust e di quella sul controllo delle concentrazioni per arginare il fenomeno delle *killer acquisitions*, simulando l'utilizzo dell'Art. 22 EUMR e degli Art. 101/102 TFUE in due ipotetici casi studio.

Le analisi svolte suggeriscono che l'Art. 22 EUMR (per le concentrazioni) e gli Art. 101/102 TFUE (per transazioni diverse dalle concentrazioni) sono strumenti adatti

(sebbene con dei limiti) ad affrontare le *killer acquisitions*. La creazione di un sistema di notifica potrebbe ulteriormente facilitare l'identificazione di transazioni potenzialmente dannose per lo sviluppo di progetti di ricerca.

Executive Summary

Negli ultimi anni, le autorità antitrust hanno mostrato una crescente preoccupazione riguardo a operazioni di concentrazione (i.e., fusioni e acquisizioni) che coinvolgono aziende altamente innovative in settori concentrati, per i loro possibili e sostanziali effetti negativi non solo sui prezzi, ma anche sul processo innovativo. Precedenti studi accademici hanno dimostrato che le fusioni possono incentivare o scoraggiare gli sforzi di ricerca e, di conseguenza, l'innovazione, a seconda di fattori come il livello di concorrenza nei mercati, il miglioramento in termini di efficienza produttiva derivante da tali operazioni ed i cambiamenti nell'appropriabilità dell'innovazione (Gilbert, 2022; Haucap & Stiebale, 2023).

Vi è inoltre una specifica preoccupazione per la "perdita di concorrenza potenziale", comunemente associata alla teoria del danno delle "killer acquisition". Questo concetto viene generalmente utilizzato per indicare l'acquisizione da parte di un'azienda di una società concorrente, spesso una *start-up*, al fine di prevenire la minaccia di una futura concorrenza sul mercato, o anche per sostituire le attività di un particolare concorrente che più si sovrappongono al *core-business* dell'azienda. Crawford et al. (2020) [82] sostengono che le acquisizioni possono anche scoraggiare la concorrenza all'interno del processo innovativo, dal momento che offrono l'opportunità di "acquistare anziché investire nello sviluppo di innovazioni rivali",[83] con il rischio di compromettere la dinamica concorrenziale ancor prima che gli sforzi di ricerca e sviluppo modellino un prodotto specifico.

Il settore farmaceutico è uno dei settori con i più alti livelli di investimento in ricerca e sviluppo, e l'innovazione svolge un ruolo fondamentale nel contribuire al progresso scientifico nel campo della sanità e alla prosperità economica (Bokhari, et al., 2021). Un risultato consistente, riportato in vari studi accademici, è che le operazioni di fusione e acquisizione nel settore farmaceutico portano a una riduzione sostanziale della spesa in ricerca e della produzione di brevetti delle aziende coinvolte in tali operazioni (Ornaghi, 2009a; Haucap, et al., 2019), nonchè a un significativo declino della produttività degli inventori delle aziende acquisite (Ornaghi & Cassi, 2023). Tuttavia, uno studio empirico sulle alleanze tra piccole aziende biotecnologiche e grandi aziende farmaceutiche, considerate come potenziali sostituti o complementi alle fusioni, offre una prospettiva più ottimistica, evidenziando una correlazione positiva tra l'esperienza di una grande azienda nello sviluppare studi clinici e la probabilità di successo per le piccole imprese (Grabowski & Kyle, 2008).

Le preoccupazioni riguardo agli eventuali effetti negativi delle operazioni di fusione sull'innovazione si sono intensificate dopo la pubblicazione del *paper* "Killer Acquisitions" di Cunningham et al. (2021). Questo studio dimostra che i progetti clinico-farmaceutici acquisiti hanno una minor probabilità di essere sviluppati quando si "sovrappongono" con (i.e. sono potenzialmente sostituibili a) al portafoglio di prodotti dell'impresa acquirente, in particolare quando il potere di mercato dell'acquirente è elevato a causa di un numero esiguo di prodotti concorrenti o di scadenze brevettuali non imminenti. Gli autori rilevano inoltre che è molto più probabile che queste operazioni di acquisizione vengano concluse per un valore appena al di sotto delle soglie rilevanti per la notifica

[82] "How tech rolls': Potential competition and 'reverse' killer acquisitions", Gregory Crawford, Tommaso Valletti, and Cristina Caffarra, VoxEU, 11 May 2020, https://cepr.org/voxeu/blogs-and-reviews/how-tech-rolls-potential-competition-and-reverse-killer-acquisitions.

[83] *Ibidem*, nostra traduzione.

alle autorità antitrust. Quest'ultimo risultato è corroborato dall'analisi di Wollmann (2019), che rileva che, dopo l'aumento della soglia di esenzione dalla pre-notifica delle operazioni di acquisizione e fusione negli Stati Uniti, l'industria farmaceutica è stata, nel periodo post-emendamento, tra i primi cinque settori per numero di fusioni orizzontali esentate. L'analisi di Cunningham et al. (2021) è anche in linea con la valutazione interna della Commissione Europea sulle operazioni che non hanno raggiunto le soglie di fatturato previste dal Regolamento UE sulle Concentrazioni (EU Merger Regulation, o EUMR). [84] Questa valutazione ha evidenziato che nel settore farmaceutico si sono verificate operazioni di fusione e acquisizione che hanno coinvolto progetti farmaceutici sovrapposti e che non hanno raggiunto le soglie di fatturato richieste per la notifica, ma per cui gli acquirenti si sono mostrati disposti a pagare un prezzo elevato per l'acquisizione di progetti innovativi con un basso fatturato.

Infine, i risultati di Cunningham et al. (2021) sono anche coerenti con quelli di uno studio su fusioni e acquisizioni nel settore farmaceutico commissionato dalla Commissione Europea e realizzato da Informa Pharma Consulting e Szücs (2020), che mostra come la probabilità di interruzione dello sviluppo di un progetto farmaceutico aumenti se questo si sovrappone, all'interno della stessa area medico-terapeutica, a un altro progetto dell'azienda acquirente. Contrariamente a quanto spesso affermato dall'industria, inoltre, lo studio non rileva un'accelerazione nei tempi di sviluppo dei farmaci a seguito di un'operazione di concentrazione.

A riprova del suo continuo impegno a preservare l'innovazione nel settore farmaceutico, la Commissione ha avviato nel 2022 un nuovo progetto – di cui questo studio presenta i risultati – per valutare la pervasività e le caratteristiche del fenomeno delle *killer acquisition*, concentrandosi su un ampio campione di transazioni (concentrazioni e altri tipi di operazioni) avvenute nel settore farmaceutico nel periodo 2014-2018.

Le specifiche tecniche del progetto definiscono le *killer acquisition* nel settore farmaceutico come transazioni che hanno come probabile obiettivo o effetto l'interruzione di progetti di ricerca e sviluppo di farmaci potenzialmente sostituibili, a danno della concorrenza futura e, in ultima analisi, dei consumatori.[85] Questa è la definizione del fenomeno adottata dal presente studio.

L'obiettivo dello studio è duplice. In primo luogo, questo intende fornire nuove evidenze sul fenomeno delle *killer acquisition* attraverso l'analisi di un ampio campione di transazioni avvenute nel periodo 2014-2018, al fine di determinare, col senno di poi, se queste operazioni abbiano probabilmente causato l'interruzione di progetti sovrapposti *e* abbiano alterato la concorrenza nel mercato ("fact-finding challenge"). A differenza della ricerca esistente, lo studio esamina *tutti* i tipi di transazioni: non solo fusioni e acquisizioni, ma anche, *inter alia*, acquisti di *asset*, accordi di licenza, e accordi di ricerca e sviluppo. Un'altra importante novità riguarda la metodologia utilizzata: diversamente dagli studi precedenti che hanno analizzato l'esistenza o la portata del fenomeno su basi teoriche o statistiche, lo studio mira a raccogliere evidenze fattuali per validare (o meno) la teoria del danno delle *killer acquisition*.

In secondo luogo, lo studio valuta anche: (i) le decisioni prese dalla Commissione in passato con l'obiettivo di analizzare possibili casi di *killer acquisition*; (ii) il quadro

[84] Commission Staff Working Document (2021), "Evaluation of procedural and jurisdictional aspects of EU merger control", SWD (2021) 66 final, 26 March.

[85] Specificazioni Tecniche del bando di concorso della Commissione Europea, *footnote* 2.

giuridico entro il quale opera la Commissione, considerando che le operazioni di *killer acquisition* possono avvenire anche al di sotto delle soglie di regolamentazione delle fusioni o non essere strutturate come operazioni di concentrazione ("evaluation challenge"). In particolare, la seconda parte di questo studio esamina le regole e le prassi attuali ai sensi del Regolamento UE sulle Concentrazioni (EUMR), nonché i meriti (e le problematiche) derivanti dall'applicazione degli Articoli 101 e 102 del Trattato sul Funzionamento dell'Unione Europea (TFUE) al fine di poter controllare le transazioni che non passano al vaglio del EUMR.

Fact-finding Challenge

Il primo capitolo di questo studio, la "fact-finding challenge", presenta l'analisi di un ampio campione di transazioni avvenute nel settore farmaceutico tra il 2014 e il 2018. L'analisi è stata condotta *ex post*, sulla base di dati disponibili pubblicamente, e, per questo motivo, ha incontrato diverse limitazioni (discusse in quanto segue). La *fact-finding challenge* mira a determinare, sulla base di evidenze fattuali, se e quali transazioni abbiano portato all'interruzione di progetti medico-farmaceutici identificati come potenziali sostituti e abbiano alterato la concorrenza nel mercato rilevante – tale analisi include casi in cui la sostituibilità si riferisce sia a progetti medico-farmaceutici entrambi in via di sviluppo, cosiddetti *pipeline-to-pipeline*, sia a un progetto in via di sviluppo e uno commercializzato nel mercato, cosiddetti *marketed-to-pipeline*.

Nell'analisi *fact-finding*, lo studio ha sviluppato una metodologia in quattro fasi che mira a identificare le fonti di dati pubblicamente disponibili e fornire strumenti per determinare se una data transazione abbia portato all'interruzione di progetti di ricerca e sviluppo di farmaci concorrenti, in linea con la teoria del danno delle *killer acquisition*:

- Identificazione delle cosiddette "sovrapposizioni strette". In linea con la prassi della Commissione e la letteratura esistente, lo studio utilizza l'indicazione terapeutica e il meccanismo d'azione per determinare se i progetti di ricerca e sviluppo di farmaci siano sostituti diretti. Questo tipo di sovrapposizione è definito come "sovrapposizione stretta" ("narrow overlap"), in contrasto con la "sovrapposizione ampia" ("broad overlap"), basata solo sull'indicazione terapeutica. Lo studio ha sviluppato, inoltre, *proxy* per identificare la potenziale sostituibilità tra progetti di ricerca e sviluppo di farmaci che possono presentare diverse indicazioni terapeutiche e/o meccanismi d'azione, a causa delle loro diverse fasi di sviluppo. In particolare, lo studio suggerisce che i cosiddetti termini MeSH (Medical Subject Headings) associati agli studi clinici nel registro di riferimento statunitense (ClinicalTrials.gov), il *database* pubblico più completo disponibile,[86] forniscono una struttura numerica e gerarchica in grado di chiarire la relazione (se presente) tra due indicazioni terapeutiche apparentemente diverse. Nel caso in cui invece i meccanismi d'azione di due farmaci non siano identici – come potrebbe accadere per trattamenti farmacologici per cui questi non sono ancora ben stabiliti – la potenziale sostituibilità può essere valutata facendo riferimento al numero di citazioni congiunte in articoli di riviste mediche specializzate, pubblicati e ricercabili *online* nella piattaforma PubMed Central® (PMC), un archivio pubblico gestito dalla National Library of Medicine degli Stati Uniti d'America.

[86] In un'analisi comparativa, abbiamo riscontrato che la stragrande maggioranza degli studi riportati nel Registro Europeo degli Studi Clinici ("EUCTR") è anche inclusa in ClinicalTrials.gov e che quest'ultimo registro offre una copertura più ampia e maggiori informazioni. Inoltre, ci affidiamo a EUCTR, per completezza, durante l'esecuzione dello *screening* manuale (i.e., la fase 4 della metodologia adottata dallo studio).

- Identificazione e classificazione delle interruzioni. Esistono numerosi modi in cui un progetto di ricerca e sviluppo di farmaci con "stretta sovrapposizione" può essere interrotto a seguito di un'acquisizione. In alcuni casi, ClinicalTrials.gov indica chiaramente che uno studio è stato interrotto o ritirato (e talvolta ne indica anche il motivo). In altri casi, non vi sono evidenze, se non l'inattività nel processo degli studi clinici, che potrebbero essere utilizzate per inferire se uno studio, o lo sviluppo ulteriore di un farmaco in una determinata indicazione terapeutica, sia stato dismesso. Infine, i progetti di ricerca e sviluppo di farmaci possono essere interrotti in un'indicazione terapeutica per essere riorientati verso un'altra indicazione terapeutica. In assenza di informazioni sull'interruzione o il ritiro, questo studio presume che un progetto sia stato interrotto quando si osservano almeno due anni di inattività nel suo sviluppo in una determinata indicazione terapeutica, e non vi è stato un ulteriore sviluppo successivo. Facendo affidamento alla struttura numerica dei termini MeSH, lo studio è in grado di individuare anche i casi in cui la sovrapposizione tra due progetti di ricerca venga eliminata a seguito di un riorientamento di uno dei due progetti verso una diversa indicazione terapeutica.[87] Le ragioni che hanno portato all'interruzione degli studi clinici (quando disponibili), il periodo di inattività osservato, la natura degli *sponsor* degli studi clinici (quali enti privati o pubblici) e l'evoluzione dell'indicazione terapeutica nel tempo per entrambi i farmaci in sovrapposizione stretta contribuiscono a filtrare, tra tutte le interruzioni osservate, quelle che sembrano non correlate alla transazione e apparentemente legate a motivi tecnici e clinici (come per esempio, una scarsa progettazione sperimentale, o una raccolta dati insufficiente). Le interruzioni che rimangono alla fine di questo processo di classificazione sono individuate come interruzioni *prima facie* rilevanti per una valutazione di *killer acquisition* (o, più semplicemente, interruzioni *prima facie* rilevanti).
- Algoritmo di *machine learning* (LASSO). Lo studio si avvale di un algoritmo di *machine learning*, (Least Absolute Shrinkage and Selection Operator, noto come "LASSO") con l'obiettivo di caratterizzare *ex ante* le transazioni che potrebbero meritare di ulteriori approfondimenti in un'ottica di valutazione di *killer acquisition*. L'analisi considera un set iniziale di caratteristiche osservabili, suggerite dalla letteratura e pre-selezionate dal gruppo di esperti farmaceutici coinvolti nello studio, che potrebbero indicare che le parti di una determinata transazione avessero l'incentivo o la capacità di eliminare la concorrenza in un mercato rilevante. Il modello LASSO include, *inter alia*, variabili che catturano l'intensità della concorrenza futura nel mercato. La metodologia LASSO viene quindi utilizzata per selezionare quali di queste caratteristiche iniziali potrebbero meglio contribuire a identificare i progetti di farmaci in sovrapposizione che probabilmente non sarebbero stati interrotti in assenza della transazione oggetto di analisi e la cui interruzione ha potenzialmente ridotto la concorrenza futura nei mercati valutati.[88] In questo modo, il metodo LASSO dovrebbe riuscire a distinguere, tra le transazioni che conducono a interruzioni *prima facie* rilevanti, quelle che sono più probabilmente coerenti con una

[87] Lo studio non tiene conto di ritardi inferiori a due anni; anche ritardi più lunghi, qualora fosse possibile osservare una qualsiasi forma di sviluppo prima della fine del periodo oggetto di studio, non sono oggetto di analisi. Tuttavia, non si può escludere che in questi casi ci sia un impatto negativo per la concorrenza dovuto al ritardo nello sviluppo di un farmaco.

[88] Il *training* del LASSO si basa su un campione limitato alle interruzioni *prima facie* rilevanti più probabilmente riconducibili a motivazioni strategiche o commerciali, a confronto con un gruppo di controllo composto da progetti di ricerca in cui non si riscontra alcuna interruzione dopo l'accordo, o la cui interruzione sembra più probabilmente legata a motivazioni tecniche e cliniche.

narrazione di *killer acquisition*. I passaggi analitici descritti fin qui fanno parte di un'analisi "su larga scala", poiché mirano a rilevare interruzioni potenzialmente anticoncorrenziali attraverso un'analisi automatizzata di un ampio numero di osservazioni, e sulla base di un set di regole predefinite.

- *Screening* manuale. Infine, lo studio conduce uno "*screening* manuale" delle interruzioni *prima facie* rilevanti che mostrano le caratteristiche validate dal modello LASSO ("LASSO-KA") e di un sottoinsieme delle (rimanenti) interruzioni *prima facie* rilevanti, per testare l'affidabilità dei risultati del modello. Lo *screening* manuale consiste, per un sottoinsieme di transazioni, in una verifica caso per caso e in un'attenta valutazione delle evidenze fattuali. L'interruzione di un progetto di ricerca e sviluppo di farmaci in sovrapposizione stretta, anche se causata da una transazione, è una condizione necessaria ma non sufficiente per concludere che l'acquisizione abbia causato (o probabilmente causerà) una riduzione della concorrenza e dell'innovazione. Nel nostro studio, la nozione di *killer acquisition* si riferisce a una teoria del danno in cui una transazione causa l'interruzione di un progetto di ricerca e sviluppo e comporta (o è probabile che comporti) un effetto negativo sulla concorrenza. In altre parole, la teoria del danno di *killer acquisition* che adottiamo esclude i casi in cui l'acquirente termina lo sviluppo di un farmaco senza, tuttavia, alterare le dinamiche competitive prevalenti nel mercato rilevante. Questo approccio richiede una piena comprensione del modello di sostituibilità tra i farmaci che vengono classificati come sovrapposti, della loro rilevanza clinica e del livello di concorrenza nel mercato rilevante, soprattutto quando la sovrapposizione nelle indicazioni terapeutiche non è perfetta e la potenziale sostituibilità deve essere stabilita con attenzione; inoltre, tale approccio richiede una valutazione degli incentivi commerciali e dei vincoli di finanziamento delle parti. L'obiettivo finale dello *screening* manuale è raccogliere evidenze che possano confermare (o al contrario, non confermare) una teoria del danno di *killer acquisition* sottostante le transazioni, tenendo conto il più possibile degli aspetti sopra menzionati e potendo far affidamento alle informazioni disponibili nel dominio pubblico. In dettaglio, lo *screening* manuale si basa su fonti di informazione e di dati più estese di quelle utilizzate per l'analisi su larga scala, inclusi i rapporti finanziari pubblicati dalle aziende farmaceutiche, e gli annunci aziendali e gli articoli sulla stampa specializzata che descrivono la transazione. Inoltre, lo *screening* manuale tiene conto della valutazione del *team* di esperti riguardo alla fattibilità tecnica e commerciale dei progetti di ricerca il cui sviluppo è stato interrotto, alla luce dei rapporti pubblici sulle attività di ricerca e sviluppo delle parti e dei loro concorrenti (disponibili su ClinicalTrials.gov o accessibili tramite PMC).

Pur basandosi su una metodologia complessa, la *fact-finding challenge* presenta le seguenti importanti limitazioni:

- Lo studio si concentra sulla concorrenza derivante dai prodotti in fase di sperimentazione clinica (*pipeline*) e, quindi, non consente di valutare del tutto l'impatto di una transazione sulla concorrenza nell'innovazione. Ad esempio, l'analisi su larga scala non copre né le sperimentazioni precliniche né le intenzioni future delle parti di perseguire una nuova indicazione terapeutica;
- Lo studio si basa su fonti pubbliche e non ha accesso a documenti o presentazioni interne delle aziende, che potrebbero aiutare a comprendere se una transazione sia stata in grado di modificare gli incentivi commerciali delle parti nel perseguire lo sviluppo di un farmaco. Inoltre, le informazioni disponibili pubblicamente spesso non consentono una chiara ricostruzione della concorrenza nel mercato rilevante, e dei vincoli esercitati da ciascun concorrente o da altre aziende.

- Nella valutazione degli accordi di licenza o di ricerca e sviluppo, è complesso identificare l'"oggetto" e il "perimetro" della transazione (rispettivamente, i farmaci e le indicazioni terapeutiche propriamente contrattati, e gli altri farmaci rilevanti, potenziali sostituti, interessati dall'accordo), e determinare la parte che beneficia dello scambio dei diritti. Di conseguenza, ciò implica che, per queste due tipologie di transazioni, lo studio potrebbe non catturare adeguatamente l'entità e la natura delle potenziali *killer acquisition*. Inoltre, nel caso degli accordi di ricerca e sviluppo, gli incentivi delle parti dipendono dall'allocazione dei diritti di *marketing* e distribuzione dei trattamenti medico-farmaceutici oggetto dell'innovazione congiunta: infatti, la teoria del danno di *killer acquisition* adottata in questo studio prevede che una transazione consenta a una parte di acquisire i diritti di controllo[89] su un progetto di ricerca e sviluppo in sovrapposizione con altri farmaci nel portafoglio della medesima parte. Tali dettagli sugli accordi di ricerca e sviluppo non sono pubblici, e non è quindi possibile comprendere se questi possano in effetti creare diritti esclusivi, anche nel caso in cui si proceda allo *screening* manuale;
- Lo studio adotta un approccio relativamente ampio nella valutazione della potenziale sostituibilità tra progetti di ricerca e sviluppo di farmaci, ma limitatamente alle sovrapposizioni strette; le sovrapposizioni ampie, e dunque le transazioni che portano una società ad avere il controllo di progetti medico-farmaceutici che condividono solo la stessa indicazione o classe terapeutica, esulano dall'ambito di questo studio – ulteriori ricerche potrebbero aiutare a chiarire in che misura questo tipo di sovrapposizioni potrebbero generare interruzioni rilevanti;
- Lo studio considera un periodo di inattività relativamente esteso come indicazione che un progetto clinico potrebbe essere stato interrotto. Tuttavia, questo criterio non si applica nel caso in cui si osservi un qualsiasi ulteriore sviluppo, come la registrazione di un nuovo studio clinico, anche dopo un lungo periodo di inattività. Di conseguenza, sebbene i ritardi nello sviluppo siano un aspetto molto rilevante per la concorrenza, questi non sono trattati nello studio;
- Lo studio considera gli interessi delle società capogruppo e delle filiali delle aziende direttamente coinvolte in una transazione, ma non prende in considerazione i casi in cui le partecipazioni di minoranza possono creare l'incentivo o la possibilita' di attuare una *killer acquisition*.

Nonostante queste limitazioni, lo studio rappresenta un contributo innovativo alla crescente letteratura che intende far luce sul fenomeno delle *killer acquisition*

[89] Lo studio intende i diritti di controllo come quelli sufficienti a fornire a un'entità la capacità giuridica - qualora ne abbia anche gli incentivi - di eliminare uno dei due progetti di ricerca e sviluppo sui farmaci che si sovrappongono e che, in assenza dell'accordo, sarebbero rivali, influenzando così potenzialmente la futura concorrenza nel mercato dei prodotti. Nelle acquisizioni e negli acquisti di *asset*, la natura delle transazioni implica un trasferimento di diritti di proprietà all'acquirente, di solito sufficiente per supporre che quest'ultimo possa disporre di entrambi i progetti di farmaci in sovrapposizione. Negli accordi di licenza, ciò che è rilevante è l'ambito della licenza: a questo proposito, oltre alle specifiche indicazioni terapeutiche oggetto dell'accordo, cerchiamo di individuare l'esclusività e di controllare l'ambito geografico della licenza, per rendere solida tale ipotesi. Negli accordi di ricerca e sviluppo, la possibilità che l'accordo modifichi la capacità e gli incentivi di una delle parti di interrompere uno dei due progetti di farmaci in sovrapposizione dipende dal modo in cui i diritti di commercializzazione e distribuzione per l'innovazione congiunta stabilita dall'accordo vengono assegnati ai *partner*, aspetto per cui, tuttavia, né il tipo di accordo stesso né le informazioni pubbliche ci aiutano a essere conclusivi.

Risultati della "fact-finding challenge"

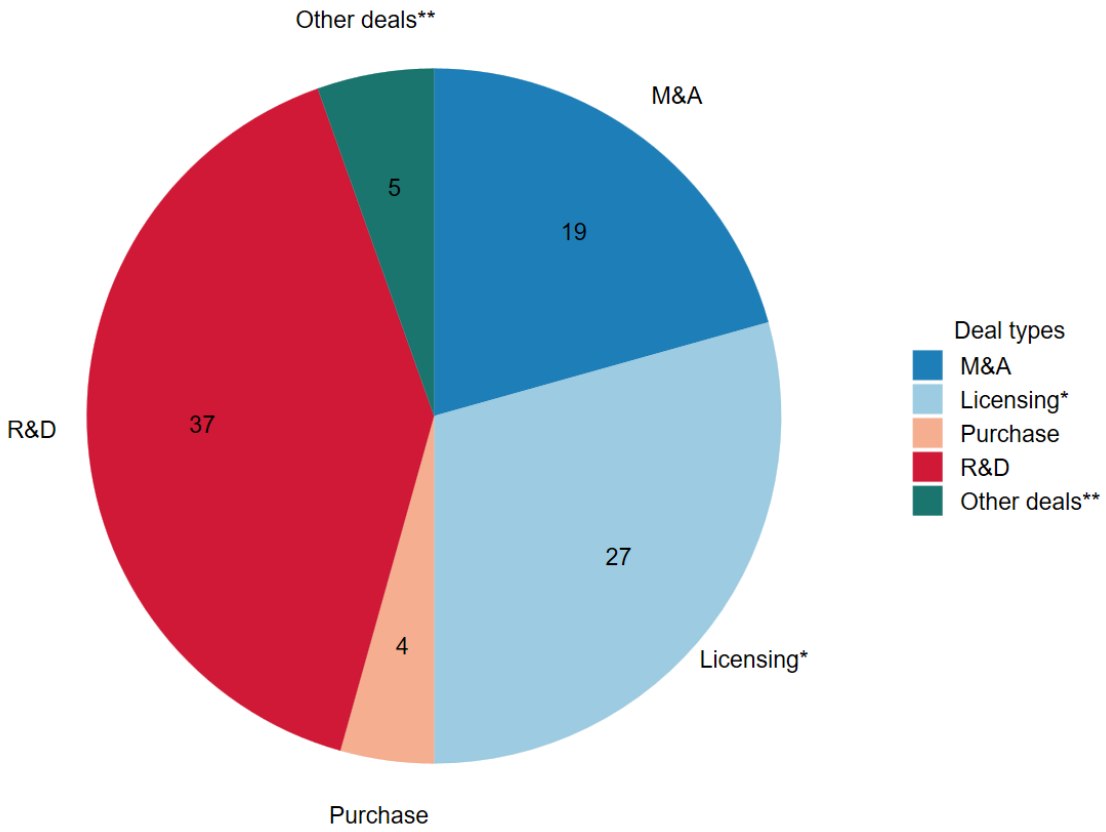
Lo studio ha identificato un totale di 6.315 transazioni nel settore farmaceutico nel periodo 2014-2018, e ne ha potute esaminare, avendone a disposizione informazioni riguardo l'oggetto, complessivamente 3.193.[90] Di queste, 240 transazioni hanno coinvolto l'acquisizione di progetti di ricerca e sviluppo di farmaci potenzialmente sostituibili, sulla base dell'individuazione di una sovrapposizione stretta (i.e., in termini di indicazione terapeutica e meccanismo d'azione). In un'imponente maggioranza di queste transazioni (183), almeno un farmaco in sovrapposizione stretta è stato interrotto dopo la transazione. Questo risultato notevole solleva la questione del motivo dell'interruzione e se questa possa essere coerente con una teoria del danno di *killer acquisition*. Lo studio rileva che per 92 transazioni (ossia il 38%) con una sovrapposizione stretta seguite dall'interruzione di almeno uno di questi progetti, tale interruzione appare *prima facie* rilevante per una possibile valutazione di *killer acquisition*.

Il grafico che segue mostra la distribuzione delle interruzioni *prima facie* rilevanti per tipologia transazione:[91]

[90] Le transazioni che hanno informato l'analisi sono quelle, incluse nel dataset iniziale, per le quali disponiamo di informazioni sufficienti per identificare i progetti di ricerca e sviluppo di farmaci delle parti interessate. Per un numero non trascurabile di transazioni, non è stato possibile identificare l'oggetto o l'obiettivo dell'accordo. Il motivo principale è che una delle aziende coinvolte non era presente nel nostro *database* di studi clinici; ciò si verifica tipicamente quando le aziende non hanno progetti di ricerca e sviluppo nel loro portafoglio (ad esempio perché producono o commercializzano piattaforme, tecnologie e dispositivi piuttosto che occuparsi dello sviluppo di farmaci, oppure i loro progetti di ricerca e sviluppo sui farmaci sono nella fase preclinica, e dunque non hanno ancora registrato studi clinici).

[91] L'analisi su larga scala è stata progettata ed eseguita separatamente per tipo di transazione, per tener conto delle specificità di ciascun tipo di transazione.

Distribuzione delle interruzioni *prima facie* rilevanti per tipo di transazione



*Fonte: analisi Lear. Note: *Tra gli accordi di licenza con un'interruzione prima facie rilevante, 12 sono "esclusivi", identificati utilizzando strumenti di ricerca testuale nella descrizione della transazione disponibile nel nostro dataset. **Per il gruppo "Altre transazioni" ("Other deals"), le interruzioni prima facie sono identificate nelle seguenti tipologie di* operazioni*: Equity investment (2 operazioni), Joint venture (1 operazione), Joint venture R&D (1 operazione), Marketing agreement (1 operazione); nessuna interruzione di sovrapposizioni strette si trova degli accordi di Partnership e Cross-Licensing.*

Nella nostra analisi, le interruzioni *prima facie* rilevanti emergono in circa il 40% delle transazioni che coinvolgono progetti di ricerca e sviluppo di farmaci identificati in sovrapposizione. In dettaglio, queste interruzioni rappresentano il 54% delle transazioni con sovrapposizioni strette tra le fusioni e acquisizioni (M&A), il 27% negli accordi di licenza (*licensing*), il 33% negli acquisti di *asset* (*purchase*) e il 43% negli accordi di ricerca e sviluppo (R&D). Inoltre, sono anche distribuite tra gli investimenti azionari (*equity investment*, 2 transazioni), *joint venture* (JV), *joint venture* R&D, e accordi di *marketing* (una transazione per ciascuno di questi tipi di accordi), mentre negli accordi di *partnership* e *cross-licensing* non è stata rilevata alcuna interruzione *prima facie* rilevante. Questi risultati suggeriscono che un'ampia proporzione di accordi che coinvolgono progetti di ricerca e sviluppo sovrapposti, in particolare tra le fusioni e acquisizioni, così come tra gli accordi di licenza e ricerca e sviluppo, sono *prima facie* rilevanti per una valutazione di *killer acquisition*.

Per individuare le transazioni in cui potrebbe essere presente o anticipata una teoria del danno di *killer acquisition*, sulla base dei dati rilevanti raccolti per i progetti di farmaci in stretta sovrapposizione, lo studio ha esplorato il metodo di analisi LASSO, seguito da

uno *screening* manuale volto a convalidare i risultati ottenuti con l'analisi automatizzata. Il LASSO, applicato alle operazioni di fusione e acquisizione, agli accordi di licenza e agli accordi di ricerca e sviluppo, ha selezionato 53 casi di interruzioni *prima facie* rilevanti come "LASSO-*killer acquisition*" (o "LASSO-KA"), distribuite su 19 diverse transazioni.

Lo *screening* manuale è stato poi condotto per: tutte le interruzioni *prima facie* rilevanti identificate tra le fusioni e acquisizioni (incluse le 6 LASSO-KA) e tra gli accordi licenza esclusivi (incluse le 9 LASSO-KA);[92] il 5% degli accordi di ricerca e sviluppo (22% in termini di transazioni, incluse le 4 LASSO-KA);[93] e tutte le interruzioni *prima facie* rilevanti identificate negli altri tipi di accordo (acquisti di *asset* e altri tipi di transazioni quali *partnership*, accordi di JV e di JV R&D, investimenti in azioni, accordi di *marketing* e *cross-licensing*, per cui l'approccio LASSO non poteva essere applicato a causa delle dimensioni ridotte del campione.

Lo *screening* manuale ha evidenziato che le interruzioni *prima facie* rilevanti sono di diversa natura, anche all'interno di ciascuna categoria di transazione e quando presentano simili "caratteristiche LASSO" (ovvero, le condizioni definite dalla soluzione del modello LASSO, sulla base delle quali sono identificate le LASSO-KA). Questo risultato dimostra che tali caratteristiche non sono sufficienti per comprendere le specificità di questi accordi. In particolare, nonostante la presenza delle caratteristiche LASSO, le evidenze disponibili (sulla base delle informazioni pubblicamente accessibili) non sono conclusive sulla narrativa di *killer acquisition* (se questa sia applicabile o meno), [94] esponendo le relative transazioni allo stesso grado di incertezza di quelle che che portano a interruzioni *prima facie* rilevanti ma che non presentano le stesse caratteristiche. Questo ostacola la capacità della soluzione LASSO di assistere le autorità della concorrenza nell'identificare *ex ante* le transazioni che meriterebbero ulteriori approfondimenti in un'ottica di valutazione *killer acquisition*.

Inoltre, senza accesso ai documenti interni delle aziende, è difficile trarre conclusioni sul grado in cui le transazioni abbiano alterato gli incentivi commerciali delle parti, anche ricorrendo allo *screening* manuale. Le evidenze pubblicamente disponibili generalmente non forniscono una base solida per determinare se le interruzioni *prima facie* rilevanti riflettono pienamente una teoria del danno di *killer acquisition*, impedendo di giungere a una valutazione conclusiva. Questo risultato vale in modo ancora più significativo per alcuni tipi di transazioni, in particolare gli accordi di ricerca e sviluppo e tutti gli altri accordi residuali ("Other deals").[95]

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[92] Un accordo di licenza non esclusivo difficilmente fornirebbe la capacità e gli incentivi per interrompere un progetto medico-farmaceutico. Pertanto, lo *screening* manuale si è concentrato sugli accordi di licenza esclusiva. Le transazioni di licenza esclusiva vengono identificate applicando strumenti di ricerca testuale alla descrizione degli accordi, disponibile nel nostro *database*.

[93] Le informazioni pubblicamente disponibili sono in genere poco informative per gli accordi di ricerca e sviluppo, per i quali non è noto neppure lo scambio di diritti relativo ai farmaci oggetto dell'accordo tra le parti. Tali limiti condizionano notevolmente l'analisi e i risultati, scoraggiando uno *screening* più esteso.

[94] Poiché i modelli LASSO sono stati stimati separatamente per ciascuna di categoria di transazione, questi hanno individuato soluzioni diverse (e quindi caratteristiche diverse) a seconda del tipo di transazione. Nella nostra prima stima del modello nel campione di accordi di fusione e acquisizione (M&A), il LASSO seleziona un solo regressore predittivo per una LASSO-KA, ovvero l'interazione tra: una delle molecole in sovrapposizione in Fase 4 (commercializzata), una delle molecole in sovrapposizione in Fase 2, e un numero massimo di concorrenti sul mercato pari a tre.

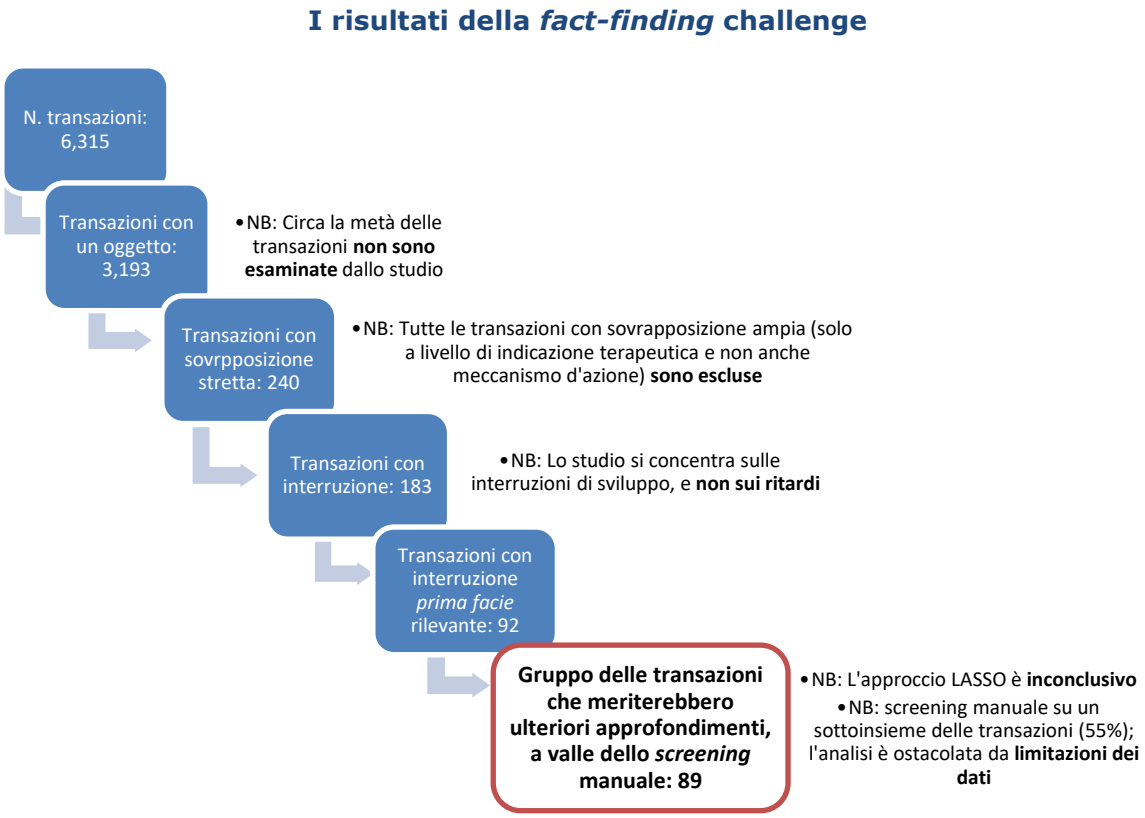
[95] Si veda la nota a piè di pagina 12.

Come discusso, la nozione di teoria del danno di *killer acquisition* adottata da questo studio implica una transazione che consente a una delle due parti di ottenere i diritti di controllo su un progetto di ricerca e sviluppo di un farmaco concorrente, provocando l'interruzione di uno dei prodotti risultati in sovrapposizione stretta, in una data indicazione terapeutica o a livello di molecola; al contempo, rileva che, attraverso queste dinamiche, sia probabile che si osservi una riduzione della concorrenza nel mercato e nel processo innovativo. Per la maggior parte delle interruzioni *prima facie* rilevanti sottoposte a *screening* manuale, le informazioni pubblicamente disponibili non hanno fornito prove sufficienti per confermare: (i) il grado di sostituibilità tra i progetti di farmaci sovrapposti (o prossimità della pressione concorrenziale, elemento fondamentale per la teoria del danno di *killer acquisition*), e, soprattutto, che i farmaci siano in grado di trattare in modo potenzialmente sostituibile la stessa malattia, piuttosto che essere adattati a diversi segmenti di pazienti, trattamenti paralleli o sequenziali, o terapie combinate; (ii) che l'interruzione manchi di una valida giustificazione clinica o tecnica; o possa essere giustificata da una valutazione commerciale che sarebbe emersa anche in assenza della transazione; (iii) che la concorrenza nel mercato rilevante sia stata influenzata negativamente dall'avvenuta interruzione del progetto (per questo esercizio, è necessaria anche una valutazione più approfondita del grado di sostituibilità con i farmaci sovrapposti delle parti per i farmaci 'concorrenti'). Inoltre, per gli accordi di ricerca e sviluppo, non è possibile trarre conclusioni generali a causa dell'opacità riguardante i diritti legali scambiati tra le parti.

Allo stesso tempo, emergono solo pochi casi in cui le evidenze pubblicamente disponibili suggeriscono più chiaramente e con un ragionevole grado di fiducia di poter escludere l'ipotesi di *killer acquisition*. Questi sono tendenzialmente casi in cui troviamo che, in contrasto con le conclusioni dell'analisi su larga scala, il farmaco non è stato interrotto ma è bensì ancora in fase di sviluppo (per esempio, ciò si verifica in due transazioni nel gruppo M&A e una nel gruppo degli accordi di licenza; rispettivamente, cinque e tre in termini di interruzioni per coppia di farmaci in sovrapposizione).

In sintesi, lo studio mostra che una proporzione significativa (89 su 240, ovvero il 37%) delle transazioni in cui si osserva una sovrapposizione stretta è stata seguita da un'interruzione che meriterebbe ulteriori approfondimenti nell'ottica di una valutazione di *killer acquisition*, nel senso che, sulla base delle informazioni pubblicamente disponibili, non emerge alcun motivo tecnico o di sicurezza chiaramente identificabile a spiegare l'interruzione. Lo studio rileva dunque che le fonti di informazione pubblicamente disponibili non sono generalmente sufficienti per valutare in modo conclusivo la sussistenza (o l'inapplicabilità) di una teoria del danno di *killer acquisition*. Qualsiasi ulteriore approfondimento volto a raggiungere conclusioni da questo punto di vista dovrebbe fare in primo luogo affidamento su informazioni privilegiate (interne alle aziende).

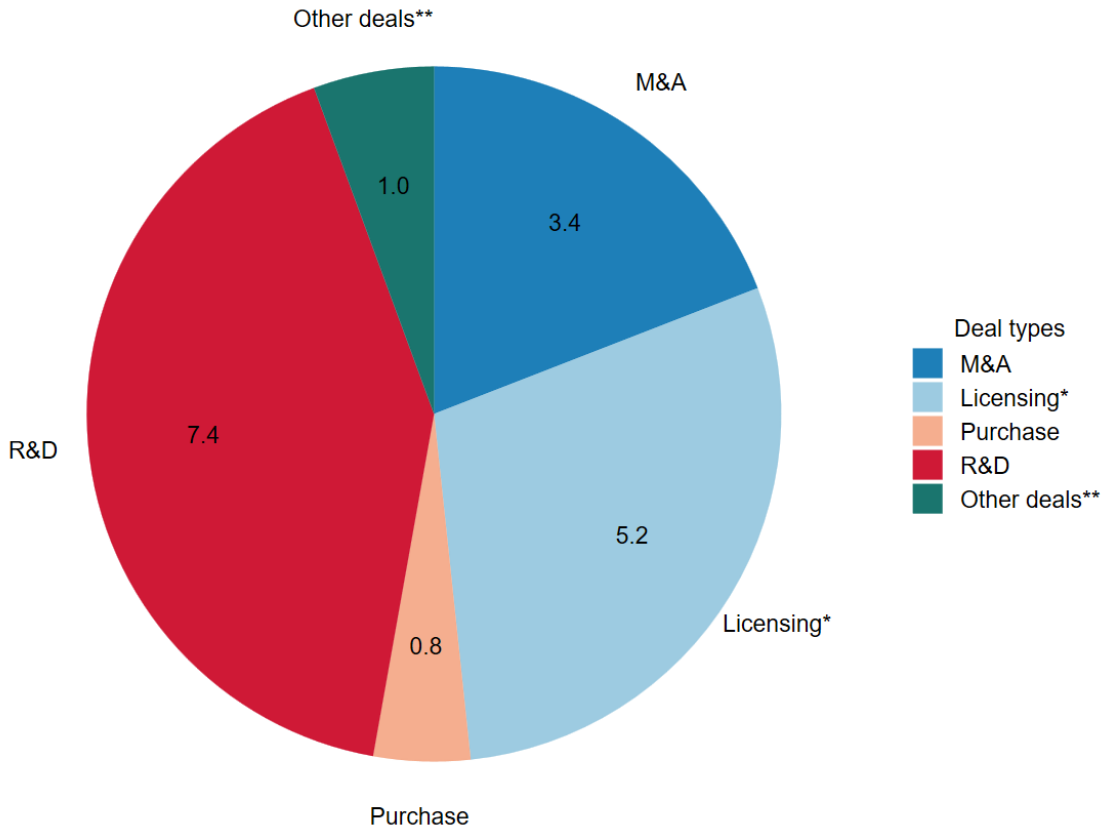
La figura sottostante riassume i principali risultati della *fact-finding challenge*:



Fonte: Lear

Per illustrare meglio l'entità del fenomeno delle transazioni che meriterebbero ulteriori approfondimenti, la figura seguente mostra il loro numero medio annuo per tipologia di transazione nel periodo analizzato:

Numero medio annuo di transazioni che meriterebbero ulteriori approfondimenti (2014-2018)



*Fonte: analisi Lear. Note: *Nel periodo 2014-2018, tra gli accordi di licenza che meriterebbero ulteriori approfondimenti, 12 sono "esclusivi", identificati utilizzando strumenti di ricerca testuale nella descrizione della transazione disponibile nel nostro dataset. **Per il gruppo "Altre transazioni" ("Other deals"), nel periodo 2014-2018, le transazioni che meriterebbero ulteriori approfondimenti sono identificate nelle seguenti tipologie di* operazioni*: Equity investment (2 operazioni), Joint venture (1 operazione), Joint venture R&D (1 operazione), Marketing agreement (1 operazione)*

Per il periodo 2014-2018, lo studio rileva una media di 3,4 accordi M&A che meriterebbero ulteriori approfondimenti all'anno, 5,2 accordi di licenza (*licensing*), 0,8 acquisti di *asset* (*purchase*), 7,4 accordi di ricerca e sviluppo (R&D) e 1 operazione nella categoria residuale.

I risultati sono ulteriormente supportati dall'analisi delle caratteristiche delle transazioni che meriterebbero ulteriori approfondimenti per gli accordi M&A, per le quali si evidenziano caratteristiche distintive rispetto alle transazioni, per lo stesso tipo di accordi, non seguite da interruzioni o seguite interruzioni apparentemente non problematiche (o benigne). In particolare, le interruzioni che richiedono ulteriori approfondimenti e le relative transazioni, spesso coinvolgono farmaci in sovrapposizione in fasi avanzate di sviluppo, il che suggerisce una potenziale significativa minaccia competitiva che potrebbe motivare una strategia di *killer acquisition*. Inoltre, questi casi tendono a verificarsi in mercati con un'alta concentrazione, dove si identificano pochi concorrenti, il che motiva ulteriormente il perseguimento di una tale strategia.

La *fact-finding challenge* suggerisce che il fenomeno delle *killer acquisition* dovrebbe continuare a sollevare preoccupazioni per le autorità della concorrenza. Sebbene confrontare i risultati quantitativi dello studio con quelli di Cunningham et al. (2021) richieda la formulazione di ipotesi e conseguenti limitazioni, le conclusioni complessive sono allineate. Lo studio di Cunningham et al. (2021) suggerisce, infatti, "cautela nell'interpretare le acquisizioni di tecnologie nascenti esclusivamente come sforzi degli *incumbent* per integrare e promuovere l'innovazione imprenditoriale".[96]

Fact-finding challenge: le raccomandazioni di *policy*

In conclusione, la *fact-finding challenge* sottolinea le crescenti preoccupazioni delle autorità per la concorrenza riguardo all'oggetto e agli effetti anticoncorrenziali delle acquisizioni che coinvolgono progetti di ricerca e sviluppo di farmaci potenzialmente sostituibili. Questo studio evidenzia l'importanza di una valutazione caso per caso, in luogo di analisi su larga scala o probabilistiche, per comprendere gli incentivi delle parti coinvolte e l'impatto di una transazione sulle dinamiche competitive. L'accesso a informazioni specifiche sulle transazioni è cruciale per comprendere fattori come la sostituibilità dei farmaci, le loro prospettive di realizzazione tecnica e commerciale e la minaccia competitiva rappresentata da altri farmaci sul mercato. Le informazioni disponibili pubblicamente possono aiutare nel vaglio preliminare di tali transazioni, specialmente per le fusioni e acquisizioni. Tuttavia, questi dati non sono sufficienti per trarre conclusioni definitive sulle implicazioni per la concorrenza futura nel mercato.

Alla luce dell'analisi, una raccomandazione per la Commissione è mantenere il suo approccio proattivo nel monitorare le concentrazioni nel settore farmaceutico, come dimostrato dalla sua attività passata nell'identificare tempestivamente potenziali concentrazioni per l'esame *ex ante* ai sensi dell'EUMR, utilizzando i rinvii di cui all'Articolo 22, come descritto più dettagliatamente di seguito. Tuttavia, analizzare gli accordi strutturati diversamente dalle concentrazioni, come gli accordi di ricerca e sviluppo e altre collaborazioni, presenta una maggiore complessità. Le informazioni pubblicamente disponibili spesso non sono sufficienti per chiarire come questi accordi siano in grado di disporre delle innovazioni oggetto della transazione e, di conseguenza, come possano influenzare gli incentivi commerciali delle parti riguardo allo sviluppo di progetti medico-farmaceutici potenzialmente sostituibili.

Nonostante le avvertenze delineate nella nostra analisi, lo studio evidenzia che il fenomeno delle *killer acquisition* può influenzare gli accordi di ricerca e sviluppo tanto quanto le fusioni e acquisizioni. Circa la metà delle transazioni con sovrapposizioni strette, per entrambi i tipi di accordi, è seguita da interruzioni dei progetti di ricerca che richiedono ulteriori approfondimenti. Pertanto, è essenziale condurre ulteriori ricerche per classificare più precisamente queste interruzioni e le relative transazioni, comprenderne le implicazioni e valutarne la suscettibilità alla narrativa di *killer acquisition*.

Evaluation challenge

Il secondo capitolo di questo studio si propone di valutare l'applicazione e, se del caso, di identificare i limiti dell'attuale EUMR, nonché di valutare i meriti dell'applicazione delle norme antitrust.

[96] Cunningham et al. (2021), p. 696, nostra traduzione.

La valutazione si basa su due pilastri. Innanzitutto, viene condotta un'analisi ex post delle valutazioni effettuate dalla Commissione per cinque concentrazioni notificate. Successivamente, viene esaminato il quadro giuridico generale in cui opera la Commissione e si simulano le applicazioni dell'articolo 22 EUMR e degli articoli 101 e 102 TFUE in due ipotetici casi studio. Entrambi gli aspetti dello studio si basano su una ricerca documentale approfondita di informazioni disponibili nel dominio pubblico. Per quanto riguarda la valutazione del quadro giuridico, ci si è basati sulla letteratura giuridica ed economica, con particolare attenzione ai precedenti legali (casi precedentemente investigati dalla Commissione) e alle decisioni dei tribunali.

È opportuno sottolineare che dal momento della stesura di questo studio (maggio 2024), la Corte di giustizia europea si è pronunciata sui ricorsi giurisdizionali di Illumina e GRAIL nelle cause C-611/22 P e C-625/22 P. Nella sua sentenza, la Corte di giustizia ha chiarito che uno stato membro deve avere competenza in base alle proprie norme nazionali sul controllo delle concentrazioni, o non avere norme sul controllo delle concentrazioni, per poter sottoporre una concentrazione all'esame della Commissione ai sensi dell'articolo 22 dell'EUMR.[97] In seguito a questa sentenza, la Commissione si è quindi allontanata dal suo approccio rivisto all'articolo 22, che consisteva nell'incoraggiare gli stati membri a sottoporgli alcune transazioni sulle quali non avevano competenza, ma che potevano incidere sul commercio e sulla concorrenza all'interno dell'UE. In futuro, e in linea con le conclusioni della Corte, la Commissione ha indicato che accetterà solo rinvii da parte di stati membri che sono essi stessi competenti a esaminare la concentrazione in questione[98] o che non hanno un regime nazionale di controllo delle concentrazioni (come il Lussemburgo) (per ulteriori dettagli si veda la sezione II.2.3). Fatte salve queste limitazioni, l'articolo 22 dell'EUMR rimane un valido strumento di applicazione per la Commissione, per esaminare concentrazioni che sembrano suscitare problemi di concorrenza nonostante non rientrino nelle soglie dell'EUMR.

Per quanto riguarda la valutazione delle singole transazioni, abbiamo utilizzato le seguenti fonti di informazione:

- Il database AdisInsight di Springer Nature sui farmaci in sviluppo commerciale in tutto il mondo;[99]
- ClinicalTrials.gov, un registro completo di studi clinici in tutto il mondo;[100]
- Risorse online per medici professionisti, compresi articoli di riviste sui risultati degli studi clinici e tendenze/sfide della ricerca e sviluppo accessibili gratuitamente

[97] Sentenza del 3 settembre 2024, Illumina, Inc. v Commissione Europea, Casi C-611/22 P e C-625/22 P, EU:C:2024:677.

[98] Ciò può includere le circostanze in cui una transazione soddisfa le soglie di controllo delle concentrazioni stabilite dalla legislazione nazionale, nonché i casi in cui le autorità nazionali garanti della concorrenza esercitano il loro potere, sulla base della legislazione nazionale, di "richiamare" (o "*call-in*") una transazione che suscita preoccupazioni in materia di concorrenza senza soddisfare le soglie nazionali applicabili (al momento della stesura del presente documento, otto Stati membri dell'UE - Danimarca, Ungheria, Irlanda, Italia, Lettonia, Lituania, Slovenia e Svezia - e due Stati membri dell'EFTA - Norvegia e Islanda - hanno previsto tali poteri di "richiamo" nelle loro legislazioni nazionali). Gli suddetti stati membri dell'UE sono competenti ad avviare le richieste di rinvio ai sensi dell'articolo 22, mentre gli Stati membri dell'EFTA non possono avviare una richiesta di rinvio, ma possono aderirvi.

[99] Una descrizione completa di questo database è fornita nella sezione I.1.2 di questo Rapporto

[100] Una descrizione completa di questo registro è fornita nella sezione I.1.3 di questo Rapporto.

tramite il database PubMed,[101] linee guida di trattamento di varie associazioni mediche (ad esempio ESMO) in vigore (e spesso modificate) nel periodo coperto dallo studio e informazioni pubblicate dall'EMA e dall'FDA sui loro siti web;
- Dichiarazioni rese dalle parti della transazione (ad esempio, nei loro comunicati stampa, relazioni annuali, depositi SEC, pipeline pubblicate, interviste alla direzione e simili), che sono state raccolte dai siti web delle parti e da altri archivi online; e
- Notizie e analisi di specialisti del settore farmaceutico (ad esempio Scrip[102] e Fierce Pharma[103]), nonché pubblicazioni online di notizie più generali orientate al business.
- Dove queste fonti pubbliche non fossero sufficientemente chiare, ci si è basati sulle conoscenze e sull'esperienza degli esperti del settore farmaceutico del Team per valutare, ad esempio, le possibilità di concorrenza tra diverse molecole, i risultati tecnici degli studi e le loro implicazioni commerciali, le prospettive di successo e i vari incentivi che potrebbero aver influenzato le decisioni strategiche delle aziende.

Evaluation challenge: i risultati

Il capitolo di evaluation challenge inizia esaminando il lavoro condotto dalla Commissione relativo alla valutazione delle transazioni avvenute nel settore farmaceutico che hanno visto coinvolti progetti di ricerca e sviluppo tra farmaci identificati come sostituibili. Questo studio include una valutazione ex post di cinque acquisizioni selezionate che sono state notificate alla Commissione e da questa autorizzate (a volte con rimedi).[104] Questi casi rappresentano, tra quelli esaminati nel periodo rilevante di questo studio,[105] quelli che coinvolgono progetti di ricerca e sviluppo di farmaci per uso umano (a differenza della R&S per dispositivi medici) e sovrapposizioni tra farmaci già nel mercato con molecole in fase di sviluppo (*market-to-pipeline*) ed esclusivamente nella fase di sviluppo (*pipeline-to-pipeline*). Tra questi casi ve ne è uno che è stato evidenziato nell'analisi di fact-finding come meritevole di ulteriore approfondimento a causa di una specifica sovrapposizione tra le molecole delle parti, che però non è stata ritenuta preoccupante nella valutazione della Commissione, in quanto quest'ultima ha avuto accesso ad informazioni non pubbliche che hanno consentito di escludere preoccupazioni concorrenziali.

La valutazione ex post mira a valutare se le acquisizioni sono state seguite da una interruzione dei progetti di ricerca e sviluppo tra molecole identificate come sostituibili a danno della concorrenza e dei consumatori. Questo include una valutazione dei rimedi

[101] PubMed (https://pubmed.ncbi.nlm.nih.gov) è un database consultabile di citazioni e abstract della letteratura di ricerca medica, gestito dalla National Library of Medicine degli Stati Uniti, che fornisce collegamenti ad altri siti web che contengono il materiale completo e pertinente.

[102] Scrip (https://scrip.citeline.com) è una fonte a pagamento di notizie e analisi farmaceutiche commerciali globali che faceva parte di Informa PLC per la maggior parte del periodo considerato da questo studio e, nel 2022, è stata ceduta e fusa con Norstella.

[103] Fierce Pharma (https://fiercepharma.com) è un servizio gratuito di notizie giornaliere (supportato dagli inserzionisti) che fornisce una copertura generale delle aziende farmaceutiche e degli sviluppi in tutto il mondo, di proprietà e gestito da Questex, LLC.

[104] M.8401 J&J/Actelion; M.7275 Novartis/GlaxoSmithKline Oncology Business; M.7872 Novartis/GSK (Ofatumumab Autoimmune Indications); M.9294 BMS/Celgene; M.9461 AbbVvie/ Allergan.

[105] Sebbene il periodo considerato nell'analisi di fact-finding vada dal 2014 al 2018, abbiamo preso in considerazione casi notificati alla Commissione anche nel 2019, perché in tale anno sono stati notificati due casi molto rilevanti per la valutazione ex-post (BMS/Celgene e AbbVie/Allergan).

e di come le molecole in fare di sviluppo si sono evolute dopo l'implementazione di tali rimedi.

Lo studio mostra che la Commissione ha generalmente identificato correttamente possibili *killer acquistions*. Sebbene, come indicato in precedenza, in uno dei casi esaminati l'analisi basata sulle prove disponibili al pubblico suggerisca una potenziale area di preoccupazione che avrebbe potuto meritare un ulteriore esame, gli autori dello studio sono consapevoli che la Commissione ha avuto accesso a dati confidenziali che avrebbero portato ad escludere ogni possibile preoccupazione. Dei cinque casi valutati in questo studio, due sono stati autorizzati dalla Commissione senza l'imposizione di rimedi e tre sono stati autorizzati con rimedi. La valutazione ex-post condotta dal Team ha rivelato che in tutti e cinque i casi almeno una delle molecole in sovrapposizione al momento dell'accordo è stata successivamente interrotta nella relativa indicazione terapeutica. Ciò non significa che l'intervento della Commissione non sia stato adeguato: infatti, la nostra valutazione ha rafforzato l'azione della Commissione (in particolare, la necessità di introdurre rimedi in tre casi e l'opportunità di autorizzare gli altri due senza rimedi). Notiamo che il semplice fatto che una molecola dismessa sia stata interrotta non significa che i rimedi fossero mal concepiti, in quanto può semplicemente riflettere il fatto che il successo dello sviluppo di farmaci è per sua natura incerto. Nei casi esaminati, non è stato possibile escludere che le pipeline cedute siano state interrotte per ragioni tecniche non legate ai rimedi, ma in un caso, J&J/Actelion, è stato anche suggerito che con misure più stringenti la molecola in questione avrebbe avuto maggiori probabilità di raggiungere il mercato. In questo caso, si ritiene che i rimedi avrebbero potuto essere concepiti meglio. In particolare, sembra che i rimedi non abbiano impedito l'interruzione di una molecola a seguito di azioni di terzi (poiché il rimedio si basava in parte sulla partecipazione attiva di un partner che aveva deciso di porre fine alla collaborazione).

Le *killer acquisitions*, tuttavia, potrebbero cadere al di sotto delle soglie di concentrazione o potrebbero non essere strutturate come concentrazioni. Le interruzioni *prima facie* rilevanti da noi rilevate – che sono possibili candidati per una valutazione dell'ipotesi di killer acquisition – coinvolgono anche tipi di accordi diversi da M&A.

Le autorità di regolamentazione della concorrenza in tutto il mondo hanno faticato a individuare mezzi sistematici per affrontare le acquisizioni di innovatori competitivamente importanti ma relativamente piccoli nei settori in rapida evoluzione senza adottare riforme dei loro programmi di controllo delle concentrazioni che probabilmente disturberanno un equilibrio costruttivo (riflesso nei loro livelli di notifica generali) tra gli oneri della notifica e i benefici della revisione ex ante. Nelle situazioni in cui uno o più stati membri hanno competenza di esaminare un'operazione, anche potenzialmente a seguito dell'esercizio dei poteri di *call-in* (o in assenza di un proprio regime di controllo delle concentrazioni), il meccanismo di rinvio previsto dall'articolo 22 EUMR può effettivamente fornire una base per facilitare l'esame di questo tipo di operazioni da parte della Commissione. L'applicazione dell'articolo 22 da parte della Commissione in alcuni casi conferma che si tratta di uno strumento che può contribuire a colmare il *gap* nell'applicazione della legge che è stato identificato nei settori altamente innovativi con imprese di piccole dimensioni ma competitivamente significative (come mostrato in J&J/TachoSil). Oltre ai limiti del suo campo di applicazione, chiariti dalla Corte di giustizia nelle cause C-611/22 P e C-625/22 P, un'ulteriore potenziale limite dell'Articolo 22 è che, pur fornendo un mezzo per affermare la giurisdizione sulle transazioni che non attivano le normali soglie di preavviso, non garantisce che le transazioni problematiche vengano portate all'attenzione della Commissione o degli stati

membri in primo luogo.[106] Sappiamo che la Commissione monitora attivamente le transazioni farmaceutiche per identificare casi candidati per l'applicazione dell'Articolo 22.[107] La procedura di monitoraggio è sviluppata lungo le stesse linee della metodologia a quattro fasi sviluppata nella *fact-finding challenge* ed è già piuttosto esaustiva. Tuttavia, potrebbe essere possibile immaginare un registro di accordi e sviluppi post-acquisizione per fornire una capacità ancora maggiore di identificare accordi rilevanti ex ante, oltre a fornire un avviso delle interruzioni pianificate. Un tale registro potrebbe essere applicabile alle aziende di dimensioni sufficienti da garantire un nesso con l'UE. Tuttavia, una valutazione costi/benefici di questa misura da parte della Commissione sarebbe appropriata.

Questo capitolo suggerisce anche che gli articoli 101 e 102 del TFUE sono strumenti preziosi per affrontare le *killer acquisitions* che non sono strutturate come concentrazioni. Partendo dai fatti di due accordi che effettivamente si sono verificati e che meriterebbero ulteriori approfondimenti secondo la *fact-finding challenge*, abbiamo sviluppato due casi studio ipotetici che ci hanno permesso di condurre valutazioni ai sensi dell'Articolo 22 EUMR e degli Articoli 101 e 102 del TFUE. In particolare, uno dei casi studio si focalizza su un caso di concentrazione al di sotto della soglia di indagine e include la valutazione ai sensi dell'articolo 22 EUMR adattata ai fatti specifici e ipotetici assunti in quel caso. L'altro caso studio considerato ha consentito di formulare due scenari distinti: uno in cui la transazione può essere vista come una concentrazione - e quindi viene effettuata la valutazione dell'Articolo 22 EUMR - e uno in cui può essere vista come un accordo di licenza - e quindi vengono condotte le valutazioni degli Articoli 101 e 102 del TFUE.

Evaluation challenge: raccomandazioni di *policy*

In conclusione, l'evaluation challenge ha evidenziato che, quando le *killer acquisitions* sono strutturate come concentrazioni e coinvolgono aziende di dimensioni sufficienti da attivare le soglie di notifica dell'EUMR, la valutazione della Commissione è tipicamente in grado di prevenire gli effetti anticoncorrenziali di tali accordi e, alla fine, il danno ai consumatori.

Inoltre, lo studio ha concluso che anche quando le *killer acquisitions* sono strutturate come concentrazioni al di sotto della soglia di notifica o in modo diverso dalle concentrazioni, esistono strumenti giuridici in alcune situazioni per affrontare tali transazioni. L'Articolo 22 dell'EUMR è un mezzo prezioso ed efficace per catturare potenziali *killer acquisitions* che assumono la forma di concentrazioni sotto soglia, a condizione che gli stati membri di riferimento siano competenti ad esaminare la transazione o non abbiano un proprio regime di controllo delle concentrazioni. Per gli

[106] Come si è detto, la Corte di giustizia europea ha anche chiarito che la Commissione può accettare rinvii ai sensi dell'articolo 22 dell'EUMR solo da parte di stati membri che sono essi stessi competenti a esaminare l'operazione o che non hanno norme nazionali sul controllo delle concentrazioni (come il Lussemburgo). Di conseguenza, il meccanismo di rinvio previsto dall'articolo 22 potrebbe non essere disponibile per alcune transazioni che non soddisfano alcuna soglia di controllo delle concentrazioni a livello nazionale o dell'UE, a meno che uno o più Stati membri non siano in grado di esercitare poteri di *call-in* (o la transazione presenti un nesso sufficiente con il Lussemburgo).

[107] Questo è indicato, ad esempio, nella Commissione Europea, Direzione Generale della Concorrenza, Aggiornamento sull'applicazione delle norme antitrust nel settore farmaceutico (2018-2022) - Autorità europee della concorrenza che lavorano insieme per farmaci accessibili e innovativi - Rapporto della Commissione al Consiglio e al Parlamento europeo, Ufficio delle pubblicazioni dell'Unione europea, 2024, https://data.europa.eu/doi/10.2763/427709.

accordi non strutturati come concentrazioni, le disposizioni antitrust sono importanti strumenti disponibili. Inoltre, per garantire che le transazioni problematiche vengano portate all'attenzione della Commissione, lo studio raccomanda di considerare l'introduzione di un registro o di un sistema di notifica degli accordi rilevanti e delle interruzioni pianificate. Questo potrebbe rivelarsi uno strumento utile per catturare le transazioni potenzialmente dannose che assumono la forma di licenze esclusive (le quali, come tali, non sono soggette a alcuna revisione ex ante ai sensi dell'EUMR).

Introduction

It is widely acknowledged that innovation serves as the primary engine for enhancing firms' productivity and product quality, while at the same time fostering economic growth. A central question that has come to the forefront among academics and antitrust authorities is how changes in market structure influence firms' incentives and ability to innovate.[108] In recent years, there has been mounting concern among antitrust authorities that mergers and acquisitions (M&As) involving highly innovative firms in concentrated industries may have substantial effects not only on prices but also on innovation and consumer choice. From a theoretical perspective, existing studies have shown that mergers may encourage or discourage research efforts and, in turn, innovation output, depending on factors such as the level of competition, efficiencies resulting from consolidation, and changes in the appropriability of innovation (Gilbert, 2022; Haucap & Stiebale, 2023).

Concerns about the detrimental effects of mergers on innovation have intensified following the publication of the "Killer Acquisitions" paper by Cunningham et al. (2021), which shows that firms may have strong incentives to engage in acquisitions with the primary objective of discontinuing the target's overlapping innovation projects, to the detriment of future competition. In addition, Crawford et al. (2020) note that the 'killer acquisition' theory of harm is related to the broader concern about a general 'loss of potential competition'. While it is often assumed that incumbents acquire a start-up to pre-empt the threat of future displacement of their core business, or to pre-empt future product market competition by eliminating a particular rival's overlapping pipeline, the authors argue that acquisitions may also deter innovation competition, i.e, be an opportunity for "'buying' instead of expending effort in rival innovation",[109] with the risk of jeopardising competitive dynamism from the outset, even before R&D efforts shape specific product development (leading also to 'reverse' killer acquisitions).

The relevance of these theories of innovation harm depends on the competitive dynamics specific to each industry, including factors such as the pace of innovation development and the predictability of its outcomes. Given the mixed results of theoretical modelling, accurate empirical investigations that consider industry-specific nuances are essential to provide robust insights into the impact of mergers on innovation.[110]

The pharmaceutical sector is one of the industries with the highest levels of research and development (R&D) investment, where innovation plays a pivotal role in contributing to advances in both economic prosperity and health outcomes (Bokhari, et al., 2021). A consistent finding of existing studies is that market consolidation in the pharmaceutical industry leads to substantial reductions in research spending and patent output among the consolidated firms (Ornaghi, 2009a; Haucap, et al., 2019), as well as a significant decline in the productivity of inventors from the target firms (Ornaghi & Cassi, 2023). However, empirical research on alliances between smaller biotech firms and larger pharmaceutical entities, considered as potential substitutes or complements

[108] See the report commissioned by European Commission's Directorate-General for Competition on "Feasibility study on the microeconomic impact of enforcement of competition policies – more details at https://op.europa.eu/en/publication-detail/-/publication/67521c90-e6d0-11e7-9749-01aa75ed71a1/language-en.

[109] Crawford et al. (2020).

[110] See, e.g., Bennato et al. (2021) for the case of the hard disk drive industry.

to mergers, offers a more optimistic perspective, as there is evidence of a positive correlation between a firm's clinical development expertise and the likelihood of successful outcomes for small firms (Grabowski & Kyle, 2008).

Focusing on the development of new treatments (the "D" in R&D), Cunningham et al. (2021) findings suggest that, in the pharmaceutical sector, acquired drug projects face reduced development prospects if they coincide with the acquirer's existing product portfolio, particularly when the market power of the acquirer is pronounced due to weak competition or distant patent expirations. Their conservative estimates, derived from a probabilistic framework, suggest that 5.3% -7.4% of acquisitions can be classified as killer acquisitions. These acquisitions tend to occur disproportionately just below thresholds that warrant antitrust scrutiny. This latter finding is reminiscent of the analysis by Wollmann (2019), which shows that following the increase in the pre-notification exemption threshold for mergers, pharmaceuticals were among the top five industries with the highest number of horizontal exempt mergers in the post-amendment period.

As part of its ongoing evaluation of the procedural and jurisdictional aspects of EU merger control, the European Commission's Directorate General for Competition (DG COMP) published the results of its internal assessment of mergers that did not meet the turnover thresholds of the EU Merger Regulation (EUMR) in 2021.[111] The assessment showed that in the pharmaceutical sector there were mergers involving overlapping drug projects which did not meet the turnover thresholds, even though the acquirers appeared to be willing to pay a high price for the acquisition of innovative targets with low turnover.

The findings in Cunningham et al. (2021) are consistent with the work on mergers and acquisitions in the pharmaceutical industry commissioned by the European Commission and carried out by Informa Pharma Consulting and Szücs (2020), which also shows that the probability of a drug project being discontinued increases if it overlaps with another drug project of the acquiring company for the same indication. In addition, the study shows no acceleration in the pace of drug development following an acquisition, contrary to industry claims that acquisitions speed up the R&D process.

Another industry where the phenomenon of killer acquisitions has recently been the subject of intense scrutiny is digital markets, with findings that present a nuanced picture. On the one hand, it appears that acquired products are not automatically abandoned after the acquisition, as suggested by an examination of competitors' official statements (Ivaldi, et al., 2023). On the other hand, in the case of technologically leading and younger firms, products of acquired targets are discontinued under their original brand names after the acquisition (Gautier & Lamesch, 2021).

As part of its continuing commitment to preserving innovation in the pharmaceutical industry, the Commission launched a new study on the phenomenon of killer acquisitions in 2022. This report is the final outcome of the project.

The objective of the study, as outlined by the Commission, is twofold. The first is to assess the actual scope and characteristics of the phenomenon of killer acquisitions (KAs) in the pharmaceutical sector, i.e. transactions that likely had as their object or

[111] COMMISSION STAFF WORKING DOCUMENT EVALUATION of procedural and jurisdictional aspects of EU merger control, available at https://competition-policy.ec.europa.eu/document/download/fec9441a-3fca-4d51-851f-6a0e22a52b35_en?filename=SWD_findings_of_evaluation.pdf.

effect the discontinuation of overlapping drug research and development projects (including both pipeline-to-pipeline overlaps and marketed-to-pipeline overlaps) to the detriment of future competition. The study aims at devising both a typology of the phenomenon's manifestations in practice and a workable methodology to identify ex ante transactions that would deserve further scrutiny ("*fact-finding* challenge").

The second objective consists in a thorough evaluation of (i) the Commission's past efforts to address the killer acquisitions phenomenon and (ii) the legal framework within which the Commission operates. In particular, the study seeks to apply, and where necessary, evaluate the aptness of the instruments that the Commission has used, and could use, to prevent harmful outcomes. Where it is found that such transactions have fallen through the regulatory grid (e.g. because they do not constitute "concentrations" or do not meet the relevant reporting thresholds under the EU Merger Regulation (EUMR)), the objective is to identify potential means of preventing such harm, whether through potential reform of the current rules and practice under the EUMR or through application of Articles 101 or 102 of the Treaty on the Functioning of the European Union (TFEU) ("*evaluation* challenge").

The study is structured in two chapters that reflect the two objectives of the research.

The first chapter relates to the *fact-finding* challenge and illustrates an analysis of all transactions that occurred in the pharmaceutical sector between 2014 and 2018, supplemented by a manual screening assessment. The analysis was conducted with the benefit of hindsight and relied on publicly available data. It sought to determine whether these transactions may have led to the discontinuation of overlapping projects, while at the same time altering the competitive landscape in the relevant market. The methodology developed for the *fact-finding* analysis identifies data and tools that would be best suited to determine in practice whether a given acquisition has led, or could lead, to the discontinuation of competing drug R&D projects.

The *fact-finding* challenge chapter includes the following:

- a detailed description of the data and other sources of information used in the study (section I.1);
- a detailed description of the methodological approach, which consists of a sequential filtering process to identify potential killer acquisitions. This process is organised in three steps: first, identifying relevant overlaps resulting from a deal (section I.2); second, pinpointing discontinuations of overlapping drug projects following a deal, and specifically identifying those likely caused by the deal, which are deemed prima facie relevant for assessing a killer acquisition (section I.3); and finally, carrying out a killer acquisition assessment on a large scale of transactions (section I.4);
- the findings of the analysis, for each of the deal types analysed, namely mergers and acquisitions, asset purchases, licensing agreements, R&D agreements and other minor deal types (section I.5).

The *evaluation challenge* chapter contains the following:

- an evaluation of the aptness of the Commission's assessment of five notified transactions to correctly anticipate possible discontinuations of competing lines of drug R&D projects, including an assessment of the remedies design (when applicable) (section II.1);
- a discussion of the opportunities and shortcomings of the merger rules to deal with killer acquisitions structured as non-notifiable concentrations. With respect to such transactions, the report discusses i) the application of the current thresholds for *ex ante* review (including aggregation of inter-related transactions), ii) lessons to be drawn from the literature regarding potential alternatives to the current jurisdictional

thresholds, and iii) the use of referrals under Article 22 EUMR to capture concentrations below threshold (section II.2);

- a discussion of the EUMR-Antitrust interface, and two case studies, showcasing how Article 22 EUMR and Articles 101 and 102 TFEU could be applied, respectively for concentrations and deals non structured as a concentration (section II.3 and II.4);
- a proposal for a "notice" system that could allow the Commission to monitor potentially harmful transactions that are currently difficult to spot (section II.5).

I Fact-finding challenge

The main objective of the fact-finding challenge is to identify potential 'killer acquisitions'. Killer acquisitions ("KA") are «'acquisitions' or other types of deals between parties, including R&D (in a wide economic sense) of innovative competitors which have as their object or effect the discontinuation of overlapping R&D projects to the detriment of innovation competition and ultimately consumers».[112]

To this aim, we follow a sequential approach consisting of the following stages:

- identification of the deals (all potentially relevant transactions in the period of interest for the analysis, i.e. 2014-2018);
- identification of deals with overlapping projects (either pipeline-to-marketed or pipeline-to-pipeline);
- identification of discontinuations of overlapping drugs;
- identification of *prima facie* killer acquisitions (*prima facie* KA).

Accordingly, this chapter is organised as follows. Section I.1 describes our data sources, detailing the data cleaning and matching processes, and illustrates descriptive statistics. Section I.2 discusses our strategy to identify overlapping projects, and section I.3 our approach to determining discontinuations and distinguishing between 'benign' and '*prima facie* relevant for a KA assessment' ones. Section I.4 presents our methodology to detect, among the latter, '*prima faci*e killer acquisitions' (*prima facie* KAs) that would deserve a case-by-case analysis. Section I.5 presents the results.

I.1 Data

Our investigation is divided into three sequential stages: (i) identification of possible overlaps between drug R&D projects, or between an R&D project and a marketed product, belonging to the parties to commercial transactions that occurred (i.e. were signed) in the period 2014-2018; (ii) identification of permanent discontinuations in the advancement of such overlapping projects; and (iii) analysis of whether the discontinuation of such projects was likely motivated by anticompetitive incentives or had the likely effect of harming competition (i.e. whether these were *prima facie* killer acquisitions). As per Technical Specifications, the focus is on R&D projects aimed at the development of an originator or branded drug with a patented Active Pharmaceutical Ingredient (API), as opposed to drug projects aimed at the development of generic[113] or biosimilar[114] drugs, or improvements in the manufacturing process. Following

[112] COMP/2021/OP/0002 - Ex Post Evaluation: EU Competition Enforcement and Acquisitions of Innovative Competitors in the Pharma Sector Leading to the Discontinuation of Overlapping Drug Research and Development Projects, footnote 2 of the Technical Specifications, page 2.

[113] European Medicines Agency (EMA) definition: A generic medicine is a medicine that is developed to be the same as a medicine that has already been authorised. Its authorisation is based on efficacy and safety data from studies on the authorised medicine. A company can only market a generic medicine once the 10-year exclusivity period for the original medicine has expired.

[114] EMA definition: A biosimilar is a biological medicine highly similar to another already approved biological medicine (the 'reference medicine'). Biosimilars are approved according to the same standards of pharmaceutical quality, safety and efficacy that apply to all biological medicines. The EMA is responsible for evaluating the majority of applications to market biosimilars in the European Union (EU).

discussions with the Commission, biosimilars are also considered as innovations being developed.[115]

To conduct our analysis, we use the following sources:

- Proprietary sources;
- Springer Nature's AdisInsight Database on deals in the pharmaceutical industry (Adis Deals) and scientific and market information on drugs in commercial development worldwide);[116]
- Non-proprietary sources;
- Clinical trials data: ClinicalTrials.gov online trial registry (CT) of the US National Library of Medicine (NLM);[117] European Union Clinical Trials Register (EUCTR) of the European Medicines Agency (EMA)[118] – the retrieval of this data benefited from the support of TRIX Srl (Trix),[119] which implemented a series of manual and automatic search queries via Python (full details are provided in Appendix A.1.3);
- Data on marketed drugs: US Food and Drug Administration (FDA), Approved Drug Products with Therapeutic Equivalence Evaluations (the "Orange Book") (OB);[120] FDA, Lists of Licensed Biological Products with Reference Product Exclusivity and Biosimilarity or Interchangeability Evaluations (the "Purple Book") (PB);[121] EMA, European public assessment reports (EPARs) for human medicines granted or denied marketing authorisation in the EU.[122]
- FDA's and EMA's lists of approved generic and biosimilar drugs.[123]

In the next subsections we explain in detail how we use the sources listed above, which variables we extract or construct from each, and how we match them to build our final dataset for the analysis.

Even though patent data, and more specifically patent expiration information, are deemed relevant in the literature in a killer acquisition analysis, we make a limited use of it in this study. The main reason is that it is difficult to associate a pharmaceutical company's patents with the specific molecules under development that may be covered by those patents and to the exact scope of the patent. Furthermore, although in the

[115] See section I.1.5.

[116] AdisInsight Database includes the following content sets: Drugs, Trials, Safety Reports, Deals and Patents. Our subscription provides us with the consultation of AdisInsight Database for the Deals and Drugs sets. https://AdisInsight.springer.com/

[117] https://clinicaltrials.gov/.

[118] https://www.clinicaltrialsregister.eu/ctr-search/search.

[119] Trix is a spin-off of the University of Bergamo (Italy), which specialises in the development of AI-based algorithms for search queries and information retrievals, especially in cloud environments, with applications to patent data, computer-aided innovations and innovation methods. Their team comprises academic and non-academic members and is composed of mechanical and software engineers.

[120] https://www.accessdata.fda.gov/scripts/cder/ob/index.cfm.

[121] https://purplebooksearch.fda.gov/.

[122]https://www.ema.europa.eu/en/medicines/field_ema_web_categories%253Aname_field/Human/ema_group_types/ema_medicine.

[123] For the US market, data are retrieved from https://www.fda.gov/drugs/first-generic-drug-approvals/anda-generic-drug-approvals-previous-years and https://www.fda.gov/drugs/therapeutic-biologics-applications-bla/purple-book-lists-licensed-biological-products-reference-product-exclusivity-and-biosimilarity-or; for the EU market, data are retrieved from https://www.ema.europa.eu/en/medicines/download-medicine-data.

case of marketed drugs this problem is softened (at least for the US)[124], patent data are often not helpful in tracking changes in ownership, as information on the assignment of a patent name may not change even after a change in drug ownership.[125]

I.1.1 AdisInsight Deals

AdisInsight is a comprehensive database that collects (*inter alia*) commercial data on pharmaceutical industry deals (Adis Deals) and scientific data on drugs in commercial development worldwide (Adis Drugs), based on sources such as published literature, medical releases, websites, and government filings from around the world.[126]

The Adis Deals dataset covers over six thousand deals in the period 2014-2018.

Each transaction profile includes information on:

- Date of agreement;
- Firms involved, i.e. name and role of the parties involved in the deal;
- Type of agreement, including mergers and acquisitions (M&As), purchases, joint ventures, licensing agreements, and R&D collaborations;
- Drugs involved, i.e. object of the deal;
- Indications involved, i.e. therapeutic indication;
- Deal value, when disclosed;
- Deal status, i.e. active, complete, pending and terminated;
- Summary of the deal, i.e. a description of the pivotal events related to the deal, which typically includes details of all the above information.

Some of the key fields of the Adis Deals dataset have been found to be incomplete or not apt for a large-scale analysis, which requires a high degree of content standardisation. For instance, our manual inspections revealed that in a non-negligible number of deals the information was not systematised into the relevant variables even when available and included in the description field. Thus, we carried out an extensive revision process through several and complex iterations. First, we asked for the support of Trix to extract through text analysis the relevant information included in natural language in the summary of the deal. Then, to obtain as accurate and comprehensive a dataset as possible, we contacted the data provider, Adis, providing it with the results of our inspections and, at the same time, requesting a review process on its part to retrieve the missing information needed for the purpose of our study (even when not included in the description field).

Appendix A.1 gives full details on the issues encountered in the original dataset and our approach to solving them, also showing examples of how we extracted the relevant information from the description field and documenting the extent of the corrections made by Adis.

[124] While the OB provides, for marketed drugs in the US, the set of unexpired patents that covers authorised drugs, this information is not available for the EU. Even for US marketed drugs, though, the patent scope is not identified.

[125] Suppose company A buys company B, which owns patent X. Company A may or may not ask the Patent Office to change the name of the owner (assignee) of patent X from company B to company A. See e.g. Graham, Marco, & Myers (2018): "Although parties to a patent conveyance face certain legal incentives to record the transaction at the USPTO, recording is not Mandatory", p. 244.

[126] https://www.springer.com/gp/adis/products-services/AdisInsight-databases.

Table I.1 shows the typology of deals we adopt for deals included in the study and the number of transactions agreed in each category in the period of interest for the analysis (i.e. 2014-2018), as in our finalised Deals dataset.[127] [128] Appendix A.1 reports additional statistics.

[127] The classification adopted does not always coincide with the original one given by Adis. Our revisions aimed at making the classification of the deals as accurate as possible and functional for the analysis. offers further details on the revision process.

[128] As illustrated in the table, Adis Deals may include deals related to products or technologies. It is important to note that we can filter out from our analysis deals that do not concern drugs or companies that develop drugs since we study the impact of the deal in a dataset that only contains information on drugs (either marketed or under development). Additional details are provided in the following subsections.

Table I.1: Type of deals included in the study[129]

Deal Type	Definition	Frequency
M&A	Transactions that entail a change in ownership of entire companies, including all associated assets and liabilities. This includes both cases where companies merge and transactions that result in the acquirer's ownership of at least a 50% interest in the acquired company.	490
Purchase	Transactions entailing the acquisition of, e.g., business units, product lines, facilities, technologies, or other assets (including patents, marketing authorisations or other types of IPR) that do not constitute all of the assets (and related liabilities) of the company from which they were acquired.	319
Joint venture	Agreements under which two or more companies conduct a specific project or business in which the parties share profits and losses.[130]	47
Equity investment	Transactions not elsewhere classified (because not combined with licensing or another deal type) consisting of capital investment in an organisation that develops products/technologies and provides financial returns not only in dividends but also in, e.g., royalties or later licensing rights.	15
Licensing	Agreements where rights for specified products or technologies are licensed from one organisation to another, or rights are shared between organisations. Based on the type of rights licensed, further distinctions could be made between licenses relating to product development, manufacturing, supply, marketing and/or distribution.	2,920
Cross-licensing	Agreements where two or more organisations license each other for the exploitation of specific products or technologies defined in their respective patents.	14
Partnership	Collaborations between two companies to carry out a specific task (e.g. clinical trial).[131]	26
R&D	Agreements (other than joint ventures) for the research and development of products (including, e.g., agreements relating to the provision of grants/funding).	2,438
Joint venture R&D	Joint ventures for research and/or development of products.	18
Marketing (not including licensing)	Agreements relating to the commercialisation of specific products but not involving licensing of technology or other intellectual property rights (e.g. promotion agreements).	28

We enriched our Deals dataset by reconstructing the corporate groups of each of the companies that are part of a deal. Indeed, while the original information provided by Adis concerns only the signatory companies, we believe that identification of their respective "corporate links" is needed for a comprehensive and accurate killer acquisition analysis. For instance, a company that intends to undertake a killer acquisition may mask this operation by interposing its subsidiary. The identification of corporate groups relies on the history of mergers and acquisitions in the period 2000-2018, as reconstructed using the external data source Zephyr, complemented with M&As included in Adis Deals in 2014-2018. Therefore, only companies connected through past M&A activity in this period are linked to each other, with the addition of some connections that we have manually included because they were outside the observed period but deemed relevant (e.g. the acquisition of Janssen Pharmaceutica by Johnson & Johnson in 1961).[132]

In light of this, we conduct our analysis of overlaps, discontinuations and killer acquisitions by looking at both the companies signing the deals and their corporate groups.

I.1.2 AdisInsight Drugs

The Adis Drugs dataset uses scientific and market information to track all new and novel prescription drugs in development, across all therapeutic areas, where a corporate entity is involved.[133] Drugs are tracked throughout the development process, from discovery to eventual launch, and continue to be monitored post-marketing.

Adis Drugs does not track generics (while it tracks biosimilars), over-the-counter (OTC) drugs, veterinary drugs, medical devices, academic or non-industrial drugs, 'drugs' that have no Active Pharmaceutical Ingredient (API) (such as osmotic solutions for bowel cleansing, dialysis solutions), and drugs approved prior to 1995.

[129] We exclude from the analysis deals in the following categories: Spin-offs; Manufacturing agreements; Manufacturing and supply agreements; Supply agreements; Marketing agreements that take the form of Promotion agreements and do not involve an identified drug. Aside from spin-offs (i.e., divestitures), all of these typologies seem to define "vertical" agreements, namely agreements between undertakings that are operating (for the purposes of the deal) at different levels of drug development/supply. By relying on a keyword search, we have verified that the deals that remain in these categories do not contain transfers of rights that would create a risk of killer acquisition (i.e., rights highlighting a non-purely vertical relationship among the parties, which would make possible an overlap between the parties' portfolios of drugs). Accordingly, these deal categories are excluded as the parties would have no ability to kill a counterparty's competing product (indeed, neither divestitures nor vertical agreements can create product/project overlaps at all). Appendix A.1 provides details and examples in support of this choice.

[130] The sharing of profits and losses in such JVs often occurs through formulas obliging each party to contribute a percentage of operating costs and entitling each party to a share of net income from venture operations. Furthermore, joint venture agreements typically establish relatively structured decision-making processes in which the parties share managerial authority (often with formal committees and detailed provisions for the resolution of disagreements) and may entail the establishment of one or more entities that have been formed specifically for that purpose.

[131] Partnerships seem to be characterised by fewer of the relatively elaborate structures and procedures that are commonly found in joint ventures.

[132] To ensure the robustness of our reconstruction, we also performed manual verifications by consulting the information on corporate groups contained on the companies' websites and annual SEC filings. Given the cumbersome nature of these dedicated searches, they were limited to the largest and most prominent corporate groups, including, for example, Johnson & Johnson, Novartis and Roche.

[133] https://support.springer.com/en/support/solutions/articles/6000231786-inclusion-criteria-for-adisinsight.

The Adis Drugs dataset includes over fifty-eight thousand drug profiles.[134] For the purpose of our analysis, it provides information on:

- Drug identifiers, i.e. unique drug IDs, drug names and synonyms (including e.g. alfa-numeric names used during the early stages of development and trade names);
- Drug class (assigned by Adis), WHO ATC classification, and EPHMRA/Intellus anatomical classification;[135]
- Mechanism of Action (MoA), i.e. the process by which drugs produce a pharmacologic effect;
- Route of Administration (RoA), i.e. the means by which drugs are delivered into the body;
- Originator and developing companies, i.e. the parties that originated the drug and are involved in developing it, respectively;[136]
- Highest development status, i.e. the highest development stage reached by a molecule in each therapeutic indication (TI) (e.g. marketed, Phase III, etc.);
- Development stages by TI and country of development.

Our use of the Adis Drugs dataset is partly aligned with a desire to assess the extent to which publicly available sources might provide information and tools that could facilitate timely identification and regulation of potential killer acquisitions. Indeed, even though AdisInsight is a proprietary dataset, the subscription-free search function available online allows some of the key information mentioned above to be gathered for the kind of case-by-case analysis that the European Commission typically undertakes in its competition policy practice.[137] In detail, a search for the name of a specific drug provides access to information on its MoAs, TIs, highest or more recent stages of development

[134] We conducted our final data extraction in October 2022. We extracted a total of 58,601 drug profiles by using the Advance search tool and the "Phase" search criterion available online from AdisInsight Database.

[135] While WHO mainly classifies substances according to the therapeutic or pharmaceutical aspects and in one class only (for international drug utilisation research and adverse drug reaction monitoring), EPHMRA (the European Pharmaceutical Market Research Association) mainly classifies products according to their indications and uses (to satisfy pharmaceutical companies' marketing needs). See: https://www.ephmra.org/sites/default/files/2022-03/WHO%20ATC%202021%20comparison%20Final%202021%20for%20web%20site.pdf.

[136] Developing companies are further subdivided into: Owner (An organisation that owns the intellectual property rights); Market Licensee (An organisation which has licensed certain rights for the drug or technology, in specified indications and/or countries); Development Licensee (An organisation which has licensed rights for carrying out trials in specific indications and countries); Licensee (The default role when it is not clear whether the agreement is for marketing or development); Sub-licensee; Technology Provider (An organisation which are licensing their technology for use with a drug); Collaborator (Any organisation where the role is unclear); Funder (An organisation involved in venture capital financing or other funding); Technology Transfer (An organisation only involved as a broker or vendor of the technology). Each of these companies might appear as Sponsor or Collaborator in registered clinical studies in which the drug is used as part of the experimental treatment or of the observed therapy. Clinical studies, however, can include a drug even when sponsors and collaborators are neither owners or developers. This can happen when clinical studies focus on combination therapies, or include active substances no longer covered by IP protection, or in observational studies.

[137] https://competition-cases.ec.europa.eu/search.

(including discontinuations and lack of recent reported development), and originator as well as developing companies.[138]

Importantly, Adis Drugs provides a static picture of a drug at the time its dataset is accessed (i.e. early 2023 for the purposes of this study). This is not a problem for the main variables we extract for our analysis, namely drug names, MoA, RoA and drug class, as these are time-invariant. On the other hand, we need to reconstruct the stage of development and ownership of the molecules of interest at the time a deal was agreed and in subsequent years, with historical detail. For this purpose, the information from Adis only serves to corroborate the other sources we employ, discussed in the following subsections.

I.1.3 Clinical Trials Data

Our data source on clinical trials is ClinicalTrials.gov (CT), a publicly available resource covering over 400,000 observational and interventional studies[139] registered in the US and 221 other countries (including the EU). We integrate CT with the Clinical Trials Transformation Initiative's database for aggregated analysis of ClinicalTrials.gov (AACT). The AACT database contains all the data elements relating to a trial's protocol and results for studies available at CT (albeit without historical details) and helps facilitate understanding and analysis by using consistent names and structures.

We also explored the possibility of including the EU Clinical Trials Registry (EUCTR) in our comprehensive analysis. However, our research showed that this data source had many limitations, as it lacked key information needed for our analysis. In addition, we conducted a comparative analysis between the EUCTR and CT, which ultimately led us to conclude that the inclusion of the former would add minimal value given the comprehensive coverage of the latter. A detailed breakdown of our assessment, which led to the final decision to extract public data on clinical trials exclusively from US sources (CT and AACT), can be found in Appendix A.1.2

We use CT data to define the portfolio of drugs held by companies at the time a deal was signed. However, to see if, after a deal, there is any further development of the drugs where we find overlapping between companies' portfolios, we use both CT and Adis Drugs (which includes information from EUCTR). In what follows we provide further details about CT.

ClinicalTrials.gov, the US clinical trial registry (CT), is a web-based resource that provides information on publicly and privately supported clinical studies in which human subjects participate over a wide range of diseases and conditions. CT is maintained by the National Library of Medicine (NLM) at the National Institutes of Health (NIH).

[138] This information is available for the subscription-free version of the site and corresponds to the "At a glance" section. Subscriber content includes additional details on: Development Overview (including Company agreements, Key development milestones, Patent information); Drug Properties & Chemical Synopsis; Biomarker; Trial Landscape; Development Status; Commercial Information; Scientific Summary; Future Events; Development History; References. This detailed information is available in a discursive text format, but not all of it is structured in the dataset that we can use for the large-scale analysis.

[139] In interventional studies, also known as clinical trials, researchers assign participants to receive one or more interventions to observe their effects. The interventions are often investigational, meaning they have not yet been approved for use by doctors. Observational studies, on the other hand, focus on collecting data from participants or using existing data about their health, habits, or environment. In observational studies, participants are not assigned interventions; if there is an intervention, it is because participants are already using it as part of their regular health care or daily life. For more details, see https://clinicaltrials.gov/study-basics/learn-about-studies.

Extensive information on each clinical trial is provided by the sponsor (or the principal investigator), who registers the study following prior assessment by the NIH.[140]

For each research project, CT reports information on:

- Unique trial identifiers, i.e. CT identifier (NCT number) and identifiers from other trial registries, including the EUCTR EudraCT (European Union Drug Regulating Authorities Clinical Trials Database) Number;
- Intervention/treatment, i.e. the drug or molecule under investigation;[141]
- Sponsor and Collaborator(s), i.e. name of the agent legally responsible for the trial and for reporting truthful information, and of the organisation(s) other than the sponsor providing support for the study;
- Condition or disease, i.e. the disease, disorder, syndrome, illness, or injury that is being studied;
- Phase, i.e. the stage of development in the trial, based on definitions developed by the US Food and Drug Administration (FDA);
- Study Type, a description of the nature of the trial (e.g. interventional or observational);
- Recruitment Status of the trial (e.g. recruiting, completed, withdrawn, terminated, suspended, unknown) and eventual reason for any termination, suspension or withdrawal;
- Relevant dates, including the study start and completion dates;
- Relevant MeSH terms, i.e. descriptors that classify the diseases and pharmacologic actions studied in the trial, coming from the Medical Subject Headings (MeSH) vocabulary, which is created and updated by the NLM[142] – this is a key feature, as we use MeSH terms to proxy therapeutical indications studied for drugs, identify and follow over time overlaps which could be affected by the deal (see section I.2);
- History of changes, i.e. dynamic changes concerning the study, including changes in the name of the sponsor and collaborators and study status (with details of when each change occurred).

A clinical trial sponsor may be an individual, company, institution, or organisation that takes responsibility for initiating, funding and/or overseeing a clinical trial, ensuring that all legal requirements regarding the safety and confidentiality of trial participants are met, and typically overseeing the collection, storage, and interpretation of data

[140] The CT registry was established under the Food and Drug Administration Modernization Act of 1997 (FDAMA) and is currently regulated by the NIH and the Food and Drug Administration (FDA), which collaborated to develop the website that was made available to the public in February 2000. In 2007, the U.S. Congress passed the Food and Drug Administration Amendments Act of 2007, which required additional, very extensive information to be submitted for the CT registry. This amendment resulted in the current publicly available database, ClinicalTrials.gov. More details are available at https://clinicaltrials.gov/ct2/about-site/background#:~:text=ClinicalTrials.gov%20is%20a%20Web,range%20of%20diseases%20and%20conditions.

[141] Using the ancillary information provided on the type of intervention, we can exclude from the data trials that do not concern drugs, i.e. trials involving behavioural aspects, devices, diagnostic tests, dietary supplements, and procedures (in line with Technical Specifications).

[142] Each clinical trial is associated with its relevant MeSH terms (or descriptors). We matched each MeSH term with the MeSH thesaurus, a controlled vocabulary produced by the NLM. The MeSH thesaurus is hierarchically organised in trees and identifies MeSH terms by numbers that indicate their location in the MeSH tree, namely MeSH codes. Given our interest in TIs and MoAs of drugs, we focused on three of the 16 main branches of the MeSH tree: Diseases [C] and Psychiatry and Psychology [F], relating to TIs, and Chemicals and Drugs [D], including Pharmacologic Actions [D27.505], which relate to MoAs. For more details on how we use MeSH terms in our analysis, see Section I.2.

generated during the trial.[143] A collaborator is an organisation other than the sponsor that provides support for a clinical trial, including activities related to funding, design, implementation, data analysis, or reporting.[144]

Two types of intellectual property rights (IPRs) may arise from a clinical trial: (i) copyrights, which cover the data generated by the clinical trial; (ii) patent rights, which cover the inventions and discoveries made during a clinical trial. The allocation of IPRs is outlined in the (legally binding) Clinical Trial Agreements (CTA). In cases where the sponsor provides funding for a trial, it generally retains ownership of the IPRs.[145]

Four features of CT are particularly relevant to our study. First, reporting on CT is generally required by law, and a study's recruitment status and results must be updated within strict deadlines by the sponsor.[146] Second, when a study is terminated, withdrawn, or suspended, the sponsor must provide an explanation.[147] As applicable law provides that submitted clinical trial information "shall not be false or misleading in any particular", and non-compliance may render the sponsor subject to substantial penalties,[148] it is reasonable to assume that the information recorded in CT is truthful. Third, CT enables users to track changes occurring during the life of a trial via its History of changes. Last, CT reports the EUCTR unique trial identifier (EudraCT number) for studies also recorded in the European register, allowing us to establish an immediate link between the two data sources.

While CT provides, to our knowledge, the most comprehensive, systematically reported, and publicly available clinical registry information, a caveat is that this information may not necessarily be complete: some trials may not be registered on CT (e.g., there is no mandatory requirement to register Phase I trials), and trial information may be missing from available records, e.g., due to incomplete compliance. Appendix A.1 reports details on the challenges posed by the data and on the data extraction process.

I.1.4 OB, Purple Book, EPARs

The data included in CT (mostly) cover molecules under development (i.e. pipelines). However, the availability of historical data on trials since 2000 ensures coverage for drugs that have entered the market in the meantime, until these have been clinically tested. CT also includes data on observational and Phase IV studies, which involve marketed drugs (from which we can also infer that a drug has been marketed).

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[143] The sponsor may act as the sponsor-investigator or may contract the investigation to a third party. A company or agency that uses its employees to conduct research is considered a sponsor, while the employees are considered investigators.

[144] For definitions, see also: https://clinicaltrials.gov/study-basics/glossary.

[145] See: https://www.ct-toolkit.ac.uk/routemap/sponsorship/downloads/sponsorship_principles_V5Jun16.pdf and https://sharepoint.healthlawyers.org/Members/PracticeGroups/PGCSToolkits/CTA/Documents/10_Intellectual_Property.pdf.

[146] Registration and reporting on clinical trials is governed by very detailed regulations, promulgated by the US Department of Health and Human Services, which establish strict requirements with respect to the timeliness, contents and other elements of each registration and update. See the Final Rule for Clinical Trials Registration and Results Information Submission, 42 C.F.R. Part 11 (2022), available online at https://www.ecfr.gov/current/title-42/chapter-1/subchapter-A/part-11?toc=1.

[147] For more details on recruitment status and eventual reasons for discontinuation, and how we use this information, see Section I.3.

[148] See generally 42 U.S.C. § 282(j)(5); 42 C.F.R. §11.66 (2022).

To ensure that we can duly track drugs that have received approval for marketing in our analysis, we use additional and specific data sources: the FDA's Orange Book (OB) and Purple Book (PB) for approved drugs and biological products in the US, and the EMA's European public assessment reports (EPARs) for drugs marketed in the EU. These sources allow us to retrieve information on market authorisation dates (also for generic versions of the same drug).

We have downloaded OB data from the FDA website, providing marketing authorisations snapshots at annual frequency, over the period 2014-2022 for the US market. Unfortunately, for biological drugs this information is available only from 2020 (in any case, each annual release also contains a record for marketing authorisations issued in the preceding years, where the historical issuance date and the current market authorisation holder are reported; the only missing information is about any past holder of the market authorisation if a change has occurred, as only the current one is reported in any subsequent release. However, we use historical clinical trial data to assign drugs to the companies taking part to a deal; the registries data are mostly used to retrieve authorisation dates). We could not find past EPARs data before 2018 either, but the EC sent us data on market authorisation transfers approved by EMA before 2018. We use such data to validate findings on marketed drugs' ownership in our results (mainly via manual inspections).

A couple of final remarks about OB/PB and EPARs are in place. First, neither the OB nor PB provide information on the therapeutic indications for which the drug has received marketing authorisation. Information on "therapeutic area" is included in the EPARs, but this is not comparable to MeSH Terms which provide a proxy for TI. To retrieve information on the marketing status of TIs, we use two sources: i) Adis Drugs, that provides the highest development status (including applications' preregistration/registration and marketing approval) of drugs at country level with relevant dates by Indication (AdisInsight uses a vocabulary of Indications largely based on MeSH Terms); ii) observational and Phase IV studies registered in CT. Second, both datasets (for US and EU) provide information on the date of approval for the marketing of generic versions of drugs, information that we use to decide whether a drug should be included in the analysis, as we explain in the next section.

I.1.5 Lists of generics

As per Technical Specifications, drug projects aimed at the development of generic or biosimilar drugs are out of the scope of the study. The Adis Drugs dataset excludes generics, whereas it includes biosimilars (which can be easily identified through specific keywords). On the other hand, the datasets for clinical trials and marketed drugs include both, generics and biosimilars.

As to generics, we consider the market entry of the first generic as the temporal discriminator that identifies the relevance of a marketed drug in our analysis. According to the literature[149] and industry experts involved in the project, once the first generic enters the market, many other generic manufacturers may decide to do the same. Moreover, patents on new indications or methods of use have traditionally not been

[149] See Ellison, Glenn and Sara Fisher Ellison, "Strategic entry deterrence and the behavior of pharmaceutical incumbents prior to patent expiration", American Economic Journal: Microeconomics, 2011, 3 (1), 1–36; and Tenn, S. and Wendling, B.W., 2014, "Entry threats and pricing in the generic drug industry", Review of Economics and Statistics, 96(2), pp.214-228.

effective in preventing the off-label use of generics. Therefore, when a transaction presents an overlap in the combined portfolio of the parties which involves a drug that has already been marketed and for which there has been at least one generic entry, for the purpose of this study, we assume that the parties have likely no appreciable incentive to undertake a killer acquisition: killing one of the overlapping drugs does not provide any competitive advantage as the firm will still face the competition of (overlapping) generics.[150]

While there is abundant literature showing that drug prices collapse once the first generic enters the market, the Experts in the Team argued that the biosimilars, that follow up on prior approved biological drugs, cannot be considered on the same ground as generics. The case of biosimilars is generally different because there are typically more research efforts and greater know-how underlying their development, and even after a biosimilar enters the market, market shares and prices tend not to be affected as much as in the case of generics. Therefore, as agreed with the European Commission, biosimilars are considered relevant drugs for the analysis.

We retrieve details on the first generic entry from the OB and EPARs data. A molecule will no longer be considered part of the portfolio of a pharmaceutical company from the date on which a generic version of the same molecule enters the market.[151]

I.1.6 The combined dataset

The use of various, primarily public data sources provides a basis on which to build an accurate and comprehensive analysis but also presents various challenges in compiling and aggregating information. Indeed, information is not always consistently reported across different datasets.

To construct the final dataset for our analysis, we need to perform two main types of matching: (i) a match based on drug names to aggregate information from the datasets on clinical trials, Adis drugs and marketed drugs, and (ii) a match based on company names between Adis Deals and clinical trials' history of sponsors and collaborators. The combined data would then allow to reconstruct the companies' portfolios at the time a deal was agreed and study their evolution over time.

We matched clinical trials, marketed drug datasets and Adis Drugs based on drug names. In parallel, we associated branded marketed drugs with the entry date of their first generic by using the active substance names to delimit the period in which the drug may be of interest in the analysis.

To perform these matching exercises, Adis Drugs proved particularly useful because it provides information on all possible synonyms of a drug (active substance name, names assigned during clinical development by the various companies that owned the molecule, trade names). Appendix A.1.3 provides full details of how we implemented the matching process between Adis Drugs and the interventions in CT.

[150] It can still happen that among competing drugs (with the same TI and MOA), there are different ones (not the same active substances) that are marketed/generics.

[151] In theory, the identification of generics can also leverage the exclusion criteria of Adis Drugs, which does not cover drugs that completed their development before 1995 or after when they do not have a novel content compared to other, previously developed drugs (see section I.1.2). Accordingly, if an intervention in a clinical trial does not have an associated profile in Adis Drugs, it can be assumed to be generic.

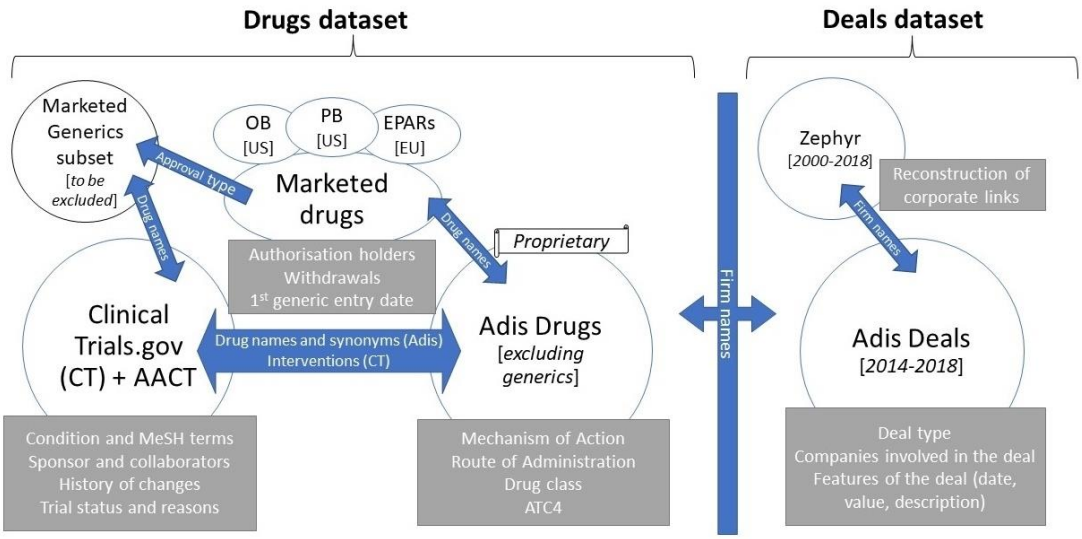
As for companies, we linked, where possible, all companies that are part of a deal (from Adis Deals) to other companies belonging to the same corporate group, as observed the month before the announcement of the relevant agreement. Then, we cleaned and standardised firms' names, as previously done in the literature (Cunningham, et al., 2021), and implemented the matching with the drugs dataset based on these names and the time the deal was agreed.

We construct historical datasets of companies' portfolios based on the information on sponsors and collaborators of all clinical studies up to the deal date. This exercise poses an important limitation related to the presence of cases where the same drug is assigned to the portfolios of different companies from clinical trials. This can be due to different reasons. First, a trial can have multiple sponsor/collaborators. Second, a company can use one drug in combination with another, and a sponsor/collaborator may be the owner only of one of these two drugs. Third, there may be a change of sponsor/collaborators over time.

To avoid the attribution of a drug to a company that does not own it, we implement the following approach. First, we compute, for each historical clinical trial dataset, the percentage of trials that have been done for a given intervention by a sponsor/collaborator up to that point in time (quarter). Next, we consider a conservative threshold of 5% to reasonably assign a given molecule to a company's portfolio. This means that we drop from firms' portfolios the drugs for which the said firms have less than or equal to 5% of the clinical trials. For example, suppose that, in the first quarter of 2014, a drug *i* has been tested (in all periods up to that quarter) in 20 clinical trials, of which 19 had company A as a sponsor or collaborator and 1 had company B (i.e., company A has done 95% of the trials while company B only 5%). By applying the threshold, we drop drug *i* from the portfolio of company B. If instead, both A and B have more than 5% of trials on drug *i*, we keep drug *i* in the portfolio of both companies. As a result, if companies A and B merge, we would have an overlap between the same drug. To avoid this issue, when we analyse such cases, we attribute the drug to the company that (1) has the highest number of clinical trials and/or (2) appears as the originator of the drug in Adis Drugs or as the market authorisation holder in the OB.

Figure I.1 provides a visualisation of the different datasets that inform our analysis, their purpose, and the key we use to perform the matching between them.

Figure I.1: Construction of the database: key information and matching



Source: Lear

As discussed, our dataset includes the entire universe of drugs, from research through commercialisation – that is, molecules at different stages of clinical development, covering the status of all the associated clinical trials (whether completed, active, suspended, terminated, etc.) and their market approval. Hereafter, we will use the term "marketed product" for a marketed molecule, "pipeline project" for a molecule under development and "relevant drugs" for any type of treatment (marketed or under development).[152]

I.2 The overlaps

The first step in evaluating a possible overlap between pipeline-to-pipeline or pipeline-to-marketed molecules is to establish a definition of overlap. The second step is to identify the "perimeter" of a deal, i.e. the set of drugs that could be affected by a deal, so that the existence of overlaps between the parties could pose a risk.

Following Technical Specifications, we focus our analysis on drug R&D projects that overlap in both Therapeutic Indication ("TI") and Mechanism of Action ("MoA"). We refer to such projects as "narrow overlaps" as opposed to "broad overlaps", which are TI-only overlaps.[153] For the purposes of this study, a narrow overlap defines the relevant market in which two drug R&D projects are assumed to be substitutes.[154]

[152] Marketed molecules in a TI can only give rise to marketed-to-pipeline overlaps.

[153] In principle, the "closeness" of overlap can be assessed in light not only of the drugs' TI and MoA but also of study descriptors (e.g. patient populations and treatment protocols), company presentations to conferences and investors, and the like. However, with the data at hand, for the fact-finding challenge, only an overlap in TI and MoA can be implemented.

[154] After several discussions with the Commission held at the beginning of the project, it was confirmed that broad overlaps may not accurately capture the substitutability between drugs, leading to too many Type I errors, and that narrow overlaps are more appropriate to answer to the research questions of the study.

CT data does not include information on preclinical projects, which represent the early stages of drug development prior to the initiation of clinical trials in humans.[155] As a result, molecules in preclinical development are not included in our reconstruction of company portfolios, leading to a downward bias in the identification of "potential" overlaps.[156] This limitation cannot be overcome (many studies of new molecules are likely to defer disclosure on company plans until clinical trials require the enrolment of subjects with a certain disease).[157]

As regards the identification of drugs that fall within the perimeter of a deal, this is a composite exercise involving two aspects. The first is to filter out from the parties' portfolios drug projects that have already been discontinued prior to the signing of the deal, which implies creating a full list of all ongoing innovative drug R&D projects (either in development or already marketed) associated with each of the parties to a deal at the time of its announcement. The second aspect is to take into account the "scope" of the deal, i.e. the areas of a company's portfolio that are affected by a deal and over which anticompetitive motives might lead to discontinuations. In the case of a merger, the scope coincides with the full set of drugs in the portfolio of both parties to the deal, whereas in other deals, such as partial acquisitions (purchases), licensing deals or R&D agreements, the scope is narrower and concerns only specific assets identified as the "object" of the deal. For instance, in licensing deals, the transaction can potentially affect the development of the licensed drugs as long as they overlap with drug projects in the licensing-in company's portfolio, while all other drug projects in the licensing-out company's portfolio can be left out of the analysis.

The rest of the section is organised as follows. Section I.2.1 discusses our strategy to identify overlapping drugs and illustrates its implications in different scenarios. Section I.2.2 introduces an ad hoc strategy for identifying narrow overlaps for vaccines: we note that in the case of vaccines, the description of the MoA tends to be homogeneous and not very informative, as most vaccines work by stimulating an immune system response to a virus or bacterium or their components. We therefore rely on TI and drug class, the latter replacing the use of MoAs, to define a narrow overlap. Finally, section I.2.3 discusses the strategy to identify the set of drugs that might be affected by a deal.

I.2.1 Strategy to identify narrow overlaps

For each molecule, our dataset includes, among other details, all TIs and associated Medical Subject Headings (MeSH) terms reported in CT, the US registry of clinical trials, as well as drug MoAs from Adis Drugs. MeSH terms include specific, hierarchically arranged categories and subcategories for both diseases and pharmacological actions.

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[155] Preclinical studies aim at providing detailed information on dosing and toxicity levels of a drug, so as to gather sufficient data to decide whether the drug should progress to human clinical trials. Preclinical studies typically involve in vitro experiments and/or animal testing. See: https://www.fda.gov/patients/drug-development-process/step-2-preclinical-research.

[156] Suppose that the target firm has a molecule in preclinical development. The potential overlap could be with other projects of the acquirer that are in the clinical or marketed phase or in the preclinical phase, but we cannot observe it in any of these instances.

[158] Based on the recommendations of the pharmaceutical experts in our team, we have grouped RoAs in the following categories: oral; injection, distinguished between subcutaneous, intramuscular, intravenous, intradermal and intraperitoneal and other injections; sublingual and buccal; rectal; vaginal; ocular; otic; intranasal; inhalation; topical; transdermal; and implant. A similar grouping is also proposed in the medical literature, which emphasises that each route has specific purposes, advantages, and disadvantages. See https://www.msdmanuals.com/home/drugs/administration-and-kinetics-of-drugs/drug-administration.

This information enables us to standardise TIs, reconstruct a hierarchy between them, and verify whether MoAs represent well-established pharmacological actions.

The hierarchical systematisation of MeSH terms proves particularly useful for identifying overlaps between molecules that are at different stages of their development and/or at different points in time. It may be the case that, as a molecule progresses through different stages of development, its TI narrows or its MoA becomes more specific and accurate, making it challenging to examine potential overlaps on a large scale. For instance, we may have to evaluate the potential overlap between a Phase I molecule with a quite broad TI (e.g. solid tumour) and a Phase III molecule that is already advanced within the same therapeutic area (e.g. sarcomas, carcinomas, and lymphomas, which are all types of solid tumours). MeSH terms help us to detect common roots within the TIs of the drugs, based on which we can establish that they overlap.

If two drugs share both a TI (as captured by MeSH terms) and a MoA, we consider them potential substitutes and label them a narrow overlap. For the purposes of this study, a narrow overlap identifies the 'product market(s)' that may be affected by a deal.

In detail, we identify narrow overlaps between the relevant drugs of the parties of a deal using the following sequential strategy:

- First, we identify relevant drugs that overlap at least in TIs (i.e., broad overlaps). In case there is no perfect overlap in TIs, we need to be sure that this is not because the relevant drugs are at different stages of development or because TIs are not sufficiently standardised. To this end, we use MeSH terms and their hierarchical systematisation (in the so-called MeSH tree) not only to identify a perfect overlap, but also to find common roots in TIs for drugs at different levels of development (i.e., to detect an imperfect overlap). The MeSH thesaurus, which is controlled by the NLM, also helps to standardise TIs that can be reported with a certain degree of variability in clinical trials. Box 1 provides details on how we use MeSH terms to trace a common root in TIs and identify broad overlaps.
- If the analysis of MeSH terms indicates that the relevant drugs of the two parties overlap in TIs (whether perfectly or not), we then aim to determine whether the two drugs also overlap in MoA, thus establishing a narrow overlap, using the following procedure:
- When two or more relevant drugs overlap in TI and share an identical MoA, we can immediately determine a "narrow overlap". Note that a drug may have multiple MoAs: if this is the case, the requirement is that at least one of the MoAs is common to both drugs.
- When two or more relevant drugs overlap in TI, but their MoAs differ, we need to investigate whether this is because the MoAs are not yet well established in their definition, in which case there may still be a narrow overlap, or whether it is because the two identified drugs serve different objectives, which would rule out a narrow overlap. In particular:
- If both MoAs are listed in the MeSH terms in the clinical trials of the molecule related to its pharmacological action, we assume that each MoA is an established term. If this is the case and the MoAs are different, we conclude that there is no narrow overlap.
- If at least one of the MoAs is not an established term (i.e. it could not be matched to the relevant MeSH terms), we check whether the two drugs share the same Route

of Administration (RoA),[158] e.g. both drugs are oral pills or intravenous (IV) treatments, as a preliminary necessary evidence of substitutability between the two drugs:

1. If they do not share the same RoA, we conclude that there is no narrow overlap.
2. If they share the same RoA, we check for a possible association between their identified MoAs in the medical literature using the National Library of Medicine (NLM) PubMed Central (PMC) full-text archive.

- We assume an association between a pair of studied MoAs if a reasonably relevant portion of the scientific literature in PMC jointly cites them, as explained in more detail in Box 2[159] If both the RoA and MoA association conditions are met, we consider that there is sufficient evidence to identify a narrow overlap.

Box 1: Overlaps in TI based on MeSH terms

Each clinical trial in CT is associated with its relevant MeSH terms. We matched each MeSH term in our data with the MeSH thesaurus, a controlled vocabulary produced by the National Library of Medicine.[160] The MeSH thesaurus is hierarchically organised in trees and branches and identifies MeSH terms by numbers (or MeSH codes) that indicate their location in the MeSH tree. There are two main branches of the MeSH tree that relate to TIs: Diseases [C] and Psychiatry and Psychology [F] (see also footnote 133).

MeSH codes consist of three digits in the first node of the tree (the broadest heading) and expand by three additional digits at a time as the MeSH term becomes more specific within the same tree. Because i) different MeSH terms can be associated with a single clinical trial and ii) a MeSH term can be associated with more than one MeSH code, we may have several MeSH codes associated with a given trial. For data tractability, i) we select the first 10 MeSH terms for each clinical trial – note that 98.98%

of trials have 10 or fewer MeSH terms; and ii) for each MeSH term, we keep the first 10 MeSH codes – the vast majority of MeSH terms have less than 10 MeSH codes, but there are some with up to 24 MeSH codes.

We establish an overlap in TI based on MeSH terms in cases where (at least):

- **Two drugs share an identical MeSH code (perfect overlap)**: this mainly helps to standardise TIs.
- **One of the MeSH codes of one of the drugs contains one of the MeSH codes of the other drug (imperfect overlap)**: this allows to establish an overlap

[158] Based on the recommendations of the pharmaceutical experts in our team, we have grouped RoAs in the following categories: oral; injection, distinguished between subcutaneous, intramuscular, intravenous, intradermal and intraperitoneal and other injections; sublingual and buccal; rectal; vaginal; ocular; otic; intranasal; inhalation; topical; transdermal; and implant. A similar grouping is also proposed in the medical literature, which emphasises that each route has specific purposes, advantages, and disadvantages. See https://www.msdmanuals.com/home/drugs/administration-and-kinetics-of-drugs/drug-administration.

[159] We developed an algorithm that automatically searches two MoAs in PMC, first on a stand-alone basis and then simultaneously, and stores the number of results for each search. The algorithm allows us to implement this strategy on a large scale for all cases where we do not observe a direct overlap of MoAs.

[160] https://id.nlm.nih.gov/mesh/.

between drugs that are at different stages of development, e.g. a Phase I drug tested for solid tumour, whose MeSH terms include "Neoplasms", and a drug at a more advanced stage tested for breast cancer, whose MeSH terms include "Breast Neoplasms". In fact, the MeSH tree structure is as follows:

Neoplasms [C04]

Neoplasms by Site [C04.588]

Breast Neoplasms [C04.588.180]

and the MeSH code C04 is included in C04.588.180.

Box 2: Overlaps in MoA based on PMC

PubMed Central (PMC), a free full-text archive of biomedical and life sciences journal literature, allows users to build complex search strings and compare the number of results, in terms of relevant publications, for different queries. PMC search algorithm is powerful and flexible as it performs an automatic term mapping process that uses appropriate translation tables. Among them, the PMC MeSH translation table contains MeSH terms, entry terms and subheadings; terms derived from the Unified Medical Language System (UMLS) that have equivalent synonyms or lexical variants in English; and supplementary substance names and their synonyms.[161] These features appear particularly useful for building associations between different MoAs for the purpose of identifying overlaps.

Thus, to establish whether two MoAs (MoA_1, MoA_2) have a close relationship based on the medical literature, we exploit PMC search and define an index that weights the joint search output of MoA_1 and MoA_2 against the highest number of publications identified by searching for each MoA individually, as follows:

$$f(MoA_1, MoA_2) = \frac{N_{12}}{\max\{N_1, N_2\}}$$

Where:

- N_{12} is the output of the joint search of MoA_1 and MoA_2,
- N_1 is the output of the individual search of MoA_1, and
- N_2 is the output of the individual search of MoA_2.

We use the function $\{\max\{N_1, N_2\}\}$ in the denominator to avoid inflating narrow overlaps: the idea is to identify close substitutability between the two MoAs, not just that they are related (hence, N1 and N2 should ideally be similar in magnitude). We have evaluated associations among a sample of MoAs in PMC with the support of the pharmaceutical experts in our Team, whom we asked to report which associations were valid (and to what extent) and which were not. Based on these tests, we have decided to employ the following conservative threshold to disentangle valid relationships between MoAs of overlapping drugs:

$$f(MoA_1, MoA_2) > 0.05$$

[161] See: https://www.ncbi.nlm.nih.gov/pmc/about/userguide/.

As the threshold is conservative, lowering it further could lead to an overestimation of narrow overlaps in a large-scale analysis.

With this threshold, we do not find a narrow overlap in MoA between the molecules Vedolizumab and Ontamalimab, which have been the focus of the EC investigation in Takeda's acquisition of Shire (case M.8955). The search for an association between their MoAs in PMC is relevant because the molecules have overlapping TIs and RoAs and have different MoAs that are not matched in MeSH terms (i.e., are not established). Although the simultaneous search for their two MoAs ("Alpha4beta7 integrin antagonists" and "MADCAM1 protein inhibitors") in PMC yields results, the association index is below the 5% threshold.[162] We believe that this is because the two MoAs are slightly different, as also noted in the EC decision. From the perspective of a large-scale analysis the exclusion is justified, because the association index cannot replace a case-specific assessment (moreover, for the case at hand, the EC has recognised that the two MoAs are indeed different, even if the conclusion is that they belong to the same relevant market definition).

I.2.2 Ad hoc strategy to identify narrow overlaps for vaccines

Vaccines differ from other drugs in many ways.[163] Vaccines are typically administered to a healthy population to prevent the onset of a medical problem; the dose, time, route and frequency of their administration are usually well defined. In contrast, other drugs are primarily given to patients when they already have a medical condition, requiring careful determination of the dose, time, and frequency of administration in response to the health problem that is occurring (He, et al., 2012).[164]

Another fundamental difference between vaccines and other drugs relates to the MoA. Understanding the MoA, i.e. how a drug produces its pharmacological effects, is crucial for drug classification as it provides insights into how the drug works in the body, as well as its toxicity and potential side effects (Trapotsi, et al., 2021). However, this is not the case for vaccines. Vaccines typically work by stimulating an immune system response to a virus or bacterium or their components. Therefore, vaccines often fall into broad categories of MoA, such as immunostimulants, immunomodulators or immunosuppressants, which does not provide sufficient information to evaluate the substitutability between two vaccines sharing the same TI.

In light of these considerations, we propose an *ad hoc* overlap identification strategy for vaccines that disregards the MoA and replaces it with another variable available in the Adis Drugs database, namely the drug class. A drug class allows the identification of a group of drugs that share common properties and action. Specifically, Adis uses a

[162] The exact value is 0.035. Using the minimum function instead of the maximum to calculate the denominator in the formula, this value would be 0.14, i.e. above the threshold. However, we believe this would also introduce too many false associations between unrelated MoAs.

[163] In our database, vaccines cover an area of 9,370 clinical studies (of which 4,889 are sponsored by the industry) relating to both interventional (clinical trials) and observational studies (which do not test potential randomised treatments but track real-world patients during treatments in their everyday routine); and to a total of 4,142 pipeline projects (of which, 963 are part of research programmes). Among the broader TIs, we have identified the following trials for vaccines: 803 Cancer, 416 Influenza, 319 Covid-19, 176 HIV, 143 Tumours.

[164] The article notes that there are exceptions to this classification in both classes of therapeutic intervention: cancer vaccines are given after the problem has been identified; protein pump inhibitors are often given to prevent gastric problems in combination with other drugs or in specific hospital settings.

thesaurus hierarchy based on MeSH terms and identifies three different categories for drug classes: i) chemical drug classes, ii) biological drug classes, and iii) indication-specific drug classes. Sometimes, the drug classes are also assigned on a case-specific basis.[165] A drug class can be identified as a composite definition, which lists more than one class definition for a single entry. Composite definitions allow for a refinement in the identification of the specific drug class and appear relevant to consider for accurate identification of overlaps.[166]

Accordingly, we intend to establish narrow overlaps between vaccines using the following sequential strategy. First, as with any other drug, we check whether two vaccines share a common TI, making use of the MeSH terms reported in CT. Second, within the vaccines with overlapping TIs, we require a perfect match in their drug class (i.e., we use the full definition of the drug class to account for composite classes).

We have also considered an alternative overlapping identification strategy for vaccines that leverages the drug-associated Anatomical Therapeutic Chemical (ATC) code (up to the fourth digit or requiring a perfect match). However, this approach showed some limitations. In particular, while the ATC code is more accurate for drugs at an advanced stage of development or already marketed, it tends to be unspecified and too broad for drugs in early development. Therefore, using the ATC code together with the TI could create an inconsistent grouping of pipeline vs marketed drugs.

Box 3 illustrates the implications of applying our strategy to identify narrow overlaps in a case investigated by the European Commission.

Box 3: Vaccine overlapping strategy in GSK/Novartis (M.7276)

We explored the implications of our strategy by assessing the existence of overlaps between the parties' portfolios in a concentration investigated by the EC, namely the GSK/Novartis vaccines business (Case M.7276). The EC identified the meningococcal vaccines as one of the areas of horizontal overlap between the parties' vaccine businesses. Meningococcal vaccines are used to prevent infections caused by Neisseria meningitidis, a bacterium responsible for diseases such as meningococcal infections and meningococcal meningitis. Focusing on one of the two TIs, meningococcal infections, it is possible to identify an overlap in TI between the following drugs: Novartis' Menveo and Bexsero, and GSK's Nimenrix and Mencevax.

While Menveo, Nimenrix and Mencevax are MenACWY-type vaccines and protect against the bacteria serogroups A, C, W, and Y, Bexsero protects against serogroup B meningococcal disease. This information is reflected in the drug class: while Bexsero is classified as "Meningococcal vaccines", Menveo, Nimenrix and Mencevax are classified as "Conjugate Vaccines; Meningococcal vaccines" – a conjugate vaccine consists of a polysaccharide antigen fused (conjugated) to a carrier molecule. Therefore, by looking at the drug class, we can more accurately identify the

[165] The following example was provided by Adis to help understanding how the drug classes are assigned: A T-cell therapy is being developed for the treatment of cancer. This is a biological therapy. Relevant biological drug classes here will be: "Immunotherapies" (as these will be involved in immunomodulation) and "T-lymphocyte cell therapies". Indication specific drug class will be: "Antineoplastics". Similarly in the case of chemical drugs, as per the chemical details and indications, chemical drug classes and indication-specific drug classes are assigned.

[166] For example, Typherix, a vaccine administered to prevent typhoid fever, has a composite drug class, defined as "Antibacterials, Bacterial vaccines, Polysaccharidesis".

substitution pattern within the same TI (i.e., meningococcal infections) and establish an overlap among Nimenrix, Menveo, and Mencevax as defined by the EC in its Decision.

I.2.3 Strategy to identify the perimeter of deals

Two aspects matter to delimit the set of drug projects whose development trajectory may be affected by a transaction, i.e. the "perimeter" of a deal: a project must be deemed "active" on a firm agenda at the time the deal is announced and fall within the deal scope.

As to the first aspect, only actively pursued drug projects by pharmaceutical firms are relevant in a killer acquisition analysis, since they may be subject to a discontinuation after a deal that would not have occurred absent the deal. Our analysis focuses on pipeline-to-pipeline overlap and marketed-to-pipeline overlap; thus, "active" drug projects include pipelines with recent clinical developments as well as marketed molecules, as the latter may overlap with pipelines. For molecules marketed in a given TI either before or after a deal, we consider them to be active in that TI both before and after that deal. For pipelines, to identify drug projects that are "active" at the time of a deal, we apply a set of rules based on the recruitment status history, as reported in clinical trials. These rules help us identify and exclude from the analysis drug projects that can be considered discontinued already before the deal. The set of rules is the same that we use to identify discontinuations that follow a deal (what changes is just the evaluation date): as this a key aspect of the analysis of discontinuations, a more detailed discussion of the rules is postponed to section I.3.1, which also provides a thorough description of the recruitment status information reported in clinical trials data.[167]

The second aspect requires to identify drug projects that fall within the "scope" of a deal, i.e. drug projects over which firms may gain decisive development rights or influence after a deal they would not otherwise hold. We restrict our analysis to narrow overlaps involving the in-scope drug projects and the substitutable drug projects that already before the deal fall under the same firm's decisive influence. This is the overall set of drug projects affected by a deal.

As deal types vary considerably in their scope, we have structured the analysis by deal type. Indeed, different deal types entail different sets of drug projects that are the "object" of the deal. Different deal types also entail allocations of different rights to the parties to the exchange. For example, between a transfer of ownership following a merger or acquisition and the rights that are allocated under a licensing or collaboration focused on the development of a specific R&D project, there is a great variation in the standard of proof required to establish the extent to which the deal can affect the ability and incentives of firms to sustain competing pipelines. While in the case of mergers and acquisitions this capability can largely be subsumed under the nature of the contract, in other deals it largely depends on the specific clauses agreed upon between the parties, which are often undisclosed.

[167] In synthesis, we exclude from the overlap analysis a drug project when all clinical trials in a given TI are either (i) completed or suspended more than 24 months before the deal is announced, or (ii) placed in unknown/ withdrawn/ terminated status, no market preregistration or authorization is observed, and no further clinical activity follows the deal.

As a matter of fact, merger and acquisitions (M&As) involve the transfer of full ownership of a target firm (or of the merging entities) to the acquirer (or to the merged entity). Accordingly, our analysis investigates the overlaps across the entire portfolio of drug projects of the companies involved in the deal.

In contrast, other deal types such as partial acquisitions (Purchase) or licensing deals (Licensing) focus only on a subset of target drugs, i.e. the set of drug projects moving from the divesting company to the acquiring company or from the licensing-out to the licensing-in company (the "object" of a deal). In these scenarios, the relevant overlaps are the narrow overlaps between the drugs identified as the object of the deal and the portfolio of the acquirer or of the licensing-in company. A different scenario is that of R&D agreements, which consist of partnerships to develop specific untested innovations, usually in selected therapeutic areas (the "TIs object" of the deal). This requires an analysis of the narrow overlaps that arise between the drugs object of the deal and the portfolio of the R&D partner that does not already own these drugs, limited to the TIs object of the deal.

The Adis Deals dataset contains some raw information on the drugs (in a field called "Drugs") and TIs (in a field called "Indications") that are the main object of the transactions and that can help to reconstruct the object of the limited scope deals. The original information has been cleaned, validated and enriched (remedying at least in part to missing data) relying on data processing routines (including manual inspections in order to test the routines) in order to: (i) increase the number of drug names associated with deals and to validate the links between deals and specific drugs in our drugs dataset, as drug names are often not unique; and (ii) link information on TIs from the deals dataset to MeSH terms. More details on the deal type-specific approach adopted to refine the data on the deal scope are provided in the following sub-sections.

I.2.3.1 Purchase deals

Our analysis of Purchase deals aims at investigating overlaps between the acquirer's portfolio and what is acquired. This is the "scope" of the deal, i.e. the drug projects' space where the deal may cause discontinuations. Deals classified as Purchase are heterogeneous acquisitions, as they may entail the acquisition of "business units, product lines, facilities, technologies, or other assets (including patents, marketing authorisations or other types of IPR) that do not constitute all of the assets (and related liabilities) of the company from which they were acquired" (Adis definition). The main challenge in analysing Purchase deals is to identify what is acquired, i.e., the drugs object of the deal.

We use the data reported by Adis Deals on the name of the drugs traded to look for a match with those reported in the Adis Drugs database, where each drug is identified by a DrugID. However, drug names recorded in the Adis Deals data are sometimes generic names (i.e., the name of the active ingredient) and may generate multiple matches to the Adis Drugs database. We validate matches where company names in the Adis Deals database (of companies involved in the deal) also match in the Adis Drugs database as either the originator or developer of the drug, and then resolve the remaining multiple matches by manual checks.

In cases where Adis Deals does not provide specific information on drug objects, we adopt a different strategy to identify the potential scope of the deal by looking for evidence of co-development of drugs by the companies involved in the deal. We follow a two-step approach: first, we identify the set of drugs that are the likely object of the acquisition relying on structured data available from CT and Adis Drugs; second, we validate the scope through a text analysis of unstructured natural language data from

the Adis Drugs database. Specifically, we identify as potential drug target both: i) drugs that are matched with clinical trials in CT where the parties to the deal are all sponsors/collaborators (not necessarily in the same trial) up to the date of the deal; and ii) drugs where the companies involved in the deal are listed among the organisations involved in the drug origination and development in Adis Drugs database. In the second step, for the drugs that are part of the identified potential object, we carefully examine the unstructured information which is provided in drug profiles that are also part of the Adis Drugs data, to confirm the possible link to the deal. This involves a thorough analysis of whether the drug profile contains any relevant references or mentions to the deal in question: if this is the case, we validate the identified link between the drug and the deal.

Conservatively, we apply the two-step strategy to identify the potential scope also to deals where some information on the drug object is available from Adis Deals. We do so to ensure that we capture all other possible drugs traded within the deal. In fact, our manual checks on deals showed that Purchase deals tend to be broad in scope, i.e., they tend to involve many drugs or entire portfolios. On the other hand, the "Drugs" field in Adis Deals sometimes only mentions one or a few drugs as examples, or drugs that were more prominent in the deal.

The final perimeter considered for the analysis includes all drugs identified by the two strategies, i.e., the direct associations based on Adis Deals that survive our validation and the indirect associations detected in the two-step approach.[168]

The subsequent analysis is designed to investigate all narrow overlaps that the deal creates between each of the drug objects and the entire portfolio of drug projects of the acquirer. Deals where we could not identify a drug object are excluded from our analysis.[169]

I.2.3.2 Licensing agreements

For Licensing agreements, our analysis aims to identify the drugs that were licensed by the licensing-out company to the licensing-in company, and to investigate all narrow overlaps arising between the licensed drugs and the portfolio of the licensing-in company.

Similarly to Purchase deals, the main challenge is to identify the drugs that are the object of the deal, i.e. the licensed drugs. Again, we rely on the available information on the drugs covered by the licensing, which we were able to retrieve and combine from the Adis Deals and Drugs datasets, by means of two strategies. First, for deals where it was possible to identify the drug object of the deal from the information compiled under the structured field "Drugs" in the Adis Deals data, we validated the association to a specific DrugID in the Adis Drugs database through careful and extensive checks. In detail, we searched the Adis Drugs dataset for drugs where the licensing-out company appears as originator and/or the licensing-in company appears as developer to ensure that the association was supported by evidence. We then supplemented the validation

[168] We also performed the analysis conservatively for the total potential object, i.e. the drugs identified in the first step of the two-step approach (together with the drugs identified by direct association based on the Adis Deals "Drugs" field). However, when we examined the results, we found that this approach led us to identify as targets drugs that had nothing to do with the specific deal. Instead, we verified that the validation of the second step, which either confirms or removes drugs from the potential object, makes the identification significantly more accurate.

[169] Appendix A.3 provides details of the deals not included in the analysis and the reasons for their exclusion.

with manual checks. For deals where the drug object information is not available in Adis Deals, we started with a tentative potential scope obtained by evaluating all drugs in the licensing-out company's portfolio that overlapped with the licensing-in portfolio at the time of the deal. For each drug in this tentative set, we relied on Adis Drugs unstructured data and looked for validations based on whether the drug profile mentioned the deal: only if this was the case, we validated the identified association of the drug as an object of the Licensing.[170]

The subsequent analysis of Licensing agreements is designed to investigate all narrow overlaps of the licensed drugs with respect to the entire licensing-in company's portfolio. On the other hand, deals for which we could not identify a drug object are not included in our analysis.

I.2.3.3 R&D agreements

R&D agreements are deals between companies for the research and development of products or technologies, which may have a more or less pronounced collaborative nature, including deals where each company contributes its drug(s) or technology and/or knowledge to the R&D in order to jointly achieve the development goal, or deals where one of the parties primarily provides the funding for the project.

R&D agreements typically focus on new drug research projects or drugs that are still at a very early, sometimes preclinical, stage of research.[171] Another common example of R&D agreements we observe in our dataset relates to the development of combination therapies, where the parties decide to collaborate with the aim of developing a therapeutic approach involving the use of two or more drugs (with at least one from each respective portfolio) to target a specific disease. Indeed, we note that Adis Deals records as R&D agreements clinical collaborations entered into by companies to test combination therapies.

R&D deals have a limited scope, not only because they focus on the development of specific drugs, but also because they typically focus on specific therapeutic indications. The first challenge is therefore to correctly identify the scope of the deal in both dimensions: the drug-object and the TI-object of the agreement.

For the purpose of identifying the drug-object, we implement a strategy similar to the one used for Purchase deals. First, we use the information reported in Adis Deals under the "Drugs" field to associate relevant drug profiles with a deal, and refine this exercise with validation checks to verify that the drug profile mentions the deal as a relevant company agreement. We then extend the latter research also to deals for which information on the drug object of the deal is not available in Adis Deals, and for which we could identify a potential object based on evidence of co-development of drugs by

[170] For licensing deals, we do not apply the strategy of reconstructing the potential object based on the evidence of co-development of a drug by the two companies, because we note that the transfer of rights that takes place in these deals is sometimes not reflected in the data of CT (e.g. the licensing-in company may never appear as a sponsor/collaborator) or even in Adis Drugs (e.g. in the case where the licensing-out company is not the originator and transfers all rights to the licensing-in company, our Adis Drugs subscription, which provides information without historical details, would not mention the licensing-out company among the organisations). In addition, we note that the licensing-out company is usually a relatively small company, in contrast to, e.g., Purchase deals, which often involve large companies divesting part of their business. This feature of licensing agreements makes it possible to perform validation against all the drugs that were in the licensing-out company's portfolio at the time of the deal.

[171] We note that this may affect the comprehensiveness of our analysis, as the data we can rely on mainly concern clinical trials, i.e. drugs that have reached the clinical research stage.

the companies involved in the deal. Taking into account the specificities of R&Ds, we identify as potential target all drug profiles that: i) are associated with clinical trials in CT in which the parties are all sponsors/collaborators (not necessarily in the same trial) up to 2 years after the date of the deal; and ii) are research programmes in Adis Drugs in which both companies are listed among the organisations. The research programme profiles in Adis Drugs refer to early-stage drug discovery projects that may form the basis for the development of one or more drugs (which are then tracked in the Adis Drugs dataset with a new, dedicated profile). By looking for evidence of co-development in these research programmes, as well as in clinical trials not only existing at the time of the deal but also initiated thereafter (within two years), our approach seeks to capture the typically prospective nature of R&D agreements. As a second and final step, we restrict the object of the agreement only to those drugs for which we are able to validate the association with the agreement based on whether the agreement is mentioned in the drug profile. This two-step approach should also limit (but not eliminate) the risk that if an R&D agreement is followed by other types of agreements between the same companies, such as licensing agreements, we may erroneously attribute to the R&D agreement overlaps and subsequent discontinuations and possible KAs that may instead relate to the subsequent agreement. This risk may otherwise be amplified in the case of R&D agreements because we track the potential object of these deals based on a future perspective and not only on past evidence (as we do for Purchases).

R&D agreements then require a refinement of the strategy to identify the scope of narrow overlaps affected by a deal with respect to other deal types, as their object should be defined in terms of both the drugs and the TIs on which these deals focus. This was confirmed by a preliminary manual screening of the object of the deals and the narrow overlaps identified on the basis of the drug object alone. To avoid including in the analysis overlaps that, although involving a drug object of the deal, are unrelated to the TI object of the deal, we rely on the information provided in Adis Deals under the field "Indication". We match the indication reported by Adis Deals to the dataset of MeSH terms for Diseases, and then match the corresponding MeSH codes to those for which we find a narrow overlap between each drug object of the deal and any drugs that belong to the portfolio of the companies taking part to the deal. As usual, an overlap can be detected if the drug object of the deal and the overlapping drug were either in clinical development or marketed in a MeSH term that matches the TI object of the deal.

Deals where we could not identify both a drug object and a TI object are excluded from our analysis.[172]

There is another important feature of R&D agreements that affects our analysis. R&D deals are by their nature collaborative, and there are no defined roles for the companies involved (they are all 'unspecified' in Adis Deals). Furthermore, the details of such deals are not public. As a result, it is not possible to understand whether the agreement provides an allocation of rights to the targeted innovation in favour of one or more of the parties (even when manually screening them) and, thus, it is not possible to conduct a conclusive killer acquisition assessment.

Finally, as long as multiple drugs are identified as the object of the deal, we need to assess overlaps with the portfolios of all companies signing the deal. Therefore, unlike other deal types, the number of overlaps to be investigated may be affected by a multiplicative effect of R&D-relevant portfolios. The only exceptions are the following: if

[172] Appendix A.3 provides details of the deals not included in the analysis and the reasons for their exclusion.

one party to the deal is not a pharmaceutical company, overlaps are only analysed with regard to the portfolios of the other companies involved; second, if a drug object of the deal belongs to one company's portfolio, the overlaps of that drug object are only analysed with regard to the portfolio of the other company(s) involved in the deal.[173]

I.2.3.4 Other deal types

The residual deal types in our dataset are: Equity investment,[174] Marketing,[175] Joint venture,[176] Joint venture R&D,[177] Cross-licensing,[178] and Partnership[179] (see Table I.1), which serve distinct purposes within the pharmaceutical and biotechnology sectors.

For Marketing agreements, we have information on the drug object (by design),[180] so we cross-referenced the "Drugs" field compiled by Adis Deals to find a match with a DrugID included in the Adis Drugs dataset and used detailed manual checks to validate or improve the associations.

For the other types of deals, the Adis Deals dataset does not identify a drug object in most cases. To address this issue, we used the Adis Drugs dataset to identify all drugs that list at least two parties involved in the deal in the "Organisation" field. Then, we followed a similar methodology to that employed for Purchase and Licensing deals to validate the matched drugs (as explained above).

As Equity investments are structured as acquisitions, for these deals we assess the overlaps between any drug object with the acquirer's portfolio and exclude deals without identifiable drug objects. Conversely, the remaining deal types by their nature involve a collaboration and, in this respect, have similarities to R&D agreements. Therefore, we assess the overlap between the drug objects and the portfolios of all companies involved in the deal. As for R&Ds, an exception is when a drug object of the deal is already part of the portfolio of one of the companies at the time of the deal: in such cases, the overlap is not analysed with respect to the portfolio of this company, but only with respect to the portfolio of the other company (or companies). Thus, as in the case of

[173] As an example, consider an agreement where firm I and firm J decide to test the development of a combination therapy between I's drug A and J's drug B to treat a disease D. In our analysis, we will evaluate all narrow overlaps traceable to disease D, between drug B and all drugs assigned to I's portfolio at the time the deal is announced; and all narrow overlaps traceable to disease D, between drug A and all drugs assigned to J's portfolio at the time the deal is announced.

[174] An Equity investment involves the investment in equity from one company to another, particularly related to funding the development of specific products or technologies. This transaction can entail some form of payback distinct from stocks or shares and may include elements such as royalties or later licensing rights (Adis definition).

[175] A Marketing agreement typically involves arrangements related to marketing and distribution strategies of specific commercial products (Adis definition).

[176] A Joint venture is an agreement involving two or more companies joining forces under a contract to undertake a specific business enterprise. Profit and loss are typically shared, and joint ventures are often project-specific rather than forming a continuous business relationship (Adis definition).

[177] A Joint venture R&D is a Joint venture agreement limited to R&D efforts (Adis definition).

[178] A Cross-licensing is an agreement where two or more organizations grant a license to each other for the exploitation of a specific product or technology defined in patents owned by them (Adis definition).

[179] A Partnership represents a deal regarding collaborations between companies to execute a specific task, such as a clinical trial (Adis definition).

[180] We excluded from our sample Marketing agreements that do not involve an identified drug.

R&D agreements, the number of overlaps (and consequently of discontinuations) is affected by the multiplicative effect of this potential multi-portfolio setting.

I.3 The discontinuations

The next step in our analysis is to identify, among the overlapping drugs in active development at the time a deal was signed, those that have been discontinued after the deal. In this respect, our approach is not limited to tracking the discontinuation of R&D projects, understood as the discontinuation of the molecule (in any TI), but also tracks redirections, i.e. the discontinuation of specific TIs.

The analysis at the molecule level alone cannot capture all cases of discontinuation of the development of the overlapping TIs at the time of the deal. Indeed, the parties to a deal may have decided to reorient one of the overlapping molecules in another TI without necessarily discontinuing any of the molecules in all TIs. In this case, the analysis at the molecule level would not detect a discontinuation potentially caused by the deal.

While redirection is in principle out of the scope of the study, we are concerned that disregarding such a potentially anticompetitive strategy would underestimate the relevance of the phenomenon of killer acquisitions. The decision to include redirection therefore allows for a more comprehensive assessment of harm and better aligns our approach with the Commission's enforcement practice. However, it poses additional challenges for the automation of large-scale analysis.

In fact, as a drug progresses through development, for example from Phase I to Phase II, there is often a narrowing of the TI (rather than a redirection): a molecule may be tested in 'solid tumours' in Phase I and then in 'ovarian cancer', a type of solid tumour, in Phase II. If the change in TI is the result of an advancement in R&D efforts, it would not be appropriate to consider it as a discontinuation.

The reliance of our strategy on MeSH terms that are used as descriptors in clinical trials and their associated MeSH codes allows us to overcome this problem. Indeed, when investigating whether further development has occurred for the overlapping molecule, we do not limit the analysis to the MeSH term(s) that overlapped at the time of the deal, but we also investigate whether development has occurred in a more advanced MeSH term within the same branch, as captured by the MeSH tree.

In detail, our approach to identifying a discontinuation in TI involves assessing the presence of any further development of the overlapping drugs in the relevant MeSH term after the deal: if a drug is observed to be marketed or if it is still in development within the same MeSH term or within a more advanced MeSH term in the same MeSH tree, we conclude that no discontinuation has occurred; conversely, we identify a discontinuation in the MeSH.

This strategy can then be easily extended to identify the discontinuation of a molecule per se, given the conceptual similarities. Indeed, the discontinuation of a molecule occurs when all lines of research related to that molecule are discontinued, i.e. when a molecule is discontinued in all its TIs (as captured by MeSH terms).

As a further step toward assessing transactions in the pharmaceutical industry, we classify discontinuations as 'benign' or '*prima facie* relevant discontinuations', the latter being the relevant cases for a KA assessment. We aim to separate those discontinuations that can be justified by credible safety or technical concerns, that do not appear driven by commercial or strategic motives, from those that may instead be problematic. To achieve this classification, we first look at evidence provided by our

analysis of discontinuations for both overlapping molecules in a deal; then, we rely on available information on the reasons for discontinuation (or lack thereof) as documented in the recruitment status of clinical trials. We also consider additional information, such as the nature of the entities involved in the trials, whether they are pharmaceutical companies or public institutions, where our assumption is that the involvement of a public entity adds credibility to the reasons for discontinuation of a trial.

Sections I.3.1 and I.3.2 provide more detail on how we identify discontinuations and on how we classify them as relevant cases for a KA assessment or benign, respectively. Section I.3.3 provides a summary of our strategy.

We are aware that our approach is not perfect. According to the pharmaceutical experts in our Team, a deeper analysis of the results of the trials testing the overlapping pipeline products would be the key piece of information to determine if there is potentially an anti-competitive behaviour (per object or effect), regardless of the reasons companies might report.[181] However, such a case-by-case approach is not applicable on a large-scale to all discontinuations. Section I.4 discusses the analytical approach we employ: a combination of quantitative methods, corroborated as much as possible by a manual screening of transactions, which serves as a complementary strategy to investigate the extent to which *prima facie* relevant discontinuations can also be considered *prima facie* KA.

I.3.1 Strategy to identify discontinuations

As a first step to identify discontinuations, we investigate whether there have been no new clinical trials or commercialisation of the overlapping molecules in the relevant (or more advanced) MeSH term(s) after the deal, leveraging all the information available in our dataset. Such lack of progress of at least one of the overlapping drugs after the deal date represents the first signal that the parties to a deal are no longer interested in investing in a given line of research, which we interpret as a discontinuation. The assumption is that companies would not invest further in a new clinical trial if the discontinuation was either the object or the direct effect of the deal. This approach implies that if the acquirer starts a new clinical trial immediately after the deal, but then discontinues it, this discontinuation would not be tracked.

Next, for molecules that did not register any such new development after a deal, we examine the trials launched before and still deemed "active" at the time the deal was announced, and how their reported recruitment status in CT[182] evolved, to determine whether and when a discontinuation occurred. We identify a discontinuation when all clinical trials evaluated as "active" at the time of the deal can no longer be deemed so by the end of the observation period, i.e. their recruitment status is one of the following:

- Terminated: a study stopped early, and it will not start again. A reason for termination should be specified – reasons for termination can vary from safety concerns to technical or commercial decisions.
- Withdrawn: a study stopped early, before enrolling its first participants. A reason for withdrawal should be specified.

[181] For example, examining if two drug products have different comparative safety may explain why one is discontinued versus another.

[182] See https://prsinfo.ClinicalTrials.gov/definitions.html#OverallStatus. We note that reports of recruitment status take into consideration all individual facilities where a study is conducted (i.e. sites).

- Unknown: a study whose last known status was recruiting;[183] not yet recruiting;[184] or active, not recruiting[185] but that has passed its completion date, and the status has not been last verified within the past 2 years.
- Suspended since more than 24 months. A study has stopped early but it may start again. A reason for suspension can be specified. We require that at least 24 months have elapsed since the suspension date for a suspended study to be marked as no longer active.
- Completed since more than 24 months. A study has been completed according to the plan (for a given phase), and participants are no longer being enrolled or treated. Medical results may be available. We require that at least 24 months have elapsed since the completion date for a completed study to be marked as no longer active.

Our assessment of discontinuations therefore also considers the time elapsed since the last reported recruitment status update on trials that were considered active at the time the deal was signed, on the assumption that if we observe a significant period of time in which there has been no further progress in the development of a drug in a given MeSH term, this is a signal of discontinuation. We use a 24-month threshold, consistent with the Code of Federal Regulation of FDA, which considers a period of at least two years to define an Investigational New Drug (IND) application as being active or inactive.[186] The implication of this approach is that we may also be capturing instances of project delays in our definition of discontinuation.

That said, it should be noted that our analysis investigates all deals signed off between 2014-2018, whereas our data on clinical trials and market authorisations is updated until mid-2022. Therefore, we can make use of a longer time span to observe possible developments of a molecule which is part of a deal. For a deal signed off in December 2018, we have at least 3.5 years of data to see if, in the post-deal period, a research project advanced to a further stage or reached commercialisation. For instance, let us assume that in 2017 a Phase II study registers a recruitment status as "completed". If until June 2022 (i.e. five years later), we do not observe any progression to Phase III for the same molecule, we can safely assume that the development of this molecule has been discontinued. On the contrary, if in June 2021 we observe a Phase III clinical trial for the same molecule, the study will not be classified as discontinued, even though more than 24 months have passed between June 2017 and June 2021. In this case, this study may show a delay but not a discontinuation.

We acknowledge that delays may still be harmful to competition, and relevant in the Commission's enforcement practice. However, in accordance with the Technical Specifications for this study, we exclude delays in project development from our *fact-*

[183] A study has been launched and is currently recruiting participants.

[184] A study has not started recruiting participants yet.

[185] A study is ongoing, and participants are receiving an intervention, but potential participants are not currently being recruited or enrolled.

[186] An IND application can be considered inactive by the Food and Drug Administration (FDA) if no subjects are entered into it for a period of two years or more, or all investigations remain on clinical hold for one year or more. A trial is placed on inactive status by either at the request of the sponsor or on FDA's own initiative. Sponsors of a clinical trial that has an inactive status is not required to submit annual reports, even when it is still in effect for purposes of the public disclosure of data and information. IND that remains on an inactive status for five years or more may be terminated. We can infer those trials with a recruitment status different than terminated, withdrawn, suspended, unknown are active. See Code of Federal Regulation, Volume 5: 21 C.F.R. § 312.45 (2022).

finding analysis,[187] with the aforementioned exception that the presence of at least two years of observable inactivity represents our lower bound to identify a discontinued research project. Thus, we may catch delays in our definition of discontinuation if, for example, the drug project we define as discontinued records progress at a later time than we can monitor with our data.

Based on our approach to identifying discontinuations, we categorise overlaps resulting from a deal as follows:

- Overlaps with evidence of ongoing development ("type A, no discontinuation"): there are new clinical trials of the overlapping molecules in the relevant (or more advanced) MeSH term(s) following the deal, or the drugs are on the market for that MeSH (before or after the deal), or at least one trial that was considered "active" at the time the deal was signed is still active or has been completed or suspended for less than 24 months up to the end of the period covered by this study's data.
- Overlaps with evidence of discontinuation based mostly on inactivity ("type B discontinuations"): there is no evidence of ongoing development as per the requirements described under item A; furthermore, all trials "active" at the time the deal was signed are either completed or suspended by more than 24 months, or in unknown recruitment status.
- Overlaps with evidence of discontinuation based on terminated or withdrawn trials ("type C discontinuations"): there is no evidence of ongoing development as per the requirements described under item A; furthermore, at least one trial among those "active" at the time the deal was signed is terminated or withdrawn, which may provide insight into the underlying motivations for discontinuations in the recruitment status.

The categorisation is also summarised in Table I.2.

[187] By contrast, in the evaluation challenge there is more scope for assessing "nuanced" impacts on competition such as project delays.

Table I.2: Types of overlaps and discontinuations (if any)

Group label	Description	Identification strategy
Type A, no discontinuation	Overlaps with no evidence of discontinuation	Drugs/TIs are marketed; OR new trial(s) started after the deal date; OR a trial completed/suspended by less than 24 months
Type B discontinuations	Overlaps with evidence of discontinuation based mostly on inactivity	All trials are completed/suspended by more than 24 months; OR in unknown recruitment status
Type C discontinuations	Overlaps with evidence of discontinuation based on terminated or withdrawn trials	There are no new or active trials or commercialisation, and at least one trial open at deal is withdrawn OR terminated (and can state reasons for discontinuation)

Source: Lear

I.3.2 Strategy to classify discontinuations

As a next step in our analysis, we classify discontinuations into two distinct categories: 'benign' and '*prima facie* relevant discontinuations'. The latter would include discontinuations that may be motivated by deal-driven commercial or strategic considerations and qualify as relevant cases for a KA analysis. Among the latter, one would expect more likely to find the discontinuations that *prima facie* might have had the anticompetitive object or effect of weakening competition, as opposed to discontinuations that do not raise competitive concerns as they appear unrelated to the deals (i.e., benign discontinuations).

To achieve this classification, first of all, we try to discriminate between cases where a 'killing' rationale appears to be present or absent from the evidence on the future development of the overlapping drugs. Specifically, we evaluate the following criteria that contribute to the classification of a discontinuation as benign:

- one molecule is discontinued, and the other is redirected; or
- both molecules are discontinued after the deal; or
- after the deal, the two molecules continue to overlap in at least one of the other MeSH terms in which they were overlapping at the time of the deal or in a related MeSH term (i.e. a MeSH term that overlaps with the former).

In our view, in all these scenarios it is unlikely that the firms are driven by an intent to harm competition or that the deal distorts innovation. Indeed, either both lines of research are discontinued by also discontinuing at least one of the overlapping drugs, or there is continued pursuit of common areas of research in a related therapeutic indication post-deal. In a large-scale analysis, which is inherently limited in tracking the nuances of each specific deal, the above criteria may help to avoid false positives (i.e. transactions that appear to have been followed by anti-competitive discontinuation but in fact did not).

It is worth noting that our analysis is conducted at the level of overlapping drug pairs (and the same molecule can be in overlap with many molecules, based on our definition of narrow overlap). Therefore, if the discontinuation of both drugs in one pair is pursued, for example, to protect the purchaser's interest in a third related product, we would still be able to capture the latter discontinuation (provided we also identify a narrow overlap between this third related drug and at least one of the two discontinued drugs), and this would not be flagged as benign based on the above rules (unless benign circumstances characterise this overlap as well).

The second strand of evidence we use to categorise discontinuations, but limited to Type C discontinuations, is the information on the reasons for discontinuation documented in the recruitment status of clinical trials and on the type of entities involved in clinical trials, whether public institutions or pharmaceutical companies.

In the case of Type B discontinuations (i.e., discontinuations identified on the basis of trials that were either active and then unknown, or completed[188] or suspended,[189] and no new trial was initiated after the deal), the absence of further activity denotes a notable lack of transparency regarding the specific reasons for the discontinuation, making these discontinuations worth considering in our KA assessment (unless the benign filtering above is satisfied).[190]

Type C discontinuations, on the other hand, allow us to examine the information on the reasons for discontinuation, as this is reported for studies that were terminated or withdrawn.[191] The benign discontinuation group includes all studies whose stop in their development occurred for a technical reason, i.e. reported reasons that are unlikely to mask a commercial or strategic decision. The remainder, including trials for which no reason is reported, are discontinuations to be further explored in the killer acquisitions analysis presented in the next section.

In detail, our approach to classifying reasons for discontinuation as benign or non-benign, is based on evidence from the medical literature and involves textual analysis of the motivations reported in CT.

First, we search for relevant keywords that are commonly associated with technical reasons, which (based on the literature) may be credible to indicate a discontinuation

[188] For completed trials, there is no additional evidence that we can automatically process in the large-scale analysis. For instance, the technical results of clinical studies are not always available in CT, and even when they are available there is no way to devise a systematic analysis as the outcomes design is heterogeneous and there is no control over the reporting format.

[189] It is worth mentioning that when a trial is suspended, a reason is reported. However, we do not use this information as it may not reflect the reason why the trial was not resumed after 24 months or more: therefore, we do not analyse it as relevant evidence for the reason for discontinuation (we consider the suspension to be a different event from the discontinuation that we ultimately infer from the lack of resumption).

[190] A case specific assessment might retrieve additional information in the public space beyond the sources we leverage in the large-scale analysis, that justify the discontinuation. Such reasons can only be considered in a case specific manual screening that we perform later on in the analysis to detect false positives among possible KAs.

[191] The information is compulsory when studies are suspended, terminated or withdrawn, if the study start date is on or after 18 January 2017. Nonetheless, for studies started before that date the information is provided in 81% of the instances in which the trial has been terminated, withdrawn and suspended. After 2017 it is provided in almost all due instances. The rate at which the information is provided increased over time (over studies with a start date preceding January 2017 by one year, the information was provided in 84% of the instances). The distribution is similar when using as reference date for the study the date the study is first submitted to CT.

that is unrelated to the deal. These keywords include different wordings of "low accrual", "poor experimental design", "lack of funding" (or financial/budgetary issues) and "futility" or "efficacy". These keywords are first searched individually to identify trials that were stopped early and where the wording of the reason given would allow establishing a link to each of these technical reasons.

Then, if certain features occur, the links to technical reasons flagged in the previous step are no longer deemed as credibly benign. One constant feature we always rely on is when the sponsor is a pharmaceutical company. For lack of funding, not even the presence of a public institution as a sponsor is considered a safeguard, because if a pharmaceutical company is reported as a collaborator, it may still easily be able to cut funding (we use additional keywords to capture this risk). Box 4 provides more details on the conditions under which a discontinuation is deemed *prima facie* relevant in the KA analysis, even if a technical reason is initially flagged.

In addition to the above, discontinuations candidate for further scrutiny in a KA analysis are flagged based on the association of an industry sponsor with the occurrence of specific keywords, which are also borrowed from the medical literature. Keywords used include: "sponsor or collaborator decision"; "business/commercial reasons"; "strategic decisions"; "risk/benefit" evaluations; "reallocation of resources"; "portfolio"; "efficiency"; "non-safety", etc. In the case of "sponsor or collaborator decision", "business/commercial reasons" and "risk/benefit" evaluations, the discontinuations are considered for further scrutiny in a KA analysis even if the sponsor is a public institution (because the keywords appear to single out decisions that are more likely to be driven by business considerations).[192]

Last, as already mentioned, withdrawn or terminated trials for which no reason for discontinuation is reported are directly classified as worth further scrutiny in the KA analysis (in line with the other scenarios).

Box 4: Reasons of discontinuations

We build on the medical literature (Kasenda, et al., 2014; Briel, et al., 2016; Vellinga, et al., 2021; Ellenberg & Shaw, 2022) to identify the most common causes of a discontinuation of a clinical trial development due to technical concerns, namely: safety concerns, low accrual, lack of funding or futility.

However, we argue that there are cases where even if a technical reason is flagged, the discontinuation may still be relevant for a KA assessment:

- Problems in accrual/enrolment/recruitment: although enrolment motivations are technical and seemingly benign, companies may be able to affect enrolment, e.g. by giving participants higher or lower incentives to take part in studies.

[192] Our coding of the different types of reasons for discontinuation has a hierarchical structure so that it avoids that the keywords characterising the second type in the structure capture also cases that have been already captured by the keywords characterising the preceding type, and so on. In fact, the reason for discontinuation can simultaneously contain references to keywords of different types, and the hierarchical organisation makes each type incremental and exclusive. This is to have greater control when selecting only some types as an input for the next step of the analysis (e.g., to identify a subset of discontinuations– that would more likely contain killer acquisitions to validate the killer acquisition indicators, as described in section I.4). The current hierarchical structure is the following: non-safety, enrolment/recruitment issues, sponsor/collaborator decision, financial reasons, futility reasons, business reasons, strategic reasons, risk/benefit evaluations, unrelated to security, portfolio related decision, closure of enrolment, funding withdrawal issues, efficacy issues.

Accordingly, terminations for enrolment or recruitment reasons are considered *prima facie* relevant for a KA assessment when the sponsor is a pharmaceutical company, and in the provided reason for discontinuation the word(s) sponsor and (or) collaborator is mentioned jointly with the word "enrolment" (or its variations). This allows to highlight cases where the sponsor/collaborator may have tried to influence the enrolment process. In other cases, the discontinuation is considered benign, as suggested by the literature.

- Lack of funding: while this may be regarded as a genuine reason for discontinuation, pharmaceutical companies may also cut funding in order to jeopardise the development of a trial. We therefore consider discontinuation due to lack of funding to be *prima facie* relevant for a KA assessment either if the sponsor of the project is a pharmaceutical company, or if the sponsor is a hospital or other public institution but one of the collaborators is a pharmaceutical company. In the latter case as additional controls the following keywords must also be mentioned in the reason of discontinuation: "collaborator", "support", "company" and "withdrew" or "pull" (in addition to the keywords used to flag that the discontinuation was due to funding reasons).
- Futility: when the motivation is based on a futility analysis, it appears likely to be legitimate, according to pharmaceutical experts in our Team. However, part of the literature points out that these analyses may be based on insufficiently strong evidence, leading to premature termination of studies that could prove effective, to the detriment of patients (Jitlal, et al., 2012; Lesaffre, et al., 2017). Accordingly, when the reason for termination/withdrawal refers to "futility" and the sponsor is a pharmaceutical company, we consider it as evidence of a *prima facie* relevant case for a KA assessment. We do the same when efficacy, or performance or efficiency (that are alternative but more ambiguous ways of referring to futility) are mentioned together with keywords such as: "sponsor", "collaborators" "financial", "business".

Table I.3 summarises our strategy, detailing how we distinguish between discontinuations that appear unlikely KA and those that, instead, look relevant cases for KA assessment.

Table I.3: Unlikely KA vs prima facie relevant discontinuations for a KA assessment

Description	Type B discontinuations	Type C discontinuations
Benign discontinuations, i.e. displaying features that seem enough to rule out *prima facie* killer acquisitions	Both molecules are discontinued after the deal; OR one molecule is discontinued and the other is redirected; OR the two molecules still overlap after the deal in at least one of the MeSH terms in overlap at the time of the deal or in another MeSH term within the MeSH tree branches that were in overlap at the time of the deal	
	No further filtering	Reasons of termination reported in CT support discontinuation is unrelated to the deal, combined, where further evidence is needed, with the presence of public institutions among sponsor/collaborators
Prima facie relevant discontinuations: these are all candidates for a killer acquisition assessment	All discontinuations that do not satisfy the benign filtering	

Source: Lear

In Appendix A.2 we provide details on the classification of all discontinuations and of *prima facie* relevant discontinuations for all deal types into Type B and Type C.

I.3.3 Summary of the strategy

By applying the strategy described so far it is possible to contrast two set of narrow overlaps between drug projects generated by a deal:

1. narrow overlaps where we identify *prima facie* relevant discontinuations: this is the set of narrow overlaps that have been followed by a discontinuation right after a deal of one of the two competing drug projects, for which the large-scale analysis cannot conclude that the discontinuation would have occurred also absent the deal, as no public evidence directly or indirectly supporting a technical reason to justify the discontinuation was found. This is the set of discontinuations that are worth investigating further to achieve the project objective of identifying *prima facie* killer acquisitions (i.e., the discontinuations that appear to have had as their most probable intent or effect the reduction or elimination of effective competition);
2. narrow overlaps where we identify either no discontinuation or benign discontinuations: the set of narrow overlaps where no discontinuation occurred after the deal, or where the large-scale analysis could instead detect direct or indirect evidence that the discontinuation probably occurred for technical reasons, suggesting that the discontinuation is justified and would have likely occurred also in the counterfactual scenario.

In section I.5 we report the number of transactions examined and those for which through the large-scale analysis we identify narrow overlaps, discontinuations as well as the number of *prima facie* relevant discontinuations detected for each deal type.

So far, the analysis of narrow overlaps builds upon a sequential filtering process, to obtain the set of discontinuations with no detected public evidence that allows excluding they are due to a deal. To summarise:

- the analysis is restricted to narrow overlaps between drug pairs. Two drugs are found in a narrow overlap if before the deal they have been tested in the same or in related TIs and they also overlap in MoA (MoA is replaced by drug class in the specific case of vaccines);[193]
- only narrow overlaps involving an ongoing innovation in the drug development process are considered relevant to the analysis, which is therefore limited to narrow overlaps between two pipelines or between a pipeline and a marketed product. Narrow overlaps between two marketed products or involving generics are excluded;
- the analysis is restricted to narrow overlaps involving as a target a drug project falling within the scope of a deal. For M&As, the deal impacts the entire portfolio of drug projects developed by the firms taking part to a deal (including their subsidiaries), if any. For deals other than M&As, it is instead necessary to identify the perimeter of the deal (as explained in section I.2.3): e.g., specific drug projects that are acquired or licensed-out, or that are the object of R&D agreements. Only narrow overlaps between these specific drug projects and all competing drug projects found in the portfolio of acquirers, licensing-in companies or R&D collaborators are relevant to the analysis;
- narrow overlaps involving – either on the acquiror side or on the target side – a pipeline that appears to have been discontinued already before a deal are also excluded from the perimeter of the analysis.

As a result, we obtain an output dataset where each narrow overlap represents one observation, in which:

- we identify narrow overlaps where either the acquiror's or the target's drug or both are discontinued in the overlapping TI after the deal. In detail, discontinuation of a pipeline is identified when after the deal no significant progress in its development is detected from processing the input data.[194] We trace discontinuation of any of the two overlapping drugs (not only of target drugs);
- when narrow overlaps are flagged as discontinued, we identify a *prima facie* relevant discontinuation where the discontinuation does not appear to be justified by benign reasons (e.g. technical reasons). Regarding the reasons for discontinuation, the large-scale analysis appraises only publicly available information reported in clinical trials associated to a drug, provided that the drug has been successfully matched to its corresponding identifier in the Adis Drugs database (i.e. DrugID) and that the companies that are parties to the deal have been identified as sponsors/collaborators in those clinical trials. The qualification of a discontinuation as *prima facie* relevant for a KA assessment is based on either the lack of further development after clinical trials are completed; or the absence or the content of the responsible party's statements when clinical trials are terminated earlier; or exploiting indirect evidence

[193] Overlaps in TI are identified based on MeSH codes that are either identical or belong to the same MeSH tree stem, as explained in sectionI.4: MeSH codes are used to standardize TIs reported in clinical trials data and in Adis Drugs, and to establish links between different TIs at different stages of development. Overlaps in MoA are then identified based on either a perfect match of at least one MoA or a high-frequency association of two different MoAs in the medical literature. For vaccines, we define overlaps in drug class based on a perfect match of the full drug class of two vaccines, as explained in section I.2.2.

[194] See section I.3.1 for more details.

that makes less credible the occurrence of a technical issue (e.g. the presence of industry sponsors in the drug development). Conversely, a discontinuation is considered benign if it seems less likely that the decision to discontinue was driven by business considerations, such as when there is a complete discontinuation of both competing molecules or where there is a narrow overlap between the same drugs that survives in other related TIs. The way the large-scale analysis interprets the evidence provided in the data inputs follows from the analysis design and is a matter of weighting the available evidence. For instance, a drug discontinuation that would be classified as *prima facie* relevant because of the absence or content of information on the reasons of the discontinuation can be re-classified as benign if also the competing drug has been totally discontinued in the overlapping TI. This second piece of evidence weighs more in our analysis design than the mere absence or tenor of company statements in CT records, because paired discontinuations conflict with the rationale of eliminating a rival to the benefit of a surviving drug project.

Prima facie relevant discontinuations, as identified through this sequential filtering process, represent the most accurate selection that can be obtained, through a large-scale analysis of the data available for this study, of discontinuations that do not appear *prima facie* justified by a more probable reason other than the deal.

In particular, they are the set of narrow-overlapping drug pairs for which there is some evidence that a deal allows one party to gain control rights over a substitutable pipeline; and a discontinuation actually occurred after – rather than before – the deal; and, last, the large-scale analysis cannot detect an alternative reason for the observed discontinuation than a deal-driven causality. However, as discussed in the next section, the notion of killer acquisition in our study refers to a theory of harm in which a transaction causes the discontinuation of an R&D project and (is likely to) determine a negative effect on competition. Therefore, a further step is needed to understand to what degree further publicly available evidence can support a killer acquisition narrative underlying the *prima facie* relevant discontinuations.

I.4 Killer acquisitions assessment: insights from the literature and analytical approach

The objective of the project is to single out discontinuations that would have not occurred in the absence of the deal and probably had the object or effect of lessening future competition and innovation to the detriment of consumers, and not just to exclude explanations alternative to deal-driven decisions, which is a necessary but non-sufficient condition.

Prima facie relevant discontinuations do not appear to be *prima facie* justified by reasons other than the deal, in the light of the public evidence available for the large-scale automatic analysis. However, this classification does not yet take into account information on the overall competitiveness of the relevant market, nor other characteristics of overlapping drug projects, such as their relative stage of development in terms of clinical trials phases reached and the closeness of the narrow overlap. These additional elements may shed light (at least partially, and to the extent possible with publicly available evidence) on the commercial incentives of the parties to the deal.

In fact, the elimination of one of two competing projects that after a deal fall in the same portfolio can still be neutral in a crowded market, in terms of effects on future product market competition, or even pro-competitive if the concentration of innovation efforts improves quality or time-to-market of the surviving project. In order to meet the goal, i.e., to reasonably assume that the deal endowed firms with the ability and the

incentives not only to eliminate an overlapping drug project that would have otherwise survived but also to profitably reduce future product market competition, thus harming consumers, evidence on the competitive landscape is fundamental. It is worth emphasising that the degree of competition measured when the deal is announced does not only speak about the effects on competition of a discontinuation, but it also provides evidence for a killer acquisition theory of harm, and thereby indirectly reveals how likely it is that the drug project would have continued its development to the market in a counterfactual scenario.

An example might help. If after a deal a pipeline shifts under the control of a firm that is developing a competing project and which decides to discontinue one of the two, but expected future competition in the relevant market remains nonetheless high, then, the narrative that the discontinuation is anticompetitive is less credible than in a scenario where potential competitors in the market are sparse. Similarly, if the acquired pipeline is at a very early stage and has been tested only in a broader TI than the acquiror's overlapping drug, but the acquiror decides to discontinue its own more advanced drug, than the KA narrative may look less solid.

The analysis of such features of overlapping drug projects and of potential competition in the relevant market at the time the deal was announced might be to some extent informative of the commercial incentives of the parties, as the literature and the Team experts suggest. Killer acquisitions in these respects might systematically differ from acquired overlapping projects that are not discontinued, or from discontinuations of overlapping projects that would have likely occurred also in a counterfactual scenario (that we classify as benign).

Given the inherent limitation of our study of being bound to publicly available information, the matter of investigating further *prima facie* relevant discontinuations consists of analysing the additional elements not so far incorporated in the filtering process, yet available in the public domain, which may tell something more about the likelihood to which they can be said to match a killer acquisition narrative. In other words, we aim to provide further elements which may support – at least *prima facie* – a "killer acquisition" theory of harm. Conclusions can be weaker or stronger depending on how strong and unambiguous this additional evidence is.

There can be two different types of information publicly available to investigate a KA narrative: information available at the time the deal was signed and information available with the benefit of hindsight. *Prima facie* relevant discontinuations have been so far identified (vs. all other discontinued and non-discontinued overlaps) based on the overall development outcomes of overlapping drug projects, from both before and after the deal.

However, information available ex ante is especially relevant as it may display typical patterns in killer acquisitions with respect to other acquisitions. If differences in ex ante observables characteristics of killer acquisitions are systematic, quantitative methods could help single out transactions that are more likely to lead to a KA from the set of *prima facie* relevant discontinuations. It would be interesting to identify such features, which could possibly help the Commission to identify ex ante transactions that would deserve further scrutiny.

Our methodology is therefore twofold. First, we employ quantitative methods to identify the *prima facie* relevant discontinuations that are more in line with a KA theory of harm based on systematic patterns of ex ante observable features of the drug projects in overlap that can plausibly indicate that the parties involved in a given acquisition had the incentive and the ability to stifle competition in a relevant market. The features are

those mentioned above: relative stage of development of overlapping molecules, closeness of the narrow overlap, information on the competitive landscape. Specifically, we use the Least Absolute Shrinkage and Selection Operator ("LASSO") regression, a machine learning ("ML") algorithm, to select which of the above ex ante observable features best predict *prima facie* relevant discontinuations that are more likely consistent with a KA theory of harm as opposed to benign discontinuations and to narrow overlaps that are not discontinued. We label as "LASSO-KAs" the *prima facie* relevant discontinuations that share exactly the features validated by the LASSO solution.

Second, we carry out a manual screening of *prima facie* relevant discontinuations predicated on the LASSO solution (LASSO-KAs) and expand the manual screening also to many of the remaining *prima facie* relevant discontinuations, to check if the former are indeed more likely to reflect a killer acquisition narrative than the latter, which do not share the same features. The manual screening is meant to corroborate or, when necessary, adjust the findings of the large-scale analysis, overcoming all the limitations deriving from ambiguities of data inputs or from the simplifying assumptions needed to implement it. In the manual screening, we rely on information sources and types of data beyond those that could possibly inform the large-scale analysis, such as company's reports, press releases or filings; articles from the medical literature and from pharma media outlets. For the more complex or interesting cases, the manual screening entailed a tailored assessment by the team of experts of the technical and commercial viability of the discontinued drug R&D projects, in light of public technical reports on the parties' and their competitors' R&D activities (referenced on ClinicalTrials.gov or accessible via PMC).

For deal types where the possibility to rely on quantitative methods was out of reach because of the small sample size, we resort directly to a manual examination of all *prima facie* relevant discontinuations.

A final remark is worth making. It is fundamental to emphasise that publicly available information hardly enables the Study Team to correctly control for the different incentives of the pharmaceutical companies as parties to the deal in the counterfactual scenario and to reach firm conclusions with on which *prima facie* relevant discontinuations likely did constitute a KA. Notwithstanding the significant work conducted, the Study Team assessment is always the result of the limited information available to it, with the implication that it will only be able to provide the Commission with a detailed account of the evidence collected on *prima facie* relevant discontinuations that is not conclusive, absent any access to private information.

The remaining part of this section is organised as follows: in section I.4.1 we motivate more in detail the choice of the observable features of narrow overlaps used as covariates in the LASSO regression; in section I.4.2 we describe the LASSO regression model; in section I.4.3 we explain the manual screening coverage. Findings are then discussed in section I.5.

I.4.1 Indicators that could support a killer acquisition narrative

The economic literature suggests a variety of *ex ante* observable features that might be meaningful in anticipating whether a given acquisition might lead to the discontinuation of a drug R&D project and reduce or eliminate competition and innovation.

The *fact-finding* challenge aims at employing variables derived from some of the "indicators" described in the economic literature, identified with the advice of pharmaceutical experts in our Team, to verify whether they can help elicit past

transactions endorsing a killer acquisition narrative (i.e. the *prima facie* killer acquisitions).

Such indicators should capture two essential dimensions: (i) the presence of an incentive to undertake a killer acquisition, as evidenced by the existence of a prospective rent that can be secured by pursuing such a strategy, and (ii) the ability to undertake a killer acquisition, which ultimately relates to the ability of the firm pursuing such a strategy to protect that rent.

In the Team experts' opinion, the stage of development of the parties' overlapping products and of each potential competing drug, as well as the number of potential competing drugs in the relevant market, are key elements in the assessment of the ability and the incentives for a killer acquisition to be captured.

This is also consistent with the findings of previous economic literature.

There is general agreement that the intensity of competition in the relevant market is a key indicator affecting both the ability and the incentives for a killer acquisition. A party with greater market power has more likely to lose if a competing innovation is successfully developed, and greater chances of effectively foreclosing competition by eliminating a single rival. Incentives and ability to kill overlapping innovation are thus higher where existing competition is limited and barriers to potential entry by new rivals are high (Arrow, 1962; OECD, 2020; Cunningham, et al., 2021). Conversely, a higher degree of residual competition also reduces the potential harm of a discontinuation after a deal, leading to better outcomes in terms of innovation and competition.

Importantly, the intensity of competition is not only related to the number of competing drugs in the relevant market, but also to the strength of the competitors in the market. The literature suggests that marketed drugs generally have, *ceteris paribus*, greater competitive significance than drugs that are still under development, as the eventual commercialisation and competitiveness of the latter are still subject to a certain degree of uncertainty (Madl, 2020-2021; OECD, 2021).[195,196] The degree of uncertainty (or weakness) surrounding pipeline prospects, in turn, is decreasing in the clinical phase (as the probability to reach the market is increasing in phase reached). Molecules at earlier stages of development, *ceteris paribus*, exert a priori less competitive pressure on the parties.

Lastly, the intensity of competition may depend on the nature of the competitors in the market. The literature suggests that competition may be more robust where studies are financed or conducted by public agencies or other non-profit entities, because such entities are less likely to discontinue drug projects for commercial reasons (Lièvre, et al., 2001). However, pharmaceutical competitors might be more focused on rapidly

[195] However, we note that in some cases a pipeline drug may be a closer competitor than a marketed drug. For example, in differentiated markets, a marketed drug with a differentiated efficacy and safety profile may not necessarily be a strong competitive constraint on a drug; conversely, a pipeline drug with a comparable profile would be a closer competitor. Similarly, a pipeline drug that is in head-to-head competition with a particular drug may be a stronger constraint on the latter than a competing marketed drug that has not been in head-to-head testing.

[196] We cannot construct an indicator for when marketed drugs, having the same TI and MoA as either of the parties' overlap drugs, already compete with generics, because we have data on generics entry at the molecule level. The existence of generics has a significant impact on competition in the supply of proprietary alternatives (Bergman & Rudholm, 2003), most likely eliminating any incentives for other producers to undertake killer acquisitions in that market. This is one of the factors that can be taken into account in the competitive assessment of a case-by-case analysis.

launching new drugs in order to capture the often-significant advantages (e.g., formulary/reimbursement approvals, adoption by prescribers who may then have little incentive to switch out drugs with which they are familiar, and the like) that are typically seized by the suppliers of first- and second-in-class drugs, i.e. drugs that are the first or second to reach the market in a given therapeutic application. This second aspect may prevail in shaping incentives for a killer acquisition, as timeliness is a key element to make entry effective and threatening, and thus mitigate market power incentives.

The economic literature also suggests that the incentives and ability to undertake a killer acquisition are shaped by the stage of development of the overlapping R&D projects. It is less costly to eliminate a drug at an early stage of development than one at a more advanced stage, *ceteris paribus*.[197] At the same time, an early-stage pipeline is more likely to fail on its own, and an innovator's low prospects to reach the market may reduce an incumbent's incentive to undertake a killer acquisition (Cunningham, et al., 2021; Madl, 2020-2021). According to the Team experts' opinion, incentives to kill competition may be stronger when the parties' overlap products are each at somewhat advanced (Phase II or later) stages of development (and there are few similarly situated rivals).

Finally, the incentives and the ability to eliminate competition may also depend on the characteristics of the deals and may be specific to certain types of deals.

There is a large debate arguing – for instance – that a relatively high price (i.e., a value that materially exceeds prices that are obtained in comparable acquisitions) suggests that the parties' valuation includes a "premium" reflecting the anticipated value of foreclosing competition (OECD, 2020).

For licensing deals, both the literature and the Team Experts suggest that a key element providing both the incentives and the ability for a killer acquisition is the presence of an exclusivity clause in the agreement. An exclusive license ensures that no party other than the named licensee can exploit the relevant intellectual property rights (absolutely or in, e.g., a geographic region or field of use), thereby limiting the number of firms that can make use of the product (Lundqvist, 2021; Newham & Vokinger, 2022). Therefore, exclusive licensing agreements may enable the licensing-in company to discontinue for an indefinite period of time the development of a project, at least in exclusive regions or fields of use. Moreover, large pharmaceutical companies can acquire control over a molecule or other innovation through an exclusive license (which is tantamount to a concentration of the parties' products) while not being subject to pre-merger review (Lundqvist, 2021). An exclusive licensing deal therefore confers on the licensee a heightened ability and concomitant incentive to foreclose actual or potential competition and harming the innovation process.

However, deal features do not vary across multiple narrow overlaps detected for the same deal: for the same deal we may have both *prima facie* relevant discontinuations and narrow overlaps that are not discontinued or benign discontinuations.

The empirical quantitative analysis described in section I.4.2 is meant to identify characteristics that vary across the most likely anticompetitive discontinuations (i.e.,

[197] The earlier-stage status of one of the overlapping drugs might be relevant ex ante, as a proxy for a more profitable (or relatively cheaper) opportunity to suppress competition prospects immediately, rather than waiting to see if they mature. Indeed, when one overlapping molecule is farther developed than the other, the owner of that molecule may feel greater pressure to protect its expectation of future net rents, which are increasing as development proceeds, and therefore may strategically kill the molecule in the earlier stage.

prima facie relevant discontinuations) and all other narrow overlaps that may occur also within the same deal. Therefore, the quantitative analysis only relies on indicators that vary across narrow overlaps.[198]

Nonetheless, in section I.5.3 we extend the analysis to deal level features to verify whether these variables exhibit informative patterns.

We provide details on the construction of the indicators used in the large-scale analysis and on deal level features in Box 5. Statistics on the indicators for the deal types where the LASSO methodology has been employed are reported in Appendix A.2

Box 5: The indicators used in the large-scale analysis

We convert each of the indicators suggested by the literature and the views of the Team Experts to measure the incentives and ability for a killer acquisition strategy into (binary, categorical or continuous) variables for use in our empirical analysis. Our selection of variables for the analysis of killer acquisitions also reflects the challenges of a large-scale assessment, which relies on automated processing of voluminous amounts of raw data to extract the necessary information.[199]

The variables that fall under the dimension of intensity of competition in the relevant market capture the intensity of residual competition for the specific parties' narrow overlap at the time of a deal. They are measured at the time of the deal to reflect the state of competition when the deal has been initiated (i.e., announced).

Our strategy for the identification of competing drugs is consistent with the sequential approach described in section I.2 for the identification of narrow overlaps between the parties of a deal. Specifically, the competing drugs are identified based on the two cumulative criteria of sharing both the same therapeutic indication (TI) and mechanism of action (MoA) of the parties' overlapping products whenever the latter show an exact match of both TI and MoA. In those cases where the Team could not rely on an exact match of either TI or MoA, or both, to identify a narrow overlap between the parties' products, the competing drugs is identified as those having: (i) the most advanced TI that defines the narrow overlap in the parties' drugs and (ii) any of the MoAs associated with the overlap in the parties' drugs.[200]

[198] One exception is that, for Licensing deals, we use the presence of an Exclusivity clause to select the subsample of observations that are identified as the treated group in the quantitative analysis, as explained in Box 7.

[199] For example, the fact-finding challenge cannot automatically retrieve and review or process large volumes of documents such as official company filings, investor presentations and presentations at industry conferences, though these are typically published online by many major pharmaceutical companies. These documents may help a competition authority find evidence of the parties' intent in undertaking an acquisition, though it is perhaps unrealistic to expect that either party might express, prior to closing of the deal, an expectation that viable projects of either party will be eliminated (rather than combined to obtain anticipated efficiencies or sold). Recommendations on such additional reliable information sources are provided in the evaluation challenge.

[200] We acknowledge that this approach is used as a proxy and might miss some competitive overlaps by focusing on more advanced TIs to identify competing drugs in cases where we do not detect a perfect overlap in TI. However, we prefer to avoid inflating residual competition by counting molecules that may never develop in the relevant TI. Consider, for example, the case of an overlap between an early-stage molecule that is

The variables we use to measure the intensity of competition are the following:

- Number of competing drugs. This consists of the total number of competing pipeline products that are in active development and drugs that have already received marketing approval (including branded drugs after the entry of generics and biosimilars). This is in line with the principle that the larger the number of competing molecules other than the two parties' molecules that are in narrow overlap with each other, the stronger the competition.
- Highest stage of development of competitors.[201] This is a synthetic discrete indicator we employ to capture the strength of competitors, spanning from a pipeline range (stages 1 to 3) to marketed drugs (stage 4) – we impute a stage 0 in markets where there are no competitors. Therefore, the indicator takes values from 0 to 4 and is increasing in the strength of residual competition. Moreover, combining the highest stage reached by competing molecules with variables that indicate the stage of development of the parties' overlapping products, allows to shape an indicator that accounts for the relative strength of competing molecules with respect to the parties' overlapping products.
- Type of competing sponsor. We construct a binary variable taking value 1 when all developers of the molecules that compete with the parties' overlapping drugs are private members of the pharmaceutical industry (i.e., where trial registration data identifies no public/non-profit institutions as a sponsor or collaborator of any competing pipelines).

The first indicator is in line with the principle that the larger the number of competitors the stronger competition. The other indicators, instead, are meant to capture the relative strength of competitors (they generally take positive or higher value when the relative strength of the competitors is higher).

Another fundamental indicator to assess the incentives and ability for a killer acquisition is the stage of development of the overlapping products at the time of a deal. We construct a variable for each R&D drug project in the overlap that measures its stage of development, spanning from a pipeline range (stages 1 to 3) to marketed drugs (stage 4). We then use dummy interactions to study the effect of the relative stage of development of the overlapping molecules.[202]

Finally, we construct a deal-level indicator for licensing deals to flag the exclusivity of licensing: we build a variable that takes value one when the terms of a licensing agreement include an exclusivity clause. Information on exclusivity is not structured in the datasets we collect. We are able to parse the information based on a keyword

being tested for treatment of "solid tumors" and a molecule at a more advanced stage of development that is being tested for treatment of "breast cancer". The parties' apparent competitive set might be too broadly defined and provide false comfort if we identified competing drugs with reference to "solid tumors". On the other side, when overlapping drugs share multiple MoAs, identifying competing drugs as any drug sharing at least one of the overlapping MoAs – as we do – imposes the least possible constraint on competitors.

[201] We prefer to assess weakness/strength of drug projects in terms of their highest stage of development which has a clearcut relationship with the overall average phase-specific probability of approval of drug projects, unconditional on firm-specific experience in clinical development. The pharmaceutical Experts on the Team note, indeed, that many (perhaps most) new drugs now originate with relatively small developers, rather than Big Pharma, and CTOs can assist small/new developers in overcoming many trial hurdles that otherwise might lead to discontinuation of a study.

[202] For pipelines, the phase will be determined using as a reference the most advanced phase for which studies are registered in the relevant TI at the time the deal was agreed.

search within an unstructured free text description of deals, which is part of the Adis Deals dataset.

I.4.2 The LASSO model

In section I.4.1 we have discussed the variables that can help predicting whether a transaction the risk of a transaction being a *prima facie* killer acquisition. These have been selected among the features proposed in the literature, with the wisdom of industry experts in the Team and in light of the limitations of the data at hand. However, we still need to investigate which values and combinations of the variables discussed are best suited to predict the risk of a killer acquisition. Knowing which values and combinations of the variables matter would help the goal of the *fact-finding* challenge of identifying *prima facie* killer acquisitions among deals occurred in the past; and may also guide competition authorities in determining which acquisitions deserve further scrutiny in the future.

With the benefit of hindsight, based on publicly available evidence on the discontinuations, we have identified narrow overlaps where there were either no discontinuations or benign discontinuations – which are *prima facie* unlikely to be KA – and, by contrast, those that *prima facie* appear relevant for a KA assessment.

A LASSO solution selects the model covariates that best replicate an observed outcome of interest. However, we do not have a real "training" sample, i.e., a set where we observe the outcome of interest (killer acquisitions and non-killer acquisitions of overlapping drugs; nor do we know in advance *prima facie* and non-*prima facie* KA) to inform the selection algorithm. There is a problem of circularity in the objectives pursued – identifying which *prima facie* relevant discontinuations display the features of a KA and identifying the features most suited to predict the risk of a KA – which impairs the assessment.

To overcome the problem, the analysis is structured into several steps:

- we first devise a hypothetical training sample that is as good as possible, consisting of a treated group and a control group, exploiting factual elements that do not depend on the variables we want to validate;
- we use LASSO, a machine learning (ML) algorithm, to obtain the combinations of the variables' values that best predict the treatment in this restricted sample; based on these results, we draw a list of the discontinuations that display the features selected by the LASSO solution (LASSO-KAs) from the larger set of discontinuations classified as *prima facie* relevant for the KA assessment;
- we corroborate the quantitative methodology with a case-specific manual screening based on desk research (details will be discussed in section I.4.3)

To build a training sample for the quantitative analysis, we need two groups of observations that act as treated group and control group: treated and control observations are those where the binary variable that indicates the treatment takes value of one and zero, respectively. Ideally, the treatment variable should equal one when there is a discontinuation that is a killer acquisition, and zero when there is no discontinuation or where the discontinuation did not occur for anticompetitive reasons. Discontinuations that likely did not have an anticompetitive object or effect should be most likely to be found among those that we classify as benign, which we therefore assign to the control group. The control group also includes narrow overlaps where no discontinuation has been detected. On the contrary, discontinuations likely having an

anticompetitive object or effect should be most likely to be found among those that we classify as *prima facie* relevant cases for a KA assessment. Therefore, the treated group is selected from observations in this set: starting from *prima facie* relevant discontinuations, we adopt a more restrictive filtering of the observable (direct or indirect) evidence on (or lack of) reasons of discontinuations, to identify a new subgroup that would more likely exclude uninteresting cases. Box 6 explains in more detail how the treated group is selected.

Box 6: The Treated Group

The treated group is selected from the set of *prima facie* relevant cases for a KA assessment. For discontinuations that follow from a lack of progress in clinical development (type B), for which there is no other meaningful evidence to be analysed, treated observations are those that do not involve public or non-profit institutions, but only pharmaceutical companies as sponsor and/or collaborators. The literature indeed suggests that competition may be more robust where studies are financed or conducted by public agencies or other non-profit entities, because such entities are less likely to discontinue drug projects for commercial reasons (Lièvre, et al., 2001).

For discontinuations that follow from the withdrawal or early termination of trials (type C), treated observations are selected based on reasons stated in the clinical trial public registry that refer to strategic considerations and financial or cost-related decisions, as also reported in the medical literature (Iltis, 2005; Scott & Magnus, 2014; Turner, et al., 2020). We carry out a textual analysis using keywords to delimit the following factors (as illustrated section I.3.2):[203]

- Business or commercial reason(s)
- Sponsor or Collaborator decision(s)
- Financial reason(s) or budget limitation(s)
- Strategic consideration(s) or change in strategy

We also include in the treated group discontinuations whose trials are terminated/withdrawn without any disclosure of the reasons. This is in line with the assignment to treatment of group B discontinuations (a lack of transparency is the hallmark of both).

The likelihood that the above reasons, or the absence of any disclosure, suggest that the acquirer discontinued the research project to kill competition is possibly higher when the sponsors and/or collaborators are pharmaceutical companies. We hence impose also to all type C discontinuations the additional condition that there are no public or non-profit institutions among the sponsors and/or collaborators.

We then use LASSO regression, an ML technique, to establish the significance of the proposed variables as predictors of a possible KA. As documented in the literature, ML techniques are particularly effective in solving prediction policy problems (Varian, 2014;

[203] The textual analysis has been shaped to capture the following occurrences, among other: "Competing studies", "Company decision to discontinue the study, not due to any safety or efficacy concerns", "Financial business decision", or "Internal company decision".

Kleinberg, et al., 2015; Decarolis & Giorgiantonio, 2022).[204] The idea behind ML algorithms is to consider a family of models and use the data to select the one that best replicates the observed data or to choose tuning parameters through cross-validation.[205]

The LASSO fits a regression (e.g., linear or logistic; we adopt a logit-based one) with the additional constraint of applying a penalty for having too many variables in the model (playing a role in identifying which predictor variables are important for the response variable). In addition to selecting the variables to include in the model, the LASSO can help to identify appropriate value thresholds above or below which an explanatory variable is significant in prediction.[206]

Thus, LASSO regression identifies the indicators and their significant values that can best predict an observed outcome of interest. In our setting, the LASSO results are driven by the differences in the values of the indicators between the treated and the control groups. In other words, the indicators that pass the validation exercise, i.e. the ones proposed in the LASSO solution, are those that are able, on average, to discriminate between observations that display a preliminary assessment – informed by the large-scale analysis – of the outcome of interest; ideally, this outcome should identify KAs, but in our setting we do not observe them directly (the treated group is composed of the *prima facie* "more likely relevant discontinuations"; the control group of no or benign discontinuations, which are *prima facie* unlikely killer acquisitions).

We identify as LASSO-KAs prima facie relevant discontinuations for a KA assessment that also satisfy the conditions defined by the LASSO model solution.[207] Box 7 provides an overview of how we build the LASSO regression model.

While the LASSO is a rigorous empirical method to test and measure the relevance of variables to be included in a model, the identification strategy in our assessment is constrained by the lack of data on the true outcome of interest: we do not observe actual killer acquisitions; we use a tentative identification of the treated and control groups for discontinued and non-discontinued overlaps. This limitation might bias results and is addressed by carrying out a manual screening on all the LASSO-KAs identified as well as on several the remaining *prima facie* relevant discontinuations (details are discussed in section I.4.3).

A typical limitation of the LASSO regression is that it does not provide a unique solution under all conditions. In quite common settings like ours (where the parameters of

[204] Varian (2014) and Kleinberg, Ludwig, Mullainathan, & Obermeyer (2015) are methodological papers. Decarolis & Giorgiantonio (2022) is an empirical study that uses ML algorithms to assess the validity of various quantitative indicators (i.e. red flags) to detect corruption in public procurement relative to a firm-level measure based on police investigations for corruption-related crimes. We note an interesting parallel between our study and the latter paper, although they explore different contexts and research questions.

[205] The goal of ML analysis is to use a training dataset to select the best prediction model that could be applied in a different dataset where only the regressors are observed.

[206] The variables of interest assume either binary or discrete values. Binary variables will take value one when indicative of a potentially anticompetitive object or effect (and zero otherwise). While for binary variables a model implicitly provides insights on whether they are significantly associated with a phenomenon of interest, for discrete or continuous variables a model should also depict whether they matter above certain specific values. We transform discrete variables into binary indicators of their categorical distinct values, or use binary transformations at significant thresholds. See Box 7 for more details.

[207] In our first estimation of the model in the sample of M&A deals, the LASSO selects only one regressor, i.e. the interaction between: one of the overlapping molecules in Phase 4 (i.e., marketed), one of the overlapping molecules in Phase 2, and maximum number of competitors in the market equal to 3.

interest are discrete, and the number of observations is greater than the number of covariates) different combinations of the regression variables might predict the outcomes of the training sample. However, the sign of a regressor coefficient is always consistent across any possible LASSO solution where that variable is part of the solution (a relevant property, that is for instance not true of normal regressions).[208] Thus, any selected regressor with a positive coefficient in one solution is positively associated with the outcome of interest in all solutions where it can be selected. The non-uniqueness of the solution may be a challenge to our goals, as a single iteration of the procedure may not capture all the relevant criteria. Therefore, we run the ML algorithm several times and collect all the different solutions, when they change, to enlarge the captured set of criteria apt at predicting possible KAs.[209]

Box 7: LASSO regression model

The goal of our analysis is to identify among the indicators discussed in section I.4.1 those that can best predict the likelihood of a killer acquisition, starting from a set of deals that we can qualify *prima facie* as such (based on factual elements that do not depend on the variables we want to validate). We employ a LASSO regression model to answer our research question.

In our setting, the "training" dataset is composed by a treated group and a control group with observations at the level of narrow overlaps: the dependent variable is an indicator variable that takes the value 1 for the treated group (*prima facie* "most likely relevant discontinuations") and 0 for the control group (narrow overlaps where no discontinuation occurred, or only benign, i.e., *prima facie* unlikely killer discontinuations).

The regressors (or predictor variables) are the indicators, when they are binary, or a binary transformation of the original indicators, that can predict the likelihood of killer acquisition ability and incentives.

For variables that can take a range of discrete values, we need to transform each regressor into a set of dummies identifying different values, so that the LASSO regression can identify the values that best predict the outcome, by selecting the relevant indicator variables.

We include the following regressors in the LASSO regression:

- Four-fold interactions between: dummy indicators for the phase of development of each overlapping molecule; a dummy indicator for the number of competitors on the market ranging from zero to five; and dummies for the maximum phase reached by the competing molecules (that share the same TI-MoA identifying the relevant narrow overlap in a transaction), where our count of competing molecules also includes pipelines and not only marketed products;

[208] A parameter is said dispensable when there are LASSO solutions where the model fit is obtained without that parameter (i.e., that LASSO's solutions shrink its coefficient to zero). Not all dispensable parameters at the same time are out of the support of a solution and in the support of another. Combinations may vary. However, the coefficient of dispensable parameters will never appear with the wrong sign (at most, the coefficient shrinks to zero in some solutions).

[209] We only ignore combinations of predictors that in all replications display a standardized coefficient always close to zero.

- an indicator for competing molecules with only pharmaceutical companies as sponsors and collaborators.

By including the four-fold interaction, we let the model select the combinations of variables that better capture the systematic features in which the *prima facie* most likely killer acquisitions differ. To select LASSO-KAs, we consider only combinations where the number of competing drug projects does not exceed a threshold of five to be indicative of a killer acquisition narrative (i.e. we impose a constraint and avoid selecting combinations that are associated with treatment but also fall into the class of more than five competitors). This is in line with findings in the literature on killer acquisitions and the advice of our Team industry experts. We deem this adjustment necessary given that we do not observe the outcome of interest. At the same time, manual checks offer the chance of also evaluating this criterion.

We also control for some factors that might indicate the degree of precision that characterises the narrow overlap identified:

- whether the narrow overlap implies a perfect match in the MeSH term that we use to delimit the therapeutic indication in which the overlapping drugs potentially compete;[210]
- whether the overlap in MoA is not perfect in structured data but established through our automatic search of the medical literature;
- whether the most advanced MeSH term in which the Parties' drugs overlap is not yet quite specific: this is a dummy taking a value of one if that MeSH term identifies only the first, broadest node of a branch in the hierarchical classification of diseases. Such a characteristic of the MeSH term of overlap can be correlated with the number of competitors we identify, because the first node is often listed in clinical trials where drugs are already being tested in more advanced TIs (e.g., when MeSH term is as broad as "Neoplasms", the number of competitors will be systematically higher than sample average).

We run the model on the treated and control groups for the different deal types separately and let the LASSO select the relevant regressor(s).

For Licensing and R&D agreements, we apply the refinements listed below to improve the quality of the training or estimation sample prior to running the model:

- Licensing deals. There are two peculiarities of licensing deals that lead us to impose a further structure on our LASSO model for predicting possible KAs. First, a licensing deal does not necessarily give the licensing-in firm exclusive control over a drug and thus the ability to implement a KA, unlike, for example, an asset purchase. Accordingly, we restrict the estimation model's dependent variable to treated discontinuations that follow licensing deals that have the characteristic of being exclusive.[211] In addition, unlike M&A and purchase deals, licensing deals may be temporary, ending with the subsequent transfer of rights back to the licensing-out firm. Therefore, we restrict the estimation sample to licensing deals

[210] An imperfect narrow overlap arises when the MeSH Terms of the two overlap drugs are different but one is an offshoot of the other based on the MeSH Tree hierarchical structure. E.g., Arthritis, Rheumatoid [C05.799.114] is an offshoot of Rheumatic Diseases [C05.799]. Thus, an imperfect overlap is found between two drugs if one drug's MeSH is Arthritis, Rheumatoid, while the other's is Rheumatic Diseases. By contrast, a perfect overlap arises if both drugs share exactly the same MeSH Term.

[211] See section I.4.1 for definition of how we measure exclusivity in licensing agreements.

with a defined drug object whose status is still 'active' (and then apply the criteria selected by LASSO to all identified discontinuations that are *prima facie* relevant for a KA assessment, including terminated/completed deals as well).[212]

- R&D agreements. Due to the specific characteristics of R&D agreements, we impose restrictions on the estimation sample to improve the precision and reliability of our predictions regarding possible KAs. First, similar to Licensing deals, we only include deals with an 'active' status. In addition, we only include cases where a drug is uniquely associated with an R&D deal. This decision is driven by our concern that multiple associations of the same drug to different R&D deals may signal a degree of ambiguity as to the accuracy of the link between the drug object and the deals in question.[213]

Last, we apply the "filters" or criteria selected by the LASSO model to the entire group of discontinuations that we have identified as *prima facie* relevant, to yield the set of LASSO-KAs that will be subject to the factual and quality verification of the manual screening.

I.4.3 Role of the manual screening

The manual screening of discontinued overlaps is used to check the inputs and the outputs, or the findings, of the large-scale analysis through the lens of a case-specific desk research. It has the advantage of overcoming at least some of the limitations of the large-scale analysis. Though always having access only to publicly available data, it relies on a reasoned analysis of evidence that is not limited to structured data and can consider information that could not be used in the large-scale assessment both in terms of diversity of sources and of more updated information.

It may highlight possible limitations deriving from ambiguities of data inputs or from the simplifying assumptions needed to standardise the large-scale analysis; and it can uncover and collect additional evidence beyond the public data sourced for the large-scale analysis. Additional evidence can originate from recent events out of the data range covered by the datasets built for the large-scale analysis (which extend until June 2022); or can originate by different sources and/or types of information, such as articles in the medical literature where clinical trials results are discussed, companies' websites, reports and filings, and pharmaceutical media outlets.

From a practical point of view, in conducting manual screening, the Team pursued two main objectives: checking the correctness of large-scale analysis findings; and carrying out desk research on the characteristics of the deal and the relevant discontinued overlaps. Further details on the type of checks and of desk research are described in Box 8.

[212] In constructing the dataset, we eliminated deals that that were terminated in the same year as they were initiated. The reason for this is that it would otherwise be difficult for us to identify their effects. The number of deals in our sample, as shown in Table I.1 and consistently in subsequent tables in this report, reflects this preliminary cleaning process. We provide further details on data cleaning and sample selection in Appendix A.1

[213] This problem is particularly pronounced for R&D agreements: among the 2,513 deal-drug associations identified, we observe that each drug generates on average three different deal associations, and, remarkably, a single drug can be the object of up to 44 deals. In comparison, the average number of deal associations for purchases is 1, with a maximum of 3 associations, while for licensing deals the average is 1.5, with a maximum of 8 associations.

There are at least two intertwined motivations for manual screening. The first is to identify transactions for which there is no publicly available evidence to justify the discontinuation for technical or commercial reasons unrelated to the deal and where, on the contrary, there is some evidence to support, at least *prima facie*, a "killer acquisition" theory of harm. The second is to validate the findings of the quantitative LASSO analysis: as long as transactions that seemingly align with a KA narrative are well predicated by the LASSO solution, or as long as the features selected by the LASSO solution are consistent with the specific KA narrative found by desk research, then they could inform, or at least complement, ex ante monitoring to flag transactions that deserve the attention of competition authorities.

However, it is important to reiterate the need for caution: information about commercial incentives of firms is quite unlikely to be found in the public domain. What can be possibly found in the public domain are only pieces of information that can appear more (or less) in line with a KA narrative, but they will hardly provide any degree of certainty. Even in cases where no evidence is found alternative to a KA narrative that explains the discontinuations, or all elements collected are aligned with that narrative, there could still be private information not accessible to the Study Team that proves that this is not the case. It would be unwise, then, to expect that availing public information only, the Study Team could be conclusive on this point, at least in most cases; and in any case the assessment cannot be claimed to provide any certainty.

The manual screening has covered different sets of discontinued overlaps to a varying extent. A more in-depth assessment has been devoted to:

- all LASSO-KAs for deal types where LASSO machine learning algorithm was applicable: M&As; Licensing and R&D agreements;
- all *prima facie* relevant discontinuations for deal types where LASSO was not applicable: Purchase, and a miscellaneous of other deal types ("Other deals").

To be able to evaluate the robustness of the LASSO results, a high-level screening of the remaining *prima facie* relevant discontinuations (those that do not share the features selected by the LASSO solution) was also performed for M&A deals; and for licensing deals where the large-scale analysis detected an "exclusivity" clause. It is worth reminding that a deal may entail many different narrow overlaps between the same drugs in different TIs or for different drug pairs at different stages of development in their TIs (one drug can be paired in multiple overlaps with different drugs, in the same TI or in different TIs). Of all the narrow overlaps found for a deal, some may be discontinued, and some of these may also be identified as *prima facie* relevant discontinuations; of the latter, it is usually the case that only some are selected by the LASSO algorithm based on the characteristics of the overlap. The manual screening, although focused on a specific *prima facie* relevant discontinuation flagged by LASSO, may also indirectly provide information on other overlaps involving the same drug for the same deal.

Box 8: Description of manual screening methodology

In conducting manual screening, the Team leveraged the technical and legal experience of the experts of the Team, with more than ten-years' experience in the assessment of commercial and technical potential of important R&D projects in the pharmaceutical industry.

The manual investigation followed a sequential approach described in detail below and can be divided in two main phases: i) checking the correctness of the findings of

the large-scale analysis, and ii) deeper desk research on the characteristics of the deal and the relevant discontinued overlaps.

1. Large-scale analysis checks

The objective of large-scale analysis checks was to ascertain, through desk research, the accuracy of the results of the large-scale analysis. These checks were carried out in several stages, divided by the relevant variables under investigation, and consisting of the following:

Reading about the deal and making sure it had taken place and that the companies involved, and the relevant TI were correct and indeed related to the deal. The main source for this step was Adis, complemented with further desk research (e.g., pharmaceutical media outlets or companies' websites).

Making sure the drugs were indeed owned by the indicated companies at the time of the deal and thereafter (the drugs might have been licensed or sold after the deal). The sources used were Adis and companies' websites and reports.

Making sure the molecule status (i.e., the highest phase reached by the molecule in any TI) was correct, through use of Adis and CT.

Ensuring that the MeSH terms and codes were correct for each drug (i.e. that the TI as identified by the MeSH term was correct and that the drugs were both actually active before the deal in that MeSH term) using Adis, CT and the MeSH vocabulary214 to cross-reference the MeSH codes.

Ascertaining the correctness of the MeSH status after the deal using Adis, CT and further desk research where necessary.

It is important to note that, in cases where the large-scale analysis checks would reveal significant errors, the manual screening would not be taken forward. For example, if the first phase of the manual screening revealed that the deal never actually took place, or that the drugs were not really owned or developed by the relevant companies, no further research would be conducted on that deal or overlap. For the vast majority of deals and overlaps, only errors of uncertain impact were identified, and the manual screening was taken to the second step.

2. Further research

The objective of this subsequent phase in the manual screening is to ascertain, through the analysis of supplementary qualitative data, whether there is sufficient publicly available evidence to build a killer acquisition narrative. This involved the following sequential checks:

Investigating whether the drugs are indeed substitutable. This step consists of ensuring that the drugs indeed have a sufficient degree of substitutability. From a TI perspective, this means that the drugs' development paths coincide, or at least that the drug which was linked to the broader MeSH had the potential to be pursued in the narrower TI. When it comes to MoA substitutability, the step consists of ensuring that the MoAs of the drugs are indeed such that both drugs can be used to treat the relevant TI with similar enough therapeutic path and potential. The research starts with relevant scientific and/or pharmaceutical website articles, which can be referred

[214] https://meshb-prev.nlm.nih.gov/search.

to the experts for confirmation if no straightforward answer is found by the Team. This step is crucial in confirming a KA narrative, as substitutability is a key element of this theory of harm.

Investigating potential technical reasons for discontinuation, if available. This step starts with Adis and CT investigations, moving on to research articles, EU CT reports or press releases related to the relevant drugs. If we find evidence that the discontinuation might be due to technical reasons, then the deal will not be a prima facie KA. For example, serious adverse events such as death or toxicity, or lack of efficacy reasons such as failure to meet primary endpoints are considered valid technical reasons for discontinuation. Other, less evident, technical issues, such as lighter adverse effects or low, but existent, therapeutic impact are then taken to the experts, who compare the discontinued drug's trial results to the latest comparable compounds that reached the relevant market (and are not owned by the companies taking part in the deal). Only if the experts confirm the discontinued drug's significant inferiority compared to competing molecules can the discontinuation be considered technical.

Investigating the competitive landscape. An anticompetitive object or effect is necessary for a deal to be considered a KA, and it is a priori unlikely that an anticompetitive effect will arise in a market with intense competition, especially when the market is not highly differentiated. Thus, in order to ascertain the likelihood of a deal being a KA, it is necessary to understand the competitive landscape in the relevant market at the time of the deal. In fact, the large-scale analysis approximates this using the number of competitors in the relevant market proxied by the combination of TI and MoA. This is manually verified using sources such as Adis, CT, Scrip[215], and any sector article or other public information that can help understand the scope of the relevant market and the number of competitors (e.g. past EC decisions). Moreover, given that the number of competitors is only a proxy for the state of competition, any qualitative information on the strength of competitors, especially the closest ones, will help conclude whether the deal could be a likely KA.

Examining the existence of patents or generics. If there are generics in the market, we assume the deal is highly unlikely to be a KA because of the above-mentioned competitive dynamics conditions. In fact, it would be a priori difficult for a discontinuation of a drug to lead to an anticompetitive effect if there are substitutable generics available on the market which would offset a possible increase in price or decrease in variety of supply. In our ex-post evaluation, generic entry is used as an indicator that the relevant patents on a drug have expired at the time of the deal or were close to expiration (with the benefit of hindsight). This helps to overcome limitations and difficulties in the use of patent data (see section I.1). However, selective desk research on the existence of patents has been used when generics have not yet entered the market in order to better understand the competitive environment.

Finally, any additional news around the dates of the deal is investigated. These can support the theory of a KA such as artificially high deal value, or a dominant position of the acquirer in the relevant market. Alternatively, they can dispute the KA theory

[215] Scrip is a website (scrip.citeline.com), for which the Team bought a subscription, that provides extensive coverage of articles on the pharmaceutical sector. The company that owns Scrip used to be a part of Informa, but that is no longer the case due to a recent restructuring.

such as any tentative by the originating company to discontinue the drug before even the closure of the deal. Sources for this are Scrip, Adis and any other sector articles or publications.

In this phase as well, it is important to point out that, if during one of the steps any evidence shedding doubts over an otherwise clean KA theory is found, further research is halted. For example, if some evidence on serious adverse effects caused by the drug is found, no further research on the competitive landscape or the likes is conducted (even if the evidence that we are able to collect is always accompanied by an unavoidable degree of uncertainty).

I.5 The findings

Having discussed the general strategy for the *fact-finding* challenge, in this section we present the findings of our analysis.

Box 9 summarises the most important challenges we have faced in constructing our data. First, our study relies on public data sources with no access to private information regarding firms ongoing and planned projects around deals. The number of deals and of narrow overlaps that have informed our analysis, based on the large-scale reconstruction of deals object and of the overall firms' portfolios, overlooks undisclosed information on the scope of the deal, projects in pre-clinical development and knowledge about internal firms' plans. The large-scale analysis also faces the additional constraints of accessing only a subset of data inputs among those available in the public domain. Box 9 summarises the caveats and challenges that might have affected the set of deals that have informed our study, the identification of narrow overlaps, discontinuations and their subsequent classification, as well as the final findings.

Box 9: Data limitations that might affect the findings

Factual and counterfactual scenarios are difficult to assess with only public information that does not help accurately addressing commercial incentives of the parties, the underlying rationale of a discontinuation, the reconstruction of the relevant market (including the closeness of competition), and potential effects on competition. This aspect has challenged both the large-scale analysis and the manual investigation of deals.

As usual, a large-scale analysis requires simplifying assumptions and the use of sufficiently structured datasets that may miss some relevant information (for instance, information contained in news releases or company filings). We also combine several complementary data sources, which may always imply some loss of information (notwithstanding the adoption of control quality procedures).

The output of the large-scale analysis is the starting point of the manual investigation, since the latter is based on the large-scale identification and classification of discontinuations of narrow overlaps. The manual investigation mostly relied on public information as well, even though the assessment combined more diverse sources in a more flexible and case need oriented fashion.

Deals and/or overlaps cannot be comprehensively analysed for several reasons:

- we do not observe pre-clinical development of drugs nor development plans of companies for the near future. In some instances, one of the parties to a deal does not have any drug project registered in clinical trial data before the deal. This

may bias results leading to an underestimation of narrow overlaps and discontinuations (the effect on the relative frequency of discontinuations could go in either direction, though). The impact on our analysis varies according to the type of deal: for M&A deals, we would still examine the deal (unless one of the parties has only preclinical projects in its portfolio), but we would only track overlaps with pipelines in clinical development; for limited scope deals, if the object of the deal is in the preclinical stage, we would not be able to identify it in our clinical trial data and thus the deal would not lead us to identify any overlap – this problem is most pronounced for collaborative agreements that are typically entered into at an early stage of research, such as R&D agreements. Another problem relates to the fact that information on the drugs and TIs targeted by deals with a limited scope is often undisclosed in retrievable data (relevant for all non-M&A deals, e.g. Purchase, licensing, R&Ds and all other types of collaborations).

- Information reported in clinical trials is key for our study: we use it to reconstruct firms' portfolio of drug projects before a deal and thereafter based on sponsors' and collaborators' status, to identify the TIs in which drugs are tested through MeSH codes listed by the responsible party, to follow development of drugs in different TIs over time through their initiation and updates, to detect drug projects termination or lack of activity once they are terminated. As with any large data source that is the result of manual compilation, information in clinical trials may suffer from inaccuracies and may not be complete – for example, reasons for discontinuation may not always be reported. However, the legal requirements that govern the registry at least partially mitigate this concern; and yet, to the best of our knowledge, no other public database would provide the same wealth of information that CT has and that the present study requires. Nevertheless, some inaccuracies and missing information may have important implications for the analysis: for example, MeSH terms related to the condition being studied in a clinical trial, although derived from a predefined dictionary, may not always provide accurate information (e.g. may refer to a broader therapeutic area). In addition, the registry does not systematically allow for the identification or differentiation of combination therapy trials, for which the association of the relevant MeSH terms may not be appropriate for all drugs tested in combination.

We investigate only drug projects that "narrowly overlap" in both TI and MoA:

- although we attempt to expand the concept of overlap to capture potential substitutability between seemingly different MoAs, overlaps in TI only (i.e. broad overlaps) fall outside the scope of this study – further research may help to shed light on the extent to which these may also motivate anticompetitive discontinuations;
- the definition of narrow overlap to identify potentially substitutable drug projects is based on TI and MoA. TI is proxied by the MeSH coding of diseases. To avoid overcounting discontinuations, we do not detect a discontinuation, for example, when a drug found in overlap before the deal in Infections [C01], is afterward tested in Corneal Ulcer [C01.375.177]. The rule is that we detect development if after a deal a drug is tested in a MeSH code that is the same or contains the MeSH of overlap before the deal.
- Publicly available information may be too limited to properly assess the closeness of competition between different drugs, even when conducting manual screening: limited information on clinical trial results may not allow a sufficiently detailed assessment of the efficacy and safety profile of a pipeline drug and how it compares to another competing drug.

- Assessing substitutability is even more challenging when studying pipelines at different stages of development, and the further they are far from the market (also because the available clinical data is more limited for early-stage pipelines). While the large-scale analysis detects such overlaps and discontinuations, a deeper assessment of substitutability between drugs when one of the two has not been tested in exactly the same TI of the other, but only in a related TI, is complex, as there may be at most indirect evidence that the discontinued drug could potentially have expanded in that TI, if at all – this assessment is made in the manual screening.[216]

Finally, the study has expanded the notion of discontinuation to track drugs' reorientation after the deal but – as per the project Technical Specifications – does not detect delay in development, which is then not considered as a potential anticompetitive outcome following deals.

Though expanding deals studied to transactions different from concentrations, and accounting for the majority interests of parents and subsidiaries of the companies directly involved in deals, the possible effects of minority shareholdings across pharmaceutical companies and of common shareholding by financial investors are out of scope of this study. Such interests may also produce effects on ability and incentives to cause a killer acquisition.

Table I.4 and Table I.5 summarise the results at the deal level and at the narrow overlap level.

[216] Suppose that prior to a deal, one of the two overlapping drugs was tested in Infections [C01] and the other in Eye Infections [C01.375]. If, after the deal, the first drug is discontinued, it will be difficult to establish whether that drug had the potential to develop into the treatment of Eye Infections. In this case, the Teams' experts can help to assess realistic prospects for the drug, e.g. by looking closely at its MoA to assess whether it may be indicative of potential development in the narrower TI (note that a narrow overlap may be established even if MoAs are not identical; also, MoAs definition in our database may be quite broad in some instances). Desk research on the companies' statements, as well as on the patient population and trial results, can help to better assess potential substitutability. Conversely, if the drug in the narrower TI is discontinued after the deal, but the surviving drug has never evolved in that TI (in the example, from Infections [C01] to Eye Infections [C01.375]), this may indicate that the discontinuation was not motivated by a KA strategy. Still, it may also be difficult to assess whether the fact that the surviving drug was never developed in the narrower indication was due to a technical reason, and whether this could have been anticipated by the acquiror, without additional clear evidence that we do not have access to in the public domain.

Table I.4: Findings at the deal level

Deal Type	Deals (total 2014-18)	Deals with an identified object or target	Deals with at least one narrow overlap	Deals with at least one narrow overlap discontinuation	Deals with at least one prima facie relevant discontinuation	Deals with any LASSO-KA
M&A	490	485	35	28	19	6
Licensing	2,920	1,219	99	72	27	9
(Exclusivity)*	(1,256)	(583)	(52)	(36)	(12)	(6)
R&D	2,438	1,169	87	69	37	4
Subtotal	5,848	2,873	221	169	83	19
Purchase	319	229	12	9	4	N.A.
Other deals**	148	91	7	5	5	N.A.
Total	6,315	3,193	240	183	92	N.A.

Source: Lear analysis.
*Notes: *Exclusivity: this row of the table provides details about "exclusive" licensing agreements, that are identified applying search text tools to the description of the deals available in our deal dataset. **For the group Other deals, prima facie relevant discontinuations are in the following deal types: Equity investment (2 deals), Joint venture (1 deal), Joint venture R&D (1 deal), Marketing agreement (1 deal). The group also includes Partnerships and Cross-Licensing agreements, for which no discontinuation of narrow overlaps is found.*

As shown in Table I.4, our data includes 6,315 transactions that took place in the pharmaceutical sector during the period 2014-2018, of which 3,193 have an identified object and therefore have informed our analysis.[217] The study shows that only 240 deals have put under the influence of the same firm at least two narrowly overlapping drug projects (based on both TI and MoA), i.e. drug projects that the large-scale analysis

[217] The difference refers to deals excluded because we could not identify one or more 'drug objects' targeted by the deal, notwithstanding the procedures to fill gaps in the sourced data, explained in section I.2.3. We might still identify a pre-clinical drug project as a deal object whenever that drug project gets an early profile in the AdisDrugs dataset. However, if we find no clinical trials for that drug dating before the deal, that project would not lead us to identify any overlap. Therefore, the deal may still be among those that informed our analysis, but that project would lead to "no overlap", as overlaps are defined only in the clinical stage drugs space.

identifies as potentially substitutes and that presumably, absent these deals, would have been rival in development.[218] While most of these transactions, 76% (i.e. 183), were followed by at least one discontinuation, about 38% (i.e. 92) were followed by at least one discontinuation that we have identified as *prima facie* relevant for a killer acquisition assessment (54% in M&As, 27% in Licensing, 43% in R&D). LASSO KAs are then identified among the types of transactions to which LASSO can be applied, namely M&A, Licensing and R&D agreements.

As shown in Table I.5, *prima facie* relevant discontinuations of drug projects, i.e. those seemingly unrelated to technical and clinical reasons, have a different relative frequency within deal types. *Prima facie* relevant discontinuations amount to 7% of the narrow overlapping drug projects in M&A, 10% in Licensing, 15% in Purchases and 12% in R&D. In "Other" deal types, *prima facie* relevant discontinuations amount to 9% of the number of narrow overlaps, explained mostly by Equity investments (with 5 *prima facie* relevant discontinuations) and Marketing Agreements (with 3), followed then by JV and JV R&D (one on each side), while in Partnerships and Cross-Licensing agreements no *prima facie* relevant discontinuation is found.

As a share of the total number of discontinuations detected among overlapping drug projects, *prima facie* relevant discontinuations represent 19% in M&As and Licensing, 33% in R&D, 37% in Purchases and 13% in "Other" deal types (24% overall).[219]

[218] This is difficult to assess for deal types as R&D agreements, where the actual exchange of rights in the deal is mostly of unknown nature, as discussed in Box 10.

[219] As an example, in M&A 19%=120/634; in Licensing 19%=97/510. That is to say, in M&A we identify 120 prima facie relevant discontinuations out of 634 discontinued narrow overlaps; and in Licensing, out of a total of 510 narrow overlaps that are discontinued, 97 of them are classified as prima facie relevant discontinuations. A similar calculation applies for the other deal types.

Table I.5: Findings at the level of narrow overlaps between drug project pairs

Deal Type	Narrow overlaps	Narrow overlaps with discontinuation	Narrow overlaps with *prima facie* relevant discontinuations	LASSO-KAs
M&A	1,723	634	120	35
Licensing	991	510	97	13
(Exclusivity)*	(298)	(198)	(30)	(9)
R&D	2,199	800	263	5
Subtotal	4,913	1,944	480	53
Purchase	65	27	10	N.A.
Other deals**	116	75	10	N.A.
Total	5,094	2,046	500	N.A.

*Source: Lear analysis. Notes: *Exclusivity: this row of the table provides details about "exclusive" licensing agreements, that are identified applying search text tools to the description of the deals available in our deal dataset. ** For the group Other deals, prima facie relevant discontinuations are in the following deal types (counts of narrow overlaps in parentheses): Equity investment (5), Joint venture (1), Joint venture R&D (1), Marketing agreement (3). The group also includes Partnerships and Cross-Licensing agreements where no discontinuation of narrow overlaps is found.*

Following the methodology described in section I.4, we have conducted further investigations of the *prima facie* relevant discontinuations: first by applying the LASSO methodology, then with a manual investigation.

The manual checks, which initially focused on LASSO-KAs, took into account several facts for which we had gathered evidence in order to further support a *prima facie* KA narrative or, conversely, contradict it. Based on this process, we conclude that the LASSO method (and probably any other large-scale statistical method, at least based on publicly available information) does not appear to be adequate to fully capture the characteristics of the phenomenon of interest. The most plausible explanation is that the features from which LASSO can choose are not enough to grasp the specificities of each case and predict the KA narrative: the LASSO picks up systematic differences between the treated and the control groups in the features included in the model specification, but those cannot entirely explain the variation in each case of all the other elements that could (or could not) support the KA narrative, which can only be observed when manually investigating the discontinuations.

For the manual inspection of the large-scale analysis findings, we have then extended the manual screening to a wider set of the prima facie relevant discontinuations than initially planned (more details are provided in section I.5.1): for instance, for M&As we have covered all the *prima facie* relevant discontinuations; and all the *prima facie* relevant discontinuations for Exclusive Licensing agreements. Moreover, for the deal types where the LASSO was not applicable because of the small sample size, it was already planned to manually investigate all prima facie relevant discontinuations. The type of evidence found for this additional set of *prima facie* relevant discontinuations was not different from that of the LASSO-KAs: in fact, we find similar evidence that may weaken the KA narrative for LASSO-KAs as well as for non-LASSO-KAs, confirming our conclusion that overlaps selected by the LASSO did not prove to be significantly more consistent with a KA narrative than other overlaps that did not share the same features.

The final result is that for the *prima facie* relevant discontinuations covered by the manual screening (either LASSO-KAs or the other *prima facie* relevant discontinuations investigated), no firm conclusion can be drawn on the basis of the evidence available in the public domain to confidently support the theory of harm. On the contrary, only in a few cases is the evidence countering a KA narrative more pronounced, to the point that a KA is considered unlikely (see section I.5.1).

Public information fails to be fully consistent with the KA narrative for the following reasons. In some instances, we miss a validation of the existence of a substitutability between the parties' drugs, or sufficient evidence suggesting the discontinued drug would have been able to continue its development in the absence of the deal. However, by relying on publicly available information, the reconstruction of parties' commercial incentives is inherently biased by subjective interpretation, and we can never exclude that a KA theory of harm might underlie the discontinuation. This is also corroborated by the fact that *prima facie* relevant discontinuations, and not only LASSO-KAs, generally occur in highly concentrated markets, where the incentive and the ability of the parties to pursue a killer acquisition is a priori higher (see also section I.5.3).

The limitations of the analysis are further exacerbated for deals other than M&A due to concerns about information opacity regarding the nature of the exchange and the object of the deal. For example, our analysis of licensing deals is affected by uncertainty regarding the object of the deal and other confidential features (e.g., the structure of payments and the detailed conditions triggering payments, which affect the licensing-out's incentives to monitor) and may require further in-depth investigation and access to confidential information in order to reach conclusions. The assessment is even more limited in the case of collaboration agreements, namely R&D agreements as well as R&D Joint Ventures and Partnerships. These deals tend to be forward-looking and focus on combining inputs to co-develop innovations – as in the case of drugs separately owned by the parties that are put together to test specific combination therapies. Therefore, lack of structured data on pre-clinical trials or firms' investment plans makes it difficult to ascertain to what extent the scope of the collaboration agreements overlaps with the parties' interests.[220] In addition, collaboration agreements do not necessarily imply a

[220] We try to address this limitation when we have to associate a DrugID to a missing drug object of the deal, as explained in the section describing the identification of the perimeter of R&D deals. However, only TIs tested in clinical trials existing at the time of the deal can give rise to narrow overlaps. If the agreement targets one drug in a given TI (drug project) that does not overlap at all with the ones for which the drug has been tested before, the timeframe of its development does not allow us to identify it as a narrow overlap put at risk by the R&D agreement in the large-scale analysis, even if data would cover the drug-project being clinically developed after the deal.

transfer of ownership over the drug projects object of the agreement, nor a specific allocation of the development and commercial rights to exploit the targeted innovation in case of success (differently from a purchase or from a licensing agreement). This information is seldom publicly available even after desk research. In fact, the available data on the agreements do not disclose relevant information on the extent to which parties retain ownership and/or commercialisation rights on the new compound that might support a killer acquisition strategy (see Box 10 for a more detailed discussion).[221]

Considering all of the above, most *prima facie* relevant discontinuations remain possible candidates for a killer acquisition assessment and no solid conclusions can be drawn based on the evidence available to the Study Team. Further and careful case-by-case assessment with access to information unavailable for this study project is therefore warranted.

The remainder of the section is structured as follows: section I.5.1 discusses the findings of the manual screening more in depth; section I.5.2 discusses the novelties of the study and compares its results with previous findings in the literature on KAs, in particular Cunningham et al. (2021); section I.5.3 provides an anonymised discussion of the features of *prima facie* relevant discontinuations for M&As: while the study lacks sufficient elements to fully support a KA narrative for any of the *prima facie* relevant discontinuations, it is also true that this narrative cannot be completely discarded (except for a small number of them). This is particularly the case for M&A deals, where the identification of the deal object, and hence the relevant overlaps and discontinuations, is least prone to error. Moreover, the focus on M&As is consistent and allows further comparison with the existing literature, which is confined to this deal type.

Box 10: R&D agreements – analysis framework

Factual and counterfactual scenarios are especially difficult to assess in R&D agreements.

R&D agreements typically involve collaborations in which companies join forces to develop new compounds, by integrating untested innovations, but also financial and/or R&D capacity that might be developed together by exploring combination therapies.

The assessment of R&D agreements more likely requires information at least on drugs in pre-clinical development. However, we do not observe this information. Moreover, R&Ds are often targeted to specific diseases and patient populations that affect the identification of overlaps. In view of this, the design of the large-scale analysis has been adapted. Specifically, for R&D agreements, the analysis:

- detects mainly through Adis Deals the object of the deal (at least one drug name and at least one TI in the development of which the parties agreed to collaborate);[222]
- matches the drug object name to our drugs dataset, delivering information (based on clinical trial data, on Adis Drugs data and on market authorisations data) to

[221] Given these analytical challenges, further research may be worthwhile in order to gain a more robust understanding of the phenomenon of killer acquisitions.

[222] See section I.2.3.3 for details on the identification of the object of the deal.

identify the drug project, namely its MoA and its development history based on MeSH codes;
- recovers the portfolio of pipelines and drug products for the parties involved in the R&D agreement at the time of the deal (including subsidiaries and/or parent companies);
- identifies all narrow overlaps between the drug object of the deal and each of the drugs in the parties' portfolio, in active development when the deal was announced;[223]
- records as an output only narrow overlaps characterized by MeSH codes that overlap with – i.e. that contain or are contained in – the MeSH codes matched to the TI object of the deal (based on the numerical MeSH Tree representation of Diseases, e.g., Eye Infections [C01.375] is contained in Corneal Ulcer [C01.375.177] – this is one type of overlap in TI that we use to expand the potential substitutability between drugs in TIs beyond the case when two drugs share exactly the same MeSH code).[224]

Narrow overlaps between the parties' interests are therefore detected indirectly, through the drug and the TI object of the agreement.

In most R&D agreements that have informed our analysis, as confirmed by the manual investigations, the deal object is a combination of one or more companies' drugs into an innovative therapy. The large-scale analysis has been designed to follow narrow overlaps between individual drugs, where development is tracked through the progress of each drug in all its clinical trials: to adapt the design to R&D, we exploit the information on the TI object of the deal to limit the analysis to the TIs that are in overlap with the TI object of the deal. However, the development of the combination therapy is followed through the separate development of the individual drug components. This may induce inaccuracies in the detection of its outcome after the deal, addressed with the manual screening.

Because of the data limitations, any interest of any of the parties in a drug that does not yet have a drug profile in Adis Drugs data, or has missing information on the MoA, or that before the deal has no active clinical trial data recorded in which the parties are listed as sponsors or collaborators, would not be detected as a relevant overlap for these deals. The drug object itself can originate an overlap only if it has been recorded in Adis data with at least a generic MoA, and has clinical trials initiated before the deal.

Moreover, the targeted therapeutic indication disclosed by the parties to the public might be quite general, making it more difficult to reach a conclusion on the causal link between a discontinuation of an overlapping drug and the deal. This is why more in-depth research is needed to investigate R&D agreements than we could invest in this study timeline.

The manual screening conducted on the findings of the large-scale analysis, supported by desk research, helps verifying the correct identification of the object of the deal

[223] Suppose that a R&D deal between Party A and Party B focuses on the development of Drug X (drug object of the deal) owned by Party A. In this scenario, only narrow overlaps, among those active when the deal was signed, between Drug X and all Party B's drugs are considered relevant.

[224] In the example above, suppose that the R&D agreement focuses on the development of Drug X in Eye Infections [C01.375]. Then, only narrow overlaps between Drug X and all Party B's drugs in a MeSH code contained or that contains Eye Infections [C01.375] are considered relevant.

and that the narrow overlaps detected by the large-scale analysis are related to the TI targeted by the deal. When the object is a combination therapy, the Team carries out further research to check whether the development of the combination therapy has advanced and, if not, for what reasons; and to check that the drugs that are found to overlap with the combination therapy would indeed be good substitutes in the TI of the combination therapy, whether they have advanced in development and, if not, for what reasons.

In the context of this study, we investigate whether killer acquisitions materialise when at least one of the parties of the deal has some interest (a marketed drug or a pipeline) in narrow overlap with the object of the R&D agreement.[225] However, incentives of the parties are difficult to evaluate because they depend on the allocation of marketing and distribution rights for the joint innovation: such details are not public, so it is not possible to understand whether they can create exclusive rights, even when manually screening them.

These circumstances make it extremely difficult to assess both the factual and the counterfactual.

When we observe a progress of the innovation targeted by the deal, while the overlapping interest of one of the parties – often unrelated to the combination therapy except for an imperfect overlap in TI – has been discontinued, absent information on the specific rights allocated through the deal, we are not able to make any assessment of whether the deal has actually decreased the party's incentives to continue the development of its own drug in order to favour the joint innovation. Such a condition may be only verified through enforcement. The manual screening faces the same constraints as the large-scale analysis on this ground. Therefore, the manual investigation simply assesses factual observable elements that may support or violate a KA narrative, such as: the degree of product substitutability; the absence/presence of data that supports valid technical reasons for the discontinuation; the degree of potential competition including both pipelines and marketed products (so that one more pipeline competitor may have heightened significantly the competitive pressure); whether any of the drug products involved has been sold or licensed after the deal.

Clearly, another implicit condition of a counterfactual in which the discontinuation of one of the parties' drugs in overlap with the surviving joint innovation would not have occurred, and which we cannot verify, is that the other party would have been a competitor absent the deal. That is because when an innovation is jointly developed, the counterfactual would require to assess whether either party was able to develop that or an equivalent innovation on its own or joining forces with a firm that was not a rival.

Similarly, if we observe no progress of the combination product, the manual screening can simply verify the same evidence mentioned above (development of the overlapping drug in the TI object of the deal; whether the discontinuation can be seen as due to reasons other than the deal and overlap, and potentially involving a market with low competition), without trying to assess the existence of the conditions necessary to justify the KA narrative that can only derive from information available to enforcers or insiders.

[225] See section I.2.3.3 for details of our strategy for identifying the perimeter of R&D deals.

I.5.1 Discussion of the findings: more details on the manual screening outcomes

Table I.6 shows the distribution of *prima facie* relevant discontinuations by deal type and the coverage of manual screenings. The first column lists the deal types, while the second and third columns provide the number and the fraction of deals, respectively, where at least one *prima facie* relevant discontinuation has been subject to this kind of examination. The last two columns of Table I.6 show the number and the fraction of *prima facie* relevant discontinuations that have been subject to the manual screening, counting the overlaps.

Table I.6: Manual screening coverage

Deal Type	Deals with at least one prima facie relevant discontinuation (count of deals)	Deals with prima Facie relevant discontinuation manually screened (% of deals)	Narrow overlaps with a prima facie relevant discontinuation (count of overlaps)	Narrow overlaps with prima Facie relevant discontinuations manually screened (% of overlaps)
M&A	19	100%	120	100%
Licensing	27	56%	97	35%
(Exclusivity)*	(12)	(100%)	(30)	(100%)
R&D	37	22%	263	5%
Purchase	4	100%	10	100%
Other deals**	5	100%	10	100%
Total	92		500	

*Source: Lear analysis. Notes: *Exclusivity: this row of the table provides details about "exclusive" licensing agreements, that are identified applying search text tools to the description of the deals available in our deal dataset. ** For the group Other deals, prima facie relevant discontinuations are in the following deal types: Equity investment (2 deals; 5 narrow overlaps), Joint venture (1 deal; 1 narrow overlap), Joint venture R&D (1 deal; 1 narrow overlap), Marketing agreement (1 deal; 3 narrow overlaps). No discontinuation of narrow overlaps is found in Partnerships and Cross-Licensing agreements.*

As discussed, the manual screening of *prima facie* relevant discontinuations entails the investigation of (at least) all the LASSO-KAs in a deal where the latter methodology has

been employed, and all the *prima facie* relevant discontinuations in other deal types where the methodology has not been employed. In practice, as the table shows, manual screening covered the full set of M&A deals, exclusive licensing deals (and 56% of all licensing deals, 35% in terms of overlaps), purchases and other deals.

In contrast, the extent of manual screening appears to be more limited for R&D agreements (22% of deals, 5% of overlaps). This is partly explained by the fact that in R&D agreements the total number of *prima facie* relevant discontinuations is much higher than in other deal types. Also, while the percentages reported in Table I.6 only account for the manual screening of *prima facie* relevant discontinuations, as a robustness check, manual screening in R&Ds has been extended beyond, to some discontinuations flagged as benign that shared the same features of the LASSO-KAs: in absolute terms, a total of 34 overlaps have been checked, the same amount as in Licensing, more than in Purchase and Other deal types altogether.[226] The manual screening confirmed that, as also noted in Box 10, R&D agreements are more difficult to investigate, notwithstanding the customisation of the large-scale framework we pursued (see section I.2.3). Public information available for desk research is also typically less informative for R&Ds than for other deal types, where at least the focal exchange of rights between the parties over the relevant drugs is known. Such limits consistently constrain our analysis and findings, discouraging more extended screening.

The evidence gathered during the manual screening is intended to verify the output of the large-scale analysis and to inform our conclusions on the assessment of the *prima facie* relevant discontinuations. The manual investigation is designed to gradually and sequentially verify whether the available public evidence could potentially support a killer acquisition theory of harm or the reverse. The notion of killer acquisition endorsed by this study, and therefore the role of manual screening, revolves around ascertaining the following key elements:

- there is a pattern of substitutability between the acquiror and the target's drugs which would provide the acquiror with the incentives to kill either its own or the target's drug: the manual screening is meant to corroborate the findings of the large-scale analysis by investigating whether the – sometimes imperfect – overlap in TI and MOA is sufficient to conclude with a reasonable degree of confidence that the drugs can similarly treat the same disease and patients;
- the discontinuation does not *a priori* seem to be grounded on technical and clinical reasons or justified by a commercial assessment that would have emerged even in the absence of the deal: by leveraging scientific articles, results of clinical trials available in the clinical trial registries and the expertise of the Team, the manual screening aims at excluding that safety or efficacy issues could have justified the discontinuation;
- the competitive dynamics in the likely relevant market are such that the discontinuation may have lessened competition: in cases where the assessment of substitutability and reasons for discontinuation could potentially support a killer acquisition theory of harm, the manual investigation collects evidence apt to verify the boundaries of the likely relevant market, and to reconstruct the number of competitors and their strength;

[226] Out of the 34 overlaps examined, 14 are prima facie relevant discontinuations, including 5 selected by the LASSO. The other 20 discontinuations manually investigated have been selected as they shared the same LASSO features but had been classified as benign.

- finally, the structure of the deal provides the acquiror with the ability and the incentives to pursue a killer acquisitions strategy: the manual screening is meant to verify whether the acquiror (i.e. the party acquiring rights over a counterparty's drug) retains control over the overlapping drug projects, or whether the evolution of the relationship between the parties would suggest the deal stifled competition in the market.

For all the prima facie relevant discontinuations manually screened, with the exception of a few cases where a KA narrative can be confidently considered unlikely, the evidence available in the public domain is not sufficiently consistent with a killer acquisition theory of harm, but at the same time does not allow such a theory of harm to be definitively ruled out, thus preventing us from making a conclusive assessment. Further research would then be required, on a case-by-case basis and with access to confidential data not available to the authors of the study, in order to fully understand the phenomenon under investigation and its extent.

Table I.7 below provides an attempt to classify the *prima facie* relevant discontinuations based on the type of evidence gathered during the manual screening to assess a potential KA narrative. We present the classification for M&As, Licensing and R&Ds, as they have been covered both with the LASSO methodology and with the manual screening. The classification is limited to the *prima facie* discontinuations (including LASSO-KAs) which have been manually inspected. The last three columns display the frequency of each type of evidence within the deal type, relative to the total number *of prima facie relevant* discontinuations that have been subject to the manual investigation (the last row shows the number of such overlaps).

Table I.7: Classification of the public available evidence gathered with the manual screening of *prima facie* relevant discontinuations (at narrow overlap level) –

Classification of the evidence	M&A- (prima-facie relevant disc. %)	Licensing- (prima-facie relevant disc. %)	R&D- (prima-facie relevant disc. %)
1) Discontinuations with evidence that would make a KA narrative not applicable			
	4%	9%	
2) Discontinuations that deserve further scrutiny ("grey area")			
Mixed evidence on the substitutability between overlapping drugs			
Uncertain substitutability	28%	21%	7%
Questions as to whether the surviving drug was ever pursued in the narrower indication (by the relevant entity)	13%		
Questions as to whether the overlapping drug was ever pursued in the relevant indication (by the relevant entity)			21%
Mixed evidence on the development of the discontinued drug in the counterfactual			
Inconclusive evidence on safety	32%	3%	
Inconclusive evidence on efficacy	9%	24%	43%
Questions as to whether the discontinuation preceded the deal	2%	3%	7%
Uncertainty regarding the ability/incentive			
Mixed evidence on the ability/incentive	8%	6%	21%
Questions as to whether the overlap involves a generic in combination therapy	3%	9%	
Questions as to whether the license over the discontinued drug returned after the deal		24%	
Uncertain timing compatibility with a KA narrative		3%	
Total 100%	**100%**	**100%**	

Total number of prima facie relevant discontinuations manually checked	**120**	**34**	**14**
Total number of prima facie relevant discontinuations at narrow overlap level	**120**	**97**	**263**

Source: Lear analysis. Note: Percentages are shares of narrow overlaps where a prima facie relevant discontinuation has been identified and covered by the manual screening

As discussed, there are only a few cases where a KA theory of harm can be confidently dismissed, representing a total of 8 *prima facie* relevant discontinuations (5 discontinuations distributed over 4 M&A deals; and 3 discontinuations distributed over 2 Licensing agreements; however, 2 of the M&As deals and 1 of the Licensing agreements also have other *prima facie* relevant discontinuations for which the evidence is less conclusive and thus remain in the grey area). These are cases based on any of the following findings:

- the manual investigation finds that the discontinued drug projects could be considered still in development for the relevant indications (3 narrow overlaps in M&A);
- the object of the deal was the acquisition of a drug-enhancing technology rather than competing drugs (2 narrow overlaps in Licensing and 1 narrow overlap in M&A pertaining to imaging agents for diagnostics purposes that do not treat diseases);
- the analysis detects two acquiror's drugs (that share the same active substance name) in narrow overlap with the same target drug in the same TI, but only one is relevant for the deal (1 narrow overlap for both M&A and Licensing).

For 96%, *prima facie* relevant discontinuations the evidence is mixed, thus highlighting transactions that merit further scrutiny (a "grey area"). Within this "grey area", no firm conclusion in either direction – full support or rejection of a KA theory of harm – is possible with the tools at hand, as outlined in Box 11 below.

In conclusion, the results of the manual screening indicate that for 3 deals a KA narrative can be reasonably ruled out (2 in M&A deals, 1 Licensing agreement), as these deals have no other *prima facie* relevant discontinuation for which they would still deserve further assessment. Instead, the remaining 89 deals fall into a grey area and would deserve further assessment. A case-by-case analysis using confidential data is required to thoroughly test a KA theory of harm for these deals. Figure I.2 provides a summary overview of all steps and related results at the deal level of the *fact-finding* challenge, while also highlighting the limitations of the analysis conducted. Finally, Figure I.3 illustrates the distribution of deals deserving further scrutiny by deal type and year to convey the scale of the phenomenon: over the 2014-2018 period, the study detects an average of 3.4 M&A deals deserving further scrutiny per year, 5.2 licensing deals, 0.8 purchase deals, 7.4 R&D agreements and 1 deal in the residual category.

Box 11: Evidence on transactions deserving further scrutiny (grey area)

It is worth noting that the categories in which we have grouped the evidence within the grey area cannot be ranked on a scale based on their strength in supporting a KA narrative. Within each category, we can find *prima facie* relevant discontinuations for which the evidence is accompanied by varying degrees of uncertainty.

- *Uncertain substitutability*: there may be cases of imperfect overlap in both TI and MoA. For the latter, we may find that although the MoAs of two drugs have been identified as substitutable based on joint citations in the medical literature, in commercial reality they may have an uncertain degree of substitutability. As for TI, a drug may have been tested to treat a different submarket in the same TI (different patient segment) or in combination with other drugs, so that the degree of substitutability remains uncertain.[227]
- *Questions as to whether the surviving drug was ever pursued in the narrower indication (by the relevant entity)*: this is a special case of imperfect narrow overlaps in TI. For example, before the deal the discontinued drug is tested in non-small-cell lung carcinoma [C04.588.894.797.520.109.220.249], while the surviving drug is tested in the general TI neoplasms [C04]; after the deal, the relevant entity (i.e. the acquiror in M&As) does not develop the latter drug in the narrower TI of the discontinued drug. On the one hand, this may refute a KA narrative, but as in some cases the discontinuation lacks an apparent sound motivation, the evidence seems inconclusive.
- *Questions as to whether the overlapping drug was ever pursued in the relevant indication (by the relevant entity):* this is similar to the category above, except that it refers to R&D agreements, where the overlapping drug is the drug attributed to the pre-deal portfolio of one of the partners and is found in narrow overlap with the object of the deal. In most instances, the manual screening finds that the deal targets a combination therapy in a TI (note that the parties do not often disclose the exact targeted TI, but a broader one) while the overlapping drug is tested only in a different TI before its discontinuation occurs, so that it cannot be established whether it had the potential to effectively compete with the TI targeted by the combination therapy.[228] Considering the above and given the overarching uncertainty that characterises the actual allocation of commercial rights between the parties over the combination product in collaboration agreements, it would not be possible in these scenarios to conclude that the deal at hand provides one partner with ability and incentives to cause a discontinuation that would not take place in the counterfactual.
- *Inconclusive evidence on safety:* evidence claiming a safety or technical problem is weak or uncertain.[229] In addition, one or more of the following may arise: published clinical trial results not available/difficult to evaluate (need relevant benchmarks); no corroborating evidence of the reason for discontinuation; additional evidence of toxicity or adverse events in articles published in scientific journals that review the results of clinical trials[230] may be inconclusive due to poor trial design, low enrolment or large dropouts; in combination therapies, safety issues may be difficult to link to a specific drug in the combination.

[227] The low substitutability label has also been used when drugs are intended for parallel treatments in the same therapeutic area.

[228] Alternatively, the combination therapy may be discontinued, and the development of the overlapping drug continues only in a TI different from that object of the deal. Neither in this case we would be able to conclude that the overlapping drug had the potential to develop in the TI object of the deal and that the overlap caused the discontinuation.

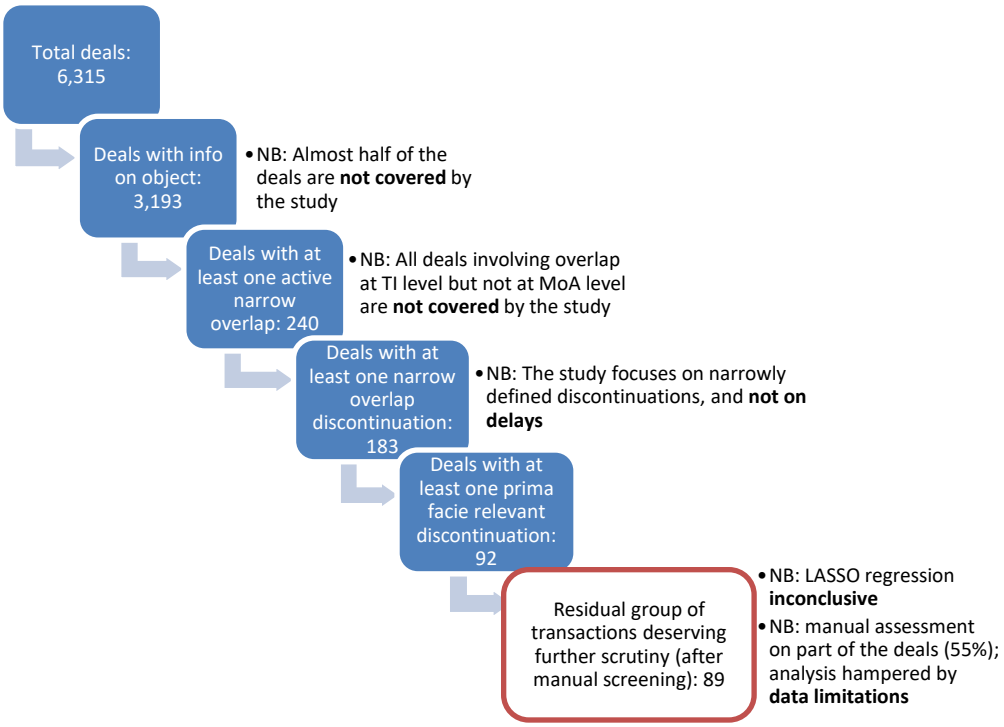
[229] Clinical trial data on safety reasons for discontinuation were already not sufficient to classify the discontinuation as benign (see section I.3.2).

[230] Available from the National Library of Medicine – PubMed Central website: https://www.ncbi.nlm.nih.gov/pmc.

- *Inconclusive evidence on efficacy*: this is similar to the "Existence of safety concerns" (just discussed above).
- *Questions as to whether the discontinuation preceded the deal:* evidence from desk research may signal that a discontinued pipeline could have been considered inactive (no longer in development) when the deal was signed. The evidence can sometimes be based on clinical trial data (where missing completion dates of the downloaded data can be missing); or other evidence uncovered (press releases, company reports, updates, media outlets), may contrast with clinical trial data.
- *Mixed evidence on ability/incentive*: it can happen because: the acquiror (or licensing-in, or partner) tested a drug in the past even if it did not own it (proving it has or had some interest in the drug, but it may not be sufficient as an incentive for a discontinuation); a spin-off occurring around the time the deal is signed (creating uncertainty surrounding the drug attribution); ambiguity in drug names can lead to multiple matches of drugs to clinical trial data.
- *Questions as to whether the overlap involves a generic in combination therapy*: generics are out of scope of the study. However, even generic drugs can be repurposed/modified to gain further protection. There are indeed several drugs that share the same active substance, are marketed or developed by different firms, and are part of the Adis dataset as different drugs. The fact that Adis does not cover purely generic drugs would then be a sign that these drugs bear some market protection, but the existence of other brands for the same drug is still evidence against possible rents. Without more detailed evidence about the relative protection obtained, we cannot conclude whether the overlaps at hand should be considered in/out of scope.
- *Questions as to whether the license over the discontinued drug was returned after the deal*:[231]. When the license is returned there is still the possibility, based on the specific circumstances, to argue a slowdown in development theory of harm (though such an outcome is out of scope of the study).
- *Uncertain timing compatibility with a KA narrative:* we find one case among licensing deals: the timing in (or a scattered) drug development suggests that the interest of the licensing-in company in its own drug may be low and thus unrelated to its acquired interest in the licensed drug. However, this kind of evidence is only speculative and thus weak.

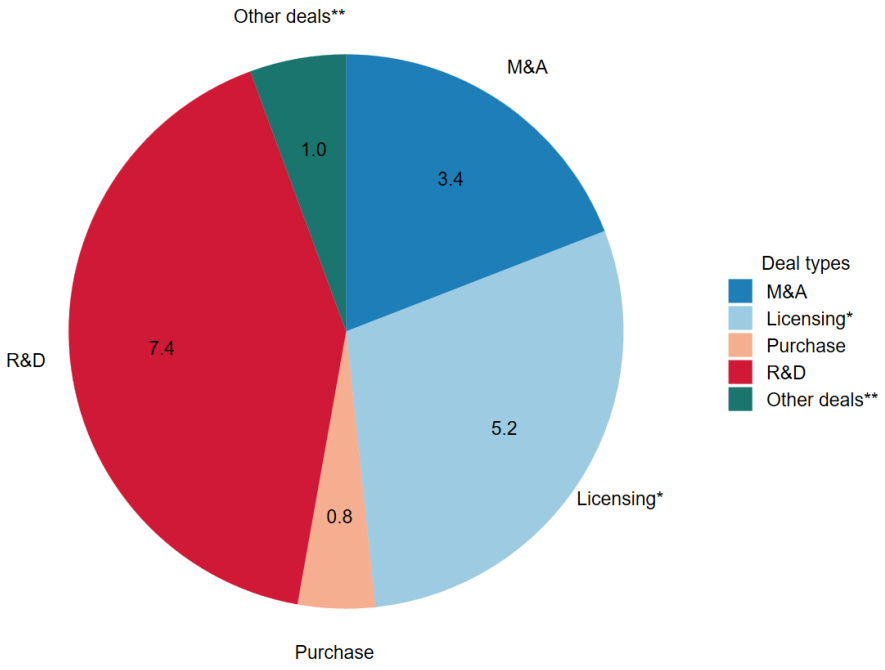
[231] This label is only used for Licensing deals, for 8 overlaps (split among 2 deals).

Figure I.2: Results of the fact-finding challenge



Source: Lear analysis

Figure I.3: Annual average number of deals deserving further scrutiny (2014-2018)



*Source: Lear analysis. Source: Lear analysis. Notes: *Over the years 2014-2018, there are 12 "exclusive" licensing agreements, identified using search text tools on the descriptions in our deal dataset, among those deserving further scrutiny.**For the group Other deals, over the years 2014-2018, deals deserving further scrutiny are in the following deal types: Equity investment (2 deals), Joint venture (1 deal), Joint venture R&D (1 deal), Marketing agreement (1 deal); no discontinuation of narrow overlaps is found in Partnerships and Cross-Licensing agreements*

I.5.2 Discussion of the novelties of our approach with respect to previous findings

The main novelty of our study is the systematic collection, for a large number of deals in the pharmaceutical industry, of factual evidence that could potentially support or dismiss a killer acquisition narrative for specific deals. Existing research mostly provides theoretical or statistical estimates of the overall magnitude of the phenomenon, that cannot be used to pinpoint specific transactions.

The most discussed contribution to the literature on killer acquisitions is Cunningham et al. (2021) (hereafter "CEM (2021)"). Given its focus on killer acquisitions, the CEM (2021) study appears to be the closest to ours, despite existing differences in approach. The remainder of this section therefore takes a closer look at the CEM (2021) study, exploring its approach and results and how they compare to our research.

CEM (2021) aims to estimate the frequency of killer acquisitions in the pharmaceutical sector by tracking the development of acquired drug projects before and after an acquisition occurs. In their main specification, they compare the development probabilities of overlapping acquired projects, which they assume are motivated by a "mix of killer and development intentions", and non-overlapping acquired projects, which they assume are motivated by "only development intentions". They estimate that acquired overlapping projects are 4.1 percentage points less likely to have a development event in the years after acquisition than non-overlapping acquired projects and explain this by the fact that 23.4% of overlapping acquisitions are pure killer acquisitions, i.e. acquisitions that imply a zero probability of development (assuming that overlapping acquired projects have otherwise the same probability of development of acquired non overlapping projects). Finally, they estimate that 5.3% of all M&A's acquisitions in the pharmaceutical sector (both overlapping and non-overlapping) are killer acquisitions (the estimate is 7.4% if non acquired projects are used as an alternative benchmark).

While CEM (2021) undertakes a top-down statistical investigation of pharmaceutical projects and estimates their likelihood of development following M&A, our study is a bottom-up exercise that attempts to single out publicly available factual evidence relevant to assess a KA theory of harm at the level of single deals and overlaps. There are many methodological differences that make a comparison difficult.

First, the notion of killer acquisition theory of harm that we adopt in our study *excludes* cases where the acquiror terminates the development of a drug without, however, altering the competitive dynamics prevailing in the relevant market. There might be instances where the seller and the acquirer value the same pipeline differently, and the acquisition alters the development of the overlapping target drug. The acquiror may more readily discontinue a relatively non-promising, though not unsafe, overlapping pipeline, whereas the seller would have still continued development absent the deal, in line with what it was doing when the deal was negotiated (to build knowledge in a new area, to exploit internal or external synergies for combination therapies or in enhancing technologies). To the extent that these discontinuations do not stifle competition, they are not candidates for the killer acquisition assessment in our study.

On the other hand, the empirical framework in CEM (2021) analysis is built on the premise that a transaction that is not consistent with the killer acquisition motive would have undergone the same development path we would have observed in the counterfactual.

This points to the set of *prima facie* relevant discontinuations that we find in M&A being our most accurate measure of the phenomenon of KAs estimated by CEM (2021), and within this framework, we endeavour to draw comparison with our results.

While the main specification examined by CEM (2021) focuses on the probability of development of target drug projects following an acquisition, as discussed above, the paper also provides a robustness check by focusing on outright project terminations, as opposed to project delays. This type of analysis seems much closer to our setting because, as also discussed above, the probability of no post-acquisition development events is a similar metric to our study of drug discontinuations. In this specification, CEM (2021) finds that the share of acquired projects for which no positive post-acquisition development event is observed is 14.9 percentage points higher for overlapping acquired projects than for non-overlapping acquired projects. Based on this, and assuming that this higher proportion of never-developed projects is due to killer acquisitions, i.e. 14.9% of overlapping acquisitions are killer acquisitions, they estimate that killer acquisitions account for 3.4% of all acquisitions (a lower estimate than that obtained from their main specification, between 5.3 and 7.4%).

We note that it is not clear from the CEM (2021) study what type of discontinuation is being captured: the overlaps are identified at the therapeutic class and mechanism of action level; however, their measure of development events (and lack thereof) also includes events related to the molecule as a whole, such as "compounds identified", "mechanism identified" and "names granted". In this respect, we also note a fundamental difference in how lack of development or project termination is tracked compared to our study, which is based solely on clinical trials and market registration or launch data.

Nevertheless, if we transform our results on *prima facie* relevant discontinuations for M&A deals (which are at the overlap level, focus only on narrow overlaps, and track post-deal discontinuations for both the acquirer and the target portfolio) to the level of counting acquired drug projects only, in line with CEM (2021), we find that they are remarkably similar to CEM (2021)'s results. Prima facie relevant discontinuations (in our view a comparable proxy for CEM (2021)'s killer acquisitions) for M&A deals account for 13.6% of overlapping acquired drug projects when looking at discontinuations at the molecule level, and 15.3% at the therapeutic indication level (as proxied by MeSH terms).[232] Thus, CEM (2021)'s estimate of 14.9% for killer acquisitions among overlapping acquisitions is within the range of our estimates for prima facie relevant discontinuations among narrow overlaps.

Finally, comparing the results at the deal level, we find that 19 M&As involved at least one prima facie relevant discontinuation, or 3.8% of all M&As in our 2014-2018 sample (490). Again, this figure is remarkably close to CEM (2021)'s estimate that 3.4% of all acquisitions are killer acquisitions.

[232] In absolute terms, we find 103 overlapping acquired drug projects and 14 prima facie relevant discontinuations at the molecule level (13.6%) and 588 overlapping acquired drug projects and 90 (15.3%) prima facie relevant discontinuations at the therapeutic indication level (as proxied by MeSH terms).

While the measures we obtain are relatively close, a comprehensive comparison may not be suitable given the significant methodological divergences between our study and CEM (2021). Additional details on the differences between the two approaches are outlined in Box 12.

Box 12: Differences in this study approach with respect to Cunningham et al, 2021 (CEM 2021)

This box lists potential differences between our study and the CEM (2021). These are to some extent also based on our interpretation of the data the authors had access to and may suffer some inaccuracies.

Our definition of narrow overlap relies on TIs, which are much more granular than therapeutical class definition used by CEM (2021), even though we allow for imperfect overlaps using the numerical and hierarchical structure of MeSH codes.

In CEM (2021)'s sample one target drug project only gives rise to one observation, even when it overlaps with multiple acquiror's drug projects, while our analysis tracks narrow overlaps between distinct pairs of acquiror's and target's drug projects. As a result, in our sample, the same target drug gives rise to distinct narrow overlaps with each of the acquiror's overlapping drugs, not only for the same TI but also for different TIs. Since discontinuations most often affect one specific TI but not others in which a target drug is involved, the number of discontinuations is diluted as a fraction of narrow overlaps generated by the same target drug.

CEM (2021) uses non-overlapping acquired and non-acquired drug projects to control for the counterfactual likelihood of discontinuations of overlapping acquired drug projects. In our project, when identifying *prima facie* relevant discontinuations, we try to control for discontinuations that would likely have occurred also in the counterfactual and are likely not driven by commercial incentives using several approaches.

- First of all, we exclude from the analysis drug projects that appear to have been discontinued before the deal. This is something that may increase the CEM (2021)'s proportion of overlapping acquired drugs with respect to ours (however, it should not affect the relative rate of discontinuations).
- When both acquiror's and target's drugs are completely discontinued in all TIs, or one is discontinued and the other is reoriented to a different TI, or when the discontinuation occurs in a given TI but the two drugs continue to overlap in a related TI, we exclude them from prima facie relevant discontinuations. In all these instances instead, CEM (2021) would track a discontinuation as they do not follow the development of overlapping acquiror's projects. We recognise that our approach is quite conservative and may overestimate discontinuations that would have likely occurred also in the counterfactual and are unrelated to a KA narrative.
- Last, we filter out discontinuations that appear justified by technical reasons claimed by principal investigators in the clinical trials, which may also overestimate the rate of counterfactual terminations as long as firms are able to manipulate the information disclosed. However, to mitigate this risk, we control for the nature of sponsors and collaborators and, when they are all private enterprises, in some instances we deem the information less credible.

I.5.3 Features of discontinuations that deserve further scrutiny for a KA assessment

This section examines the 17 M&A transactions that would deserve further scrutiny: i.e. *prima facie* relevant discontinuations in M&A deals, after excluding the two for which a KA narrative can be confidently dismissed. While the characteristics of this "grey area" of *prima facie* relevant discontinuations may appear to be of limited relevance, as the study lacks sufficient elements to fully support a KA narrative, it also lacks sufficient evidence to dismiss it based on the available data. Consequently, this set still represents deals that could potentially conceal a KA.

In addition, the focus on M&A deals facilitates direct comparisons with previous research, notably CEM (2021). Moreover, the scope of M&A deals is readily identifiable, and coincides with the portfolio of the target company, making the identification of both overlapping drugs and competing drugs more reliable.

We examine the characteristics of discontinuations and corresponding transactions that would deserve further scrutiny at both the overlap and the deal level. At the overlap level, we analyse the development phases of the overlapping drugs, market concentration and the strength of competitors in the relevant market. At the deal level, we analyse the size of the companies involved in the deal and the deal's value.

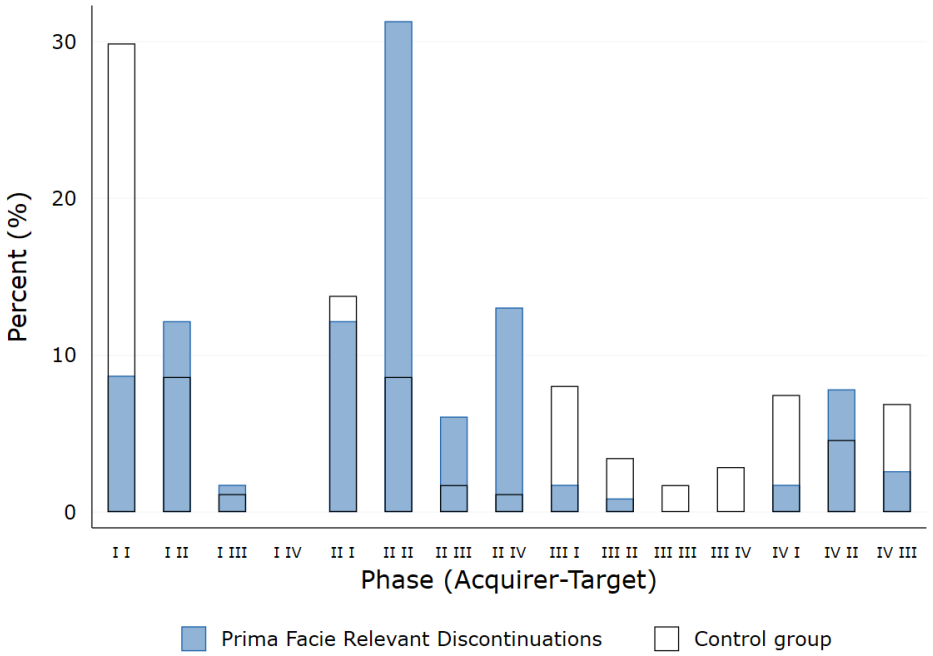
In order to determine whether the identified features exclusively characterise this set of discontinuations within M&A deals that merit further scrutiny, we extend the analysis to include a control group consisting of all M&A deals without prima facie relevant discontinuations (and their respective overlaps).

While the assessment conducted in this study could not ultimately lead to sufficient evidence to support a KA narrative for any of these discontinuations, it remains a possibility that undiscovered prima facie KAs may exist within this pool and therefore merit in-depth assessment, provided access to broader data beyond that available in the public domain.

This conclusion is reinforced by analysing the features of prima facie relevant discontinuations deserving further scrutiny in M&A deals.

Regarding the development phases of overlapping drugs, we find that "grey area" discontinuations in M&A deals tend to involve overlapping drugs in relatively higher phases of development, as shown Figure I.4. The prevalence of overlapping drugs both in Phase II and where one drug is in Phase II while the other is already on the market (commonly referred to as Phase "IV") for prima facie relevant discontinuations sets a pattern that differs from the control group, where overlaps where both drugs are instead in Phase I are more frequent.

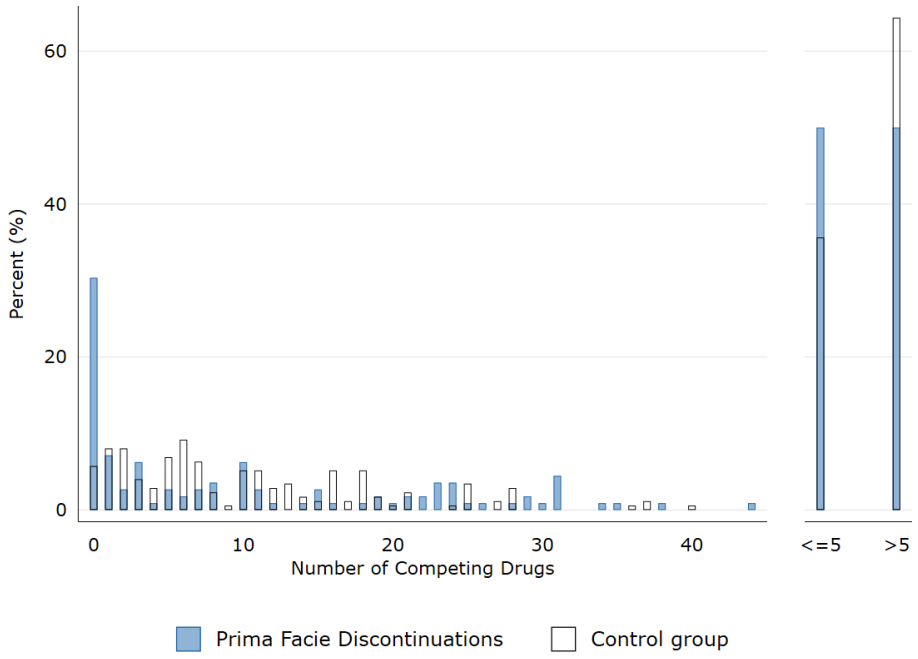
Figure I.4: Phases of the overlapping drugs: prima facie relevant discontinuations that deserve further scrutiny vs. control group



Source: Lear analysis. Phase numbering refers to research phases I-III (1-3) and market drugs IV (4)

Turning to market concentration and the competitive landscape, we find that the grey area discontinuations tend to occur in concentrated markets, as shown in Figure I.5. The figure plots the distribution of competing drugs for them and for the control group, as well as the distribution for a dichotomous definition of market concentration, with markets with a maximum of five competitors as proxies for concentrated markets. Both plots show that the relevant markets in which *these* discontinuations occur tend to be more concentrated on average. In addition, when looking at the full distribution of competing drugs, a notable feature is the presence of a pronounced spike when there are no competitors. Assuming that these discontinuations can be compared to killer acquisitions in CEM (2021) analysis, the patterns highlighted are consistent with CEM (2021)'s finding that killer acquisitions are more likely in less competitive markets.

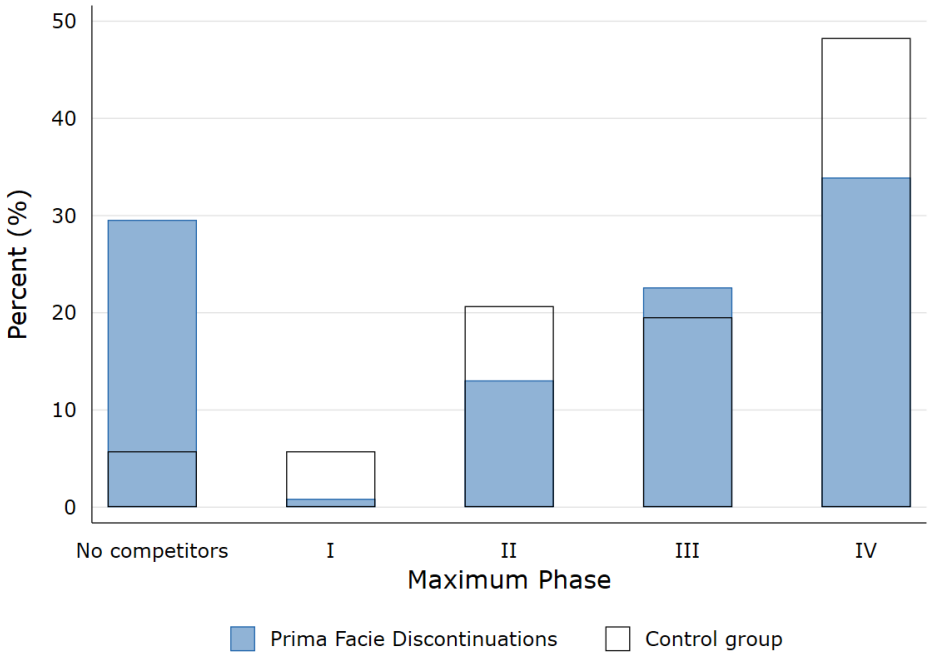
Figure I.5: Number of competing drugs: prima facie relevant discontinuations deserving further scrutiny vs. control group



Source: Lear analysis

Looking further into the competitive landscape by assessing the strength of the most advanced competitor in the relevant markets, Figure I.6 reveals an interesting pattern. Overlaps associated with grey area discontinuations often face a competitor characterised by a less advanced stage of development, in contrasts to the control group where the prevalence of at least one marketed competitor is more pronounced.

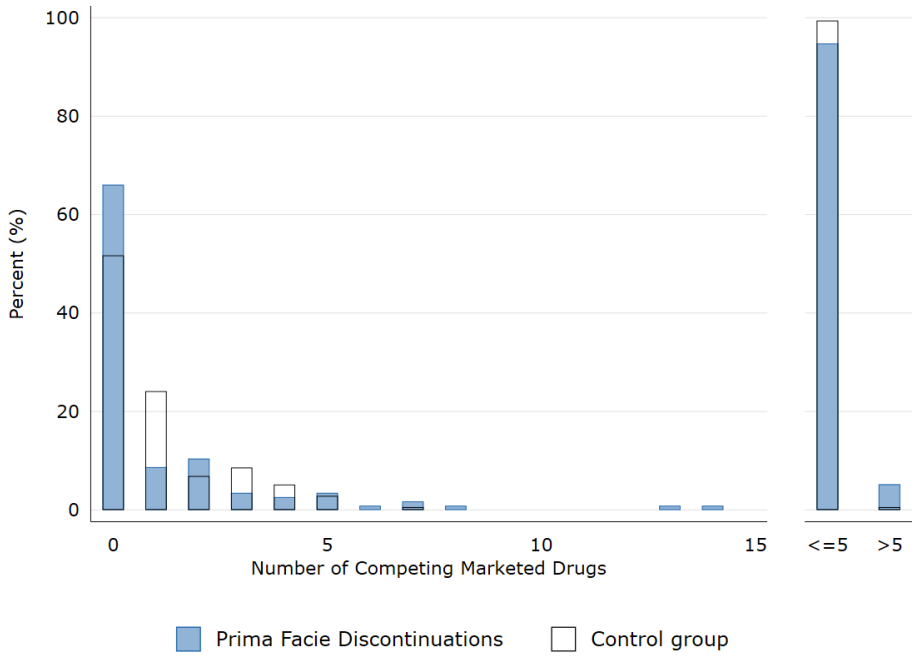
Figure I.6: Maximum phase of competing drugs: prima facie relevant discontinuations deserving further scrutiny vs. control group



Source: Lear analysis. Phase numbering refers to research phases I-III (1-3) and market drugs IV (4)

A more nuanced picture emerges when focusing only on marketed competitors, as shown in Figure I.7. While there is still a peak where there is no marketed competitor for grey area discontinuations, the distribution shows a longer tail, i.e. there are instances where the number of marketed competitors is higher than in the control group. This apparent contradiction is potentially reconciled by looking at the definition of the relevant markets for these cases characterised by a high number of marketed competitors: we find that they fall into relevant markets where the therapeutic indications are predominantly in the area of cancer (the most common being multiple myeloma and non-small cell lung cancer) and the overlap in MoA is not perfect, but is established by an association in the literature through PMC. In these cases, any competing drug that shares at least one of the MoAs of the two overlapping drugs is considered a candidate competitor, potentially inflating the number. The same relevant markets are not observed in the control group.

Figure I.7: Number of competing marketed drugs: prima facie discontinuations deserving further scrutiny vs. control group



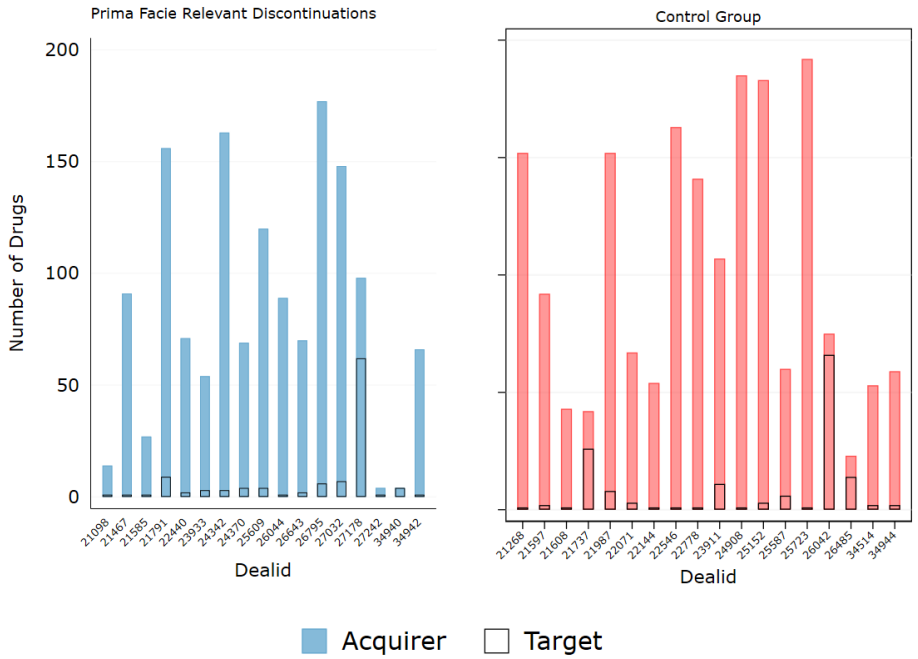
Source: Lear analysis

The evidence gathered on grey area discontinuations reveals distinctive features when compared to a control group of deals and corresponding overlaps with no discontinuation or only benign discontinuations:

- grey area discontinuations entail overlapping drugs at a relatively advanced stage of development, which fosters more informed expectations about their potential in the relevant therapeutic area. Firms are more likely to be threatened by the competitive pressure exerted by drugs that have at least passed the Phase I of the R&D cycle. Furthermore, we note that grey area discontinuations often occur when there is an overlapping marketed drug, which can be rationalised by the higher risk of losing future stream of profits due to the threat exerted by a nascent competitor;
- grey area discontinuations generally occur in most concentrated markets, and less-likely face marketed competitors overall.
- This interplay of factors supports a potential killer acquisition narrative, as it describes a scenario where there is a stronger incentive and ability to eliminate a competitive threat in order to win the market.

Shifting our focus to deal-level attributes, we observe a notable trend in the relative size of the acquirer and target companies involved. As shown in Figure I.8, deals with discontinuations deserving further scrutiny often feature an acquirer with an extensive drug portfolio acquiring a smaller, nascent target with a more limited portfolio. However, we note that the feature of a large acquirer relative to the target goes beyond discontinuations deserving further scrutiny and shapes the landscape of narrow overlap deals that we observe in our sample; indeed, it is also observed for the control group. This feature would be consistent with the CEM (2021) study, which considers the entire set of deals with overlap in therapeutic class and MoA as "killer-acquisition suspects" (CEM (2021), p. 685).

Figure I.8: Number of drugs for acquirer and target in M&A deals: prima facie relevant discontinuations deserving further scrutiny vs. control group



Source: Lear analysis

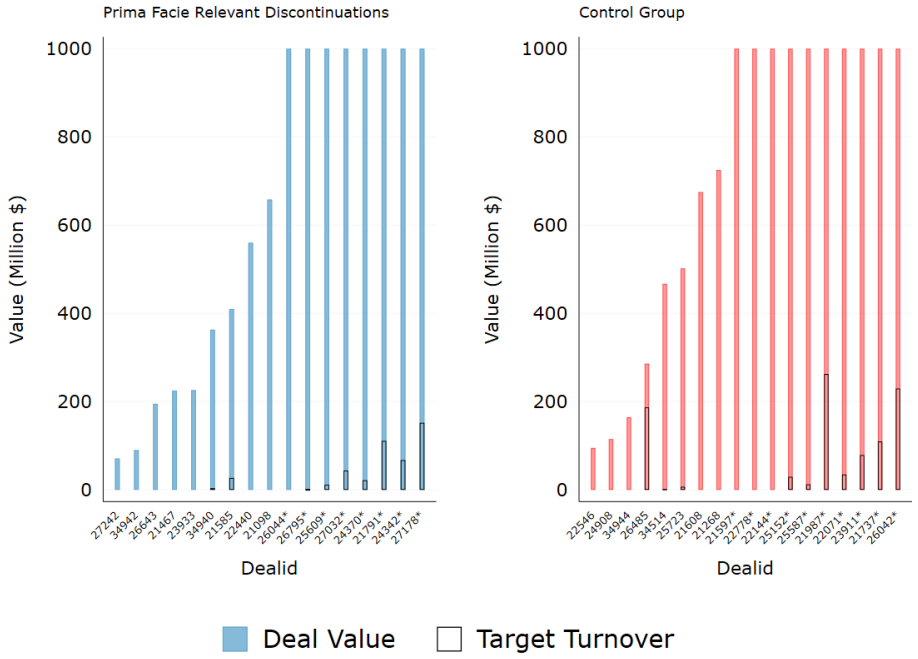
Finally, we look at the deal value and how it compares to the turnover of the target company. Figure I.9 shows that:

- deals with discontinuations deserving further scrutiny are all characterised by values strictly above $50 million;
- deals with discontinuations deserving further scrutiny have disproportionately high deal values compared to the turnover of the target companies, which often have no revenues from sales and limited revenues from other sources (typically collaboration agreements).

Similar features emerge when looking at the control group.

The observed deal value seems to diverge from CEM (2021): they indeed find a clear bunching of deals with overlaps just below the US antitrust review threshold of $50 million (in their sample period). We attribute such results to at least two factors: first, our deal database is mainly based on public sources, and we may have a sample selection bias towards relatively larger deals; second, our analysis of company portfolios, overlaps and discontinuations is primarily based on public clinical trial data, which means that we would only be able to analyse a deal if each company involved had conducted at least one clinical trial, leaving out of our analysis all deals where, for example, the target is a very small, nascent company that has only done preclinical research. However, we note that such deals are a priori less likely to give rise to killer acquisition concerns given the uncertainty inherent in preclinical pipelines.

Figure I.9: Deal Value and Target Turnover (Total) in M&A Deals: Prima Facie Relevant Discontinuations deserving further scrutiny vs. Control Group



Source: Lear analysis. Note that the deal value has been capped at $1000 million for scaling purposes. This cap applies to all deals marked with an asterisk (*) whose actual values range from 1.6 to $70.5 billion. In these cases, the target turnover has been proportionally adjusted to accurately reflect its relative value.

II Evaluation Challenge

This part of the study aims at providing an assessment of the suitability of merger and antitrust rules to deal with killer acquisitions that, as such, deserve further scrutiny.

Killer acquisitions may fall in one of the following three groups, depending on the modalities of the acquisition and consequently on the available tools to capture them:

- concentrations that were notified to and examined by the Commission. These cases fall within the scope of the EUMR, and for a sample of such mergers we evaluated if the Commission's clearance decision (with or without remedies) was followed by a harmful discontinuation, or whether any remedies imposed were effective in impeding competitive distortions;
- transactions that are structured as concentrations but fall outside the EUMR because they are below its reporting thresholds. For these cases we considered how the Commission or relevant National Competition Authorities (NCAs) could have detected the potential harmful effects of those killer acquisitions;
- transactions that fall outside the EUMR because they do not constitute concentrations within the meaning of the EUMR (e.g. licensing agreements). The aim with reference to this group of deals has been investigating to what extent the Commission could rely on Articles 101 and 102 TFEU to deal with those killer acquisitions.

The report first seeks to find out how well did the Commission's substantive merger assessment deal with five transactions involving overlapping R&D projects that were notified to the Commission in the period 2014-2019.[233] The analysis aims at ascertaining whether the Commission has correctly anticipated the risk of discontinuation, and in case of remedies, whether the remedies have effectively addressed the concern raised.

We then turn to a discussion that relates primarily to a different kind of transaction – that is, acquisitions of small innovators whose turnovers may not reflect their competitive importance or trigger review at the time they are acquired. The fundamental question here is not whether the Commission's substantive assessments are sound, but whether the Commission and other competition regulators have appropriate notice and opportunity to address such transactions *ex ante* in the first place.

We begin our assessment in this area by considering key parameters of the Commission's competence under the EUMR, and then briefly review various alternatives to the current notification thresholds that have been proposed and some of the challenges they present. We then discuss a different approach to the problem, in the use of referrals under Article 22 EUMR as a corrective mechanism to address cases where regulatory competence otherwise might be lacking or misplaced. We conclude that the referral process is workable in specific situations and has enabled the Commission to address some anticompetitive transactions more effectively.

We then conduct two hypothetical case studies, to show how Article 22 EUMR and Articles 101 and 102 TFEU might be applied in practice to deal with potentially harmful transactions. In particular, we start from the facts of two cases that were highlighted in the fact-finding challenge as deserving further scrutiny, and – after having made some

[233] Although the period considered in the fact-finding challenge analysis goes from 2014 to 2018, we considered cases notified to the Commission also in 2019, because two very relevant cases for the ex-post evaluation were notified in such year (BMS/ Celgene and AbbVie/ Allergan).

assumptions that allow us to obtain two fictitious cases that clearly support a killer acquisition narrative – we evaluate the available tools to deal with such cases. The first case study includes the assessment under Article 22 EUMR tailored to the specific, hypothetical, facts assumed in that case. The second case study allows to formulate two distinct hypothetical scenarios: one where the transaction can be seen as a concentration - and hence the Article 22 EUMR assessment is conducted - and one where it can be seen as a license agreement - and hence we assess whether Article 101 and 102 TFEU would have been well suited to deal with it.

Finally, we observe that a singular challenge in addressing potential killer transactions is detecting them in the first place, given the many ways they might be structured and their possible execution with respect to small, innovative targets. As discussed in Chapter I, many (particularly licensing) transactions are not publicized in any meaningful fashion, and there appear to be very few features by which competitively benign and killer transactions can be systematically distinguished from each other. We therefore suggest that the Commission might consider establishing an online registry of newly acquired interests in pharmaceutical pipelines (of which we provide a model) for a trial period that would enable it to monitor developments and to determine whether the maintenance of such a registry might be a proportionate and effective supplement to current enforcement tools.

Box 13: Facts used in our assessments of transactions and case studies

It is important to note that in assessing individual transactions and preparing this Report, we have relied solely on publicly available information, and did not have access to the companies involved in the relevant transactions or any confidential business information. We relied, in particular, on the following sources of information:

- Springer Nature's AdisInsight database on drugs in commercial development worldwide;[234]
- ClinicalTrials.gov (i.e. the most comprehensive registry of clinical trials worldwide);[235]
- online resources for medical professionals, including journal articles regarding the results of clinical trials and R&D trends/challenges that were accessible free of charge through the PubMed database,[236] treatment guidelines of various medical associations (e.g. ESMO) that were in force (and often amended) over the period covered in this study, and information published by the EMA and FDA on their official websites;
- representations made by transaction parties (in, e.g. their press releases, annual reports, SEC filings, published pipelines, management interviews, and the like), which were assembled from the parties' websites and other online archives; and

[234] A full description of this database is provided in section I.1.2 of this Report.

[235] A full description of this registry is provided in section I.1.3 of this Report.

[236] PubMed (https://pubnmed.ncbi.nlm.nih.gov) is a searchable database of citations and abstracts of medical research literature, maintained by the U.S. National Library of Medicine, that provides links to other websites carrying the relevant, full-text material.

- news reports and analyses by specialists in the pharmaceuticals sector (e.g. Scrip[237] and Fierce Pharma[238]), as well as more general, business-oriented news publications online.

Where these public sources were not sufficiently clear, we drew on the knowledge and experience of pharmaceutical industry experts in the Team to assess, e.g. the scope for competition between different molecules, technical trial results and their commercial ramifications, pipeline prospects for success, and the various incentives that might have shaped firms' strategic decisions.

Our desk research into numerous transactions confirms that it is often impossible to reach definitive conclusions, on the basis of public information alone, regarding the reasons companies discontinued various pipelines or the competitive effects of such discontinuations. Accordingly, all references in this Report (whether express or implied) to facts that are not established as matters of public record must be regarded as hypothetical and a means of facilitating the discussion of points of law. They are neither allegations of wrongdoing nor statements of actual fact, and the authors expressly disclaim any interpretation or use of all or any part(s) of this Report that is inconsistent with the foregoing.

II.1 Concentrations notified to the European Commission

Concerning the first group of cases, that is concentrations that were notified to the Commission, we evaluated the following list of five transactions:

- M.8401 J&J/Actelion;
- M.7275 Novartis/GlaxoSmithKline Oncology Business;
- M.7872 Novartis/GSK (Ofatumumab Autoimmune Indications);
- M.9294 BMS/Celgene;
- M.9461 AbbVie/ Allergan.

To select the above cases, the Team only considered cases that were in scope for the study (e.g. they took place in the time period of interest, involved human drug R&D projects, as opposed to R&D for medical devices, involved market-to-pipeline overlaps or pipeline-to-pipeline overlaps, etc). The deals M.9294 BMS/Celgene and M.9461 Abbvie/ Allergan are an exception, as they happened a few months after the relevant time period considered in the study. However, they were included as they meet the other criteria for inclusion in the study, and appear to be interesting cases, the evaluation of which can provide useful lessons. It should be noted that this list of cases ensures that a variety of features across cases is reached (e.g. different markets are covered, cases where the Commission required remedies as well as cases cleared unconditionally are included).

[237] Scrip (https://scrip.citeline.com) is a subscription-based source of global commercial pharmaceutical news and analysis that was part of Informa PLC for most of the period covered by this study and, in 2022, was divested and merged with Norstella.

[238] Fierce Pharma (https://fiercepharma.com) is a free (advertiser-supported) daily news service providing general coverage of pharmaceutical companies and developments worldwide that is owned and operated by Questex, LLC.

In the assessment of each of these cases, the following methodology has been adopted. We first assess the evolution of the overlapping drug R&D projects following the acquisition by examining whether the R&D project has been further developed (e.g. has been moved to a subsequent phase of clinical trials) and/or commercialized. In cases cleared with divestiture, this amounts notably to examining whether the divested asset has been developed and commercialized.

When the evidence collected suggests that there has been a discontinuation, the Team first investigates whether the firms' decision to discontinue the pipeline project is grounded on technical reasons (e.g. safety reasons, poor accrual, poor experimental design). In case the discontinuation can be technically motivated, it can be concluded that it would have happened anyway, and it is unrelated to the merger.

When there is not enough or solid evidence suggesting there are technical reasons behind the decision of discontinuing the pipeline project, the Team performs an overall assessment of the Commission's decision. The key dimensions that typically characterize the Commission's assessment and that the Team evaluates are:

- the definition of the relevant market: are the relevant drugs close substitutes?
- the assessment of the existing and potential competitors in the relevant market: are there viable and strong competitors to preserve and stimulate the race to innovation? The competitive landscape may also provide useful insights on the chance of success of a pipeline, i.e. the technical and commercial value, regardless of the firms' incentives.
- in case of remedies: have the remedies been properly designed to mitigate firms' incentives to distort competition?

The rest of this section presents the ex-post assessment for each of the five cases listed above.

II.1.1 Notified concentration #1: J&J/Actelion

II.1.1.1 Background

On 12 April 2017 the European Commission received notification of the proposed acquisition by Johnson & Johnson ("J&J")[239], through Janssen Holding GmbH ("Janssen"), of control (at least 67% of the shares) of Actelion Pharmaceuticals Ltd ("Actelion")[240] (the "Transaction"). J&J and Actelion (collectively the "Parties") announced that the value of the Transaction was approximately $30 billion.

As part of the Transaction, J&J also proposed to acquire a 16% interest (and option to acquire a further 16% interest with rights to board representation) in Idorsia Ltd ("Idorsia"), a newly-formed company into which Actelion would spin off the majority of its drug discovery operations and early-stage pipeline assets. The investment was part of a broader package of agreements relating to J&J's extension of long-term financing, technology licenses and cross-licenses, and collaboration agreements regarding several experimental compounds.

[239] J&J is a US company whose pharmaceuticals business (Janssen) specializes in five therapeutic areas: (i) cardiovascular and metabolic diseases; (ii) immunology; (iii) infectious diseases and vaccines; (iv) neuroscience; and (v) oncology.

[240] Actelion is a Swiss company that is focused on prescription medicines in a number of therapeutic areas, most notably cardiovascular diseases.

The Commission reviewed the Transaction and approved it, subject to remedies, in a decision dated 9 June 2017 (the "Decision"). The Parties completed the Transaction on 16 June 2017.

II.1.1.2 The Commission's Decision

In the Decision, the Commission identified the following two overlaps between the Parties' activities:

- an overlap between two pipeline products (orexin receptor antagonists) that the Parties were developing as treatments for insomnia; and
- an overlap between a pipeline product (ponesimod) that Actelion was developing for multiple sclerosis and several older drugs that J&J distributed for Biogen, Inc. ("Biogen") in a number of EU Member States.

Details of the second overlap are provided in Appendix A.4.1, as we found no discontinuation of the relevant products. The rest of the assessment for this case addresses the overlap in insomnia, where we found a refocusing of development that entailed the discontinuation or delay of an overlap product.

The overlap in therapies for insomnia involved two molecules that inhibit the action of certain proteins (orexins) that transmit signals in the brain. Orexins promote arousal, and therefore play an important role in the sleep/wake cycle, motivation and mood. Because pharmacological blockage of orexin receptors facilitates sleep, drugs having that effect were being developed, and the Commission concluded that they would occupy a distinct product market (when commercialised) based on their unique mechanism of action and consequent differences in efficacy, safety and potential pricing.

The Commission identified a pipeline overlap between Actelion's ACT-541468 (daridorexant) and J&J's JNJ-7922 (seltorexant). ACT-541468 is a dual orexin receptor antagonist ("DORA") that Actelion was developing (in Phase II trials) as a treatment for primary insomnia. This pipeline was to be transferred to Idorsia, in which J&J would take a minority stake. JNJ-7922 is a selective orexin-2 receptor antagonist ("SORA") that J&J and Minerva Neurosciences, Inc. ("Minerva")[241] were co-developing (in Phase II trials) as potential treatments for primary insomnia and major depressive disorder ("MDD"). The agreement between J&J and Minerva (the "Co-Development Agreement") provided that the drug was to be commercialised by Minerva in the EEA and by J&J elsewhere.[242]

This information is summarised in Table II.1 below.

[241] Minerva is a US company in which J&J held an 11% interest at the time of the Decision, and was focused on clinical development of four potential therapies for diseases of the central nervous system.

[242] A copy of the Co-Development Agreement can be found as an attachment to one of Minerva's SEC filings (see: https://fintel.io/doc/sec-nerv-minerva-neurosciences-ex107-2014-june-10-18513-773).

Table II.1: the overlap in insomnia identified by the EC (June 2017 Decision)[243]

Product market	Geographic market	Pipeline/ drug	Owner	Phase
Orexin-antagonists for the treatment of insomnia	Global or at least EEA-wide	ACT-541468 (daridorexant)	Actelion pre-Transaction; spun off to Idorsia for post-Transaction development	Phase II
		JNJ-7922 (seltorexant)	J&J; being co-developed with Minerva for commercialisation by Minerva in the EEA and by J&J elsewhere	Phase II

Source: Lear

Following the market investigation, the Commission concluded that J&J would have the incentive and the ability to discontinue, delay or re-orient one of the overlapping pipelines. In particular, J&J was the originator and co-developer of JNJ-7922, and therefore could directly influence its development and commercialisation. J&J also was likely to have the ability to influence Idorsia's development of ACT-541468 given its extension of long-term financing and a 15-year credit facility, licensing and cross-licensing of various technology rights, and rights and options to co-develop and commercialise various compounds. J&J could nominate members of Idorsia's board if it opted to convert certain financing into a shareholding of more than 20% and, in that capacity, would have access to sensitive information regarding Idorsia's strategy that J&J might use in deciding how to develop JNJ-7922.

In light of the concerns expressed by the Commission, the Parties offered remedies to ensure the maintenance of effective competition notwithstanding J&J's post-acquisition involvements with Idorsia and Minerva. In particular, these included:

- Idorsia commitments: J&J committed, inter alia, not to increase its shareholding in Idorsia beyond certain thresholds (at most 16%); to waive any right to nominate board members in Idorsia; not to acquire (directly or indirectly) the possibility of exercising influence over the whole or part of Idorsia; and not to obtain any non-public, commercially sensitive information about Idorsia's activities regarding orexin-antagonist products (described in the Decision as ACT-541468 for insomnia).

[243] The EC defined the product market as the one for orexin-antagonists for the treatment of insomnia, based on the TI, the MoA and a further sub-segmentation. Orexins are small proteins that work as neurotransmitters, i.e. to transmit signals between neurons in the brain. Orexins impact arousal and sleep: a loss of the orexin-producing neurons causes sleepiness. Orexin-antagonists (drugs that inhibit the effects of orexins) were, at the time of the Decision, a novel approach for promoting sleep and treating insomnia. Consistently with the precedents when defining geographic markets for pipeline products, the EC defined the geographic market for the development of orexin-antagonists for insomnia as global or at least EEA-wide.

- Minerva commitments: J&J committed to cancel its minority shareholding in Minerva (and thereafter not to acquire, directly or indirectly, the possibility of exercising influence over Minerva); "to continue supporting Minerva in relation to JNJ-7922"; to grant Minerva the "final say" on all decisions concerning the development of JNJ-7922 for insomnia on a global basis; to continue funding development of JNJ-7922 in insomnia, with an up-front payment of $30 million, forgiveness of $11 million in accrued Phase II costs, and various Phase III milestone payments "should Minerva conclude that the clinical trials show technical success and have a positive regulatory pathway"; and to forego its right to royalties on Minerva's future sales for insomnia in the EEA.

II.1.1.3 The evolution of the overlapping pipelines after completion of the Transaction

Based on information in AdisInsight and ClinicalTrials.gov, we tracked the evolution of ACT-541468 and JNJ-7922 after completion of the Transaction, to determine whether either of them was discontinued.

Our analysis shows that Actelion/Idorsia's pipeline project (ACT-541468) was successfully commercialised as a treatment for primary insomnia. Idorsia completed 18 of the 21 clinical trials of ACT-541468 undertaken prior to launch, obtained its first marketing authorisation in January 2022, in the US, and launched the drug there under the brand name QUVIVIQ® in May 2022. Idorsia also obtained an EU marketing authorisation in April 2022, launched QUVIVIQ in Germany and Italy in November 2022, in Spain and the UK in the second half of 2023 and launch in France is set for the first half of 2024.[244]

In contrast, it appears that J&J (more specifically Minerva, as explained below) stopped developing JNJ-7922 as a treatment for primary insomnia sometime after April 2019 (when it completed its most recent clinical trial, in Phase II, for that indication).[245]

Other facts that are relevant to the assessment include the following:

- In May 2019, J&J published a summary of its pipelines showing that it planned to develop JNJ-7922 first as a treatment for MDD and, after obtaining marketing authorisation in that indication, to seek a line extension authorizing it to market JNJ-7922 for insomnia.[246]
- In June 2020, Minerva exercised its option under the Co-Development Agreement not to participate in further development of JNJ-7922. Since then, Minerva has not been involved in developing JNJ-7922 for any indication.

[244] Idorsia Media Release (25 July 2023) (https://www.idorsia.com/documents/com/media-releases-hy2023-financial-reporting-final-en.pdf). Idorsia also obtained approval to market QUVIVIQ in the UK (September 2022), Switzerland (December 2022) and Canada (May 2023), and licensed a pharmaceutical company in China to develop and commercialise QUVIVIQ there (September 2022).

[245] Although Minerva announced upon completion of that trial that the results "will help to define a Phase 3 clinical development program for seltorexant that potentially will encompass both MDD and insomnia" (https://www.globenewswire.com/en/news-release/2019/06/24/1872915/32445/en/Minerva-Neurosciences-Announces-Achievement-of-Primary-and-Key-Secondary-Objectives-in-Phase-2b-Clinical-Trial-of-Seltorexant-MIN-202-in-Insomnia.html), J&J appears to have done no further work to develop JNJ-7922 as a treatment for primary insomnia.

[246] J&J Investors' Presentation (15 May 2019) (https://johnsonandjohnson.gcs-web.com/static-files/99720898-6788-4bad-b066-a1b53212629d).

- From July 2020 through September 2023, J&J began six clinical trials of JNJ-7922 for treatment of MDD.[247] J&J initiated no new trials in primary insomnia, but all of its studies in MDD relate to some extent to secondary insomnia; two of them enlisted only MDD patients with insomnia symptoms, and the other four included some sleep-related measures of the drug's effect.

II.1.1.4 Reasons for discontinuation

The evidence collected suggests that Minerva opted out of further development of JNJ-7922 because it could realize immediate and substantial financial benefits by doing so. Minerva was developing several drugs (including its lead compound, roluperidone, for treatment of schizophrenia) but had generated losses and a negative cash flow since its inception in 2007.[248] Its decision to opt out of the project with J&J eliminated its obligation to fund some Phase III trials, allowed it to focus its limited financial resources on roluperidone, and enabled it to realize $41 million in previously deferred revenue.[249] After its opt-out, Minerva also was able to sell its interest in royalties on future sales of JNJ-7922, for an upfront payment of $60 million and up to $95 million in future milestone payments.[250]

J&J's interests in JNJ-7922 were different; it could comfortably invest in the development of numerous drugs for a variety of uses, and its compound had shown promise in several indications (including as a treatment for primary insomnia that J&J had exclusive rights to sell outside the EEA). Presentations that J&J made to investors shortly before and after it agreed to acquire Actelion suggest that the company might have refocused its pipeline as a result of the acquisition.[251] However, it appears more likely that J&J shifted its focus from primary insomnia to MDD with insomnia symptoms ("MDDIS") as a series of trials begun in 2014 made it increasingly clear that JNJ-7922 not only alleviated sleep disturbances but also significantly improved the core symptoms of depression.[252] As results were obtained from these trials, it appears that what began

[247] As reported in ClinicalTrials.gov, these consisted of three Phase III trials (NCT04532749, NCT04513912, and NCT0453352), two Phase I trials (NCT04451187 and NCT0495160), and a standard-of-care study (NCT05109195). As of 1 October 2023, two Phase III trials and one Phase 1 trial were ongoing.

[248] Minerva stated in its 2020 annual report that "We have no products approved for commercial sale and have not generated any revenue from product sales to date. . . . As of December 31, 2020, we had an accumulated deficit of $284.8 million. We expect to continue to incur significant losses for the foreseeable future, and we expect these losses to increase. . .. [W]e may never generate revenue or become profitable" (https://www.sec.gov/ix?doc=/Archives/edgar/data/1598646/000156459021011340/nerv-10k_20201231.htm). Minerva continued to report losses and negative cash flow in 2023 (see: https://www.sec.gov/ix?doc=/Archives/edgar/data/1598646/000095017023036159/nerv-20230630.htm).

[249] Minerva Neurosciences, Form 10-Q for the quarter ended 30 June 2020 (https://www.sec.gov/ix?doc=/Archives/edgar/data/1598646/000156459020035289/nerv-10q_20200630.htm).

[250] GlobeNewswire (19 January 2021) (https://www.globenewswire.com/news-release/2021/01/19/2160616/0/en/Royalty-Pharma-Acquires-Royalty-Interest-in-Seltorexant-From-Minerva-Neurosciences.html).

[251] Compare J&J 3Q16 Earnings Call (18 Oct. 2016) (https://johnsonandjohnson.gcs-web.com/static-files/663d615f-0546-40d1-a196-c24908464233) with J&J Investors' Presentation (17 May 2017) (https://static.seekingalpha.com/uploads/sa_presentations/998/9998/original.pdf).

[252] See NCT02067299, NCT02476058 and NCT03227224; K Recourt et al., Seltorexant shows antidepressant and sleep-promoting effects (2019) (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6722075/); A Savitz et al., Efficacy and Safety of Seltorexant as Adjunctive Therapy in Major Depressive Disorder (2021) (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8653874/).

as a project addressing primary insomnia with adjunctive MDD gradually became a project addressing MDD with adjunctive insomnia.

A review of various business publications and discussions with the Team's pharmaceutical experts suggest that J&J might well have refocused its development of JNJ-7922, given the results emerging from its clinical trials, because treatment of MDD is an unmet need with greater commercial potential than treatment of insomnia.[253] As discussed with our findings in section II.1.1.4.1 below, although several DORAs for treatment of insomnia have been launched in the US since 2015, they have been generating relatively little revenue. Accordingly, once it had supporting trial data, J&J may have seen a commercial benefit in making MDD its project focus.

There is a sound clinical explanation for the fact that J&J's development strategy differed from that of Idorsia: while the blockade of a single orexin receptor with a SORA (like JNJ-7922) can alleviate depression, there is troubling evidence that the blockade of two orexin receptors (with a DORA like ACT-541468) can aggravate depression and prompt suicidal ideation in persons with MDD.[254] Accordingly, Idorsia did not have the same range of options that J&J had.[255]

In conclusion, J&J discontinued or delayed development of JNJ-7922 in primary insomnia and focused development on MDD. However, this appears to have been motivated by data emerging from a series of trials begun in 2014 and by the fact that Merck/MSD's Belsomra did not perform as well as anticipated following its launch in 2015. Accordingly, it appears that development of JNJ-7922 would have taken the same course absent the acquisition. This will be further investigated below.

II.1.1.4.1 The evolution of the competitive landscape after the merger

We looked at how competition in the relevant products evolved after the Transaction, for several reasons. First, this can further clarify J&J's likely motivations in refocusing its development of JNJ-7922, because incentives to kill an overlapping product are inversely related to the number and strength of rivals. Second, although we do not observe what would have happened in the absence of the deal (and of the remedies), understanding how the competitive landscape has evolved can shed light both on the Commission's ex ante assessment of the Transaction's likely competitive effects and on whether the remedies adopted by the Commission were fit for purpose.

The Decision states that at the time of the investigation, no orexin antagonists for treatment of insomnia were being sold in the EEA, and only three firms had them in Phase II or Phase III trials with an intention to launch them in the EEA. Those were:

- Actelion's daridorexant (ACT-541468) (Phase II);
- J&J's seltorexant (JNJ-7922) (Phase II); and

[253] Pharmaceutical experts in the Team also suggested that J&J might differentiate JNJ-7922 from other MDD drugs, and further enhance its value, by obtaining approval to market it as a treatment for MDD with secondary insomnia.

[254] See: C Summers et al., Orexin/hypocretin receptor modulation of anxiolytic and antidepressive responses (2018) (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6591110/)).

[255] Indeed, persons who were using antidepressants were ineligible to participate in Idorsia's trials of ACT-541468, and the Product Information package approved by the EMA states that QUVIVIQ "should be administered with caution in patients exhibiting symptoms of depression." See: Eligibility Criteria as reported on ClinicalTrials.gov for trials of ACT-541468; EMA, EPAR – Quviviq (Annex I) (https://www.ema.europa.eu/en/documents/product-information/quviviq-epar-product-information_en.pdf).

- Eisai's lemborexant (Phase III).

In addition, Merck/MSD was supplying suvorexant (Belsomra®) in the US, Japan and Australia, but there was no indication that it had any intention to supply its drug elsewhere.[256]

Table II.2 presents the progress made after the Transaction by each of these molecules.

Table II.2: Developments in competing molecules after the Transaction

Drug	Status at time of Transaction	Developments	Marketed in EU?
Idorsia's QUVIVIQ® / ACT-541468 (daridorexant)	Phase II	Authorised in the US (January 2022) and launched there in May 2022. Authorised in the EU (April 2022) and first launched in EU Member States in November 2022.	Yes
J&J/Minerva's JNJ-7922/MIN-202 (seltorexant)	Phase II	Now in Phase III development for treatment of major depressive disorder, may be covered by future application for a post-approval line extension in primary insomnia.	No
Eisai's Dayvigo® (lemborexant)	Phase III	Launched in the US (2020), Canada, Japan, India and several smaller Asian countries; marketing authorisations obtained by mid-2023 in over 15 countries in Asia and the Americas. No EU marketing authorisation appears to have been sought, for unknown reasons.	No
Merck/MSD's Belsomra® (suvorexant)	Marketed	Launched in Japan (2014), the US (2015), and Australia (2017). Approved in Canada (2018) but either was not launched there or has been withdrawn. No EU marketing authorisation appears to have been sought, for unknown reasons.	No

Source: Lear

[256] J&J/Actelion, paragraph 36.

As shown in Table II.2, of the few molecules that were being sold or were in advanced development for treatment of insomnia, only Idorsia's daridorexant (QUVIVIQ) has been commercialised in Europe. Furthermore, it appears that no other molecule that was in pre-clinical trials at the time of the Decision (nor molecules for which trials may have started after the Decision) made it to the market.

In our assessment of the evolution of competition, we considered the prices of orexin antagonists and other treatments for primary insomnia, as a means of evaluating the drugs' competitive viability and interactions. While general public sources provide little readily accessible information about prices nearly ten years ago, we noted two points of interest.

First, we noted that Merck sold Belsomra in the year it was launched at an average wholesale price ($10.52/tablet) that was higher than that of the #3 non-benzodiazepine (Pfizer's Sonata, $8.23/tablet) but lower than that of the #2 non-benzodiazepine (Sepricor's Lunesta, $14.90/tablet) and Sanofi-Aventis' best-selling Ambien ($17.42/tablet).[257] That is a bit surprising, given the Commission's finding in J&J/Actelion that orexin antagonists would be a significant improvement over non-benzodiazepines (the existing standard of care) and were expected to command higher prices as a result. Merck's pricing of Belsomra suggests that Merck may have felt competitively constrained by the other non-benzodiazepines, perhaps in light of market studies it is likely to have conducted in order to assess demand before establishing its own price point.

In light of this finding, it appears that when innovative drugs have not yet been launched in the EEA, general information about their pricing and performance outside the EEA might usefully inform the Commission's market definitions (bearing in mind that the way different countries price and purchase medicines necessarily limits the inferences that can be drawn). The US in particular might provide a useful referent because its sizeable pharmaceutical markets typically draw early launches, and the state's limited role in pharmaceutical pricing/procurement might facilitate an assessment of the extent to which different drugs are potential substitutes. In addition, where the Commission finds that a future market exists, it might usefully broaden its competitive assessments to consider information regarding the market(s) for the closest substitute(s) for the pipeline drugs. In some cases, such information might demonstrate the existence of competitive constraints that operate across the boundaries of the defined product markets. More generally, it may help to make the Commission's decisions more robust because they are based on actual evidence (rather than predictions) of competitive dynamics that may be common to both markets.

We noted a second point of interest, relating to the price impact of generic drugs. Around the time Belsomra was launched, competition with generics had caused a serious decline in total US sales of insomnia medications, from $2.1 billion in 2013 to $1.4 billion by 2016.[258] However, industry observers often suggested that the imminent launch of orexin antagonists might revitalise the category, and a leading analyst forecast in 2015

[257] See: JD Lie et al., Pharmacological Treatment of Insomnia (2015), Table 1 (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4634348/).

[258] See, e.g.: Sleep Review (18 February 2015) (https://sleepreviewmag.com/sleep-disorders/insomnia/insomnia-treatment-market-decline-new-drugs-aid-recovery/); Fierce Pharma (14 December 2021) ("the extremely low cost of established, generic insomnia drugs have dragged down the overall value of the market for sleep medicines").

that they would reverse the downward spiral and push total sales in the category up to $2.3 billion in 2023.[259] Such forecasts were not borne out. An influential provider of product ratings/reviews advised consumers in 2015 to "think twice" before buying Belsomra, given its limited efficacy and a retail price that was more than four times the retail price of zolpidem (the active ingredient in Ambien).[260] Similarly, a study in 2016 noted that "[t]he biggest foreseeable barrier to the widespread use of suvorexant is availability and cost. The estimated cost of suvorexant is between $200 and $300 per month . . . compared to generic [non-benzodiazepines] and benzodiazepines that can cost as low as $5–$10 per month."[261]

Such substantial price differences almost certainly depressed demand for Belsomra, which was the only orexin antagonist approved for treatment of insomnia in the period 2014-2020 but was unable to show appreciably greater efficacy than older/cheaper drugs because marketing approvals required that it be supplied in relatively low doses. Moreover, it has been suggested that a marked susceptibility to pricing pressures may distinguish sleep aids from most pharmaceuticals. Because insomnia is not regarded as a serious/life-threatening disorder, patients may be prescribed an unusually broad range of therapies that form a chain of substitutes, transmitting competitive pressures through a series of common trade-offs from the low end (antihistamines) to the high end (orexin antagonists) through approved or off-label use of, e.g. benzodiazepines, sedating antidepressants, atypical antipsychotics, mood stabilisers, and conventional non-benzodiazepines – virtually all of which are genericised.

Pharmaceutical companies clearly rely on branded medicines to deliver high value, and it seems unlikely that the prospect of eventual generic competition would deter a firm from making a killer acquisition when the relevant drugs are in development or recently commercialised. However, pricing pressure doubtless contributed to the limited success of orexin antagonists following their introduction in 2015, providing further corroboration that J&J is likely to have had commercial incentives to focus its development of JNJ-7922 on something other than primary insomnia.

In sum, although we do not observe the counterfactual, our ex post assessment of developments following completion of the Transaction supports the Commission's determination in 2017 that competition in the global development of orexin antagonists is limited, and that competing drugs were not likely to be launched in sufficient time to constrain potentially anti-competitive effects of the Transaction. This case shows clearly the competitive importance of products in Phase II, despite clinical uncertainties and the existence of rivals with drugs in more advanced stages of development, and supports the ex ante adoption of remedies.

II.1.1.4.2 Lessons learned on the EC remedies

The evaluation conducted so far suggests that J&J's decision to discontinue (or delay) development of JNJ-7922 for primary insomnia might well have been unrelated to its acquisition of Actelion. However, there does not appear to have been clear evidence of that in 2017. While the series of trials that supported J&J's refocusing of development began in 2014, reasonably definitive results from that line of research were not available until 2019. Moreover, it was difficult to dismiss forecasts made in 2015, that orexin

[259] See: Sleep Review (18 February 2015) (discussing study by GlobalData).

[260] Consumer Reports (12 July 2015).

[261] J Lee-Iannotti & J Parish, Suvorexant (2016) (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4772996/).

antagonists could revitalize the pricing and profitability of sleep medications, until they were discredited by Merck's inability to make serious inroads with Belsomra over several years. Accordingly, for reasons discussed above, the ex ante adoption of remedies in 2017 appears to have been warranted.

Despite the foregoing, a thorough analysis of the remedies adopted by the Commission suggests that they may not have been sufficient to ensure that competition between the parties' pipelines remained as robust post-completion as it was prior to the Transaction.

In order to assess this, we analyzed how the remedies may have changed the Parties' incentives to continue developing their pipeline products, and whether they were optimally designed to anticipate the parties' actions following clearance.

It appears that Idorsia's post-closing incentives to continue developing ACT-541468 as a treatment for insomnia were largely consistent with Actelion's incentives prior to the Transaction. Idorsia obviously had an interest in ensuring the success of one of its most promising assets (i.e. one of the four compounds moving to Phase III trials in 2018), and the remedy ensured that J&J could not directly influence its efforts to do so. While Idorsia's management might have had some incentive to avoid displeasing a significant (albeit passive) shareholder, that appears unlikely to have appreciably influenced company operations given Idorsia's need to generate turnover and management's fiduciary duty to the other shareholders. Moreover, the remedial "firewall" prohibiting the disclosure to J&J of non-public, competitively sensitive information regarding Idorsia's activities in orexin antagonists provided an important assurance of Idorsia's ability to benefit fully from its development efforts.

Evidence that these measures have been effective can be seen in Idorsia's further development and commercialisation of ACT-541468, as has already been described.

It appears that J&J also had appreciable incentives, after it acquired Actelion, to continue developing JNJ-7922 as a treatment for primary insomnia, given its right to commercialise the finished drug outside the EEA (including, e.g. in the US and Japan, reportedly the two largest markets for prescription sleep aids). However, it appears that these incentives may have been diminished to some extent as a result of the Transaction and the Commitments given to the Commission, for several reasons:

- J&J could no longer ensure that decisions taken by Minerva concerning the development of JNJ-7922 would best position the resulting product for successful commercialisation. For example, Minerva might decide to formulate the drug in sub-optimal ways; conduct essential trials in the EEA (rather than the US), so that FDA approval might be more difficult to obtain; design clinical trials with comparators or end points that J&J considered ill-suited to effective commercialisation; or market the finished drug in the EEA in ways that could reduce J&J's ability to achieve optimal pricing/listing elsewhere.
- If JNJ-7922 was successfully developed as a treatment for insomnia, J&J would neither earn royalties on Minerva's sales of it in the EEA nor share in profits earned on those sales through its former 11% interest in Minerva.
- Finally, commercialisation of JNJ-7922 as a treatment for insomnia could reduce the sales or profitability of ACT-541468 (QUVIVIQ), from which J&J might benefit through its 16% interest in Idorsia.

Some of these concerns might be more hypothetical than real. For example, J&J must have been reasonably confident, when it undertook its collaboration with Minerva, that Minerva had sound R&D capabilities and incentives to make the project a success. In contrast, J&J may have had less confidence that Idorsia, a new company with little

marketing infrastructure, could effectively commercialise its product (assuming that the drug was successfully developed). Such elements aside, J&J's incentives also would depend, e.g. on the costs of further development, sales projections for the two products, and the royalties payable by J&J on its sales outside the EEA. Accordingly, while commercial prospects outside the EEA might have provided sufficient post-closing incentives for J&J to continue developing JNJ-7922 for insomnia, this was not assured.

As discussed above, it appears likely that J&J eventually refocused its development of JNJ-7922 in light of technical and commercial developments that were unrelated to the Transaction. However, the decision to discontinue/delay development of the compound as a treatment for primary insomnia highlights the fact that, under the remedy design, the development of JNJ-7922 in primary insomnia was dependent on the active participation of a partner, Minerva, that instead took the decision to discontinue it.

Several alternatives might have provided greater assurance that JNJ-7922 would not be discontinued/delayed in order to reduce competition. The most obvious remedy might have required J&J to divest its 16% stake in Idorsia, eliminating any interest in ACT-541468 that might dampen J&J's incentives to develop JNJ-7922. Alternatively, the remedy might have required that J&J divest JNJ-7922 to another company that would develop it as a treatment for primary insomnia (if Minerva was willing to consent to novation of J&J's obligations under the Co-Development Agreement). Either option would have made a clean break between J&J and one of the overlapping pipelines, helping to ensure that any later developments were not motivated by a desire to eliminate competition.

A third option might have entailed commitments that J&J would continue to develop JNJ-7922 as a treatment for primary insomnia, assumedly pursuant to pipeline plans made prior to negotiation of the Transaction (which would provide an objective standard against which to assess J&J's compliance with its obligations). However, variables in the design and execution of clinical trials might make it difficult to ascertain whether these obligations were being met and, at a minimum, the oversight of a Monitoring Trustee almost certainly would be required. Further, such commitments assumedly would have to be subject to a review clause, so that J&J could respond to significant clinical developments or evolving market circumstances with a more appropriate use of the compound or related development resources.[262]

It is somewhat more difficult to assess how the remedy might have affected Minerva's incentives to continue development of JNJ-7922, because the measures that were adopted were likely to have mixed effects. On one hand, they enhanced Minerva's position with a greater ability to direct the project and guarantees of future funding. Moreover, Minerva's incentives to continue development were doubtless enhanced by the greater profit potential created through elimination of its obligation to pay royalties to J&J on its sales in the EEA.

That said, the Commitments may have created more immediate (albeit unintended) incentives for Minerva to opt out of further co-development in order to alleviate some of the financial constraints on its business (as noted in section II.1.1.2 above). The remedy does not appear to have established sufficient incentives or conditions to ensure that Minerva continued to co-develop JNJ-7922 despite its financial constraints. A

[262] See: Commission Notice on remedies acceptable under Council Regulation (EC) No 139/2004, [2008] OJ C267/1, paragraphs 70-76.

requirement in the Commitments that J&J support continued development "should Minerva conclude that the clinical trials show technical success and have a positive regulatory pathway" protected Minerva's right to continue development, but did not establish any obligation to do so. Accordingly, the remedy may have made opting out more attractive to Minerva (with positive benefits on top of more typical cost avoidance) than it otherwise would have been.

It is not clear whether Minerva's opt-out had any material effect on J&J's subsequent development of JNJ-7922. We have seen no indication that Minerva opposed a developmental plan that prioritized MDD; to the contrary, the parties' Co-Development Agreement makes clear that they had a shared interest in MDD as early as 2014;[263] Minerva highlighted the relevance of MDD in public statements throughout its participation in co-development; and the pipeline showing that J&J planned to apply for a line extension covering insomnia, after JNJ-7922 was approved for MDD, was published while Minerva had global strategic control over the development of JNJ-7922 for insomnia (Commitments section B.2(c)i). Moreover, while publicly available information does not permit a definitive assessment of J&J's legal position, it appears that Minerva's withdrawal did not deprive J&J of any rights it needed in order to continue developing JNJ-7922 for insomnia. Accordingly, J&J's prioritization of MDD as a therapeutic target may be consistent with what J&J and Minerva would have done together as co-developers.

That said, it is clear that Minerva's independent management of the project was fundamental to the remedy, and that the remedy therefore could have been compromised by Minerva's decision not to continue. This highlights an inherent weakness in remedies that depend on the actions of a third party (i.e. a firm that is not a party to the transaction under review, and therefore is not an undertaking with respect to whom commitments can be accepted or enforced[264]). However, even in the absence of a formal enforcement mechanism, regulatory risk might have been reduced if the benefits that Minerva obtained under the remedy had been made contingent on its performance of its envisaged role. For example, J&J might have been obliged under the Commitments to provide its up-front payment and waiver of Minerva's accumulated costs on terms requiring a refund and recission of the waiver if Minerva did not continue to manage the project (assumedly until an EU marketing authorisation was obtained, JNJ-7922 definitively failed clinical trials, or an assessment of changed circumstances under a review clause demonstrated that the remedy should be reformed).

Other protective measures might have been adopted. For example, the Commitments might have required that J&J divest JNJ-7922 to a buyer approved by the Commission if at any time Minerva declined to perform the role detailed in the Commitments. Alternatively, the Commitments might have provided that if Minerva withdrew from co-development, J&J had an obligation to collaborate with another partner (approved by the Commission) who operated under terms ensuring that development of JNJ-7922 for insomnia continued untainted by J&J's interest in Idorsia/ACT-541468.

Such measures would not provide the definitive solution and ease of administration that a simple divestiture of JNJ-7922 would have done (and it is not clear why that wasn't agreed, unless perhaps Minerva had made known that it would not consent to any

[263] See: Co-Development Agreement sections 3.10(g), 11.5(a) and 11.6(b).

[264] See: Article 6.2 EUMR; T-162/10 Niki Luftfahrt v Commission, ECLI:EU:T:2015:218, paragraph 303.

novation of the Co-Development Agreement). However, if such remedies are adopted in future cases, this case clearly suggests that it might be prudent to establish greater incentives for third-party performance, or legally enforceable fallback protections if a third party fails to perform as expected.

In conclusion, our findings suggest that development of JNJ-7922 for insomnia was probably discontinued (or delayed) in response to technical and commercial developments, rather than in furtherance of a strategy to eliminate competition. However, the remedies adopted in this case might not have been sufficient, in different circumstances, to foreclose the anticompetitive discontinuation of an overlap asset. Remedies that might have been more effective in ensuring continued competition between the parties' pipeline products include:

- requiring modification of the deal so that J&J did not acquire an ownership (or other) interest in Idorsia (which would have been the kind of structural remedy that was least dependent on the parties' future incentives or behaviour);
- conditioning clearance on J&J's divestiture of JNJ-7922 to a Commission-approved buyer (which also could have been a relatively simple and definitive way to eliminate the Commission's competition concerns if Minerva was willing to accept novation of the Co-Development Agreement); or
- conditioning the benefits that Minerva received under the remedy on its continued performance of the role envisaged in the remedy (which would not have reduced the regulatory risk as effectively as either of the first two options, but could have helped to ensure that the remedy was effective despite the Commission's inability to enforce it directly against the third party).

II.1.1.5 Conclusions

The Commission found a pipeline-to-pipeline overlap in the Parties' development of orexin receptor antagonists for treatment of primary insomnia. At the time of the Decision, Actelion was to transfer its overlap pipeline (ACT-541468) to Idorsia, whose further development of the compound might be influenced by J&J given its acquisition of certain minority interests and option to have board representation in Idorsia, as well as various financing, co-licensing and collaboration agreements with the company. At the same time, J&J was co-developing its overlap pipeline (JNJ-7922) with Minerva. The Commission determined that J&J would have the incentives and ability to discontinue one of the two pipelines after completing the Transaction, and that actual and potential competition would not develop in time to avoid the likely creation of a substantial impediment to effective competition. Accordingly, the Commission approved the Transaction subject to remedies, which were meant to ensure that J&J's interests in, and interactions with, each of Idorsia and Minerva did not threaten existing competition in the development, or future competition in sales, of the pipeline drugs.

Our ex post assessment showed that Idorsia further developed one of the two pipelines (ACT-541468) and is now commercializing it as a treatment in the overlapping therapeutic indication (primary insomnia), while Minerva discontinued or delayed further development of the other pipeline (JNJ-7922) as a treatment for primary insomnia, with J&J instead prioritizing development of the compound in a therapeutic indication (major depressive disorder (MDD)) where there was no competitive overlap and the drugs' different mechanisms of action effectively ensured that none could arise. Based on a review of material in the public domain, assessment of how competition evolved post-Transaction, and consultation with pharmaceutical experts in the Team, our review suggests that this discontinuation is most likely to have been motivated by the results of ongoing clinical trials showing that JNJ-7922 had greater therapeutic value in MDD than was previously known, and by limited sales of the first orexin-antagonist

drug for insomnia suggesting that JNJ-7922 had less commercial potential as a sleep aid than was previously believed, rather than by an anticompetitive incentive or opportunity arising as a result of the Transaction.

We do not observe what would have happened absent the deal (i.e. if the market would have evolved differently and how), but our assessment of how the competitive landscape evolved after completion of the Transaction supports the Commission's determination that competition with the Parties' few existing and potential rivals could not be expected to prevent a possible discontinuation, redirection or delay of one of the Parties' competing pipelines, and suggests that the ex ante adoption of remedies was appropriate. However, a thorough analysis of the remedy, and of actions taken after they were adopted, also suggests that the remedies were not entirely fit for purpose, as they did not prevent Minerva's discontinuation of its role in co-developing JNJ-7922, and did not prevent the discontinuation or delay of further development of JNJ-7922 in the overlapping therapeutic indication (as such development, under the remedy design, was depended on Minerva's active participation). While it appears likely that J&J's refocusing of its pipeline was a legitimate response to an evolving appreciation of the technical and commercial potential of JNJ-7922, and was not related to J&J's acquisition of Actelion, experience with the implementation of this remedy suggests that any similar remedies in future cases might be improved by providing more robust protections to ensure that they are implemented pursuant to expectations shared by the Commission and the parties at the time the remedy is adopted, unless a waiver, modification or substitution of the commitments is granted by the Commission at a request of the parties.

II.1.2 Notified concentration #2: Novartis/GSK Oncology Business

II.1.1.6 Background

On 28 November 2014, the European Commission received notification of the proposed acquisition by Novartis AG ("Novartis")[265] of a portfolio of oncology products from GlaxoSmithKline plc. ("GSK")[266] (the "GSK Oncology Business"), by way of a purchase of assets (the "Transaction"). Novartis and GSK are jointly referred to as "the Parties".

The Commission reviewed this proposed acquisition and published its decision (the "Decision") on 28 January 2015, where it announced approval of the Transaction subject to remedies.[267]

[265] Novartis is a Swiss healthcare company, active globally in the development, distribution and marketing of medical products. Its main areas of activity cover pharmaceuticals, eye care, generics, OTC products and vaccines.

[266] GSK is a British company, active globally in the development, distribution and marketing of medical products in three main areas: pharmaceuticals, vaccines and consumer healthcare products. The GSK oncology business consists in the research, development and marketing of oncology products for various indications worldwide.

[267] This transaction forms part of a three-part transaction whereby GSK has agreed to acquire sole control over Novartis' vaccine business (excluding the influenza business) and GSK and Novartis have agreed to combine their non-prescription ("OTC" or "consumer health") businesses into a new venture (both these parts of the deal are assessed by the Commission in case M.7276). The Parties later, in December 2015, notified another transaction whereby Novartis would acquire the rights to the auto-immune indications of the ofatumumab molecule from GSK (assessed separately as case M.7872).

The Decision has focused on cancer targeted therapies that, differently from traditional forms of therapy (e.g. surgery, chemotherapy), are used primarily at advanced stages of the tumour, and their goal is to slow down cancer progression.[268]

Three classes of targeted therapies are of interest for this case, which differ according to the type of protein inhibited: i) B-Raf inhibitors, ii) MEK inhibitors, and iii) VEGF inhibitors. In particular, the Commission found overlaps in the Parties' B-Raf and MEK inhibitors in the following cancer types:

- advanced melanoma;
- ovarian cancer;
- colorectal cancer;
- non-small-cell lung cancer (NSCLC);
- melanoma brain metastases;
- uveal melanoma.

In addition to the B-Raf and MEK inhibitors, the EC found that the Parties' activities overlapped with regard to other targeted therapies (non MEK and B-Raf inhibitors) in the following other cancer types:[269]

- neuroendrocrine tumors of pancreatic origin ("pNET");
- breast cancer;
- multiple myeloma.

Details of the overlaps in the treatments for ovarian cancer, uveal melanoma and melanoma brain metastases are provided in Appendix A.4 to this report, as for the former two cancer types we found that there wasn't a discontinuation of the relevant molecules, and for the latter cancer type that the discontinuation was not of interest for our ex-post evaluation.[270] The rest of the assessment for this case is therefore focused on the overlaps where at least one of the Parties' molecules has been discontinued and where the discontinuation merited attention.

II.1.1.7 MEK and B-Raf inhibitors for advanced melanoma

II.1.1.7.1 The Commission's Decision

The Commission considered that the relevant product and geographic market is the global or at least EEA-wide market for pipeline targeted therapies for the treatment of advanced melanoma.[271] Table II.3 shows the overlap found by the Commission in the treatments for advanced melanoma, including both the Parties' monotherapies and combination therapies. It is to be noted that, while Novartis was developing its MEK

[268] The Decision, paragraphs 9 and 10.

[269] We only report the overlaps in scope for this study (i.e. excluded marketed/ marketed overlaps and overlaps involving biosimilars).

[270] The discontinuation involves the projects of GSK, which through the merger were acquired by Novartis, and after the merger Novartis lacks the ability to influence Array (the receiver of the divestment business), thus the discontinuation of GSK's (then Novartis') projects is unrelated to Array.

[271] The product market is defined at the level of the type of cancer, as the Commission considered that it was not necessary to reach a conclusion on possible further delineations of this market by lines of treatment or mechanism of action, since the Transaction raised competitive concerns irrespective of any possible further segmentation of the market. More granular definition of the relevant market was instead adopted for the use of B-Raf and MEK inhibitors in other cancer types, and more specifically, the EC relied on the cancer type, the MoA and the pipeline phase of development.

inhibitor for N-Ras mutated melanoma, GSK was developing its MEK inhibitor for B-Raf mutant melanoma.[272]

Table II.3: Overlaps in treatments for advanced melanoma identified by the EC (Jan 2015 Decision) [273]

Product market	Geographic market	Owner	B-Raf inhibitor	MEK inhibitor	B-Raf/MEK combination
Pipeline targeted therapies for the treatment of advanced melanoma	Global or at least EEA-wide	Novartis	LGX818 (encorafenib)	MEK162 (binimetinib)	LGX818 and MEK162
			B-Raf mutated melanoma	N-Ras mutated melanoma	B-Raf mutated melanoma
			Phase III	Phase III	Phase III
		GSK	Tafinlar (dabrafenib)	Mekinist (trametinib)	Tafinlar and Mekinist
			B-Raf mutated melanoma	B-Raf mutated melanoma	B-Raf mutated melanoma
			Approved	Approved	Phase III

Source: Lear

Following the market investigation, the Commission found that there were only three companies holding B-Raf and MEK inhibitors marketed or in phase III clinical trials for the treatment of advanced melanoma, Roche, GSK and Novartis. It also considered that combination treatments of all three firms were likely to enter the market and that the monotherapies and combination therapies of the three firms were close competitors.

The EC concluded that the Transaction was likely to reduce Novartis' incentives to launch LGX818 and MEK162, to the benefit of Tafinlar and Mekinist, both as combination therapy (where the latter two were at a more advanced stage in the phase III trials) and as monotherapy (where GSK's molecules were approved, while Novartis' were on Phase III trials). The likely elimination of Novartis' pipeline B-Raf and MEK inhibitors following the Transaction would, according to the Commission, result in the loss of a credible competitor, and the only other player that was on the market, Roche, would not exert sufficient competitive pressure on the merged entity post-Transaction.

Due to those concerns, the Commission imposed remedies, based on which:

[272] In fact: i) GSK did not do any studies on N-Ras mutant melanoma after a single Phase I trial (NCT04511013) that was completed on 8 November 2011, almost three years before the Transaction; and ii) an article co-authored in 2012 by some of those working on the Phase 1 trial makes clear why GSK could have decided that the project was not worth pursuing ("NRAS-mutant melanoma appears less responsive to trametinib than BRAF-mutant melanoma"). See: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC4109286/

[273] The product market is defined at the level of the type of cancer, as the Commission considered that it was not necessary to reach a conclusion on possible further delineations of this market by lines of treatment or mechanism of action, since the Transaction raised competitive concerns irrespective of any possible further segmentation of the market. More granular definition of the relevant market was instead adopted for the use of B-Raf and MEK inhibitors in other cancer types, and more specifically, the EC relied on the cancer type, the MoA and the pipeline phase of development.

- Novartis committed to returning MEK162 and divesting LGX818 to Array BioPharma Inc. ("Array") (together, the "Divestment Business");
- Array was obliged to negotiate appropriate agreements to partner with a suitable company (the "Suitable Partner"), which shall have the ability and incentive to develop worldwide and commercialise in the EEA MEK162 and LGX818.

II.1.1.7.2 The evolution of the relationship between the Parties and of the overlapping projects after the merger

Our ex-post assessment confirmed that the EC remedies were implemented, and also found that after the merger Array was involved in another transaction. In particular:

- Following the January 2015 approval of the Transaction subject to remedies, in March 2015 Novartis completed the acquisition of the GSK oncology portfolio, for a cash consideration of $16 billion.
- In adherence to the commitments, in December 2015, following approval by the EC, Pierre Fabre acquired from Array the rights to LGX818 and MEK162 in selected countries. Array retained exclusive commercialization rights in the U.S., Canada, Japan, South Korea and Israel, and handed over the rest of the world (including Europe, Asia and Latin America) to Pierre Fabre. Array and Pierre Fabre agreed to split future development costs on a 60:40 basis (Array:Pierre Fabre), and all ongoing LGX818 and MEK162 clinical trials would remain substantially funded through completion by Novartis.
- Array was then, in July 2019, acquired by Pfizer.

Table II.4 and Table II.5 below detail the evolution of the Parties' B-Raf and MEK inhibitors in the advanced melanoma indication after the Transaction, both as monotherapies and as combination therapy.

As Table II.4 shows, none of GSK's molecules were discontinued, as both the monotherapies and the combination therapy progressed after the merger. In particular, we found that Tafinlar and Mekinist were first licenced as monotherapies in BRAF melanoma and then combined as the combination therapy was more efficacious. The combination therapy has in fact become the standard of care (both in first line and second line treatment) for B-Raf-mutated melanoma as it is superior to single-agent BRAF therapy in terms of response rates, progression-free survival and overall survival.[274] However, we found that in certain patients, exceptionally, the B-Raf monotherapy is advised, as MEK inhibition adds specific toxicities and thus, single-agent B-Rafs should be used in case of a contraindication for MEK inhibitors.[275] Also, certain side effects can be stronger with the combined therapy compared to B-Raf inhibitor monotherapy.[276]

As per Novartis' molecules, we found that its monotherapy of MEK162 was discontinued, while the monotherapy of LGX818 and the combination therapy were not discontinued.

[274] See ESMO guidelines (2019) and EMA's Assessment report.

[275] See ESMO guidelines (2019).

[276] For example, Novartis website reports that more frequent or severe fever can be observed in the combined therapy compared to BRAF inhibitor monotherapy.

Table II.4: Evolution of GSK's Tafinlar and Mekinist for advanced melanoma after the Transaction

Owner pre-merger	Drug/pipeline	Phase at time of merger	Evolution of project
GSK	B-Raf inhibitor: Tafinlar (dabrafenib)	Approved in the EU (September 2013)	September 2015: Marketed in several European countries
	MEK inhibitor: Mekinist (trametinib)	Approved in the EU (July 2014)	July 2019: Marketed in Canada and the US
	Trialed in combination	Phase III	September 2015: Approved in the EU June 2015 - 2019: Marketed in Australia, Canada, Japan, USA, EU (e.g. UK, Italy, Spain)[277]

Source: Lear

[277] Marketing authorization is based on the results from the Phase III COMBI-d and COMBI-v studies, in which the Tafinlar/Mekinist combination demonstrated overall survival (OS) benefit compared to Tafinlar and Zelboraf monotherapies. See: https://www.novartis.com/news/media-releases/novartis-receives-eu-approval-tafinlar-and-mekinist-first-combination-approved-patients-aggressive-form-melanoma

Table II.5: Evolution of Novartis' LGX818 and MEK162 for advanced melanoma after the Transaction

Owner pre-merger	Drug	Phase at time of merger	Evolution of project
Novartis (Array)	B-Raf inhibitor: LGX818 (encorafenib)	Phase III	Divested to Array following EC Commitments Phase III study referred to by the Commission in the Decision: a study comparing combination of LGX818 Plus MEK162 Versus Vemurafenib and LGX818 Monotherapy in BRAF Mutant Melanoma (COLUMBUS). This found that better results were given by the combination therapy than the LGX818 monotherapy.[278] No other trials for the monotherapy of LGX818. The COLUMBUS study is "Active, not recruiting" and as such we wouldn't characterise this as a discontinuation. It appears to be correct to have an "active" status as e.g. in July 2022 a 5-year update was published. The study started in 2013, results were posted in 2021, and estimated completion is in 2023.
	MEK inhibitor: MEK162 (binimetinib)	Phase III	Returned to Array following EC Commitments Phase III study referred to by the Commission in the Decision: Study Comparing the Efficacy of MEK162 Versus Dacarbazine in Unresectable or Metastatic NRAS Mutation-positive Melanoma (NEMO trial, completed June 2019). Pierre Fabre first applied for marketing authorization and then in January 2018 withdrew it as the EMA raised questions related to the molecule's effectiveness.[279] No progress nor new trials in the monotherapy, so this molecule appears to have been discontinued as a monotherapy agent.
	Trialed in combination	Phase III	September 2018: EC approval February 2019: Marketed in several EU countries (UK, Austria, Netherlands, Germany), Japan, USA. There is also a new Phase III trial with a "recruiting" status, which started in May 2022.[280]

Source: Lear

II.1.1.7.3 Reasons for discontinuation

The collected evidence suggests that Array discontinued MEK162 as a monotherapy for N-Ras mutated melanoma. The discontinuation, however, does not seem to indicate that the remedies were not effective and not apt to keep alive competition and innovation in the relevant market of targeted therapies for advanced melanoma, but appears to be grounded on technical reasons.

Firstly, it should be noted that, as mentioned in section II.1.2.2.1, before the merger the MEK162 monotherapy was being trialed by Novartis for N-Ras mutated melanoma, while GSK's Mekinist was approved for B-Raf mutated melanoma. Therefore, this is not an exact project overlap when further looking at the type of mutation.

As per the technical reasons for the discontinuation, we found that the EMA raised questions related to the efficacy of the molecule, following which application for authorization was withdrawn.[281] In addition, the ESMO guidelines for skin melanoma (2019)[282] report that "for NRAS-mutated melanoma, due to the limited efficacy of MEKis [based on NEMO trial results], first-line immunotherapy options are the first choice".

Therefore, as this discontinuation appears to be due to technical reasons, it does not seem to suggest either that the remedies were not effective or that, in absence of the merger, such discontinuation would not have occurred.

II.1.1.8 Innovation in MEK and B-Raf inhibitors (for colorectal cancer, NSCLC and advanced melanoma brain metastases)

II.1.1.8.1 The Commission's Decision

At the time of the Decision, GSK and Novartis had early stage clinical trials (Phase I or II) involving MEK and B-Raf inhibitors, used either as monotherapies or in combination, in a number of other types of cancer, namely colorectal cancer, non-small-cell lung cancer (NSCLC) and advanced melanoma brain metastases.

The Commission concluded that the Parties' clinical research programs in the above indications were competing research programs, because aimed at developing substitutable products (assessed with reference to the molecules' MoA[283] and cancer type) and having similar timings (assessed with reference to the phase of the trial).

The relevant product market was defined by the Commission as the one for innovation concerning the development of MEK and B-Raf inhibitors for the treatment of colorectal cancer (or NSCLC or advanced melanoma brain metastases). The relevant geographic market was considered to be at least EEA-wide, consistently with the Commission's approach when pipeline products (at any stage) are involved.

The ex-post assessment will be focused on the concerns raised by the Commission in the market for the treatment of colorectal cancer and NSCLC. We found no relevant discontinuation in the market for the treatment for advanced melanoma brain metastases, which is discussed in Appendix A.4 to this report.

Table II.6 shows the overlaps identified by the Commission at the time of the Decision between the Parties' MEK and B-Raf inhibitors for the treatment of colorectal cancer, and NSCLC.

[281] Withdraw EU Marketing Authorisation Application for Binimetinib (esmo.org)

[282] See ESMO guidelines (2019).

[283] The MoA in this case is the feature of being a MEK/ B-Raf inhibitor.

Table II.6: Overlap in treatments for colorectal cancer and NSCLC identified by the EC (January 2015 Decision)

Owner	B-Raf inhibitor (Novartis: LGX818 GSK: Tafinlar)	MEK inhibitor (Novartis: MEK162 GSK: Mekinist)	B-Raf/ MEK combination (Novartis: LGX818+ MEK162 GSK: Tafinlar+Mekinist)
Colorectal cancer			
Novartis	Phase I/II	Phase I/II	
GSK			Phase II
NSCLC (lung cancer)			
Novartis	Phase II	Phase II	Phase II
GSK	Phase II		Phase II

Source: Lear

In its market investigation, the Commission found that only Roche had a pair of MEK and B-Raf inhibitors that could compete with the Parties' pairs of MEK and B-Raf inhibitors in these types of cancer and that therefore, the transaction would bring together under a single ownership two among the only three competing clinical research programs based on the MEK and B-Raf inhibitors in the markets for colorectal cancer, and NSCLC.

The EC concluded that given the more advanced stage of development of GSK's Mekinist and Tafinlar combination therapy for the treatment of advanced melanoma, the merged entity was likely to prioritise the development of a clinical research program for this pair of MEK and B-Raf inhibitors also in other types of cancer, either as monotherapies or as combination therapies. Therefore, the Transaction would reduce the merged entity's incentive to develop the broader clinical research program for LGX818 and MEK162, either as monotherapies or as combination therapies, for the various cancer types for which they were at early stages of clinical development and for potential further indications.

Due to these concerns, the Commission introduced remedies, requiring Novartis to return MEK162 and divest LGX818 to Array. For more details on the commitments see section II.1.2.2.1. As described in section II.1.2.2.2, the remedies were implemented by the Parties, with Array partnering with Pierre Fabre for the development and commercialisation of MEK162 and LGX818.

II.1.1.8.2 The evolution of the overlapping projects after the merger

We found that, both in the colorectal cancer and lung cancer indication, Array discontinued its monotherapies of MEK162 and LGX818 and directed its investments towards the combination therapy, which had become the new standard of care in both cancer types.

Table II.7 and Table II.8 below detail the evolution of the Parties' combination therapies for colorectal cancer and lung cancer respectively after the Transaction. In colorectal cancer, Array's MEK162 and LGX818 were discontinued as monotherapies and progressed as a combination therapy, where several trials are ongoing. Also GSK's combination therapy was not discontinued, as there are several ongoing trials.

In lung cancer, we found that Array's MEK162 and LGX818 monotherapies were discontinued after the Transaction. Regarding the combination therapy, which was on Phase II trials at the time of the Decision, we didn't find a phase progress, but several new trials are ongoing, implying that the combination therapy was not discontinued. As per GSK's targeted therapies, we found that GSK's monotherapy of Tafinlar was discontinued while the combination therapy made progress (it was approved in April 2017 and also new trials are ongoing).

Table II.7: evolution of Novartis' and GSK's combination therapies for colorectal cancer after the Transaction

Owner pre-merger	Drug and phase pre-merger	Evolution of project
Novartis (Array)	No trials in the combination therapy of MEK162 and LGX818	The molecules advanced as combination therapy, where progress was made and new trials started. EU relevant developments: Phase III trial (BEACON CRC trial) started in October 2016, and was completed in November 2022.[284] Patients were randomly assigned in a 1:1:1 ratio to receive encorafenib, binimetinib, and cetuximab (triplet-therapy group); encorafenib and cetuximab (doublet-therapy group); or either cetuximab and irinotecan or cetuximab and FOLFIRI (control group). The trial results for the double and triplet arms were significantly superior compared to the control group, which was the standard of care at the time of the trial. This study led to the EC approval of the encorafenib–cetuximab combination in June 2020 for the treatment of adult patients with BRAFV600E-mutant metastatic colorectal cancer (mCRC) who have received prior systemic therapy. For this patient population this has become the new standard of care.[285] Pfizer is continuing investigating the prospects of the triplet therapy: ANCHOR Phase II study (for previously untreated patients) so far gave encouraging results (still "active", but the est. completion date passed in April 2023).[286] Several other ongoing trials on these molecules as combination therapy, e.g. see here (binimetinib in combination with encorafenib) and here (binimetinib, encorafenib and cetuximab in combination).
GSK	Combination Mekinist (trametinib) & Tafinlar (dabrafenib) Phase II	No phase progress, but several new ongoing trials, therefore we wouldn't charachterise this as a discontinuation: Phase II trial (Dabrafenib + Trametinib + PDR001 In Colorectal Cancer) started in October 2018 and has an estimated study completion date in December 2022. The status is still "recruiting", so it is unclear whether the trial has been completed.[287] Phase I trial (A Study of Select Drug Combinations in Adult Patients With Advanced/Metastatic BRAF V600 Colorectal Cancer) started in July 2020 and has an estimated completion date in May 2024.[288]

Source: Lear

Table II.8: evolution of Novartis and GSK's combination therapies for lung cancer after the Transaction

Owner pre-merger	Drug and phase pre-merger	Evolution of project
Novartis (Array)	Combined therapy of MEK162 and LGX818 Phase II	No phase progress, but several new ongoing trials in the combination therapy, which is therefore not discontinued. A 2022 investor presentation[289] only mentions the combination therapy (Phase II), further suggesting that the monotherapies have been abandoned. Most relevant trials (ongoing): ▪ Started June 2022: Phase II Study Investigating the Combination of Encorafenib and Binimetinib in BRAF V600E Mutated Chinese Patients With Metastatic Non-Small Cell Lung Cancer.[290] ▪ Started June 2019: Encorafenib + Binimetinib in Patients With BRAFV600-mutant Non-small Cell Lung Cancer.[291] ▪ Started June 2019: An Open-label Study of Encorafenib + Binimetinib in Patients With BRAFV600-mutant Non-small Cell Lung Cancer.[292] ▪ Started Jan 2021: ENCOrafenib With Binimetinib in bRAF NSCLC.[293]

[284] See here and here.

[285] See ESMO guidelines and Pfizer prescribing information.

[286] https://www.esmo.org/oncology-news/first-line-encorafenib-binimetinib-and-cetuximab-combination-provides-clinical-benefit-and-manageable-safety-in-braf-v600e-mutated-mcrc

[287] https://clinicaltrials.gov/ct2/show/NCT03668431?term=trametinib&cond=colorectal+cancer&draw=2&rank=1

[288] https://clinicaltrials.gov/ct2/show/NCT04294160?term=trametinib&cond=colorectal+cancer&draw=2

[289] https://cdn.pfizer.com/pfizercom/product-pipeline/Pipeline_Update_28JUL2022_0.pdf?v9aJurw3hqVCO8AwGCx9M_cnB3qJiKCc

[290] https://clinicaltrials.gov/ct2/show/NCT05195632?term=encorafenib&cond=lung+cancer&draw=2&rank=1

[291] https://clinicaltrials.gov/ct2/show/NCT03915951?term=encorafenib&cond=lung+cancer&draw=2&rank=2

[292] https://clinicaltrials.gov/ct2/show/NCT03915951?term=encorafenib&cond=lung+cancer&draw=2&rank=2

[293] https://clinicaltrials.gov/ct2/show/NCT04526782?term=encorafenib&cond=lung+cancer&draw=2&rank=4

		▪ Started Jan 2021: ENCOrafenib With Binimetinib in bRAF NSCLC.[294]
GSK	Combination of Mekinist (trametinib) &Tafinlar (dabrafenib) Phase II	April 2017: approval in the EU June 2017- March 2018: approval in the US, Japan and Canada Moreover, a new trial is ongoing: Started August 2020: A Study of Dabrafenib in Combination With Trametinib in Chinese Patients With BRAF V600E Mutant Metastatic NSCLC[295]

Source: Lear

II.1.1.8.3 Reasons for discontinuation

We detected a discontinuation of Array's monotherapies of MEK162 and LGX818 for colorectal cancer and lung cancer and in GSK's Tafinlar monotherapy for lung cancer. We also found that after the Transaction, Array's MEK162 and LGX818 progressed as a combination therapy both in colorectal cancer and lung cancer.

Our analysis showed that technical reasons appear to support the choice to focus on the combined therapy rather than the monotherapies and thus that the discontinuation of the monotherapies appears to be unrelated to the merger.

In particular, both in colorectal cancer and in lung cancer, better results of the combination therapy and the fact that this became the standard of care[296] warrant Array's choice to focus on progressing the combination therapy and to discontinue the monotherapies. Similarly, GSK's Tafinlar monotherapy in lung cancer was discontinued as the combination therapy was more efficacious than the monotherapy.[297]

These findings suggest that the EC remedies were effective at ensuring that competition and innovation were kept alive in the market for targeted therapies for colorectal cancer and lung cancer (since in both indications Array's molecules were taken forward in their most efficacious form, i.e. the combined therapy), and that the discontinuation of the MEK162 and LGX818 monotherapies is grounded on technical reasons and could have therefore happened independent of the merger.

II.1.1.9 Evaluation of the Commission's assessment

Our ex-post evaluation reaffirms the rationale leading the Commission to conclude that the deal raised competition concerns in the markets for treating advanced melanoma,

[294] https://clinicaltrials.gov/ct2/show/NCT04526782?term=encorafenib&cond=lung+cancer&draw=2&rank=4

[295] https://clinicaltrials.gov/ct2/show/NCT04452877?term=tafinlar&cond=lung+cancer&draw=2&rank=6

[296] For colorectal cancer, the encorafenib–cetuximab combination gained EC approval in June 2020. For lung cancer, see ESMO guidance.

[297] The combination therapy gave stronger results than the monotherapy in terms of overall response rate (ORR), median progression free survival (mPFS), and median duration of response (mDoR). See ESMO guidance, page 17.

ovarian cancer[298], colorectal cancer and NSCLC (in light of the limited number of competitors, the likely entry of the parties' molecules and the closeness of competition between them) and warranted the introduction of remedies. The analysis suggests that the Commission's remedies worked in ensuring that continued effort was put into the development of both Parties' targeted therapies for the treatment of those cancer types. In fact, the remedies were effective at ensuring that the projects of both parties were taken forward in their most efficacious form (i.e. combined therapy), and thus the discontinuation of the monotherapies in these indications, which happened for technical reasons, does not warrant further investigation.

Our findings suggest that the Commission assembled an appropriate package of assets to be divested by Novartis and adopted sufficient other measures to ensure that Array had the incentive and ability to continue development in the therapeutic areas of advanced melanoma, ovarian cancer, colorectal cancer, NSCLC, and melanoma brain metastases.[299]

We note that after the completion of the deal, Array started collaborating with Merck on the development of its MEK and B-Raf inhibitors.[300] Moreover, in June 2019 Array was acquired by Pfizer.[301] These developments suggest that the Commission's requirement that Array partnered with a suitable company with the ability and incentives to commercialise the relevant compounds (which ended up being Pierre Fabre) might have been unnecessary, as its alliance with Merck and then acquisition by Pfizer might have been sufficient to ensure that the molecules reached the market. However, these developments could not have been anticipated by the Commission at the time of its review, and thus it appears that the Commission's remedies were appropriate at the time they were designed.

II.1.1.10 Other targeted therapies (non MEK and B-Raf inhibitors): several other cancer types

The Commission found the following overlaps[302] in other targeted therapies (i.e. non MEK or B-RAF inhibitors):

- neuroendrocrine tumors of pancreatic origin ("pNET"): marketed / pipeline overlap (Phase undisclosed);
- breast cancer: marketed / Phase III pipeline overlap;
- multiple myeloma: Phase III pipeline / Phase II pipeline overlap.

[298] Details for this cancer type are provided in Appendix A.4 to this report because no discontinuation was found.

[299] No counterfactual analysis has been carried out (i.e. it is not known what would have happened absent the remedies).

[300] In May 2017, Array partnered with Merck for the development of a combination therapy of Array's MEK162 and Merck's KEYTRUDA® in colorectal cancer (see: https://www.prnewswire.com/news-releases/array-biopharma-announces-strategic-collaboration-with-merck-300452843.html); in June 2016, Merck jointly announced with Array and Pierre Fabre the initiation of a Phase III trial of BRAF-mutant metastatic colorectal cancer (mCRC), investigating a new combination of Erbitux® (cetuximab), plus encorafenib (LGX818) with or without binimetinib (MEK162) (see: https://www.merckgroup.com/en/news/array-biopharma-and-pierre-fabre-04-06-2016.html).

[301] https://www.cnbc.com/2019/06/17/pfizer-to-buy-array-biopharma-for-48-a-share-in-cash.html#:~:text=Pfizer%20is%20acquiring%20Array%20Biopharma,the%20stock's%20close%20on%20Friday.

[302] We report only the overlaps in scope for this study (i.e. excluding marketed/ marketed overlaps and overlaps involving biosimilars).

In the Decision, in all those cases the product market definition was left open. In particular, it was not concluded whether to further distinguish between lines of treatment in addition to cancer type. Also the geographic market definition was left open because the Commission had no competitive concern under any plausible geographic market definition.

II.1.1.10.1 Targeted therapies for pNET

The Commission's Decision

Table II.9 shows the overlap between the Parties' activities in pNET (neuroendrocrine tumors of pancreatic origin) identified by the Commission.

Table II.9: Overlap in treatments for pNET identified by the EC (January 2015 Decision)

Owner pre-merger	Drug	Phase at time of merger
Novartis	Afinitor (everolimus), mTOR inhibitor	Marketed
GSK	Votrient (pazopanib), Tyrosine kinase inhibitor	Phase II

Source: Lear

In its market investigation, the Commission found that the only marketed treatment competing with Afinitor was Pfizer's Sutent (sunitinib), a multiple kinase inhibitor. It also found that other firms had trials for targeted treatments for pNET, all no further than Phase II.[303]

The Commission concluded that the Transaction did not raise competitive concerns in this cancer type for two main reasons. Firstly, it was argued that even if Votrient obtained authorization (considered uncertain since the molecule was in phase II), it likely wouldn't be a close competitor of Afinitor because the two were expected to be used in different lines of treatment. Secondly, "Afinitor and Votrient were already approved for several other, significantly larger cancer indications, where they did not overlap. When negotiating reimbursement conditions with national health authorities in Europe, it is difficult to differentially price across indications. Accordingly, Novartis would have no ability or incentive to increase the price of Afinitor or Votrient with respect to pNETs".[304]

The evolution of the overlapping projects after the merger

In our ex-post assessment we found that Novartis' Afinitor is still marketed, while GSK's Votrient was discontinued in pNET.

[303] Novartis with BKM120 (a P13K inhibitor), Roche with Avastin, Bayer/Onyx with Nexavar, and Pfizer with Torisel (an mTOR inhibitor).

[304] The Decision, paragraphs 175 and 178

Results of the Phase II study of Votrient (pazopanib)[305] were positive, finding that "Pazopanib showed a comparable efficacy to other targeted agents not only in pancreatic NETs but also in NETs originating from gastrointestinal (GI) tract"[306] and that "[it] provides impetus for further study of this potential agent for consideration in the area of neuroendocrine tumors"[307]. However, no further studies were undertaken and statements, annual reports and investor presentations from GSK (before the merger) and Novartis (after the merger) do not mention pazopanib in the pNET indication among the pipelines.

Reasons for discontinuation

Feedback from pharma experts in the Team highlighted that Afinitor (everolimus) is an mTOR inhibitor while Votrient (pazopanib) is a Tyrosine Kinase inhibitor and so the drugs have different targets and might also be used in different lines of treatment. This implies that there don't seem to be the incentives to discontinue Votrient, and confirms the EC conclusion that the Parties' molecules appear not to be close competitors and thus there are no anticompetitive concerns arising from the Transaction in this indication.

As per the reasons for the discontinuation of Votrient, this appears to be due to lack of compelling efficacy and the resulting negative commercial impact of progressing an indication with only comparable efficacy to established targeted agents. In fact, experts in the Team highlighted that:

- Comparable efficacy (or Non-Inferiority) is not always sufficient to be successful in oncology unless the asset is a fast follower or has significantly better safety. Even if it is possible to obtain regulatory approval without a head-to-head[308] Phase 3 trial, you might need this type of data to support successful reimbursement and maintenance of pricing versus existing marketed indications. That might be risky as well as expensive, unless it is possible to beat existing therapies by a good margin.
- Votrient is a Tyrosine Kinase inhibitor and is most similar to Pfizer's sunitinib in terms of mode of action. In fact, GSK was willing to perfom a head-to-head study of the two drugs in renal cell carcinoma (COMPARZ) where succeeded on safety. It is possible that GSK were unable to see a successful path forward for pazopanib in pNET based on the Phase 2 data generated.
- Moreover, Votrient would mainly have been a competitor to Pfizer's sunitinib if it had been taken forward (not Afinitor). Sunitinib produced positive Phase 3 outcomes in pNET in 2010 and Votrient was only in phase 2 in 2015 for this indication. Even if Votrient had progressed to Phase 3, the study readout would have been much later and the product would have been closer to loss of exclusivity (LOE) - taking significant market share from a well-established sunitinib in time to make robust returns might have been seen as challenging.

Therefore, the discontinuation of GSK's Votrient appears to be grounded in technical reasons and thus to be unrelated to the merger.

[305] https://clinicaltrials.gov/ct2/show/NCT01099540?term=01099540&draw=2&rank=1

[306] https://pubmed.ncbi.nlm.nih.gov/23989950/

[307] https://pancreatica.org/clinical-trial-with-votrient-for-advanced-nets/

[308] Two therapies are placed in head-to-head clinical trials when they are compared against each other as opposed to a standard of care.

II.1.1.10.2 Other targeted therapies for breast cancer

The Commission's Decision

Table II.10 shows the overlap identified by the Commission between the Parties' activities in a specific type of breast cancer, called HER2+ breast cancer.

Table II.10: Overlap in treatments for HER2+ breast cancer identified by the EC (January 2015 Decision)

Owner pre-merger	Drug	Phase at time of merger
Novartis	Afinitor (everolimus)	Phase III (two trials: Bolero 1 for first line of treatment, Bolero 3 for second or later lines of treatment)
GSK	Tyverb (lapatinib)	Approved (second or later lines of treatment)

Source: Lear

The Commission, based on several submissions to its market investigation, considered that in light of negative results of the Bolero 1 and 3 trials, it was unlikely that Afinitor received approval. Based on that, it concluded that the Parties' activities were not materially overlapping regarding targeted therapies for the treatment of advanced HER2+ breast cancer and that the Transaction raised no competitive concerns in this indication.

The evolution of the overlapping projects after the merger

In our ex-post assessment we found that Tyverb is still marketed throughout the EU.[309] As per Novartis' Afinitor, trials did not progress to a later phase nor there are new recent trials for HER2+ breast cancer, and thus we can conclude that the molecule was discontinued in this indication.

Reasons for discontinuation

The discontinuation of Novartis' Afinitor for HER2+ breast cancer appears to be grounded on technical reasons. In particular, the results of the Bolero 1 and 3 trials were not encouraging:

[309] https://www.novartis.com/about/products?search_api_fulltext=tyverb&sort_by=title&sort_order=ASC

- Bolero 1 - in December 2014, Novartis reported that the primary endpoint was not met as there was no statistically significant difference in the progression free survival between the Afinitor treatment group and the placebo group.[310]
- Bolero 3 – trial results showed that overall survival was lower in the group treated with Afinitor than the placebo group.[311]

The Commission had anticipated that this discontinuation was likely to happen for technical reasons. Thus, our ex-post assessment provides support for the EC decision not to intervene with remedies for this indication, as Novartis' molecule was unlikely to progress in its development independent of the merger.

II.1.1.10.3 Other targeted therapies for multiple myeloma

The Commission's Decision

Table II.11 shows the overlap identified by the Commission between the Parties' activities in multiple myeloma. As shown, at the time of the Decision, Novartis' LBH589 was in Phase III clinical trials and GSK's GSK2110183 was in Phase II clinical trials.

Table II.11: Overlap in treatments for multiple myeloma identified by the EC (January 2015 Decision)

Owner pre-merger	Drug	Phase at time of merger
Novartis	LBH589 (panobinostat)	Phase III
GSK	GSK2110183 (afuresertib)	Phase II

Source: Lear

In its Decision, the Commission concluded that the Transaction did not raise competitive concerns in the multiple myeloma indication because Novartis' molecule received negative feedback from the FDA in November 2014, which made approval unlikely in the US and therefore also in the EU.

The evolution of the overlapping projects after the merger

Our ex-post assessment contradicted the expectations of the Commission, as we found that Novartis' LBH589 was approved[312] and marketed in the EU (contrary to the EC's

[310] https://storage.googleapis.com/pcf_sb_39_1613727931605803249/assets/supporting/mediarelease/1835/809172591.html?GoogleAccessId=pcf-binding-6c96771b@sn-paas-sb-gcp.iam.gserviceaccount.com&Expires=1668622229&Signature=VGj78yHedANQvikwUL2ZzSmWlQSpELV9GzInsCbnU03Ov49rYkTA0CiPwTPjwXvjJJ7ycWF3MKYfrpQ5yT%2FvacKZObfArwAXMnARvMA6ECQnrJmjRynRYKgppG7MVHQAb3dHc%2FLNbQRZwcymkgo2W7RCI%2Bw4%2BYJDCwIJyhMNT8lopvKE5FgitpLjy2wtgeapGGrE1K7tiwWo5hLYKE8tOKD4bf1gbNG%2B973kzmtY3g7sPep2LbqsVmflRLs0pSDKf28VuZLySFHN%2BsC1StlasZ9OluDD%2BkxjoL%2BxCvhcJimV6ddNeMAMbOO3ZAJYXm8lwwc0IGzeg1SjMIPEpr0tQw%3D%3D

[311] https://clinicaltrials.gov/ct2/show/results/NCT01007942?view=results

[312] https://www.ema.europa.eu/en/medicines/human/EPAR/farydak#authorisation-details-section

forecast), while GSK's molecule was discontinued.[313] Table II.12 summarises the most recent trials of GSK's GSK2110183, and shows that three out of four trials were terminated early. In two of these trials the reasons for termination were reported: one trial was terminated for safety reasons, and the other because the standard of care in multiple myeloma had evolved compared to the time when the trial was started, and thus the study was obsolete.

[313] However, Novartis' Panobinostat is not marketed in the US. In February 2015, the US FDA approved (under the accelerated approval program) panobinostat in combination with bortezomib and dexamethasone. In November 2021, Secura Bio (which acquired panobinostat in March 2019 from Novartis) announced that, based on discussions with the US FDA, the company submitted for the withdrawal of the approval for panobinostat because it was not feasible for the company to complete the required post-approval clinical studies as designed as part of the accelerated approval process. Panobinostat is still marketed in countries (including the EU) where it received approval. See here: https://www.prnewswire.com/news-releases/secura-bio-announces-us-withdrawal-of-farydak--panobinostat-nda-301434428.html

Table II.12: Evolution of GSK's GSK2110183 for multiple myeloma after the Transaction

Owner pre-merger	Drug and phase pre-merger	Evolution of project
GSK	GSK2110183 (afuresertib) phase II	No development nor new recent trials, thus this molecule was discontinued. Most relevant trials: ▪ A phase I/II trial was completed by GSK in March 2013 for the combination of afuresertib and trametinib.[314] Results showed that continuous daily dosing of the afuresertib+trametinib combination was poorly tolerated. Further studies were warranted.[315] ▪ Phase II study (for afuresertib in combination with carfilzomib (Part 1) and the combination compared with carfilzomib alone (Part 2)).[316] The study was terminated in May 2016 because "the protocol defined study treatment was no longer aligned with the evolving standard of care [SoC]".[317] Feedback from our pharma experts confirmed that given the SoC at the time, this appears to be a reasonable justification for termination. ▪ A Phase 1b study to evaluate afuresertib in combination with bortezomib and dexamethasone was completed in Oct 2015 but results are not available on clinical trials nor other medical journals.[318] ▪ A phase I study of afuresertib monotherapy which had been started in August 2014 was terminated in August 2019 (primary completion date is February 2017 and no significant changes were reported between February 2017 and August 2019 other than updating the "study status"). The Recruitment status on clinicaltrials.gov is "Terminated (Company decision)". No further information or study results were published.[319]

Source: Lear

Reasons for discontinuation

We found that GSK's GSK2110183 was discontinued, and the main reason appears to be the evolved standard of care (SoC) for treating multiple myeloma compared to the SoC when GSK's trials were started.

[314] https://clinicaltrials.gov/ct2/show/study/NCT01476137?term=NCT01476137&draw=2&rank=1

[315] https://pubmed.ncbi.nlm.nih.gov/25417902/

[316] https://clinicaltrials.gov/ct2/show/study/NCT02235740?term=NCT02235740&draw=2&rank=1

[317] https://clinicaltrials.gov/ct2/show/study/NCT02235740?term=NCT02235740&draw=2&rank=1

[318] https://clinicaltrials.gov/ct2/show/record/NCT01428492?term=NCT01428492&draw=2&rank=1

[319] https://clinicaltrials.gov/ct2/show/study/NCT02177682?term=NCT02177682&draw=2&rank=1

In particular, in 2016 the SoC for the treatment of multiple myeloma had become the combination therapy of an immunomodulatory drug (typically lenalidomide), a proteasome inhibitor (i.e. chemotherapy with an agent like bortezomib) and an anti-inflammatory (typically dexamethasome). This warrants GSK's decision, in May 2016, to terminate the trials for GSK2110183 in combination with its molecule carfilzomib.

Moreover, in 2016 the first monoclonal antibody (mAb) was introduced as a new treatment for multiple myeloma, and later became the new SoC (used in combination with the above triplet).[320] The introduction of mAbs in 2016, despite not being yet the SoC, may have also been a factor in the decision to discontinue trials for GSK2110183.

Therefore, it appears that GSK2110183 has been discontinued for technical reasons, and thus that the discontinuation is unrelated to the merger.

Moreover, it is important to note that in March 2019 Novartis sold Panobinostat to Secura Bio.[321] We believe that by 2019, the emergence of mAbs combined into existing combinations might have put the use of panobinostat into decline. Thus, this does not appear to be a case where an overlap compound was discontinued in order to eliminate competition with the owner's other compound. Rather, Novartis evidently decided that it didn't want to keep/develop both its molecules for multiple myeloma. Given that business decision, it doesn't seem that discontinuance of GSK2110183 should be regarded as evidence of a killer acquisition.

II.1.1.11 Evaluation of the Commission's assessment

The Commission concluded that the Transaction did not raise competitive concerns in the multiple myeloma indication because it believed that Novartis' panobinostat was unlikely to reach the European market. However, we found that Novartis' molecule was approved in the EU, while GSK's GSK2110183 was discontinued due to the evolved SoC (which implied that prior trials were obsolete).

Regarding Novartis' panobinostat, the evidence available to the Commission in January 2015 (i.e. the month of publication of the Decision) could not have led it to predict that the drug would be approved in the EU. In fact, panobinostat was approved in the EU only in August 2015, even though the drug had received negative feedback at the end of 2014 in the US.

As per GSK's GSK2110183, the turning year for the discontinuation of the molecule was 2016 (i.e. after the Decision), when the SoC for multiple myeloma changed and when the first monoclonal antibody was introduced as a new treatment. Therefore, at the time of the Decision, these developments were unpredictable by the Commission.

We believe that the Commission's assessment, based on the information available at the time of the Decision, was fit for purpose. The discontinuation of GSK's GSK2110183, which was not anticipated by the Commission, appears to be due to technical reasons and is thus independent of the merger.

II.1.1.12 Conclusions

The Commission found overlaps in i) MEK and B-Raf inhibitors for the treatment of advanced melanoma, ovarian cancer, colorectal cancer, NSCLC and melanoma brain

[320] See the ESMO guidance.

[321] https://www.prnewswire.com/news-releases/secura-bio-acquires-global-rights-to-farydak-300810566.html

metastases, and ii) other targeted therapies for the treatment of pNET, breast cancer and multiple myeloma.

As per the overlaps in MEK and B-Raf inhibitors, where the clearance decision required the divestiture of Novartis' pipelines, our assessment (which we note does not extend to evaluating the counterfactual scenario without the deal) supports the Commission's decision to intervene to remedy competition concerns. We found that after the deal the pipeline projects of both parties were taken forward in advanced melanoma, colorectal cancer, NSCLC, and ovarian cancer (in their most efficacious form, i.e. combined therapy). Thus, the remedies implemented by the Commission regarding MEK and B-Raf inhibitors appear to have been effective at ensuring that Array had the incentive and ability to continue development in all cancer types where an overlap was found.

Regarding the overlaps in other targeted therapies for the treatment of pNET, breast cancer and multiple myeloma, our evaluation confirmed that – given the information available to the Commission at the time of the Decision – its assessment was fit for purpose. In all three indications, one of the Parties' molecules was discontinued, but in all cases the discontinuation appears to be grounded in technical reasons and thus to be unrelated to the merger. Moreover, in the breast cancer indication, the discontinuation had been anticipated by the Commission. Where the discontinuation wasn't anticipated (pNET and multiple myeloma), we believe that the information available to the Commission at the time of the Decision did not allow this to be predicted.

II.1.2 Notified concentration #3: Novartis/ GSK (Ofatumumab autoimmune indications)

II.1.2.1 Background

On 18 November 2015 the European Commission received notification of a proposed concentration by which Novartis AG ("Novartis")[322] would acquire control of the autoimmune indications of the pharmaceutical substance ofatumumab (the "Target") owned by GlaxoSmithKline plc ("GSK")[323] by way of a purchase of assets (the "Transaction").[324]

The autoimmune indications of ofatumumab, an anti-CD20 monoclonal antibody, at the time of the decision ("the Decision") were still in development.[325]

The Commission reviewed this proposed acquisition and published its decision on 18 December 2015, where it announced approval of the Transaction unconditionally.

[322] See footnote 31.

[323] See footnote 32.

[324] Under the agreement entered into between Novartis and GSK, the consideration for this business would be paid in a staggered form: Novartis would pay US$ 300 million at closing. An additional US$ 200 million would be payable when Novartis started the Phase III study for the use of ofatumumab in multiple sclerosis. Novartis had also agreed to make additional payments of up to US$ 534 million to GSK in the future, if certain pre-determined milestones were achieved. Novartis had also agreed to pay to GSK royalties of up to 12% on any future net sales of the drug in the auto-immune indications.

[325] Ofatumumab is developed both for autoimmune and oncology indications. Novartis acquired the oncology indications from GSK as part of a broader, initial, transaction, which was authorised by the EC subject to commitments on 28 January 2015 (see Case M.7275). The transaction was completed on 2 March 2015.

II.1.2.2 The Commission's Decision

As described in the Decision, the Commission found that the Transaction led to one overlap between Novartis' activities and ofatumumab autoimmune indications, namely in the treatment of multiple sclerosis (MS).

The overlap identified by the Commission involves the Parties' drugs for the treatment of a specific type of multiple sclerosis, called relapsing-remitting multiple sclerosis (RRMS). In particular, GSK owned the Phase II pipeline ofatumumab, while Novartis owned two marketed drugs (Gilenya and Extavia) and two pipelines (BAF312 and CJM112). This information is summarized in Table II.13.

Table II.13: The overlap in RRMS identified by the EC (December 2015 Decision)[326]

Owner	Drug/ pipeline	Phase
Novartis	Gilenya (fingolimod), oral therapy	Marketed d
	Extavia (interferon beta-1b), injectable therapy	Marketed
	BAF312 (siponimod), oral therapy	Phase II
	CJM112, anti-IL17 monoclonal antibody	Phase II not yet initiated
GSK	Ofatumumab, anti-CD20 monoclonal antibody	Phase II

Source: Lear

The Commission considered that:

after the Transaction Novartis would continue to face strong competition from four other firms (Teva, Bayer, Sanofi and Biogen);

ofatumumab was not a close competitor of Novartis' other RRMS treatments given its different mode of action and efficacy/safety profile.[327] The EC considered that Novartis' CJM112 (an anti-IL17 monoclonal antibody) was the closest to GSK's ofatumumab (an anti-CD20 monoclonal antibody), although the two still have a different mechanism of action;

[326] The EC did not conclude on the exact product and geographic market definition since it considered that the Transaction was unlikely to give rise to serious doubts as to its compatibility with the internal market for MS, irrespective of the product and geographic market definition.

[327] The Commission considered that treatments for RRMS can be classified according to their modes of action and efficacy/ safety profiles into three groups : i) interferon-based drugs (mostly injectables), generally considered as less efficacious but safer than oral therapies and monoclonal antibodies and generally used as first line of treatment, ii) oral therapies, and iii) monoclonal antibodies, generally considered high-efficacy drugs, used as second- or third-lines of treatment, after injectables and oral therapies.

ofatumumab's closest future competitor would be Roche's pipeline ocrelizumab which has the same mechanism of action (CD20 inhibitor).

For these reasons, the EC concluded that the Transaction did not raise competitive concerns and approved it unconditionally.

II.1.2.3 The evolution of the overlapping projects after the merger

As shown in Table II.14, we found that GSK's (then Novartis') ofatumumab (which was on Phase II trials at the time of the Decision) was approved in 2021, while one of Novartis' molecules, CJM112, was discontinued. In particular, looking at Novartis' annual reports, it appears that the decision to discontinue CJM112 was taken between 2015 and 2017.[328]

[328] Novartis 2015 annual report mentions CJM112 among the pipelines for multiple sclerosis. The 2016 annual report mentions CJM112 but doesn't specify the indication, so we cannot exclude that in 2016 CJM112 was still being considered for the multiple sclerosis indication. The 2017 report mentions CJM112 only as a pipeline in development for asthma. The 2018 and 2019 reports don't mention CJM112 at all.

Table II.14: Evolution of Novartis' and GSK's molecules for RRMS after the Transaction

Owner (pre-merger)	Pipeline/ drug	Phase at time of deal	Evolution of project
GSK	Ofatumumab (Kesimpta), anti-CD20 monoclonal antibody	Phase II	Following the Transaction, the molecule was acquired by Novartis. Approved in the US (August 2020) Approved in the EU (March 2021) Other approvals: Canada and Japan (March 2021).
Novartis	Gilenya (fingolimod), oral therapy	Marketed	Still marketed
	Extavia (interferon beta-1b), injectable therapy	Marketed	Still marketed
	BAF312 (siponimod), oral therapy	Phase II	Approved in the US (March 2019) Approved in the EU (Jan 2020) Other approvals include Canada and Australia.
	CJM112, anti-IL17 monoclonal antibody	Phase II not yet initiated	No recent trials nor phase progress, thus this pipeline was discontinued. Phase II trials were never initiated.[329]

Source: Lear

II.1.2.4 Reasons for discontinuation

Desk-based research and the opinion of the pharmaceutical experts in the Team suggest that the discontinuation of CJM112, an anti-IL17 monoclonal antibody, may have been a reasonable commercial decision which was unrelated to the merger.

In the window when Novartis decided to discontinue CJM112 (i.e. 2015-2017), three pathways among monoclonal antibodies were available (i.e. already marketed) for the treatment of multiple sclerosis:

- one anti-alpha4 integrin monoclonal antibody (natalizumab, by Biogen);
- one anti-CD52 monoclonal antibody (alemtuzumab, by Sanofi); and

[329] The Phase II study identified by the Commission in its Decision (not yet initiated at the time of the Decision) is mentioned as a planned trial (comparing CJM112 to fingolimod in a population who stopped natalizumab) in this presentation (dated October 2015) but it appears that it was then never initiated, as it was never registered on clinicaltrials.gov.

- two anti-CD20 monoclonal antibodies (ocrelizumab and rituximab[330] both by Biogen/ Genentech).

The former two types of monoclonal antibodies were found to cause very serious side effects, so that both needed to be put on special monitoring programs. Instead, anti-CD20 monoclonal antibodies proved to cause much less serious side effects and it is likely that they were considered the most promising treatment strategy at the time. Since ofatumumab is an anti-CD20 monoclonal antibody, one may think that in the absence of the merger Novartis would not have had an anti-CD20 inhibitor in its portfolio and may have continued researching the viability of its IL17 monoclonal antibody, CJM112. However, we found key evidence suggesting that the discontinuation of CJM112 was a reasonable commercial decision and unrelated with the incentives that may have arisen after the merger.

Firstly, IL17 protein inhibitors may not yet have been fully elucidated as a viable target for multiple sclerosis at the time of the discontinuation (i.e. between 2015 and 2017). In fact, sector articles suggest that this was fully confirmed more recently in February 2020[331] and prior to that, it appears that the pathway for multiple sclerosis, which allows to fully understand whether a molecule worsens or improves a condition, was not clear. Therefore, it appears that back in 2015-2017, there was a lot of uncertainty about the efficacy of IL17 inhibitors in treating MS, and this may have discouraged Novartis from further developing and commercialising the molecule.

Secondly, no other companies developed anti-IL17 monoclonal antibodies for multiple sclerosis. As of September 2018, only two other companies tested an IL17 protein inhibitor for multiple sclerosis, Genentech and Pfizer, and both decided to discontinue the projects.[332] The fact that other companies discontinued their molecules suggests that abandoning the IL17-inhibition route may have looked like the most sensible decision at the time. Following the research published in 2020, there may be renewed interest in the viability of IL17 protein inhibition as a target for multiple sclerosis, and so it is possible that new trials on this type of asset might be started in the future.

Lastly, the discontinuation of CJM112 took place in the period when Roche's ocrelizumab (considered by the EC the closest competitor to ofatumumab because sharing the same mechanism of action) entered the market. This makes it unlikely that CJM112 was discontinued to eliminate competition with ofatumumab, because knowing that there is competition in the market undermines the incentives to kill competition.

In conclusion, the evidence collected and the expertise of the team suggest that discontinuing this molecule was a reasonable commercial decision and was not spurred on by the merger.

II.1.2.5 Evaluation of the Commission's assessment

One key factor of the assessment of this decision is that the Novartis' molecule that has been discontinued – CJM112 – was a close substitute of the target's molecule,

[330] Used off-label even before the approval of ocrelizumab. See: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6466331/

[331] https://www.tcd.ie/news_events/articles/new-discovery-provides-hope-for-improved-ms-therapies/

[332] Genentech tested afasevikumab and discontinued it for unspecified reasons. in April 2015 Pfizer terminated a Phase I study of its PF-06342674 molecule "due to a corporate decision and not related to the safety or efficacy seen in the trial". See: https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7879974/

ofatumumab. The Commission deemed the two pipeline projects to be competing in the same relevant market, although they were not sharing the same mechanism of action, and hence somehow departing from the criteria generally used to define relevant markets in these cases. Our desk research confirms such conclusions. The latest guidelines for the treatment of multiple sclerosis state that choosing between the wide range of available treatments for RRMS (including oral therapies, injectable therapies and monoclonal antibodies) depends on a number of factors, such as patient characteristics, disease severity/activity, drug safety profile and the accessibility of the drug.[333] This suggests that, depending on those factors, drugs with a different mechanism of action and/or efficacy/safety profile can be to some extent substitutable. Therefore, as also evidenced by the Commission, despite not sharing the same mechanism of action, CJM112 (an anti-IL17 monoclonal antibody) and ofatumumab (an anti-CD20 monoclonal antibody) could be considered substitute drugs. We also agree with the Commission's consideration that the closest competitor to ofatumumab would be Roche's ocrelizumab (another anti-CD20 monoclonal antibody).

Although the counterfactual scenario in the absence of the deal is unknown, we looked at how the competitive landscape for the treatment of RRMS evolved after the merger, to understand how harmful this discontinuation was to competition and innovation as well as to figure out whether the Commission's assessment of existing and potential competition (and the consequent decision not to impose remedies) was fit for purpose.

In the Decision, the Commission anticipated that in the field of MS, Novartis would continue to face competition by four main companies after the Transaction: Teva, Bayer, Sanofi and Biogen. Our ex-post assessment confirms that these companies are still Novartis' competitors in 2022. Moreover, several new drugs have been approved since publication of the Decision, implying that Novartis faces competition from additional firms, namely Mylan, Merck, Roche, Bristol-Myers Squibb and Janssen. Table II.15 lists all the disease modifying therapies[334] for RRMS approved in the EU after the Decision (as of 2022) with the corresponding year of approval.

Moreover, the Commission's Decision to clear the Transaction unconditionally was also grounded on the consideration that Roche's ocrelizumab, considered the closest competitor to ofatumumab, was likely to enter the market. Our evaluation found that Roche's ocrelizumab was indeed approved in the EU in 2018. The fact that CJM112 was discontinued in the period when Roche's ocrelizumab entered the market is important, because it makes it unlikely that the Transaction was a killer acquisition: knowing that there are other close competitors in the market undermines the incentives to kill competition.

These factors show that the Commission's expectations were realized and suggest that the conclusion that the Transaction could be cleared unconditionally was fit for purpose. Given the high number of competitors in the MS space and the entry of Roche's ocrelizumab in the market (an anti-CD20 monoclonal antibody similarly to ofatumumab), it seems unlikely that the discontinuation of CJM112 (an anti-IL17 monoclonal antibody) had the object or the effect to kill competition.

[333] https://pubmed.ncbi.nlm.nih.gov/29353550/

[334] As reported in the Decision (cfr. paragraph 19), there is no curative therapy for MS but only long term disease modifying therapies ("DMT") aimed at reducing the disease activity.

Table II.15: Disease modifying therapies for RRMS approved in the EU after the Decision[335]

Chemical name	Generic available	Brand name (owner)	Year of approval
Glatiramer acetate, injectable therapy	Yes	Glatiramer Mylan (Mylan – generic version of Copaxone)	2016
Cladribine, oral therapy	No	Mavenclad (Merck)	2017
Ocrelizumab, anti-CD20 monoclonal antibody	No	Ocrevus (Roche)	2018
Ofatumumab, anti-CD20 monoclonal antibody	No	Kesimpta (Novartis)	2021
Ozanlimod, oral therapy	No	Zeposia (Bristol-Myers Squibb)	2020
Ponesimod, oral therapy	No	Ponvory (Janssen)	2021
Siponimod, oral therapy	No	Mayzent (Novartis)	2020

Source: Lear

II.1.2.6 Conclusions

The Commission found one overlap between Novartis' treatments for RRMS and GSK's ofatumumab, which represents the target in this acquisition. Our ex-post assessment found that following the EC's clearance of the Transaction, ofatumumab was acquired by Novartis and approved for MS in March 2021, while one of Novartis' drugs for MS, CJM112 (an anti-IL17 monoclonal antibody), was discontinued. Our assessment suggests that this is not a likely killer acquisition, and rather that it may have been a commercial decision due to the fact that IL17 protein inhibitors were not yet known to be a viable target for MS at the time of the discontinuation.

Our assessment of the evolution of competition after the Transaction confirmed that the drug expected by the EC to become ofatumumab's closest competitor (Roche's ocrelizumab) entered the market, and found that several other treatments for MS were approved after the Transaction, implying that - as expected by the EC - Novartis

[335] Based on Emps and NMSS information. See https://emsp.org/about-ms/ms-treatments/ and https://www.nationalmssociety.org/Treating-MS/Medications/Aubagio

continues to face strong competition from a large number of firms. These factors show that the Commission's expectations were realized and suggest that its decision to clear the Transaction unconditionally was fit for purpose. However, this assessment does not extend to evaluating a counterfactual scenario where the deal did not take place.

II.1.3 **Notified concentration #4: BMS/Celgene**

II.1.3.1 Background

On 24 June 2019, the European Commission received a notification of a proposed concentration by which Bristol Myers Squibb Company ("BMS")[336] would acquire sole control of Celgene Corporation ("Celgene")[337] through a cash and stock transaction ("The Transaction"). BMS and Celgene are jointly referred to as "the Parties".

The European Commission reviewed the acquisition and published its decision on 29 July 2019, clearing the transaction unconditionally.

The Commission found overlaps in the following treatment activities of the Parties:

- autoimmune diseases;
- fibrotic diseases;
- oncology treatments.

This section provides an ex post evaluation of the overlaps previously assessed by the Commission, as well as for two possible additional potential overlaps revealed by the fact-finding challenge, based on publicly available evidence, and not included in the Commission decision.

II.1.3.2 Autoimmune diseases

Autoimmune diseases result from a dysfunction of the immune system in which the body attacks its own organs, tissues, and cells. In the autoimmune therapeutic space, the Parties' activities overlapped in the following therapeutic indications:

- Psoriasis ("PsO");
- Psoriatic Arthritis ("PsA");
- Inflammatory Bowel Diseases ("IBD");
- Systemic Lupus Erythematosus ("Lupus").

II.1.3.2.1 Psoriasis (PsO)

The Commission's Decision

The Commission found that the Transaction gave rise to overlaps between the marketed and pipeline products of the Parties in the market for moderate-to-severe psoriasis treatments. These overlaps are described in Table II.16 below.

[336] BMS is a global pharmaceutical company headquartered in the United States. BMS is engaged in the development and commercialisation of innovative medicines in four main therapeutic areas: oncology, autoimmune diseases, cardiovascular diseases, and fibrotic diseases.

[337] Celgene is a global pharmaceutical company headquartered in the United States. Celgene is engaged primarily in the development and commercialization of innovative therapies in oncology and autoimmune diseases.

Table II.16: Overlaps in psoriasis treatments identified by the EC[338]

Product market	Geographic market	Owner (pre-merger)	Drug	MoA/MoD	Line of treatment	Phase at time of Decision
Treatments for moderate-to-severe PsO (further segmentation left open)1	National for marketed, global or at least EEA for pipeline products	Celgene	Otezla	PDE-4/Oral	3rd	Marketed
			NDI-0348581	TYK2 inhibitor/Oral	3rd	Preclinical stage
		BMS	BMS-986165	TYK2 inhibitor/Oral	3rd	Phase III
			BMS-986251	RORγt antagonist/Oral	unknown	Phase I

Source: Lear

Regarding the overlap between Celgene's marketed Otezla and BMS' pipelines in a possible relevant market comprising all third-line treatments for moderate-to-severe PsO, the Commission found that it was improbable that the Transaction would give rise to competitive disruptions, because: i) none of the Parties' drugs was or was expected to hold a particularly strong position in the relevant market, ii) there were multiple other competitors in the market, and iii) the drugs were differentiated in terms of MoA as well as efficacy and safety profile, which is the key factor in the choice of treatment in the EEA.

With regard to the overlap between the Parties' pipeline programmes in a possible relevant market for TYK2 inhibitors for the treatment of moderate-to-severe PsO, the Commission didn't raise competitive concerns. The market investigation concluded that there were strong competitive constraints from other pipelines in the market and that each of the Parties' pipeline products appeared to compete more closely with other competitors' pipelines.[339]

The evolution of the overlapping projects after the merger

The evolution of the Parties' projects after the merger is described in Table II.17. As shown, we found that BMS' BMS-986251 was discontinued.

[338] Prior to the Transaction, BMS owned Kenalog, an injectable corticosteroid marketed in Spain, Italy and France. Since this drug was used for short-term relief of the symptoms as opposed to the long-term treatment of the underlying disease, and was being overtaken by a large number of generic alternatives, it was not taken into account in the Commission's, nor our assessment.

[339] Given that Celgene owned an option to acquire NDI-034858 from Nimbus, the EC concluded that there was a lack of incentives for the combined entity to exercise the option, purchase the Nimbus pipeline asset, and then discontinue it.

Table II.17: Evolution of the overlapping projects post-Transaction

Owner (pre-merger)	Drug/ pipeline	Phase at time of the deal (2019)	Evolution of the project
Celgene	Otezla, PDE-4	Marketed d	Marketed (by Amgen, to whom it was divested in the merger due to FTC concerns).[340]
	NDI-034858, TYK2 inhibitor	Preclinical stage	Celgene's option over this molecule was not exercised. In December 2020 BMS (after the acquisition of Celgene) declined the option, as it decided to 'streamline and prioritize its portfolio'.[341] December 2022: announcement of purchase of this molecule from Nimbus by Takeda.[342] September 2022: Phase II completed.[343] November 2023: two Phase III trials commenced.[344]
BMS	BMS-986165, TYK2 inhibitor	Phase III	Approved in the US, Canada and Japan.[345] March 2023: Marketing authorization issued by the EMA.[346]
	BMS-986251, RORγt antagonist	Phase I	June 2018: Phase I/II Terminated. Discontinued

Source: Lear

[340] See: https://news.bms.com/news/corporate-financial/2019/Bristol-Myers-Squibb-Announces-Agreement-Between-Celgene-and-Amgen-to-Divest-OTEZLA-for-134-Billion/default.aspx

[341] See the Company Agreements section at https://adisinsight.springer.com/drugs/800060068

[342] https://www.takeda.com/newsroom/newsreleases/2022/takeda-to-acquire-late-stage-potential-best-in-class-oral-allosteric-tyk2-inhibitor--ndi-034858-from-nimbus-therapeutics

[343] https://clinicaltrials.gov/ct2/show/NCT04999839

[344] https://clinicaltrials.gov/study/NCT06088043?intr=tak-279&rank=5; https://clinicaltrials.gov/study/NCT06108544?intr=tak-279&rank=6

[345] See Key Development Milestones, Psoriasis subsection: https://adisinsight.springer.com/drugs/800043162

[346] https://www.ema.europa.eu/en/medicines/human/EPAR/sotyktu#ema-inpage-item-authorisation-details

Reasons for discontinuation

The collected evidence suggests that BMS discontinued BMS-986251 for safety reasons. The reason for termination reported by BMS is the occurrence of an 'adverse change in the risk/benefit'.[347] More specifically, desk research conducted by the Team found that:

- the first arm of the study (on healthy volunteers), before it was terminated, yielded "adverse events" such as headaches, diarrhoea, dry mouth etc. in some individuals in the treatment groups. Some adverse events were reported also in the placebo group, though they were fewer and/or lower than in the treatment group[348];
- BMS-986251 is a RORγt inverse agonist, and concerns had been raised about the risk of deep immunosuppression because RORyt is needed at the earliest stage of T cell development (in the Thymus). Additional concerns relate to opportunistic infections (a major cause of morbidity and mortality in immunocompromised patients) as these were encountered in patients with hereditary RORyt deficiency[349];
- a lot of studies were previously terminated, in various phases of development, for RORγt inhibiting substances. The reason, where disclosed, is mostly related to safety.[350]

In light of the above, the Team considers that this discontinuation was due to safety reasons, and as such, was unrelated to the merger.

II.1.3.2.2 Psoriatic Arthritis (PsA)

The Commission's Decision

The Commission found overlaps in the market for moderate-to-severe PsA treatments between Celgene's marketed Otezla, and BMS' pipelines BMS-986165 and BMS-986251. These are described in Table II.18 below.

[347] https://www.clinicaltrials.gov/ct2/show/NCT03329885

[348] https://www.cdek.liu.edu/trial/NCT03329885/

[349] See: https://www.frontiersin.org/articles/10.3389/fimmu.2021.621956/full

[350] https://www.evaluate.com/vantage/articles/news/snippets/abbvies-ror-ends-whimper

Table II.18: Overlaps in psoriatic arthritis treatments identified by the EC[351]

Product market	Geographic market	Owner (pre-merger)	Drug	MoA/MoD	Phase at time of Decision
Moderate-to-severe PsA treatments (further segmentation left open)[352]	National for marketed, global or at least EEA for pipeline products	Celgene	Otezla	PDE-4/Oral	Marketed
		BMS	BMS-986165	TYK2 inhibitor/Oral	Phase II
			BMS-986251	RORγt agonist/Oral	Phase I

Source: Lear

The Commission did not raise competitive concerns emerging from the Transaction with respect to the above overlaps because: i) Otezla had limited market shares in each of the relevant national markets, while also being less efficacious than biologics, ii) the overlapping products were differentiated in terms of MoA and expected efficacy and safety profiles, and iii) post-Transaction, the merged entity would continue to face a high number of actual and potential competitors (including under the narrowest market definition giving rise to an overlap, i.e. oral third-line treatments for PsA).

The evolution of the overlapping projects after the merger

The evolution of the Parties' projects after the merger is described in Table II.19. Similarly to PsO, we found that BMS' BMS-986251 was discontinued in PsA as well.

[351]Prior to the Transaction, BMS owned Kenalog, an injectable corticosteroid marketed in Spain, Italy and France. Since this drug was used for short-term relief of the symptoms as opposed to the long-term treatment of the underlying disease, and was being overtaken by a large number of generic alternatives, it was not taken into account in the Commission's, nor our assessment.

[352] Possible further segmentation by line of treatment, Mode of Action (MoA) or Mode of Delivery (MoD) is left open due to a lack of concern regarding the potential anti-competitive outcomes of the Transaction in even the narrowest possible market delineation.

Table II.19: Evolution of the overlapping projects post-Transaction

Owner (pre-merger)	Drug	Phase at time of deal (2019)	Evolution of project
Celgene	Otezla	Marketed	Marketed (by Amgen, to whom it was divested in the merger due to FTC concerns).[353]
BMS	BMS-986165	Phase II	Phase III (active trial with estimated completion in 2026).[354]
	BMS-986251	Phase I	There are no records on AdisInsight or CT of this molecule ever being in clinical trials for PsA. However, there is a Phase I trial in rheumatoid arthritis which is quite similar to PsA, thus it is likely that the Commission is referring to that study. Note that it is the same trial[355], terminated early, previously mentioned for PsO.[356] This molecule did not progress further to Phase I in this indication, thus we can conclude that it was discontinued.

Source: Lear

Reasons for discontinuation

As explained in Section II.1.4.2.1.3, the Phase I trial conducted in PsO and rheumatoid arthritis led to several disturbances already in healthy volunteers. The third arm of the study, which was supposed to treat psoriasis patients, never commenced as the trial was terminated early. It seems plausible that developers hoped for a safer profile in healthy volunteers before proceeding to patients, and it is also reasonable that activity in psoriasis would have flagged likely activity in other autoimmune diseases (such as rheumatoid arthritis or PsA). Since the safety concerns described above emerged in healthy individuals, they are valid throughout all autoimmune indications for which the compound was being developed. Therefore, we can conclude that the discontinuation of BMS-986251 in PsA was due to safety reasons and thus was unrelated to the merger.

II.1.3.2.3 Inflammatory Bowel Disease (IBD)

IBD typically refers to two conditions: Ulcerative colitis (UC) and Crohn's disease (CD), which are inflammatory diseases that affect the digestive system.

[353] https://news.bms.com/news/corporate-financial/2019/Bristol-Myers-Squibb-Announces-Agreement-Between-Celgene-and-Amgen-to-Divest-OTEZLA-for-134-Billion/default.aspx

[354] https://clinicaltrials.gov/ct2/show/NCT04908189

[355] See the study here: https://www.clinicaltrials.gov/ct2/show/NCT03329885

[356] Alternatively, inability to find this trial may be due to the fact that it is not mandatory to record Phase I trials on CT.

The Commission's Decision

The Commission found that the Transaction gave rise to pipeline-to-pipeline overlaps in IBD treatments between Celgene's Ozanimod on the one hand, and BMS' TYK2 inhibitor and RORγt agonist on the other. These overlaps are described in Table II.20 below.

Table II.20: Overlaps in IBD treatments identified by the EC

Product market	Geographic market	Owner (pre-merger)	Drug	MoA/MoD	Phase at time of Decision
IBD treatments (further segmentation left open)[357]	Global or at least EEA-wide	Celgene	Ozanimod	S1P1 agonist/Oral	Phase III (UC and CD)
		BMS	BMS-986165	TYK2 inhibitor/Oral	Phase II (UC and CD)
			BMS-986251	RORγt agonist/Oral	Phase I (UC)

Source: Lear

[357] Possible further segmentation by line of treatment, within each of UC and CD, by Mode of Action (MoA) or Mode of Delivery (MoD) is left open due to a lack of concerns regarding the potential anti-competitive outcomes of the Transaction in even the narrowest possible market delineation.

The Commission concluded that the Transaction did not give rise to serious competitive concerns in IBD treatments. In particular, the Parties' pipelines are differentiated in terms of MoA, which also makes it likely that their efficacy and safety profiles would be differentiated if they were to reach the market. Moreover, the Parties' products were expected to compete more closely with pipeline products of their competitors. Finally, the combined entity would continue to face competitive constraints from several actual and potential competitors (even in the narrowest possible market, i.e. oral third-line treatments for UC/CD).

The evolution of the overlapping projects after the merger

Table II.21 below describes the evolution of the overlapping projects after the merger. Similarly to PsO and PsA, BMS-986251 was discontinued in IBD.

Table II.21: Evolution of the overlapping projects post-Transaction

Owner (pre-merger)	Drug	Phase at time of deal (2019)	Evolution of project
Celgene	Ozanimod	Phase III (UC and CD)	Approved for UC.[358] Multiple active Phase III studies for CD.[359]
BMS	BMS-986165	Phase II (UC and CD)	October 2023: Phase II in CD terminated due to lack of efficacy[360] November 2023: Phase II in UC completed[361]
	BMS-986251	Phase I (UC)	Same study identified for PsO. June 2018: Phase I/II Terminated.[362] Discontinued.

Source: Lear

Reasons for discontinuation

As described in the sections above, the Team's assessment suggests that BMS-986251 was discontinued for technical reasons (safety concerns) which plausibly apply to all autoimmune indications for which the molecule was being tested, including IBD.

[358] See the Introduction section: https://adisinsight.springer.com/drugs/800033563

[359] A list of studies can be seen here: https://clinicaltrials.gov/search?cond=crohn%27s%20disease&intr=Ozanimod

[360] https://clinicaltrials.gov/ct2/show/NCT03599622

[361] https://clinicaltrials.gov/ct2/show/NCT04613518

[362] See the trial here: https://www.clinicaltrials.gov/ct2/show/NCT03329885

II.1.3.2.4 Systematic Lupus Erythematosus (Lupus)

The Commission's Decision

Regarding Lupus treatments, the Commission found that the Transaction gave rise to pipeline-to-pipeline overlaps between Celgene's CC-220 on the one hand, and BMS' TYK2 inhibitor, BTK inhibitor, TLR antagonist and RORγt agonist on the other. The identified overlaps are described in Table II.22 below.

Table II.22: Overlaps in Lupus treatments identified by the EC

Product market	Geographic market	Owner (pre-merger)	Drug	MoA/MoD	Phase at time of Decision
Pipeline products for Lupus treatment (further sub-segmentation left open)[363]	Global or at least EEA	Celgene	CC-220	Cereblon receptor/Oral	Phase II
		BMS	BMS-986165	TYK2 inhibitor/Oral	Phase II
			BMS-986195	BTK inhibitor/Oral	Phase II
			BMS-986256	TLR 7/8 antagonist/Oral	Phase I
			BMS-986251	RORγt agonist/Oral	Phase I

Source: Lear

The Commission's assessment allowed us to exclude serious doubts about the competitive outcomes of the Transaction. Firstly, the Parties' compounds were very differentiated: they had different MoAs and thus would likely serve different patient groups and have different efficacy and safety profiles. Secondly, post-Transaction, the combined entity would continue to face competitive constraints from a large number of actual and potential competitors. Finally, as evidenced by a KOL in the market investigation, at the time of the deal there was still a need for an efficacious lupus treatment, making it unlikely that the combined entity would decide to discontinue one of the Parties' pipeline projects.

The evolution of the overlapping projects after the merger

We found that, similarly to the autoimmune diseases detailed in the previous sections, BMS' BMS-986251 was discontinued in Lupus as well. Moreover, there seems to have been a discontinuation of Celgene's CC-220 in Lupus (specifically a redirection to multiple myeloma and lymphoma treatments).

[363] Possible further segmentation by line of treatment, Mode of Action (MoA) or Mode of Delivery (MoD) is left open due to a lack of concern regarding the potential anti-competitive outcomes of the Transaction in even the narrowest possible market delineation.

Table II.23: Evolution of the overlapping projects post-Transaction

Owner (pre-merger)	Drug	Phase at time of deal (2019)	Evolution of the project
Celgene	CC-220	Phase II	August 2021: Phase II study completed. No new studies.[364] Starting from BMS' Q1 2022 investor presentation, this molecule is mentioned only as a part of the hematology portfolio.[365] It is possible that this drug is being pursued only in multiple myeloma and lymphoma treatments (both within Hematology), where it is in Phase III according to CT, AdisInsight and BMS' website.[366] Reoriented to hematology after the deal.
BMS	BMS-986165	Phase II	November 2022: Phase III initiated, still active.[367]
	BMS-986195	Phase II	December 2022: Phase II completed according to CT and AdisInsight.[368]
	BMS-986256	Phase I	June 2021: Phase II initiated, recruiting.[369]
	BMS-986251	Phase I	There is no information about this drug ever being tested for Lupus on AdisInsight nor CT.[370] It does appear in the BMS Annual report 2018[371] on Phase I trials for 'Autoimmune disease', but it is not mentioned from 2019 onwards. Discontinued.

Source: Lear

[364] https://clinicaltrials.gov/study/NCT03161483

[365] See the presentation here: https://s21.q4cdn.com/104148044/files/doc_presentations/2022/BMY-2022-Q1-Results-Investor-Presentation.pdf

[366] See the study here: https://clinicaltrials.gov/ct2/show/NCT05560399, AdisInsight profile here: https://adisinsight.springer.com/drugs/800037266 , and BMS website here: https://www.bms.com/researchers-and-partners/in-the-pipeline.html

[367] Study details here: https://clinicaltrials.gov/ct2/show/NCT05620407

[368] See the study: https://clinicaltrials.gov/ct2/show/NCT04186871 , and AdisInsight: https://adisinsight.springer.com/drugs/800044925

[369] Study profile: https://clinicaltrials.gov/ct2/show/NCT04895696

[370] This could be due to the fact that it is not mandatory to record Phase I trials on CT.

[371] https://s21.q4cdn.com/104148044/files/doc_financials/annual_reports/2018/2018-BMS-Annual-Report.pdf

Reasons for discontinuation

Celgene's CC-220 was discontinued after a Phase II trial in Lupus, and redirected to multiple myeloma and lymphoma. The evidence that emerged in our assessment suggests that the drug was discontinued on a technical basis. Namely, we compare the Phase II trial data of CC-220 with the Phase II trial data of the most recently approved drug in the same indication, AstraZeneca's Saphnelo.[372] It should be noted that the CC-220 and Saphnelo studies looked into the same primary outcome measure, but Saphnelo was trialed in a significantly harder to treat population (moderate to severe disease with steroid tapering).[373] Nevertheless, both drugs showed efficacy, with the significant difference in the primary endpoint measure between treated and placebo group being 19.4 and 16.7 percentage points, respectively. However, CC-220 seems to have led to higher instance of non-serious adverse events (40.96% in placebo group vs. >70% in most treated groups) than Saphnelo (35.64% in placebo vs. 40.4% and 43.81% in treatment groups).[374] The observed higher incidence of non-serious adverse events for CC-220 suggests a relatively poor tolerability profile, with a broader range of tolerance issues compared to Saphnelo. Additionally, the absence of steroid sparing exacerbates concerns about steroid tolerability for CC-220 patients. When considering these factors alongside efficacy, the risk-benefit assessment is notably skewed against CC-20, contributing to the decision not to pursue further development in this specific indication. Moreover, it should be acknowledged that SLE is a challenging disease to treat, making market entry difficult (looking at the history of approval, GSK's Benlysta was approved in 2011, followed by Saphnelo in 2022).

As described in the sections above, the reasons that led to the discontinuation of BMS-986251 in PsO (i.e. safety concerns) appear to be sufficient to warrant the discontinuation in Lupus as well, i.e. another disease in the autoimmune group (especially given the early trial phase).

II.1.3.3 Fibrotic diseases

Fibrotic diseases include a broad range of diseases (e.g. idiopathic pulmonary fibrosis, non-alcoholic steatohepatitis, advanced liver fibrosis) that involve fibrosis in some part of the body. Fibrosis is the formation of excessive tissue scarring and can occur in different organs, such as the lungs, liver, skin, eyes, heart, and kidneys.

In fibrotic diseases, at the time of the Transaction the Parties' activities overlapped with respect to the following indications:

- Idiopathic Pulmonary Fibrosis ("IPF");
- Non-alcoholic steatohepatitis ("NASH").

[372] For CC-220 see: https://clinicaltrials.gov/study/NCT03161483 and https://pubmed.ncbi.nlm.nih.gov/35294813/For Saphnelo see: https://clinicaltrials.gov/study/NCT01438489 and https://pubmed.ncbi.nlm.nih.gov/28130918/

[373] While steroids are a mainstay of SLE treatment, their use is accompanied by a myriad of adverse effects. Consequently, healthcare practitioners aspire to employ alternative interventions that are steroid-sparing, aiming to enhance the overall efficacy while mitigating the associated side effect profile.

[374] Since steroid tapering likely reduced the instance of adverse events in the Saphnelo trial, we look at the differences between the control and treatment groups which would cancel out the population effect.

The overlaps in IPF are presented in Appendix A.4 to this report as no discontinuations were found in that indication.

II.1.3.3.1 Non-alcoholic steatohepatitis (NASH)

The Commission's Decision

With regard to NASH treatments, the Commission identified pipeline-to-pipeline overlaps between Celgene's CC-90001 on the one hand, and BMS' BMS-986263 and BMS-986036 on the other. These overlaps are described in Table II.24 below.

Table II.24: Overlaps in NASH treatments identified by the EC

Product market	Geographic market	Owner (pre-merger)	Drug	MoA/MoD	Phase at time of Decision
Pipeline products for NASH treatment (further segmentation left open)[375]	Global or at least EEA	Celgene	CC-90001	JNK inhibitor/Oral	Phase II
		BMS	BMS-986263[376]	HSP47 inhibitor/Injectable	Phase II
			BMS-986036	Pegylated FGF21/Injectable	Phase II

Source: Lear

The Commission considered that the Transaction did not give rise to competition concerns in the market for NASH treatments. In particular, Celgene's and BMS' pipeline products are very differentiated in terms of MoA and MoD, making it very likely that these drugs, if they were to reach the market, would have different efficacy and safety profiles and thus serve different patient groups. Secondly, post-Transaction, the combined entity would continue to face competitive constraints from a large number of actual and potential competitors. Finally, the Commission found that, given the absence of an effective treatment available on the market, there was high unmet demand for NASH therapies. As such, it was considered unlikely that the combined entity would have incentives to discontinue, delay or reorient any of its pipeline products, especially given their differentiation.

The evolution of the overlapping projects after the merger

Our research found that Celgene's CC-90001 was redirected from NASH to advanced solid tumours treatment. Moreover, through qualitative assessment, we found a discontinuation in BMS-986036, which wouldn't be identified as a discontinuation in our large-scale analysis as the last clinical trial was completed less than 24 months ago. The evolution of the overlapping projects in NASH is detailed in Table II.25 below.

[375] As the Commission concluded there were no serious concerns about anti-competitive outcomes of the Transaction even under the narrowest possible market definition.

[376] BMS had a financial option over ND-L02-s0201 (i.e. BMS-986263), an asset that was being developed by Nitto Denko at the time of the Decision.

Table II.25: Evolution of the overlapping projects post-Transaction

Owner (pre-merger)	Drug	Phase at time of deal (2019)	Evolution of the project
Celgene	CC-90001	Phase II	October 2021: BMS terminated the Phase II trial (since "Business objectives have changed").[377] December 2022: Phase I study in advanced solid tumors.[378] Redirection to oncology.
BMS	BMS-986263	Phase II	Phase II trial initiated in March 2021 (active).[379]
	BMS-986036	Phase II	September 2021: Phase II study completed.[380] Our large-scale analysis would not identify this as a discontinuation (since the study was completed less than 24 months ago). However, our qualitative assessment found that this drug has been discontinued.[381]

Source: Lear

Reasons for discontinuation

Regarding the discontinuation of BMS-986036, this appears to be due to technical reasons. In particular, the sector journal Fierce Biotech explains that the compound didn't meet its primary endpoints in Phase II studies, which warranted the discontinuation.[382]

As per Celgene's CC-90001, based on desk-research and the views of pharmaceutical experts in the Team, it appears that the compound was redirected from NASH to advanced solid tumours due to commercial reasons that are unrelated to the merger.

In particular, it is important to note that there are currently no FDA- or EMA-approved medicines for NASH.[383] Although this would suggest that the NASH market is a promising one for the companies that manage to develop a successful drug, it is expected that

[377] See AdisInsight: https://adisinsight.springer.com/drugs/800040481 and clinical trial: https://clinicaltrials.gov/ct2/show/NCT04048876

[378] https://clinicaltrials.gov/ct2/show/NCT05625412

[379] See the clinical trial: https://clinicaltrials.gov/ct2/show/NCT04267393. Moreover, this drug is mentioned in the BMS Annual report 2021 (https://annual-report.bms.com/assets/bms-ar/documents/2021-annual-report.pdf) as being developed in partnership with Nitto Denko for NASH treatment.

[380] https://clinicaltrials.gov/ct2/show/NCT03486912

[381] See the Fierce Biotech article: https://www.fiercebiotech.com/biotech/bristol-myers-becomes-latest-victim-unforgiving-nash-as-mid-stage-asset-shelved

[382] https://www.fiercebiotech.com/biotech/bristol-myers-becomes-latest-victim-unforgiving-nash-as-mid-stage-asset-shelved

[383] https://www.nature.com/articles/s41401-022-00900-y

slow reimbursement rates, cumbersome diagnostic procedures[384] and high therapy costs would likely impede the uptake of pipeline drugs in the future.[385] Moreover, the market for NASH pipelines is crowded, with approximately 120 assets in development, including eight assets in Phase III and one asset in Pre-registration.[386] This implies that a very reliable product is required in order to succeed in the potential NASH treatments market.

Moreover, the efficacy of selectively inhibiting one pathway of injury alone (as it is done by CC-90001) is questionable. Despite the appeal of directly targeting mechanisms of liver damage in steatohepatitis rather than the upstream cause, some of these methods have failed to demonstrate clear benefits.[387] In fact, given the complex pathophysiology of NASH, diverse pathways including metabolism (glucose, fat, cholesterol), inflammation, and fibrosis are being targeted by therapies in development.[388] It is believed that engagement of multiple targets simultaneously could increase the likelihood of success.

Therefore, based on the above, it appears that CC-90001 was likely redirected due to the difficulty of pioneering in the (still inexistent) NASH treatment market. The compound was redirected to cancer treatment - a bigger and more cost-effective market, with higher expected value (especially due to the low probability of developing a successful NASH treatment) - suggesting that the redirection may be due to commercial reasons and be unrelated to the merger.

II.1.3.4 Oncology treatments

Cancer treatments include traditional types of therapies (such as surgery, radiotherapy and chemotherapy) and newer forms of treatment (such as targeted therapies and immunotherapies). Within oncology, the Transaction gave rise to overlaps with respect to: i) BET inhibitors (belonging to targeted therapies)[389] and ii) various immunotherapies.[390]

The overlaps in BET inhibitors are presented in Appendix A.4 to this report, as no discontinuations were found among them post-Transaction. Regarding immunotherapies, the Commission identified overlaps in the following therapeutic indications:

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[384] There are a few cumbersome options available for NASH diagnosis, such as liver biopsy, which is a painful, costly, and invasive method that creates patient hindrance. Owing to such factors, the non-alcoholic steatohepatitis global average diagnosis rate lies at only around 20%. This affects the treatment rate negatively.

[385] https://www.grandviewresearch.com/industry-analysis/non-alcoholic-steatohepatitis-nash-treatment-market-report#:~:text=Report%20Overview,39.2%25%20from%202022%20to%202030.

[386] https://www.smartanalyst.com/wp-content/uploads/2021/12/Updates-in-hepatology-NASH.pdf

[387] For example, chemokine antagonists, anti-apoptotics, or VAP1 (also known as AOC3) inhibitors. See https://www.sciencedirect.com/science/article/pii/S0168827822002100

[388] https://www.smartanalyst.com/wp-content/uploads/2021/12/Updates-in-hepatology-NASH.pdf

[389] BET inhibitors are inhibitors of Bromodomain and Extra-Terminal (BET) proteins, which are involved in the expression of several genes controlling activities which are key for cancer development, such as cell proliferation and metastatic spreading.

[390] Immunotherapies are products that utilise a patient's own immune system to fight cancerous cells. Immunotherapies do not attack cancerous cells directly but are designed to enhance the body's natural mechanisms to fight cancer, helping the immune system to increase its natural ability to eliminate cancer cells.

- Colorectal cancer;
- Head and neck squamous cell cancer (HNSCC);
- Non-small cell lung cancer (NSCLC);
- Small cell lung cancer (SCLC);
- Ovarian cancer;
- Pancreatic cancer;
- Multiple myeloma.

It should be noted that since Celgene's products involved in the overlaps in immunotherapies for colorectal cancer and HNSCC were not disclosed in the publicly available Decision, these overlaps are not discussed further in our evaluation. Moreover, we found no discontinuations in the immunotherapies for NSCLC, SCLC, ovarian cancer and pancreatic cancer, so these overlaps are presented in Appendix A.4 to this report.

The next subsection contains remarks which are worth making with regard to a specific molecule involved in the overlaps in NSCLC, ovarian cancer and pancreatic cancer, despite no discontinuation was detected in these indications. The following subsection discusses the only indication within immunotherapies where we found a discontinuation, multiple myeloma.

II.1.3.4.1 MSC-1: an "escaped" discontinuation

At the time of the merger, Celgene had exercised a financial option[391] over MSC-1, a pipeline immunotherapy that was being developed by Northern Biologics. The pipeline was overlapping with BMS' pipelines and marketed immunotherapies for NSCLC, ovarian cancer and pancreatic cancer. The overlap was found by the Commission as unlikely to lead to an anti-competitive outcome, due to (i) the differentiated MoA of MSC-1 and the overlapping products, (ii) the uncertainties resulting from the early stage of development of MSC-1 (Phase I at the time of the Decision), (iii) the existence of several competing pipelines at a more advanced stage of development (in some of the overlapping indications) and (iv) the absence of competition concerns raised by market participants during the Commission's market investigation.

The following events took place after the merger in relation to the MSC-1 compound:

- BMS decided to no longer exercise the financial option over MSC-1;[392]
- in January 2020, Northern Biologics' Phase I study of MSC-1 in advanced solid tumors (which comprises also the more granular indications mentioned above) was terminated, with the reported explanation "Safety and PK/PD data from Dose Escalation support further development; Dose Expansion canceled". This seems to suggest that termination was not due to technical reasons;[393]
- in May 2020, Boehringer Ingelheim acquired Northern Biologics (excluding the MSC-1 asset);[394]

[391] Celgene exercised the option to acquire certain, undisclosed, rights to the MSC-1 development program. We can assume that the deal involved funding at least a part of the compound's development. See: https://www.versantventures.com/portfolio/northern-biologics

[392] https://web.archive.org/web/20220925111512/https://xconomy.com/new-york/2020/05/14/boehringer-ingelheim-acquires-northern-biologics-preclinical-pipeline/

[393] See the study here: https://clinicaltrials.gov/ct2/show/NCT03490669

[394] https://www.boehringer-ingelheim.com/press-release/acquisitionofnorthernbiologics

- in November 2020, AstraZeneca acquired MSC-1 from Northern Biologics[395], and in December 2021 started a Phase II study of this compound in advanced solid tumors (note that the name of the molecule is now AZD0171).[396]

Thanks to AstraZeneca acquiring the molecule and resuming trials, MSC-1 was not discontinued. However, the events above suggest that, had AstraZeneca (or other third parties) not got involved, the molecule would have been discontinued for non-technical reasons that could potentially be related to the merger. In particular, the Team and its experts consider it likely that originally Celgene's rights over MSC-1 required it to fund at least part of the molecule's development. Therefore, BMS' decision post-merger not to exercise its option over MSC-1 could have potentially led to lack of funding for the compound's development, explaining the termination of the Phase I study by Northern Biologics.

Post-merger, BMS could have been uninterested in pursuing MSC-1 because BMS had a couple of successful mega Immuno-Oncology (IO) blockbusters in its portfolio (i.e. Opdivo and Yervoy) and thus it is possible that other IO assets would have to be very promising to compete with these or be suitable for combining with these mega IOs. Indeed, BMS focused a lot of resources on trials for various mono- or combination therapies including Opdivo.[397] Moreover, Opdivo was reported as one of BMS' main brands, with a world-wide revenue of $1.36 billion in 2017.[398] Finally, the fact that MSC-1 was taken forward by an established oncology player (AstraZeneca) indicates that it was likely to be promising enough not to be discontinued, but perhaps had to compete for resources with other massive drivers for BMS such as Opdivo.

Therefore, initial termination of the study on MSC-1 may be seen as potentially related to the merger (i.e. absent the merger, Celgene may have continued financing trials on MSC-1). However, the involvement of AstraZeneca guaranteed that the molecule was taken forward, implying that this was an "escaped" discontinuation.

In any event:

- It is unclear whether the discontinuation of MSC-1 would have been detrimental to competition (and, thus, harmful for consumers). In fact, the Commission's decision suggests that it would not have been the case given notably the existence of several (more advanced) competing pipelines and the absence of concerns raised by market participants during the Commission's market investigation;
- The fact that BMS did not exert the option to acquire MSC-1 tends to dismiss a potential killer acquisition narrative.

[395] https://www.metrixpartners.com/northern-biologics-announces-global-acquisition-of-clinical-stage-antibody-msc-1-by-astrazeneca/

[396] See the study here: https://clinicaltrials.gov/ct2/show/NCT04999969

[397] See the load of trials here: https://clinicaltrials.gov/ct2/results?cond=&term=opdivo+bms&cntry=&state=&city=&dist=&Search=Search

[398] https://news.bms.com/news/corporate-financial/2018/Bristol-Myers-Squibb-Reports-Fourth-Quarter-and-Full-Year-Financial-Results/default.aspx

II.1.3.4.2 Immunotherapies for multiple myeloma

The Commission's Decision

In the market for immunotherapies for multiple myeloma, the Commission found a number of Celgene's drugs and pipeline programmes overlapping with BMS' Opdivo (which was in Phase I/II trials at the time of the Transaction).[399] The overlaps identified by the Commission are described in Table II.26 below.

Table II.26: Overlaps in immunotherapies for multiple myeloma identified by the EC

Product market	Geographic market	Owner (pre-merger)	Drug	MoA	Phase at time of Decision
Immunotherapies for multiple myeloma (sub-segmentation left open)[400]	National for marketed, global or at least EEA-wide for pipelines	Celgene	Imnovid	IMid[401]	Marketed + Pipelines (Phase II, III)
			Revlimid	IMid	Marketed + Pipelines (Phase II)
			Thalidomide	IMid	Marketed
			bb2121	CAR-T	Phase I, II and III
			JCARH125	CAR-T	Phase I
			bb21217	CAR-T	Phase I
			CC-92480	Cereblon modulator	Phase I
			CC-220	Cereblon modulator	Phase I/II
			CC-93269	T-cell engager CD3/BCMA	Phase I
		BMS	Opdivo (combination)	PD-1 inhibitor and others	Phase I/II

Source: Lear

[399] For the multiple myeloma indication, Opdivo was being trialed as a combination therapy.

[400] As the Transaction raised no concerns even when taking into account the narrowest possible relevant product market.

[401] Immunomodulator

The market investigation conducted by the Commission did not reveal any concrete elements supporting the existence of serious doubts regarding anticompetitive outcomes of the Transaction in this indication. Firstly, it concluded that the Parties' pipelines were differentiated products, with distinct MoA and different lines of treatment,[402] implying that if they were to reach the market, there was no indication that their efficacy and safety profiles would be similar. Secondly, BMS' Opdivo was at a very early stage in trials and was not expected to reach the market before many years. Moreover, prospective indications remained uncertain and subject to change, especially with respect to immunotherapies. Finally, the combined entity would face competition from several pipeline programmes, including pipelines which were at a more advanced stage of development than BMS' pipeline and pipelines with the same MoA as the Parties'.

The evolution of the overlapping projects after the merger

Our assessment of the evolution of the overlapping projects post-Transaction found that one compound, bb21217, was discontinued, while all others are marketed or still in development. The evolution of the overlapping drugs after the merger is described in Table II.27 below.

[402] BMS' Opdivo combination was being trialed for a very late line of treatment whereas Celgene's marketed and pipeline products were mostly prescribed or trialed as earlier lines of treatment.

Table II.27: Evolution of the overlapping projects post-Transaction

Owner (pre-merger)	Drug	Phase at time of deal (2019)	Evolution of the project
Celgene	Imnovid	Marketed + Pipeline (Phase II, III)	Marketed + multiple Phase II and III trials[403]
	Revlimid	Marketed + Pipelines (Phase II)	Marketed + multiple ongoing studies[404]
	Thalidomide	Marketed	Marketed[405]
	bb2121	Phases I, II and III	Approved in the EU and the US[406]
	JCARH125	Phase I	February 2018: Phase I/II study initiated, completed in March 2023[407]
	bb21217	Phase I	Discontinued in January 2022.[408]
	CC-92480	Phase I	Multiple ongoing studies, most advanced being Phase III[409]
	CC-220	Phase I/II	Multiple ongoing studies, most advanced being Phase III[410]
	CC-93269	Phase I	April 2018: Phase I study initiated, estimated completion date August 2029[411]
BMS	Opdivo (comb.)	Phase I/II	Multiple ongoing studies, most advanced being Phase III (completed March 2022).[412]

Source: Lear

[403] https://clinicaltrials.gov/ct2/results?cond=multiple+myeloma&term=imnovid&cntry=&state=&city=&dist=&Search=Search

[404] https://clinicaltrials.gov/ct2/results?cond=multiple+myeloma&term=Revlimid&cntry=&state=&city=&dist=&Search=Search

[405] https://adisinsight.springer.com/drugs/800004827

[406] https://adisinsight.springer.com/drugs/800042787

[407] https://clinicaltrials.gov/ct2/show/NCT03430011

[408] See article: https://www.fiercebiotech.com/biotech/bristol-myers-2seventy-cull-multiple-myeloma-car-t-as-abecma-sales-pick-up

[409] https://clinicaltrials.gov/ct2/results?cond=multiple+myeloma&term=CC-92480&cntry=&state=&city=&dist=&Search=Search

Reasons for discontinuation

Our evaluation found that bb21217 (a CAR-T programme) was discontinued for commercial reasons unrelated to the merger, in particular because after the merger BMS marketed a very similar drug (bb2121, also a CAR-T programme) which had immense success, and the characteristics of CAR-T therapies suggest that it may not be commercially sensible to own multiple programmes of this type.

More specifically, at the time of the merger, Celgene had three ongoing CAR-T programmes in its multiple myeloma treatment portfolio: bb2121, JCARH125 and bb21217, while BMS had none. CAR T-cell therapy is approved for multiple myeloma that has relapsed after or is refractory to at least four prior treatments. It is a highly-specialized therapy that involves genetically modifying a patient's own T-cells to attack their multiple myeloma using a target called B-cell maturation antigen (BCMA).[413] According to pharmaceutical experts in the Team, CAR-T is complex to make and deliver to patients, resulting in high costs and lower margins than comparable off-the-shelf products. This is confirmed by pharmaceutical websites.[414]

Celgene's (then BMS's) bb21217 was supposed to be an improvement over bb2121 (Abecma), in particular yielding longer-lasting results.[415] Results of the Phase I trial of bb21217 continued to support the hypothesis that bb21217 would lead to a longer-lasting duration of response.[416] However, bb21217 was discontinued by BMS after the Phase I study (in January 2022). Pharmaceutical journals explain that the discontinuation was due to the fact that BMS had already marketed a very similar drug, bb2121 (Abecma), which proved very successful.[417] Given the nature of CAR-T therapy, experts in the Team consider that having three such products in a company's portfolio may not have been commercially sensible.

Thus, the discontinuation appears to be due to commercial considerations which are unrelated to the merger. Moreover, it should be noted that bb21217 and bb2121 (Abecma) were both a part of Celgene's portfolio before the merger. Thus, in the absence of the merger, also Celgene would have likely discontinued bb21217 in light of the success of bb2121.

Concerning harm, we note that the discontinuation could be seen as somewhat harmful for consumers, as they will not get the opportunity to be treated by a possibly longer lasting drug. However, the merged company is left with two other CAR-T programmes,

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[410] https://clinicaltrials.gov/ct2/results?cond=multiple+myeloma&term=CC-220&cntry=&state=&city=&dist=&Search=Search

[411] https://clinicaltrials.gov/ct2/show/NCT03486067

[412] https://clinicaltrials.gov/ct2/show/NCT02726581

[413] See https://www.dana-farber.org/cellular-therapies-program/car-t-cell-therapy/car-t-cell-therapy-for-multiple-myeloma/

[414] For example, https://www.pharmaceutical-technology.com/features/off-the-shelf-car-t-precision-medicine/

[415] https://www.medpagetoday.com/meetingcoverage/ashvideopearls/91305

[416] https://www.sciencedirect.com/science/article/pii/S0006497121025404

[417] https://www.pmlive.com/pharma_news/bms_and_2seventy_bio_move_away_from_car-t_programme_1386216

and nine overall multiple myeloma marketed/pipeline treatments, so choice for consumers appears to be potentially high, reducing the impact of the discontinuation.

II.1.3.5 The additional potential overlaps revealed by the fact-finding challenge

In addition to the overlaps described in the Commission decision, the large-scale analysis revealed that the deal may have given rise to two additional potential overlaps, ultimately leading to discontinuations, that do not appear in the decision.

The first potential additional overlap was flagged as a LASSO KA in the large-scale analysis and is between BMS' BMS 986166 and Celgene's Ozanimod in Ulcerative Colitis ("UC").

BMS 986166 was found in perfect MoA and TI overlap with Celgene's Ozanimod, both drugs being S1P1 agonists trialled in UC. BMS 986166 was discontinued after a Phase I trial to assess safety and tolerability in healthy individuals, completed in August 2017.[418] There is no publicly available evidence suggesting technical issues warranting the discontinuation, and on the contrary, the drug seems to have been well tolerated.[419] Ozanimod, on the other hand, was in Phase III in UC prior to the deal, and got approval for this TI in the EU in March 2020.[420]

The focal point of this assessment revolves around determining whether the discontinued molecule, BMS' BMS 986166, was in active development at the time of the deal, which, based on publicly available evidence, is unclear. In fact, if the molecule was active at that time, then its discontinuation after the deal makes this transaction a possible killer acquisition, as the existing evidence in the public domain is consistent with a potential killer acquisition narrative.

We note that the decision extensively discusses the parties' compounds in UC[421], but does not include the examined overlap. Although the evidence available in the public domain suggests that BMS 986166 may have been in active development at the time of the deal (see below), the Team understands that the Commission had access to confidential information indicating that the pipeline was no longer active at the time of the deal. This is another illustration of the limitation of relying exclusively on public sources, which are by nature fragmented, for this type of assessment.

The publicly available evidence suggesting that BMS 986166 may have been in active development at the time of the deal is described below:

- the drug was listed in BMS active pipeline in Phase I at the time of the deal in the broader area of "immunoscience" (noting that the Team suppose it is the Phase I "S1P1 Agonist" listed in the pipeline);[422]
- there is an article published in October 2020 (i.e. one year after the deal completion), and sponsored by BMS, showing an improved cardiac safety profile of

[418] Even though, according to the title, the study was conducted in healthy individuals, the relevant indication flagged on CT is ulcerative colitis. See: https://clinicaltrials.gov/study/NCT03038711

[419] See results: https://pubmed.ncbi.nlm.nih.gov/32306792/

[420] See trial: https://clinicaltrials.gov/study/NCT02435992; and authorization details: https://www.ema.europa.eu/en/medicines/human/EPAR/zeposia#ema-inpage-item-authorisation-details

[421] An overview of the Commission's assessment of the overlaps between the parties' compounds in ulcerative colitis, as well as our ex-post evaluation, can be seen in section II.1.4.2.3.

[422] https://web.archive.org/web/20190114114857/https:/www.bms.com/researchers-and-partners/in-the-pipeline.html

BMS 986166 compared to other S1P1 agonists, including Ozanimod.[423] This article also mentions BMS 986166 being under development for ulcerative colitis. However, we note that the article was submitted for publication in September 2018 (i.e. 9 months before the formal notification of the Transaction), and thus is likely to only imply that BMS 986166 was active 9 months before the deal notification;

- BMS 986166 was listed in BMS' website as an active pipeline in Phase I (and later Phase II) in "immunoscience" and then "autoimmune disease" until the beginning of 2022. Then, the TI was narrowed to Atopic Dermatitis in February 2022. In fact, a Phase II trial in Atopic Dermatitis was started in August 2021.[424] Importantly, this proves that the safety data observed in the Phase I trial in healthy volunteers didn't warrant a discontinuation in autoimmune diseases. As of today, the drug appears to be no longer in pipeline. Based on Adis and CT, Ozanimod has not been in development for Atopic Dermatitis, meaning that BMS 986166 might have been reoriented to a TI with no overlapping compounds within the newly created entity.

Considering only the above publicly available information, the Team and its experts concluded that the evidence gathered for this case, including that related to the activity of BMS 986166 at the time of the deal, could potentially be consistent with a killer acquisition narrative, especially if the market is defined narrowly as a combination of TI and MoA. Most notably: i) the two overlapping drugs can be seen as substitutable in ulcerative colitis; ii) the discontinuation seems to lack a valid technical, clinical or commercial justification that would have emerged even in the absence of the transaction; and iii) in the potential relevant market defined narrowly as a combination of TI and MoA, competition at the time of the deal appears to be sufficiently limited that the incentives for a killer acquisition would be present. Specifically, in such market, at the time of the deal there appears to have been only one competitor to BMS' and Celgene's compounds, Arena's Etrasimod, approved by the FDA for the treatment of moderate to severe ulcerative colitis in October 2023.[425] Taking into consideration a broader market for moderate to severe UC (with no MoA distinction), the Team experts' opinion is that there is a high unmet need for treatments (especially at the time of the deal, prior to the approval of Rinvoq), and that therefore it would have been reasonable to progress a promising candidate with a recognized MoA such as BMS 986166. However, the Commission decision[426] suggests that in the broader market for UC actual and potential competition may not have been limited, implying that even if we concluded that the discontinuation of BMS 986166 was related to the transaction, it is unclear that this discontinuation would be detrimental to competition should the market be defined on a broader basis. The Commission precedents show that the exact scope of the market is not obvious.[427]

[423] https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7821288/

[424] https://clinicaltrials.gov/study/NCT05014438

[425] https://www.pfizer.com/news/press-release/press-release-detail/us-fda-approves-pfizers-velsipitytm-adults-moderately

[426] BMS/ Celgene decision, §§133-136.

[427] Concerning precedents, in M.7379 – AbbVie/Shire and M.8955 – Takeda/Shire, the Commission has typically segmented the market based on the line of treatment, distinguishing between conventional

Therefore, based on publicly available information, assuming BMS 986166 was still active in UC at the time of the deal (*quod non* – see above), our ex-post assessment suggests that BMS' acquisition of Celgene may have led to the anti-competitive discontinuation of BMS' BMS 986166. Under a narrow definition of the relevant market, based on both the TI and MoA, this discontinuation would be worrying, given the very limited competition in the market; if instead the market is more widely defined, then the anti-competitive impact of the discontinuation is not obvious, given a larger number of available competing products. We note that our assessment refrains from drawing firm conclusions, as it does not rely on companies' internal technical and commercial documents. These documents could have offered additional insights into the development status of BMS 986166 at the time of the deal and its technical and commercial viability/prospects.

For simplicity, the second overlap that does not appear in the Commission decision is described in the appendix, because based on the Team's assessment the discontinuation appears to be unrelated to the BMS/ Celgene deal.

II.1.3.6 Evaluation of the Commission's assessment

Our ex-post assessment detected three discontinuations and two redirections in treatments where the Parties' activities overlapped before the merger (and which had been ex ante evaluated by the Commission). The Team concluded that all of them were unrelated to the merger, i.e. absent other differences in the market conditions, they would have likely happened also in the absence of the merger.

BMS' BMS-986251, which prior to the merger was in Phase I clinical trials for the treatment of Psoriasis, Psoriatic Arthritis, Inflammatory Bowel Diseases and Systemic Lupus Erythematosus, was discontinued. We found that the discontinuation was due to safety reasons, and specifically the fact that disturbances emerged already in trials on healthy individuals, suggesting they would be valid throughout all autoimmune indications for which the compound was being developed and warranting the discontinuation in all those indications.

BMS' BMS-986036, which prior to the merger was in Phase II clinical trials for the treatment of Non-alcoholic steatohepatitis (NASH), was discontinued for technical reasons, and in particular the fact that it did not meet primary endpoints in the relevant trial.

Celgene's CC-220, which was in a Phase II trial in SLE prior to the deal, was redirected to multiple myeloma and lymphoma. This redirection seems to have occurred due to technical inferiority of CC-220 when compared to the most recently marketed drug in SLE, coupled with the difficulty in entering that market.

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treatments and post-conventional treatments, the latter being a later line of treatment. Within post-conventional treatments (which would include BMS' BMS 986166 and Celgene's Ozanimod), the Commission in those precedents envisaged a segmentation based on the MoA. In Takeda/Shire, in addition to the MoA distinction, even a further segmentation was deemed appropriate, separating anti-integrin biologics from anti-TNFs and IL-12/23 inhibitors based on the safety profile. As described above, in the BMS/Celgene decision, the Commission considered potential segmentations of the IBD treatments market by line of treatment, MoA or MoD, but ultimately left the relevant product market definition open. Also in AbbVie/ Allergan (the fifth notified case we ex-post evaluated) the Commission left open the exact market delineations, considering both a narrow segmentation based on the MoA but also broader market delineations. These precedents show that the exact scope of the market is not obvious.

It appears that Celgene's CC-90001, which prior to the merger was in Phase II clinical trials for NASH, was redirected to advanced solid tumours for commercial reasons not related to the merger. In particular, the redirection appears to be due to the difficulty of pioneering in the NASH treatment market. In fact, no compound made it to the market yet, and the pipeline market is crowded with a number of compounds in more advanced stages of development. The pipeline was redirected to cancer treatment, a bigger and more cost-effective market than NASH, with higher expected value.

Celgene's bb21217, a CAR-T therapy which prior to the merger was in Phase I clinical trials as immunotherapy for multiple myeloma, appears to have been discontinued for commercial reasons unrelated to the merger. In particular, after the merger BMS marketed a very similar drug (also owned by Celgene prior to the merger) which had immense success, and it appears that it would not be commercially sensible to own multiple CAR-T therapies in the same portfolio.

Our evaluation confirmed the suitability of the Commission's assessment for those overlaps addressed in the decision. The assessment of the evolution of the markets post-merger endorses the reasoning that led to the Commission's unconditional clearance. The collected evidence substantiates the presence of a large number of existing and potential competitors, differentiated products with varying efficacy and safety profiles, and an early stage of development of the pipeline development at the time of the deal. While no counterfactual analysis was conducted, these conditions persist post-merger.

However, the large-scale analysis revealed a potential additional overlap not addressed in the Commission decision, between BMS' BMS 986166 and Celgene's Ozanimod in ulcerative colitis. Although publicly available information suggests that the molecule was still active at the time of the deal and discontinued afterward, the Team understands that the Commission had access to confidential evidence indicating that BMS 986166 was no longer under development at the time of the deal. This is an illustration of the limitation of this study relying exclusively on public sources, which are by nature fragmented.

Considering only the above publicly available information and, thus, assuming that BMS 986166 was still being developed for UC at the time of the deal (*quod non* – see above), the Team and its experts consider that this discontinuation does not seem to be justified on technical and clinical grounds, and occurred in a market where competition may potentially have been scarce depending on the exact scope of the relevant market (which is unclear). These factors collectively make this case one deserving further scrutiny, as the publicly available evidence potentially supports a killer acquisition narrative.

II.1.3.7 Conclusion

In summary, our ex-post assessment revealed three discontinuations and two redirections in treatments where the Parties' activities overlapped at the time of the deal (and which had been ex ante evaluated by the Commission). We concluded that these actions were unrelated to the merger and would likely have occurred independently of it. Specifically, all the discontinuations and redirections occurred were based on technical or commercial reasons unrelated to the deal. Our ex-post evaluation reaffirms the rationale leading the Commission's conclusion that the deal did not pose competition concerns and did not require any remedies. However, this assessment does not extend to evaluating a counterfactual scenario without the deal.

Furthermore, we addressed an additional potential overlap not included in the Commission's assessment, which resulted in a discontinuation found in our large-scale

analysis based on public sources. The Team understands that the Commission had access to confidential evidence indicating that the concerned pipeline was no longer in active development at the time of the deal.

Despite the above, considering only the above publicly available information and, thus, assuming that BMS 986166 was still being developed for UC at the time of the deal (*quod non*), the Team and its experts consider that the collected publicly available evidence suggests that this potential overlap would have warranted further scrutiny, as it led to a discontinuation seemingly unrelated to technical reasons in a market where competition may have been scarce depending on the exact scope of the relevant market (which is unclear).

II.1.4 Notified concentration #5: AbbVie/Allergan

II.1.4.1 Background

On 12 November 2019, the European Commission received notification of a proposed concentration by which AbbVie Inc. ("AbbVie") would acquire sole control of Allergan plc ("Allergan") through a cash and stock transaction ("The Transaction"). AbbVie and Allergan are jointly referred to as "the Parties".

The European Commission reviewed the acquisition and published its decision on 10 January 2020, announcing approval of the Transaction subject to remedies.

The Transaction gave rise to limited horizontal overlaps in marketed and/or pipeline treatments in the following indications:[428]

- Inflammatory Bowel Diseases (IBD), covering:
  - Ulcerative Colitis (UC)
  - Crohn's disease (CD)
- Uveitis[429]

This assessment will focus on the treatments of inflammatory bowel disease, as the overlap in uveitis contains only marketed products and it is out of the scope of this study.

II.1.4.2 The Commission's decision

The Commission found that the Transaction gave rise to overlaps between the marketed and pipeline products of the Parties in the market for post-conventional UC and CD treatments. The Commission's findings can be seen in Table II.28 below.

[428] The Transaction also gave rise to potential minor horizontal overlaps in relation to (i) Parkinson's disease, (ii) Alzheimer's disease, (iii) cystic fibrosis and (iv) oncology, where it was unlikely to raise serious doubts as to its compatibility with the internal market (see footnote 28 of the Decision for more details). Due to the lack of competitive concerns in these indications, they are not discussed in the EC Decision, implying that the overlapping products in these indications are not disclosed in the Decision.

[429] As the overlap in uveitis contains only marketed products, it is out of the scope of this study and won't be further researched.

Table II.28: Overlaps in IBD treatments identified by the EC

Product market	Geographic market	Owner (pre-merger)	Drug	Indication	Line of treatment[430]/MoA	Phase at time of Decision
Post-conventional[431] treatments for UC and CD (Possibility of further segmentation by MoA[432])	National for marketed, global or at least EEA for pipeline products	AbbVie	Humira (adalimumab)	UC/CD	post-conv./ anti-TNF	Marketed
			Skyrizi (risanikumab)	UC/CD	post-conv./ IL-23 inhibitor	Phase III
			Upadacitinib	UC/CD	post-conv./ JAK inhibitor	Phase III
			ABBV-323	UC	post-conv./ CD40 antagonist	Phase II
		Allergan	Brazikumab	UC/CD	post-conv./ IL-23 inhibitor	Phase II (UC) Phase II/III (CD)
			ABI-M201	UC	post-conv./ Microbiome biologic drug	Phase I

Source: Lear

In the potential (narrowest) market for IL-23 inhibitors for the treatment of UC and CD, the Transaction gave rise to a pipeline-to-pipeline overlap between two advanced-stage pipelines of the Parties: AbbVie's Skyrizi and Allergan's brazikumab. In the market investigation, concerns were raised regarding a possible discontinuation of one of the pipelines post-Transaction (most likely brazikumab), as the new entity was expected to have limited incentives to develop two drugs with the same MoA in parallel. Moreover, competition in the market was scarce, with only two other companies developing IL-23 inhibitors for UC and CD treatment:

- Eli Lilly at the time of the deal was developing mirikizumab (Phase III for UC and CD). Mirikizumab (Omvoh) was authorized[433] by the EMA for UC (26/5/2023) and is still in Phase III for CD.
- Johnson & Johnson was developing guselkumab (Phase II for UC and Phase II/III for CD). Guselkumab is now in Phase III for UC and CD.

[430] The treatment of IBD usually consists of two lines of treatment: first, the conventional treatment and in case of the failure/contraindication of this treatment, a post-conventional one is prescribed. These are considered to belong to two separate markets (as seen in M.7379 – AbbVie/Shire and M.8955 –Takeda/Shire).

[431] The EC found that Allergan had marketed a conventional drug, Asacol, which will not take part in the assessment as it does not belong to the same product market (i.e. market for post-conv. treatments for UC and CD), and thus is not relevant.

[432] i.e., a market excluding anti TNFs or a market for IL-23 inhibitors only.

[433] https://www.ema.europa.eu/en/medicines/human/EPAR/omvoh

As a result, the Transaction would lead to a reduction in the already limited number of competitors active on the market for IL-23 inhibitors from four to three, assuming that all IL-23 inhibitor pipelines were to reach the (EEA) market, which was highly uncertain at that stage. As a result of potential anti-competitive effects in the plausible market for IL-23 inhibitors, in particular the potential discontinuation of Allergan's brazikumab, the Transaction was seen to raise serious doubts as to its compatibility with the internal market and the functioning of the EEA Agreement.

In a potential (and broader) market for post-conventional treatments of UC and CD excluding anti-TNFs, the Transaction gave rise to several pipeline-to-pipeline overlaps, the main one being the overlap between the Parties' IL-23 inhibitors.[434] The risk of discontinuation of brazikumab would also have a detrimental impact on this potential market for several reasons: (i) the market investigation revealed the need for new alternative treatments, as most respondents confirmed the importance of having several MoA options in order to be able to cover all patients' needs, and there were at the time only three drugs in this potential market; (ii) IL-23 inhibitors were expected to have a better safety profile than existing post-conventional treatments; (iii) the discontinuation of brazikumab would remove a promising competitive constraint on the market, compared to the situation absent the Transaction.[435] Due to the above-mentioned concerns, the Transaction raised serious doubts as to its compatibility with the internal market and the functioning of the EEA Agreement.

Finally, the Commission also raised concerns related to the marketed-to-pipeline overlap between AbbVie's Humira (anti-TNF) and Allergan's brazikumab (IL-23 inhibitor). Several factors were considered by the Commission: (i) the market investigation revealed Humira's leadership on the market of post-conventional treatments; and (ii) the number of competitors active at national level was limited in several EEA countries (e.g., duopoly or quasi duopoly in Hungary, Ireland and Romania). As a result of potential competition-distorting effects (in particular the strengthening of AbbVie's dominant position, and the potential discontinuation of Allergan's brazikumab), the Transaction raised serious doubts as to its compatibility with the internal market and the functioning of the EEA Agreement.

The sole commitment proposed was a full divestiture of the development, manufacturing and marketing rights related to Allergan's brazikumab at worldwide level (the Divestment Business) to a suitable purchaser (the Purchaser). The compound was divested back to AstraZeneca, its originator, thereby terminating the license Allergan had over the compound.[436] Under the termination agreement, Allergan would fund up to an agreed amount, estimated to be the total costs expected to be incurred by

[434] The focus is on IL-23 inhibitors as the other overlapping pipelines have very different MoAs and there was no indication at the time of the Decision that the drugs would have similar safety and efficacy profiles.

[435] In fact, brazikumab had a potential competitive advantage due to the head-to-head trials comparing its efficacy and safety to the leading drug in the market (Takeda's Entyvio).

[436] In 2016, Allergan purchased a license from AstraZeneca, covering exclusive worldwide patent and know-how rights to develop, manufacture, commercialize and otherwise exploit brazikumab. Under the terms of the agreement, Allergan would make an upfront payment to AstraZeneca of $250 million for the exclusive, worldwide license to develop and commercialize brazikumab. In addition, Allergan would make potential additional payments to AstraZeneca of up to $1.27 billion, dependent on the achievement of agreed upon success-based development and sales-related milestones, and pay tiered royalties on potential sales of the medicine. See: https://www.astrazeneca.com/investor-relations/stock-exchange-announcements/2016/medimmune-out-licenses-potential-medicine-for-inflammatory-diseases-to-allergan-03102016.html#

AstraZeneca until completion of development for brazikumab in CD and UC, including the development of a companion diagnostic. When it comes to potential sales, AstraZeneca would own all rights and benefits arising from the product, apart from a high single-digit to low double-digit royalty on sales that it would have to pay out to Amgen due to their collaboration agreement.[437]

II.1.4.3 The evolution of the overlapping projects after the merger

The evolution of the Parties' projects after the merger is described in Table II.29. As can be seen, while the divested compound, brazikumab, has been discontinued, all other drugs are marketed or in development.

Table II.29: Evolution of the overlapping projects post-merger

Owner (pre-merger)	Drug	MoA	Phase (at time of the deal)	Evolution of the project
AbbVie	Humira (adalimumab)	anti-TNF	Marketed	Marketed[438]
	Skyrizi (risankizumab)	IL-23 inhibitor	Phase III	November 2022: Approved for CD in the EU[439] Phase III study in UC (est. completion September 2028)[440]
	Upadacitinib	JAK inhibitor	Phase III	Registered for UC Under regulatory review for CD[441]
	ABBV-323	CD40 antagonist	Phase II	January 2022: Phase II for UC completed[442]
Allergan	Asacol (mesalazine)	Lipoxygenase-cyclooxygenase inhibitor	Marketed	Marketed[443]

[437] https://www.astrazeneca.com/media-centre/press-releases/2020/astrazeneca-to-recover-the-global-rights-to-brazikumab-medi2070-from-allergan-27012020.html#

[438] https://adisinsight.springer.com/drugs/800008414

[439] https://adisinsight.springer.com/drugs/800035998

[440] https://classic.clinicaltrials.gov/ct2/show/NCT03398135?term=skyrizi&draw=2

[441] https://adisinsight.springer.com/drugs/800037410

[442] https://classic.clinicaltrials.gov/ct2/show/NCT03695185?term=abbv+323&draw=2&rank=1

[443] https://adisinsight.springer.com/drugs/800023243

	Brazikumab	IL-23 inhibitor	UC/CD	Discontinued[444]
	ABI-M201	Microbiome biologic drug	UC	Phase I for UC Terminated (Sponsor decision)[445] – completion date is Jan 2021). April 2022: acquired by Xbiome.[446] There are no new trials on CT, thus the large-scale analysis will conclude that this molecule was discont. However, qualitative analysis of the eval challenge found that the molecule was acquired in April 2022 by Xbiome (i.e., there have been developments < 24 months ago), thus we wouldn't characterize this as a discontinuation. The molecule was renamed to LBP02 and Xbiome is planning a phase Ib trial in UC in the US.[447]

Source: Lear

II.1.4.4 Reasons for discontinuation

In their press release, AstraZeneca claims to have discontinued the development following "a recent review of brazikumab's development timeline and the context of a competitive landscape that has continued to evolve", noting that "the timeline was impacted by delays that could not be mitigated following global events".[448] We note that as part of its investigation to decide whether to waive the commitments imposed in the Takeda/ Shire deal, the Commission found that multiple players developing IBD treatments were facing difficulties recruiting patients for clinical trials, due to the COVID-19 pandemic as well as an increasing number of pipeline drugs competing for the limited pool of patients eligible in clinical trials for IBD treatments. This is among the reasons why the Commission, in May 2020, accepted Takeda's request to waive the commitments.[449]

[444] https://www.astrazeneca.com/media-centre/press-releases/2023/update-on-brazikumab-development-programme.html

[445] https://classic.clinicaltrials.gov/ct2/show/NCT03923478?term=abi-m201&draw=2&rank=1

[446] Note that the link indicates that ABI-M201 was acquired from Assembly Biosciences rather than from Allergan. That is because the molecule was owned by Assembly Biosciences, with whom Allergan had entered an exclusive worldwide licensing agreement in 2017. In June 2020 Abbvie (formerly Allergan) terminated the agreement (not based on efficacy or safety data).

[447] https://www.xbiome.com/pipeline

[448] https://www.astrazeneca.com/media-centre/press-releases/2023/update-on-brazikumab-development-programme.html

[449] https://ec.europa.eu/competition/mergers/cases1/202037/m8955_1874_8.pdf

It is believed that when mentioning a changed development timeline for brazikumab, AstraZeneca might be referring to the difficulties in recruiting patients encountered by companies in that period. In fact, AstraZeneca reported high difficulty enrolling patients in three out of four Phase 2 and 3 trials of brazikumab that it took over from Allergan.[450] However, a comparison of AstraZeneca's efforts to develop brazikumab and its competitors' efforts to develop other IL-23 inhibitors suggests that, in the possibly challenging environment faced by all firms, AstraZeneca lagged behind its competitors. In fact, while AstraZeneca pursued the trials it took over from Allergan and initiated no new trials, the competitors, Eli Lilly and J&J, initiated 5 and 6 Phase 3 trials since 2020, respectively. Moreover, several developers of other IL-23 inhibitors did not have any apparent difficulty reaching, and often surpassed, the large enrolments envisaged when they launched their trials.

The Team also notes that AstraZeneca may have come to the conclusions that brazikumab was not as promising as its competing post-antiTNF rivals. The results of brazikumab in a Phase II double-blind placebo-controlled trial in CD[451] showed clinical remission rates not significantly larger than placebo in week 12, whereas the results of competing post-antiTNF rivals seem to be much more robust. While these results have become available only after AstraZeneca's decision to set back the development of brazikumab, they may signal that there were technical reasons deterring AstraZeneca to further invest into the compound.

Thus, while the Team cannot draw firm conclusions based on publicly available evidence on the reasons for the discontinuation of brazikumab, it is possible that the molecule was discontinued for technical reasons.

II.1.4.5 The evolution of the competitive landscape

The evolution of the competing IL-23 inhibitors for UC/CD in development at the time of the deal can be seen in Table II.30 below.

[450] For example, original anticipated enrolment for NCT03961815 was 1000 at the beginning of the trial. It dropped to 161 mid-2021, whereas the final (actual) enrolment ended up being only 18.

[451] https://pubmed.ncbi.nlm.nih.gov/28390867/

Table II.30: Evolution of competition

Company & Drug	MoA	Phase at deal time	Evolution of project
Eli Lilly's mirikizumab	IL-23 inhibitor	Phase III for UC and CD.	Authorized by the EMA for UC (26/5/2023).[452] Phase III for CD.[453]
J&J's guselkumab	IL-23 inhibitor	Phase II for UC and Phase II/III for CD	Phase III for UC and CD.[454]

Source: Lear

The only two marketed IL-23 inhibitors currently available are Eli Lilly's mirikizumab for UC and AbbVie's Skyrizi (risankizumab) for CD, with J&J's guselkumab in development for both indications. Thus, the potential IL-23 inhibitor markets are in a state of very scarce competition, with one marketed option in each.

II.1.4.6 Evaluation of the Commission's assesment

The investigation conducted by the Team confirmed the Commission's rationale leading it to conclude that the deal would pose competition concerns and warranted the introduction of remedies, mainly due to the state of competition at the time of the decision. This opinion is reinforced by the fact that, as can be seen in Section II.1.5.5, the potential market currently stands at three competitors with no new candidates emerging in the meanwhile. However, it should be noted that what would have happened in the counterfactual scenario in the absence of the deal is unknown.

When it comes to the design of the remedy, two main questions arose in the evaluation: i) whether the Purchasing party, i.e. AstraZeneca, was adequately chosen; and ii) whether the commitment posed on the Purchasing party to pursue the compound's development was stringent enough.

Publicly available information suggest there might have been multiple reasons informing the Commission's decision to approve AstraZeneca: i) it is likely that AstraZeneca could have prohibited the sale of Allergan's license on brazikumab under the clauses of the licensing agreement; ii) AstraZeneca's Research and Development programme and organisational structure expansion toward a Respiratory and Immunology group may have signalled AstraZeneca's commitment to develop brazikumab thereby reinsuring the Commission on AstraZeneca's incentives[455]; and iii) the terms of payments under

[452] https://www.ema.europa.eu/en/medicines/human/EPAR/omvoh#ema-inpage-item-authorisation-details

[453] https://clinicaltrials.gov/search?intr=mirikizumab&cond=ulcerative%20colitis

[454] For UC see: https://clinicaltrials.gov/search?intr=TREMFYA&cond=ulcerative%20colitis; for CD see: https://clinicaltrials.gov/search?intr=TREMFYA&cond=crohn%27s%20disease

[455] Indeed, the Commission noted in its Purchaser Approval that AZ's primary therapeutic areas included inflammation and autoimmunity, and that an acquisition of brazikumab was "in line with AstraZeneca's business strategy" . Some confirmation that the Commission correctly apprehended AstraZeneka's intentions

the 2016 license, which include large milestone payments, may have suggested the company would have incurred substantial opportunity costs if it delayed or discontinued work on the compound.[456]

Concerning the stringency of the commitment, the Team believes that it provided the right incentives to AstraZeneca to further develop the compound. In fact, under the commitment, AstraZeneca received a pipeline whose future development was fully funded by the seller (i.e. Allergan), and thus had strong incentives to continue the development of the molecule.

While the choice of the Purchasing party and the design of the remedy appear to be adequate, we nonetheless observed a discontinuation of brazikumab after the divestiture. The publicly available evidence suggests that it is possible that the discontinuation is grounded on technical reasons, and thus would have happened also in the absence of the deal, but this cannot be firmly concluded, as doubts concerning the reasons for such discontinuation remain.

II.1.4.7 Conclusion

The Transaction between AbbVie and Allergan gave rise to a significant overlap between the Parties' compounds in the market for IBD treatments, leading to the divestiture of one of Allergan's compounds, brazikumab, back to its original owner, AstraZeneca. This remedy was accepted by the Commission based on the scarce competitive constraints on the relevant market at the time of the decision. Although the counterfactual scenario in the absence of the deal is not observed, the Team's evaluation supported the rationale leading the Commission to require remedies and also concluded that the choice of purchaser and remedy design was adequate. The ex-post evaluation revealed that, nevertheless, brazikumab was discontinued by AstraZeneca post-divestiture. As for the reason for the discontinuation, although no firm conclusion can be drawn based on publicly available information, it is possible that it is a technical discontinuation, as : i) in its press release AstraZeneca appears to refer to a difficult environment for enrolling patients into clinical trials, and ii) clinical trial results showed that the compound was not as promising as certain rivals (although this is less likely as the relevant trial results became available after AstraZeneca had already announced the discontinuation).

II.2 EUMR: Jurisdictional thresholds for *ex ante* review

Concentrations that are large enough to trigger a filing obligation under the EUMR almost certainly have as their primary purpose continued utilisation of the acquired company's assets (with a possible reorganisation and on-sale of those that are outside the acquirer's fields of interest). While parties may not even have recognised the

may be found in later public statements of the company, including a statement in early 2023 that AZ's strategy in Immunology was to "establish a presence in gastroenterology . . . targeting diseases such as inflammatory bowel disease". See AstraZeneca Annual Report & Form 20-F Information 2022, page 26 https://www.astrazeneca.com/content/dam/az/Investor_Relations/annual-report-2022/pdf/AstraZeneca_AR_2022.pdf

[456] Some indication of this can be found in the 2016 license, under which AZ's potential revenues from Allergan's development of brazikumab included around $847 million in milestone payments and later sales-based royalties (https://www.astrazeneca.com/investor-relations/stock-exchange-announcements/2016/medimmune-out-licenses-potential-medicine-for-inflammatory-diseases-to-allergan-03102016.html#). While circumstances may have changed somewhat over four years, AZ assumedly had strong incentives to preserve such a potentially significant income stream, either by licensing another developer or by developing brazikumab itself.

potential "killer" aspects of their deal when it was being negotiated, review under the EUMR gives the Commission a meaningful opportunity to detect and address them. For example, in *J&J/Actelion* (2017), statements by the parties and industry analysts make clear that the deal was undertaken primarily because Actelion's drugs for pulmonary arterial hypertension fit well with J&J's focus on cardiovascular and metabolic diseases; therapies for insomnia do not appear to have figured in the parties' transaction planning at all. Nonetheless, upon notification and review, the Commission identified an overlap between drugs that each of the parties had in Phase II development for insomnia, and concerns about that overlap were ultimately resolved with remedies.[457]

More problematic transactions are those in which the acquisition targets are small firms that are engaged in early-stage discovery and development of novel compounds. Such firms are of particular concern because they play a vital role in the pharmaceutical sector. Analysts report that emerging biotechs now account for the discovery of more than two-thirds of the innovative new drugs that make it to market,[458] and some of these firms are beginning to take their discoveries through more advanced stages of development.[459] Such firms may launch (or license out) innovative therapies that significantly increase competition, drive down prices, and enhance therapeutic choices. However, these benefits of innovation may be lost if such firms are absorbed through mergers and acquisitions before they have begun to generate sufficient turnover to trigger *ex ante* review.[460]

II.2.1 Current rules

There are two basic prerequisites to review under the EUMR, and issues with respect to each of them may arise in addressing potential killer acquisitions. First, the relevant transaction must be a concentration (i.e. a transaction that results in a lasting change

[457] Case M.8401 - J&J/Actelion (2017) (discussed further in section II.1.2 of this Report).

[458] See, e.g. A. Schuhmacher et al., Investigating the origins of recent pharmaceutical innovation (2023) (https://www.alexandria.unisg.ch/server/api/core/bitstreams/1e9878d0-3c52-4dc4-813b-af22b7966a92/content); R. Robinson, Small Pharma Driving Big Pharma Innovation (1 January 2020) (https://www.pharmavoice.com/news/2020-01-pharma-innovation/612330/); NDA, New drug product approvals in Europe & US during 2020 (2021) (https://ndareg.com/news/new-drug-approvals-in-europe-us-during-2020/).

[459] See, e.g. E. Harputlugil et al., First-time launchers in the pharmaceutical industry (2021) (https://www.mckinsey.com/industries/life-sciences/our-insights/first-time-launchers-in-the-pharmaceutical-industry). Small biotech firms can undertake such downstream activities because there are growing numbers of independent contract providers of clinical, regulatory and commercial support. While such outsourcing was not a subject of this study, we have observed small companies using a range of these services, from a start-up's early-stage work with contract research and manufacturing organisations (see the case study discussed in section II.3.1 of this Report) to a developer's product launch in partnership with a pharmaceuticals marketing services organisation (see J&J/Actelion (2017), discussed in section II.1.3 of this Report).

[460] It should be noted that the preponderance of transactions that are followed by the discontinuation of a pipeline must be negotiated. It seems likely that larger firms have more resources available to "invest" in non-productive (i.e. killer) acquisitions than their smaller rivals, but such an expectation may be too facile. In any event, it has been reported that in the period 2021-3Q22, small-cap biotech companiess accounted for the largest share (35%) of 145 biotech-to-biotech M&A transactions. "Big Pharma" firms (i.e. firms with a market capitalisation over $50 billion) reportedly accounted for the second-largest share (26%), followed by privately owned biotech companies (21%) and mid-cap biotech companies (18%). J.P. Morgan, Biopharma Therapeutics Licensing and Venture Deals (Oct 2022) (https://www.jpmorgan.com/content/dam/jpm/commercial-banking/insights/startups-innovation-economy/jpmorgan-chase-q3-2022-biopharma-report.pdf). While these data are limited to transactions in which both the acquirer and acquired firm are active in the pharmaceuticals industry, they do not identify how many of those transactions involved actual or potential competitive overlaps.

of control of an undertaking). Second, the magnitude and geographic distribution of the parties' turnovers must meet one of several tests of a Union dimension or, failing that, the transaction must satisfy the prerequisites for application of a corrective mechanism established in the EUMR. We address the first two issues below, and the third in section II.2.3.

II.2.1.1 Acquisition of a business

Issues regarding the existence of a concentration are most likely to arise when an acquirer is purchasing less than all of a seller's assets, because these may not be sufficiently comprehensive to constitute an undertaking.[461] In this regard, the Consolidated Jurisdictional Notice establishes that an undertaking is "a business with a market presence, to which a market turnover can be clearly attributed."[462] Two cases, summarised in Box 14 below, illustrate how the rule has been applied in the pharmaceutical sector.

[461] Article 3(1) EUMR. It might be noted that a variety of arrangements that are relatively common in the pharmaceutical sector (e.g. forms of collaboration that entail minority investments and sometimes board representation, some technology licenses, and the like) may create the kind of rights or dependencies that amount to de facto control (and the acquirer's ability to kill a pipeline). However, current rules and practice provide for realistic, fact-based assessment whether a transaction confers de facto control (either by itself or in combination with other aspects of the parties' dealings), and potential killer acquisitions do not appear to raise particular issues in that regard. Accordingly, the following discussion relates to the object (rather than the existence) of control.

[462] Commission Consolidated Jurisdictional Notice under Council Regulation (EC) No 139/2004 on the control of concentrations between undertakings (2008/C 95/01) ("CJN"), paragraph 24. Similarly, the Court of Justice (CJEU) has made clear that, for purposes of Articles 101 and 102 TFEU, "any entity engaged in an economic activity . . . must, as such, be categorised as an undertaking, irrespective of its legal form." Judgment of 21 December 2023, European Superleague Co v Fédération internationale de football association (FIFA), C-333/21, EU:C:2023:1011, sections V.A.2 and 3.

Box 14: Acquisitions of several businesses in Novartis/GlaxoSmithKline (2015)[463]

In 2014, Novartis contracted with GSK to acquire the rights, licenses, marketing authorisations and employee contracts relating to its ten marketed and two pipeline drugs for treatment of cancer. Novartis did not acquire any manufacturing assets or R&D operations, but had agreements under which GSK would supply it with the relevant drugs and opt-in rights relating to GSK's current and future oncology pipelines. The Commission concluded that the acquisition was a concentration because the assets comprised what was necessary for commercialisation and R&D relating to GSK's portfolio. Because GSK's prior-year sales from that portfolio (together with Novartis' turnover) triggered notification under the EUMR, the Commission conducted a review, and identified several market-to-pipeline and pipeline-to-pipeline overlaps that might have made this a killer acquisition had remedies not been adopted.

In 2015, shortly after Novartis completed its acquisition of GSK's oncology assets, the parties agreed to Novartis' acquisition of exclusive rights to develop, manufacture, promote and market ofatumumab, which GSK was developing for treatment of autoimmune (AI) diseases. Under the parties' agreements, Novartis also would acquire "core" tangible assets (apparently those that related specifically to ofatumumab, but not more general R&D assets), including biological materials and cells, product inventory, supply contracts, approved Investigational New Drug Applications, and clinical trial data. The Commission found that this acquisition constituted a concentration because the acquired assets provided means to enter the market and the parties expected Novartis to complete a timely and profitable launch.[464] Finding a Union dimension pursuant to Article 5(2) EUMR (discussed in section II.2.2 below), the Commission reviewed the transaction and cleared it unconditionally.

These decisions contribute to a growing body of precedent that may support future assertions of competence to regulate potential killer acquisitions under the EUMR. Moreover, it might be noted that the Commission presented its assessment in *Novartis/Ofatumumab* as findings relating to the particular facts in that case. This appears to be in accord with the Commission's obligation to make a careful and

[463] Case COMP/M.7275 - Novartis/GlaxoSmithKline Oncology Business (2015) (discussed further in section II.1.1 of this Report) and Case M.7872 - Novartis/GSK (Ofatumumab Outoimmune Indications) (2015) (discussed further in section II.1.2 of this Report).

[464] The Commission cited, as proof of the parties' expectations, the contingent developments upon which GSK would receive sizeable payments for the assets, and an internal Novartis document assessing the probabilities of a successful launch. It also suggested another line of analysis, in stating that "assets that are already in phase III clinical trials can be reasonably assumed to be capable of generating a turnover in the foreseeable future." Id. paragraph 11. However, such a "bright line" test could be either overbroad (as approximately 50% of Phase III trials are unsuccessful) or too narrow (as the Commission in some cases has found that overlaps in earlier stages of development may require a remedy). Moreover, it appears that the probabilities that a drug will progress from Phase III trials to marketing authorisation may vary significantly for different types of disease (with estimates of, e.g. 36% in oncology and 64% in autoimmune/inflammatory disorders). CH Wong and KW Siah, Estimation of clinical trial success rates and related parameters (2019) (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6409418/). Accordingly, while the performance or completion of Phase III trials might be used as a guideline, it is questionable whether it should be treated as a conclusive test.

unfettered analysis of all of the available evidence, including economic and commercial realities specific to the case at hand.[465]

These decisions also may be helpful in preserving the competitive potential of firms that face somewhat uncertain prospects. For example, they make clear that an undertaking (and, therefore, a concentration) can be found to exist even where an acquirer is purchasing less than all of the assets that the seller has used in conducting the acquired business, if they provide the acquirer with the necessary means to enter (or remain in) the market. In addition, while the decision in *Novartis/Ofatumumab* is based on a set of facts that is unlikely to arise often (as discussed in section II.2.1.3 below), the decision may prove to be valuable in highlighting the possibility of future reviews under Article 22 EUMR.

Two points might be noted with respect to potential killer acquisitions in particular. First, as a practical matter, the decisions discussed here support assertions of competence to review potential killer acquisitions in which the acquirer purchases most or all of a rival's pipeline, with the intention to further develop that pipeline while discontinuing its own. However, they provide little support for intervention when an acquirer intends to discontinue a target pipeline (while continuing to develop its own). Such an acquiror need not purchase all (or even most) of the pipeline assets; it is enough to acquire assets that the seller needs in order to continue development. In fact, a "buy and delay" strategy might be as effective as a "buy and bury" one, if work on a target pipeline is set back far enough that the seller has little motivation to continue (e.g. in light of the possibility that rivals may capture durable commercial advantages by launching similar drugs more quickly). While such an acquirer doubtless would have to pay significantly more than the value of the assets being acquired, it might be willing to do so if it anticipated sufficiently large returns from a reduction of competition. Given the fundamental importance of the concept of a concentration in delineating the separate (albeit complementary) fields of merger control and antitrust law, it appears likely that antitrust rules provide the best (and perhaps only) means of addressing such acquisitions.

II.2.1.2 Union dimension

As a rule, a concentration may be reviewed under the EUMR only if the parties' annual turnovers (worldwide and within the EEA) satisfy a set of thresholds showing that their transaction has a Union dimension.[466] Relevant turnovers are the "amounts derived by the undertakings concerned in the preceding financial year from the sale of products

[465] See Judgment of 22 June 2022, ThyssenKrupp v Commission, T-584/19, EU:T:2022:386 (affirming the Commission's obligation to consider the best available evidence in assessing individual firms' business plans and capabilities). For example, the decision does not elaborate on what the Commission regarded as a "reasonable period of time" for market entry, or whether its assessment was made with reference to competitive effects (e.g. the two years that is typically regarded as timely in merger reviews), commercial incentives (e.g. a prospect of returns sufficiently imminent to ensure assiduous pipeline development), the credibility that might be accorded the parties' expectations (e.g. as sufficiently near-term to be reliable), or something else. That the Commission was not more prescriptive may provide valuable latitude in addressing other, potentially problematic transactions.

[466] Two general sets of thresholds defining a Union dimension are established in Article 1 EUMR, without prejudice to Article 22(1) EUMR, which provides for Commission review at the request of a Member State when a concentration affects trade between Member States and threatens to significantly affect competition in the Member State making the request. Three other corrective mechanisms (Articles 4(4), 4(5) and 9 EUMR) provide that the Commission and Member States may reallocate between themselves concentrations that have (or are deemed to have) a Community dimension.

and the provision of services falling within the undertakings' ordinary activities," and very few adjustments to audited financial statements are permitted.[467]

These rules lie at the heart of concerns that there may be a "gap" in merger control as regards particular sectors (pharmaceutical and digital) where competition is driven to a significant extent by the innovations of relatively small firms.[468] While annual turnovers provide an initial measure of the economic resources that are being brought under common control and therefore operate as a simple and objective test of jurisdiction, they also are founded on an implicit premise – that a company's turnover is a useful, *prima facie* signifier of its likely competitive significance – that may not be true where the acquisition target is an emerging biotech company whose competitive significance lies in its innovations and innovative potential.

Recent transactions show that such concerns may be valid. For example, Illumina's $7.1 billion acquisition of GRAIL, a company that had not yet begun to generate turnover, was found to raise serious competition issues requiring its divestment.[469] Similarly, regulators required that Meta (formerly Facebook) unwind its $315 million acquisition of Giphy, which generated only about $27 million in annual turnover around the time it was acquired. The fact that Meta divested Giphy for only $53 million – less than 20% of what it paid for the company three years earlier – suggests that the original purchase price may have included a premium for anticipated returns in the elimination of a competitor.[470]

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[467] Article 5(1) EUMR; CJN paragraph (169). As a rule, figures taken from an undertaking's most recent audited accounts may be adjusted only to reflect permanent changes in the structure of the undertaking (i.e. completed acquisitions, divestitures, or closures of parts of its business). CJN paragraphs (170)-(174). The only instance where current Commission practice permits the use of revenue forecasts appears to be where a business that is being spun off previously recorded only intra-group sales at values that do not correspond to a market valuation of its activities, in which case the CJN suggests that publicly quoted prices or an extant agreement with the divesting parent may be used as an objective and readily determinable proxy for actual turnover. Id. paragraph (163).

[468] See generally OECD Roundtable, Start-ups, killer acquisitions and merger control (June 2020) (collected materials available online at https://www.oecd.org/competition/start-ups-killer-acquisitions-and-merger-control.htm). A number of studies indicate that, in the digital sector, leading companies have made hundreds of acquisitions in recent years, most of which were not subject to ex ante review (see, e.g. European Commission, 2021; US Federal Trade Comm'n, Non-HSR Reported Acquisitions by Select Technology Platforms, 2010-2019 (2021) (https://www.ftc.gov/reports/non-hsr-reported-acquisitions-select-technology-platforms-2010-2019-ftc-study); Digital Competition Expert Panel, 2019; and Argentesi et al., 2019). Gautier & Lamesch (2021) examined 175 acquisitions by Amazon, Facebook, Google and Microsoft over a three-year period and found that in 105 cases the brands of the target firms were discontinued within a year after their acquisition. Care obviously must be taken in interpreting the results of such studies, which might easily overstate the problem (for example, discontinuation of a brand need not mean that formerly branded products were discontinued, as they might simply have been rebranded) or understate it (for example, a focus on what happened to the target's products will miss potential killer acquisitions that were executed through a post-merger discontinuation of the acquirer's overlap products). However, the magnitude of findings like this provides strong indications that a number of these transactions are likely to have reduced direct competition, entrenched the acquirers, and dampened innovation (with a consequent reduction in product variety and quality).

[469] See Section II.2.3.1 of this Report.

[470] See S. McCallum, Meta loses millions as made to sell Giphy to Shutterstock (23 May 2023) (https://www.bbc.co.uk/news/technology-65684986). Alternatively, Meta may have been unable to recover much of the value of its purchase because the supply of GIFs was a declining business (see A. Hern, 'Gifs are cringe' (16 September 2022) (https://www.theguardian.com/technology/2022/sep/16/gifs-are-cringe-and-for-boomers-giphy-claims-in-meta-takeover-filing)), or because Meta was unable to get more than a "fire sale" price under a divestiture order.

The EUMR and current practice make no provision for the use of turnover forecasts or other measures that might reflect the future competitive significance of a nascent business. That has led to various proposals for reform which, in turn, have attracted strong critiques. These are briefly summarised in section II.2.2 of this Report.

II.2.1.3 Interrelated transactions

II.2.1.3.1 Multi-stage acquisitions of a single business

The rules described above might give rise to the possibility that acquirers try to evade review by dividing a single acquisition into several transactions, none of which can be regarded as the purchase of a business on its own. However, such stratagems are clearly addressed in the EUMR and existing Commission practice, and we see little empirical reason to question their effectiveness.

Article 3 EUMR, as interpreted by the Commission and the courts, requires that multiple acquisitions be treated as a single concentration when they result in a change in control of a business and are either linked by mutual condition or otherwise shown to be interdependent.[471]

We were advised by industry experts on the Team that parties who contemplate the purchase and sale of a business require legal certainty that they will be able to complete the entire transaction before investing in parts of it. An acquirer is unlikely to take the risk of buying some assets and being unable to use them as intended if its counterparty then refuses to sell others, and a seller is unlikely to accept the risk that it may wind up with "stranded" assets (which it can neither use nor sell elsewhere) if the purchaser of some of its assets refuses to buy the rest. Accordingly, while various assets of a business might be (and often are) conveyed under separate agreements,[472] the parties normally execute a contemporaneous master agreement specifying how all of the subsidiary agreements are to be performed, and a material failure to follow through on one or more of the subsidiary agreements constitutes a breach of the overall contract.

We also were advised that transaction parties normally want to complete an acquisition quickly, while their findings from due diligence, deal valuations, financing arrangements and the like are current, and in order to minimise the risks that a drawn-out process might compromise relationships with their employees and customers.[473]

Insofar as pharmaceutical killer acquisitions are concerned, further incentives to move quickly are likely to arise from the fact that many drug development efforts are very time-sensitive given, e.g. the substantial commercial value of being the first or second to market with a new drug, and possibilities that the technical/commercial landscape may change as new data emerge from the parties' and others' trials of various

[471] See generally CJN paragraphs (36)-(40) and (43)-(45); Judgment of 23 February 2006, Cementbouw Handel & Industrie v Commission, EU:T:2006:64, appeal on other grounds dismissed, Judgment of 18 December 2007, Cementbouw Handel & Industrie v Commission, C-202/06 P, EU:C:2007:814.

[472] For example, separate agreements are often used to itemize and convey intangible assets, and a number of agreements may be used where the acquired enterprise is present in countries that have different corporation, tax, or other legal requirements.

[473] In this regard, the US antitrust agencies appear to have concluded that multi-step acquisitions are likely to be done with sufficient dispatch that acquirers are required to aggregate only those assets that they have acquired (or agreed to acquire) from the same seller within 180 days of their latest acquisition. 16 C.F.R § 801.13(b).

compounds. A desire to avoid duplicative development or marketing costs also may make delays unacceptable to an acquirer who intends to discontinue an overlap drug.

Given the foregoing, substantial delay in completion of a deal appears likely to hold little appeal for an acquirer. Moreover, our industry experts were confident that although the buyer and seller of a business might execute a single deal through multiple contracts and acquisitions, the interdependence of those acquisitions can almost certainly be established both *de jure* and *de facto*.

This view has not been tested with respect to the deals that were analyzed as part of the fact-finding challenge, which was based on public information that, in many cases, was not sufficiently detailed to permit such an assessment. However, we did not observe instances in which it was obvious that the same parties transferred assets relating to overlapping pipelines in more than one transaction before one of the pipelines was discontinued. Accordingly, the results of the fact-finding challenge were consistent with, but did not independently corroborate, what our industry experts anticipated.

II.2.1.3.2 "Step" transactions constituting implementation of a concentration

Aside from the foregoing business considerations, it might be noted that step transactions, like those addressed above, may expose parties to the risk of significant fines under recent Court rulings that parties may be deemed to have implemented a concentration under Article 7 EUMR as soon as they take one or more steps that contribute to a lasting change in control of the target, even if those steps alone do not make the intended change.[474] However, such risks arise only when a step transaction is necessary to (i.e. has a "direct functional link" to) the envisaged change of control, and not merely because the transaction has some factual, but non-essential, relationship to it.

It might be noted that this rule clarifies what constitutes the implementation of a concentration and the consequences under Article 7 EUMR for an acquirer's infringement of the standstill obligation pending completion of a review (rather than defining what might constitute a concentration under Article 3, as discussed above, or providing for the aggregation of turnover where parties have undertaken two concentrations, as discussed below with respect to Article 5(2) EUMR). Insofar as it might deter parties' intentional efforts to evade review, it has largely the same practical effect. However, it has different practice effects from the regulatory point of view, for at least two reasons. First, it provides grounds for intervention as soon as the first step transaction is completed, so that the harmful effects of such a strategy can be prevented before further steps have been taken and a concentration (i.e. a change of control) has actually taken place. However, the rule can be applied (at least as a technical matter) only through an enforcement action, and therefore may require time and resources where a recalcitrant acquirer refuses to acknowledge the nature of the transactions at issue.

II.2.1.3.3 Acquisitions of more than one business from the same seller

Finally, Article 5(2) EUMR provides that two or more concentrations occurring in a two-year period between the same buyer and seller also are to be treated as a single concentration for purposes of calculating turnover. An example of how this rule applies in practice is provided in Box 15 below.

[474]Judgment of 31 May 2018, Ernst & Young v Konkurrencerådet, C-633/16, EU:C:2018:371; Judgment of 18 May 2022, Canon v Commission, T-609/19, EU:T:2022:299.

Box 15: Turnover assessment in Novartis/GlaxoSmithKline[475]

In 2014, Novartis agreed to acquire key assets in GSK's portfolio of drugs (including ofatumumab) that were approved or in development for treatment of cancer. The acquisition was recognised as a concentration and GSK's annual sales of the acquired drugs (together with Novartis' annual turnovers) triggered a review under the EUMR before the deal closed in 2015.

Later that year, Novartis agreed to acquire from GSK assets that would enable it to develop and commercialize ofatumumab for treatment of autoimmune (AI) disorders. The Commission found that although ofatumumab was still in clinical trials for AI indications, the parties expected Novartis to use the assets to obtain marketing approval and launch ofatumumab as an AI treatment that produced a market turnover within a reasonable timeframe. The Commission concluded that Novartis was acquiring a business to which a market turnover could be clearly attributed, and therefore was a concentration. Because the transaction took place within two years of Novartis' acquisition of GSK's oncology business, the turnover attributed to the oncology business was taken into account under Article 5(2) EUMR and this second acquisition triggered a new obligation to file for review under the EUMR.

Article 5(2) EUMR appears unlikely to contribute appreciably to the Commission's ability to address potential killer acquisitions, for several reasons.

First, such sequential transactions are infrequent, and the chance that one of them is a killer acquisition is rather remote. Because Article 5(2) relates only to transactions that are sufficiently comprehensive to constitute a concentration, an acquirer might take this rule into account in avoiding the two-year window if it was concerned about the competitive implications of a deal.

Second, the first acquisition might well be completed and a competitive overlap eliminated (with little prospect that the discontinued product can be effectively resuscitated) before a subsequent acquisition brings the transactions within the scope of review. In such cases, although the Commission may order interim measures, divestiture of the first-acquired business, and other measures to restore competition,[476] these may be too late to restore competition fully.

Despite the foregoing, there might be cases where Article 5(2) contributes to the regulation of killer acquisitions because it operates as a deterrent. If an acquirer identified the opportunity to make a killer acquisition soon after acquiring another business from the same seller, it might be put off by the prospect of either a difficult review or a lengthy wait while continued investments were being made in both of the overlap drugs. That said, the existence of any such deterrent effect is obviously rather speculative.

II.2.2 Alternative tests of regulatory competence

The development of sectors in which competition is driven to a significant extent by the innovations of relatively small firms has given rise to questions whether turnover-based

[475] See Novartis/Oncology (2015) and Novartis/Ofatumumab (2015), discussed in section II.2.1 above.

[476] See Articles 8(4) and 8(5)(c) EUMR.

tests always provide an appropriate foundation for merger control, given the possibility that nascent competitors may be acquired by more sizeable competitors (or may decide to merge themselves) before they begin to generate sufficient turnover to trigger review.[477] Below is a brief summary and assessment of various changes and proposals for change that have been considered in this regard.

II.2.2.1 Turnover forecasts

Some have suggested that the current thresholds might be adjusted to take into account the turnovers that a nascent competitor is expected to achieve within 1-2 years after its innovation is launched commercially.[478]

While the idea might have some immediate appeal as a direct response to current concerns, its development into a workable rule would raise numerous difficulties. For example, such a rule would have to establish when a firm is a "nascent" competitor – whether that is based, e.g. on its years in existence, years to (or since) a product launch, business plan, number/quality of employees or assets, capital structure, financial performance, or some other criteria, singly or in combination. Such a test would risk being either discretionary or arbitrary and might readily be evaded (e.g. if shareholders of a start-up wanted to cash out with a competitively problematic sale). Further, a start-up's successful development of a new drug typically requires a lengthy amount of time before the period for which turnovers might reasonably be forecast.

Such a rule might be easier to craft if it were applicable to pipeline products, rather than to firms. Again, however, it is unclear how such a rule might work as a practical matter: forecasts are inherently uncertain and susceptible to manipulation; any such rule would require a relatively detailed set of turnover forecasts (for individual Member States) in order to permit application of Article 1(3) EUMR; and the current thresholds in the EUMR might capture the acquisition of "blockbusters" but provide little opportunity to detect competitors' elimination of smaller drugs (including orphan drugs, which small innovators are particularly well positioned to develop, account for an increasing share

[477] See generally OECD Roundtable, Start-ups, killer acquisitions and merger control (June 2020) (collected materials available online at https://www.oecd.org/competition/start-ups-killer-acquisitions-and-merger-control.htm). This has been a particular focus of discussion with respect to the digital sector. A number of studies indicate that leading companies in that sector have made hundreds of acquisitions in recent years and that most of those were not subject to ex ante merger control (see, e.g. European Commission, 2021; US Federal Trade Comm'n, Non-HSR Reported Acquisitions by Select Technology Platforms, 2010-2019 (2021) (https://www.ftc.gov/reports/non-hsr-reported-acquisitions-select-technology-platforms-2010-2019-ftc-study); Digital Competition Expert Panel, 2019; and Argentesi et al., 2019). Aside from their potential elimination of competition in the supply of goods and services and entrenchment of the acquiring companies, it appears likely that many of these acquisitions reduced competition in innovation. For example, Gautier & Lamesch (2021) examined 175 acquisitions by Amazon, Facebook, Google and Microsoft over a three-year period and found that in 105 cases the brands of the target firms were discontinued within a year after their acquisition. Care must be taken in assessing such studies, to ensure that the problem is not either overstated (e.g. discontinuation of a brand might simply mean that a product was rebranded, rather than discontinued) or understated (e.g. studies that focus on what happened to the targets' products do not capture killer acquisitions that might have occurred when an acquirer discontinued one or more of its own projects in order to pursue those of the target). In any event, however, the magnitude of findings like this provides strong indications that a number of these transactions are likely to have dampened innovation rivalry, with a consequent reduction in product variety and quality.

[478] Current rules and practice provide, with limited exceptions, that competence under the EUMR is to be established with reference to the amounts that an undertaking derived from the sale of products and services in the ordinary course of business in its most recent fiscal year, as reported in its audited accounts for that year (see section II.2.1.2 of this Report).

of new product launches, and often appear to be highly profitable if competition is limited).

Apart from their practical difficulties, proposals like this would expose assessments of regulatory competence to potential disagreement or manipulation, undermine parties' ability to determine their filing obligations, and compromise the legal certainty that companies and investors need to have in knowing that their transactions will not be challenged after completion.[479]

The Commission long has recognized "the need for precision and certainty in the criteria used for calculating turnover so that jurisdiction can be readily verified."[480] This is in line with court judgments. The CJEU has recognized that given the need for legal certainty, Articles 1 and 5 EUMR establish "precise and objective criteria" for jurisdiction.[481] The General Court[482] likewise has held that "the very foundation of the system of thresholds established by Article 1 [EUMR] is to provide a simple and effective method" for determining jurisdiction, and that it would be "neither reasonable nor prudent" to rely on unaudited numbers.[483] It therefore is not clear whether a jurisdictional test based on sales forecasts would survive judicial review.[484]

That said, because parties that are engaged in R&D projects normally have developed a business case for them, the Commission might base its jurisdictional assessments on internal sales projections prepared by the parties in the ordinary course of business. Parties assumedly have ready recourse to their own projections, and the fact that those projections were made (and relied upon) in the ordinary course of business should provide some of the guarantee of reliability that the Commission traditionally has attributed to audited accounts. However, regulatory reliance on such projections may enable parties to hedge against the likelihood of review through careful drafting of their internal documents. Moreover, this approach might be difficult to implement in practice if parties have conflicting projections (as might exist, e.g. in "best case/worst case" assessments), assessments that vary significantly over a short period of time, internal assessments that vary significantly from external analysts' predictions, and the like. Further complicating the use of such assessments is the fact that they might well reflect not only a party's expectations for its own drug but also predictions about the likely

[479] The application of such a rule also might be challenged as a denial of equal treatment, unless the Commission were prepared to accept parties' claims that forecasts of declining sales should be deducted from their turnovers.

[480] CJN paragraph (184). See also id. paragraph (127) (the turnover thresholds are intended to provide "a simple and objective mechanism that can be easily handled"); Commission Notice on Case Referral in respect of concentrations (2005/C 56/02) ("Referral Notice"), paragraph 3 (determining jurisdiction exclusively by reference to fixed turnover-related criteria is a "bright line" scheme that is meant to provide legal certainty).

[481] Cementbouw (2007), paragraph 38.

[482] Consistent with our use of the current numbering of relevant Treaty provisions, and for purposes of clarity, we refer to the Court of First Instance as the General Court throughout this Report.

[483] Judgment of 14 July 2006, Endesa v Commission, T-417/05, EU:T:2006:219, paragraphs 130, 146, 170, 180 and 209.

[484] The high hurdle that such a test would have to overcome is evident in the CJEU's judgment that "the principle of legal certainty requires that Community rules enable those concerned to know precisely the extent of the obligations which are imposed on them. Individuals must be able to ascertain unequivocally what their rights and obligations are and take steps accordingly." Judgment of 10 March 2009, Gottfried Heinrich, C-345/06, EU:C:2009:140, paragraph 44.

pace and technical merit of rivals' pipeline projects and the commercial prospects of drugs that are already on the market.

More importantly, perhaps, this approach appears unlikely to capture many killer acquisitions, for several reasons. First, as noted above, many new drugs may be competitively important but not the kind of "blockbuster" innovations that would trigger one of the EUMR turnover tests within a year or two of launch. Second, if many killer acquisitions occur when a target's product is at a relatively early stage of development (as is suggested in some of the literature[485]), detailed sales forecasts are likely to be non-existent or highly speculative. This approach therefore does not appear to be particularly promising.

II.2.2.2 Transaction value

Some have suggested that the current turnover-based tests might be supplemented with an alternative test based on the value of potentially reportable transactions.

Recent regulatory initiatives and studies suggest a growing appreciation that this type of test may capture some acquisitions of competitively important innovators that have not yet established a market presence. Such a test assumedly would reflect the best available estimate of the future commercial and competitive importance of the target, made by the parties themselves (who, being directly involved in the business and having strong incentives to negotiate the best possible deal, are likely to be the most knowledgeable and diligent assessors). It must be borne in mind, however, that deal valuations also may reflect some considerations that are unique to the acquirer, with varying implications from a regulatory perspective. For example, the parties' valuation may reflect synergies from a combination of complementary assets or operations (so that it overstates the target's general commercial/competitive importance, giving rise to unwarranted reviews and transaction costs). However, an acquirer's willingness to pay a relatively high price also may reflect unique benefits that the acquirer expects to achieve through the elimination of a rival (in which case an inflated transaction value should be of little concern because it may promote effective regulation).

Some Member States (e.g. France) have considered the adoption of a value-of-transaction test but ultimately rejected the idea because such a threshold would not be sufficiently precise and would be both under- and over-inclusive.[486] However, both Austria and Germany supplemented their turnover-based tests with value-of-transaction tests in 2017.[487]

Initial experience suggests that these new tests have generated few filings where regulatory intervention was required.[488] However, Facebook recently was required, under Austria's € 200 million value-of-transaction test, to notify its $315 million acquisition of Giphy, an innovator in social media services and online advertising that was founded in 2013. In their review, the regulators determined that the acquisition

[485] E.g. Cunningham et al. (2021).

[486] OECD Roundtable, DAF/COMP/WD(2020)16, Note by France (9 June 2020) (https://one.oecd.org/document/DAF/COMP/WD(2020)16/en/pdf).

[487] Section 35(1a) GWB; Section 9(4) KartG.

[488] European Commission, 2021.

would strengthen Facebook's dominant position in social media and online advertising, and approved the transaction only subject to conditions.[489]

A critical issue, if a value-of-transaction test were adopted, would be how to ensure that it does not capture numerous, otherwise non-reportable transactions where sole application of the current turnover-based thresholds appears to work well. While an unduly low threshold could impose unnecessary burdens on transaction parties and the Commission, a threshold that is too high may not capture significant acquisitions of nascent competitors. In this regard, the Commission services recently estimated that the use of a € 1 billion value-of-transaction test over the 2015-2019 period would have brought in around 300 additional filings per year – a roughly 75% increase in the Commission's merger control caseload. However, this threshold still would not have required notification of various transactions that the Commission found to be of serious concern or that seem likely to have elicited serious concern had they been notified.

The imposition of unjustified costs of notification where current turnover-based thresholds work well might be mitigated to some extent if a value-of-transaction test were made applicable only to transactions in specified industries with high rates of innovation by small and medium-size enterprises (e.g. the pharmaceuticals and digital sectors).[490] Difficulty drawing sufficiently precise boundaries around discrete sectors/industries where the test is meant to apply might be mitigated to some extent through the use of CPA (Classification of Products by Activity) codes or NACE (*Nomenclature statistique des activités économiques dans la Communauté européenne*) codes in establishing the scope of the rule.[491]

The establishment of an appropriate value-of-transaction test might improve the regulation of potential killer acquisitions in two respects: first, by expanding the scope of *ex ante* review, and second, by deterring some potentially anticompetitive transactions. Wollmann (2019) shows that the likelihood of competitors merging increases as the probability of merger control decreases. Moreover, Cunningham et al. (2021) has observed that possible killer acquisitions in the pharmaceutical sector seem

[489] See AFCA Press Release (4/3/2022) (https://www.bwb.gv.at/en/news/detail/meta-facebook-giphy-merger-afca-appealing-against-conditional-clearance); AFCA Press Release (24/6/2022) (https://www.bwb.gv.at/en/news/detail/submetering-cartel-decision-relating-to-ista-oesterreich-gmbh-final-1). The UK's Competition & Markets Authority ("CMA") also reviewed the Facebook/Giphy transaction, under its "share of supply" test, and ultimately required Meta to divest the company. CMA, Completed Acquisition by Facebook (now Meta Platforms) of Giphy (Final Report 30 November 2021), appeal dismissed, Meta Platforms v CMA [2022] CAT 26; CMA, Meta Platforms/Giphy (Final Order 6 January 2023).

[490] It might be noted in this regard that the US competition regulators have adopted specific rules for transactions in the pharmaceutical sector, which they have concluded gives rise to unique considerations. See Premerger Notification: Reporting and Waiting Period Requirements, 78 Fed. Reg. 68705 (15 November 2013) (https://www.ftc.gov/system/files/documents/hrs_statements/pharmaceutical-licensing/131115premergerfrn.pdf).

[491] The US antitrust agencies have adopted a similar approach with the use of NAICS (the North American Industry Classification System) to establish the scope of a rule requiring HSR notification when exclusive patent rights are being transferred in the pharmaceutical industry. The rule (16 C.F.R. § 801.2(g)(1)) establishes that an obligation to notify applies with respect to patents covering products whose manufacture and sale would generate revenues in NAICS Industry Group 3254 (Pharmaceutical and Medicine Manufacturing).

to occur disproportionately just below the size-of-transaction merger control thresholds applied by the US competition authorities.[492]

A second issue, if a value-of-transaction test were adopted, would be the need to ensure that transactions falling within their scope have an appropriate nexus to trade within the EEA. What constitutes evidence of a sufficient nexus is not obvious; for example, the NCAs in Austria and Germany have adopted somewhat different approaches in assessing whether transaction targets are active in-country to a significant extent.[493] Thus, the BWB focuses to a significant extent on whether the target has a physical presence (e.g. sites or subsidiaries) in Austria.[494] The BKartA, in contrast, generally focuses on whether a target's current turnover reliably reflects its market position in Germany,[495] or various facts indicating that a target that does not yet have any in-country turnover nonetheless is likely to be active in Germany to a significant extent in the reasonably near term.[496] In this regard, the BKartA has acknowledged that the factors to be considered "are context and case-specific" and that "[a] definitive list of possible criteria cannot be provided."[497]

In proposals for amendment of the EUMR, a variety of criteria demonstrating a Union nexus have been suggested, including, e.g. patenting of the relevant innovations in Europe, the parties' activities (e.g. performance of clinical trials) in the EEA, or an expectation that the parties will be engaged in future marketing or licensing in the EEA.[498] However, while a variety of approaches might be adopted, it appears likely that there would be an inherently discretionary element (and concomitant uncertainty in assessments of competence) in all of them.

Finally, a value-of-transaction test would require the adoption of clear rules for how transaction values are to be calculated. One purpose of such rules would be to ensure that all appropriate components of value are included in the calculation. For example, the FTC concluded in a recent review of hundreds of acquisitions made over a 10-year period by Amazon, Apple, Facebook, Google and Microsoft that 79% entailed deferred or contingent compensation of founders and key employees, and that adding that compensation to nominal transaction value would have resulted in 10% fewer

[492] Cunningham et al. (2021) examined acquisitions whose transaction values fell just above and below the Hart-Scott-Rodino (HSR) notification thresholds, and compared the merged companies' post-closing project developments. They observed clear bunching of deals just below the $50 million size-of-transaction threshold, but only for deals in which the target had projects that overlapped with those of the acquirer. Moreover, they found that the merged companies' project termination rate was higher (94.6% versus 83.3%) and product launch rate was lower (1.8% versus 9.1%) for deals that were, respectively, just below and above the reporting threshold.

[493] See generally BKartA and BWB, Transaction Value Thresholds (2022), paragraphs 64-106 (https://www.bundeskartellamt/de/SharedDocs/Publikation/EN/Leitfaden/Leitfaden_Transaktionswertschwelle.pdfjsessionid=F2Da).

[494] An additional consideration is whether the target has at least € 1 million annual in-country turnover, unless it can be concluded that its lower (or non-existent) turnover does not adequately reflect its market position and competitive potential.

[495] This might be the case, for example, if the target has made initial efforts to enter the German market, and its commercial launch of the relevant product elsewhere suggests that its sales will grow rapidly.

[496] Accordingly, acquisitions of R&D undertakings might be assessed in light of, e.g. their stage of clinical testing, laboratory location, level of resources, successful patent prosecutions, and the like.

[497] OECD Roundtable, DAF/COMP/WD(2020)20, Note by Germany (28 May 2020) (https://one.oecd.org/document/DAF/COMP/WD(2020)20/en/pdf).

[498] European Commission, 2021.

transactions falling below the HSR size-of-transaction threshold.[499] A second purpose of such rules would be to ensure that all elements of value are properly calculated, particularly where an agreement provides for contingent forms of consideration (e.g. milestone and earn-out payments). Guidance published by the BKartA and BWB for application of their new value-of-transaction tests makes clear how complex such calculations may be.[500]

II.2.2.3 Hybrid (value : turnover) threshold

Some have suggested that a "hybrid" test of jurisdiction, reflecting the ratio of transaction value to turnover of the target, might be adopted, and that regulatory competence might appropriately extend deals where the amount being paid for a company is disproportionate to what would normally be expected given its current commercial performance (i.e. turnover).[501] The Commission has noted in the past that such disproportionality is a factor that may be considered in its evaluation of requests for referral under Article 22 EUMR.[502]

It should be noted that this "hybrid" proposal entails the same difficulties in establishing the transaction "price" and local nexus that a value-of-transaction test would do. Moreover, it is not clear what ratio would be appropriate as a jurisdictional test; recent assessment by the Commission services suggests that anything from 4:1 to 10:1 might be instructive.[503] However, such a test might provide at least a partial remedy to the shortcomings that have been identified in the use of party turnovers alone. Given recent cases, as noted above, it is evident that some potential killer acquisitions (and other acquisitions of small but competitively significant businesses) would be flagged with a hybrid test. Indeed, the use of a ratio would capture all acquisitions of pipelines and start-ups that have not begun to generate appreciable turnover.

II.2.2.4 Other asset-based approaches

Some have suggested that the definition of a 'concentration' might be expanded to capture certain acquisitions of assets that do not constitute a discrete business.

One means of addressing this might be to expand the definition of a concentration to include some types of asset acquisitions and, in particular, the acquisition of a wider

[499] FTC, 2021.

[500] See BKartA and BWB, Transaction Value Thresholds (2022), paragraphs 11-63.

[501] European Commission, 2021.

[502] European Commission, Guidance on the application of the referral mechanism set out in Article 22 of the Merger Regulation to certain categories of cases (2021/C 113/01) ("Referral Guidance"), paragraph 19.[503] European Commission, 2021, paragraphs (100 (note 130)) and (103). It might be noted that even the lowest ratio identified here (4:1) would not have flagged for review a recent pharmaceuticals case (J&J/Tachosil (2020)) where the acquiror proposed to pay $400 million for a product that had prior-year sales of $155 million (a ratio of 2.6:1). This transaction, which bore some of the hallmarks of a potential killer acquisition (and which the parties abandoned in the face of regulatory concerns), is discussed in section II.2.3.1 of this Report.

[503] European Commission, 2021, paragraphs (100 (note 130)) and (103). It might be noted that even the lowest ratio identified here (4:1) would not have flagged for review a recent pharmaceuticals case (J&J/Tachosil (2020)) where the acquiror proposed to pay $400 million for a product that had prior-year sales of $155 million (a ratio of 2.6:1). This transaction, which bore some of the hallmarks of a potential killer acquisition (and which the parties abandoned in the face of regulatory concerns), is discussed in section II.2.3.1 of this Report.

range of exclusive IPRs than is provided for in current rules.[504] Such a reform would be consistent with US rules under the HSR pre-merger review programme, under which the antitrust authorities can review *ex ante* the purchase or exclusive licensing of patents or other IPRs (whether that package of IPRs may be regarded as a discrete business or not).[505] However, it might be noted that such a rule is found in a minority of jurisdictions, and this study has not identified any clear examples of likely killer acquisitions of this type (though the limits of publicly available information make an assessment of licensing transactions particularly challenging).

Another means of addressing this might be to amend current rules so that a concentration can be identified on the basis that a discrete business will be created through a combination of the assets being acquired and the acquirer's own assets.[506] In order to avoid catching numerous asset acquisitions that are not of concern, such a rule might include a requirement that the jurisdictional assessment have full regard for all actions the acquirer planned to take in connection with the transaction (including redeployment or retirement of its pre-existing assets) in determining whether the assets held post-transaction constitute a discrete business. An acquirer of material assets is likely to have prepared internal investment proposals, requests for approval, or operating plans showing how the acquired assets will be used. These arguably would provide an appropriate means for an acquirer to determine its notification obligations, and for the Commission (or NCAs) to assess compliance in individual cases. However, it appears that the difficulties and uncertainties arising in practical application of such a rule might render it unworkable.

II.2.2.5 Market shares

The current turnover-based tests might be supplemented with an alternative test based on the market share(s) of the parties.

Market share tests currently are included in the notification thresholds of Portugal,[507] Slovenia,[508] and Spain.[509] An obvious shortcoming of this approach is that the

[504] See CJN, paragraph (24). These extent to which grants of IPRs might be regarded as concentrations is discussed in section II.3.2 of this Report.

[505] A focus on exclusive IPRs would appear to be appropriate because without exclusivity, the acquirer in a potential killer acquisition cannot effectively preclude others from developing the product it may be trying to eliminate. As discussed in Section II.3.2 of this Report, it would be important to provide that an acquisition of non-exclusive IPRs on terms making it highly unlikely that third parties can (or would attempt to) exploit the underlying technology is regarded as a de facto acquisition of exclusive IPRs.

[506] It might be possible to establish such a test as a matter of interpretation, rather than through amendment of the EUMR, given a literal reading of its provisions. However, such an interpretation would represent a significant departure from general understandings that a concentration arises only where there is a change of control of the whole or parts of an undertaking other than the acquirer. See Article 3(1) EUMR; CJN paragraphs (7) and (136) ("a concentration only covers operations where a change of control in the undertakings concerned occurs" and "the undertakings concerned will be the acquirer(s) and the acquired part(s) of the target undertaking").

[507] In Portugal, a transaction may trigger notification if a share of at least 50% is acquired, created or increased, or if a share of at least 30% is acquired, created or increased and each of two parties has annual in-country turnover of more than € 5 million.

[508] In Slovenia, transaction parties are required to inform the competition authority (which may then require formal notification) if they have a share of 60% or more.

[509] In Spain, a transaction may trigger notification if a share of at least 30% is acquired or increased, unless the target's annual in-country turnover does not exceed € 10 million and the parties do not have an individual or combined share of at least 50%.

jurisdictional assessment is conflated with what might more appropriately be addressed in a substantive assessment of the deal, complicating parties' efforts to determine (and the regulators' ability to confirm) their filing obligations. Such a test is used by only a few regulators worldwide.

A share-based approach might be a viable means of capturing at least some killer acquisitions. In cases giving rise to a market-to-pipeline overlap, one of the parties has sales (i.e. a determinable share) on an existing market and, although the other party is not yet present on the market, the test may not require that the transaction will result in an increment to share.[510] Where a transaction gives rise to a pipeline-to-pipeline overlap, an equal share might be attributed to each similarly situated developer (having due regard, in particular, to the stage of clinical trials currently underway of drugs having the same mechanism of action (MoA) and therapeutic indication (TI)).[511] Similarly, in cases raising concerns about innovation competition *per se*, an equal share might be attributed to each properly resourced R&D operation.[512]

A different approach exists in the United Kingdom, which relies on shares of any identifiable "supply" found to be relevant to an acquisition (whether or not that "supply" constitutes a properly defined market).[513] Critics have charged that this test is so flexible it rarely amounts to a genuine test at all. However, that flexibility also has been cited as something that can help to ensure effective regulatory oversight when nascent but important competitors are acquired.[514]

II.2.2.6 Sector-specific requirements

Objective jurisdictional tests might be supplemented with additional notification requirements targeted at specific areas of concern.

The EU recently adopted a series of measures meant to promote more effective, *ex ante* regulation in the digital sector, including a requirement that leading online platform operators ("gatekeepers") must inform the Commission in advance of any intended concentrations where the target provides services in the sector, whether or not the

[510] Neither Portugal nor Spain requires a competitive overlap in order to assert jurisdiction under its market share test.

[511] In assessments of pipeline-to-pipeline overlaps, the Commission might count the number of similarly situated innovators and impute an equal share to each of them (e.g. if there were three companies conducting Phase 3 clinical trials, each of them and the parties combined would be deemed to have a 25% share). Because such assessments are meant to identify genuine competitive constraints, it would be appropriate to disregard or discount companies that are in earlier-stage trials or have only limited resources.

[512] See, e.g. Case M.7932 – Dow/DuPont (27.3.2017). It seems somewhat unlikely that concerns about innovation competition per se would arise with respect to parties that do not trigger the basic turnover-based thresholds for notification; if the relevant companies are not large, one would expect that their capabilities (particularly in emerging technologies) are evidence that others could enter the field relatively easily. However, it cannot be excluded that an identifiable group of undertakings with unique R&D capabilities might exist in specialized areas of pharmaceutical research where entry is more difficult.

[513] Under section 23 of the UK's Enterprise Act 2002, in deciding whether a 25% share exists, "the decision-making authority shall apply such criterion (whether value, cost, price, quantity, capacity, number of workers employed or some other criterion, of whatever nature), or such combination of criteria, as the decision-making authority considers appropriate". For example, the CMA recently asserted jurisdiction over a pharmaceutical transaction giving rise to a market-to-pipeline overlap, where the target had no UK sales but, together with the acquirer, accounted for more than 25% of UK-based employees engaged in activities relating to the overlap products. See CMA, Anticipated acquisition by Roche Holdings of Spark Therapeutics (16 December 2019) (https://assets.publishing.service.gov.uk/media/5e3d7c0240f0b6090c63abc8/2020207_-_Roche_Spark_-_non-confidential_Redacted-.pdf).

[514] See OECD, Start-ups, killer acquisitions and merger control (2020), page 19.

transaction satisfies the EUMR notification thresholds.[515] The Commission is to share such information with the NCAs, who may then request review under Article 22 EUMR (provided they have competence themselves, or no national merger control regime at all).

Norway's merger control law enables the NCA to impose similar disclosure requirements on individual firms operating in industries that are sufficiently concentrated that an *"enhanced focus"* is justified. After being informed of a transaction, the NCA may impose a duty to notify it (and to suspend further implementation of it) if the agency has reasonable grounds to assume that it will adversely affect competition.[516]

More effective control of potential killer acquisitions might be advanced by the adoption of similar measures for the pharmaceuticals sector. For example, such measures might require the largest pharmaceutical companies (i.e. companies of sufficient size they may be presumed to have competitively significant activity in the EEA) to provide advance or contemporaneous notice of acquisitions that entail a direct competitive overlap between the parties' pipeline or marketed drugs, with follow-on notice for several years if development of an overlap drug is discontinued or redirected.[517] The costs entailed in the operation of such a system (for both the Commission and the parties) could be minimised if it were a simple online registry, enabling the Commission and NCAs to enquire further if a competition assessment appears to be warranted in particular cases. Such a system is discussed further in section II.4 of this Report.

II.2.2.7 Discretion

Finally, provision might be made for the discretionary assertion of competence (the normal reporting thresholds notwithstanding) in cases raising particular competition concerns.

The merger control laws of Denmark, Hungary, Iceland, Ireland, Latvia, Lithuania, Norway, Slovenia and Sweden reportedly provide that if an NCA that has particular competition concerns about a transaction, it may require notification even though the parties' turnovers do not meet the standard filing thresholds.[518] Italy likewise amended its competition law in 2022 to provide that the IAA may require notification of transactions that present "concrete risks for competition" on a market in Italy where only one of its (normally cumulative) in-country turnover tests is met or the combined

[515] Regulation (EU) 2022/1925 of the European Parliament and of the Council of 14 September 2022 on contestable and fair markets in the digital sector and amending Directives (EU) 2019/1937 and (EU) 2020/1828 (Digital Markets Act), 2022/L 265/1, Article 14.

[516] See OECD Roundtable, DAF/COMP/WD(2020)21, Note by Norway (25 May 2020) (https://one.oecd.org/document/DAF/COMP/WD(2020)21/en/pdf)

[517] While the appropriate levels of turnover would have to be considered, it might be noted as an indicative matter that the top 20 pharmaceutical companies worldwide, listed by 2022 revenues, are Pfizer, Johnson & Johnson, Roche, Merck & Co, AbbVie, Novartis, Bristol Myers Squibb, Sanofi, AstraZeneca, GSK, Takeda, Eli Lilly, Gilead Sciences, Bayer, Amgen, Boehringer Ingelheim, Novo Nordisk, Moderna, Merck KGaA, and BioNTech. K. Dunleavy, The top 20 pharma companies by 2022 revenue, FIERCE Pharma (18 April 2023) (https://www.fiercepharma.com/pharma/top-20-pharma-companies-2022-revenue).

[518] See also OECD Roundtable, Note by France, paragraph 40. Iceland and Norway both have call-in powers but, as they are not part of the EU, they cannot initiate Art. 22 referrals. The EEA Agreement only allows them to join such referrals.

worldwide turnovers of the parties exceed € 5 billion.519 France also has proposed to introduce a measure that would enable its competition authority to require notification where its global turnover test is met and a transaction raises "significant competition concerns".520

An obvious concern regarding discretionary competence to review non-notifiable transactions is that such intervention may complicate parties' ability to organise already complex transactions and, where transactions have already closed, may compromise significant investments and settled expectations. Accordingly, we understand that the NCAs in some Member States (e.g. Finland, Germany, the Netherlands and Portugal) generally cannot intervene in transactions that fall below their merger control thresholds.

Despite this, such powers would appear to be consistent with recent modernisation of EU competition law, and an appreciation that sizeable businesses normally are well placed to assess competition law issues with the assistance of counsel. Moreover, concerns that such powers could undermine businesses' ability to plan and execute transactions might be met by regulators' willingness to provide confidential assessments of deals that the parties present on a voluntary basis (with appropriate assurances of a genuine intention to proceed). While such assessments might be made contingent on the results of an eventual market investigation, frank discussion of the issues in advance may enable parties to structure their transaction timetables and condition their agreements appropriately.

Competition regulators worldwide have struggled to identify systematic means of addressing acquisitions of competitively important but relatively small innovators without disrupting a constructive balance, reflected in their general notification thresholds, between the burdens of notification and the benefits of *ex ante* review. Italy's recent amendment of its law (and France's similar proposal), supplementing fixed reporting requirements with agency discretion, may herald an emerging trend. In combination with Article 22 EUMR, these provisions may contribute to filling the jurisdictional gap by allowing some below-threshold transactions to be referred to and reviewed by the Commission where Member States are competent to do so. However, it must be borne in mind that such powers are only a partial solution to the problem of killer acquisitions; while they empower the regulator to act, they provide little assurance that the regulator will receive notice of deals in which it might be appropriate to do so.

II.2.3 Regulatory competence under Article 22

The EUMR grants the Commission exclusive jurisdiction to review concentrations with an EU dimension, defined by the application of combined turnover-based thresholds set out in Article 1 EUMR. Such thresholds delineate the transactions which have an EU dimension (i.e. whose impact on the market is assumed to go beyond the national borders of any one Member State) and which, as such, are in principle best dealt with at the EU level. The EUMR contains corrective mechanisms to the application of these

519 Law n. 118/2022, amending Law n. 287/1990. Italy's notification thresholds (which are updated annually) currently require filing if the parties' combined in-country turnover exceeds € 532 million and each of at least two parties has annual in-country turnover exceeding € 32 million.

520 See OECD Roundtable, Note by France, paragraphs 40-43. Similar to the EU Member State rules noted above, transactions that do not trigger the procedural benefits afforded by an HSR filing in the US nonetheless may be investigated, preliminarily enjoined pending the completion of any investigation and, if appropriate, prohibited under the substantive antitrust laws.

quantitative jurisdictional thresholds, allowing, under specific circumstances, a referral of individual cases between the Commission and one or several Member States. This system of referrals aims to ensure that the most appropriate authority or authorities is(/are) responsible for carrying out a particular merger investigation review(s) for a case, even if jurisdictional rules mean they would not initially be competent.

Article 22 EUMR allows for one or more Member States to request the Commission to examine, for those Member States, any concentration that does not have an EU dimension but affects trade between Member States and threatens to significantly affect competition within the territory of the Member State or States making the request. Until very recently, it was the Commission's view, based on the wording and the purpose of Article 22 EUMR, that Article 22 was applicable to all concentrations, not only those meeting the respective jurisdictional criteria of the referring Member States. However, over time, the Commission had developed a practice of discouraging referral requests under Article 22 EUMR from Member States that did not have original jurisdiction under their respective national laws over the transaction at stake.

More recently, the Commission found that market developments resulted in a gradual increase of concentrations involving firms that play or may develop into playing a significant competitive role on the market(s) at stake despite generating little or no turnover at the moment of the concentration. Therefore, it considered that a number of cross-border transactions which could potentially also have a significant impact on competition in the EU internal market may have escaped review by both the Commission and the Member States.[521]

In light of these developments, the Commission announced in March 2021 its intention, in certain circumstances, to encourage and accept referrals in cases where the referring Member State does not have initial jurisdiction under national law over the case (but where the criteria of Article 22 EUMR are met), issuing new guidance on the matter.[522] This would notably be the case where the turnover of one of the merging parties does not reflect its actual or future competitive potential. This could be relevant for companies developing promising pharmaceutical pipelines: the Commission identified that this could include examples where the target is a start-up or recent entrant with significant competitive potential, an important innovator or is conducting potentially important research, or has access to competitively significant assets, such as intellectual property rights.

The Illumina/GRAIL case was the first case in which the Commission applied this recalibrated approach towards referrals under Article 22 EUMR, by accepting referral requests from six Member States despite Illumina's acquisition of GRAIL not being notifiable in any of these Member States.[523] After a full investigation, and in one of its relatively rare challenges to a vertical acquisition, the Commission prohibited Illumina's acquisition of GRAIL as incompatible with the internal market. However, the parties contested the Commission's jurisdiction to review the transaction (since it did not meet EU or national merger control thresholds). While the General Court initially upheld the Commission's interpretation of Article 22, in Joined Cases C-611/22 P and C-625/22 P,

[521] See European Commission, 2021.

[522] Communication from the Commission Guidance on the application of the referral mechanism set out in Article 22 of the Merger Regulation to certain categories of cases ("Referral Guidance"), OJ C 113, 31.3.2021, p. 1–6.

[523] See https://competition-cases.ec.europa.eu/cases/M.10188

the European Court of Justice on appeal ruled in favour of Illumina and GRAIL, set aside the judgement of the General Court and annulled the Commission's referral decisions under Article 22 EUMR in the Illumina/GRAIL case.[524] The case is described briefly in Box 16 below.

Box 16: Illumina/GRAIL[525]

In 2021, the Commission accepted requests from France, three other Member States and two EFTA States that it review the proposed $7.1 billion acquisition by Illumina, a US supplier of advanced genomic sequencing instruments, consumables and services, of GRAIL, a US developer of blood-based cancer screening tests that had not yet begun to generate turnover. The requests followed on the Commission's receipt of a complaint about the transaction and provision of notice inviting requests under Section 22(5) EUMR.[526]

The Commission found that Illumina was the only credible supplier of technology that could be used to process blood-based cancer detection tests, with an installed base of instruments, reliable support network, and IPRs that constituted significant barriers to entry by other instrument suppliers. It also determined that, post-transaction, Illumina would have incentives and the ability to disadvantage GRAIL's rivals through a variety of tactics (e.g. refusals to supply, selective price increases, and the untimely provision of inferior service/supplies) that would not be adequately constrained by Illumina's offer to extend technology licenses and to contract on standard terms. Because such tactics might undermine competition in innovation that would shape the emerging market for tests being developed by GRAIL and its rivals, and in order to ensure that tests with different features and price points became available, the Commission declared the transaction incompatible with the internal market and ordered Illumina to divest GRAIL.[527]

[524] More specifically, the following events took place. On 9 March 2021, the French competition authority made a referral request asking the Commission to examine the Illumina/GRAIL case pursuant to Article 22(1) EUMR, which was subsequently joined by the national competition authorities of Belgium, Greece, Iceland, the Netherlands, and Norway (together the "Referring Countries"). On 19 April 2021, the Commission adopted six decisions pursuant to Article 22(3) EUMR accepting the requests of the Referring Countries (the "Referral Decisions"). On 28 April 2021, Illumina sought the annulment of the Referral Decisions before the General Court of the European Union (Case T-227/21). On 13 July 2022, the General Court upheld the Referral Decisions confirming the Commission's jurisdiction to examine the transaction (judgment of 13 July 2022, Case T227/21, Illumina, Inc. vs European Commission, EU:T:2022:447). On 22 September 2022, Illumina lodged an appeal against the judgment delivered by the General Court (Case C-611/22 P). On 30 September 2022, GRAIL also lodged an appeal against the judgment delivered by the General Court (Case C-625/22 P). On 3 September 2024, the European Court of Justice upheld Illumina's and GRAIL's appeals and annulled the Commission's Referral Decisions. As a result, the Commission withdrew all decisions subsequently adopted as part of that procedure.

[525] Cases M.10188, M.10483, M.10493, M.10.938, and M.10939 – Illumina/GRAIL.

[526] After clarifying with several NCAs that they did not have competence under their national merger controls, the Commission invited requests for referral, which it received from Belgium, France, Greece, the Netherlands, Iceland and Norway. Case M.10188 – Illumina/GRAIL (reported in EC Press Release (20/4/2021) (https://ec.europa.eu/commission/presscorner/detail/en/MEX_21_1846)) (appeal dismissed by the General Court in Illumina (2022), appeal pending in Case C-611/22 P Illumina v Commission).

[527] Case M.10188 – Illumina/GRAIL (reported in EC Press Release (6/9/2022) (https://ec.europa.eu/commission/presscorner/detail/en/ip_22_5364)) (appeal pending in Case T-709/22 Illumina v Commission); Case M.10939 – Illumina/GRAIL (Restorative measures) (reported in EC Press Release (12/10/2023) (https://ec.europa.eu/commission/presscorner/detail/en/IP_23_4872)) (appeal pending in Case T-1190/23 Illumina v Commission).

During its procedure, the Commission imposed interim measures establishing "hold separate" and related obligations after Illumina completed the transaction in violation of its standstill obligation under Article 22(4).[528] After reaching its final determination on the merits, the Commission also imposed a fine on Illumina amounting to 10% of its annual turnover for its intentional infringement of that provision.[529]

All these decisions were appealed by Illumina and GRAIL, who had also challenged the Commission's competence to review this transaction (since it did not meet EU or national merger control thresholds). While the General Court initially upheld the Commission's interpretation of Article 22, the European Court of Justice found on appeal that the Commission should not have accepted referral requests from Member States lacking jurisdiction to review the transaction under their own national laws. Consequently, the Court annulled the decisions whereby the Commission had accepted to review the case on behalf of the six referring Member States. As this meant that the Commission had effectively no jurisdiction to review Illumina's acquisition of GRAIL, the Commission formally withdrew all decisions adopted as part of this procedure on 6 September 2024.

II.2.3.1 The importance of Article 22 review

In all sectors combined, the Commission reviewed 33 transactions under Article 22 from 2004 (when the EUMR entered into force) through the end of 2023. Seventeen of those reviews (49%) entailed an in-depth (Phase II) investigation, and almost half (48%) resulted in substantive changes to the parties' proposals: ten were cleared subject to remedies, while one was prohibited and five were abandoned following the Commission's decision to open Phase II proceedings.[530] Accordingly, experience over the last ten years shows fairly conclusively that requests for referral under Article 22 enable the Commission to address a significantly higher proportion of problematic transactions than is found in its overall caseload.[531]

The Commission initiated its first Article 22 review in the pharmaceutical sector in 2019, when Germany, which was competent to review the subject transaction, filed a request for referral. After the Commission gave notice pursuant to Article 22(2), Germany's request was joined by the other two NCA's that were competent to review the deal and by three countries that were not. The facts in this case are summarised in Box 17 below.

[528] Cases M.10493 – Illumina/GRAIL (Interim measures under Art. 8(5)a) (reported in EC Press Release (29/10/2021) (https://ec.europa.eu/commission/presscorner/detail/en/IP_21_5661)) (appeal pending in Case T-755/21 Illumina v Commission); Case M.10.938 – Illumina/GRAIL (Interim measures under Article 8(5)c) (reported in EC Press Release (28/10/2022) (https://ec.europa.eu/commission/presscorner/detail/en/MEX_22_6467)) (appeal pending Case T-5/23 Illumina v Commission).

[529] Case M.10483 – Illumina/GRAIL (Article 14 procedure) (reported in EC Press Release (12/7/2023) (https://ec.europa.eu/commission/presscorner/detail/en/ip_23_3773) (appeal pending in Case T-591/23 Illumina v Commission).

[530] European Commission, Competition Policy - Competition case search (https://competition-cases.ec.europa.eu/) (results 2/2/2024).

[531] Out of 6744 notifications over the last 10 years (2004-2023), 171 transactions (3%) were subject to in-depth (Phase II) investigation, 334 transactions (5%) were cleared subject to remedies, and 15 transactions (<1%) were prohibited. EC Statistics (https://competition-policy.ec.europa.eu/mergers/statistics_en).

Box 17: Johnson & Johnson/Tachosil[532]

In 2019, the Commission accepted requests from Germany, four Member States and an EFTA State that it review the proposed $400 million acquisition by Johnson & Johnson of the assets associated with Takeda Pharmaceuticals' manufacture, licensing and commercialisation of dual haemostatic patches, which generated around $155 million in annual sales. Germany requested referral after receiving a merger control filing from the acquirer, and its request was joined when the Commission notified the other Member States and the EFTA Surveillance Authority that it had received Germany's request.[533]

At the time of the transaction, Takeda's *TachoSil*-branded patch was the only haemostatic patch being sold in the EEA because, 18 months earlier, J&J had stopped supplying its own patch (*Evarrest*) in the EU and requested for "commercial reasons" that its EU marketing authorisation be withdrawn.[534] The Commission accepted the referral, noting that it would, *inter alia,* clarify why J&J had withdrawn *Evarrest*.

After in-depth investigation, the Commission concluded that J&J would have strong incentives to (re-)enter EEA markets for haemostatic patches if it did not acquire *TachoSil* (either with *Evarrest*, which was still marketed in the US by Baxter, or with a newly developed patch) and that the acquisition could hinder competitors' ability to enter or expand.[535] Faced with strong expressions of concern by both the Commission and the FTC, the parties abandoned the deal.[536]

In sum, Article 22 reviews have proved to be – in certain situations – a tool in ensuring that transactions involving small but competitively significant targets are properly regulated, both generally and with respect to competition in pharmaceuticals and medical devices.[537] Although the judgement of the European Court of Justice in the *Illumina / GRAIL* case has tightened the conditions under which Article 22 referrals can be accepted by the Commission, these remain a tool to address the enforcement gap with regard to potential killer acquisitions falling below applicable merger control thresholds in specific instances. As is clear from the ruling of the Court of Justice, the Commission may still accept such referrals from Member States with competence to review under national rules or no merger control regime of their own (like Luxemburg).

[532] Case M.9547 – Johnson & Johnson/Tachosil.

[533] Germany's request was joined by Austria and Spain (each of which was competent to review the transaction) and by France, Finland and Norway (which were not). Case M.9547 – Johnson & Johnson/Tachosil (Article 22 Decision) (26/9/2019).

[534] EMA Public Statement, EMA/24202/2018 (12/1/2018) (https://www.ema.europa.eu/en/documents/public-statement/public-statement-evarrest-withdrawal-marketing-authorisation-european-union_en.pdf).

[535] EC Press Release (25/3/2020) (https://ec.europa.eu/commission/presscorner/detail/en/IP_20_529).

[536] Withdrawal of notification of a concentration (Case M.9547 – Johnson & Johnson/Tachosil (17/4/2020) 2020/C 124/01 (https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=OJ:C:2020:124:FULL)).

[537] Following the Commission's intervention in Illumina/GRAIL, Spain filed an Article 22 request (which was joined by 12 other Member States) upon its receipt of a notification relating to a transaction that gave rise to a horizontal overlap in the supply of hearing implants. After the Commission accepted referral, the UK's Competition & Markets Authority issued a partial prohibition decision that eliminated the overlap of concern, and the Commission cleared the remainder of the transaction unconditionally in a Phase 1 review. Case M.10966 – Cochlear/Oticon Medical (2023).

In that context, as pointed out above, there is an increasing trend of Member States adopting "call-in" provisions or alternative jurisdictional tests in their national law to be able to review transactions falling below traditional turnover-based thresholds but giving rise to significant competition concerns[538]. This somewhat widens the scope for possible Article 22 referrals to the Commission. For example, the Commission is currently reviewing the proposed acquisition of Run:ai by NVIDIA following an Article 22 referral from Italy, whose national competition authority requested notification of the transaction (which fell below the national merger control thresholds) using the "call in" powers provided for in the Italian Competition Act[539].

In any case, if protecting competition against potential killer acquisitions remains a key enforcement priority for the Commission, a further possible avenue would be to make targeted amendments to the EUMR to close the jurisdictional gap. This could be achieved through amendments to the thresholds set out in Article 1(5) EUMR, by revising Article 22 to clarify that it can be used by Member States without competence under national rules, or by introducing properly regulated "call-in" powers at EU level similar to those in force in the Member States referred to above.

II.2.3.2 Preparation and assessment of Article 22 requests for referral

Review may be requested under Article 22(1) EUMR if the transaction of interest is a concentration that "affects trade between Member States" and "threatens to significantly affect competition within the territory of the Member State or States making the request." Because potentially problematic transactions may not trigger automatic notification or suspension requirements under the merger control laws of the Member States, effective use of this provision requires diligent efforts to detect those transactions that may give rise to actual or potential overlaps in the parties' products and pipelines. In this regard, we are aware that the Commission actively monitors financial news reporting services and other sources of information regarding transactions in the pharmaceutical sector. Deals that might be of interest can readily be followed up with recourse to online news reports, and parties will often announce a transaction for the benefit of investors in press releases that highlight similarities in their respective businesses. Trade analysts likewise often publish such assessments shortly after a deal is announced. In addition, a transaction may come to the Commission's attention if concerned competitors, customers, or suppliers register complaints. In any event, regular coordination through the European Competition Network (ECN) and other inter-agency contacts can be a helpful means of sharing intelligence about potential transactions that may have come to the attention of one regulator while remaining below the radar of others.

The following discussion relates to various legal and practical considerations in the framing and assessment of Article 22 requests for referral.

II.2.3.2.1 Effect on trade between Member States

The General Court has held that Article 22(1) EUMR must be interpreted in line with Articles 101 and 102 TFEU, under which the Commission is competent to intervene when

[538] See at Section II.2.2.7 above.

[539] Press release available at: https://ec.europa.eu/commission/presscorner/detail/en/mex_24_5623.

potential infringements "may affect trade between Member States."[540] As noted by the Commission, "the effect on trade criterion is a jurisdictional one, which serves to distinguish those agreements and practices which are capable of having cross-border effects, so as to warrant an examination under the Community competition rules, from those agreements and practices which do not."[541]

As a preliminary matter, it might be noted that competence to address some potential killer acquisitions may exist (insofar as the targets are doing business in the EU) by virtue of the fact that such acquisitions may appreciably alter the structure of competition in the EU.[542] However, it appears likely that the Commission is competent to review even acquisitions of small innovators that are not doing business in the EU because they may appreciably affect trade between Member States.

The Commission regulates many infringements, even if they occur outside the EU and have not produced any observable changes in cross-border trade, because they are presumed to be capable of having effects in the EU (e.g. by inhibiting the development of new products/services that would lead to faster and more extensive integration of the common market).[543]

A robust case can almost certainly be made that the development of pharmaceuticals, wherever it occurs, and the sale of pharmaceuticals that have been placed on the market with an EU marketing authorisation, can cause appreciable effects on trade between Member States.

Medicines are developed in a transparent environment, fostered by the online publication of information regarding clinical trials that sponsors must register on

[540]Judgment of 15 December 1999, Kesko Oy v Commission, T-22/97, EU:T:1999:327, paragraph 106. The Commission has taken the position that it is now "settled case law [that] an agreement that has an impact on the competitive structure in more than one Member State is by its nature capable of affecting trade between Member States." Case AT.39612 – Perindopril (Servier) (9/7/2014), paragraphs 1401-1405 (for appeal on other grounds, see Judgment of 12 December 2018, Servier and Others v Commission, T-691/14, EU:T:2018:922, further appeal pending in Cases C-176/19 P Commission v Servier and C-201/19 P Servier v Commission).

[541] Commission Notice – Guidelines on the effect on trade concept contained in Articles 81 and 82 of the Treaty, 2004/C 101/07 ("Effect on Trade Guidelines"), paragraph 35.

[542] See, e.g. Judgment of 6 March 1974, Istituto Chemioterapico Italiano and Commercial Solvents v Commission, 6/73 and 7/73, EU:C:1974:18, paragraphs 32-33 (competence exists under Article 102 where the elimination of a competitor would have "repercussions on the competitive structure within the Common Market" even though it might be difficult to show an appreciable effect on trade between Member States); Judgment of 14 February 1978, United Brands v Commission, 27/76, EU:C:1978:22, paragraph 201 (competence under Article 102 does not require a showing of effects relating to trade between Member States if it has been shown that the elimination of a competitor would have "repercussions on the patterns of competition in the Common Market"); Judgment of 8 October 1996, Compagnie Maritime Belge Transports and Others v Commission, T-24/93, T-25/93, T-26/93 and T-28/93, EU:T:1996:139, paragraphs 201-203 (Commission is competent to challenge exclusionary conduct that is so "inherently capable of affecting the structure of competition" on a market that the existence of an effect on trade between Member States can be assumed).

[543] Under a standard formulation of the rule, competence to address an activity or operation exists if it is "possible to foresee with a sufficient degree of probability and on the basis of objective factors of law or fact that it may have an influence, direct or indirect, actual or potential, on the pattern of trade between Member States, such as might prejudice the realisation of the aim of a single market in all the Member States." Kesko (1999), paragraph 103; Judgment of 30 June 1966, Société Technique Minière v Maschinenbau Ulm, 565/65, EU:C:196:38. While this test does not require evidence of actual effects, potential effects must be supported by more than mere conjecture. Cf. Judgment of 31 May 1979, Hugin Kassaregister v Commission, 22/78, EU:C:1979:138.

government websites and for which they are required to provide regular updates and results. Accordingly, a firm's decisions about whether and how to develop a particular pipeline may both influence and be influenced by others' management of their pipelines. For example, a Belgian pharmaceutical company might be considering development of a treatment for a particular condition but, if public databases reveal that companies in Germany and the US have already begun clinical trials of a similar drug, may decide not to pursue the project, with consequences that are likely to be felt in Member States if the availability of only two drugs keeps prices high or when one or both of the drugs that are being developed in Germany and the US fail in clinical trials.[544] Accordingly, online transparency contributes to competitive interactions worldwide in the management of pharmaceutical pipelines. Consistent with this, the Commission has consistently found, over the course of its reviews under the EUMR, that competition to develop new pharmaceuticals is at least EEA-wide (and probably global).

Competitive interactions occur not only in developers' choice of pipeline projects but also in how they pursue development, because there is significant competition worldwide among the sites at which clinical trials are conducted. Pharmaceutical companies are increasingly willing and able to move their trials around in order to manage their development costs and reduce competition with other trials when recruiting trial participants.[545] The flexible siting of trials is facilitated by the use of contract research organisations (CROs) who have established investigational sites and employ trained clinicians around the world, and these sites often receive investigational drugs and other supplies from contract manufacturing organizations (CMOs) that typically operate cross-border. Accordingly, transactions that affect developers' decisions to develop (or discontinue) a drug must have substantial effects on trade between Member States in the EEA, where approximately 2,800 clinical trials are authorised every year.[546]

Once two drugs having the same MoA and TI(s) have entered clinical trials, an acquisition that brings both pipelines under common control almost certainly reduces actual competition, either because the acquirer discontinues a pipeline, or because the intensity of competition is lessened if the acquirer delays progress on one of them or redirects it to a different TI. The effects of such changes are felt by CROs, CMOs and others at the investigational sites where trials are (or might have been) conducted. Accordingly, transactions that impact whether and how clinical trials are pursued may have both direct and indirect effects on trade between Member States.[547]

[544] In addition, the online publication of information regarding clinical trials offers opportunities for an acquirer in a killer acquisition not only to eliminate competition from one of its overlap pipelines but also to deter competition from independent developers of similar projects, if it terminates a trial or publishes discouraging analyses of trial results for a pipeline that it does not intend to continue.

[545] See generally, e.g. EFPIA, Pharmaceutical Industry in Figures – Key Data 2023 (https://www.efpia.eu/media/rm4kzdlx/the-pharmaceutical-industry-in-figures-2023.pdf); S. Jeong et al., Current globalization of drug interventional clinical trials (2017) (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5480138/); PK Drain et al., Global migration of clinical research (2018) (https://journals.plos.org/plosone/article?id=10.1371/journal.pone.092413).

[546] EMA, Clinical Trials in Human Medicines (www.https://www.ema.europa.eu/en/human-regulatory-overview/research-and-development/clinical-trials/human-medicines) (undated, accessed 25 January 2024).

[547] Moreover, if competition is limited, the acquirer may reduce its efforts to develop both pipelines, and competitors taking notice may discontinue or delay some of their R&D as well, so that an immediate loss of actual competition between the parties to a killer acquisition may be a precursor to other reductions in the scope or pace of innovation.

The Commission has recognised in past cases its powers to regulate new product development, despite its uncertainties, in light of the potential effects that successful development may have on future competition.[548] Successful development activity worldwide enables pharmaceutical companies to file applications for marketing authorisations (MAAs) in the EEA, and the EMA has reported its regular receipt of MAAs based on pivotal trials that have been conducted in countries around the world.[549] Moreover, receipt of an EU marketing authorisation initiates a cascade of effects that, singly or in combination, almost certainly have an appreciable impact, notwithstanding the fact that finished drugs are sold in national markets.[550] For example, the formulary listing, pricing, and use of a newly developed drug in one Member State may impact the pharmaceutical trade in other Member States given, e.g. the operation of healthcare authorities' reference pricing policies, the fact that suppliers may sequence their national launches of a new drug in order to obtain the most favourable prices/terms they can, and the fact that one Member State's experience with a drug may influence other Member States' cost/benefit assessments and evolving standards of care. The launch of a new drug also may pressurise demand for older drugs, leading to adjustments in their prices and availability not only in Member States where the new drug is available but also in others where the supplier(s) of older drug(s) may try to recover sales volumes lost to their new rival. Once a new drug is placed on the market, some parallel trading is likely to occur.[551] And Member State responses to a launch may inform suppliers' assessments of the relative profit potential in various diseases or drugs, thereby affecting the course of future innovation.

In sum, it seems clear that drug development worldwide, and the supply of drugs in the EU, are likely to affect trade between EU Member States to some extent. However, such effects can support an assertion of jurisdiction only if they are appreciable.

As noted in Commission Guidelines, appreciability "is to be appraised in particular by reference to the position and the importance of the parties on the market for the products concerned."[552] It may be somewhat challenging to make such assessments with respect to potential killer acquisitions in the pharmaceutical sector, when one or

[548] See, e.g. Case IV/27.442 — Vacuum Interrupters (1977/L 48 /32) and (1980/L 383/1); Case IV/32.363 — KSB/Goulds/Lowara/ITT (1991/L 19/25).

[549] For example, the EMA has reported that, in one five-year period (2007-2011), it received MAAs supported by the results of pivotal trials that were conducted in 72 countries outside EFTA, including the US, Canada, Australia, Turkey, Russia, Ukraine, Israel, South Africa, India, China, Japan, South Korea, Taiwan, Thailand, Argentina, Brazil, Chile, and Mexico. EMA, Clinical trials submitted in marketing-authorisation applications to the European Medicines Agency, EMA/INS/GCP/676319/2012 (2013) (https://www.ema.europa.eu/system/files/documents/other/wc500016819_en.pdf). The EMA is supported in its evaluation of these MAAs by widespread adoption of common norms of Good Clinical Practice and increasing standardization of records and formats. Such measures are promoted primarily through the International Council for Harmonization of Technical Requirements for Pharmaceuticals for Human Use (ICH), an organization formed in 1990 of which the EMA, the FDA, and Japan's PMDA are the founding members.

[550] Although the Commission has confirmed in countless pre-merger reviews that finished drugs are sold in national markets, its Guidelines make clear that the existence of an appreciable effect on trade between Member States is determined with regard to different criteria and may be confirmed where markets are national or smaller. See Effects on Trade Notice, paragraph 22.

[551] The effects mentioned above are not necessarily limited by the scope of the EU marketing authorisation because a drug, once it is placed on the market, may lawfully be used off-label for non-approved indications.

[552] Judgment of 28 April 1998, Javico International v Yves Saint Laurent Parfums, C-306/96, EU:C:1998:173, paragraph 17.

both of the parties' products are still in development and a market for them may not yet exist.

Determining whether the parties' position and importance in an area of competitive overlap are such that their combination can appreciably affect trade is likely to require a preliminary assessment whether their pipeline drugs are sufficiently similar to existing drugs that healthcare providers might consider both the new and existing drugs in selecting a course of treatment. If they are likely to do so, jurisdiction might be confirmed with reference to the shares of the parties and their rivals on the markets for the existing drugs (assumedly in EU Member States where they are sold).[553] Pipeline competition between the parties would be of limited significance to the jurisdictional assessment (though it could carry greater weight in a substantive assessment) because the existing drugs would be regarded on a *prima facie* basis as effective competitive constraints in the development and supply of the newer ones. However, the threshold for a finding of appreciability is not high; the transaction might be deemed incapable of appreciable effects only if the parties' combined share of the existing market does not exceed 5% and their combined turnover in that market is not over €40 million.[554] Because a potential killer acquisition is likely to arise only where the parties' pipelines are competitively important, it appears unlikely that they would escape review under this test.

A different assessment must be made if the parties' pipelines might be regarded as sufficiently unique that they are likely to create their own demand in a future market where the existing drugs are not regarded as acceptable substitutes for them. If that is the case, an evaluation of appreciability might well entail the identification of other firms who are developing drugs that may compete with the parties' drugs in the future market and who are similarly situated (given, e.g. their development timetables and stages of development, resources for further development, and the like). Because the innovators who are relevant to the assessment are those that are similarly situated to the parties, equal shares might be attributed to each of them, after which it might be concluded that a combination of the parties is unlikely to have appreciable effects if their combined share is below 20-25%.

In any case, we note that an assertion of regulatory competence under Article 22 need not be based on the rigorous factfinding and analysis that the Commission must undertake in a substantive review. Accordingly, it appears likely that the Commission can establish that a transaction is capable of affecting trade between Member States to an appreciable extent, and that it therefore is competent to conduct a review.

II.2.3.2.2 Effect on competition in Member States

Reasoned requests for referral under Article 22 must address not only a transaction's ability to affect trade between Member States but also the threat that it may have a significant effect on competition in the Member State that requests referral. In this regard, materials that are readily available either through normal regulatory contacts or through desk research online are likely to provide the requisite information.

[553] See Effect on Trade Notice, paragraph 52. While shares normally are assessed in individual Member States when concentrations are reviewed under the EUMR, it would appear reasonable to consider the parties' share in the EU as a whole in a jurisdictional assessment that turns on potential effects among two or more Member States.

[554] Effect on Trade Notice, paragraph 52.

Some referral requests may be initiated by NCAs that have received filings under their merger control laws, which should have sufficient information in them to provide a basis on which a request for referral can be made (or further information sought).[555] In other cases, where a transaction comes to the attention of an NCA that is not in receipt of a notification, previous decisions of the Commission or other competition regulators who publish reasoned decisions in their reviews may provide some background that is of assistance in preparing a request. In any event, online industry newsletters and blogs regarding recently announced transactions, while typically lacking much detailed information, often provide entry points (i.e. the names of leading companies and products that can be used as search terms) for further online research.

In assessing parties' notifications and regulatory precedents, as well as in cases where such material is not available, an NCA that is preparing a request for referral can be guided by the methodology that is typically used in reviews under the EUMR, in which potential pharmaceutical overlaps are identified in the first instance (and subject to later investigation) with reference to drugs' therapeutic indications (TIs) and mechanism of action (MoA).[556] These can be identified for drugs that are already on the market with reference to online databases that are intended for consumer use (of which one that is well regarded and generally free of commercial bias is Drugs.com). The MoA and potential TIs of experimental drugs and drugs that are being developed for new therapeutic uses can readily be identified on ClinicalTrials.gov (which is relatively comprehensive and accessible free of charge) or on subscription databases like Biomedtracker and AdisInsight Drugs.[557]

Some desk research online can provide extensive amounts of information very quickly, given the frequent publication of articles by researchers (regarding clinical trials and the preclinical development of promising treatments) and by healthcare providers (setting out their observations regarding the clinical/cost effectiveness of particular products and their substitutes). These can often be accessed on PubMed (www.pubmed.ncbi.nlm.nih.gov), an online database of professional articles, accessible to the public internationally free of charge, that is maintained as part of the National Library of Medicine of the U.S. National Institutes of Health. Accordingly, a productive research strategy is often to identify basic search terms (i.e. company and product names) from online newsletters/blogs, use a general search engine (e.g. Google) to find a professional article on PubMed that is reasonably on point, and then follow a link from that article (which might well be too narrow or technical for present purposes) to more general material (typically an overview of current research or metanalysis of numerous studies) through a review of the titles of earlier articles that are cited by, and later articles that cite, the entry-point article. An alternative means of accessing relevant material on PubMed is to follow links to specific articles that are included in the

[555] This was the case in the initial requests for referral of J&J/TachoSil (Germany) and Cochlear/Oticon Medical (Spain). The Illumina/GRAIL transaction, for which the initial referral request was made by France, was not notified in any Member State.

[556] See generally, e.g. Novartis/Oncology, paragraphs (24)-(33) (assessment of pipeline overlaps) and (89)-(94) (assessment of overlapping clinical research programs).

[557] The extent to which drugs might be substitutable for each other (in cases where generics are not an issue) depends primarily on their safety and efficacy, rather than pricing or other commercial data points. See generally, e.g. Judgment of 1 July 2010, AstraZeneca v. Commission, T-321/05, EU:T:2010:266, appeals dismissed, Judgment of 6 December 2012, AstraZeneca v. Commission, C-457/10 P, EU:C:2012:770.

descriptions of specific trials on ClinicalTrials.gov.[558] In any case, the professional articles that can be accessed on PubMed follow a fairly standardized format, and the information that is most relevant to a preliminary competition-law assessment is typically found in the abstract and Introduction at the beginning of the article and in the Discussion at the end.[559]

While different research strategies will work best for different people, the material that is relevant for a basic competition assessment, prior to the initiation of a formal review, can normally be retrieved online very quickly. It appears likely that the Commission and NCAs can optimise the results of such research if it is done by someone who has read about treatments for a variety of diseases, so that the landscape and jargon are familiar, but professional medical qualifications are not required. A review of this nature will often be enough to identify candidate markets and the drugs that are being supplied or developed by leading companies (and, therefore, is likely to afford a reasonable understanding whether an inquiry might be warranted).[560]

Further information might be obtained by issuing RFIs to, and having distance interviews with, the parties and other market participants (e.g. customers, competitors, and knowledgeable opinion leaders), as is commonly done in the Commission's pre-notification preparations for receipt of a formal filing. Proactive complainants also may be a source of relevant information.

In cases presenting a potential competitive threat to innovation competition *per se*, it appears reasonably likely that the area of overlap will be apparent without extensive analysis. Because this analysis focuses on competitors' R&D capabilities (rather than their commitments to the development of particular products), innovation spaces can be defined much more broadly than the product markets they supply.[561]

[558] While PubMed has a search function itself, it caters to professional researchers and can yield unwieldy volumes of material for the layperson, while the kinds of search strategy suggested in the text may yield useful results more quickly.

[559] Indeed, it is frequently easier to obtain reliable information about drugs that are in development than it is about drugs that are on the market, because searches relating to the latter often yield results that are laden with relatively basic material that reflects the bias of industry sponsors and advertisers. In any case, while materials available on PubMed are usually prepared for a professional readership and therefore are of reasonably high quality, it is always necessary to ascertain the financing and purpose for a publication in order to ensure proper sensitivity to any biases it might reflect.

[560] Our desk research suggests that oncology (and, secondarily, autoinflammatory diseases) may be the most difficult areas for the non-specialist to assess, because companies are pursuing many new therapies, the science is complex, and it often is not clear what drugs might be acceptable substitutes for each other in treating different patient populations. Such questions can arise, e.g. because a single type of cancer may result from a number of different genetic mutations (so that a drug that targets one mutation will not work for patients who have the same type of cancer as a result of different genetic mutations) or, in some cases, a therapeutic indication (e.g. rheumatoid arthritis) is not a single disease but a syndrome (i.e. a group of symptoms that have a variety of causes). While we were able to assess these with the assistance of pharmaceutical experts on the team, a regulator may simply note such uncertainties as reason to investigate, as the standard that must be met in order to justify the initiation of a review is less demanding than what is required for a final determination.

[561] Thus, for example, the innovation spaces defined in Dow/DuPont were much more general (i.e. herbicides, fungicides, and insecticides) than the related commercial markets (which were defined with reference, e.g. to specific types of weeds and crops). Case M.7932 – Dow/DuPont (27.3.2017); see also Case M.8084 – Bayer/Monsanto (21.3.2018).

II.2.3.2.3 Effects outside the EU

Despite the foregoing, once a transaction has been announced, it is not always possible to detect potential issues in a timely manner, before the parties have completed their deal and "scrambled the eggs." While an informal review of readily available information (e.g. the parties' public statements, analysts' reports and the like) and direct inquiries to the parties or other industry sources may go some way in clarifying matters, essential information and cooperation may be limited prior to the initiation of a formal review. In such cases, it appears that the Commission's understanding of facts and concerns that might warrant an Article 22 referral may be further clarified by reference to developments in the US (which, as the world's largest pharmaceuticals market, is often deeply involved in both the commercial and regulatory aspects of the sector).

While we did not consider the relevance of developments outside the EU in any systematic way in this study, the research we conducted as part of the fact-finding challenge shows that the same molecules and therapeutic indications often are studied in clinical trials in both the US and the EU.[562] Moreover, the cases we reviewed as part of the evaluation challenge, while they were more limited in number and had *prima facie* relevance to different issues, also indicate that drugs that are launched successfully in the US are often launched in the EU. Other studies that we have reviewed over the course of this study confirm that the EMA and FDA each receive significant numbers of MAAs from the same applicants, for the same drugs, and reach broadly consistent results.[563]

Similarities in regulatory approaches and outcomes of the EMA and the FDA appear to be far larger than any differences, and such differences as exist appear to be narrowing. Moreover, it is reasonably clear that the assessments made and positions taken by the EMA and FDA are not influenced by commercial considerations that otherwise might reduce their utility in analyses of competition.[564] Accordingly, our assessments appear to confirm that evidence and insights from the US may have some utility in assessing the merits of referral under Article 22.

II.2.3.2.4 Cautionary observations

A number of cautionary observations are worth making. Firstly, the judgement of the European Court of Justice in the Illumina / GRAIL case has shed light on the conditions under which referrals based on Article 22 EUMR can be accepted by the Commission. As made clear in that ruling, such referrals may only be made by Member States having competence over the concentration they intend to refer to the Commission, or by Member States having no merger control regime of their own. On the contrary, Member

[562] More specifically, our comparison of data in the EUCTR and ClinicalTrials.gov for the period 2000-2022 found that 59% of the trials registered on the EUCTR also were registered on ClinicalTrials.gov, and that 98% of the 6783 drugs studied in the 16,656 trials that were reported only in the EUCTR also were the subject of studies that were registered on ClinicalTrials.gov.

[563] See, e.g. UP Rohr et al., A decade comparison of regulatory decision patterns for oncology products to all other non-oncology products among Swissmedic, European Medicines Agency, and US Food and Drug Administration (2023) (https://ascpt.onlinelibrary.wiley/com/doi/full/10.1111/cts.13567); M. Kashoki et al., A Comparison of EMA and FDA Decisions for New Drug Marketing Applications 2014-2016 (2020) (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC6977394/).

[564] See generally, e.g. T. Teixeira et al., Are the European Medicines Agency, US Food and Drug Administration, and Other International Regulators Talking to Each Other? (2019) (https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7028217/); J. Sederstrom, The Geography of Drug Approvals (2017) (https://ashpublications.org/ashclinicalnews/news/3315/The-Geography-of-Drug-Approvals).

States with a national merger control regime but lacking competence over a concentration may neither initiate nor, join, in a referral request under Article 22 EUMR.

Secondly, it might be noted that there is a potential downside to relatively expansive application of the EUMR (whether through the review of transactions referred under Article 22 or, more generally, revision of the current, turnover-based tests of jurisdiction). Recent experience from merger reviews in innovation-intensive industries has highlighted the difficulty of predicting how those industries will develop, and the corresponding risk of "false negatives" (i.e. clearance of transactions *ex ante* that might have drawn greater regulatory scrutiny or intervention several years later, as their competitive significance became more apparent). This appears to be particularly true in the digital sector.

In *Towercast*, Advocate General Kokott highlighted issues that might arise if a regulator attempted to challenge *ex post* a transaction that was previously cleared *ex ante*. Her conclusion was that, given the principle of legal certainty, "the legislature intended to exclude such a double assessment in principle, as is apparent from Article 21(1)":

> Article 102 TFEU would indeed remain applicable in principle. However, a concentration which has been approved under the more specific rules of merger control, and the effects of which on market structure and competition conditions have been declared to be compatible with the internal market, could not as such be qualified (any longer) as an abuse of a dominant position within the meaning of Article 102 TFEU, unless the undertaking concerned has engaged in conduct which goes beyond that and could be found to constitute such an abuse.[565]

The same risk might exist under Article 101. Accordingly, the benefits of an *ex ante* review undertaken before any competition concerns have materialised (in order to prevent possible harm to the market or irremediable integration of the parties' operations) may have to be balanced against the risks of regulatory preclusion (where a transaction is approved and later developments make clear the need for *ex post* intervention that then cannot be pursued).[566]

Lastly, as a cautionary observation, it should be highlighted that the Commission cannot unilaterally call in a deal that it considers may merit review under Article 22 EUMR; the Commission can only invite, but not compel, Member States to request a referral.[567] Consequently, if a Member State does not make a timely referral request, either on its own initiative or in response to the Commission's invitation, the Commission is unable

[565] Towercast, Opinion of AG Kokott, paragraphs 59-60.

[566] This situation might be contrasted with that in the US, where the antitrust regulators are currently seeking to compel the divestiture, under laws prohibiting anticompetitive conduct and monopolisation, of companies that Facebook (Meta) and Google acquired without challenge during HSR pre-merger review. The cases are not subject to legal preclusion in the US, as might apply in the EU, because lack of a challenge during HSR review does not constitute approval of a transaction; rather, it simply reflects the government's decision not to avail itself of the procedural advantages afforded during ex ante review. See Case 1:23-cv-00108, United States et al. v. Google (E.D.Va. filed 24 January 2023) (https://www.justice.gov/opa/pr/justice-department-sues-google-monopolizing-digital-advertising-technologies) and Case 1:20-cv-03590-JEB, FTC v. Faceboook (D.D.C. filed 9 September 2021) (https://www.ftc.gov/system/files/documents/cases/2021-09-08_redacted_substitute_amended_complaint_ecf_no._82.pdf).

[567] Article 22(5) EUMR.

to assess or to remedy any potentially anticompetitive effects of the deal on national markets in that Member State.

II.3 The EUMR-Antitrust interface

Prior to adoption of the first Merger Regulation, the CJEU held that the Commission could review potentially problematic transactions under Articles 101 (as unlawful coordination) and 102 TFEU (as abuses of dominance).[568] However, the first Merger Regulation[569] established a clear distinction between concentrations, which are subject to merger control, and other acts and agreements that are subject to antitrust law.[570] The EUMR now operates as a part of a unified system in which these elements complement each other in protecting and promoting undistorted competition.[571] The CJEU recently made clear, in *Towercast*, that Article 21(1) EUMR does not preclude an NCA's application of Article 102 TFEU to a completed concentration that did not trigger *ex ante* review at the EU or Member State levels and was not reviewed under Article 22 EUMR.[572]

Immediately after the CJEU issued its judgment, the Belgian Competition Authority (BCA) gave it practical effect, opening an investigation into the acquisition by Proximus, a leading operator in Belgium's telecommunications sector, of EDPnet, a competing retail operator and wholesale customer. The € 20 million transaction was undertaken in a judicial reorganisation with EDPnet's creditors, and was not subject to *ex ante* review. The BCA secured a ruling from the Competition College that a *prima facie* case of abuse of dominance had been made under Article 102 TFEU and corresponding national law, and obtained interim measures to ensure EDPnet's operational and commercial independence pending its investigation.[573] The hearing in that case was the first opportunity to address various questions left open in *Towercast*, including uncertainty about the legal standard to be applied in an *ex post* merger review,[574] the kind of

[568] Judgment of 18 April 1975, Europemballage and Continental Can v Commission, C-6/72, EU:C:1973:22; Judgment of 17 November 1987, British-American Tobacco and R.J. Reynolds Industries v Commission, C-142/84 and C-156/84, EU:C:1987:490.

[569] Council Regulation (EEC) No 4064/89 of 21 December 1989 on the control of concentrations between undertakings (1989/L 395/1) (ECMR), repealed and replaced in 2004 by the EUMR.

[570] That boundary, now found in Article 21(1) EUMR, was initially established in Articles 22(1)-(2) ECMR.

[571] See, e.g. Judgment of 31 May 2018, Ernst & Young v Konkurrencerådet, C-633/16, EU:C:2018:371 (rejecting an interpretation that would treat non-full function JVs as concentrations); Austria Asphalt (2017) (rejecting an interpretation that would treat non-contributory transactions as implementation of a concentration).

[572] Judgment of 16 March 2023, Towercast v Autorité de la Concurrence, C-449/21, EU:C:2023:207.

[573] BCA, Competition College Decision N° 23-RPR-17 of 21 June 2023, Proximus/EDPnet, CONC-RPR-23/0002 (https://www.belgiancompetition.be/en/decisions/23-rpr-17-proximus-edpnet) (French language).

[574] The BCA took the position that the standard discussed briefly at the end of the CJEU's judgment in Towercast is essentially the same as the SIEC standard applied in ex ante reviews under the EUMR, while Proximus argued for a more restrictive standard based on the nature of an ex post review.

remedies that might be sought,[575] and other procedural questions.[576] However, none were resolved definitively because Proximus voluntarily divested itself of EDPnet a few months after interim measures were imposed, and the BCA then terminated proceedings.[577] In any event, the BCA's initiation of this case so soon after the CJEU delivered its judgment in *Towercast* suggests that some NCAs may regard Article 102 TFEU as an important tool in closing a perceived enforcement gap.

The CJEU's judgment in *Towercast* maintains a clear distinction between merger control and antitrust, recognising that an NCA must proceed under national rules of procedure in challenging a concentration under Article 102 TFEU, as described above.[578] However, the Commission and the NCAs also may apply antitrust rules to address competitive harms that are separate from but related to a concentration, as exemplified in the case studies section below (see section II.4). Article 101 TFEU and Article 102 TFEU may be valuable tools to address killer acquisitions that are not structured as concentrations within the meaning of the EUMR. The applicability of these rules depends on various elements, such as the specific features of the case, the companies involved and their market position, the agreements concluded, or the type of conduct observed as well as the potential harm to competition.

In particular, in the following sections we describe two case studies, where we show how the Commission could apply the tools at its disposal to deal with two fictitious potentially harmful transactions. We started from the facts of two cases that were highlighted in the fact-finding challenge as warranting further scrutiny, and then, using a number of assumptions that allow to conduct the analysis, we simulate the assessments that could be conducted under Article 22 EUMR and Articles 101 and 102 TFEU.

The first case study starts from the facts of a concentration below threshold and provides the assessment under Article 22 EUMR tailored to the specific, hypothetical, facts

[575] While Advocate General Kokott suggested in her opinion that fines rather than dissolution of the concentration would be expected in view of the primacy of behavioural remedies and the principle of proportionality (Opinion delivered 13 October 2022 (KOKOTT, A.G.), Towercast v Autorité de la concurrence, C-449/21, EU:C:2022:777, paragraph 63), the BCA's request for a Hold-Separate order and arguments made during the hearing suggest that they may well have been preparing to seek divestiture.

[576] Among them was Proximus' argument that, in the interests of a speedy resolution, legal certainty and good administration, the BCA should have sought referral under Article 22 EUMR rather than proceeding under Article 102 TFEU. The Competition College disagreed.

[577] BCA Press Release (6 November 2023) (https://www.belgiancompetition.be/sites/default/files/content/download/files/20231106_Press_release_51_BCA_pdf).

[578] We note that the Commission has a duty under Article 105 TFEU to ensure application of the principles laid down in Articles 101 and 102 TFEU, and that its ability to do so prior to the adoption of the first implementing regulation (as anticipated in Articles 104 and 105) was confirmed in the Judgment of 6 April 1962, Kledingverkoopbedrijf de Geus en Uitdenbogerd v Robert Bosch, 13/61, EU:C:1962:11, paragraph 1. It therefore might be argued that the Commission can apply Articles 101 and 102 to concentrations even without recourse to the powers of investigation and enforcement established in Regulation No 1/2003 and with the kind of assistance at the national level that was envisaged when the Treaty was first ratified. It might be noted in this regard that the ECMR was based on Articles 235 and 87 of the EC Treaty (as the EUMR was based on Articles 308 and 83 TEC), which provided only for additions to the powers, and measures that give effect to the principles, established in the Treaty, and the Commission reserved its right to challenge concentrations that do not have a Community dimension during discussions about adoption of the ECMR (Interpretive Notes on Council Regulation (EEC) 4064/89 (https://ec.europa.eu/competition/mergers/legislation/ notes_reg4064_89_en.pdf)). However, we note that this is the view of the authors of this Report, and may not accord with the current views of the Commission.

assumed in that case. The other case study uses the facts of another deal as a starting point. Since there are questions about whether it is appropriate to characterise that deal as a concentration or as a technology transfer, we formulated two distinct scenarios: one where the transaction can be seen as a concentration - and hence the Article 22 EUMR assessment is conducted - and one where it can be seen as structured as a license agreement - and hence the Article 101 and 102 TFEU assessments are carried out.

II.4 Case studies

II.4.1 Case Study #1

II.4.1.1 The Parties

Company A is a global pharmaceutical company headquartered in Japan that was focused, when it acquired Company B, on the development and commercialization of drugs to treat various therapeutical indications ("TIs"). Among its numerous pipelines, Company A was developing a molecule (*Pipeline a*) that was in a Phase II trial in the US for treatment of TI 1.

Company B was a US-headquartered biotech company. The company was developing *Pipeline b*, which was in a Phase III trial internationally for treatment of TI 1, and two other molecules that were in early stages of discovery/development. Company B had not yet developed a marketable product and was consistently loss-making, with forecast losses and negative cash flows for another three years.

II.4.1.2 The Transaction

In December 2013, Company B began an extensive effort to develop partnerships outside the US, in order to obtain resources required to develop *Pipeline b* for additional TIs and to ensure that *Pipeline b* could be commercialised effectively outside the US. However, those efforts met with little success, and were particularly challenging because volatility in Company B's stock price made it difficult for Company B and potential partners to agree on how a deal should be valued.

Company A appears to have shown relatively little interest in acquiring Company B, despite earlier (inconclusive) discussions about partnering possibilities, until sometime in 2014, when the parties appear to have begun serious discussions about a possible acquisition. Following due diligence and negotiations, the companies signed a definitive merger agreement, under which Company A would complete the transaction by means of a tender offer that had the unanimous support of Company B's Board.

II.4.1.3 Identifying cases for review (competitive overlaps and landscape)

The Team's desk research revealed that Company A's acquisition of Company B might merit further inquiry, as there are elements of the case supporting a killer acquisition narrative.

First, there was a pipeline-to-pipeline overlap, based on the products' common mechanism of action ("MoA 1") and TI, between Company A's *Pipeline a* and Company B's *Pipeline b* for TI 1. The relevant market appears to be appropriately defined based on the MoA and the TI, without distinction by lines of treatment.

Second, we observed an unexplained elimination of the overlap. Although Company A was conducting a Phase II trial of *Pipeline a* for treatment of TI 1 in late 2014, when it acquired Company B, it announced that the pipeline had been discontinued. Moreover, in contrast to its announcement of other pipeline discontinuations around the same time, Company A did not explain this as a decision made in light of its review of clinical trial results – instead, Company A noted that its decision was based on strategic

considerations. In fact, when the trial was completed in 2018, company researchers reported that the results were supportive of the further development of the molecule.

The Team's pharmaceutical experts reviewed the results of Company A's trial, and concluded that although they were not as strong as the results that were obtained in clinical trials of a competitors' pipeline (*Pipeline c*, which was approved as a treatment for TI 1 in 2018), they supported further development of *Pipeline a* as a treatment for TI 1 patients who are newly diagnosed (an easier-to-treat population). Indeed, *Pipeline b* was approved for marketing as a first-line treatment in both the US and EU after approvals to market it as a second-line treatment were refused.

Finally, there were relatively few competitors: No MoA 1 drugs had been approved for treatment of TI 1 when Company A acquired Company B, and there were only four other MoA 1 molecules in development. Moreover, the failure of other pipelines over the last 10-15 years (with the consequent exit of several of the earliest developers) gave reason to assume that not all of those who were testing MoA 1 compounds would succeed. Accordingly, an acquirer might have considered it likely that there would be sufficiently few competitors to make a killer acquisition attractive.

Given the foregoing, this transaction appears to have presented several hallmarks that might be indicative of a killer acquisition. However, the information available in the public domain is not sufficient to conclude whether this transaction is a killer acquisition, and actually certain elements could represent evidence (or at least be interpreted as) discrediting a killer acquisition narrative. Therefore, in the following section we make a number of assumptions that allow us to create a hypothetical case supporting a killer acquisition narrative. Under these assumptions, we then assess whether this fictitious case – being a concentration below threshold - would warrant review under Article 22 EUMR.

II.4.1.4 Case assumptions

We make the following assumptions, which allow us to eliminate possible doubts regarding the killer acquisition nature of this case:

- the relevant market, where the above assessment of the number of competitors has been conducted, is the one MoA 1 pipelines for the treatment of TI 1, without distinction by line of treatment. If the market was defined also based on the line of treatment, we would conclude that both *Pipeline b* and *Pipeline a* had been discontinued in the market for second-line treatment; instead, in the unique market including multiple lines of treatment we have identified, *Pipeline a* has been discontinued and *Pipeline b* was marketed (as first-line treatment);
- the Team's interpretation of trial results (according to which *Pipeline a* merited further development for treating first-line TI 1) is correct; and
- the various merger and pre-merger documents developed by the parties (that are available in the public domain) do not hinder a killer acquisition narrative.

II.4.1.5 Detecting and evaluating referral under Article 22 EUMR

Because Company B had no product sales in 2013, and had very limited turnover (from, e.g. its role in co-operative development programmes), its acquisition by Company A received little *ex ante* review. The parties notified the transaction in the US, and the HSR waiting period (which is only 15 days for cash tender offers) expired without challenge. The transaction did not trigger any pre-merger filing requirements in Europe, and no request for referral was made under Article 22 EUMR. Accordingly, detection of this transaction would have required review of the kinds of material identified in section II.2.1 above.

As discussed more generally in section II.2.3 of this Report, there appear to be good arguments that a transaction like this was capable of causing an appreciable effect on trade between Member States. First and foremost, it should be noted that amongst the most appropriate cases for referral there are those where the affected markets are wider than national and the main impact of the concentration is on such markets. [579] Since the concentration considered in this case study affects pipeline markets, that are typically EEA-wide or global in scope, this case appears to fall in that category.

The most direct and immediate effects of the transaction were likely to be seen in trade in the services (and, secondarily, goods) related to the performance of clinical trials. Company B was conducting its Phase III trial of *Pipeline b*, at the time it was acquired, at 70 investigational sites in eleven EU Member States. Trial sponsors sometimes add, drop, or limit activity at their investigational sites during a trial (given, e.g. the ease or difficulty of enrolling patients, accruing costs, and other considerations), and Company A's control of the trial, following its acquisition of Company B, might well have led to decisions different than Company B was making in how the trial would be completed. It also might be noted that Company A was an active sponsor of clinical trials in the EU; indeed, it had recently sponsored a Phase I trial of *Pipeline a* (for treatment of a different TI than TI 1) in 2 Member States and, less than six months after it acquired Company B, initiated a Phase III trial of *Pipeline a* for yet another TI in nine EU Member States. Moreover, when Company A initiated a Phase III trial of *Pipeline b* as a first-line therapy for TI 1, after it acquired Company B, it included 13 EU Member States among the 28 countries in which it conducted the trial. As discussed in section II.2.3, since the parties were active drug developers in the EU, suggesting that they had intentions to launch their products in the EU, the transaction appears capable of having an effect on trade between EU Member States.

Insofar as neither Company A nor Company B had begun to market a MoA 1 drug for treatment of TI 1 in 2014, it might be questioned whether their concentration was capable of having an effect on trade that was appreciable.[580] However, several considerations might be noted in that regard.

First, the magnitude of the requisite effect on trade is not high. It might be shown that the concentration could have an appreciable effect because the trial activity by Company B and Company A could impact the maintenance or cost of the relevant services in the Member States concerned (as, for example, contract research organisations (CROs) must have some scale of operations in order to maintain the local infrastructure and professional staff that are required to carry out trials on a cost-effective basis). Moreover, it might be relevant that Company A had a tendency (or not) to concentrate its trials in specific Member States (so that a change of control of its new business came at the expense of other Member States). In any event, the range of decisions to be made regarding the location of clinical trials, how they are carried out (e.g. with

[579] Commission Notice on Case Referral in respect of concentrations, paragraph 45.

[580] Cf. J&J/Tachosil (2019), where the Commission found that the transaction for which referral was sought "gives rise to overlaps involving products sold in several Member States and, therefore, is by its very nature capable of affecting trade between Member States" (Decision regarding the request for referral by Germany, paragraph 19).

particular CROs, through local in-house facilities, and the like) or, indeed, how many trials to perform, is likely to have some effect on local suppliers.[581]

More generally, it might be argued that Company A's acquisition of Company B was capable of causing an appreciable effect on trade between Member States because it involves an overlap in pipelines that the parties intended to launch in Europe and that the EMA has designated of high importance, affording it "orphan drug" status, fast-track treatment and quickly approving each of the three MoA 1 drugs that are available on the market now. In *Illumina/GRAIL*, where the target had not yet launched a product on the market, the Commission found the requisite effect on trade between Member States when considering that "the combined entity could restrict access to or increase prices of next generation sequencers and reagents to the detriment of GRAIL's rivals," noting further that referral was appropriate because "[g]enomic cancer tests, having the potential to identify a wide variety of cancers in asymptomatic patients, are expected to be game-changers in the fight against cancer" and it was "important to ensure that patients get access to this technology as quickly as possible, from as wide sources as possible, and at a fair price."[582]

While the Commission focused its comments for purposes of a brief press notice on immediate effects relating to the pipeline products at issue, it also might be noted that the elimination of a pipeline (if there are indications that it is intended to be or would likely be marketed in Europe), where competing alternatives are limited, is likely to affect inter-state trade in medicines, impact healthcare systems, and have all the repercussions of effective (or ineffective) healthcare delivery that are likely to result when the scope or pace of drug development are reduced or the prices of finished drugs are increased. Even an attenuated or uncertain effect therefore might justify the assertion of jurisdiction to review a transaction that resulted in ownership of two (rather than one) of the few MoA 1 compounds being developed for TI 1, when the odds of all of the pipelines succeeding were not high and there is a need for multiple drugs in order to combat the adaptive resistance of TI 1.

Substantial amounts of information about the nature of the parties' negotiations and Company A's plans for post-closing operations was publicly available before this transaction was consummated, because the acquisition of a publicly held company by means of a tender offer requires extensive disclosures to actual and potential shareholders. While a review of some of the other kinds of material identified in section II.2.1 above would have been necessary to place these disclosures in context, these filings might well have flagged this transaction as one that merited *ex ante* review.

This transaction appears to be among the types of cases that would likely be considered to deserve scrutiny and appropriate for an Article 22 referral, to the extent that the target was an innovator that was conducting important research and had turnover that did not reflect its future competitive potential, and insofar as the transaction gave rise to a pipeline-to-pipeline overlap in a therapeutic indication where there was unmet demand at the time of the deal and limited competition.[583] Would such a transaction be assessed in the light of publicly available information and a request been made, it

[581] Cf. Judgment of 30 January 1985, Bureau national interprofessionnel du cognac v Guy Clair, 123/83, EU:C:1985:33, paragraphs 28-30; Judgment of 28 February 2002, Compagnie Générale Maritime v Commission, T-86/95, EU:T:2002:50, paragraphs 145-149.

[582] EC Press Release (20/4/2021).

[583] See Section II.2.3 above.

appears likely that the Commission would accept referral, provided that the requesting Member State is competent to review the transaction under its national merger control rules, or does not have any merger control regime.

II.4.2 Case Study #2

II.4.2.1 The Parties

Company A is a global pharmaceutical company whose leading product at the time of the acquisition was *Drug a* for various therapeutical indications ("TIs"). *Drug a* was (and is) supplied only to trained professionals for precisely targeted injections into target muscles/tissues in order to achieve the desired effect. It was the first drug with that Mechanism of Action (hereinafter, also "MoA 1") to be approved for human use, and Company A was (and remains) the leading supplier of such group of drugs worldwide.

Company B was a clinical stage biotech company that was developing *Pipeline b*, a molecule with the same MoA as *Drug a*, that was formulated with proprietary excipients that reportedly made it possible to administer the drug transdermally (rather than by injection). At the time of the acquisition, Company B was developing *Pipeline b* as a treatment for TI 1, TI 2 and TI 3. In April 2015 (roughly nine months before it was acquired by Company A), Company B announced an intention to list its stock on NASDAQ, with plans to use the proceeds principally to fund Phase II and III trials of *Pipeline b* for treatment of TI 1 and TI 2, as well as to further develop an injectable molecule (*Pipeline c*) for TI 1 (for which a transdermal drug is ineffective). However, Company B had the ill fortune to attempt its initial public offering (IPO) just as the market for new issues went into a substantial dive.[584] Company B withdrew from its IPO – the fourth company to do so that week – after several weeks of unsuccessful efforts to price made it apparent that the company was unlikely to raise the amount that was originally anticipated.

II.4.2.2 The Transaction

In January 2016, Company A announced that it had acquired Company B and the price included an upfront payment and unspecified future milestone payments. Two facets of the deal might be noted in an assessment of what Company A's intentions might have been with respect to further development of *Pipeline b* after closing.

First, Company A disclosed in its annual report for 2016 the amount of the milestone payments it had agreed with respect to *Pipeline b* and its delivery technology. We note that such milestone payments were a very substantial part of the purchase price, and this fact might suggest that the parties expected Company A to continue developing Company B's pipeline. Alternatively, it also might have been the case that the parties negotiated these payments with little expectation that the milestones were likely to be met; negotiating a relatively low upfront payment against higher milestone payments would have been the optimal strategy for Company A if it planned to discontinue *Pipeline b*, and the Company B shareholders may have believed that the upfront payment itself

[584] See, e.g. Bob Pisani, CNBC, *Is biotech topping out? Markets shrugs at big week of IPOs* (7 May 2015) (https://www.cnbc.com/2015/05/07/is-biotech-topping-out-markets-shrug-at-big-week-of-ipos.html); Bob Pisani, *Stay calm, despite a poor end to the month* (30 April 2015) (noting that Biogen lost almost 12% of its market value in one week after disappointing earnings from several biotech firms). A brief review of blogs from the IPO sector suggests that it didn't recover until the latter half of July. Rennaissance Capital, *IPO market back on track* (July 17, 2015) (https://renaissancecapital.com/IPO-Center/News/334546/US-IPO-Weekly-Recap-IPO-market-back-on-track-as-tech-and-biotech-deals-fly-)

represented good value for the company. Accordingly, no firm conclusions can be drawn about the significance of these terms. However, it might be noted that although Company A routinely listed its potential liabilities for milestone payments on other projects in its annual reports, the only year for which it included any potential payments to Company B' shareholders were 2016 (the year it acquired the company).

Second, in the most fulsome description of the deal we have been able to find, Company A announced that it had acquired *Pipeline b*'s delivery technology and "global rights to *Pipeline b*," while a newly formed company (Company C) that was owned by Company B' shareholders received "certain assets" that were spun off by Company B and "certain non-exclusive rights to *Pipeline b*." As with the milestone payments, various inferences might be drawn from this. One might infer that Company A would not have agreed to Company C's acquisition of any of Company B' former assets or rights had it intended to kill Company B's pipeline. However, in the authors' view, any such inference appears speculative without more information about what assets and rights Company C actually obtained. Moreover, if Company B' shareholders made clear that they were not willing to sell all of the IPRs (and other assets) used in their former business, Company A may simply have decided that it was preferable to acquire some of them rather than nothing (particularly if doing so would at least delay, and perhaps deter, development of a competing technology). In any case, given the limited evidence available in the public domain, no firm conclusion can be reached either way.

II.4.2.3 Identifying cases for review (competitive overlaps and landscape)

The results of work on the fact-finding challenge revealed that Company A's acquisition of Company B might merit further inquiry, as some elements of the case support a killer acquisition narrative.

First, there were several market-to-pipeline overlaps, based on the products' common mechanism of action (MoA) and therapeutic indications (TIs) as reported by Adis:

- Company A's *Drug a* and Company B' *Pipeline b* for treatment of TI 1; and
- Company A's *Drug a* and Company B' *Pipeline b* for treatment of TI 2.

Company B completed its last trial of *Pipeline b* for the treatment of TI 1 in January 2014 and announced its plans three months later to conduct two more Phase 2 trials of *Pipeline b*, for treatment of TI 1 and TI 2, respectively. Company B initiated the first of those trials (for TI 2) in June, and it seems plausible that it would have initiated the second trial (for TI 1) had it not been drawn into negotiations with Company A instead. Accordingly, the authors believe that Company B was actively developing *Pipeline b* for treatment of both TI 1 and TI 2 at the time it was acquired, and that both projects are properly included in this study.

It should be noted that these overlaps might well be assessed, as a substantive matter, in candidate market(s) that are significantly broader (or narrower) (as discussed more fully below). However, the Commission often uses the MoA/TI pair to identify competitive overlaps, and the existence of such an overlap obviously is characteristic of potential killer acquisitions, so that this transaction might be flagged as one meriting closer assessment.

Second, we observed an unexplained delay of development of one of the overlapping molecules. The last clinical trials of *Pipeline b* conducted by Company B for TI 1 and TI 2 were a Phase II study for TI 1 completed in 2014, and a Phase II study for the treatment of TI 2 completed in February 2016. Similarly, we found no appreciable mention of Company B' delivery technology in company reports or materials relating to the pharmaceutical sectors following completion of the deal. Results from the last clinical

trials in TI 1 that Company B prepared were positive, showing both efficacy and a lack of notable side effects. Company A published results from a final trial in TI 2 that are instead negative, but (as discussed further below) the Team believes that this may have to do with the methodology adopted by Company A to report the results, and that under more frequently used methodologies the results could be seen as acceptable. Company C is now further developing *Pipeline b* (though under a different name) for TI 2 and TI 1 (and the pipeline is in Phase II trials). Accordingly, development of *Pipeline b* in the indications of overlap appears to have been delayed for several years. The discontinuation or the significant delay of overlapping products is an essential characteristic of potential killer acquisitions, and the facts noted above appeared to be clear indications that further assessment was merited here.

Third, we noted that the number of competitors might be limited to an appreciable extent. At the time of the transaction, there were only three competing suppliers of MoA 1 drugs approved for TI 1 or TI 2 use in Europe: Company A and two others. The number of companies conducting clinical trials for MoA 1 molecules in TI 1 and TI 2 was also limited. The number of competitors here invites a closer assessment whether there might have been appreciable incentives to invest in a killer acquisition.

Finally, the acquirer here appears to have a substantial long-term revenue stream at risk if competition increases materially. As has been noted previously, an acquirer that anticipates future revenues over a long period of time (e.g. because its product is covered by patents having lengthy terms yet to run) will have correspondingly greater incentives to protect its future revenue streams by eliminating a nascent competitor. In this case, Company A was earning a very substantial turnover from sales of *Drug a*, for which trade secrets (if carefully maintained) may afford protection of essentially limitless duration. Accordingly, the prospect of open-ended and substantial revenues might be regarded as another reason this transaction merits closer assessment.

While the foregoing elements obviously are not in themselves sufficient to conclude that Company A acquired Company B in order to eliminate potential competition, the conjunction of these four elements, in the authors' view, may be indicative of potential competition concerns that possibly could have drawn an in-depth investigation had the transaction been notified anywhere (as apparently it was not) or otherwise come to a competition agency's attention. In the following sections, under a set of assumptions that allow to eliminate possible doubts regarding the killer acquisition nature of the case and that ultimately allow to conduct an *ad hoc* assessment, we turn to consideration of various challenges the Commission might have met had it investigated this hypothetical case.

II.4.2.4 Case assumptions

The aim of the next sections is to simulate the assessments that the Commission would undertake if this was indeed a potentially problematic transaction. Since a number of elements of the case might potentially call into question a killer acquisition narrative (as detailed above), or because the evidence needed to conduct part(s) of the assessment may not be available in the public domain, we make a number of assumptions. In particular, we assume that:

- all exclusive rights over *Pipeline b* were granted by Company B to Company A as part of the transaction (i.e. no rights over the molecule were given to any third party, such as Company C). Accordingly, we consider that development of *Pipeline b* has been discontinued rather than delayed (as the fact that Company C is currently further developing the same compound, under a different name, is not taken into account);

- the results of the final clinical trial of *Pipeline b* in TI 2 were promising, i.e. they did not warrant the discontinuation of the molecule based on technical grounds;
- inactivity of *Pipeline b* in TI 1 for about two years prior to the deal does not mean that development of the molecule in that indication had been abandoned, i.e. *Pipeline b* was active in both TI 1 and TI 2 at the time of the deal;

Moreover, it should be noted that based on the very limited information that is available in the public domain, it is not clear whether the transaction should be qualified as a concentration or a license agreement. Information in the public domain is so limited that it is not clear whether Company A acquired the securities or assets of Company B. Accordingly, we develop two different scenarios: in the first one, the transaction is assumed to qualify as a concentration, and hence the Article 22 EUMR assessment (specifically tailored to the hypothetical facts of this case) is conducted; in the second one, it is assumed that it is structured as a license agreement, and hence the Article 101 and 102 TFEU assessments are carried out, again with reference to the specific, hypothetical, facts assumed in this case.

II.4.2.5 Scenario #1 (concentration): detecting and evaluating referral under Article 22 EUMR

Assuming that the transaction is a concentration, the deal would not trigger pre-merger filing requirements in the EU, because Company B was not yet marketing any products at the time of the transaction, and thus was not generating turnover.[585] The relevant question in this scenario is whether the case meets the requirements for review under Article 22 EUMR, and it appears that it does provided that the referring Member State would be competent under its national merger control rules, or not have a merger control system at all.

In addition to the possible the prima facie competition concerns outlined above, it appears that this transaction was capable of having appreciable effects on trade between Member States. Although Company B conducted all of its trials in the US,[586] it stated in 2015 that it intended to commence clinical trials in Europe and to seek marketing authorisation from the EMA. Company A, in turn, has conducted numerous trials of *Drug a* for treatment of TI 1 and TI 2 in various EU Member States (e.g. Belgium, France, Germany, Hungary, Ireland, Poland, and Sweden)[587] and now supplies *Drug a* for treatment of TI 1 and TI 2 throughout Europe under an EMA marketing authorisation. Accordingly, in the authors' view, it appears likely that Company A's acquisition of Company B was capable of appreciably affecting trade between EU Member States and may have merited *ex ante* review pursuant to Article 22 EUMR provided that the referring Member State was competent under its own national merger rules, or did not have any merger control system.

II.4.2.6 Scenario #2 (license agreement): assessment under Article 102 TFEU

Under the assumption that the transaction is a license agreement, in the present section we carry out the assessment that the Commission (or, similarly, a NCA) would have to

[585] Likewise, the transaction was too small to trigger the only value-of-transaction test (in the US) that is likely to have applied.

[586] ClinicalTrials.gov. This website reports the Locations at which the originator of a drug sponsored a registered trial. Investigator sponsored Trials (e.g. trials undertaken by research universities or other non-profit organizations) are excluded from this assessment because they do not have any evidentiary value regarding the commercial intentions of the originator of the drug.

[587] ClinicalTrials.gov.

conduct to investigate the case under Article 102 TFEU. The assessment under Article 101 TFEU is simulated in the following section.

The existence of a dominant position is not in itself an infringement of the EU competition laws or cause for censure; indeed, it may simply be evidence of strong competition on the merits. However, a dominant firm has a special responsibility to ensure that its conduct does not impair the maintenance or emergence of effective competition, so that even conduct that is normally lawful for firms that do not hold a dominant position can be unlawful under Article 102 TFEU if pursued by a dominant undertaking.[588]

II.4.2.6.1 Market definition

Market definition is a critical element in cases brought under Article 102, because it is a prerequisite to a finding that an alleged infringer has sufficient market power to be dominant.

In pharmaceutical cases, the Commission typically begins its assessment of candidate markets with reference to the overlap drugs' mechanism of action (MoA) and therapeutic indication(s) (TIs).

Insofar as treatments for TI 1 are concerned, it appears that the MoA and TI are likely to establish the outer boundaries of the relevant product market. However, the Commission might well find the existence of possible sub-markets/segments.

For example, the Commission sometimes refers to drugs' modes of administration in its pharmaceutical market definitions, and topical formulations (like Company B' *Pipeline b*) might be found to meet a discrete demand from patients who are intolerant of injections, while injectable formulations (like *Drug a*) might well occupy a market that is comprised of both injectable and topical formulations (given a likely asymmetry of demand). Similarly, the Commission might distinguish among drugs by their efficacies (e.g. duration of effect).

Insofar as TI 2 is concerned, different questions arise, but it is still plausible that the relevant market may be defined based on the MoA and TI.

Another issue arising with molecules having MoA 1, in particular, is that attempts to define markets for specific therapeutic indications may be difficult to defend because the identical product is typically sold for multiple TIs. Even where package sizes or branding differ, off-label sales may readily erode any meaningful distinction between markets defined with reference to product use. However, a limiting principle may exist in the fact that structural differences in various therapeutic indications could lead to sufficiently different conditions of competition that different markets must be defined.

In sum, an Article 102 investigation would likely require substantial efforts to establish the relevant product market(s). However, for reasons discussed below, while the Commission would be required to define the exact scope of the relevant market(s), it appears to be reasonably likely that *Drug a* commands a sufficiently significant position in them (howsoever defined) that this element would not pose a substantial impediment to a challenge under Article 102.

[588] Case 322/81 NV Nederlandsche Banden Industrie Michelin v Commission [1983] ECR 3461.

II.4.2.6.2 Dominance

A fundamental challenge in applying Article 102 TFEU to killer acquisitions is proving that the alleged infringer is dominant in the relevant market. While proving dominance may be challenging in cases giving rise to pipeline-to-pipeline overlaps, cases giving rise to a market-to-pipeline overlap are more easily addressed. In this case study, we do not intend to prove that Company A had a dominant position in the relevant markets, as that will be assumed to be able to go on with the assessment under Article 102; however, the rest of this section shows that this assumption is a reasonable one.

We have not found in publicly available information any very reliable estimates of Company A's share in potential markets defined based on the MoA or MoA+TI. However, it was reported that *Drug a* accounted for 70% of the US market for TI 1 injections in 2019. It cannot be excluded that Company A's share may be smaller in Europe, where two of the other leaders in drugs featuring MoA 1 are based. However, this seems unlikely; a common theme running through virtually every trade article in this area is the mention of Company A's dominant or leadership position.

Similarly, publicly available sources do not seem to report Company A's share of sales for treatment of TI 2 through its MoA 1 drug (probably because the same product is sold for many therapeutic indications, so no one knows exactly what that is). However, it was recently reported that *Drug a* is the standard of care for TI 2.

In an investigation under Article 102 TFEU, the Commission can obtain proprietary information from the parties and third parties that provides a basis for reasonably precise market share estimates. Findings of dominance may also be supported in some cases by the fact that shares other than those of the allegedly dominant firm are fragmented among a number of smaller rivals; however, depending on the case, small market shares may also point to a large number of start-ups and mavericks having entered the market. As shown in the discussion of a potential investigation under Article 101, below, competition with *Drug a* appears to have been limited and relatively fragmented at the time Company A acquired Company B.

Further evidence of dominance may be found in the fact that there are relatively high barriers to entry/expansion. For instance, an undertaking owning important intellectual property, has the benefit of "first mover" advantages, or commands superior financial and human resources for R&D.[589] In this regard, it might be noted that Company A has frequently challenged new rivals with trade secret and patent litigation that may be indicative of strong IPR protection. Company A also has a significant "first mover" advantage in the development of MoA 1 drugs, as *Drug a* was the first MoA 1 drug approved for human use and remains the leading supplier of MoA 1 drugs worldwide. Moreover, Company A has a large portfolio of complementary products that can provide substantial marketing and other commercial advantages. Evidence that such advantages pose substantial barriers to entry may be found in the fact that a large pharmaceutical company abandoned plans to launch a competitor of *Drug a* in 2014.

Given the foregoing, it appears possible that the Commission could potentially have established that Company A has a dominant position in a market for MoA 1 drugs for human use or such sub-markets/segments as ultimately might be identified.

[589] AstraZeneca (2010) paras 270-286.

II.4.2.6.3 Abuse

If it can be demonstrated that an undertaking has a dominant position in the relevant market, it can be argued that an acquisition (of a business or of IP rights to a technology) made by that firm that is capable of foreclosing competition may constitute an abuse.

The existence of a pattern of acquisitions (of businesses or exclusive licenses) that had the effect of co-opting potential rivalry could a fortiori represent evidence of an anticompetitive strategy put in place by the acquiring firm. This case study considers whether the exclusive license agreement between Company A and Company B could be challenged under Article 102 TFEU, and the existence of a pattern of several acquisitions of businesses/ exclusive licenses by the same dominant undertaking with potentially exclusionary effects would be relevant in assessing the abuse. In that respect, it might be noted that Company B was one of at least three nascent competitors that Company A acquired over a roughly five-year period. Concerning the other two acquisitions, each of them added to Company A's portfolio a molecule with the same MoA as *Drug a*. In one of the two, Company A acquired exclusive rights to a pipeline overlapping with *Drug a,* pursued little active development and then more than seven years later returned it to its original owner. In the other, Company A acquired a pipeline that has the same MoA as *Drug a* but differs in other features and thus is considered by Company A complementary, rather than substitute, to *Drug a*. Consistent with that view, Company A continued to develop such acquired pipeline.

Whether these acquisitions were undertaken pursuant to an exclusionary strategy or were simply a response to opportunities as they arose might be determined by direct evidence from internal company documents showing, e.g. that the company acted (or did not act) pursuant to a deliberate plan to pre-empt the introduction of innovative products that might compete with its own, or that it approved the capital expenditures required to complete such acquisitions with an assessment of the potential profits that might be put in jeopardy otherwise. In any case, these are only examples of documentary evidence that might be found, as an anticompetitive intent is not a requirement to qualify an abuse of dominance.

Whatever Company A's motivations might have been in acquiring an exclusive license over Company B' molecule, the transaction eliminated some competition in innovation; we have found no indication (on ClinicalTrials.gov or elsewhere) that Company A ever initiated any trials of *Pipeline b*, and little indication that Company A has pursued any trials of topical drugs (having MoA 1 or even a different MoA) that might make use of Company B' delivery system.[590]

The acquisition of exclusive rights over a costly compound (like *Pipeline b*) by a dominant undertaking - that appears to have done little or nothing to develop - could be - depending on the circumstances of the case and the evidence on the motivation for the acquisition - considered to constitute recourse to methods different from those

[590] For the purpose of this hypothetical case study, we assumed that all exclusive rights over *Pipeline b* were granted by Company B to Company A (i.e. no rights over the molecule were given to any third party, such as Company C).

that condition normal competition.[591] Accordingly, under this hypothetical case study, this deal raises a threshold question whether there is a reasonable case to be made that Company A might have wanted to eliminate a competing molecule rather than acquiring and further developing it.[592] Given its position in the relevant markets, Company A assumedly was uniquely positioned to develop and launch a MoA 1 drug at prices comparable to what it was already charging for its injectable drug (possibly increasing demand for it at the same time). Accordingly, one might conclude that Company A's apparent decision to forego development of *Pipeline b* was based on concerns that the technology simply would not work. However, it can't be excluded that Company A might have had various competitive/commercial reasons for wanting to eliminate *Pipeline b*, not least of which is that Company A may have seen little reason to invest in the development of a substitute for what it was already supplying very profitably with limited competition.

In light of the foregoing, obvious difficulties arise in trying to characterise Company A's apparent decision to forego further development of *Pipeline b*, after it acquired Company B, as an infringement of Article 102. While such a claim might have a conceptual foundation in Article 102(b) TFEU (where unilaterally "limiting production, markets or technical development" are listed as examples of abuse), there is little precedent for a successful challenge to the discontinuation or withholding of a product that does not already have customers on the market and is not an essential facility. Considering the above and the limitations of publicly available data on which the study relies, it appears difficult to challenge Company A's discontinuation of *Pipeline b* after it has been acquired.

A different case might be made with respect to a dominant acquirer's use of pipeline assets to undermine or deter others' efforts to develop a product that might compete with the acquirer's existing products. In the authors' view, an example might potentially be found in Company A's post-acquisition reporting of results of Company B' final trial of *Pipeline b*.[593] While trial results are reported on ClinicalTrials.gov in a standard tabular format without discussion or conclusions, sponsors still have substantial discretion in choosing how to interpret and report their data, and Company A chose a method of statistical analysis – which it does not appear to have used in reporting on any other trials completed in the years immediately before and after the relevant trial was completed – that, according to the authors of the study, gave a distorted and negative view of the efficacy of *Pipeline b*. Company A also failed to provide materials that might have enabled readers to make a fairer assessment of the study data (in particular, copies of the study protocol and the results of any statistical analyses it may have made – both of which are supposed to be provided). It might be inferred from such reporting that Company A may have regarded its report as an opportunity to undermine further

[591] As stated the now classic formulation, abuse "is an objective concept relating to the behaviour of an undertaking in a dominant position . . . which, through recourse to methods different from those which condition normal competition in products or services on the basis of the transactions of commercial operators, has the effect of hindering the maintenance of the degree of competition still existing in the market or the growth of that competition." Case 85/76 Hoffmann-La Roche v. Commission EU:C:1979:36, paragraph 91.

[592] While intent is not an essential element of a case under Article 102, the CJEU has noted that an assessment of the conduct of a dominant undertaking under Article 102 necessarily entails an assessment of the business strategy pursued by that undertaking. Case C-549/10 P Tomra Systems v Commission ECLI:EU:C:2012:221.

[593] We recall that for the purpose of this case study we assumed that results of the final clinical trial of *Pipeline b* in TI 2 were promising, i.e. they did not warrant the discontinuation of the molecule based on technical grounds.

development of other topical toxins.[594] Should it be the case (which remains to be established), such reporting could potentially fall within the scope of Article 102.[595]

II.4.2.7 Scenario #2 (license agreement): assessment under Article 101 TFEU

This section provides the steps of the assessment that would have to be conducted to prove an infringement of Article 101 TFEU.

II.4.2.7.1 Market definition

In assessments under Article 101 TFEU, the Commission uses market definition in particular to determine whether an appreciable restriction of competition exists or to establish whether the condition in Article 101(3), point (b), TFEU for an exemption from the application of Article 101(1) TFEU is met. In practice, the Commission tends to use market definition when assessing agreements that have as their effect the prevention, restriction or distortion of competition. By contrast, the Commission is not required to (and usually does not) define the relevant market when assessing agreements that represent an infringement by object (e.g. cartel agreements).[596]

Issues regarding the definition of the relevant markets in which this transaction might be assessed were discussed above, with respect to Article 102, and will not be repeated here.

II.4.2.7.2 Agreement

In an Article 101 TFEU investigation of a pharmaceutical transaction as a killer acquisition, the most delicate theme to assess appears to be whether the license agreement contemplated the discontinuation of an overlapping molecule, and what documents are apt to prove such a link between the license agreement and the discontinuation. In the case at hand, we do not have sufficient elements to draw a conclusion on this aspect, and thus – for the purpose of continuing this hypothetical assessment – we assume that the license agreement between the parties envisaged the discontinuation of *Pipeline b*. In other words, the pipeline discontinuation is specifically linked to the license agreement. This aspect implies that the license agreement can be seen as anti-competitive, warranting the analysis of the next steps of the assessment under Article 101.

II.4.2.7.3 Potential competition

As noted previously, the deal gave rise to two market-to-pipeline overlaps. Because Company B had already completed a number of Phase II trials of *Pipeline b*, which offered an easy mode of transdermal administration that could create a significant competitive advantage vis-à-vis older injectable toxins, it is likely that it was exerting an immediate competitive constraint on other toxin producers as a developer. Further, given the fact that it had advanced so far in development (i.e. completion of Phase II trials), Company B might reasonably be regarded as a potential market entrant in the supply of finished medicines in the foreseeable future.

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[594] Failure of *Pipeline b* might have convinced competitors that molecules with the same TI and MoA were also unlikely to succeed. However, molecules with the same TI and MoA may be characterised by other differences, so failure of one does not necessarily imply failure of the others.

[595] Cf. Hoffmann-La Roche (2018) (parties' public distortion of data in order to reduce competitive pressures created by authorized and off-label uses of a drug infringed Article 101 by object).

[596] Market Definition Notice, paragraph 9.

Company B commented positively the Phase II trial results of its topical drug, including its performance against controls, and said that it would be studied further in Phase IIb clinical trials. A key opinion leader and professor likewise stated that a topical molecule would be a significant advance for treating T1 and T2 in individuals seeking non-invasive approaches. In any case, we recall that for the purpose of this case study we assumed that results of the final clinical trial of *Pipeline b* in TI 2 were promising (and those of the final clinical trial in TI 1 were announced to be positive, so no assumption is needed in that regard).

In light of the foregoing, in the authors' view, it would appear relatively easy to show that Company B was a potential competitor of Company A.

II.4.2.7.4 Restriction of competition

The next step of the assessment involves a determination whether the alleged infringement constitutes a restriction of competition by object or by effect. It is likely that agreements providing for the purchase and sale of a business, or the licensing of a technology cannot be regarded as anticompetitive in nature, so that an investigation into the effects of the agreement (including its negative effects on potential competition and innovation) must be required. In such cases, the Commission generally must take into account all relevant factual developments up to the time it adopts its decision.[597]

Insofar as is relevant here, the CJEU has noted that the counterfactual for purposes of a 'by effect' assessment of a market-exclusion agreement must reflect the "realistic possibilities" of how a potential competitor who has been excluded would have acted, and how the market is likely to have been structured and operate, in the absence of that agreement.[598]

It is clear that Company B was competing in efforts to develop a new MoA 1 drug and publicly available information suggests that the trials of *Pipeline b* up to the time it was acquired had been successful, and that the molecule was seen as a promising candidate in the market. Moreover, absent the deal Company B would likely have had the incentive to continue investing in the development of *Pipeline b*, as competition in the relevant market(s) at the time of the deal was limited.[599]

Based on online desk research, we identified the "MoA 1 molecules" that were available or in development at the time of the deal for the treatment of TI1 and TI2.

Three companies supplied MoA 1 drugs for TI1 in the EU at the time of the deal, Company A and two others. Five companies were pursuing pipeline projects in the area, Company B and four others. While most of the treatments being supplied or in development were injectable, Company B and one more firm also were developing topical/transdermal treatments.

A full competition assessment requires consideration of not only the structure, but also the dynamics, of the relevant market. Evidence of the latter can be obtained in the context of an Article 101 investigation (in, e.g. the parties' and third parties' answers to interrogatories, internal company strategic plans, marketing studies and the like). However, the results of our desk research suggest that competition at the time of the

[597] Servier, paragraphs 1130, 1184.

[598] Generics (UK).

[599] We note that for the purpose of this case study we assumed that results of the final clinical trial of *Pipeline b* in TI 2 (completed shortly after the deal) were promising.

licensing agreement was limited, as i) only a few marketed drugs existed, ii) they were in injectable form as opposed to the more innovative transdermal mode of administration, and iii) they were exerting limited competitive pressure (as can be inferred by Company A's extremely large market shares. Moreover, while late-stage clinical development may pose an immediate competitive constraint on producers of rival products to continue innovating, the products that were being developed when Company A acquired Company B, in 2016, were not commercialised quickly enough to competitively constrain actual sales in TI 1 for a number of years. Accordingly, it appears that Company B' *Pipeline b* would have represented an important competitive force.

Competition in the development and supply of MoA 1 drugs for the treatment of TI 2 appears to have been even more limited. However, it must be borne in mind that MoA 1 drugs are used extensively off-label, i.e. in a different way than indicated in the marketing authorisation (for example, for a different indication or in a different dosage). Accordingly, marketing authorisations for a specific therapeutic indication may not reflect the true extent of competition between MoA 1 drugs that have been approved for TI 2 and other MoA 1 drugs that have been approved for different therapeutic indications.

Only two companies, one of which is Company A, supplied MoA 1 drugs under marketing authorisations for treatment of TI 2 in the EU at the time of the deal. Two other companies supplied such drugs under EU marketing authorisations for other therapeutic indications and, because of extensive off-label use, may have provided some competition in the sale of drugs to treat TI 2.

Two companies, one of which is Company B, were pursuing Phase II trials in TI 2 at the time of the deal. As has been noted previously, Company A did not undertake any further trials of Company B' drug after the licensing agreement.

Thus, in view of the above discussion and under the assumptions of this case study, the authors consider that the license agreement, which also envisaged the discontinuation of the development of *Pipeline b* by Company A, may have warranted an investigation under Article 101 TFEU.

II.5 Spotting potentially harmful transactions

This section of the report provides a brief discussion of "gap" transactions (section II.5.1) and proposes one possible means of spotting potentially harmful deals, in particular through a registry that would allow the Commission to receive notice of transactions that might merit regulatory review (section II.5.2).

II.5.1 Licensing and other "gap" transactions

As noted previously, it appears highly likely that potential killer transactions may be made not only through acquisitions of companies/businesses, but also through the licensing of exclusive rights either to a target's technology *in toto* or to specific fields of use, territories, or customer groups. Exclusivity appears to be required for an effective killer strategy, because otherwise the acquirer/licensee has no means of ensuring that it will not face competition from the licensor or other licensees of the same technology.

Given the large volume of licensing transactions (and transactions that almost certainly included licensing, such as the formation of non-full function joint ventures and, potentially, co-marketing/co-distribution agreements), as well as the number of mergers and acquisitions (from a much smaller group of transactions) that appear to be potential candidates for a killer acquisition assessment, it seems plausible that some potential killer acquisitions, made through exclusive in-licensing of a target's

overlapping pipeline technology, could not be found simply because publicly available information was insufficient to reasonably identify them.

Given the foregoing, the difficulty to effectively monitor and review transactions in which IPRs are licensed on an exclusive basis may lead to an enforcement gap that might need remedies, as discussed in the next section.

II.5.2 The proposal for a registry or "notice" system

As has been noted throughout this Report, a potential "gap" in the Commission's ability to detect killer acquisitions – and one that is imperfectly addressed through the use of Article 22 referrals – is that the Commission may be unaware of transactions that might merit regulatory review. The Commission could make use of a number of monitoring resources and data mining processes to identify concentrations that may not trigger *ex ante* review. We understand that the Commission already carefully monitors concentrations in the pharmaceutical industry to identify appropriate candidate cases for an Article 22 referral, notably those where there is a risk of a killer acquisition and where, following the ruling of the Court of Justice in *Illumina / GRAIL*, some Member States have (or are able to claim, by way of "call-in" powers) jurisdiction based on their national laws. We have not evaluated the approach currently used by the Commission, or the merits or possible downsides thereof. However, given that the applicability of Article 22 is limited to concentrations, such a system may not capture exclusive licenses, which might be an area in which acquisitive companies can deploy "buy and bury" strategies.

One means to bridge this "gap", and to further strengthen the Commission's ability to monitor potential killer acquisitions, might be to establish a registry on which companies (possibly above a certain turnover threshold to ensure their nexus with the EU and likely competitive significance) would be required (or have the possibility) to file notice whenever they acquired an interest in a pharmaceutical pipeline giving rise to any market-to-pipeline or pipeline-to-pipeline overlaps. Registrants then might be required to provide periodic (e.g. quarterly or annual) updates on development and commercialization of the overlap drugs for a period of, say, two years (the period adopted in this study as a reasonable basis on which to detect any pipeline discontinuations) and, should they intend to discontinue any of them, report the reasons. In order to minimize the burden on companies and the Commission, information in the registry could be relatively high-level (e.g. overlaps might be identified solely by therapeutic indication and mechanism of action, rather than through a full competition analysis), so that the registry would serve as a "notice" system rather than the basis for full assessment. After each entry or update in the registry, the Commission might have a limited time frame (e.g. three or six months) to open an inquiry, after which any Commission inaction would be deemed tacit approval of the steps reported in the most recent update.

A possible feature of such a registry would be the suspension for a short period, and upon an indication of interest by the Commission, of steps taken or proposed in a company's most recent entry regarding a transaction in the registry. This could afford some of the benefits of *ex ante* review, ensuring that the Commission could pursue interim measures (e.g. hold-separate and project-maintenance obligations) during the investigation period if the Commission had concerns about a reported discontinuation.

We are not aware of any jurisdiction operating such a systematic registry in the pharmaceutical sector today. However, in a recent merger review in Spain, regarding ceramic tile coatings (where innovation plays an important role), the CNMC approved

the transaction with R&D reporting-and-review commitments like the ones proposed above.[600]

Whether the system should be mandatory or voluntary is a policy judgment (but a mandatory system would require a legislative reform). On one hand, a mandatory system would help to ensure that the Commission did not miss transactions. On the other hand, it might be easier to establish a voluntary system, and companies might be incentivized to use it as a means to obtain, e.g. legal certainty, immunity from fines, or consideration of registration as a mitigating factor in fining decisions. Either way, the establishment of such a system on a trial basis would enable the Commission to assess its utility and cost:benefit implications.

There is recent precedent for both approaches. In particular, the Commission has recently established a system in the Digital Markets Act under which leading online platforms are required to report *ex ante* their proposed acquisitions in the digital sector.

We are cognizant that there is little appetite, either at the Commission or among businesses, for anything like the notification procedures that were utilised prior to the modernisation of EU competition law in 2004. Accordingly, it appears likely that such a system could win support only if it were relatively easy to use (by both the Commission and businesses) and entailed the minimum burden that might ensure the Commission's receipt of sufficient notice to exercise its regulatory responsibilities. An online registration, run through the Commission's secure servers, therefore would appear to be appropriate. Moreover, a "checklist" type of approach to the information which must be registered would be manifestly easier to use, for both the Commission and businesses, than submissions in hard copy, and might enable automated processing of incoming data so that only transactions that were likely to be of interest would require the attention of Commission personnel.

A mock-up of what we believe might be appropriate in this regard is included in Appendix A.5 to this Report. The proposed Notice consists of two forms (which, again, would be opened for users of an online system). In short:

- Form A would be used to register a new acquisition of interest, and assumedly would be required to be filed, e.g. prior to or within seven days of that acquisition. All of the information required would be data that the registrant almost certainly would have readily available as a result of its due diligence for the transaction. Section 1 would require basic information about the parties, as currently defined under the EUMR. Sections 2-4 would require very basic information about the interest being acquired, including the type of transaction, degree of exclusivity in any licenses, and summary details of any collaborative arrangements, as well as summary identification of the drugs in which the acquirer was obtaining an interest or a collaboration was established with contribution from each of the parties. Sections 5-7 would require information regarding the value of the transaction and the means by which it is to be paid, shown in the Annex in a level of detail that might help to ensure appropriate registration of all components of the transaction value, but readily reduced to a single line item if the Commission determined that a "top line" valuation was all that was required in a notice system. Item 8 would be completed for each overlap product, noting the most recent three trials at its most advanced

[600] Case C-1116/20 Pigments/Ferro Corporation (available in Spanish on the CNMC's website).

stage of development, with summary details regarding its status and reason for any discontinuation.

- Form B is a single page form, which would be identified with Form A by the registrant's provision of the registration number provided by the Commission's system upon completion of a Form A, and would provide for periodic (e.g. semi-annual or annual) updating on the status of each overlap product.

The foregoing is just a first attempt to craft a model of the type of system (if any) the Commission might choose to deploy, but might help to address the problem of notice, and the potential "enforcement gap," that gives rise to current concerns about potential killer acquisitions.

Conclusions

The fact-finding challenge chapter provides a detailed explanation of the data sources and methodological approach used in this study to identify potential killer acquisitions that occurred between 2014 and 2018 in the pharmaceutical sector, as well as a detailed discussion of the resulting findings.

The study adopts the notion of a killer acquisition as a theory of harm in which a transaction causes the discontinuation of an R&D project and is (likely to be) detrimental to competition.

The approach developed to identify such transactions involves a large-scale analysis, complemented by a thorough manual screening to identify those cases of discontinuations that merit further investigation. In detail, it consists of a sequential filtering process organised as follows:

- identification of the relevant narrow overlap: The analysis focuses on narrow overlaps between drug pairs at the time of the deal, determined on the basis of identical or sufficiently comparable therapeutic indication (TI) and mechanism of action (MoA). Narrow overlaps are relevant to the analysis if they involve ongoing innovation. Accordingly, the analysis is limited to pipeline-to-pipeline or pipeline-to-market overlaps, while it excludes overlaps between two marketed products, overlaps involving generics and overlaps involving pipelines already discontinued prior to the deal. Finally, the analysis focuses on overlaps arising from target drug projects within the scope of a deal. While for mergers and acquisitions the deal affects the entire portfolio of drug projects of the companies involved, for other deals it specifically affects the drug projects that are the object of the deal; therefore, only overlaps arising between these traded projects and the other party to the deal portfolio (e.g. acquirer, licensor or partner to a collaboration agreements) are considered;
- identification of discontinuations and prima facie relevant discontinuations: we identify narrow overlaps where the acquirer's drug or the target's drug, or both, are discontinued post-deal in the overlapping TI. Specifically, the discontinuation of a pipeline is determined by a lack of post-deal progress in both clinical trial data and drug registration or launch data. Within the detected discontinuations, we then identify those that are prima facie relevant to a killer acquisition assessment, weighing the available evidence in the large-scale analysis. Prima facie relevant discontinuations are those that may be motivated by deal-driven commercial or strategic considerations and qualify as relevant cases for a KA analysis. These include discontinuations following completion of a clinical trial, as evidenced by the absence of further development, or discontinuations following early termination of a trial for unmotivated or seemingly strategic reasons, such as business considerations. In essence, their identification requires either a lack of transparency about the observed discontinuation, or the existence of reasons for discontinuation that would presumably not have been observed in a counterfactual without the deal;
- evaluation of evidence consistent with a killer acquisition narrative: this final step aims at identifying the set of discontinuations deserving further scrutiny. This objective is pursued by evaluating the extent to which the publicly available evidence would potentially endorse a killer acquisition theory of harm. The study cannot draw firm conclusions on whether discontinuations are ultimately killer acquisitions, as the lack of access to companies' internal documents and other confidential information prevents any definitive assessment of whether the transaction indeed altered the parties' incentives. Despite this inherent limitation, the study aims to identify the

transactions that would deserve further scrutiny, at least based on publicly available information; this is done using a twofold methodology.

- First, quantitative, machine-learning methods (specifically, LASSO, i.e. Least Absolute Shrinkage and Selection Operator, regression) examine systematic patterns of ex ante observable characteristics of the overlapping drug projects and their competitors that may plausibly indicate that the parties involved in a given acquisition had the incentive and the ability to stifle competition in a relevant market. Factors considered are those collected from publicly available datasets for all narrow overlaps and include the stage of development of the overlapping drugs, as well as the number and strength of competitors at the time the deal was signed.
- Second, a manual screening closely inspects any piece of additional publicly available information, obtained from company websites, reports or filings, the medical literature and the pharmaceutical industry news outlets, covering both the pre- and post-transaction periods, that cannot be processed in the large-scale analysis.

Conclusions regarding the qualification of a prima facie relevant discontinuation and of the related transaction as deserving further scrutiny may be weaker or stronger depending on the strength and clarity of this additional evidence.

Using this approach, the study finds that out of the 3,193 transactions that informed our analysis (out of a total of 6,315 in the period 2014-2018), 240 brought at least two narrowly overlapping drug projects under the influence of the same company, and 38% of these transactions (i.e. 92 in total) have been followed by at least one discontinuation that was identified as prima facie relevant for a killer acquisition assessment. Prima facie relevant discontinuations of drug projects are distributed differently across deal types, amounting to 54% of the deals with narrow overlaps in mergers and acquisitions, 27% in licensing agreements, 33% in purchases and 42.5% in R&D agreements. The remaining prima facie relevant discontinuations are distributed across equity investments (with 2 deals), followed then by joint ventures, joint venture R&D and Marketing agreements (one deal in each of these deal types), while in partnerships and cross-licensing agreements no prima facie relevant discontinuation is found.

Despite their potential to highlight observable ex ante patterns that may be indicative of a killer acquisition theory of harm, machine learning methods proved inadequate for selecting covariates that could consistently characterise the phenomenon of interest. Therefore, manual screening plays a crucial role in systematically verifying whether the public evidence may support or contradict a killer acquisition theory of harm.

This comprehensive, in-depth review was carried out for a large number of deals and corresponding overlaps with a prima facie relevant discontinuation. Specifically, the manual screening covered 55% (51 deals) of the 92 deals with prima facie relevant discontinuations and 38% (188 overlaps) of the 500 overlaps involving a prima facie relevant discontinuation. At both deal and overlap level, the screening provided full coverage of mergers and acquisitions, exclusive licensing agreements, purchase deals and other transactions, with only a subset of non-exclusive licensing and R&D agreements excluded from it.

Out of all the prima facie relevant discontinuations manually screened, our findings reveal that the information in the public domain does not provide solid unambiguous evidence that would fully support all the elements of the killer acquisition narrative, but at the same time does not allow such a theory of harm to be definitively ruled out, thus preventing us from making a conclusive assessment. In most cases, publicly available information could not provide compelling evidence to more firmly suggest: (i) the substitutability between acquirer and target drugs, and most notably, that the drugs can similarly treat the same disease and patients; (ii) that the discontinuation lacks a

valid technical or clinical justification or can be justified by a commercial assessment that would have emerged even in the absence of the transaction; (iii) that competition in the relevant market was adversely affected by the discontinuation.

On the other hand, only in a very few deals the evidence collected suggests that a killer acquisition narrative can be confidently dismissed (2 M&A deals and 1 licensing agreement). These are the cases where, for instance, the closer inspection reveals that the discontinuation was announced well ahead of the date of the deal.

Therefore, the study concludes that, with the exception of these few deals where a killer acquisition narrative can be reasonably ruled out, the 89 deals accounting for the remaining prima facie relevant discontinuations fall into a grey area where a conclusive assessment is not possible based on publicly available information: a case-by-case analysis using confidential data is required to thoroughly test a KA theory of harm for these deals.

In terms of methodology, manual screening proved to be indispensable in shaping the study's findings and introduced a crucial novelty in emphasising the role of factual evidence in the assessment process, marking a departure from previous literature that relied solely on theoretical and statistical evidence. A fundamental conclusion in this respect is the need for careful case-by-case assessment.

However, the analysis and resulting findings are significantly affected by the inherent uncertainty and incompleteness of publicly available evidence. This evidence includes data disclosed by companies to regulators, investors and the media, or published in the medical literature based on clinical trial results, subject to company disclosure policies. Despite the expertise of the team, which can draw on a deep understanding of the legal, technical and commercial aspects of the viability of pharmaceutical projects, it is difficult to reach a final verdict because of the inability to assess confidential "private" information that is critical to an accurate understanding of the parties' commercial incentives, including R&D plans, business strategies and funding constraints. This limitation extends to a full understanding of the pattern of substitutability between overlapping drugs and the level of competition in the relevant market, especially when the overlap in TI is not perfect and potential substitutability has to be evaluated.

Relying on publicly available data is less challenging for analysing deals such as mergers and acquisitions, where at least the scope of the deal is easily identifiable. Conversely, for other types of deals, which may vary quite a lot in scope and duration, there may be a lack of publicly available information on what the parties agreed upon, making reliance on public data a significant limitation. This challenge is particularly pronounced in the case of R&D agreements, where it is crucial to determine whether there is an actual exchange of rights between the parties to the agreement, a task that appears to be unachievable with the available information.

In conclusion, the fact-finding challenge has provided valuable insights for appraising the killer acquisition theory of harm in the pharmaceutical sector. However, the inherent limitations of publicly available data preclude any definitive certainty in the assessment. Accordingly, most prima facie relevant discontinuations remain as potential candidates for a killer acquisition assessment.

This conclusion is reinforced by analysing the features of prima facie relevant discontinuations deserving further scrutiny in mergers and acquisitions (after removing the few cases where a killer acquisition narrative can be reasonably ruled out). Indeed, the analysis of prima facie relevant discontinuations deserving further scrutiny and the corresponding deals, when compared to a control group consisting of mergers and acquisitions that do not involve any prima facie relevant discontinuations, reveals

distinct characteristics. Such discontinuations involve overlapping drugs at a relatively advanced stage of development, which fosters more informed expectations about their potential in the relevant therapeutic area and thus signals the presence of a more serious threat that may motivate a killer strategy. In addition, these discontinuations tend to occur in markets that are more concentrated, including markets where there is often no competitor, increasing the incentive and ability for a potential killer acquisition. This evidence therefore supports the conclusion that overlaps and deals that merit further scrutiny are potentially consistent with a killer acquisition theory of harm.

The evaluation challenge chapter aims at providing an assessment of the suitability of merger and antitrust rules to deal with possible killer acquisitions. To this aim, in addition to a thorough review of the relevant literature, this part of the study ex-post evaluates a number of deals.

First, it provides an assessment of five mergers in the pharmaceutical sector that have been notified to the Commission. The ex-post evaluation aims at assessing, with the benefits of the hindsight, whether the Commission has successfully identified any area of concern that could potentially feed a killer acquisition strategy and effectively addressed them. The analysis seeks to ascertain whether the evolution of the overlapping drug R&D projects post-merger supports the Commission's assessment, even though it does not extend to evaluating the counterfactual with no merger.

Second, it discusses the extent to which the merger and antitrust rules are well suited to tackle potential killer acquisitions that escape ex-ante review because structured as concentrations below the EUMR thresholds or because not structured as concentration. This includes two fictitious case studies, showcasing how Article 22 EUMR, and Articles 101 and 102 TFEU could be applied to tackle potentially harmful transactions.

The ex-post evaluation of the notified transactions reveals that the Commission's substantive assessment is overall effective in detecting possible killer acquisitions. However, in one case we found that the Commission remedies could have been better designed.

For the cases ultimately cleared with no conditions (Novartis/GSK *Ofatumumab,* BMS/Celgene), when the evolution of the overlapping drug R&D projects reveals that either of the two has been discontinued, either the collected evidence points to commercial and/or technical reasons for the discontinuation or the competitive conditions at the time of the deal make a killer acquisition theory of harm not applicable. In BMS/Celgene, however, the ex-post evaluation based on public sources identified a further potential area of concern that was not addressed in the Commission's decision, which resulted in a discontinuation *prima facie* relevant for a killer acquisition assessment. The publicly available evidence suggests that the deal created a possible additional overlap between substitutable drugs in a market with apparently limited competition, potentially leading to a discontinuation. However, the Team understands that the Commission had access to confidential information indicating that the concerned pipeline was no longer in active development at the time of the deal. This illustrates the limitation of this study relying exclusively on public sources, which are by nature fragmented.

For the cases ultimately cleared with conditions (J&J/Actelion, Novartis/GSK Oncology Business and AbbVie/Allergan), the evolution of the competitive landscape post-merger reaffirms the Commissions' decision to intervene. In all three cases at least one of the molecules in overlap at the time of the deal was subsequently discontinued in the relevant therapeutic indication. However, it is important to note that this does not automatically mean that the remedies were ill-designed, as it can simply reflect the fact

that the successful development of pipeline drugs is by nature uncertain. Indeed, in all three cases it cannot be excluded that the discontinuation is grounded on technical reasons unrelated to the remedies. In only one out of the three cases (J&J/Actelion), the ex-post evaluation suggests that remedies could have been better designed, as they appear to have been too dependent on the active participation of a partner which ultimately ended the collaboration.

In particular, the remedies failed to prevent Minerva from withdrawing its participation in co-developing JNJ-7922 and did not prevent J&J from discontinuing or delaying further development of JNJ-7922 in the overlapping therapeutic indication. Similar remedies in future cases could be enhanced by offering stronger protections to ensure their implementation aligns with the expectations shared by the Commission and the parties at the time the remedy is adopted, unless the Commission grants a waiver, modification, or substitution of the commitments upon request by the parties. While remedies in J&J/Actelion may not seem suitable for their intended purpose, their ultimate impact on competition remains uncertain. J&J's refocusing of its pipeline from primary insomnia (the indication where there was an overlap at the time of the deal) to MDD (where no overlap existed) was driven by technical and commercial considerations[601] that would have likely emerged also in absence of J&J's acquisition of Actelion. In particular, the remedies also consisted in J&J not controlling the competing ACT-541468 pipeline, so any decision related to JNJ-7922 was in all likelihood not driven by any anticompetitive consideration. However, if it had been the case, and while we cannot exclude that the Commission had exchanges with the parties and took the latter into consideration, the remedies would not have been effective in preserving competition. In any case, it should be noted that the Commission cannot impose any remedy, as the remedies are proposed by the Parties and only accepted by the Commission. In this light, the Commission also cannot impose measures that are binding on third parties.

The two fictitious case studies investigate the extent to which antitrust and merger rules can effectively deal with killer acquisitions, especially when they escape ex-ante review under EUMR or because they are not structured as concentrations. The large-scale analysis shows that, in our sample, *prima facie* relevant discontinuations are typically not structured as concentrations. Additionally, the majority of M&A has not been scrutinized by any competition authority.

Jurisdiction under the EUMR is based primarily on the size and geographic distribution of the turnovers of the merging parties. While large transactions are routinely subject to *ex ante* review, smaller but yet competitively important acquisitions may escape review, particularly when the target is an important innovator but does not yet generate a turnover. The study offers a review of the available options for reforming the current jurisdictional thresholds and suggests that such alternatives may not be justified as they could disrupt the delicate balance between the burdens of notification and the benefits of *ex ante* review.

Article 22 EUMR appears to be a helpful corrective mechanism to ensure regulatory review of below-threshold concentrations. So far, that provision has enabled the Commission to regulate a number of problematic transactions that did not meet its normal jurisdictional thresholds. However, resort to Article 22 also has its limitations, the main one being the fact that identifying potentially harmful transactions that are

good candidates for referral is not immediate. The fact-finding challenge itself revealed the challenges of identifying systematic features that allow to distinguish potentially problematic transactions *ex ante.* In fact, the *fact-finding* challenge suggests that killer acquisitions have a diverse nature and each merits its *ad hoc* assessment. The two fictitious case studies we conducted show that pharmaceutical transactions appear to lend themselves well to meeting the requirements for a referral request under Article 22. Another important limitation has to do with the fact that, as recently clarified by the Court of Justice in *Illumina / GRAIL*, referrals under Article 22 EUMR are only possible where the referring Member States have jurisdiction under their own national rules or no merger control regime of their own.

Antitrust rules, that intervene *ex post*, may be a powerful tool to deal with killer acquisitions that are not structured as concentrations. The study goes through the steps of the assessment that could be conducted under Article 101 and 102 TFEU in the second of our case studies, under the assumption that the hypothetical case at hand is a licensing agreement. The assessment under article 101 TFEU suggests that a crucial part of the analysis consists in understanding whether the licensing agreement contemplated the discontinuation of an overlapping molecule, and what documents could prove it. In the case we considered, the publicly available evidence did not allow to draw conclusions on this aspect, and therefore we assumed – for the purpose of conducting the assessment - that the licensing agreement between the parties envisaged the pipeline discontinuation.

Moreover, our analysis raises questions regarding the applicability of Article 102 TFEU when a company appears to have in-licensed a small developer's molecule or technology with the effect of eliminating the threat of future competition from a new product that otherwise might undercut demand for a product in which the acquirer has a dominant position. The existence of serial acquisitions by the same company of emerging rivals (involving subsequent discontinuations) is an element that would be considered in an evaluation under Article 102. Another important step of the assessment where issues could arise is proving the relevant market, as mentioned in the case study.

Finally, we note that the limits of our fact-finding analysis are exacerbated when it comes to licensing and collaboration agreements (including R&D and joint venture R&D agreements) as publicly available information do not sufficiently disclose the nature of such agreements. The Commission may encounter comparable gaps in monitoring such transactions. The establishment of a registry where companies acquiring interests in pharmaceutical pipelines provide notice, would enable the Commission to monitor developments and intervene if necessary. Whether the system should be mandatory or voluntary is a policy judgment. The success of such a system hinges on its ability to provide adequate notice to the Commission while remaining accessible and manageable for businesses operating within the EU.

References

Argentesi, E. et al., 2019. *Ex-post Assessment of Merger Control Decisions in Digital Markets,* s.l.: Document prepared by Lear for the Competition and Markets Authority..

Arrow, K., 1962. Economic Welfare and the Allocation of Resources for Invention. In: *The Rate and Direction of Inventive Activity: Economic and Social Factors.* s.l.: National Bureau of Economic Research, Inc., pp. 609-626.

Ballantyne, A., 2008. Benefits to research subjects in international trials: do they reduce exploitation or increase undue inducement?. *Developing world bioethics,* 8(3), pp. 178-191.

Bennato, A., Davies, S., Mariuzzo, F. & Ormosi, P., 2021. Mergers and innovation: Evidence from the hard disk drive market.. *International Journal of Industrial Organization,* Volume 77, p. 102755.

Bergman, M. A. & Rudholm, N., 2003. The Relative Importance of Actual and Potential Competition: Empirical Evidence From the Pharmaceuticals Market. *The Journal of Industrial Economics,* Volume 51, pp. 455-467.

Bokhari, F., Mariuzzo, F. & Bennato, A., 2021. Innovation and growth in the UK pharmaceuticals: the case of product and marketing introductions.. *Small Business Economics,* Volume 57, pp. 603-634.

Bower, P. et al., 2014. Interventions to improve recruitment and retention in clinical trials: a survey and workshop to assess current practice and future priorities.. *Trials,* 15(399).

Briel, M. et al., 2016. A systematic review of discontinued trials suggested that most reasons for recruitment failure were preventable.. *J Clin Epidemiol.,* Volume 80, pp. 8-15.

Chaudhari, N., Ravi, R., Gogtay, N. & Thatte, U., 2020. Recruitment and retention of the participants in clinical trials: challenges and solutions.. *Perspectives in Clinical Research,* 11(2), pp. 64-69.

Comanor, W. & Scherer, F., 2013. Mergers and innovation in the pharmaceutical industry.. *Journal of Health Economics,* 32(1), pp. 106-113.

Crawford, G., Valletti, T. & Caffarra, C., 2020. 'How tech rolls': Potential competition and 'reverse' killer acquisitions. *Vox EU.*

Cunningham, C., Ederer, F. & Ma, S., 2021. Killer Acquisitions. *Journal of Political Economy,* 129(3), pp. 649-702.

Decarolis, F. & Giorgiantonio, C., 2022. Corruption red flags in public procurement: new evidence from Italian calls for tenders. *EPJ Data Science,* 11(16).

Digital Competition Expert Panel, 2019. *Unlocking digital competition,* s.l.: s.n.

Ellenberg, S. & Shaw, P., 2022. Early Termination of Clinical Trials for Futility - Considerations for a Data and Safety Monitoring Board.. *NEJM Evidence,* 1(7).

European Commission, Directorate-General for Competition; Montjoye, Y.; Schweitzer, H.; Crémer, J., 2019. Competition policy for the digital era. *Publications Office,* p. https://data.europa.eu/doi/10.2763/407537.

European Commission, Directorate-General for Research and Innovation; Pang, T.; Folwell, B.; Osborne, A.; et al., 2020. Study on the impact of mergers and acquisitions

on innovation in the pharmaceutical sector. *Publications Office,* p. https://data.europa.eu/doi/10.2777/323819.

European Commission, 2021. Evaluation of procedural and jurisdictional aspects of EU merger control. *Commission Staff Working Document 66,* p. https://ec.europa.eu/competition/consultations/2021_merger_control/SWD_findings_of_evaluation.pdf.

European Commission, D.-G. f. R. a. I., Pang, T., Folwell, B. & Osborne, A. e. a., 2020. Study on the impact of mergers and acquisitions on innovation in the pharmaceutical sector. *Publications Office of the European Union.*

Facoetti, G., Mariani, M., Montecchi, T. & Russo, D., 2017. *Method and tool for the automatic reformulation of search keyword strings in document search systems..* s.l. Patent No. EP3163467.

Gautier, A. & Lamesch, J., 2021. Mergers in the digital economy. *Information Economics and Policy,* Volume 54, p. 100890.

Gautier, A. & Lamesch, J., 2021. Mergers in the digital economy. *Information Economics and Policy,* Volume 54, p. 100890.

Gilbert, R., 2022. Innovation matters: competition policy for the high-technology economy.. *MIT Press.*

Goldacre, B. et al., 2018. Compliance with requirement to report results on the EU Clinical Trials Register: cohort study and web resource.. *BMJ,* Volume 362, p. k3218.

Grabowski, H. & Kyle, M., 2008. Mergers and Alliances in Pharmaceuticals: Effects on Innovation and R&D Productivity. In: K. Gugler & B. B. Yurtoglu, eds. *The Economics of Corporate Governance and Mergers.* s.l.:Edward Elg.

Graham, S. J. H., Marco, A. C. & Myers, A. F., 2018. Patent transactions in the marketplace: Lessons from the USPTO Patent Assignment Dataset. *Journal of Economics & Management Strategy,* 27(3), pp. 343-371.

Haucap, J., Rasch, A. & Stiebale, J., 2019. How mergers affect innovation: Theory and evidence.. *How mergers affect innovation: Theory and evidence,* 63(C), pp. 283-325.

Haucap, J. & Stiebale, J., 2023. Non-price effects of mergers and acquisitions.. *DICE Discussion Paper No. 402.*

He, Y. et al., 2012. A 2012 Workshop: Vaccine and Drug Ontology in the Study of Mechanism and Effect (VDOSME 2012. *J Biomed Semantics,* 18 Dec, 3(1), p. 12.

Hull, D. W. & Clancy, M. J., 2006. Pharma and biotech in-licensing and collaboration agreements: a deal lawyer's guide to EU anti-trust pitfalls. *Covington & Burling LLP,* pp. https://uk.practicallaw.thomsonreuters.com/1-205-6037?transitionType=Default&contextData=(sc.Default)&firstPage=true.

Iltis, A., 2005. Stopping trials early for commercial reasons: the risk–benefit relationship as a moral compass.. *Journal of medical ethics,* 31(7), pp. 410-414.

Ivaldi, M., Petit, N. & Unekbas, S., 2023. Killer Acquisitions: Evidence from EC Merger Cases in Digital Industries. *forthcoming in Antitrust Law Journal - TSE Working Paper No. 13-1420.*

Jitlal, M., Khan, I., Lee, S. & Hackshaw, A., 2012. Stopping clinical trials early for futility: retrospective analysis of several randomised clinical studies.. *Br J Cancer,* Volume 107, pp. 910-917.

Kasenda, B. et al., 2014. Prevalence, characteristics, and publication of discontinued randomized trials.. *JAMA,* 311(10), pp. 1045-51.

Kleinberg, J., Ludwig, J., Mullainathan, S. & Obermeyer, Z., 2015. Prediction Policy Problems. *American Economic Review: Papers \& Proceedings,* 105(5), pp. 491-495.

Lesaffre, E. et al., 2017. Statistical controversies in clinical research: futility analyses in oncology–lessons on potential pitfalls from a randomized controlled trial. *Annals of Oncology,* 28(7), pp. 1419-1426.

Lièvre, M. et al., 2001. Premature discontinuation of clinical trial for reasons not related to efficacy, safety, or feasibility.. *BMJ,* 322(7286), pp. 603-5.

Lundqvist, B., 2021. Killer Acquisitions and Other Forms of Anticompetitive Collaborations (Part I). *European Competition and Regulatory Law Review,* 5(3), pp. 186-199.

Madl, A. C., 2020-2021. Killing Innovation?: Antitrust Implications of Killer Acquisitions.. *Yale Journal on Regulation Bulletin,* Volume 38, pp. 28-52.

Marthan, J., Kuhn, T., Powell, M. & Wendebourg, R., 2021. Latest developments on the Article 22 EUMR referral mechanism: the only thing that's certain is the uncertainty. *White & Case LLP,* pp. https://www.whitecase.com/publications/alert/latest-developments-article-22-eumr-referral-mechanism-only-thing-thats-certain.

Moher, D. et al., 2016 . Increasing value and reducing waste in biomedical research: who's listening?. *Lancet,* 387(10027), pp. 1573-1586.

Newham, M. & Vokinger, K., 2022. Adverse effects of acquisitions in the pharmaceutical industry.. *Nature Medicine.*

OECD, 2020. Start-ups, Killer Acquisitions and Merger Control. pp. http://www.oecd.org/daf/competition/start-ups-killer-acquisitions-and-merger-control-2020.pdf.

OECD, 2021. Methodologies to Measure Market Competition. *OECD Competition Committee Issues Paper,* p. https://oe.cd/mmmc.

Ornaghi, C., 2009a. Mergers and innovation in big pharma. *International Journal of Industrial Organization,* 27(1), pp. 70-79.

Ornaghi, C., 2009b. Positive assortive merging. *Journal of Economics & Management Strategy,* 18(2), pp. 323-346.

Ornaghi, C., 2009. Mergers and innovation in big pharma. *International Journal of Industrial Organization,* Volume 27, pp. 70-79.

Ornaghi, C. & Cassi, L., 2023. Acquisitions, Inventors' Turnover, and Innovation: Evidence from the Pharmaceutical Industry.. *University of Southampton Discussion Papers in Economics and Econometrics n.2306..*

Scott, C. & Magnus, D., 2014. Wrongful termination: lessons from the Geron clinical trial.. *Stem cells translational medicine,* 3(12), pp. 1398-1401.

Snapinn, S., Chen, M. G., Jiang, Q. & Koutsoukos, T., 2006. Assessment of futility in clinical trials.. *Pharmaceutical statistics,* 5(4), pp. 273-281.

Trapotsi, M., Hosseini-Gerami, L. & Bender, A., 2021. Computational analyses of mechanism of action (MoA): data, methods and integration.. *RSC Chem Biol.,* 22 Dec, 3(2), pp. 170-200.

Turner, B. et al., 2020. Characteristics of ophthalmology trials registered in ClinicalTrials. gov, 2007-2018. *American Journal of Ophthalmology,* Volume 211, pp. 132-141.

U.S. Department of Justice & Federal Trade Commission, 2017. Antitrust Guidelines for the Licensing of Intellectual Property.

Varian, H. R., 2014. Big Data: New Tricks for Econometrics. *Journal of Economic Perspectives,* 28(2), pp. 3-28.

Vellinga, A., Lambe, K., O'Connor, P. & O'Dea, A., 2021. What discontinued trials teach us about trial registration?. *BMC Research Notes,* 14(1), pp. 1-5.

Wollmann, T. G., 2019. Stealth Consolidation: Evidence from an Amendment to the Hart-Scott-Rodino Act. *American Economic Review: Insights,* 1(1), pp. 77-94.

Appendices

Table of Contents

A.1 Detailed description of data sources, problems encountered, and solutions adopted

A.1.1 AdisInsight Database: issues encountered, and revisions made

As discussed in section I.1.1 of the Final Report, the original version of the AdisInsight Deals dataset was incomplete or not readily amenable to large-scale analysis. This circumstance has hindered an outright extraction of the relevant data. Our manual inspections and checks revealed that, in a non-negligible number of deals, the information was not systematised into the relevant variables even when available and included in the description field. This field summarises in natural language the pivotal events related to the deal and its details, including the parties and their roles, the financial terms and the object of the deal (consisting of the relevant drugs and rights for transactions other than M&As).

We undertook an extensive review process. First, with the support of Trix, we extracted relevant deal details using automated semantic search of key terms within the generic description field, to fill in the gaps found in other purpose-specific fields. We then shared the results of our inspections and suggested revisions with Adis, asking them to intervene directly on the dataset with the appropriate corrections. This process took place through complex iterations and has allowed us to gradually overcome the problems encountered while at the same time ensuring cross-validation of the data, which we can now consider to be as complete and reliable as possible. More details on the specific issues and revisions made are provided below.

Name and role of the organisations involved in a deal. There is a field in the raw data that should record the names and roles of the organisations that are parties to the deal (i.e. acquiring and acquired company, acquiring and divested company, licensor and licensee, etc.). We found instances where the categorisation was not accurate or systematic, posing an overall challenge in our analysis, e.g. "unnamed" or "unknown" companies in a deal and "unspecified" roles. We extracted the problematic records and shared them with Adis, which intervened to correct all deals where possible, i.e. where information was available and deemed reliable.[602]

Drugs object of the deal. Information about the drug(s) involved in a transaction is fundamental in assessing, e.g., licensing agreements, R&D ventures, and other deals that are specific to a drug or set of drugs, while it is less relevant for M&As (as those involve a concentration of ownership of all the products of the parties). We noticed that the purpose-specific drug field had many missing values, while information was usually reported in the description field. To solve this problem, we used the AdisInsight Drugs dataset and scanned the names of the over fifty-eight thousand treatments included against the description field of the Deals dataset, using a semantic algorithm (with the support of Trix). We then shared the retrieved drug names for each deal with Adis, asking them to make the appropriate corrections. This resulted in a significant

[602] We reported 97 records where companies were "unnamed" or "unknown"; Adis amended 74 records (the remaining 23 concern deals where the company name was not disclosed, adding to a further 42 deals with "undisclosed" companies, which we dropped from the analysis). We reported over 800 records with "unspecified" roles where they should be indexed based on Adis editorial tools and practices (M&A, purchases and licensing); Adis corrected 554 records. The remaining "unspecified" roles were dealt with through dedicated desk research or directly in the analysis (e.g. in M&A deals, roles do not necessarily need to be specified as the result of the deal is the merging of the two companies' portfolios anyway). In the end, the problem remained for only 32 licensing deals, while it was overcome for all M&As and purchases (see Appendix A.3 - Deals that have not been analysed).

improvement in the data.[603] Moreover, as explained in detail in section I.2.3, several strategies have then been adopted to enrich further and validate this information.

Value of the deal. The deal value in the raw data is missing for many transactions. With the help of Trix, we managed to retrieve many of the missing values from the description field. However, in many instances, we extracted multiple values and could not devise a rule for how they should be treated. For example, some transactions may involve multiple payments at different stages, so summing the different values would be appropriate. However, there are also instances where the description of a deal reports a valuation range (e.g., that the deal value is "70-75 million dollars"), so summing the extracted values ($70 million and $75 million) would be erroneous. Therefore, we shared with Adis the list of records for which we extracted a value and requested a revision. Adis compiled the data where the information was available and deemed reliable.[604] Unfortunately, there remains a considerable number of deals with a missing value, i.e., 4,616 in the sample of 6,315 deals of interest. Consequently, we will not apply any sample selection based on the deal value – contrary to the provisions of the Technical Specifications that required considering only transactions with a deal value above EUR 50 million to maintain the study's focus on the discontinuation of significant overlapping drug R&D projects. In any case, it is interesting to note that for the 1,699 transactions with a compiled value, the median is $ 100 million, and the value is greater than or equal to $ 50 million for 1,044 deals.

Status of the deal. We noticed that a non-negligible number of deals were classified as "pending" years after their announcement or as "active" for too long, the latter in deal types where "active" is a temporary status which should then result in a completion (i.e., M&A or purchases). Therefore, we asked Adis to amend these records.[605] After their revision, we decided to keep only "completed" deals or, in the case of deals that may have a duration (deals other than M&As or Purchases), to keep "active", "completed", or "terminated" deals (the latter only if concluded in years other than the year of initiation because it would be difficult for us to identify their effects otherwise). After this selection, of the 6,315 deals of interest in the period 2014-2018, 5,246 are "active", 903 "completed", and 166 "terminated".

The required additional processing of the deal data caused a delay, relative to the timeline, in the construction of the final dataset. Nevertheless, the application of tailored, large-scale semantic searching and matching algorithms to the rich raw information provided by AdisInsight in natural language, coupled with the data provider's willingness to revise the data, ultimately yielded more informational inputs to the fact-finding challenge.

[603] Through an automatic search, we identified 2,826 records mentioning drug names or synonyms in the description field while having a missing drug field. Adis amended 2,385 records. The remainder were false positives, e.g., due to the fact that drugs can also be mentioned in deals of which they are not the object. We, therefore, consider the results of Adis review as definitive.

[604] Through an automatic search, we flagged 657 records mentioning monetary values in the description field while having a missing value field. Adis made 396 corrections, explaining that the remaining instances could not be verified or identified.

[605] We asked Adis to revise all deals with a "pending" status, 289 in total, and 152 deals among mergers, acquisitions or purchases with an "active" status. After Adis revision, there only remain 14 deals with a "pending" status and 5 among mergers, acquisitions or purchases with an "active" status (therefore not completed).

Type of deals. There are many different categories of deals in the AdisInsight Deals database.[606] In some instances, the categorisation of a given deal is incorrect or not informative, and what is being traded (in term of property rights) can be determined only by reading into the description field. This information is pivotal to understand whether a deal type is relevant to the scope of the project and also to set up the analysis itself (as we apply different routines for examining deals of different categories). We performed a manual inspection to identify, in the description field, keywords that could help improve the classification for the purpose of the analysis, e.g. detecting an exchange of rights to qualify licensing agreements.[607]

Table I.1 shows the deal type definitions used by Adis and clarifies whether and how we have changed them. Table I.2 provides details on the number of deals in each category according to our reclassification, disaggregating it by the original distribution of Adis deal types. The data refer to the period of interest for the analysis, i.e. 2014-2018.

Table I.1: Deal types recommended for inclusion in the study: definitions

Adis Deal Type	Adis Definition of the Deal Type	Lear Deal Type Issues identified and changes applied (if any)
		M&A
Merger	Companies merge to form one. Usually involves a name change. More often, stocks/shares are exchanged, rather than cash.	We noticed inconsistencies in the classification used by Adis between Merger and Acquisition. Therefore, we reclassified as M&A all transactions that (either through alternative data sources or text analysis) we could identify as indeed a change in ownership of entire companies – including all associated assets and liabilities. This includes both cases where companies merge and transactions that result in the acquirer's ownership of at least a 50% interest in the acquired company. This group also includes those deals for which we were unable to identify an inconsistency in the original Adis classification as Mergers.
		Purchase
Purchase	Refers to purchase of products/assets/technologies by a company.	We reclassified as purchases all transactions that we have identified as entailing the acquisition of parts of a company, such as business units, product lines or simply products, facilities, technologies or other assets that did not constitute all of the assets (and related liabilities) of a company.

[606] https://adis.springer.com/help#Deal_Type.

[607] Although Adis reported a correction of the deal type was not feasible because the categorisation adopted reflects specific editorial choices, we found that 258 corrections were made based on our suggestions.

		The group also includes those deals for which we were unable to identify an inconsistency in the original Adis classification (either through alternative data sources or text analysis).
Acquisition	Refers to acquisition or divestiture of, a) whole or b) part of the company. a) Must involve a 50% or more share ownership in the company. B) Includes acquisition of a working part of a company such as division/department.	Using alternative data sources, text analysis, and manual inspection, we have reclassified these deals into M&A or Purchase, depending on their features.
Joint venture	We only use when specified in the source document. two or more companies joining hands under a contractual agreement to conduct a specific business enterprise, with both parties sharing profits/losses. Usually for a specific project only, rather than a continuing business relationship.	**Joint venture**
Equity investment	Investment of money from one organisation to another related to development of products or technologies which involves some payback, (additional to stocks or shares), for the investing organisation (e.g. royalties, later licensing rights etc). Only used when not in combination with some other deal type such as an acquisition or licensing agreement. NOTE: a company often includes an equity payment in a licensing/ collaboration deal. We do not process a separate equity deal for this.	**Equity investment**
Licensing	Licensing rights to products/ technologies etc. are acquired from a company, or rights are shared between companies.	**Licensing** Based on text analysis and manual sample inspection, we found that all deals included in the original Adis groups listed on the left-hand side can be broadly categorised as licensing agreements, the only difference being the type of right licensed (e.g.,
Licensing and supply	Licensing rights to products/ technologies etc. are acquired from a company. Additionally supply of products/ technologies is provided by Out-licensing company	

Development and marketing	Development (i.e. composition) and commercialisation of products/ technologies etc.	development and marketing v. marketing).
Marketing	Relates to the commercialisation of specific products	An exception concerns a small subset of marketing agreements, which cannot be reclassified as licensing agreements: we label these as **Marketing (not including licensing rights)**.
Distribution	Relates to the distribution of specific products in specific countries/ markets	
Manufacturing and marketing	Includes both the manufacturing and commercialisation of specific products	Using the same techniques and criteria, we included in the new Licensing group also few Manufacturing agreements and Manufacturing and Supply agreements.
Cross-licensing	An agreement where 2 or more organisations grant a license to each other for the exploitation of a specific product or technology defined in patents owned by them. Only use when specified in the media release.	**Cross-licensing**
Partnership	Collaboration between companies to carry out a specific task e.g. a clinical trial. Use this term when mentioned in the source document.	**Partnership**
R&D	Deal between companies for the research and development of products/ technologies etc. (e.g.: grants/ funding etc.)	**R&D**
Joint venture R&D	Only use when specified as a joint venture for R&D in the media release.	**Joint venture R&D**
Agreement	A general agreement relating to specific products or technologies. Only used where the actual type of agreement is not clearly specified.	Based on text analysis and manual verification, we have reclassified some of these deals as Licensing, as suggested by the compiled roles of the companies. The remainder has been reclassified as R&D agreements: we have manually inspected a random sample of 10% of these deals and verified that they were equivalent to R&D ones.

Source: Lear

Table I.2: Deal types recommended for inclusion in the study: frequencies

Lear Deal Type	Frequency	(Of which) Adis Deal Type: Frequency
M&A	490	Merger: 56 Acquisition: 433 Agreement: 1
Purchase	319	Purchase: 287 Acquisition: 30 Partnership: 2
Joint venture	47	Joint venture: 47
Equity investment	15	Equity investment: 12 Acquisition: 3
Licensing	2,920	Licensing: 2,227 Licensing and supply: 60 Development and marketing: 185 Manufacturing and marketing: 29 Marketing: 253 Distribution: 128 Manufacturing: 2 Manufacturing and supply: 8 Acquisition: 2 Joint venture: 1 Agreement: 25
Cross-licensing	14	Cross-licensing: 14
Partnership	26	Partnership: 26
R&D	2,438	R&D: 2,030 Acquisition: 1 Agreement: 407
Joint venture R&D	18	Joint venture R&D: 18
Marketing (not including licensing rights)	28	Marketing: 28
Total	6,315	6,315

Source: Lear

We exclude from the analysis deals in the following categories: Spin-offs, Manufacturing agreements, Manufacturing and supply agreements, Supply agreements, and Marketing

agreements that take the form of Promotion agreements when no drug is identified (for a total of 301 deals). Spin-offs are divestitures and as such cannot create any product/project overlaps. Manufacturing agreements, Manufacturing and supply agreements and Supply agreements are labels that seem to define a purely "vertical" relationship between undertakings that are operating (for the purposes of the deal) at different levels of drug development/supply. Indeed, by relying on a textual analysis based on keywords, we have identified and moved away from these categories the few deals that entailed the transfer of licensing or commercialisation rights that would create a risk of an anticompetitive object or effect (i.e., that kind of transaction that can create an horizontal overlap in the parties' ownership and control over drugs). These deals have been moved to the licensing agreement group. Accordingly, deals that remain in these deal types are residuals excluded from the analysis as they do not create the ability to eliminate a counterparty's competing product.

In what follows, we provide details and examples in support of this choice.

- Spin-off: deal made between the company wanting to spin-out (divesting company) and the management of the new company (divested company). It is a type of divestiture, so it is not a relevant deal type for an analysis of killer acquisitions. *Example*: "In 2018, Array BioPharma spun-off Yarra Therapeutics to develop and commercialise therapeutics targeted towards rare diseases, including PF 07265803.".
- Manufacturing agreement: refers to the production of products/technologies etc. on a large scale but also includes clinical development. This category covers deals concerning the manufacture of products. Where deals involve only product manufacturing (i.e. commercialisation rights are not transferred), there are no incentives for a killer acquisition. Indeed, deals that remain in this group can be assumed not to include relevant licensing rights related to commercialisation: using text analysis and manual verification, we found two deals that involved such licensing rights and moved them into the Licensing category. *Example*: "In January 2014, Lonza established an agreement with Pharmacyclics, Inc. to support the commercial and clinical production of its oral oncology drug, Imbruvica™ (Ibrutinib). The agreement follows a multi-year partnership, including the development and clinical manufacturing, which was utilized for Pharmacyclics' NDA submission and now first FDA approval of their lead product for oncology treatment. Under the long term agreement, Lonza will continue to support the production of commercial and clinical material.".
- Manufacturing and supply agreements: deals that include the manufacturing and the selling of the product to a purchaser. This category typically includes agreements according to which one firm engages in the production and supply of a product of the other firm. When control over the commercialisation of the drug remains within the firm that owns the drug, there is no ability to discontinue the product. This category also includes deals which, more broadly, involve some form of collaboration between the parties in the production and supply phase (e.g. supporting the production of the other party or the preparation of NDAs). *Example*: "In January 2014, Relypsa entered into an agreement with Lanxess Corporation to manufacture and supply Relypsa's Patiromer for commercial sale and to support Relypsa in preparing and filing its NDA.".
- Supply agreements: selling of goods to the purchaser on a large scale. If the purchaser of the goods is restricted as to where or to whom the goods may be on-sold, the arrangement is usually called a Distribution Agreement. Not used for supply of products for clinical trial only. This category typically includes deals whereby one party supplies to the other an input necessary in trials or a production input. As

such, this category cannot include candidate killer acquisitions. *Example*: "In February 2014, Bionor Pharma ASA entered into a supply agreement with Celgene Corp for supply of Istodax® for the REDUC trial. This agreement secures Bionor Pharma free supply of study drug of Istodax®.".

- Marketing agreements that take the form of Promotion agreements when no drug is identified: Deals different from licensing ones where Adis does not report any drugs as the object of the deal in its Deal data export in Excel format. *Example*: "In December 2013, Boston Scientific Corporation and The Medicines Company announced a co-promotion agreement for the Boston Scientific Promus Premier™ stent system. Under the terms of the agreement, The Medicines Company's acute cardiovascular care sales force will collaborate with the Boston Scientific Interventional Cardiology sales force to provide promotional support for the Promus Premier™ stent system in US hospitals beginning 1 January 2014.".

A.1.2. Clinical Trials Datasets

ClinicalTrials.gov. Employing the expertise of Trix, we retrieved data from ClinicalTrials.gov adopting a series of manual and automatic procedures via the following sequential steps. First, to identify the web address (i.e. URL pattern) which leads from the main web-search page of CT to each single recorded webpage of the registry, a manual analysis has been conducted to explore the HTML structure of the main search page and its relative extensions. Note that each single clinical trial is recorded in a dedicated webpage, which includes various hyperlinks that open to new webpages disclosing new details (for instance, the webpage where the history of changes of a study is recorded). Second, once we identified the pattern of the clinical trial webpages along with addresses of hyperlinks, and therefore relative URLs, we downloaded all webpages of the entire registry by implementing an automatic procedure built upon an AI algorithm. To make sure that we collected all needed pages, we implemented an automatic count. This count allows us to have full control of which page we downloaded automatically. Third, once we downloaded all the data, for each webpage, through HTMLParser we collected the text elements of our interest, using clues such as HTML tags, CSS classes, ID values, etc. Fourth, we normalized all collected data by converting them into the same format (for instance, we manipulated the dates to have the same format) and transferred the data into an Excel file (cvs), where each row identifies a clinical trial, and each column identifies the collected variable (i.e. interventions, sponsor, collaborators, recruitment status, last update posted date, etc.). For the data collected from the history of changes, we created a new Excel file where each row corresponds to a specific version of the study, and we use an additional helper column to track the study number. Finally, to control that we have correctly collected the data, we employ an ex-post analysis of the data. Specifically, we created specific sets to verify the information recorded in each column, checking for possible outliers or whether the converted format was inconsistent with the rest of the data (for instance, in a column where dates are collected, finding another type of data that is not a date would be an error).

The entire process was implemented by using the Python Programming Language. To create the final dataset, we used the following two packages: *beautifulsoup4* and *openpyxl*.[608]

European Union Clinical Trials Register. The EU Clinical Trials Register (EUCTR) is the database used by regulators in the European Union for data related to clinical trial protocols. It includes information on: (i) interventional clinical trials conducted in the EU and the European Economic Area (EEA);[609] and (ii) clinical trials conducted outside these two areas that are linked to European paediatric-medicine development.[610]

Below we provide details of the data contained in the EUCTR, how we retrieved it, and discuss the relevant limitations of the data that led us not to rely on the EUCTR for the present study.

The EUCTR contains the following information:

- EudraCT Number, i.e. the unique identifier for each study recorded in the EUCTR;
- Start Date, i.e. the date when the record was first entered in the database;
- Sponsor Name, i.e. the agent responsible for the information provided;
- Trial Status: authorized, ongoing or complete, temporarily halted, prematurely ended, restarted, prohibited by CA, suspended by CA;
- Full title of the study, i.e. the official scientific title of a recorded study;
- Term and Medical condition or disease under investigation;
- MedDRA term, i.e. an internationally used set of terms relating to medical conditions, medicines and medical devices;
- Status of the sponsor: e.g. Commercial, Non-Commercial, etc.;
- Pharmaceutical form: e.g. coated tablet, injection, etc.;
- Product name: i.e. name of the drug;
- Trade name: i.e. trade name of the drug;
- INN and Proposed INN, i.e. the International Non-proprietary Name for an active substance;
- Standard of Care (SOC) Term, i.e. it is the treatment accepted by medical experts as the most appropriate for a certain type of disease in a particular setting and is widely used by healthcare professionals. Also called best practice, standard medical care, best available therapy and standard therapy;
- Condition being studied is a rare disease: i.e. yes/no;
- Therapeutic exploratory, i.e. Phase of study development;
- End of Trial Status: i.e. complete;
- Date of the global end of the trial.

[608] Both beautifulsoup4 and openpyxl are library which allow to scrape information from web pages, and to read/write Excel 2010 xlsx/xlsm/xltx/xltm files, respectively.

[609] After a preliminary validation of the data, the sponsor of the clinical trial registers in full all data related to the trial protocols at the National Competent Authority of the Member State(s) in which the sponsor plans to conduct the study. This latter is responsible to upload the trial application in the EudraCT register.

[610] The EUCTR validates report details about clinical trials conducted outside the EU/EEA when (i) they form part of a paediatric investigation plan, or (ii) the registered clinical trials are sponsored by a marketing authorisation holder and involve the use of a medicine in the paediatric population as part of an EU marketing authorisation.

After downloading the EUCTR data, we used the same approach and tools to normalise, convert into a usable format and validate it as we did for the US data retrieved from ClinicalTrials.gov. However, the EU register turned out not as rich in information as ClinicalTrials.gov.[611] In fact, we encountered a number of challenges related to the quality of the data in the EU register.[612] In particular:

- The output of search engine queries provides only a summary of the registered trial, and this information is not complete (for instance, the Phase reached by a study is not labelled, unless explicitly stated in the full title of the study).
- Information on clinical trials entered into the database between May 2004 and March 2011 might be incomplete or contain inconsistencies. This has an impact on this project, as even if our analysis focuses on 2014-2018, data related to earlier years are used to feed our datasets. For instance, the end date of a trial might be missing, or the trial status might be 'Ongoing' even after completion. This is due to the different dates when Member States implemented the Directive and started using the EUCTR between 2004 and 2006.[613]
- The records do not show any historical changes that occurred in the recorded trials: EUCTR only provides access to the basic information on when a study was first posted, while information on the recruitment status and on sponsors, collaborators and investigators refers to the latest update. Therefore, the historical changes that occurred in the recruitment status and in sponsor and collaborators cannot be observed, and we can only observe the latest recruitment status and the latest sponsor and collaborators reported to the registry. This is a major limitation for our analysis, as the history of changes of clinical studies is the essential feature we use to reconstruct the retrospective evolution of firms' portfolios and of the recruitment status of trials over time (at the time a deal was signed and thereafter).
- Reasons why a trial has been "temporarily halted" or "prematurely ended" are never reported (and this information is relevant in our strategy to identify discontinuations and possible KAs, as explained in sections I.3 and I.3.3).
- The register does not guarantee consistency between records entered by different countries for the same trial, as it lacks central monitoring by the European Medicines Agency (EMA) and the absence of a data quality verification system between the registry and National Competent Authorities causes updates to take a long time (Goldacre, et al., 2018).[614] The results of the recorded trials are entered into the database directly by the responsible sponsors and are published in the EUCTR only after the sponsors have validated their data through the National Competent Authority of the relevant Member State(s).[615]

[611] The number of clinical trials recorded in EUCTR is far lower than that in CT. As a comparison, on January 2023 EUCRT displays a total of 43,135 clinical trials, against a total of 437,588 currently listed in CT. Moreover, CT keeps track of historical changes occurred to the pivotal actors and dimensions of a trial, whereas this piece of information is missing in EUCTR.

[612] It is worth noting that the EU clinical trial registry is currently undergoing a process of changes. See https://euclinicaltrials.eu/about-this-website/.

[613] "Delays in setting up links to NCAs and implementing a data verification system has led to known data issues such as missing completion or trial status data for records up to March 2011". See: https://www.medrxiv.org/content/10.1101/2021.06.29.21259627v1.full, accessed on July 9th.

[614] See: https://www.medrxiv.org/content/10.1101/2021.06.29.21259627v1.full, accessed on July 9th.

[615] For more detail, see: https://eudract.ema.europa.eu/protocol.html.

We therefore highlight that i) EUCTR does not provide the historical data needed for our analysis, unlike CT, and ii) our comparative analysis shows that CT comprehensively covers almost all drugs registered in EUCTR, presumably all the most relevant ones. In addition, we note that we rely on both CT and Adis Drugs to examine whether there is further development of the overlapping drugs between the companies' portfolios after a deal, and that the latter source includes information from EUCTR and from EU Member States' national registers. Taking all of this into account, we conclude that reliance on clinical trial data extracted from CT is appropriate and provides reliable results.

To assess the impact of not sourcing data from the EUCTR in the present study (net of duplicated information), we compare it against CT by studying the EU trials recorded from 2000 to 2022.[616] The EUCTR includes 40,839 trials, of which 10,828 were recorded in 2014-2018 (we excluded duplicates, herbal products, devices, homoeopathic products, etc.). Leveraging the information on the EudraCT code (i.e. the unique trial identifier of the EUCTR) included in CT, we found that 59.22% (24,183) of EU trials are also recorded in CT, while the remaining 40.78% (16,656) are only in EUCTR. We have found that the trials reported exclusively in the EUCTR concern a total of 6,783 studied molecules, and through textual analysis of drug names we found that 98% (6,647) of these molecules are also studied in CT. This confirms that the most relevant or promising molecules (most likely to be marketed in the US) are also recorded in the US register.

A.1.3 The matching of Adis and Clinical Trials dataset

In this section, we provide details of the approach we have taken to match each drug investigated and reported in CT to an Adis Drugs profile. The association of the investigated molecules recorded in CT with an Adis Drugs profile represents an important step in the construction of our final database. Indeed, their association allows us to identify pivotal aspects about the studied drugs, i.e. the originator, the class to which the drug belongs to, its MoA, the highest development phase, etc.

The process of pairing the investigated molecules recorded in CT to an Adis Drugs profile required a detailed manual analysis of the data on both extracted datasets before designing a set of rules which we implemented to perform the matching. This phase was quite demanding, because the name of a molecule or a drug is not standardised, therefore their definition can vary broadly. For a large-scale type of exercise, as the one we performed for this process, these preliminary steps demonstrated to be pivotal. The ex-ante matching analysis, indeed, included a series of steps which helped us to consolidate the type of rules to implement.

First, we employed a semi-manual semantic analysis of the words adopted to define a drug/molecule, along with the length (min and max) of the name of a drug/molecule. We also inspected the design of the name of molecules at the early definition stage (Phase II), where the name is usually defined by an alphanumeric string. Within this preliminary phase, we also identified the common terms used to define the scientific name of a molecule (e.g. sodium). This last step helped us to identify which common names could be excluded from the matching rules, and also helped us to establish a rule that would prevent a molecule under development from being associated with a generic term. Secondly, we carried out a series of interactive trial and error processes which helped us to refine the rules used.

As a result, with the support of Trix, we have developed an *ad hoc* algorithm to perform the matching exercise. This exercise involves using the comprehensive list of molecules investigated in CT (focusing on interventional drugs), by retrieving their names from the *Arms and Interventions* section. Then, starting from Adis Drugs, we seek to establish associations between each molecule and the drugs catalogued in CT. We do this by matching the names and related synonyms of the molecules according to the following set of rules:

1. Each Adis Drugs profile is searched in CT making use of both the drug name (term), and its relative synonyms.

2. The search is conducted term by term, considering alphanumeric names, and relative spaces. Each single name, as it appears in Adis Drugs must match with the equivalent in CT.

3. In case of composite names (multiple terms), the matching occurs only if the drug name in Adis Drugs appears in CT with at most two terms of distance between them.

4. All special characters, such as ® or ™, are ignored.

5. All drug names whose length is below three digits (excluding spaces) are dropped; for drug names defined by numbers, the relevant threshold is five digits.

6. Interventional treatments (in CT), which are classified as: "behavioural", "device", "diagnostic test", "dietary supplement", "procedure", "other" are not considered, because they do not identify any new molecular entry.

7. Each drug name is cleared by the company name extracted from the field "Organisation" in Adis Drugs; the only exception is for vaccines where the name of the company is part of the drug name (these drugs are identified by looking at the word "vaccine" in their name).

8. If in Adis Drugs the drug name includes common terms between brackets (e.g., sodium, disodium, fluoride, etc.), these are not searched as standing alone terms.

We apply an additional, specific rule for drugs whose name is a composite alphanumeric term:, i.e. an alphanumeric drug name is searched for an exact matching in its total length and its variations. For instance, a drug whose name in Adis Drugs is "ABC123" is searched as "ABC123"; "ABC 123"; and "ABC-123". The same rule is applied for drugs whose name appears as "ABC-123" or "ABC 123".

A.2 Additional results on the fact-finding challenge

A.2.1 M&As

Table I.3: Overlaps and discontinuations for M&A deals

	Number of deals
M&As (2014-2018)	490
with at least one overlap in TI (MeSH)	72
with at least one narrow overlap	35
(of which) narrow overlap in MeSH + MoA	35
(of which) narrow overlap in MeSH + Drug class (vaccines)	0
with at least one discontinuation in MesH	28
with at least one prima facie relevant discontinuation	19

Source: Lear analysis

Table I.4: Distribution of overlaps and discontinuations for M&A deals

	Total number	Median by deal	5th percentile by deal	95th percentile by deal
Narrow overlaps	1,723	5	1	70
Discontinuations in MeSH	634	2	0	35
(of which) Type B	402	2	0	28
(of which) Type C	232	0	0	35
Prima facie relevant Discontinuations	120	1	0	7
(of which) Type B	68	0	0	7
(of which) Type C	52	0	0	1

Source: Lear analysis

Table I.5: Indicators for KA analysis (M&A): Intensity of competition

	All Discontinuations			Prima Facie Relevant Discontinuations		
	Number of Overlaps	Mean	Standard Deviation	Number of Overlaps	Mean	Standard Deviation
Number of competing drugs	634	8.98	12.70	120	12.93	20.90
Number of competing drugs (weighted by phase)	634	18.00	23.59	120	25.36	33.86
Number of competing marketed drugs	634	0.61	1.40	120	1.25	2.41
Absence of competitors	634	0.18	0.38	120	0.28	0.45
Absence of generic competition	634	0.71	0.46	120	0.68	0.47
Fraction of competing molecules that lag behind [(1)]	523	0.41	0.39	86	0.43	0.35
Fraction of competing molecules that lag behind and are in Phase I [(2)]	368	0.71	0.39	66	0.62	0.42
All competitors are pharma companies	634	0.11	0.31	120	0.08	0.28

Source: Lear analysis. (1) The statistics for this indicator are computed only when the number of competitors is greater than zero. (2) The statistics for this indicator are computed only when both the number of competitors is greater than zero and the competing drugs are in Phase I.

Table I.6: Indicators for KA analysis for M&A: Intensity of competition (Continued)

	No Discontinuations		
	Number of Overlaps	Mean	Standard Deviation
Number of competing drugs	1089	14.56	16.02
Number of competing drugs (weighted by phase)	1089	27.61	28.35
Number of competing marketed drugs	1089	0.93	1.51
Absence of competitors	1089	0.10	0.30
Absence of generic competition	1089	0.79	0.40
Fraction of competing molecules that lag behind [(1)]	982	0.58	0.36
Fraction of competing molecules that lag behind and are in Phase I [(2)]	853	0.66	0.36
All competitors are pharma companies	1089	0.07	0.25

Source: Lear analysis. [(1)] The statistics for this indicator are computed only when the number of competitors is greater than zero. [(2)] The statistics for this indicator are computed only when both the number of competitors is greater than zero and the competing drugs are in Phase I.

Table I.7: Indicators for KA analysis (M&A): Features of the parties and of overlapping drugs projects (1)

	All Discontinuations			Prima Facie Relevant Discontinuations		
	Number of Overlaps	Mean	Standard Deviation	Number of Overlaps	Mean	Standard Deviation
Highest phase at deal acquirer drug (MeSH)	634	1.96	0.91	120	2.09	0.89
Highest phase at deal target drug (MeSH)	634	1.94	0.84	120	2.15	0.95
Overlap between Phase I relative to Phase II	634	0.28	0.45	120	0.24	0.43
Overlap between Phase I relative to Phase III	634	0.03	0.16	120	0.03	0.18
Overlap between Phase II relative to Phase III	634	0.09	0.29	120	0.07	0.25

Source: Lear analysis

Table I.8: Indicators for KA analysis (M&A): Features of the parties and of overlapping drugs projects (1, Continued)

	No Discontinuations		
	Number of Overlaps	Mean	Standard Deviation
Highest phase at deal acquirer drug (MeSH)	1089	2.20	0.93
Highest phase at deal target drug (MeSH)	1089	2.26	0.97
Overlap between Phase I relative to Phase II	1089	0.21	0.41
Overlap between Phase I relative to Phase III	1089	0.05	0.22
Overlap between Phase II relative to Phase III	1089	0.10	0.30

Source: Lear analysis

Table I.9: Indicators for KA analysis (M&A): Features of the parties and of overlapping drugs projects (2)

	All Discontinuations			Prima Facie Relevant Discontinuations		
	Number of deals	Mean	Standard Deviation	Number of deals	Mean	Standard Deviation
Deal Value (Million $)	25	5713.70	14467.56	16	2384.30	4099.51
Normalised Deal Value	25	1007.29	1624.69	16	692.77	1174.87

Source: Lear analysis. The number of observations for these indicators is limited due to missing data for numerous transactions in the AdisInsight database.

Table I.10: Indicators for KA analysis (M&A): Features of the parties and of overlapping drugs projects (2, Continued)

	No Discontinuations		
	Number of Deals	Mean	Standard Deviation
Deal Value (million $)	7	14580.80	22538.15
Normalised Deal Value	7	1871.71	1018.93

Source: Lear analysis. The number of observations for these indicators is limited due to missing raw data for numerous transactions in the AdisInsight database.

A.2.2 Purchase

Table I.11: Overlaps and discontinuations for Purchase deals

	Number of deals
Purchase deals (2014-2018)	319
Purchase deals with an identified drug object	229
with at least one overlap in TI (MeSH)	37
with at least one narrow overlap	12
(of which) narrow overlap in MeSH + MoA	12
(of which) narrow overlap in MeSH + Drug class (vaccines)	0
with at least one discontinuation in MesH	9
with at least one prima facie relevant discontinuation	4

Source: Lear analysis

Table I.12: Distribution of overlaps and discontinuations for Purchase deals

	Total number	Median by deal	5th percentile by deal	95th percentile by deal
Narrow overlaps	65	3.5	1	18
Discontinuations in MeSH	27	1	0	12
(of which) Type B	26	1	0	12
(of which) Type C	1	0	0	1
Prima facie relevant discontinuations	10	0	0	4
(of which) Type B	9	0	0	4
(of which) Type C	1	0	0	1

Source: Lear analysis

A.2.3 Licensing

Table I.13: Overlaps and discontinuations for Licensing deals

	Number of deals
Licensing deals (2014-2018)	2,920
Licensing deals with an identified drug object	1,219
with at least one overlap in TI (MeSH)	223
with at least one narrow overlap	99
(of which) narrow overlap in MeSH + MoA	99
(of which) narrow overlap in MeSH + Drug class (vaccines)	0
with at least one discontinuation in MesH	72
with at least one prima facie relevant discontinuation	27

Source: Lear analysis

Table I.14: Distribution of overlaps and discontinuations for Licensing deals

	Total number	Median by deal	5th percentile by deal	95th percentile by deal
Narrow overlaps	991	2	1	70
Discontinuations in MeSH	510	1	0	29
(of which) Type B	378	1	0	25
(of which) Type C	132	0	0	7
Prima facie relevant discontinuations	97	0	0	5
(of which) Type B	85	0	0	5
(of which) Type C	12	0	0	1

Source: Lear analysis

Table I.15: Indicators for KA analysis (Licensing): Intensity of competition

	All Discontinuations			Prima Facie Relevant Discontinuations		
	Number of Overlaps	Mean	Standard Deviation	Number of Overlaps	Mean	Standard Deviation
Number of competing drugs	510	7.19	8.18	97	8.81	9.65
Number of competing drugs (weighted by phase)	510	14.95	19.05	97	20.11	26.79
Number of competing marketed drugs	510	0.79	2.19	97	1.66	3.82
Absence of competitors	510	0.21	0.40	97	0.19	0.39
Absence of generic competition	510	0.79	0.40	97	0.71	0.46
Fraction of competing molecules that lag behind (1)	405	0.37	0.37	79	0.38	0.39
Fraction of competing molecules that lag behind and are in Phase I (2)	258	0.73	0.37	48	0.60	0.40
All competitors are pharma companies	510	0.14	0.34	97	0.10	0.31

Source: Lear analysis. (1) The statistics for this indicator are computed only when the number of competitors is greater than zero. (2) The statistics for this indicator are computed only when both the number of competitors is greater than zero and the competing drugs are in Phase I.

Table I.16: Indicators for KA analysis (Licensing): Intensity of competition (Continued)

	No Discontinuations		
	Number of Overlaps	Mean	Standard Deviation
Number of competing drugs	481	8.54	10.14
Number of competing drugs (weighted by phase)	481	17.86	22.09
Number of competing marketed drugs	481	1.00	2.28
Absence of competitors	481	0.16	0.37
Absence of generic competition	481	0.84	0.37
Fraction of competing molecules that lag behind [(1)]	403	0.52	0.37
Fraction of competing molecules that lag behind and are in Phase I [(2)]	324	0.63	0.40
All competitors are pharma companies	481	0.11	0.32

Source: Lear analysis. [(1)] *The statistics for this indicator are computed only when the number of competitors is greater than zero.* [(2)] *The statistics for this indicator are computed only when both the number of competitors is greater than zero and the competing drugs are in Phase I.*

Table I.17: Indicators for KA analysis (Licensing): Features of the parties and of overlapping drugs projects (1)

	All Discontinuations			Prima Facie Relevant Discontinuations		
	Number of Overlaps	Mean	Standard Deviation	Number of Overlaps	Mean	Standard Deviation
Highest phase at deal acquirer drug (MeSH)	510	1.85	0.91	97	1.95	1.05
Highest phase at deal target drug (MeSH)	510	1.71	0.84	97	1.62	0.92
Overlap between Phase I relative to Phase II	510	0.37	0.48	97	0.31	0.46
Overlap between Phase I relative to Phase III	510	0.07	0.26	97	0.12	0.33
Overlap between Phase II relative to Phase III	510	0.04	0.20	97	0.04	0.20

Source: Lear analysis

Table I.18: Indicators for KA analysis (Licensing): Features of the parties and of overlapping drugs projects (1, Continued)

	No Discontinuations		
	Number of Overlaps	Mean	Standard Deviation
Highest phase at deal acquirer drug (MeSH)	481	2.23	1.11
Highest phase at deal target drug (MeSH)	481	2.09	0.71
Overlap between Phase I relative to Phase II	481	0.22	0.41
Overlap between Phase I relative to Phase III	481	0.05	0.23
Overlap between Phase II relative to Phase III	481	0.09	0.28

Source: Lear analysis

Table I.19: Indicators for KA analysis (Licensing): Features of the parties and of overlapping drugs projects (2)

	All Discontinuations			Prima Facie Relevant Discontinuations		
	Number of Deals	Mean	Standard Deviation	Number of Deals	Mean	Standard Deviation
Deal Value (Million $)	43	710.06	1116.09	20	830.60	824.25
Normalised Deal Value	41	539.91	712.23	19	649.11	456.08
Exclusivity of licencing	72	0.50	0.50	27	0.44	0.51
Upfront payments only	72	0.01	0.12	27	0.00	0.00

Source: Lear analysis. The number of observations for these indicators is limited due to missing raw data for numerous transactions in the AdisInsight database.

Table I.20: Indicators for KA analysis (Licensing): Features of the parties and of overlapping drugs projects (2, Continued)

	No Discontinuations		
	Number of Deals	**Mean**	**Standard Deviation**
Deal Value (Million $)	17	559.21	460.93
Normalised Deal Value	16	535.48	479.87
Exclusivity of licencing	27	0.59	0.50
Upfront payments only	27	0.00	0.00

Source: Lear analysis. The number of observations for these indicators is limited due to missing raw data for numerous transactions in the AdisInsight database.

A.2.4 R&D

Table I.21: Overlaps and discontinuations for R&D agreements

	Total
R&D deals (2014-2018)	2,438
R&D deals with an identified object (TI & drug)	1,169
with at least one overlap in TI (MeSH)	219
with at least one narrow overlap	87
(of which) narrow overlap in MeSH + MoA	87
(of which) narrow overlap in MeSH + Drug class (vaccines)	0
with at least one discontinuation in MesH	69
with at least one prima facie relevant discontinuation	37

Source: Lear analysis

Table I.22: Distribution of overlaps and discontinuations for R&D agreements

	Total number	Median by deal	5th percentile by deal	95th percentile by deal
Narrow overlaps	2199	12	1	120
Discontinuations in MeSH	800	4	0	32
(of which) Type B	718	4	0	27
(of which) Type C	82	0	0	5
Prima facie relevant Discontinuations	263	0	0	13
(of which) Type B	238	0	0	12
(of which) Type C	25	0	0	1

Source: Lear analysis

Table I.23: Indicators for KA analysis (R&D): Intensity of competition

	All Discontinuations			Prima Facie Relevant Discontinuations		
	Number of Overlaps	Mean	Standard Deviation	Number of Overlaps	Mean	Standard Deviation
Number of competing drugs	800	8.52	9.23	263	11.34	10.65
Number of competing drugs (weighted by phase)	800	17.05	19.25	263	22.30	21.28
Number of competing marketed drugs	800	0.62	1.40	263	0.88	1.53
Absence of competitors	800	0.16	0.37	263	0.09	0.29
Absence of generic competition	800	0.77	0.42	263	0.75	0.43
Fraction of competing molecules that lag behind (1)	671	0.42	0.39	239	0.38	0.34
Fraction of competing molecules that lag behind and are in Phase I (2)	449	0.67	0.39	167	0.77	0.34
All competitors are pharma companies	800	0.10	0.31	263	0.11	0.32

Source: Lear analysis. (1) The statistics for this indicator are computed only when the number of competitors is greater than zero. (2) The statistics for this indicator are computed only when both the number of competitors is greater than zero and the competing drugs are in Phase I.

Table I.24: Indicators for KA analysis (R&D): Intensity of competition (Continued)

	No Discontinuations		
	Number of Overlaps	Mean	Standard Deviation
Number of competing drugs	1399	8.85	9.11
Number of competing drugs (weighted by phase)	1399	16.98	17.42
Number of competing marketed drugs	1399	0.50	1.11
Absence of competitors	1399	0.13	0.34
Absence of generic competition	1399	0.87	0.34
Fraction of competing molecules that lag behind [1]	1213	0.54	0.39
Fraction of competing molecules that lag behind and are in Phase I [2]	957	0.61	0.37
All competitors are pharma companies	1399	0.06	0.24

Source: Lear analysis. [1] The statistics for this indicator are computed only when the number of competitors is greater than zero. [2] The statistics for this indicator are computed only when both the number of competitors is greater than zero and the competing drugs are in Phase I.

Table I.25: Indicators for KA analysis (R&D): Features of the parties and of overlapping drugs projects (1)

	All Discontinuations			Prima Facie Relevant Discontinuations		
	Number of Overlaps	Mean	Standard Deviation	Number of Overlaps	Mean	Standard Deviation
Highest phase at deal acquirer drug (MeSH)	800	1.57	0.88	263	1.25	0.57
Highest phase at deal target drug (MeSH)	800	2.10	0.91	263	2.06	0.82
Overlap between Phase I relative to Phase II	800	0.38	0.49	263	0.48	0.50
Overlap between Phase I relative to Phase III	800	0.10	0.30	263	0.14	0.35
Overlap between Phase II relative to Phase III	800	0.07	0.25	263	0.03	0.18

Source: Lear analysis

Table I.26: Indicators for KA analysis (R&D): Features of the parties and of overlapping drugs projects (1, Continued)

	No Discontinuations		
	Number of Overlaps	Mean	Standard Deviation
Highest phase at deal acquirer drug (MeSH)	1399	2.13	1.11
Highest phase at deal target drug (MeSH)	1399	2.14	0.86
Overlap between Phase I relative to Phase II	1399	0.29	0.45
Overlap between Phase I relative to Phase III	1399	0.10	0.30
Overlap between Phase II relative to Phase III	1399	0.08	0.27

Source: Lear analysis

Table I.27: Indicators for KA analysis (R&D): Features of the parties and of overlapping drugs projects (2)

	All Discontinuations			Prima Facie Relevant Discontinuations		
	Number of Observations	Mean	Standard Deviation	Number of Observations	Mean	Standard Deviation
Deal Value (Million $)	6	1818.67	4424.44	4	2723.75	5417.51
Normalised Deal Value	6	913.67	2210.12	4	1366.88	2705.44
Normalised Deal Value (by phase)	6	266.50	628.88	4	396.50	769.11
Overlap ratio [1]	87	0.13	0.15	41	0.11	0.05

Source: Lear analysis. The number of observations for all indicators in the table is limited due to missing raw data for numerous transactions in the AdisInsight database. For additional information, please refer to section I.1.1.[1] Moreover, for R&D deals involving more than two companies, statistics that take into account the number of overlaps (such as the Overlap ratio in this table) are calculated for each company's portfolio.

Table I.28: Indicators for KA analysis (R&D): Features of the parties and of overlapping drugs projects (2, Continued)

	No Discontinuations		
	Number of Observations	**Mean**	**Standard Deviation**
Deal Value (Million $)	1	30.00	
Normalised Deal Value	1	15.00	
Normalised Deal Value (by phase)	1	5.00	
Overlap ratio (1)	18	0.27	0.32

Source: Lear analysis. The number of observations for all indicators in the table is limited due to missing raw data for numerous transactions in the AdisInsight database. For additional information, please refer to section I.1.1. (1) *Moreover, for R&D deals involving more than two companies, statistics that take into account the number of overlaps (such as the Overlap ratio in this table) are calculated for each company's portfolio.*

A.2.5 Other types of deals

Table I.29: Overlaps and discontinuations for other types of deals at the deal level

	Equity	Marketing	JV R&D	JV	Cross-Licensing	Partnership	Total
Number of deals (2014-2018)	15	28	18	47	14	26	148
Number of deals with identified drug object	7	28	7	20	9	20	91
with at least one overlap in TI (MeSH)	4	4	1	2	1	1	13
with at least one narrow overlap	2	2	1	1	1	0	7
(of which) narrow overlap in MeSH + MoA	2	2	1	1	1	0	7
(of which) narrow overlap in MeSH + Drug class (vaccines)	0	0	0	0	0	0	0
with at least one discontinuation in MesH	2	1	1	1	0	0	5
with at least one prima facie relevant discontinuation	2	1	1	1	0	0	5

Source: Lear analysis

Table I.30: Distribution of overlaps and discontinuations for other types of deals

	Equity	Marketing	JV R&D	JV	Cross-Licensing	Partnership	Total
Narrow overlaps	5	98	6	6	1	0	116
Discontinuations in MeSH	5	64	3	3	0	0	75
(of which) Type B	5	50	3	3	0	0	61
(of which) Type C	0	14	0	0	0	0	14
Prima facie relevant discontinuation	5	3	1	1	0	0	10
(of which) Type B	5	3	1	1	0	0	10
(of which) Type C	0	0	0	0	0	0	0

Source: Lear analysis

Table I.31: Distribution of overlaps and discontinuations for Equity investments

	Total number	Median by deal	5th percentile by deal	95th percentile by deal
Narrow overlaps	5	2.5	1	4
Discontinuations in MeSH	5	2.5	1	4
(of which) Type B	5	2.5	1	4
(of which) Type C	0	0	0	0
Prima facie relevant discontinuations	5	2.5	1	4
(of which) Type B	5	2.5	1	4
(of which) Type C	0	0	0	0

Source: Lear analysis

Table I.32: Distribution of overlaps and discontinuations for Marketing deals

	Total number	Median by deal	5th percentile by deal	95th percentile by deal
Narrow overlaps	98	49	1	97
Discontinuations in MeSH	64	32	0	64
(of which) Type B	50	25	0	50
(of which) Type C	14	7	0	14
Prima facie relevant discontinuations	3	1.5	0	3
(of which) Type B	3	1.5	0	3
(of which) Type C	0	0	0	0

Source: Lear analysis

Table I.33: Distribution of overlaps and discontinuations for Joint venture R&D

	Total number	Median by deal	5th percentile by deal	95th percentile by deal
Narrow overlaps	6	6	6	6
Discontinuations in MeSH	3	3	3	3
(of which) Type B	3	3	3	3
(of which) Type C	0	0	0	0
Prima facie relevant discontinuations	1	1	1	1
(of which) Type B	1	1	1	1
(of which) Type C	0	0	0	0

Source: Lear analysis

Table I.34: Distribution of overlaps and discontinuations for Joint venture deals

	Total number	Median by deal	5th percentile by deal	95th percentile by deal
Narrow overlaps	6	6	6	6
Discontinuations in MeSH	3	3	3	3
(of which) Type B	3	3	3	3
(of which) Type C	0	0	0	0
Prima facie relevant discontinuations	1	1	1	1
(of which) Type B	1	1	1	1
(of which) Type C	0	0	0	0

Source: Lear analysis

Table I.35: Distribution of overlaps and discontinuations for Cross-licensing deals

	Total number	Median by deal	5th percentile by deal	95th percentile by deal
Narrow overlaps	1	1	1	1
Discontinuations in MeSH	0	0	0	0
(of which) Type B	0	0	0	0
(of which) Type C	0	0	0	0
Prima facie relevant discontinuations	0	0	0	0
(of which) Type B	0	0	0	0
(of which) Type C	0	0	0	0

Source: Lear analysis

A.3 Deals that have not been analysed

In our KA analysis, a non-negligible number of deals are excluded because an overlap in a MeSH Term (our definition of TIs) could not be established, for possibly different

reasons. In this section, we explore the reasons that led to the exclusion of these deals. As the reasons can vary depending on the type of deal, we have organised the discussion to provide specific details for each deal type.

Table I.36 provides a breakdown of the relevant exclusion criteria for the M&A deals. Of the 490 M&A deals in our sample, 72 deals (around 15%) had overlapping MeSH terms and thus met the initial criteria for inclusion in our analysis. These deals were then subjected to the further scrutiny associated with the identification of narrow overlaps. The remaining 418 deals (85%) were excluded for the following reasons:

- 353 deals (72%) were not analysed because at least one of the companies involved and its group was not present in our clinical trials (CT) dataset. This typically occurs when a company has no R&D projects in its portfolio, or where its drugs are only at the pre-clinical stage. It is worth noting that the Adis Deals dataset also includes deals involving companies focused on platforms, technologies and devices rather than drugs. For example, it includes deals such as Baxter's 2014 acquisition of Chatham Therapeutics, a company specialising in gene therapy platform technology, and BTG plc's 2014 acquisition of PneumRx, a medical device company.
- 19 deals (4%) were excluded from the analysis because at least one of the companies or its group had no active molecules in its portfolio.
- 41 deals (8%) met these initial filters but were excluded because the companies involved had active portfolios that did not overlap in MeSH terms.
- 4 deals (0.8%) took place between companies of the same group and were therefore excluded as our approach considers the group as a single entity.
- Finally, one deal (0.2%) was excluded because it was a duplicate entry in the dataset.

Table I.36: Categorisation of issues for M&A deals not covered in the analysis

Issue (if any)	Number of deals	Percentage of deals
At least one overlap in MeSH terms between companies	72	14.7
Deals not covered by M&A deal analysis		
At least one of the companies in the deal (including its group) does not appear in CT	353	72.0
At least one of the companies in the deal (including its group) has no active molecules in its portfolio	19	3.9
Companies have active portfolios that do not overlap in MeSH terms	41	8.4
Acquisitions between companies of the same group	4	0.8
Duplicate deal	1	0.2
Total	490	100

Source: Lear analysis

Table I.37 focuses on purchases. Of the 319 purchases in our sample, 37 (12%) result in at least one overlap in MeSH terms. The remaining 282 deals (88%) were excluded for the following reasons:

- As detailed in section I.5 of the Final Report, our analysis of purchase deals is limited to deals for which we could identify a drug object, i.e., a (set of) drug(s) traded through the deal. This preliminary filtering produced the exclusion of 90 deals (28%).
- 58 deals (18%) were excluded because the acquiring company (and its group) had no active or relevant molecules in its portfolio.
- 85 deals (27%) were excluded because the drug(s) object of the deal did not appear in our clinical trials (CT) dataset.
- 13 deals (4%) involved drugs that were already generic.
- 6 deals (2%) were not analysed because the drug(s) were not in the CT dataset at the time of the deal.
- The remaining 30 deals (9%) had no overlap in MeSH terms.

An issue that characterises purchase deals (and all deal types except M&A) is that the inability to identify a drug target leads to the exclusion of the deal from the analysis. A possible concern is that this inability is due to data limitations and therefore may lead to the exclusion of relevant deals (although the extensive checks carried out and the coverage achieved in terms of deals with an identified target should reassure in this regard).

Table I.37: Categorisation of issues for Purchase deals not covered in the analysis

Issue (if any)	Number of deals	Percentage of deals
At least one overlap in MeSH terms	37	11.6
Deals not covered by purchase deal analysis		
Purchase without an identified drug object	90	28.2
The acquiring company (including its group) has no active/relevant molecules in its portfolio	58	18.2
The drug(s) object of the deal does not appear in CT	85	26.6
The drug(s) object of the deal is already a generic	13	4.1
The drug(s) object of the deal is not in CT at the time of the deal	6	1.9
No overlap in MeSH terms	30	9.4
Total	319	100

Source: Lear analysis

Table I.38 focuses on licensing deals. Of the 2,920 licensing deals included in our sample, 223 (8%) have at least one overlap in MeSH terms. The remaining 2,697 deals (92%) were excluded for the following reasons:

- 1,701 deals (58%) lacked an identified drug object.
- 32 deals (1%) were excluded due to the fact that the licensing roles, i.e., licensing-in vs licensing-out, were not specified in Adis Deals. The role is fundamental to the analysis as, once the object of the deal is identified, we examine overlaps relative to the licensing-in company's portfolio.
- 266 deals (9%) were not analysed because the licensing-in company and its group are not included in the clinical trials (CT) dataset.
- 27 deals (0.9%) were excluded because the licensing-in company had no active or relevant molecules in its portfolio.
- 474 deals (16%) were not analysed because the licensed drug was not in the CT dataset.
- 13 deals (0.45%) involved licensed drugs that were already generic at the time of the deal.
- 33 deals (1.13%) were excluded because the licensed drugs were not in the CT dataset at the time of the deal.
- Finally, 151 deals (5.17%) were excluded from the analysis because they lacked any overlap in MeSH terms.

Table I.38: Categorisation of issues for Licensing deals not covered in the analysis

Issue (if any)	Number of deals	Percentage of deals
At least one overlap in MeSH terms	223	7.6
Deals not covered by licensing deal analysis		
Licensing without an identified drug object	1,701	58.3
Licensing roles not specified	32	1.1
The licensing-in company (including its group) does not appear in CT	266	9.1
The licensing-in company (including its group) has no active/relevant molecules in its portfolio	27	0.9
The licensed drug does not appear in CT	474	16.2
The licensed drug is already a generic	13	0.5
The licensed drug is not in CT at the time of the deal	33	1.1
No overlap in MeSH terms	151	5.2
Total	2,920	100

Source: Lear analysis

The categorisation of the challenges encountered in R&D agreements and in other deal types, which include equity investments, marketing agreements, R&D joint ventures, joint ventures, cross-licensing and partnerships, mirrors that already discussed for purchase and licensing deals. This categorisation is presented in Table I.39, Table I.40 and Table I.41.

Table I.39: Categorisation of issues for R&D deals not covered in the analysis

Issue (if any)	Number of deals	Percentage of deals
At least one overlap in MeSH terms	219	9.0
Deals not covered by R&D deal analysis		
R&D without an identified drug object	652	26.7
The company (including its group) has no active/relevant molecules in its portfolio	259	10.6
The drug(s) object of the deal is already part of the company's portfolio	94	3.9
The drug(s) object of the deal does not appear in CT	1,132	46.4
The drug(s) object of the deal is not in CT at the time of the deal	28	1.1
No overlap in MeSH terms	54	2.2
Total	2,438	100

Source: Lear analysis

Table I.40: Categorisation of issues for 'other' types of deals not covered in the analysis

Issue (if any)	Equity		Marketing agreement		Joint Venture R&D	
	N	%	N	%	N	%
At least one overlap in MeSH terms	4	26.7	4	14.3	2	11.1
Deals not covered by the analysis						
Deal without an identified drug object	6	40	0	0	6	33.3
The company (including its group) has no active/relevant molecules in its portfolio	0	0	9	32.1	0	0
The drug(s) object of the deal is already part of the company's portfolio	0	0	3	10.7	0	0
The drug(s) object of the deal does not appear in CT	5	33.3	6	21.4	10	55.6
The drug(s) object of the deal is not in CT at the time of the deal	0	0	1	3.6	0	0
No overlap in MeSH terms	0	0	5	17.9	0	0
Total	15	100	28	100	18	100

Source: Lear analysis

Table I.41: Categorisation of issues for 'other' types of deals not covered in the analysis (cont.)

Issue (if any)	Joint venture		Cross-licensing		Partnership	
	N	%	N	%	N	%
At least one overlap in MeSH terms	2	4.3	1	7.1	1	3.8
Deals not covered by the analysis						
Deal without an identified drug object	21	44.7	5	35.7	5	19.2
The company (including its group) has no active/relevant molecules in its portfolio	2	4.3	0	0	2	7.7
The drug(s) object of the deal is already part of the company's portfolio	0	0	0	0	0	0
The drug(s) object of the deal does not appear in CT	22	46.8	8	57.1	18	69.2
The drug(s) object of the deal is not in CT at the time of the deal	0	0	0	0	0	0
No overlap in MeSH terms	0	0	0	0	0	0
Total	47	100	14	100	26	100

Source: Lear analysis

A.4 Further details on the evaluation challenge

For each case assessed as part of the evaluation challenge in section II.1 of the Final Report, this section reports the overlaps that were found by the Commission and for which no discontinuation took place or those that are not relevant for our ex-post assessment. As the methodology, described in section II.1.1.2 of the Final Report, explains, for those overlaps no further analysis is necessary.

A.4.1 J&J/ Actelion

The Commission found an overlap between marketed products of Biogen, Inc. ("Biogen") distributed by J&J in a number of Central and Eastern European countries and one pipeline product of Actelion for the treatments for multiple sclerosis.

Table I.42 below shows the evolution of the Parties' projects after the merger. As shown, Actelion's molecule, which was a pipeline at the time of the merger, was marketed in the US and registered in Europe in March 2022. As per Biogen's drugs, these were all marketed at the time of the merger and they are all still marketed today. Therefore, no discontinuation of the Parties' molecules for the treatments of multiple sclerosis took place.

Table I.42: Parties' treatments for multiple sclerosis - evolution of projects

Product market	Drug	Owner pre-merger	Phase at time of deal	Evolution of the projects
Disease-modifying therapies for multiple sclerosis	ACT-128800 (ponesimod)	Actelion	Pipeline (phase unknown)	Ponesimod was marketed in the US and registered in Europe in March 2022
	Avonex Plegridy Tysabri Tecfidera	Biogen (distributed by J&J in Central and Eastern Europe)	Marketed	Marketed

Source: Lear

A.4.2 Novartis/ GSK Oncology

MEK inhibitors for ovarian cancer

The Commission found an overlap between Novartis' and GSK's MEK inhibitors for low-grade serous carcinoma ("LGSC"), a rare type of ovarian cancer. In particular, Novartis' and GSK's MEK inhibitors (MEK162 and Mekinist respectively) were both in phase III clinical trials for LGSC at the time of the Decision.

Table I.43 below shows the evolution of the Parties' projects after the merger. As shown, a new trial for MEK162 in ovarian cancer is due to start in December 2022, implying that this molecule was not discontinued. As per GSK's drug, Mekinist, the Phase III study identified by the Commission in the Decision is still "active". The results, published in February 2022, are positive, and suggest that "Mekinist should be considered a new standard of care for LGSC".[617] Therefore, no discontinuation of the Parties' molecules for the treatments of LGSC took place.

[617] See the interpretation of the results here, here and here.

Table I.43: Evolution of of Novartis' MEK162 and GSK's Mekinist for LGSC after the Transaction

Owner	Drug and phase pre-merger	Evolution of project
Novartis	MEK162 (binimetinib) Phase III	Returned to Array following the EC Commitments Phase III study (MILO Study)[618], which started in June 2013, was discontinued in April 2016. Array announced this decision[619], after a planned interim analysis showed that the Hazard Ratio for Progression Free Survival (PFS) - which was the study's primary end point - crossed the predefined futility boundary. This means that the study was terminated earlier than anticipated because, based on defined thresholds, it appeared impossible to reach the trial's aim. Top-line results from the study had been expected in 2017. Note that the MILO study was launched well before the Novartis/GSK deal was agreed, so it's clear that the deal had no effect on how "futility" was defined in the study. Phase II trial for the ovarian cancer indication is due to start in December 2022.[620] Therefore, this molecule was not discontinued.
GSK	Mekinist (trametinib) Phase III	Phase III study identified by the EC[621] is still "active", thus we wouldn't charachterise this as a discontinuation.

Source: Lear

MEK inhibitors for uveal melanoma

The Decision reports that at the time of the Transaction Novartis had an on-going Phase III clinical trial for the use of its MEK inhibitor (MEK162) in uveal melanoma, while GSK was not developing its MEK inhibitor (Mekinist) for uveal melanoma. The Commission was concerned that, given the more advanced stage of development of GSK's molecules in other indications (such as advanced melanoma), it was unlikely that the merged entity would have the incentives to pursue MEK162 only for uveal melanoma. The

618 https://clinicaltrials.gov/ct2/show/NCT01849874

619 https://storage.googleapis.com/pcf_sb_39_1613727931605803249/assets/supporting/mediarelease/1839/809193588.html?GoogleAccessId=pcf-binding-6c96771b@sn-paas-sb-gcp.iam.gserviceaccount.com&Expires=1666707129&Signature=L7abdPgotf3m11DdCgTeiq2oIABjLAwifmj3R7ZmDs%2F7CMcFFC1TQ0DJYQGPMa%2F%2BVvTn%2Fnlpn4xlRznoAc9i4sEr94db5lVhcUgrr%2BaTwNApiOCFIaUoI%2B2KAccvlBEfpb%2B%2F%2B42n2gI6G%2FhVVCWcwyHvg8n2WpfFbUsEoeAml3v3b4VcNzO75Auy4vZksYblm4TOm8gROrx%2FNRS0REckZd8%2FiUMc2uYUNrsDbY8pEkRcwUAzo%2Fyi%2F091NM6cxQxY6qPLoAyqDeL41XJ%2FpvVpBv3992TEaFlb7%2F7vp3u3V%2Bn3NiTX8IxvZPlm%2Fg%2BfxcP3DA97xqGjW%2FMDycdzXRDZJw%3D%3D

620 https://clinicaltrials.gov/ct2/show/NCT05554367?term=MEK162&cond=Ovarian+Cancer&draw=2&rank=3

621 https://clinicaltrials.gov/ct2/show/study/NCT02101788?term=Mekinist&cond=Ovarian+Cancer&draw=2&rank=1

Commission cleared the merger subject to remedies, which involved the divestiture of MEK162 and another of Novartis' molecules (LGX818) to Array.

In our ex-post assessment, we noticed that Novartis' Phase III study referred to by the Commission couldn't be found. Array was conducting a Phase I/II trial of MEK162 during the Commission's review. The study[622] was begun in August 2013 and terminated for technical reasons in May 2015. The Commission's reference to a Phase III study may come from there (as uveal melanoma was a minor detail in the Commission's review, "I/II" may have been transcribed as "III" and the study then erroneously attributed to Novartis).

Pfizer, which acquired Array in 2019, is currently trialling MEK162 for uveal melanoma (its most recent study started in December 2021 and is recruiting).[623]

As per GSK's activity in uveal melanoma, The EC did not mention it in the Decision, but ClinicalTrials.gov reports that GSK also conducted two Phase II trials of Mekinist for uveal melanoma before the merger: one begun in October 2013 and completed in September 2017[624], the other begun in 2010 and was then cancelled before any patients were enrolled.[625]

Thus, if our intuition regarding the Array Phase I/II trial having been mistakenly attributed to Novartis is correct, then Novartis would have had no trials for MEK162 in uveal melanoma at the time of the Transaction, and the EC concerns that MEK162 could be discontinued in uveal melanoma would not stand.

MEK and B-Raf inhibitors for melanoma brain metastases

The evolution of the overlapping projects after the merger

Table I.44 details the evolution of Novartis' combination therapy of MEK162 and LGX818 for the treatment of melanoma brain metastases after the Transaction. As shown, we found that no progression to a later phase was reached for the combination therapy, but new trials are ongoing. Thus, the combination therapy was not discontinued.

[622] https://clinicaltrials.gov/ct2/show/NCT01801358?term=NCT01801358&draw=2&rank=1

[623] https://clinicaltrials.gov/ct2/show/study/NCT05170334?term=MEK162&cond=Uveal+Melanoma&draw=2&rank=2

[624] https://clinicaltrials.gov/ct2/show/study/NCT01979523?term=NCT01979523&draw=2&rank=1

[625] https://clinicaltrials.gov/ct2/show/NCT01328106?term=NCT01328106&draw=2&rank=1

Table I.44: Evolution of Novartis' LGX818 and MEK162 for melanoma brain metastases after the Transaction

Owner pre-merger	Drug and phase pre-merger	Evolution of project
Novartis (Array)	Combined therapy MEK162 (binimetinib) + LGX818 (encorafenib) Phase II	MEK162 was returned to Array, LGX818 was divested to Array following the EC Commitments, then Array was acquired by Pfizer (2019)
		There are new ongoing studies, thus no discontinuation:
		Started September 2020: A Study to Compare the Administration of Encorafenib + Binimetinib + Nivolumab Versus Ipilimumab + Nivolumab in BRAF-V600 Mutant Melanoma With Brain Metastases (Phase II, "recruiting", estimated completion date is June 2027).[626]
		Started July 2019: Encorafenib and Binimetinib Before Local Treatment in Patients With BRAF Mutant Melanoma Metastatic to the Brain (Phase II, "active, not recruiting", estimated completion date is November 2023).[627]
		Started September 2022: Binimetinib Encorafenib Pembrolizumab +/- Stereotactic Radiosurgery in BRAFV600 Melanoma With Brain Metastasis (Phase II, "recruiting", estimated completion date: April 2029).[628]

Source: Lear

Table I.45 details the evolution of GSK's Mekinist and Tafinlar for melanoma brain metastases after the Transaction. We found that both GSK's monotherapy of Tafinlar and its combination therapy were discontinued. Since Novartis after the Transaction is not able to influence Array, the discontinuation of GSK's projects (which were, through the Transaction, acquired by Novartis) is not of interest for our ex-post evaluation.

626 https://clinicaltrials.gov/ct2/show/NCT04511013?term=MEK162&cond=Brain+Metastases&draw=2&rank=3

627 https://clinicaltrials.gov/ct2/show/NCT03898908?term=MEK162&cond=Brain+Metastases&draw=2&rank=4

628 https://clinicaltrials.gov/ct2/show/record/NCT04074096?term=NCT04074096&draw=2&rank=1

Table I.45: Evolution of GSK's Mekinist and Tafinlar for melanoma brain metastases after the Transaction

Owner pre-merger	Drug and phase pre-merger	Evolution of project
GSK	Tafinlar (dabrafenib) Phase II	No development nor new recent trials for this monotherapy, thus it was discontinued.
	Combination Mekinist (trametinib) &Tafinlar (dabrafenib) Phase II	No development nor new recent trials for the combination therapy, thus it was discontinued. Most recent studies: In February 2018, GSK/ Novartis completed the phase II COMBI-MB trial[629] that evaluated the safety and efficacy of dabrafenib + trametinib. Interpretation of the results[630] says that "Dabrafenib plus trametinib was active with a manageable safety profile […], but the median duration of response was relatively short. These results provide evidence of clinical benefit with dabrafenib plus trametinib and support the need for additional research to further improve outcomes in patients with melanoma brain metastases." A Phase II study[631] of dabrafenib in combination with trametinib continuously with stereotactic radiotherapy (SRS), started in February 2018, was terminated due to very slow accrual. In April 2017, GlaxoSmithKline completed a phase IIb trial[632] of pre-operative therapy with dabrafenib and a combination of dabrafenib and trametinib. The trial was initiated in April 2014, but was terminated due to limited enrolment.

Source: Lear

Reasons for discontinuation

We found that GSK's monotherapy of Tafinlar, as well as GSK's combination therapy were discontinued. Our analysis suggests that these discontinuations were grounded in technical reasons.

The ESMO guidelines[633] report that there are a number of therapies (or modalities) that can be applied for melanoma brain metastases depending on the individuals' needs,

[629] https://clinicaltrials.gov/ct2/show/NCT02039947?term=NCT02039947&draw=2&rank=1

[630] See here.

[631] https://clinicaltrials.gov/ct2/show/NCT02974803?term=tafinlar&cond=Brain+Metastases&draw=2&rank=1

[632] https://clinicaltrials.gov/ct2/show/NCT01978236?term=tafinlar&cond=Brain+Metastases&draw=2&rank=3

[633] https://www.annalsofoncology.org/action/showPdf?pii=S0923-7534(20)32563-1

including targeted therapy with B-Raf/MEK combination (dabrafenib + trametinib). However, they also note that "the optimal sequence or combination of these modalities has not been fully determined, but recent results [including the COMBI-MB trial of dabrafenib + trametinib] can help with decision making until ongoing clinical trials bring more definitive answers." Therefore, the guidelines seem to flag the importance of new clinical trials to determine the optimal therapeutic approach in this indication.

Interpretation of the trial results and feedback from the pharmaceutical experts in the Team suggest that the discontinuation of GSK's molecules for melanoma brain metastases is due to lack of sufficient efficacy. In fact, our experts advise that the language "it is active" and "there is evidence of clinical benefit" (see the results of the COMBI-MB trial reported in Table I.45) is entirely consistent with when a study doesn't produce compelling data. Limited enrolment, which as highlighted in Table I.45 brought two trials to termination, is likely to be a secondary effect that demonstrates lack of investigator buy-in to the treatment.

Moreover, our pharmaceutical experts suggest that an indication for metastatic melanoma will cover the use in brain metastases, unless it is contra-indicated. The actual use/uptake of the product in brain metastases (an underserved and difficult to treat population) would be driven by evidence and that data if positive could be added to the Summary of Product Characteristics (SPC) to support prescribing. The performed trials show that there has been an attempt to generate this evidence but the data does not seem to be compelling enough to take it further.

Therefore, it appears that GSK's molecules were discontinued for technical reasons, and therefore these discontinuations were unrelated to the merger.

A.4.3 BMS/Celgene

Idiopathic Pulmonary Fibrosis (IPF)

In the market for IPF treatments, the Transaction gave rise to pipeline-to-pipeline overlaps between Celgene's CC-90001 (JNK inhibitor, Phase I at the time of the Decision) on the one hand, and BMS ND-L02-s0201[634] (HSP74 inhibitor, Phase II) and BMS-986278 (LPA(1) antagonist, Phase I) on the other.

The relevant product market was defined as IPF treatments, with further sub-segmentation left open as even in the narrowest possible market delineation (e.g., oral treatments for IPF), no competitive concerns arose due to the Transaction. The relevant geographic market was defined as global or at least EEA wide. Based on the available information, the Commission considered that the Transaction did not raise serious doubts as to its compatibility with the internal market. Firstly, Celgene's CC-90001 and BMS' pipeline products are very differentiated in terms of MoA that affect different inflammatory pathways. It was also likely that these drugs would serve different patient groups and would likely have different efficacy and safety profiles. Secondly, post-Transaction, the combined entity would continue facing competitive constraints from a large number of actual and potential competitors. Moreover, the Commission found that, given the absence of cure or disease-modifying treatment available on the market, there was high unmet demand for IPF therapies. As such, it was unlikely that the combined entity would have had incentives to discontinue, delay or reorient any of its pipeline

[634] BMS had a financial option over ND-L02-s0201, an asset that was being developed by Nitto Denko at the time of the Decision

products, especially as they were differentiated. In view of the above, no commitments were proposed.

Our investigation of the evolution of the IPF programmes post-Transaction can be seen in Table I.46 below. As shown, no discontinuations were detected.

Table I.46: Evolution of IPF programmes post-Transaction

Owner (pre-merger)	Drug	Phase at time of deal (2019)	Evolution of the project
Celgene	CC-90001	Phase II	December 2021: Phase II trial completed according to AdisInsight[635] and CT[636]
BMS	ND-L02-s0201	Phase II	August 2022: Phase II completed by Nitto Denko[637]
	BMS-986278	Phase I	Phase II initiated in July 2020, and completed in September 2023[638]

Source: Lear

BET inhibitors

In the market for pipeline BET inhibitor drugs, the Commission found overlaps between Celgene's CC-90010 and CC-95775 on the one hand, and BMS' BMS-986158 on the other. The relevant geographic market was defined as global or at least EEA-wide. The Commission excluded serious doubts as to the compatibility of the Transaction with the internal market regarding BET inhibitor drugs. According to the assessment, post-Transaction, the combined entity would continue facing competitive constraints from a large number of actual and potential competitors in BET inhibitor drugs. Thus, no commitments were proposed.

An overview of our investigation regarding the evolution of the projects post-Transaction can be seen in Table I.47 below. As shown, no discontinuations were detected.

[635] https://adisinsight.springer.com/drugs/800040481

[636] https://clinicaltrials.gov/ct2/show/NCT03142191

[637] https://clinicaltrials.gov/ct2/show/NCT03538301

[638] https://clinicaltrials.gov/ct2/show/NCT04308681

Table I.47: Evolution of BET inhibitors post-Transaction

Owner (pre-merger)	Drug	Phase at time of deal (2019)	Evolution of the project
Celgene	CC-90010	Phase I	There are multiple Phase I active trials regarding this drug in various oncology diseases: Non-Hodgkin's Lymphomas[639] SCLC[640] Astrocytoma[641] and glioblastoma[642] Pediatric cancer[643]
BMS	CC-95775	Phase I	October 2021: Phase I(b) study in Non-Hodgkin's Lymphomas was completed[644]
	BMS-986158	Phase I/II	March 2021: Phase I/II in myelofibrosis was initiated, it is currently active and recruiting[645]

Source: Lear

Immunotherapies for NSCLC

In the market for immunotherapies for NSCLC, the Transaction gave rise to overlaps between Celgene's pipeline MSC-1 on one hand, and BMS' marketed Opdivo monotherapy, as well as pipelines of Opdivo combination therapy and Yervoy on the other. The market investigation did not reveal any concrete elements supporting the existence of serious doubts regarding anticompetitive outcomes of the Transaction. Firstly, it was concluded that the MoA of Celgene's pipeline is very different from BMS' marketed and pipeline immunotherapies for NSCLC. This meant that if the Parties' pipelines were to reach the market, there was no indication that the drugs' efficacy and safety profiles would be similar. Secondly, the development of MSC-1 was at a very early stage (Phase I). At this stage, prospective indications remain uncertain and subject to change especially with respect to immunotherapies. Finally, the combined entity would face competition from at least three marketed products, and several pipeline programmes. In view of the above, no commitments were proposed.

Our investigation revealed no discontinuations, Table I.48 below shows.

[639] https://clinicaltrials.gov/ct2/show/NCT03220347

[640] https://clinicaltrials.gov/ct2/show/NCT03850067

[641] https://clinicaltrials.gov/ct2/show/NCT04047303

[642] https://clinicaltrials.gov/ct2/show/NCT04324840

[643] https://clinicaltrials.gov/ct2/show/NCT03936465

[644] https://clinicaltrials.gov/ct2/show/NCT04089527

[645] https://clinicaltrials.gov/ct2/show/NCT04817007

Table I.48: Evolution of NSCLC immunotherapies post-Transaction

Owner (pre-merger)	Drug	Phase at time of deal (2019)	Evolution of the project
Celgene	MSC-1	Phase I	September 2019: Phase I study Terminated (Safety and PK/PD data from Dose Escalation support further development; Dose Expansion canceled). The study wasn't only in NSCLC, but also other cancer types as well as advanced solid tumors more broadly. It was conducted by Northern Biologics.[646] After the BMS-Celgene merger, BMS decided not to exercise the financial option over MSC-1.[647] November 2020: AstraZeneca acquires MSC-1 from Northern Biologics.[648] December 2021: Phase II study, again in advanced solid tumors, initiated by AstraZeneca on a drug called AZD0171 which is another name for MSC-1. Completion estimated in October 20234
BMS	Opdivo	Marketed + Pipelines in Phase I/II, II and III	Still marketed, with multiple ongoing studies as well.[649]
	Opdivo (comb.)	Phase I, I/II, II and III	Approved in the EU, Japan, and Taiwan as a combination and first-line therapy for NSCLC, with multiple ongoing studies as well.[650]
	Yervoy	Phase III	Marketed in the US and Japan[651] Approved in the EU, Taiwan and South Korea[652]

Source: Lear

Immunotherapies for SCLC

In the immunotherapies for SCLC market, the Commission found that the Transaction gave rise to overlaps between Celgene's pipeline CC-90011 (Phase I) and BMS pipeline combination of Opdivo and Yervoy (Phase II). The market investigation did not reveal any concrete elements supporting the existence of serious doubts regarding anticompetitive outcomes of the Transaction. Firstly, the MoA of Celgene's pipeline is

[646] https://clinicaltrials.gov/ct2/show/NCT03490669

[647] https://web.archive.org/web/20220925111512/https://xconomy.com/new-york/2020/05/14/boehringer-ingelheim-acquires-northern-biologics-preclinical-pipeline/

[648] https://www.metrixpartners.com/northern-biologics-announces-global-acquisition-of-clinical-stage-antibody-msc-1-by-astrazeneca/

[649] https://clinicaltrials.gov/ct2/results?cond=&term=opdivo&cntry=&state=&city=&dist=

[650] https://clinicaltrials.gov/ct2/results?cond=&term=opdivo&cntry=&state=&city=&dist=

[651] https://adisinsight.springer.com/drugs/800006680

[652] https://adisinsight.springer.com/drugs/800006680

very different from BMS' marketed and pipeline immunotherapies for SCLC. If the Parties' pipelines were to reach the market, there was no indication that the drugs' efficacy and safety profiles would be similar. Secondly, both Parties' pipelines were at an early stage of development, i.e. many years away from a hypothetical launch on the market, which remained highly uncertain. Finally, the combined entity would face competition from several pipeline programmes, including three Phase III pipelines. In view of the above, no commitments were proposed.

Our investigation found no discontinuations, as can be seen in more detail in Table I.49 below.

Table I.49: Evolution of SCLC immunotherapies post-Transaction

Owner (pre-merger)	Drug	Phase at time of deal (2019)	Evolution of the project
Celgene	CC-90011	Phase I	July 2020: Phase II initiated for this drug in combination with Opdivo, with an estimated completion date in December 2023.[653] Moreover, multiple Phase I studies are active.[654]
BMS	Opdivo + Yervoy	Phase II	November 2021: Phase III completed and has results.[655]

Source: Lear

Immunotherapies for ovarian cancer

In the immunotherapies for ovarian cancer market, the Commission found that the Transaction gave rise to overlaps between Celgene's pipeline MSC-1 (Phase I), and BMS Yervoy pipelines (Phase II). The market investigation did not reveal any concrete elements supporting the existence of serious doubts regarding anticompetitive outcomes of the Transaction. Firstly, Celgene's and BMS' pipelines have very different MoA, implying that in case the Parties' pipelines reached the market, there was no indication that the drugs' efficacy and safety profiles would be similar. Secondly, the development of MSC-1 was at a very early stage. At this stage, prospective indications remain uncertain and subject to change especially with respect to immunotherapies. Finally, the combined entity would face competition from several pipeline programmes, including three Phase III pipelines. In view of the above, no commitments were proposed.

Our investigation of the evolution of the overlapping programmes revealed no discontinuations, as can be seen in Table I.50 below.

[653] https://clinicaltrials.gov/ct2/show/NCT04350463

[654] https://clinicaltrials.gov/ct2/results?cond=&term=CC-90011&cntry=&state=&city=&dist=&Search=Search

[655] https://clinicaltrials.gov/ct2/show/results/NCT02538666

Table I.50: Evolution of ovarian cancer immunotherapies post-Transaction

Drug	Owner (pre-merger)	Phase at time of deal (2019)	Evolution of the project
MSC-1	Celgene	Phase I	September 2019: Phase I study Terminated (Safety and PK/PD data from Dose Escalation support further development; Dose Expansion canceled). The study was not only in ovarian cancer, but also advanced solid tumors more broadly. It was conducted by Northern Biologics.[656] After the BMS-Celgene merger, BMS decided not to exercise the financial option over MSC-1.[657] Nov 2020: AstraZeneca acquires MSC-1 from Northern Biologics.[658] December 2021: Phase II study, again in advanced solid tumors, initiated by AstraZeneca on a drug called AZD0171 which is another name for MSC-1. Est. completion date October 2024.[659]
Yervoy	BMS	Phase II	Multiple ongoing and completed (within the last two years) Phase II studies where Yervoy is included in combination with other drugs.[660]

Source: Lear

Immunotherapies for pancreatic cancer

In the market for pancreatic cancer immunotherapies, the Transaction gave rise to overlaps between Celgene's pipeline MSC-1 (Phase I) on one hand, and BMS Opdivo (combination, Phase I/II and III), BMS-813160 (Phase II) and Cabiralizumab (Phase II) on the other[661]. The Commission's market investigation did not reveal any concrete elements supporting the existence of serious doubts regarding anticompetitive outcomes of the Transaction. Firstly, the Parties' pipelines are differentiated products, with distinct MoA and thus likely different efficacy and safety profiles. Secondly, the development of MSC-1 was at a very early stage. At this stage, prospective indications remain uncertain and subject to change especially with respect to immunotherapies. Finally, the combined entity would face competition from several pipeline programmes, including pipelines which are at an advanced stage of development. In view of the above, no commitments were proposed.

[656] https://clinicaltrials.gov/ct2/show/NCT03490669

[657] https://web.archive.org/web/20220925111512/https://xconomy.com/new-york/2020/05/14/boehringer-ingelheim-acquires-northern-biologics-preclinical-pipeline/

[658] https://www.metrixpartners.com/2020/11/10/northern-biologics-announces-global-acquisition-of-clinical-stage-antibody-msc-1-by-astrazeneca/

[659] https://clinicaltrials.gov/ct2/show/NCT04999969

[660] https://clinicaltrials.gov/ct2/results?term=Yervoy&cond=ovarian+cancer&draw=2&rank=1

[661] Note there were two more BMS compounds which were not disclosed, thus couldn't be investigated.

Our investigation of the evolution of the programmes post-Transaction found no discontinuations, as shown in Table I.51 below.

Table I.51: Evolution of pancreatic cancer immunotherapies post-Transaction

Drug	Owner (pre-merger)	Phase at time of deal (2019)	Evolution of the project
MSC-1	Celgene	Phase I	September 2019: Phase I study Terminated (Safety and PK/PD data from Dose Escalation support further development; Dose Expansion canceled). The study was not only in pancreatic cancer, but also advanced solid tumors more broadly. It was conducted by Northern Biologics.[662] After the BMS-Celgene merger, BMS decided not to exercise the financial option over MSC-1.[663] Nov 2020: AstraZeneca acquires MSC-1 from Northern Biologics.[664] December 2021: Phase II study, again in advanced solid tumors, initiated by AstraZeneca on a drug called AZD0171 which is another name for MSC-1. Est. completion date October 2024.[665]
BMS-813160	BMS	Phase II	August 2017: Phase I/II study was initiated, completed in June 2023.[666]
Cabiralizumab		Phase II	December 2017: Phase II study was initiated, completed in June 2023.[667]
Opdivo (comb.)		Phase I/II, III	Multiple Phase II studies are active.[668]

Source: Lear

[662] https://clinicaltrials.gov/ct2/show/NCT03490669

[663] https://web.archive.org/web/20220925111512/https://xconomy.com/new-york/2020/05/14/boehringer-ingelheim-acquires-northern-biologics-preclinical-pipeline/

[664] https://www.metrixpartners.com/2020/11/10/northern-biologics-announces-global-acquisition-of-clinical-stage-antibody-msc-1-by-astrazeneca/

[665] https://clinicaltrials.gov/ct2/show/NCT04999969

[666] https://clinicaltrials.gov/ct2/show/NCT03184870

[667] https://clinicaltrials.gov/ct2/show/NCT03336216

[668] https://clinicaltrials.gov/ct2/results?cond=pancreatic+cancer&term=opdivo&cntry=&state=&city=&dist=&Search=Search

The overlap revealed by the fact-finding challenge in non-small cell lung cancer (NSCLC), gastric cancer and pancreatic cancer

The fact-finding challenge revealed two discontinued overlaps that do not appear in the Commission decision. The first one is described in section II.1.4.5 of the Final Report, while the second one is covered in this section, since the Team's assessment revealed that it does not appear to be related to the BMS/ Celgene deal.

This overlap is between BMS' BMS 986148 and Celgene's Paclitaxel in several indications: non-small cell lung cancer (NSCLC), gastric cancer and pancreatic cancer.[669] It should be noted that this overlap was identified in a therapeutic indication proxied by MeSH codes and in a MoA proxied by PMC correlation. Such an approach is used in the fact-finding challenge when perfect overlaps between therapeutic indications and MoAs cannot be established, and implies that it is not clear cut whether there is indeed substitutability between compounds. Further manual scrutiny in order to ascertain the relationship between the drugs is required.[670] At the time of the deal, BMS' compound was in a Phase I study in advanced solid tumors, among which the above-mentioned narrower indications, whereas Celgene's compound was marketed in all those indications. After the deal, BMS' compound's Phase I study was terminated "for business reasons not related to safety".[671]

With regard to this discontinued overlap, the Team's experts advised that: i) even though the large-scale analysis established a close relationship between the drugs' mechanisms of action based on PMC, BMS 986148 is an Antibody Drug Conjugate, and Paclitaxel a chemotherapy agent, and as such they are not substitute with each other in the commercial reality, ii) in 2019, Paclitaxel was already nearing the end of its life cycle (3-4 years until US generic entry and a European generic already present in 2019), thus a targeted agent like BMS' compound would have been a good way to extend the franchise, implying that if possible the acquirer would have avoided the discontinuation, and iii) there were a lot of other BMS' compounds competing with BMS 986148 to be used in combination with another of its drugs, nivolumab, and possibly some of them had more compelling results. In summary, the drugs weren't directly substitutable, so the discontinuation of BMS' compound wouldn't have had an impact on the market positioning of Paclitaxel. Furthermore, the Team and its experts deem that the discontinuation was most likely due to commercial reasons related to BMS having other better performing compounds.

[669] The imperfect overlap identified by the fact-finding challenge as a LASSO KA was in large cell carcinoma, subtype of NSCLC. Manual screening led us to include in the report the overlaps in (broader) NSCLC, as well as gastric and pancreatic cancer, as the two drugs seem to overlap perfectly in those indications. These overlaps were classified as leading to prima facie relevant discontinuation by the large-scale analysis but were not detected as LASSO KAs. They indeed arose after a detailed reading of the narrower cancer types included in BMS 986148's trial in advanced solid tumors. Consequently, we considered these the most appropriate overlaps to include in the assessment.

[670] The relationships between therapeutic uses are established by use of MeSH codes, which act as a proxy for therapeutic indications in large scale analysis. An imperfect overlap suggests that the drugs were not intended for precisely the same medical condition, but were instead pursued in two separate therapeutic indications that can be categorized under a more general, overarching indication. More on this methodology can be seen in section I.2.1 of the Final Report. The relationships between MoAs are established by measuring the frequency of joint appearance of the two MoA in medical literature. It is represented as a ratio between the number of joint occurrences in medical literature over the multiple of individual occurrences. The threshold for considering the two MoA related is a frequency over 0.05, and the number in this specific case was 0.09. More on the PMC methodology can be seen in section I.2.1 of the Final Report.

[671] https://clinicaltrials.gov/study/NCT02341625

A.5 Notice of interest: Forms A and B

	FORM A: PHARMACEUTICAL DEVELOPMENT NOTICE OF INTEREST		
	Name(s) of filing party/parties:	Date of Agreement:	Filing Date:

	I. THE PARTIES	
1	1a Acquiring party (Party A):	1b Party acquired/transferring interest (Party B):

II. THE ACQUISITION

2 □ **Investment in an existing company/business**

Interest acquired

2a □ Controlling interest (sole or joint) in an existing company

2b □ Greater than 10% in voting shares or other management decision making

2c □ Assets comprising a business to which a market turnover can be attributed

□ Other

Drug(s) being developed and/or marketed by the acquired company/business		
2d **INN *(pINN, USAN, BAN etc)***	2e **Mechanism of action**	2f **Therapeutic indications**

3 □ **Technology transfer / asset acquisition**

3a □ Technology purchase or assignment

3b □ Acquisition of license

3c □ Cross-license

3d License of rights to –
□ Develop
□ Produce/have produced
□ Use (as input/process)
□ Commercialise

3e Exclusive license to –
□ Technology
□ Territory/customers
□ Field of use/TI
□ None

3f Acquisition of –
□ R&D assets (data, trial samples, cell lines, etc.)
□ Facilities/equipment
□ Regulatory materials (e.g. approvals, applications)
□ Supply contracts
□ Option to purchase or license
□ Other

3g

Drug(s) to which the acquired rights/assets relate		
INN *(pINN, USAN, BAN, etc)*	**Mechanism of action**	**Therapeutic indication(s)**

4 □ **Joint venture / collaboration agreement**

4a Structure of collaboration
- □ Full function joint venture
- □ Non-full function joint venture
- □ Other

4b Scope of collaboration
- □ Discovery/development
- □ Specialisation
- □ Co-promotion
- □ Co-marketing

4c

Drugs (and/or related assets) contributed to the collaboration by Party A		
INN *(or pINN, USAN, BAN, etc)*	**Mechanism of action**	**Therapeutic indication(s)**

Drugs (and/or related assets) contributed to the collaboration by Party B		
INN *(or pINN, USAN, BAN, etc)*	**Mechanism of action**	**Therapeutic indication(s)**

III. VALUE OF TRANSACTION

		€ million
5	**Total approved investment** (acquirer valuation of transaction)	

		€ million
6	**Upfront consideration**	
	Cash and listed securities	
	Other *(specify)*	

7	**Contingent consideration**	Nominal value (€ million)	Present value (€ million) *(est.)*
	Milestone payments		
	(describe)		
	Other (e.g. earn-outs, deferred compensation)		

(describe)			
Royalties	[Year 1] (€ million) *(est.)*	[Year 2] (€ million) *(est.)*	[Year 3] (€ million) *(est.)*
(specify base and rate)			

IV. OVERLAP PROJECT/PRODUCT		
Mechanism of action: Narrowest common therapeutic indication (TI):		
Party:	INN (or pINN, USAN, BAN, etc):	
Pending (or most recent completed) trials in the latest stage of development:		
Trial number: Designated TI: Phase: □ I □ II □ III Original end date: / / Status: □ Active Est. completion: / / □ Completed Date: / / □ Suspended/Terminated for: □ Safety/efficacy/futility □ Design/accrual/funding □ Regulatory reasons □ Commercial reasons Date: / /	Trial number: Designated TI: Phase: □ I □ II □ III Original end date: / / Status: □ Active Est. completion: / / □ Completed Date: / / □ Suspended/Terminated for: □ Safety/efficacy/futility □ Design/accrual/funding □ Regulatory reasons □ Commercial reasons Date: / /	Trial number: Designated TI: Phase: □ I □ II □ III Original end date: / / Status: □ Active Est. completion: / / □ Completed Date: / / □ Suspended/Terminated for: □ Safety/efficacy/futility □ Design/accrual/funding □ Regulatory reasons □ Commercial reasons Date: / /
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□ In EU	MAA filed (date): / /	MA issued (date): / /
□ Outside EU *(specify where)*	MAA filed (date): / /	MA issued (date): / /

<table>
<tr><td></td><td colspan="3">FORM B:
STATUS OF PHARMACEUTICAL DEVELOPMENT</td></tr>
<tr><td>1</td><td>Name(s) of filing party/parties:</td><td>Registration number:</td><td>Filing Date:</td></tr>
<tr><td>2</td><td>Party A:</td><td colspan="2">Party B:</td></tr>
</table>

<table>
<tr><td colspan="4">OVERLAP PROJECT/PRODUCT</td></tr>
<tr><td></td><td colspan="3">Mechanism of action:
Narrowest common therapeutic indication (TI):</td></tr>
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