



## Roche/Spark and pharma mergers: acquiring a 'pipeline' potential competitor and 'killer acquisition' concerns

Competition authorities are increasingly concerned that merger control may be missing acquisitions of *early stage* potential competitors. Roche's \$4.3 billion acquisition of Spark Therapeutics, recently cleared in the UK, brought together an existing treatment with a potential treatment still in clinical trials. The case signals increasing interest in highly uncertain potential competition concerns in the pharma sector, with possible read across to other sectors.

Roche launched a new and successful treatment for Haemophilia A in 2018, which significantly reduced the necessary frequency of doses for patients. Spark Therapeutics is currently undertaking Stage 2 clinical trials with a potentially game-changing gene-therapy based treatment that would provide a one-time non-recurring treatment for patients.<sup>1</sup>

If Spark's pipeline product was to launch, it would treat broadly the same patient group as Roche's existing treatment, and so represents a potential competitor. Initial concerns were raised as to whether Roche would have an incentive to 'kill' or delay the development of Spark's pipeline product to protect the revenue generated from its existing product, or raise the price of either treatment. Commentators called for the deal to be blocked due to such 'killer acquisition' concerns.

The challenge with such theories of harm is that projects like Spark's are in such an early stage of development that prospects for the success of clinical trials and future launch (and over what time period this might occur) are extremely uncertain.

This uncertainty is compounded by other factors affecting entry: requisite funding must be obtained to continue development, regulatory approval obtained, and reimbursement obtained from the NHS in the UK (and equivalent health insurance providers in other countries).

Only when taking these factors (and thus entry) as given can a forward-looking assessment of substitution between Roche, Spark and competitor treatments (existing and pipeline) be made, particularly as a number of other gene therapy treatments are being developed and appear well-placed to launch before Spark. Estimating likely elasticities in this context can be challenging.

Commonly there is also a credible rationale for such acquisitions that do not involve 'killing' the target, making it difficult for competition authorities to distinguish between pro-competitive and anti-competitive motivations. Roche, rather than removing a potential competitor, was seeking to acquire Spark's wider gene-therapy capabilities.

Assessing the potential for such pipeline acquisitions to result in competitive harm stretches the forward-looking nature of merger control to periods of time in which the counterfactual becomes increasingly uncertain and difficult to predict. This in turn makes it challenging for merging parties to rebut the authorities' concerns. However, the wider context – which we go on to outline – suggests authorities will be increasingly inclined to look at these types of transactions.

This note provides an overview of this wider context, the assessment in *Roche/Spark*, the approach to assessing potential competition – the CMA's divergence from the established approach of the European Commission in similar cases – as well as policy implications for the pharma sector and possible read across to other sectors.

### Increased concerns about the 'kill' motivation in pharma

Concerns over possible 'kill' or delay motivations for acquisitions have been invigorated by recent empirical research suggesting that killer acquisitions are occurring in the pharma sector and being missed by antitrust authorities.<sup>2</sup>

From a large sample of over 16,000 pharmaceutical drug projects undertaken by almost 7,000 companies over 25 years, the research finds that around 6% of acquisitions could be thought of as

'killer acquisitions' (i.e. where the acquiring company has an overlapping product or project and development is stopped) and that acquired drug projects are less likely to be developed when the acquired project overlaps with the acquirer's portfolio of products and projects.<sup>3</sup> This pattern is more pronounced when the acquirer has strong incentives to protect its market power (i.e. where existing competition is weak).

The results suggest such killer acquisitions lowered the overall industry drug development rate by 4%, which would equate to significant consumer harm. This evidence is helping to spur increased interest by authorities in pharma sector mergers.

The results have also been used to suggest similar issues in digital markets but such extensions are inappropriate: one of the key distinctions between pharma and recent digital sector concerns is that pipeline drugs are developed to treat a particular condition (reflecting extensive testing and regulatory requirements), making it relatively easy to identify future product overlaps. While there are exceptions – Pfizer famously originally discovered Viagra while seeking treatments for angina – this contrasts with recent concerns in digital markets, which have focused on complementary products that may (or may not) become future competitors, or with data where the front-end product overlap is less relevant.

### Stretching jurisdiction: to intervene the authority must first be able to look

The medical treatments for Haemophilia A are not specific to any country. In theory, there is a global competitive overlap but as pipeline treatments have no revenue the European Commission did not have jurisdiction. In the UK, the CMA applied the share of supply test.

Spark makes no revenue or sales from its Haemophilia A treatment, given it is still being developed, and has no R&D activity in the UK. Despite this, the CMA considered that Spark's development activity meant that it was active in the supply of Haemophilia A treatments and qualified the deal on two grounds, both of which led to a share of "supply" greater than 25%.

First, based on full-time employees: Spark has a very small number of staff based in the UK. This provides a cautionary lesson for pharma companies with staff working on future commercialisation across Europe: locating them in the UK may raise additional regulatory risks. Second, based on "procurement" or "acquisition" of patents. The CMA takes the position that a pharma company has "procured" a patent even if it has developed the know-how itself and then applied for and been granted a patent and no "procurement" has actually taken place.

While this indicates the CMA's willingness to stretch the bounds of the share of supply test to ensure it captures these transactions (in other circumstances such a jurisdictional assessment might have been appealed), it also highlights the inability of the European Commission and other authorities to review transactions with a similar set of circumstances, including those that, unlike *Roche/Spark*, may raise concerns.

Given it is relatively common for large pharma companies to 'restock' their pipelines through acquiring early stage projects developed in universities, hospitals or research labs, we expect competition authorities to show increased interest in this area. Such acquisitions can bring vital resources and expertise to projects while acting as an exit strategy for research teams and venture capital.<sup>4</sup> Such funding can therefore drive incentives to invest and innovate *ex-ante*, particularly for researchers or venture capital that have no experience or intention of commercialising and marketing a product themselves.

### How likely does likely need to be?

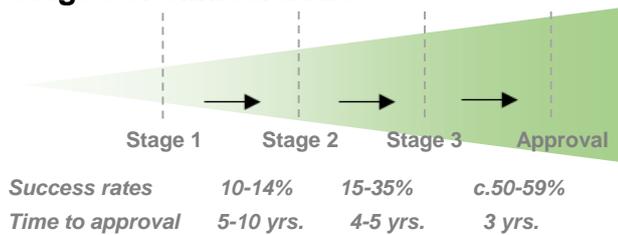
The CMA assessed the case through a framework of potential competition. As we go on to outline, this diverges from the standard approach of the European Commission in assessing acquisitions of pipeline projects still in Stage 2 clinical trials.

Under the CMA's approach, the analytical framework is that for assessing the possible removal of a potential entrant in any sector: is the entrant "likely" to enter absent the merger and, if so, would this entry lead to greater competition?<sup>5</sup> The likelihood is an absolute and relative assessment with greater concerns where the entrant is the "most likely" or "best placed" entrant.<sup>6</sup>

In the UK at Phase 2 the counterfactual must be the most likely scenario.<sup>7</sup> This raises significant issues for these types of transactions: research in the pharma sector shows that the likelihood of progressing from Stage 2 (where Spark's treatment is currently) through Stage 3 to approval is only around one-third or less<sup>8</sup> (i.e. less likely than not) and therefore the relevant counterfactual would be *no entry* (even before taking into account additional uncertainty of funding, obtaining NHS reimbursement, and becoming an effective competitor). Indeed, the risk of failure even in Stage 3 clinical trials can be greater than 50%.<sup>9</sup>

While the exact likelihood will be specific to the facts of a case (including the medical indication and novelty of treatment), the levels of uncertainty in clinical trials are so high (the merging parties themselves will have only limited knowledge) that it may be difficult to depart from general estimates of likelihoods without documentary evidence or an

## Stages of clinical trials



objective basis.<sup>10</sup> In the *Roche/Spark* case, the development of novel treatments such as gene-therapy might reasonably be expected to have an even lower likelihood of success compared to the average.

Cleared at Phase 1, the CMA did not need to meet the Phase 2 “most likely” test and so this issue did not arise. However, despite the significant uncertainty inherent in Stage 2 clinical trials, the CMA stated that Spark “would be likely” to commercialise its product and enter suggesting the CMA believed that entry by Spark met the higher ‘most likely’ threshold.

Potentially worrying for future pharma mergers, the CMA assessment of the likelihood of entry did not reflect the possibility that Spark’s product may not be reimbursed by the NHS, even though there are rival gene-therapy pipeline treatments currently on track to come to market before Spark.<sup>11</sup>

The CMA pointed to Spark’s “*clear intention to commercialise*” its product as one of the key factors indicating likely entry. Given an intention to commercialise is self-evident from any development process (why else would a company develop a product?) and says little about the prospect of the development being successful, it is unclear why such intentions should feature in an assessment of likelihood.

### Possible risk of divergent outcomes?

The European Commission has traditionally considered only treatments in Stage 3 clinical trials sufficiently advanced to compete with either existing or other pipeline products, noting the low likelihoods of projects progressing from earlier stages of clinical testing and the length of time for projects at those stages to launch if successful.<sup>12</sup> For earlier stage clinical trials, the Commission focused on overlapping R&D efforts and innovation (e.g. do the merging parties have similar R&D capabilities? Are limited players engaged in similar R&D?).<sup>13</sup>

However, more recently, it has extended the potential competition framework to early stage pipeline pharma products (e.g. Novartis/GSK oncology<sup>14</sup>), similar to the CMA in *Roche/Spark*, and accepted remedies to address concerns that the acquirer would discontinue development.

The different approaches can lead to different (and possibly divergent outcomes). *Roche/Spark* provides a good example of when this might be the case. Under the EC’s traditional approach, the extent to which there would have been a material overlap in is unclear: Spark’s R&D is focused on gene-therapy, while Roche has limited activity in gene-therapy (which is why it was acquiring Spark).

To the extent the EC’s approach has evolved, the risk of divergent outcomes is no more than it always has been. The European Commission guidelines allow for a lower threshold for potential competition than the CMA: there must be a “*significant likelihood* of [the entrant] growing into an effective competitor”, not necessarily more likely than not, although it also notes that “plans to enter in a significant way” can inform this assessment of likelihood,<sup>15</sup> which parallels the CMA’s interpretation of ‘intentions to commercialise’.

### Future competition between Roche and Spark

In assessing the incentive for Roche to delay development of Spark’s product (or increase price of either), three factors were noteworthy in the CMA’s clearance decision:

**Competing pipelines:** There are a number of rivals also developing gene-therapy treatments in different stages of clinical trials, amongst which BioMarin Pharmaceutical (already reporting interim Stage 3 trial results) is expecting to launch in the EU in 2021 on the basis of an EU accelerated pathway.<sup>16</sup> Spark is behind BioMarin (having not yet progressed to Stage 3) while Sangamo Therapeutics released positive Stage 2 clinical trial data in July 2019.<sup>17</sup>

**First-mover advantage:** Common to many novel treatments, there is likely a pool of existing Haemophilia A patients that are unhappy with their current treatment and likely to switch to the first available gene-therapy treatment. As gene-therapy is aiming to be a one-time treatment, if BioMarin launches first it would capture most of this pool, giving it a first-mover advantage. Patients responding well to current treatment would be more difficult for BioMarin (and subsequent entrants) to persuade to switch.

**Pricing:** Roche’s existing product is reimbursed in the UK at a price negotiated with the NHS. While gene-therapy offers the potential for one-time treatment, the absence of long-term clinical trial data supporting this means that, if successful, those cost savings relative to existing treatments might not be reflected in the price. Competing drug prices are also generally set with reference to existing drugs, and as such Spark’s price is likely to be set with reference to BioMarin’s already approved treatment.

The incentive to kill or delay Spark's development or raise the price of either product can be modelled using cash flow forecasts for each product.<sup>18</sup> These forecasts can provide a baseline from which the change in the merging parties' incentives can be examined. An incentive to delay requires the gains from protecting the revenues of Roche's existing product (against sales lost to Spark) to outweigh the lost sales of the (delayed) Spark product. An incentive to raise price requires a significant proportion of the sales lost following the price rise to be captured by the other product (once launched).

## Shifting sands for assessing potential entry?

More widely, competition authorities have been debating how potential entry should be assessed with suggestions that greater uncertainty should be allowed in the counterfactual. For example:

- The Furman Report proposed allowing a lower likelihood for potential entry where the benefits of entry on competition against the incumbent could be large.<sup>19</sup>
- The CMA's Chief Executive, recognising the difficulties predicting how nascent firms develop, suggested that the time-frame for assessing entry of a competitor could be extended as "*becoming successful can take longer than the two years normally considered for entry*".<sup>20</sup>
- Most recently, DG COMP's Deputy Chief Economist stated that he believed the standard for enforcers to show that companies will compete in the future, as set out in the EC's merger guidelines (i.e. significant likelihood), is "*slightly too high*".<sup>21</sup>

These proposals were made in the context of digital markets but raise a number of important concerns about risk of wider application including to pharma mergers.

First, as noted above, the focus of the 'likelihood' assessment is different between pharma and digital markets: in pharma identifying an overlap is more straightforward so the focus is on likelihood of success (as well as efficacy, approval and reimbursement) while in digital markets the focus is on whether there is an overlap (direct product overlap or indirect data overlap).

Second, allowing increased uncertainty in the counterfactual by loosening the time frame for potential entry by one of the merging parties must be accompanied by a symmetrical loosening of the time frame for entry by rivals as a countervailing constraint. Similarly, any reduced likelihood for entry cannot be applied while maintaining the extremely high threshold for efficiencies, particularly in sectors characterised by high levels of innovation where the impact of increased concentration on

innovation is specific to the circumstances of a case and must be assessed in detail (not mechanically dismissed).<sup>22</sup> Otherwise the result is a significant shift in merger policy favouring Type I errors (blocking pro-competitive mergers) over Type II errors (allowing anti-competitive mergers).

Third, reducing the threshold for the likelihood of entry in pharma would mean treating products in early stages of clinical trials as future overlaps, despite the low probability of the overlap occurring and the time period when the overlap would occur extending the forward outlook of merger control to potentially seven years or more. This potentially leads to speculative theories of harm and impractical assessment trying to compare very small and poorly informed likelihoods of competing pipelines set against the benefits of well-established exit strategies and funding mechanisms that can encourage investment. Given standard patents last 20 years, the first 10 to 15 years of which are typically required to develop the treatment and obtain approval, this would risk significant costs with limited benefit.

Finally, the US Horizontal Merger Guidelines make it explicitly clear that the lessening of competition from removing a potential competitor is more likely to be substantial, the larger is the market share of the incumbent.<sup>23</sup> This seems a more pragmatic approach that can be applied consistently across sectors, including pharma: if the incumbent has a particularly strong market position, then the SLC test is more likely to be met by a potential entrant. This does not reduce the threshold for likelihood and so avoids engaging in speculative theories of harm and the practical difficulties of comparing small likelihoods of competing potential entrants.

In summary, these types of transactions can raise competition concerns and competition authorities are signalling an increased interest in them. The *Roche/Spark* case illustrates the CMA taking an aggressive approach to ensure it has jurisdiction. In doing so it has raised some policy issues as to how best to assess these cases.

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*The views in this article are the authors and do not represent the views of any client or of CRAs other experts.*

<sup>1</sup> Gene-therapy involves the transfer of a therapeutic or working gene copy into the patient's cells in order to repair a faulty gene copy or to introduce a new gene and is considered the next frontier in the treatment of genetic and rare diseases.

<sup>2</sup> *Killer acquisitions*, Cunningham, C., Ederer, F. and Song, M., working paper (17 June 2019). Available at: [https://papers.ssrn.com/sol3/papers.cfm?abstract\\_id=3241707&download=yes](https://papers.ssrn.com/sol3/papers.cfm?abstract_id=3241707&download=yes)

<sup>3</sup> Specifically, acquired projects are 47% less likely to move from Stage 1 to Stage 2 clinical trials where there is an overlap. See *ibid*, page 4.

<sup>4</sup> Venture capital is increasingly common in drug development. For example, in 2018 over half of newly approved drugs were by venture capital backed firms. See *Small companies are the engine of drug R&D in Novartis cholesterol deal highlights mass-market opportunity*, Financial Times, 28 November 2019.

<sup>5</sup> See CMA Merger Assessment Guidelines, paragraph 5.4.15.

<sup>6</sup> See, for example, *Air France/KLM/VLM*, OFT, May 2008, paragraph 111; and COMP/M.3280 *Air France/KLM*, European Commission paragraph 92.

<sup>7</sup> *Merger Assessment Guidelines*, CMA, September 2010, paragraph 4.3.6.

<sup>8</sup> See *Estimation of clinical trial success rates and related parameters*, Wong, Siah and Lo, *Biostatistics*, 20 (2) April 2019, 273–286. The figures in the chart are sourced from this paper, which also summarises estimates from previous studies. See also *Clinical Development Success Rates, 2006-2015*, Bio Industry Analysis and Trial watch.

<sup>9</sup> *Ibid*. See also: *Trial watch: Phase III and submission failures: 2007–2010*, Arrowsmith, J., *National Review of Drug Discovery*, 10 (2): 87.

<sup>10</sup> The CMA has recently suggested that the target valuation and purchase price can be seen an indicator of likelihood. In pharma the valuation will incorporate the likelihood of failure in clinical trials.

<sup>11</sup> A new product will only be reimbursed if it is cheaper and/or more effective than existing treatments. The NHS currently approves only a single provider for current blood clotting treatment (Factor VIII) playing suppliers off against each other for the tender.

<sup>12</sup> See, for example: COMP/M.5661 *Abbot/Solvay Pharmaceuticals*, paragraph 37; Comp M. 1846 – *Glaxo*

*Wellcome/Smithkline Beecham*, paragraph 70; COMP/M7975 *Mylan/Meda*, paragraph 581; and COMP/M.9461 *Abbvie/Allergen* (yet to be published).

<sup>13</sup> The Commission laid out its approach to assessing innovation in a number of recent policy speeches. See, for example, Remarks prepared for the 66<sup>th</sup> ABA Section of Antitrust Law Spring Meeting, Washington, D.C., 12 April 2018, by Deputy Director General for Mergers, Carles Esteva Mosso. Available at: [https://ec.europa.eu/competition/speeches/text/sp2018\\_05\\_en.pdf](https://ec.europa.eu/competition/speeches/text/sp2018_05_en.pdf), page 7.

<sup>14</sup> Comp/M.7275 – *Novartis/GSK Oncology Business*

<sup>15</sup> *Guidelines on the assessment of horizontal mergers under the Council Regulation on the control of concentrations between undertakings*, European Commission, February 2004, paragraph 60.

<sup>16</sup> See: <https://www.biopharmadive.com/news/biomarin-confirms-timeline-for-hemophilia-gene-therapy-putting-pressure-on/558279/>. Accelerated assessment reduces the time taken by the European Medicines Agency (EMA) to review applications for marketing authorisation on grounds of public health and therapeutic innovation.

<sup>17</sup> *Ibid*.

<sup>18</sup> Revenue and cost projections can be obtained from valuations undertaken of the pipeline product used to determine the purchase price or built based on modelling the target patient population, take-up of rival products, and assumptions on price and cost.

<sup>19</sup> *Unlocking digital competition, Report of the Digital Competition Expert Panel*, March 2019.

<sup>20</sup> *Competition in the digital age: reflecting on digital merger investigations: A speech delivered by Andrea Conscelli to the OECD/G7 conference on competition and digital economy*. <https://www.gov.uk/government/speeches/competition-in-the-digital-age-reflecting-on-digital-merger-investigations>.

<sup>21</sup> Remarks by Svend Albaek at Chillin' Competition 2019 conference.

<sup>22</sup> For a discussion of mergers and innovation in the pharma sector, see the article by our colleague Raphaël De Coninck: *Innovation in EU merger control: in need of a consistent framework*, *Competition Policy & Debate*, 2(3), September 2016.

<sup>23</sup> US Horizontal Merger Guidelines, Section 5.3

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