

Anticipated acquisition by Roche Holdings, Inc. of Spark Therapeutics, Inc.

Decision on relevant merger situation and substantial lessening of competition

ME/6831/19

The CMA's decision on reference under section 33(1) of the Enterprise Act 2002 given on 16 December 2019. Full text of the decision published on 10 February 2020.

Please note that [X] indicates figures or text which have been deleted or replaced in ranges at the request of the parties or third parties for reasons of commercial confidentiality.

SUMMARY

1. Roche Holdings, Inc. (**Roche**) has agreed to acquire Spark Therapeutics, Inc. (**Spark**) (the **Merger**). Roche and Spark are together referred to as the **Parties**.
2. The Competition and Markets Authority (**CMA**) believes that it is or may be the case that each of Roche and Spark is an enterprise; that these enterprises will cease to be distinct as a result of the Merger; and that the share of supply test is or may be met. Accordingly, arrangements are in progress or in contemplation which, if carried into effect, will result in the creation of a relevant merger situation.
3. The Parties both supply prophylactic (ie preventative) treatments for congenital Haemophilia A (**Hem A**) in the UK. Hem A is a rare genetic condition that manifests in insufficient or deficient clotting factor, Factor VIII (**FVIII**), which negatively affects sufferers' ability to form clots and stop bleeding. More specifically:
 - (a) Roche manufactures and supplies emicizumab, which is sold under the brand name 'Hemlibra'. Unlike traditional FVIII treatments that require patients to be frequently injected with FVIII, Hemlibra is an innovative

non-factor based (**novel**) Hem A treatment which is subcutaneously administered and mimics the action of FVIII in a patient in order to prevent or reduce bleeding.

- (b) Spark is currently developing two Hem A gene therapy (**GT**) products based on SPK-8011 and SPK-8016 compounds. GT treatment involves a one-time administration after which, if successful, patients will start to produce their own FVIII.
4. For the purposes of the jurisdictional assessment of the Merger, the CMA notes that significant competition exists between firms in the Hem A treatment space before their products are fully commercialised and that therefore competitive interactions between firms should not be reduced to overlaps in directly-marketed products. Roche (a firm with a currently marketed product) and Spark (a firm with products still in clinical development) have both altered their commercial strategies to compete against one another and other firms (with marketed and/or pipeline products). In order to reflect the commercial realities of the Merger, the CMA believes Spark should be considered, for the purpose of assessing whether the share of supply test is or may be satisfied, to be active in the supply of Hem A treatments in the UK. Accordingly, the CMA believes that the share of supply test is or may be met on the basis that the Parties overlap in the supply of novel non-GT and GT Hem A treatments in the UK and have a combined share of approximately [40-50]% with an increment of [5-10]% (based on the number of UK-based, full time equivalent, employees engaged in activities relating to novel non-GT and GT Hem A treatments).
5. The CMA has assessed the impact of the Merger in relation to the supply of all Hem A prophylactic treatments, including traditional FVIII treatments and novel non-GT treatments and GT treatments, considering differences in the characteristics of these treatments within its competitive assessment. While certain competitive parameters relevant to Hem A treatments are likely to be set on a global basis, the CMA has considered the impact of the Merger within a national frame of reference due to differences in national regulatory schemes, prescribing practices, pricing policies and marketing strategies used by pharmaceutical firms.
6. For the substantive assessment of the Merger, the CMA has applied an economic assessment consistent with its established guidance (ie to consider the competitive interaction between the Parties within the framework of actual potential competition) on the basis that Spark's products are not currently marketed to UK patients. The CMA therefore assessed whether the Merger leads to horizontal unilateral effects from a loss of actual potential competition in the supply of Hem A prophylactic treatments by reference to: (i) whether

Spark would be likely to commercialise its GT products in the absence of the Merger; and (ii) whether this would lead to greater competition, taking into account other potential entrants as part of its assessment (ie on this basis, the CMA has considered whether the loss of the constraint posed by Spark would give rise to a realistic prospect of a substantial lessening of competition (SLC)).¹

7. The CMA found that Spark would be likely to commercialise its GT products in the absence of the Merger. Spark has already taken clear and concrete steps towards commercialisation: in particular, its products are at a relatively advanced phase of clinical development and it has UK-based staff working on the commercialisation of its GT products in Europe (including the UK). Spark's internal documents demonstrate a clear intention to commercialise its products in the UK, and third parties consider Spark to be a potentially significant player in the supply of Hem A prophylactic treatments (and, moreover, that Spark's relatively advanced pipeline products are in practice, operating as a constraint on the suppliers with marketed and/or pipeline products). While Spark's products [X] have [X], the available evidence does not indicate that [X].
8. The CMA found that the loss of the constraint posed by Spark would not, however, give rise to a realistic prospect of an SLC in the supply of Hem A prophylactic treatments in the UK. While Roche's recently-launched Hemlibra has already made Roche a significant competitor whose strength is likely to grow, Roche will continue to be sufficiently constrained by several other competing treatments (that are already being commercialised or at a relatively advanced stage of development). In particular, Roche will continue to be constrained by other GT treatments developed by BioMarin and Sangamo, with BioMarin in particular being likely to be commercialised sooner than Spark's products and to gain some first mover advantage. The evidence available to the CMA indicates that Spark's GT product is unlikely to have [X] those rival products.
9. In addition, the CMA's investigation found that there are several novel non-GT products (from suppliers such as Sanofi, Novo Nordisk and Pfizer) that have a realistic potential of being commercialised and are likely, because of their product characteristics, to compete particularly closely with Roche's Hemlibra. The available evidence therefore does not suggest that Spark would be a particularly close or significant constraint on Roche (as compared to other GT treatments and novel non-GT treatments).

¹ *Merger Assessment Guidelines* (OFT1254/CC2), September 2010, paragraph 5.4.15. The *Merger Assessment Guidelines* have been adopted by the CMA (see *Mergers: Guidance on the CMA's jurisdiction and procedure* (CMA2), January 2014, Annex D).

10. Given this strong constraint from rivals, the CMA believes that the Merger does not give rise to a realistic prospect of a substantial lessening of competition (**SLC**) as a result of horizontal unilateral effects in the supply of Hem A prophylactic treatments in the UK.
11. The Merger will therefore **not be referred** under section 3(1) of the Enterprise Act 2002 (the **Act**).

ASSESSMENT

PARTIES

Roche

12. Roche is a wholly-owned subsidiary of Roche Holding AG, a global biotechnology company headquartered in Basel, Switzerland. Roche Holding AG is listed on the SIX Swiss Exchange. Roche offers medicines in oncology, immunology, infection diseases, ophthalmology and neuroscience. It is also active in in-vitro diagnostics and tissue-based cancer diagnostics, as well as diabetes management. For the financial year ending 31 December 2018, Roche's global turnover was approximately £43.5 billion, of which £[~~3~~] million was attributable to the UK.²
13. Amongst other treatments, Roche supplies emicizumab (Hemlibra) for the prophylactic treatment of Hem A. In the UK, Hemlibra has been marketed to and used in certain patient groups since July 2018.³

Spark

14. Spark is a biotechnology company headquartered in Philadelphia, Pennsylvania and is listed on the Nasdaq Global Select Market. Spark is active in the development of GT treatment for genetic diseases, including blindness, haemophilia, lysosomal storage disorders and neurodegenerative disorders. For the financial year ending 31 December 2018, Spark's global turnover was approximately £48.2 million. Spark did not generate any turnover in the UK in 2018.⁴
15. Spark has two GT products in development for the prophylactic treatment of Hem A (the compounds SPK-8011 and SPK-8016).

² Final merger notice submitted by the Parties on 18 October 2019 (**Final Merger Notice**), paragraphs 67-69.

³ A more detailed overview of the Parties' activities in treatments for Hem A prophylaxis is provided later on in this decision.

⁴ Final Merger Notice, paragraphs 70-71.

TRANSACTION

16. The Parties announced on 25 February 2019 that they had entered into a definitive merger agreement for Roche to fully acquire Spark (the **Merger Agreement**). Roche made a cash tender offer to purchase all of the outstanding shares of common stock of Spark for net \$114.50 (equivalent to approximately £90.25) per share, amounting to total consideration of approximately \$4.3 billion (approximately £3.4 billion).⁵
17. The Merger is also the subject of review by the US Federal Trade Commission (**FTC**).
18. The CMA's mergers intelligence function identified this transaction as warranting an investigation.⁶

Transaction rationale

19. The Parties submitted that:
 - (a) For Roche, the Merger was an opportunity to become an effective developer of GT treatments (over a broad platform including but not limited to Hem A). Roche submitted that GT remains the next frontier in the treatment of genetic and rare diseases, will be an important component for Roche's future competitive position and that GT development is a strategy already being followed by its competitors.⁷
 - (b) For Spark, [REDACTED]:⁸
 - (i) [REDACTED];⁹
 - (ii) Roche has experience dealing with regulatory authorities and securing patients for clinical trials and has the financial resources to fund Spark's development efforts; and
 - (iii) The Merger was preferable to collaborations with third-party pharmaceutical companies as it offered more security and backing.

⁵ The price represents a 122% premium on Spark's closing share price on 22 February 2019. Figures have been converted from USD to GBP using the Bank of England's monthly average exchange rate for February 2019 of USD 1 = GBP 0.7882.

⁶ See [Mergers: Guidance on the CMA's jurisdiction and procedure](#) (CMA2), January 2014, paragraphs 6.9-6.19 and 6.59-60.

⁷ Final Merger Notice, paragraph 26.

⁸ Final Merger Notice, paragraphs 27-32.

⁹ Spark's submissions in this respect are considered in further detail in the competitive assessment.

20. Roche's internal documents are broadly consistent with its submission that it has been seeking to expand its presence as a GT developer more broadly than for just Hem A. For example, several of Roche's internal documents indicate Roche's interest in building a wider GT platform across rare diseases, with the Spark acquisition serving as a starting point to broaden Roche's scope with further expansion into GT across various therapeutic areas.¹⁰
21. Roche's interest in Spark's GT platform as a whole is also evidenced by the fact that Roche attributed a [REDACTED] illustrative net present value to Spark's unallocated research and development (**R&D**) [REDACTED] (whilst noting the difficulty of knowing how productive the R&D would be).¹¹
22. Roche's valuation further suggests that Roche also attributed [REDACTED] value to Spark's Hem A portfolio (that is, over Spark's other GT products). [REDACTED].¹²
23. The CMA recognises that these valuations were based on information available to Roche at the time of its valuation of Spark in early 2019 [REDACTED].¹³ The CMA nevertheless considers that these valuations evidence the confidence that Roche places in the future commercial success of the Spark Hem A business, particularly taking into account [REDACTED] (which Roche would have been aware of at the time the Merger Agreement was entered into). [REDACTED],¹⁴ [REDACTED].
24. The CMA has also considered Spark's submissions as to [REDACTED], to the extent relevant, within its competitive assessment.

BACKGROUND

25. By way of background to the analysis set out in this decision, this section provides an overview of:
 - (a) the structure of supply in the pharmaceutical sector, including:
 - (i) an overview of the key stages of the supply cycle: (1) early R&D; (2) clinical development; (3) obtaining of regulatory approvals (namely, the process of acquiring marketing authorisations); and (4) patient use (namely, the UK reimbursement and tendering process and prescription by clinicians);

¹⁰ Final Merger Notice, [REDACTED].

¹¹ Final Merger Notice, [REDACTED].

¹² This is also consistent with Roche's internal documents which suggest that [REDACTED]. Final Merger Notice, [REDACTED].

¹³ [REDACTED].

¹⁴ [REDACTED].

- (ii) the role of intellectual property (**IP**) and other market exclusivity rights; and
 - (iii) the product development process and competitive dynamics;
- (b) treatments for Hem A, including an overview of:
- (i) marketed and pipeline treatments for patients with Hem A;
 - (ii) the Parties' Hem A activities; and
 - (iii) parameters of competition in Hem A.

Supply in the pharmaceutical sector

Key stages of the supply cycle

26. In broad terms, pharmaceutical products pass through three key stages before they are accessible by patients: (i) early R&D; (ii) clinical development, comprised of sequential phases of clinical trials known as Phases I, II and III; and (iii) the obtaining of regulatory approvals.¹⁵ On average, it may take some time (ie a number of years) to develop one new treatment from the earliest stages of discovery to the time it is available for treating patients.

Early R&D

27. The initial stages of discovery will generally involve researchers identifying target compounds and testing them for factors such as safety, efficacy and dosage to ensure these compounds are suitable for human testing in clinical trials. A relatively small percentage of drugs and biologics proceed past this stage.¹⁶

Clinical development

28. It is widely recognised that the success of products in clinical trials are a particularly important determinant of whether these products are authorised for eventual commercialisation. The amount and quality of clinical data obtained from trials are therefore key factors in product development, with clinical trials accounting for a significant proportion of the financial investment incumbent in the development costs of a new product.¹⁷

¹⁵ Roche response to CMA request for information dated 16 August 2019 (**RFI 3**), question 5.

¹⁶ Parties' responses to RFI 3, question 5.

¹⁷ As recognised in, for example, Case M.7326 – *Medtronic/Covidien* (2015), paragraph 74.

Phase I

29. Phase I aims to evaluate the safety of drug compounds and product candidates. It is the first stage of clinical human trials and bears the risk that compounds showing efficacy in cellular or animal testing will not show the same results in human testing. In most circumstances, testing takes place on healthy volunteers (which can involve patients) and generally lasts several months.¹⁸ Testing on healthy volunteers at Phase I is generally not, however, appropriate for GT (due to the potential for unknown risks and the fact that the effect of GT is intended to be long-lasting (ie it cannot be removed once administered)).¹⁹

Phase II

30. Phase II aims to test further the safety, efficacy and appropriate dose of a drug compound or product candidate. The length of this process can vary significantly. Typically, for drug compounds, this process can last from between several months to two years; for GT, timing can differ greatly depending on the product.²⁰ The number of patients involved can also vary. For non-GT drug compounds, Phase II testing can involve up to several hundreds of patients. However, as many GT treatments are aimed at treating serious and rare diseases, the pool of potential patient participants may be smaller, given the specific qualifications patients must have.²¹
31. It is not uncommon for pharmaceutical companies to begin marketing activities in relation to their treatment-in-development from this stage, or even earlier, to ensure brand recognition before the product enters the market. For example, internal documents relating to Spark's Hem A brand strategy [REDACTED].²²

Phase III

32. Phase III tests the efficacy and safety of the drug compound or product candidate on a larger scale than at Phase I or II. For GT treatments, Phase III focuses primarily on testing efficacy and typically involves the investigation of just one 'dose' (that is, the one identified from Phase I/II as being the most effective without exposing the patient to untoward safety risks). This phase can last any number of years. Similarly, the number of participants can also vary considerably, from between hundreds to thousands for non-GT drug compounds (and considerably fewer for GT).

¹⁸ Roche response to RFI 3, question 5, paragraph 5.5.

¹⁹ Spark response to RFI 3, question 5, paragraph 5.5.

²⁰ Parties' responses to RFI 3, question 5.

²¹ Parties' responses to RFI 3, question 5.

²² Spark response to section 109 notice dated 8 July 2019, [REDACTED].

33. The CMA notes that the location of the R&D activities does not determine whether pipeline products have a competitive impact in a given market. Global R&D is how the Parties (and other market players with pipeline and marketed treatments for Hem A) set the quality (and in doing so, influence the potential competitive significance) of their products in every market they operate in.

Obtaining of regulatory approvals

34. On completion of clinical testing, manufacturers/pharmaceutical companies will apply to a relevant competent authority for a marketing authorisation licence, which would allow the product to be placed on the market for sale in the territory concerned.²³ Once approved, the applicant will receive authorisation to market the product for a set period and be subject to continued evaluation during the product's post-marketing phase.²⁴ It can take approximately two years to obtain marketing authorisation in the UK.²⁵

Patient use

- *UK reimbursement and tendering process*

35. In the UK, the final part of the process for supplying new Hem A products to patients consists of two stages:
- (a) First, novel Hem A treatments must be assessed by the National Institute for Health and Care Excellence or Clinical Priority Advisory Group (**CPAG**) in order to agree product reimbursement.²⁶ Both processes take into account the value for money that the new treatment may bring and how it compares to other treatment options available, with novel Hem A treatments being expected to agree a 'cost neutral' price (ie a price that does not cost more than existing Hem A treatments).²⁷
- (b) Second, in order to be prescribed, Hem A treatments must go through the National Health Service (**NHS**) tendering process.²⁸ Separate tendering

²³ In the UK this is the Medicines and Healthcare products Regulatory Agency (**MHRA**) and in the US it is the Food and Drug Administration (**FDA**). A central application can be made to the European Medicines Agency (**EMA**) to obtain European-wide marketing authorisation valid in all EU and European Economic Area states. The EMA is a decentralised agency of the European Union responsible for the scientific evaluation, supervision and safety monitoring of medicines in the EU.

²⁴ Roche response to RFI 3, question 5.

²⁵ Teach-in with the Parties, 24 July 2019.

²⁶ Reimbursement refers to whether the NHS will pay for a particular treatment as part of the standard NHS care.

²⁷ Failure to agree a cost-neutral price tends to make the reimbursement process longer and more uncertain. For example, all treatments which require additional investment (not only those limited to Hem A) are assessed by the CPAG twice a year, where it is agreed which of these drugs will be allocated the available funding; see [NHS England Specialised Commissioning Service Development Policy](#). Note of call with NHS England Commercial Medicines Directorate, 11 September 2019.

²⁸ Hem A treatments are currently procured and paid for by the NHS (rather than private providers).

frameworks are run for different treatment groups; however, these frameworks do not allow pharmaceutical companies to discriminate between (ie set separate prices for) different patient groups or between on-demand and prophylactic treatments.²⁹ Only the products which are selected by the tender can be prescribed. Prescribers may sometimes be required to switch patients from one brand/manufacturer to another depending on which manufacturer has presented the winning bid.³⁰

- *Prescription by clinicians*

36. A large majority of Hem A treatments are prescribed by consultant haematologists specialising in haemophilia treatment and are administered in Haemophilia Comprehensive Care Centres, which provide specialist haemophilia care. The consultants generally select which medicine to prescribe based on what is therapeutically most appropriate and effective, although patients may be able to express their preferences for a particular treatment. Consultants' ability to prescribe a particular Hem A treatment will be limited by criteria set out in the marketing authorisation issued to a particular medicinal product and the NHS reimbursement and procurement regimes discussed above.

The role of IP and other market exclusivity rights

IP rights

37. The Hem A sector is characterised by a significant degree of investment by market players in innovation in relation to both GT and future non-GT treatments.³¹ To protect these innovation efforts, market players developing treatments for Hem A will often, as can be typical for pharmaceutical companies, seek patent protection to protect their innovation efforts from an early stage (including during the early R&D stage of the supply cycle).
38. The European Patent Office (**EPO**) is responsible for granting European patents. The filing of the application for a European patent can be made to the EPO or a national patent office, including the UK patent office (UK Intellectual Property Office (**UKIPO**)).³² The UK is a party to the European Patent Convention which means that, on request for a grant of a European patent,

²⁹ An overview of different patient groups and treatment types is provided later below.

³⁰ Under the current FVIII tendering framework, winning bids are ranked in descending order and the top three products are awarded indicative volumes. The products ranked fourth and fifth are not awarded volumes but will still be prescribed to a smaller number of patients. NHS Commissioning Board response to CMA section 109 notice dated 13 September 2019, page 6. Roche response to CMA request for information dated 8 July 2019 (**RFI 1**), question 8.

³¹ Final Merger Notice, paragraph 125.

³² Article 75 European Patent Convention 1973.

the UK, as a contracting State at the time such an application is filed, would be deemed a designated State in which protection is required.³³ The patent granted by the EPO will therefore benefit from, and be subject to, the same conditions as if it had been granted in the UK.³⁴

Orphan designation rights

39. Market players developing products for the treatment of rare diseases or conditions such as Hem A can also file an application with the EMA (or the relevant regulatory body in a particular jurisdiction, for example the FDA in the US) to obtain an orphan drug designation. An orphan drug designation protects a medicinal product, for a period of seven years in the US and generally for a period of ten years in Europe, by preventing the grant of a marketing authorisation or extension of existing marketing authorisations for any 'similar medicinal products' for the same therapeutic indication.³⁵ Where medicinal products are determined to be similar, however, authorisation can still be granted at the consent of the orphan drug designation holder, if the holder cannot supply sufficient quantities of the drug, or if it can be shown that the treatment under application is superior.³⁶

The product development process and competitive dynamics

40. Many markets in the pharmaceuticals sector (including the market for the supply of Hem A products) are characterised by significant switching costs, in particular because patients may be highly reluctant to switch treatments.³⁷ In practice, this means that incumbent firms have the incentive to compete not only against the products that are already in the market, but also against known pipeline products, in order to win as many patients as possible before the pipeline product is commercialised so as to reduce the eventual impact of the new product on the incumbents' sales.

³³ Part III, Chapter I, Article 79 European Patent Convention 1973.

³⁴ Part I, Chapter I, Article 2(2) and Part II, Chapter IV, Article 74 of the European Patent Convention 1973 and section 77 of the Patents Act 1977. The patent application process typically involves four stages: (i) submission of the application; (ii) an examination report issued by the UKIPO; (iii) a patent search request by which the UKIPO checks whether the matter being patented is new and inventive; and (iv) publication of the application, followed by a substantive examination of the invention to ensure it meets the necessary legal requirements. This process can take up to five years to be completed ('Patenting your invention' at <https://www.gov.uk/patent-your-invention/before-you-apply>).

³⁵ 'Similar medicinal product' is defined as a medicinal product containing a similar active substance or substances as contained in a currently authorised orphan medicinal product, and which is intended for the same therapeutic indication, see article 3 of the Commission regulation (EC) No 847/2000.

³⁶ Ie the product is safer, more effective or otherwise clinically superior. Parties' response to RFI 3, question 10.

³⁷ Various factors may limit patients' willingness to switch treatments, eg patients may experience initial side effects when switching to new treatments; it may take them time to identify the most effective dosage, during which time they experience more symptoms; and they also may be loyal to a treatment that they know to be safe and effective based on their own experience. [X].

41. Pharmaceutical markets are also characterised by a degree of transparency as to the relevant rivals active in the sector and the stage of development of a rival firm's pipeline products (as pharmaceutical firms will typically announce this publicly, for example at industry conferences and through news announcements and shareholder updates). The attainment of, and notable delays in the attainment of, important milestones within the key stages of the supply cycle can be tracked by rivals. This means that products at the product development stage play an integral role in the competitive process.³⁸ The CMA found evidence that market players react to pipeline products by seeking to improve their own competitive offer to compete – both before these rival products are commercialised and with a view to doing so after these products obtain marketing authorisation and are commercialised.
42. For example, Roche's internal documents provide [REDACTED] evidence of Roche responding to the threat of GT entry (at a point that is several years before patients will have access to these products), [REDACTED].³⁹ Indeed, several third parties confirmed Roche's significant efforts in globally marketing Hemlibra through active promotions by spokespersons and ambassadors, and noted that Roche's actions to establish a strong presence in the haemophilia community was likely to be in part a competitive reaction to pipeline treatments.⁴⁰
43. In addition, Roche has also engaged in several activities aimed at increasing the rate of Hemlibra's uptake. These include the [REDACTED].⁴¹ Roche's internal documents indicate that at least some of these activities have been undertaken in response to the threat of GT entry.⁴²
44. This trend was also corroborated by evidence of third parties closely monitoring the Hem A treatment pipeline and tracking the development of individual pipeline products. Most suppliers of Hem A treatments indicated that they pay particular attention to clinical trial data released by market players developing Hem A treatments.⁴³ Further, one competitor noted that it tries to anticipate how regulatory authorities will evaluate a product under review for marketing authorisation to form a view as to the likelihood and timing of its launch.⁴⁴ Third parties, including clinicians and haematologists, also indicated that they monitor the pipeline for Hem A treatments, and were able to provide detailed insight on specific developments, further confirming

³⁸ This feature of the pharmaceutical industry has been recognised in a number of cases, including for example Case M.7275- *Novartis/Glaxosmithkline Oncology Business*, 2015, paragraph 24.

³⁹ Roche internal documents received from FTC: [REDACTED].

⁴⁰ [REDACTED].

⁴¹ Roche response to CMA request for information dated 19 August 2019 (**RFI 4**), question 2.

⁴² For example, see Roche response to section 109 notice dated 8 July 2019, [REDACTED].

⁴³ [REDACTED].

⁴⁴ [REDACTED].

the competitive constraint these developments place on existing players. It is also apparent that firms with pipeline products that are nearing commercialisation in the UK often reach out to clinicians to promote their treatment.⁴⁵ Spark also confirmed that, within the UK, Spark's EU Advocacy Lead has already had periodic engagement with the UK Haemophilia Society (to deliver corporate updates and answer questions) and has supported engagement with a UK-based haemophilia advocate.⁴⁶

45. In the light of the evidence of their competitive relevance, the CMA has therefore given material weight to both Parties' activities concerning pipeline and existing Hem A products in both its assessment of jurisdiction and in the substantive assessment of the Merger.

Treatments for Hem A

46. Hem A is a rare genetic condition affecting the blood's ability to clot. People with Hem A either have insufficient or deficient FVIII clotting factor, which negatively affects their ability to form clots and stop bleeding. Depending on the level of FVIII, Hem A patients can be split into the following categories:
- (a) Mild (FVIII levels of 5-40%);
 - (b) Moderate (FVIII levels of 1-5%); and
 - (c) Severe (FVIII levels <1%).⁴⁷
47. The CMA estimates that in 2017/18 severe Hem A patients accounted for nearly two thirds (57%) of all treated patients in the UK, followed by patients with mild (25%) and moderate (16%) Hem A.⁴⁸

⁴⁵ [REDACTED].

⁴⁶ Spark response to CMA request for information dated 17 September 2019 (**RFI 6**), question 3.

⁴⁷ [EMA Hemlibra assessment report](#), page 10.

⁴⁸ In 2017/18, there were 8,159 registered patients who were diagnosed with Hem A in the UK, of which only half received treatment (UKHCDO 2018 Annual Report, page 16). The CMA considers that for the purposes of this merger investigation it is appropriate to refer to the number of patients *receiving* Hem A treatment (ie rather than referring to the total number *diagnosed*).

Marketed and pipeline treatments for patients with Hem A

48. Treatments for Hem A can be split into the following categories:
- (a) On-demand episodic treatments, which are aimed at stopping a bleed when it occurs (a category that includes non-GT treatments only); and
 - (b) Prophylactic treatments, which are aimed at preventing bleeding from occurring (a category that includes both non-GT treatments and GT treatments).
49. As set out below, the type of treatment available to the patient depends on the severity of the condition and the presence of FVIII inhibitors. The need for treatment is currently lifelong.

On-demand episodic treatments

50. Mild and moderate Hem A patients may not need prophylactic treatment and may only require episodic on-demand treatment to stop existing bleeds.⁴⁹ Typically, these types of treatments comprise high levels of FVIII or bypassing agents (**BPA**s) up to every two hours.

Prophylactic treatments

51. The majority of patients receiving prophylactic treatment will have severe Hem A.⁵⁰ The treatment options will differ depending on whether a patient has persistent FVIII ‘inhibitors’ (ie antibodies which attack FVIII), as further set out below.

Patients without FVIII inhibitors

52. For patients without FVIII inhibitors, preventative treatment usually currently requires:
- (a) Injecting FVIII three to four times a week.⁵¹ Although effective in reducing bleed rates, FVIII treatments are given intravenously, which requires long intravenous (**IV**) infusion times, and may be more difficult for some patients to maintain as they require frequent access to veins. Many

⁴⁹ Roche response to RFI 1, question 33.

⁵⁰ Note of call with Consultant in Paediatric Haemostasis and Thrombosis, 12 August 2019; Note of call with Consultant Haematologist, 25 July 2019. For instance, based on data provided by one third party, the CMA estimates that severe patients represent 81% of all prophylaxis patients. [§].

⁵¹ FVIII treatments can be split into (i) human plasma derived treatments and (ii) recombinant (ie synthetic) treatments. Human plasma derived FVIII treatments were the first generation FVIII treatments, now largely replaced by recombinant FVIII treatments in the UK.

patients may require central venous access devices (**CVADs**) to be inserted surgically,⁵² or

- (b) Using other novel non-GT Hem A treatments, such as Roche's Hemlibra,⁵³ which is administered intravenously once a week or, in some cases, more rarely.⁵⁴

53. In addition, a number of GT treatments are also being developed for patients without inhibitors. Unlike conventional treatments, GT involves a one-time administration, after which – if successful – patients start to produce their own FVIII.⁵⁵ GT treatments typically work by using a synthetic virus' outer coat or capsid (known as a 'vector') which is infused and finds its way into the patient's liver. While often referred to as a 'life-long treatments', GT treatments currently in development (**first generation GT treatments**⁵⁶) are expected to stay effective for only a finite number of years. At present, there is limited clinical evidence on the average duration of GT treatments' efficacy. However, some evidence suggests that treatments which stay effective for five to ten years are likely to be considered as 'effective' by regulatory authorities.⁵⁷

54. In addition to uncertainties around treatment durability, first generation GT treatments face other challenges which further limit the population of GT-eligible patients. More specifically:

- (a) Since all GT treatments currently in development use viral vectors, previous exposure to similar viruses may lead to patients developing cross-reacting antibodies, making a particular GT treatment ineffective for such patients.⁵⁸ Therefore, patients' eligibility for a particular GT product will depend on whether they have been exposed to the virus used by that particular GT product. Further, as a result, 're-dosing' (ie repeated

⁵² While CVADs allow for easier administration, they also increase the risk of infection and thrombosis.

⁵³ Roche's Hemlibra is the only marketed treatment belonging to this category, having agreed reimbursement for severe non-inhibitor patients with NHS England on 21 August 2019, although several other novel Hem A treatments are currently being developed by a number of players (see Table 1) .

⁵⁴ 52% of Hemlibra patients use it once a week, 44% every two weeks and 4% every four weeks. This corresponds to between 13 to 52 injections a year. By contrast, traditional FVIII treatments require from 156 to 208 injections per year. Roche response to RFI 1, question 39.

⁵⁵ Final Merger Notice, paragraphs 7 and 24-26.

⁵⁶ This includes GT products which use adeno-associated viral (**AAV**) vectors, including but not limited to those developed by Spark, BioMarin and Sangamo.

⁵⁷ Spark response to section 109 notice dated 8 July 2019, [§]. [§]. Some of the Parties' internal documents also suggest that [§]. Final Merger Notice, [§]; Spark response to section 109 notice dated 8 July 2019, [§].

⁵⁸ It may be possible to limit the activity of antibodies by using steroids following a GT treatment dose, although very limited clinical data on the efficacy of this approach currently exists.

treatment with the same manufacturer's product) will not be possible with first generation GT treatments.⁵⁹

- (b) It is also unclear whether a patient will be able to repeat a GT treatment with a different manufacturer's GT product using a different viral vector. While this is theoretically possible, no evidence examining the cross-reactivity of different manufacturers' GT treatments currently exists.⁶⁰ Since all first-generation GT treatments currently being developed use AAV vectors, it remains possible that patients may develop an immune response which is robust enough to react to a range of AAV vectors used by different AAV therapies.⁶¹
- (c) Absent further clinical evidence, it remains unclear whether patients with FVIII inhibitors, either persistent or historic, would be eligible for GT treatments.⁶²

Patients with FVIII inhibitors

55. Around one in three people with Hem A who are treated with FVIII replacement therapy may develop inhibitors, thus making such treatment ineffective. It is estimated that between 60 to 80%⁶³ of patients that develop inhibitors can have them eradicated by ITI treatment and can subsequently resume FVIII replacement therapy.⁶⁴ However, patients for which the ITI was unsuccessful (representing around 6% of all treated Hem A patients in the UK⁶⁵) have more limited Hem A treatment options. For those patients with persistent inhibitors, treatment options include:

- (a) Novel non-GT Hem A treatments which are not affected by inhibitors, such as Roche's Hemlibra; and

⁵⁹ Re-dosing will also have an effect on whether GT will be available to children who, if treated with GT early, would need to repeat GT once their liver has fully formed. Spark response to section 109 notice dated 8 July 2019, [redacted].

⁶⁰ Note of call with Consultant Haematologist, 25 July 2019.

⁶¹ [redacted].

⁶² It is not currently clear whether the GT would be able to achieve FVIII levels high enough to mitigate the effect of persistent inhibitors or to ensure inhibitors do not reappear in patients who have had immune tolerance induction (ITI) therapy (see following paragraph and footnote 64), making them ineligible for GT. Spark currently excludes patients with both persistent and historic FVIII inhibitors from its potential patient population. Spark response to CMA request for information dated 8 July 2019, question 19 and 36; Note of call with Consultant in Paediatric Haemostasis and Thrombosis, 12 August 2019.

⁶³ [EMA Hemlibra assessment report](#), page 11.

⁶⁴ ITI treatment involves administering very high doses of FVIII. While it is possible that some patients may decide not to undergo ITI, prescribers usually consider it very important to have FVIII inhibitors eradicated before proceeding to any other treatment. Failing to eradicate inhibitors would also make patients ineligible for gene therapy. Note of call with Consultant in Paediatric Haemostasis and Thrombosis, 12 August 2019.

⁶⁵ CMA analysis using as a proxy the number of patients that had inhibitors reported in the previous year in the UKHCDO 2018 Annual Report. Spark's research provides similar estimates; Spark response to section 109 notice dated 8 July 2019, [redacted].

(b) Treatment using BPAs every two to three days (some of which may be administered daily).⁶⁶ Like FVIII, BPAs can only be given intravenously which requires long IV infusion times,⁶⁷ can cause pain and stress, and carry the same risks associated with CVADs. In addition, BPAs are usually considered to be less effective in reducing bleed rates than other alternative treatments (ie traditional FVIII treatments or Hemlibra).⁶⁸

56. An overview of suppliers of different Hem A treatments (both currently marketed and in development) is provided in Table 1 below.

Table 1: Overview of Hem A treatments in the UK

Treatment	Manufacturer	Brand	Type of administration	Stage	Use for Hem A prophylaxis		
					With inhibitors	Severe without inhibitors	Other
<i>Human plasma derived FVIII</i>	Biotest	Haemoctin	IV	Marketed	✓	✓	✓
	BPL	FVIII 8Y	IV	Marketed	✓	✓	✓
	BPL	Optivate	IV	Marketed	✓	✓	✓
	Grifols	Alphanate	IV	Marketed	✓	✓	✓
	Grifols	Fanhdi	IV	Marketed	✓	✓	✓
	Octapharma	Octanate	IV	Marketed	✓	✓	✓
<i>Recombinant FVIII</i>	Octapharma	Wilate	IV	Marketed	✓	✓	✓
	Octapharma	Nuwiq	IV	Marketed	✓	✓	✓
	Bayer	Kogenate	IV	Marketed	✓	✓	✓
	CLS Behring	Helixate Nexgen	IV	Marketed	✓	✓	✓
	Novo Nordisk	NovoEight	IV	Marketed	✓	✓	✓
	Pfizer	Refacto AF	IV	Marketed	✓	✓	✓
<i>Enhanced half-life recombinant FVIII¶</i>	Shire	Advate	IV	Marketed	✓	✓	✓
	SOBI/Biogen	Elocta	IV	Marketed	✓	✓	✓
<i>BPA</i>	Sanofi/Bioveratiiv	BIVV-001	IV	Phase II/III*	✓	✓	
	Shire	FEIBA	IV	Marketed	✓		
<i>Anti-tissue factor pathway inhibitor therapy</i>	Novo Nordisk	NovoSeven	IV	Marketed	✓		
	Novo Nordisk	Concizumab	Subcutaneous	Phase III	✓	✓	
<i>Emicizumab</i>	Pfizer	PF-06741086		Phase II	✓	✓	
	Roche	Hemlibra	Subcutaneous	Marketed	✓	✓	
<i>Antithrombin targeted siRNA</i>	Sanofi	Fitusiran	Subcutaneous	Phase III	✓	✓	
<i>GT</i>	Spark	SPK-8011		Phase II		✓	
	Spark	SPK-8016		Phase I		✓	
	BioMarin	BMN-270		Phase III		✓	
	Sangamo/Pfizer	SB-525		Phase II		✓	

Source: CMA analysis based on the Parties' data

* Sanofi is expected to start Phase III clinical trials by the end of 2019.⁶⁹

¶ Enhanced half-life FVIII products which are expected to bring improvements to the frequency of standard FVIII treatment administration, see further paragraph 220 of this decision.

⁶⁶ EMA Hemlibra assessment report, page 11.

⁶⁷ Eg 25-50 minutes, see EMA Hemlibra assessment report, page 11.

⁶⁸ EMA Hemlibra assessment report, page 10.

⁶⁹ See press article *New data to be presented at ASH 2019 highlight Sanofi's commitment to treat challenging blood cancers and rare blood disorders*, 6 November 2019, <https://www.bloomberg.com/press-releases/2019-11-06/new-data-to-be-presented-at-ash-2019-highlight-sanofi-s-commitment-to-treat-challenging-blood-cancers-and-rare-blood-disorders>.

Notes: (1) Save for Spark's SPK-8016, the pipeline treatments listed in this table only include products that have reached Phase II clinical trials; (2) GT and other novel non-GT treatments may not be reimbursed for children/adolescents, at least initially, due to the need to conduct additional clinical trials. It remains unclear whether GT would be reimbursed for children at all, as there are some concerns that children's livers may not be sufficiently developed for GT; (3) Spark submitted that both SPK-8011 and SPK-8016 were currently in Phase I/II. However, since SPK-8016 is still at the relatively early stages of its clinical trials and SPK-8011 already had a follow-up study and was about to start an observational study to recruit subjects for its Phase III trials [§], the CMA considers it appropriate to view SPK-8011 as currently in Phase II and SPK-8016 in Phase I of clinical trials; (4) While the Parties' data suggests that traditional FVIII and enhanced half-life FVIII treatments can be used for Hem A prophylaxis in patients with inhibitors, in light of the evidence described from paragraph 55 above, the CMA believes that these treatments are primarily used for the purposes of ITI rather than in patients with persistent FVIII inhibitors.

The Parties' Hem A activities

57. Both Roche and Spark are active in the supply of prophylactic treatments for Hem A.⁷⁰ Roche manufactures and supplies Hemlibra and Spark is currently developing two Hem A first generation GT products – SPK-8011 and SPK-8016. The Parties' activities are further described below.

Roche

58. Roche's product Hemlibra 'mimics' the action of FVIII in a patient in order to prevent or reduce bleeding. Hemlibra is currently only reimbursed for the treatment of patients with persistent FVIII inhibitors and for the treatment of patients with severe Hem A without inhibitors. This means that it is prescribed for only those patient groups (which account for around 60% of treated Hem A patients in the UK).⁷¹

59. Roche is currently at the commercialisation stage of supply in the UK. Roche told the CMA that it had incurred a series of costs, both globally and in the UK, in developing its supply operations, including product marketing costs, R&D costs and distribution costs.⁷²

60. Roche's Hem A business in the UK is comprised of certain activities that are carried out centrally (ie on global basis) and certain activities that are carried out locally in the UK (to provide additional support for the UK business). For example:

- (a) All discovery and preclinical research within the Roche Group relating to Hem A is carried out by Chugai, Roche's pharma affiliate in Japan;

⁷⁰ The Parties also overlap in treatments for retinal disease and Huntington's disease. However, given that the Parties' overlap in these activities is limited, this is not addressed further in this Decision.

⁷¹ Roche response RFI 1, question 8; Note of call with Lead Commissioner for Specialised Blood Disorders, 9 August 2019 (relevant only to the first sentence of paragraph 58).

⁷² Parties' responses to response to CMA request for information dated 2 August 2019 (RFI 2), question 1.

- (b) Roche's drug development activities relating to Hem A are managed by employees (a category that includes Roche's in-house clinical scientists) located across a number of Roche's global sites (such as Basel, San Francisco, Welwyn as well as Shanghai, for clinical trial activities related to China), with clinical trials taking place in several hospitals/clinics around the world;⁷³
- (c) Roche UK employs [REDACTED] individuals who are fully dedicated to Hemlibra. In addition, Roche UK employs [REDACTED] individuals who are partly dedicated to Hemlibra;⁷⁴
- (d) From a global perspective, the wider Roche group also employs a number of individuals who are assigned to supporting Hem A trials in the UK. For each of these individuals, Hem A constitutes only a small part of their overall role;⁷⁵
- (e) Roche UK provides grants to a number of UK healthcare organisations;⁷⁶
- (f) Roche holds 12 UK patents in relation to the treatment of Hem A in the UK;⁷⁷
- (g) Roche holds a marketing authorisation issued by the EMA in respect of Hemlibra (covering the inhibitor and non-inhibitor indications). This EMA authorisation allows Roche to market Hemlibra throughout the EU (including the UK); and
- (h) Roche has conducted a number of clinical trials in relation to Hem A treatments in the UK and is in the process of conducting or planning to conduct more. Those trials that have been already completed involved more than 60 patients in the UK, and those on-going around 50 patients in the UK.⁷⁸

Spark

61. As explained above at paragraph 53 above, GT involves a one-time administration after which, if successful, patients start to produce their own FVIII. Spark's two Hem A GT compounds, SPK-8011 and SPK-8016, are currently intended for the treatment of Hem A patients without inhibitors. [REDACTED].

⁷³ Roche response to CMA request for information dated 14 October 2019 (RFI 7), question 2.

⁷⁴ Parties' responses to RFI 1, question 29.

⁷⁵ Parties' responses to RFI 1, question 29.

⁷⁶ Parties' responses to RFI 1, question 30. One of the three grants paid out by Roche UK in relation to Hem A relates to the provision of equipment.

⁷⁷ The patents held by Roche are EU patents which have been validated in the UK.

⁷⁸ Roche response to RFI 3, question 4, [REDACTED].

62. Spark is currently at the clinical development stage of supply (SPK-8016 and SPK-8011 are respectively at the Phases I and II stages) and continues to take steps to proceed to the commercialisation stage, including in the UK,⁷⁹ in the foreseeable future.
63. Spark's Hem A business in the UK is also comprised of a mix of activities that are carried out centrally and certain activities that are carried out locally in the UK. For example:
- (a) Most of Spark's current Hem A R&D activities are carried out in Philadelphia, where Spark's laboratory space and R&D professionals dedicated to SPK-8011 and SPK-8016 are located. Spark's clinical trials for SPK-8011 and SPK-8016 are also managed from Spark's Philadelphia-based operations. Of Spark's eleven open clinical trial sites for SPK-8011, two are outside of the United States;⁸⁰
 - (b) Spark's subsidiary in the UK, Spark Therapeutics UK Ltd, has [REDACTED] employees who undertake activities relating to Hem A;⁸¹
 - (c) Spark has been granted a UK patent related to the treatment of Hem A (including methods of manufacture) in the UK;⁸²
 - (d) Spark has a number of patent applications currently pending in the EU relating to SPK-8011 and SPK-8016. These will be validated in the UK upon patent issuance;⁸³ and
 - (e) Spark has not initiated any clinical trials for Hem A in the UK. However, Spark intends to include UK sites [REDACTED].

Parameters of competition in the supply of Hem A treatments

64. Pharmaceutical companies focus on different competitive aspects, depending at which stage the product is. The key parameters of competition in relation to: (i) pipeline Hem A treatments; and (ii) marketed Hem A treatments are set out below.

⁷⁹ [REDACTED].

⁸⁰ [REDACTED].

⁸¹ [REDACTED].

⁸² Spark has been granted an EU patent (EU 11737508.9) which has been validated in the UK, that relates to SPK-8011/SPK-8016 manufacturing. Spark response to RFI 2, question 6.

⁸³ Spark response to RFI 2, question 6.

Pipeline products

65. At the product development stage, pharmaceutical companies primarily compete by investing in improving product efficacy and safety profile, as well as other product-specific quality parameters. For instance, with regard to non-GT Hem A treatments, manufacturers compete by seeking to improve the mode of treatment administration and the frequency of dosing. GT manufacturers will compete on the basis of various clinical parameters⁸⁴ that will influence its attractiveness relative to other types of treatments including:⁸⁵
- (a) Efficacy, ie reduction of bleed rates;
 - (b) Variability/predictability, ie the certainty of a particular clinical outcome being achieved;
 - (c) Durability, ie how long the effects of GT product are expected to last;
 - (d) Safety, ie whether the GT product could lead to significant adverse effects; and
 - (e) Immunogenicity, ie the proportion of patients that have been exposed to a particular virus and are therefore ineligible for a particular GT product. This would influence the number of patients which would be eligible for a particular GT product.
66. In addition, manufacturers of pipeline GT treatments also compete to come to market earlier than rivals, with the treatment that succeeds in being first to market possibly gaining certain competitive advantages.⁸⁶ With regard to first generation GT manufacturers, these advantages may include access to a wider patient pool,⁸⁷ as well as the opportunity to gain greater historical data on their product's safety and efficacy, making the treatment more attractive, in particular to risk-averse patients/prescribers.⁸⁸

Marketed products

67. When a product is marketed, manufacturers primarily compete on product pricing. Pricing is particularly important in jurisdictions such as the UK, which is characterised by a single buyer (the NHS), tender frameworks and budget

⁸⁴ See for example [REDACTED].

⁸⁵ Parties' responses to RFI 4, question 19.

⁸⁶ See for example [REDACTED].

⁸⁷ For example, given that re-dosing with first generation GTs is not expected to be possible, subsequent GT products will face a reducing eligible patient population.

⁸⁸ Spark response to RFI 4, question 19.

constraints.⁸⁹ For instance, when negotiating the reimbursement of Hemlibra, Roche and the NHS England agreed a [REDACTED] price.⁹⁰ In addition, during the most recent tendering process, the winning bids were selected primarily on the basis of price, which accounted for 80-85% of the overall score, with the remainder being accounted for by security of supply and ease of use.⁹¹ The Parties and third parties told the CMA that they expect GT treatments to compete in the same way on product pricing when they reach the commercialisation stage.⁹²

68. Once the reimbursement and price have been agreed with the NHS, the suppliers of different Hem A treatments continue to compete with each other in terms of investment in sales, marketing and other activities in order to 'educate the healthcare professionals on the safe and effective use of their particular medicine'.⁹³
69. Local competitive conditions in each jurisdiction will influence competition on price and investment in sales and marketing activities. While global competitive conditions will influence the overall timing of entry, manufacturers' decisions to market products in specific jurisdictions (and which jurisdictions to enter first) will be influenced by the size of that market, the local competitive conditions in each jurisdiction and the incremental cost of entry in a particular jurisdiction.⁹⁴
70. In addition, Hem A treatment manufacturers may continue to invest in improving product quality or extending the treatment to patients not yet covered by the marketing authorisation. GT treatment manufacturers, particularly in the initial years following commercialisation, will also compete on the basis of adequate manufacturing.⁹⁵ Similar to pipeline products, these parameters are also likely to be influenced by global competitive conditions.

⁸⁹ Third parties explained that price is the most important competitive parameter for marketed Hem A treatments. [REDACTED].

⁹⁰ The CMA understands there have been examples of the NHS taking steps to ensure that only the less costly treatments are prescribed, [REDACTED]. Note of call with Consultant Haematologist, 25 July 2019; Note of call with Consultant Haematologist, 16 August 2019.

⁹¹ When competing for tenders, third parties noted that commissioners would usually expect the manufacturers to bid below their list price. Note of call with NHS England Blood Products and Vaccine team, NHS England and NHS Improvement, 14 August 2019; [REDACTED].

⁹² Parties' responses to RFI 4, question 19. BioMarin also mentioned that securing reimbursement will influence the success of GT products. See BioMarin response to CMA questionnaire dated 27 September 2019, question 12.

⁹³ Roche response to RFI 1, question 18.

⁹⁴ For instance, Spark and at least one other competitor have taken decisions to [REDACTED]. Final Merger Notice, footnote 14; [REDACTED].

⁹⁵ Parties' responses to RFI 4, question 19.

JURISDICTION

Relevant framework

71. In the context of an anticipated transaction, a relevant merger situation exists where the following conditions are satisfied:⁹⁶
- (a) two or more enterprises will cease to be distinct; and
 - (b) either:
 - (i) the value of the target enterprise's UK turnover exceeded £70 million in its last fiscal year (the **turnover test**); or
 - (ii) the enterprises ceasing to be distinct will have a share of supply in the UK, or in a substantial part of the UK, of 25% or more in relation to goods or services of any description (the **share of supply test**).

Enterprises ceasing to be distinct

72. Each of Roche and Spark is an enterprise. As a result of the Merger, Roche will acquire 100% of the shares (and therefore a controlling interest) in Spark. Therefore, these enterprises will cease to be distinct.

The turnover test

73. The Merger does not satisfy the turnover test in section 23(1)(b) of the Act, since Spark does not have turnover in the UK.

The share of supply test – general framework

74. The Guidance on the CMA's jurisdiction and procedure (**Guidance**) sets out that the share of supply test is satisfied if the merged enterprises both either supply or acquire goods or services of a particular description, and will, after the merger, supply or acquire 25% or more of those goods or services in the UK.⁹⁷
75. The share of supply test therefore contains the following three key elements:
- (a) a product element (ie the supply or procurement of goods or services of any description);

⁹⁶ Section 23 of the Act.

⁹⁷ *Mergers: Guidance on the CMA's jurisdiction and procedure* (CMA2), January 2014), paragraph 4.53.

- (b) a geographical element (ie the UK or a substantial part of it); and
- (c) a quantitative element (ie the 25% threshold).

76. With regard to the first element, the Act confers on the CMA a broad discretion to choose a specific category of goods or services supplied or procured by the merging parties.⁹⁸ The Guidance identifies a number of considerations to which the CMA will have regard when choosing this category.⁹⁹ In particular, the Guidance provides that the share of supply test is not an economic assessment of the type used in the CMA's substantive assessment and need not amount to a relevant economic market. Rather, the Guidance requires the CMA to have regard to any reasonable description of a set of goods or services to determine whether the share of supply test is met.¹⁰⁰
77. With regard to the second element, the Act does not provide specific rules on determining whether, and to what extent, an enterprise's activities should be deemed to be in the UK for the purposes of the share of supply test. The Guidance states that as a general rule, goods or services are deemed to be supplied in the UK if customers are located in the UK. The Guidance also states that the CMA will apply this general rule in a flexible and purposive way, with regard to all relevant factors, including where relevant procurement decisions are likely to be taken and, where in turn, any competition between suppliers takes place.¹⁰¹
78. With regard to the third element, the Act gives a wide discretion to the CMA to apply whatever measure (including value, cost, price quantity, capacity, and number of workers), or combination of measures, it considers appropriate to calculate the merging parties' share of supply or procurement and to determine whether the 25% threshold is satisfied.¹⁰²

The application of the share of supply test

79. The Parties submitted that the CMA does not have jurisdiction to review the Merger as the share of supply test is not met.
80. The CMA has considered the Parties' submissions along with information provided by third parties. As further explained below, the CMA considers that the share of supply test is or may be satisfied in this case.

⁹⁸ Section 23(8) of the Act.

⁹⁹ *Mergers: Guidance on the CMA's jurisdiction and procedure* (CMA2), January 2014, paragraph 4.56.

¹⁰⁰ *Mergers: Guidance on the CMA's jurisdiction and procedure* (CMA2), January 2014, paragraph 4.56.

¹⁰¹ Guidance, paragraph 4.58.

¹⁰² Section 23(5) of the Act.

81. The overall purpose of merger control is to regulate the conduct of companies in the market and to enable competition authorities to examine mergers which may have a detrimental effect on competition and consumers. This is confirmed by the Competition Appeal Tribunal's statement that '[t]he CMA's role in regulating merger activity, and its ability to do so effectively, is a matter of public importance.'¹⁰³ As part of the assessment of whether a relevant merger situation exists, the intention of the Act is for the share of supply test to be a key gateway to providing the CMA with the power to intervene in transactions which, like the present one, are relevant to UK markets or activities and may be expected to raise competition concerns that could impact UK consumers.¹⁰⁴
82. The CMA's well-established approach in carrying out its statutory duties in relation to merger control is to consider the commercial realities and results of transactions, focussing on the substance rather than the legal form of arrangements.¹⁰⁵ Markets can be characterised by a variety of different business models and that the ways in which firms interact (with each other and other market participants) to win business over time can vary significantly. In practice, this means that competitive interactions between firms may not be reduced to overlaps in directly-marketed products or services (as they may in more traditional markets) but can result from overlaps involving pipeline products or services.
83. In the present case, the available evidence shows that significant competition exists between firms well before their products are fully commercialised (ie a firm with a currently-marketed product will alter its commercial strategy to compete against a product that is still in clinical development and *vice versa*).
84. The way in which suppliers compete with each other is similar even where products are at a different stage of the supply cycle. For example, prior to Hemlibra's entry into the market in the US in November 2017, Roche incurred product promotion and marketing costs associated with Hemlibra in 2016. Similarly, Spark has incurred costs related to 'Commercial and Medical Affairs' including market access, marketing and sales while it is still at the clinical development stage of its Hem A GT treatments.¹⁰⁶ Spark's internal

¹⁰³ *Electro Rent Corporation v CMA* [2019] CAT 4, para. 120.

¹⁰⁴ Whether from horizontal unilateral effects from the loss of actual or potential competition or from other forms of competitive harm. In the parliamentary debate at the time of proposed amendments of the Act, it was stated that '*The purpose of the test is to take out of scope of merger control a larger number of transactions that are of no economic concern to give business regulatory certainty that they will not fall within merger control. The share of supply test is a more workable test for those purposes.*' [...] '*The definition in the Bill is simpler, more flexible and the right text context. ...*' [emphasis added] (Source: [Hansard Record](#): Commons Standing Committee B, 30 April 2002).

¹⁰⁵ *Mergers: Guidance on the CMA's jurisdiction and procedure* (CMA2), January 2014, paragraphs 4.7 and 4.21.

¹⁰⁶ Parties' responses to RFI 2, question 1; see also reference in paragraph 44 above in which it is noted that Spark has already engaged with UK-based industry professionals in the haemophilia space.

documents further demonstrate a focus on marketing activities and brand recognition [redacted] and Spark has already engaged in certain types of marketing activity in the UK through UK-based employees.¹⁰⁷

85. Accordingly, the CMA considers that the available evidence indicates that, in order to properly reflect the commercial realities of the Merger, Spark should be considered, for the purpose of assessing whether the share of supply test is or may be satisfied, to be active in the supply of Hem A treatments in the UK.
86. For completeness, the CMA has also considered whether the share of supply test is or may be satisfied on the basis of procurement of Hem A patents in the UK.

The supply of novel non-GT and GT Hem A treatments in the UK

87. For the reasons set out below, the CMA considers that Roche and Spark overlap in the supply of novel non-GT and GT Hem A treatments in the UK; that this is a reasonable description of goods; and that the 25% threshold is satisfied on the basis of the number of workers employed to undertake activities related to novel non-GT and GT Hem A treatments in the UK.

The Parties supply novel non-GT and GT Hem A treatments in the UK

88. The CMA's starting point has been to consider whether both Roche and Spark supply novel non-GT and GT Hem A treatments in the UK.
89. The Parties submitted that the share of supply test is not met because Spark is not active in the supply of any goods or services – ie that it does not supply any marketed Hem A products, whether novel or otherwise – in the UK today. The Parties also submitted that Spark will not commence the supply of a marketed Hem A treatment to patients in the UK for at least another [redacted], and that section 23 of the Act does not permit the CMA to take jurisdiction based on a prospective assessment of the Merger potentially creating or enhancing a 25% share of supply for the Parties in the future.¹⁰⁸
90. Given the commercial realities of the pharmaceutical sector, the CMA considers that the supply of a given product typically encompasses several stages.¹⁰⁹ R&D undertaken in the first research and early development stages

¹⁰⁷ Spark response to section 109 notice dated 8 July 2019, [redacted].

¹⁰⁸ Jurisdiction paper submitted by the Parties on 4 November 2019 (**Jurisdiction Paper**).

¹⁰⁹ First, pharmaceutical companies conduct research and early development. Second, pharmaceutical companies conduct clinical development and obtain marketing authorisation approvals from relevant health authorities in order to commercialise the product. Third, pharmaceutical companies market and sell the treatments they have developed, including by competing to offer them at an attractive price.

is a core determinant of a pharmaceutical company's ability to subsequently market and sell a treatment. Similarly, without the prospect of marketing and selling the treatment, firms will generally not undertake the first stage of R&D. The CMA considers that R&D activities are therefore integral (along with activities such as marketing and selling) to the process of supplying pharmaceutical treatments.

91. The available evidence also shows that a firm at a relatively developed stage of R&D for a given treatment is liable to provoke competitive responses from firms with existing marketed products. Accordingly, as explained above, material competitive interactions between market players developing Hem A treatments are not limited to overlaps between directly-marketed treatments or services, but also take place between pipeline treatments, and between pipeline treatments and marketed treatments. The CMA considers that these interactions are consistent with the position that pipeline treatments form part of the broader supply process within this sector.
92. The CMA therefore considers that a firm engaged in R&D activities relating to Hem A treatments in the UK, in particular where those activities are at a relatively advanced stage, should be understood to be active in the process of supplying such pharmaceutical treatments in the UK, even in cases where that process has not yet culminated in actual sales of that treatment.¹¹⁰ Specifically, the CMA considers that treatments at the Phase II (or more advanced) stage of development to be particularly relevant in the circumstances of this case (see paragraph 96 and following).
93. In this case, Roche is, as explained above, active in the supply of novel non-GT Hem A treatments in the UK through its marketed product Hemlibra. Spark is active in the supply of GT treatments for Hem A through its ongoing clinical development of SPK-8016 and SPK-8011 (which are respectively at the Phase I and Phase II stages of clinical development).
94. With regard to the UK nexus of Spark's activities, the CMA notes that while some of Spark's current Hem A R&D activities are carried out globally:¹¹¹
 - (i) these activities form an integral part of the process of making the treatment available in the UK;¹¹² and
 - (ii) several of Spark's activities relevant to the R&D

¹¹⁰ The statutory definition of 'supply' is extremely broad and does not require sales. This approach is consistent with CMA and Office of Fair Trading (OFT) decisional practice in markets involving innovation. For instance, in *Hutchinson 3G UK/Transvisions Investments*, the CMA found the share of supply test was met on the Parties' procurement not just of currently useable spectrum, but also of prospectively useable spectrum (*Hutchinson 3G UK/Transvisions Investments*, 2017, paragraphs 19 to 25). Similarly, in *Vodafone/Telefonica*, where the OFT assessed the share of supply test by reference to the Parties' capacity to provide access (*Vodafone/Telefonica JV*, 2012, paragraphs 36 to 41).

¹¹¹ See paragraph 63(a).

¹¹² See paragraph 90.

and/or its intended commercialisation already take place in the UK. Spark has various UK/EU patents (both granted and pending) related to Hem A treatment in the UK¹¹³ and has employees undertaking activities related to the commercialisation of Hem A in the UK.¹¹⁴ In addition, Spark intends to have UK patients participating in the Phase III SPK-8011 clinical trials at UK sites.¹¹⁵ Therefore, the CMA considers that Spark is active in the supply of GT Hem A treatments in the UK.

95. The CMA therefore considers that the Parties overlap in the supply of novel non-GT and GT Hem A treatments (including commercialised products and pipeline treatments which are at Phase II (or more advanced) stage of clinical development) in the UK.¹¹⁶

Reasonable description of goods

96. The Parties submitted that, in order to devise a ‘particular description’ of Hem A-relevant goods or services in which both Parties are ‘active’, the CMA would need to capture all actual and potential non-GT Hem A treatments in the UK, as well as all potential GT Hem A treatments in the UK. The Parties further submitted that such an approach would not comprise a ‘reasonable’ description of goods within the scope of the Guidance.¹¹⁷
97. In this case, however, the CMA considers focusing on novel non-GT and GT Hem A treatments (including commercialised treatments and pipeline treatments which are Phase II (or more advanced) stage of clinical development) for the purposes of the application of the share of supply test is a reasonable approach based on the evidence available. In reaching this conclusion, the CMA carried out a two-staged assessment.
- (a) First, it considered whether it was reasonable to distinguish traditional non-GT treatments (both commercialised and pipeline) from novel non-GT treatments and GT Hem A treatments (both commercialised and pipeline).
- (b) Second, it considered whether it was reasonable to distinguish pipeline novel non-GT and GT Hem A treatments at Phase II (or more advanced) stage of clinical development from pipeline novel non-GT and GT Hem A treatments at Phase I stage (or earlier) of clinical development.

¹¹³ Spark response to RFI 2, question 6.

¹¹⁴ Spark response to RFI 7, question 3

¹¹⁵ See paragraph 63(e).

¹¹⁶ The Parties’ overlap in this respect is based on Spark’s SPK-8011 compound, which is currently at Phase II. SPK-8016 is at a less advanced stage of development at Phase I; whilst SPK-8016 is considered in the CMA’s competitive assessment of Spark’s Hem A activities, it is not included as part of Spark’s overlap with Roche for the purposes of the CMA’s application of the share of supply test.

¹¹⁷ Jurisdiction Paper dated 4 November 2019.

98. The CMA considers that the exclusion of traditional non-GT treatments from the relevant description of goods is reasonable in this case in particular because:
- (a) As further explained below from paragraph 135, the available evidence in this case indicates that the traditional FVIII non-GT treatments may, in some aspects, have significant disadvantages relative to novel non-GT treatments (such as Roche's Hemlibra) and GT treatments (such as Spark's products), in particular with regard to the mode and frequency of administration. Novel non-GT and GT treatments therefore display similar characteristics and will accordingly be expected to compete with each other more closely than as against the existing traditional FVIII non-GT treatments. Whilst the CMA's description of goods for the purposes of the share of supply test need not equate to an economic market, the fact that novel treatments compete more closely with one another than as against traditional treatments supports the position that it is reasonable to categorise all types of novel treatments within the same description of goods and services.
 - (b) Such a distinction is also consistent with the internal categorisations used by several market players. The CMA notes, in this regard, that the Parties and several third parties tend to split out traditional non-GT treatments from other treatment types when discussing the Hem A landscape.¹¹⁸
99. In addition, the CMA considers that basing the relevant description on novel non-GT and GT pipeline treatments that are at Phase II (or more advanced) stage of clinical development is a reasonable approach to take in this case in particular because:
- (a) Treatments that have reached the Phase II stage of clinical development have shown some efficacy in human patients and can be tested in larger patient populations. In Phase III, companies have generally identified a workable/effective dose and are primarily testing the efficacy of this specific dose with a larger patient population. In contrast, Phase I bears significant risk that compounds showing efficacy in cellular or animal testing will not show the same results in human testing.¹¹⁹
 - (b) Phase II treatments are considered by market players to have a realistic potential to be commercialised in the foreseeable future. As explained further in the competitive assessment, Roche's internal documents indicate that it considers [REDACTED] GT treatments [REDACTED] to be a competitive

¹¹⁸ Spark response to section 109 notice dated 8 July 2019, [REDACTED], [REDACTED].

¹¹⁹ See paragraph 29.

threat.¹²⁰ This is also consistent with the position represented in recent press articles reporting on developments in gene therapy treatments for Hem A.¹²¹

100. With regard to the overall ‘reasonableness’ of the CMA’s description of goods in this case, the Parties also submitted that any approach by the CMA to capture all marketed Hem A treatments and all potential non-GT and GT Hem A treatments for the share of supply test would depart from the CMA’s approach in *Tiancheng/Biotest* where the CMA focused on a product market for FVIII.¹²² The Parties submitted that in *Tiancheng/Biotest*, the CMA did not seek to include in its frame of reference either: (i) all marketed non-GT Hem A treatments; (ii) all actual *and* potential non-GT Hem A treatments; or (iii) all potential GT Hem A treatments.¹²³
101. As the assessment of jurisdiction is case-specific, and the relevant description of goods or services chosen for the purposes of the share of supply test need not amount to a relevant economic market, the CMA considers that the approach taken in a previous case to assessing possible substantive competition concerns has limited relevance in this context.
102. In any case, the CMA notes that there have been a number of industry developments in Hem A treatments since the *Tiancheng/Biotest* case. These include significant advances in GT treatments and the entry of Hemlibra into the UK market. Such market changes limit the relevance of *Tiancheng/Biotest* for this case (both with regard to the assessment of the share of supply test and the competitive assessment). See paragraph 132 for further discussion of this case.
103. For the reasons set out above, the CMA therefore considers that the supply of novel non-GT and GT Hem A treatments (including commercialised and pipeline treatments which are, at least, at Phase II stage of clinical development) is a reasonable description of goods. The third-party suppliers and products which fall within the relevant description and which the CMA has considered for the purposes of calculating the Parties’ share of supply are: (i) BioMarin (GT pipeline BMN-270; Phase III); (ii) Sangamo (GT pipeline: SB-525, Phase II); (iii) Sanofi (non-GT pipeline: Fitusiran, Phase III); (iv) Novo

¹²⁰ Roche internal documents received from FTC: [REDACTED].

¹²¹ See press article *BioMarin talks down worries on gene therapy data differences*, 10 September 2019, <https://www.biopharmadive.com/news/biomarin-explains-hemophilia-gene-therapy-differences-steroids-valrox/562626/>.

¹²² CMA decision in *Completed Acquisition by Tiancheng International of Biotest AG* (2018).

¹²³ Jurisdiction Paper dated 4 November 2019.

Nordisk (non-GT pipeline: concizumab, Phase III)¹²⁴; and (v) Pfizer (non-GT pipeline: PF-06741086, Phase II).

Calculation of the 25% threshold

104. The Parties submitted that, even if the CMA were to adopt a description of goods or services comprising all actual and potential non-GT and GT Hem A treatments in the UK, the Merger would not meet the 25% threshold on the basis that Hemlibra has a share of supply of c. [0-5]% based on UK patients diagnosed with Hem A in 2017/18, and the Merger will not give rise to a >[20-30]% increment.¹²⁵
105. The CMA notes that the Act gives a wide discretion to the CMA to apply whatever measure, or combination or measures, it considers appropriate to calculate the merging parties' share of supply or procurement and to determine whether the 25% threshold is satisfied. Section 23(5) of the Act provides that the CMA shall apply such criterion as it considers 'appropriate' and, in doing so, specifically cites 'number of workers employed' as an example of such an appropriate criterion.¹²⁶
106. In this case, the CMA considers that the share of supply test is or may be satisfied by the number of UK-based employees engaged in activities relating to novel non-GT and GT Hem A treatments (including commercialised treatments and pipeline treatments at Phase II (or more advanced) stage of clinical development) in the UK. The CMA has collected the relevant data on full-time equivalent employees from the Parties and from the third parties identified in paragraph 103 above. Based on this data, the CMA estimates that the Parties would have a combined share of approximately [40-50]%, with an increment of [5-10]%, as a result of the Merger.
107. The Parties submitted that, unlike measuring assets which contribute to the actual marketed activities of an entity, R&D-centred metrics (such as units of full-time equivalent employees engaged in R&D activity) would be 'preliminary in nature'; would not relate to a 'supply'/'acquisition' of 'goods' or 'services' from or to the Parties; and would not therefore comprise any reliable basis on which to determine the extent of the Parties' UK presence, so as to determine

¹²⁴ Concizumab started Phase III clinical trials in October 2019. See Novo Nordisk investor presentation, *Conference call – First nine months of 2019*, 1 November 2019, page 4, https://www.novonordisk.com/content/dam/Denmark/HQ/investors/irmaterial/investor_presentations/2019/20191101_Q3_2019_Conference%20call.pdf.

¹²⁵ Jurisdiction Paper dated 4 November 2019. The CMA's assessment of the Parties' estimated shares of supply is provided in the competitive assessment from paragraph 181.

¹²⁶ Section 23(6) of the Act.

whether the Merger does in fact have a meaningful nexus with the UK today.¹²⁷

108. However, as explained above, the CMA considers that the Parties are active in the supply of novel non-GT and GT Hem A treatments in the UK. The Parties employ staff related to the supply of novel non-GT and GT Hem A treatments in the UK. These employees are either fully or partially dedicated to activities relating to the research and early development and/or to the commercialisation of Hem A treatments (ie their activities are not solely limited to R&D).¹²⁸ Therefore, the CMA considers that the measure chosen relies on 'assets'; which contribute to the supply of goods or services in the UK and reflects the Parties' presence in the supply of novel non-GT and GT Hem A treatments in the UK (and the UK nexus of the Merger).
109. The Parties also submitted that any quantitative exercise based on counting units of employees presents a number of methodological flaws which would undermine the robustness of the test.¹²⁹ In particular, a simple quantitative counting exercise would fail to take into account the qualitative differences (in terms of, eg, value and strength) between units of full-time employees engaged in R&D.
110. The CMA considers the Parties' submission on this point to be misplaced. While any qualitative differences between units may be relevant to the competitive assessment they are not a necessary factor for the purposes of assessing whether the share of supply test is or may be met by units of goods procured or supplied by the merging parties. The CMA therefore considers that it would not be appropriate to take a different, additionally weighted approach in this case beyond having collected the relevant data on full-time equivalent employees.
111. Accordingly, the CMA believes that it is or may be the case that the share of supply test in Section 23 of the Act is met.

The procurement of Hem A patents

112. As noted above, for completeness, the CMA also considers that Roche and Spark overlap in the procurement of patents for Hem A treatments in the UK; that this is a reasonable description of goods; and that the 25% threshold is satisfied on the basis of the number of UK patents procured in relation to the

¹²⁷ Jurisdiction Paper dated 4 November 2019.

¹²⁸ Parties' response to RFI 1, question 29.

¹²⁹ Jurisdiction Paper dated 4 November 2019.

treatment of Hem A by the Parties and the third parties identified in paragraph 103 above. The basis for the CMA's reasoning is explained further below.

The Parties procure patents for novel non-GT and GT Hem A treatments in the UK

113. The CMA's starting point has been to consider whether both Roche and Spark procure patents for Hem A treatments in the UK.
114. The Parties submitted that the mere grant or holding of a patent (or the submission of a patent application) cannot qualify as an 'acquisition' of relevant 'goods' or 'services'. The Parties submitted that, in deciding whether to grant or decline patent applications, patent authorities exercise an administrative and legal function rather than engaging in a commercial activity. The Parties concluded that there is, therefore, no overlap in the 'purchase', 'acquisition', or 'procurement' of IP rights which are 'held' or 'owned' by the Parties in relation to all (actual and potential non-GT and potential GT) treatment of Hem A in the UK.¹³⁰
115. However, the CMA considers that patents qualify as goods¹³¹ and the acquisition of patents qualifies as procurement of goods. As indicated above from paragraph 57 and following, the evidence received from the Parties indicates that Roche has obtained (and still holds) 12 UK patents in relation to its Hem A activities and Spark has obtained (and holds) one UK patent granted in relation to its Hem A activities. Therefore, the CMA considers that the Parties overlap in the procurement of patents for Hem A treatments in the UK.
116. Consistent with the above approach regarding the application of the share of supply test in relation to the supply of novel non-GT and GT treatments, the CMA has focused its assessment on the procurement of patents by suppliers of novel non-GT and GT Hem A treatments (including commercialised treatments and pipeline treatments which are at the Phase II (or more advanced) stage of clinical development). The CMA considers that this is a reasonable approach based on the evidence available as the strategic value of a given patent (which is still valid) for a market player with a Hem A treatment at Phase II is likely to be materially different to that of a player at an earlier stage of R&D. This reflects the fact that a treatment at Phase II

¹³⁰ Jurisdiction Paper dated 4 November 2019.

¹³¹ The CMA considers that the definition of 'goods' under section 129 of the Act includes patents. This is supported by section 30(1) of the Patents Act 1977 stating that patents are personal property and not things in action.

development stage is considered likely to have a more realistic potential of being commercialised than at an earlier stage.

Calculation of the 25% threshold

117. The Parties submitted that the Merger will not satisfy the 25% threshold in relation to the purchase/acquisition/procurement of IP rights relevant to all (actual and potential non-GT and potential GT) treatments of Hem A in the UK.¹³²
118. In addition, the Parties noted potential counting and methodological flaws. In particular, the Parties noted various challenges related to the ‘counting’ of third parties’ self-reported patents (eg whether they include granted patents only or a mixed of granted patents alongside patent applications; whether the patents relate to the UK; whether they include ‘divisional’ applications;¹³³ whether discrepancies between different patent identifying numbers (eg when they are part of the same family) have been settled to avoid double-counting applications; and whether patents owned by one entity and licensed to another entity(ies) are included in any calculation to avoid double-counting). In addition, the Parties submitted a number of concerns arising from counting pending patent applications.¹³⁴
119. However, the CMA considers that the potential methodological flaws identified by the Parties do not, in practice, affect the CMA’s calculation of the share of supply in this case. With regard to the Parties’ share of supply, the CMA considers that this may be satisfied by number of UK patents procured in relation to activities relating to novel non-GT and GT Hem A treatments (including commercialised treatments and pipeline treatments at Phase II (or more advanced) stage of clinical development) in the UK. The CMA gathered data on the number of individual UK patents¹³⁵ procured in relation to the treatment of Hem A by the Parties and the third parties identified in paragraph 103 above.
120. As outlined above, the CMA generally does not attach different weights to units of measure (eg value or strength of the individual units) to calculate the share of supply of the merging parties and does not consider it would be appropriate in this case to consider claimed qualitative differences between patent units. On the basis of this data, the Parties would have a share of

¹³² Jurisdiction Paper dated 4 November 2019.

¹³³ ie patent applications which share the same filing date and claim subject matter as their ‘parent’ application, and which relate to broadly the same technology.

¹³⁴ Jurisdiction Paper dated 4 November 2019.

¹³⁵ Including EU patents validated in the UK.

procurement of Hem A patents of [40-50]% in the UK, with an increment of [0-5%], as a result of the Merger.¹³⁶

Conclusion on jurisdiction

121. The CMA therefore believes that it is or may be the case that arrangements are in progress or in contemplation which, if carried into effect, will result in the creation of a relevant merger situation.
122. The initial period for consideration of the Merger under section 34ZA(3) of the Act started on 22 October 2019 and the statutory 40 working day deadline for a decision is therefore 16 December 2019.

COUNTERFACTUAL

123. The CMA assesses a merger's impact relative to the situation that would prevail absent the merger (ie the counterfactual). For anticipated mergers the CMA generally adopts the prevailing conditions of competition as the counterfactual against which to assess the impact of the merger. However, the CMA will assess the merger against an alternative counterfactual where, based on the evidence available to it, it believes that, in the absence of the merger, the prospect of these conditions continuing is not realistic, or there is a realistic prospect of a counterfactual that is more competitive than these conditions.¹³⁷
124. In the present case, the Parties have not proposed an alternative counterfactual to the prevailing conditions of competition.¹³⁸
125. The CMA has considered the broader market context of Hem A treatments. In particular, the available evidence indicates that this is a dynamic sector in which all players invest significantly in R&D to improve existing or develop new treatments. Recent developments in novel non-GT and GT products for Hem A by Spark and other players such as BioMarin and Sangamo may have a significant impact on their competitive interactions with Roche, absent the Merger.
126. In light of the available evidence, the CMA has considered the impact of the Merger relative to the prevailing conditions of competition. Given the dynamic nature of the market, the CMA considers that the prevailing conditions of competition involve an environment where both the Parties (and other market

¹³⁶ The CMA's share of supply calculation relies on the number of individual patents for Hem A activities granted to the relevant companies.

¹³⁷ [Merger Assessment Guidelines](#), from paragraph 4.3.5.

¹³⁸ [REDACTED].

players) would have continued with levels of investment and innovation commensurate with their pre-merger business plans. Specifically in relation to Spark, the CMA acknowledges that this continued investment may have been in conjunction with a strategic partner or by means of an acquisition by another third party that would not give rise to competition concerns.¹³⁹ The relevant factors and their implications for future competitive conditions (including the implications of the launch of Spark's Hem A GT product for Spark's competitive position *vis-à-vis* Roche, along with the available evidence relating to entry by other suppliers and to future product development more generally) are discussed in more detail in the competition assessment.

FRAME OF REFERENCE

127. Market definition provides a framework for assessing the competitive effects of a merger and involves an element of judgement. The boundaries of the market do not determine the outcome of the analysis of the competitive effects of the merger, as it is recognised that there can be constraints on merging parties from outside the relevant market, segmentation within the relevant market, or other ways in which some constraints are more important than others. The CMA will take these factors into account in its competitive assessment.¹⁴⁰
128. The Parties overlap in the supply and development of Hem A prophylactic treatments on a global basis.¹⁴¹

Product scope

129. The Parties submitted that the relevant product scope for the assessment of the Merger should be non-GT treatment options for Hem A in the UK (ie including Hemlibra and non-GT treatments but excluding GT treatments). The Parties argued that GT is expected to create a new segment within the existing Hem A treatment landscape, separate from that comprising non-GT treatments.¹⁴² The Parties also referred to the CMA's decision in *Tiancheng/Biotest*, in which the CMA focused on a market for FVIII and not on a broader product market comprising other non-GT Hem A treatments.¹⁴³

¹³⁹ [REDACTED].

¹⁴⁰ [Merger Assessment Guidelines](#), paragraph 5.2.2.

¹⁴¹ Since the Parties only overlap in the supply and development of prophylactic treatments for Hem A, the terms 'Hem A treatments' and 'Hem A prophylactic treatments' are used interchangeably in this decision.

¹⁴² Final Merger Notice, paragraphs 92, 97 and 114-115. The Parties did not consider it necessary to focus on any potential sub-segments (eg the severity of symptoms, the existence of FVIII inhibitors or patients' age) for the purposes of defining the relevant product scope.

¹⁴³ Final Merger Notice, paragraph 57 and paragraphs 98-100 and 111-115.

130. The CMA has considered whether consumers (in this case, patients and/or prescribers) view different Hem A treatments as close substitutes, by reason of their characteristics, their prices and their intended use. While Hem A treatments may differ with regard to a range of parameters, such as the mode of action, efficacy, type and frequency of administration and associated side effects, they are all developed with the ultimate aim of preventing or managing bleeds in Hem A patients.
131. Given that several novel non-GT and GT products are currently in development and are expected to enter the market in the foreseeable future, the CMA has taken a forward-looking approach and has not limited its assessment to currently-marketed products. The CMA notes that the relevant frame of reference will include the most significant competitive alternatives available to customers of the Parties. The CMA's approach to assessing the product frame of reference is to begin with the overlapping products of the merger parties in the narrowest plausible candidate product frame of reference and then to see if this can be widened on the basis, primarily, of demand or supply-side considerations.¹⁴⁴ The CMA has considered this by reference to: (i) GT and non-GT treatments; (ii) traditional non-GT and novel non-GT and GT treatments; and (iii) patient characteristics, as set out further below.
132. *Tiancheng/Biotest* concerned an overlap between FVIII products (in contrast to this case, which concerns an overlap between novel non-GT and GT treatments for Hem A). The CMA considers this decision to have limited relevance for the purposes of the current decision. First, in *Tiancheng/Biotest*, the Parties both supplied Factor VIII derived from human blood plasma and no concerns arose even on the narrowest plausible candidate product frame of reference (and accordingly, it was not necessary to consider competitive interactions with broader product categories in that case). Second, there have also been significant industry developments since that decision – namely, advances in GT treatments and the entry of Hemlibra into the UK market – that further limit the relevance of *Tiancheng/Biotest* to this case.
133. As set out in more detail below, the evidence indicates that the market for Hem A treatments is differentiated, with different types of treatments having a likely competitive constraint on each other.

¹⁴⁴ In accordance with *Merger Assessment Guidelines*, section 5.2.

GT vs non-GT treatments

134. The CMA considers that pipeline GT treatments are viewed by prescribers as likely future alternatives to currently marketed non-GT Hem A treatments, including novel non-GT treatments. This is corroborated by the Parties' internal documents, [REDACTED], and by feedback from third parties.¹⁴⁵ As discussed in more detail below in the competitive assessment, Roche's internal documents suggest that GT treatments already exert some competitive constraint on Hemlibra [REDACTED]. Accordingly, the CMA considers that both GT and non-GT Hem A treatments form part of the relevant product frame of reference.

Traditional non-GT treatments vs novel non-GT and GT treatments

135. On one hand, the available evidence indicates that traditional non-GT treatments may, in some aspects, be considered inferior to novel non-GT treatments and GT treatments due to factors such as their frequency and mode of administration. As such, patients that have switched away from these traditional non-GT treatments to novel non-GT or GT treatments may no longer see them as a viable alternative.

136. On the other hand, the Parties' internal documents often examine and compare different Hem A treatments, including traditional non-GT treatments such as FVIII, in addition to novel treatments, indicating that traditional non-GT treatments exert at least some competitive constraint on novel non-GT and GT products.¹⁴⁶

137. In light of the above, the CMA considers that there is significant uncertainty as to whether traditional non-GT treatments will exert a significant constraint on novel non-GT and GT treatments. For the purposes of its assessment, the CMA has expanded the product scope to include traditional non-GT treatments. The CMA takes the potential weakness of the constraint from traditional non-GT treatments into account in its competitive assessment.

Narrower frames of reference based on patient age and severity of condition

138. The CMA also considered whether the product frame of reference should be segmented by patient segment based on patient age, severity or the presence of FVIII inhibitors.

¹⁴⁵ Final Merger Notice, Annex 9-015 – [REDACTED]; Final Merger Notice, Annex 9-022 – [REDACTED]; Spark response to section 109 notice dated 8 July 2019, [REDACTED]. See also Spark response to section 109 notice dated 8 July 2019, [REDACTED]. [REDACTED].

¹⁴⁶ Final Merger Notice, Annex 9-001 - [REDACTED], pages 16, 17 and 29; [REDACTED], page 10-14; [REDACTED], page 31; [REDACTED], pages 11, 16-17, 20, 29. Spark internal documents received from FTC: [REDACTED], pages 32, 36.

139. While the vast majority of traditional Hem A treatments as well as Hemlibra are indicated for all ages, the CMA has received mixed evidence on whether it may be possible to use GT in children and it has been suggested that regulators may impose restrictions on the use of GT in patient segments including children and those with irreversible joint damage (see notes to Table 1 above).¹⁴⁷
140. Similarly, potential treatment options can differ between patients with and without FVIII inhibitors and between those with severe and mild or moderate Hem A. For example, at least initially, some novel non-GT and GT treatments are likely to be limited to severe patients.¹⁴⁸
141. While the degree of substitutability between different Hem A treatments may vary by patient group, as certain patients are limited in the treatment options available to them, the NHS tendering process does not recognise these differences. Different treatments are procured by the NHS as part of the same tendering framework for all patient groups and a supplier can only charge a single price for its product notwithstanding the fact that the product may be indicated for the use in different patient categories.
142. As competitive parameters are set uniformly across all patient categories, the CMA has accordingly considered the overall closeness of competition between the Parties for all patient categories that the Parties' treatments can be used for.

Conclusion on product scope

143. For the reasons set out above, the CMA has considered the impact of the Merger in the supply of all Hem A prophylactic treatments, including traditional and novel non-GT treatments and GT treatments.¹⁴⁹
144. Notwithstanding the above assessment, the CMA has left open the exact product frame of reference since, as set out below, the CMA considers the Merger does not give rise to a realistic prospect of an SLC. The frame of reference used does not determine the outcome of the analysis or the evidence considered in assessing the competitive effects of the Merger, and the CMA has taken all relevant competitive constraints into account within the competitive assessment.

¹⁴⁷ The CMA understands that a child's liver may not be sufficiently developed for GT to be effective. Note of call with Consultant in Paediatric Haemostasis and Thrombosis, 12 August 2019, [REDACTED].

¹⁴⁸ Spark response to section 109 notice dated 8 July 2019, [REDACTED].

¹⁴⁹ The CMA has considered any constraint from on-demand treatments within the competitive assessment.

Geographic scope

145. The Parties submitted that the R&D activities associated with the development of pipeline Hem A GT treatments take place on a global basis and therefore a UK-wide frame of reference would not be appropriate in this case. The Parties also referred to the CMA's decision in *Tiancheng/Biotest* in which the relevant geographic frame of reference was considered to be no wider than the UK.¹⁵⁰ The Parties recognised that the CMA did not have to conclude on the geographic frame of reference in *Tiancheng/Biotest* as no competition concerns arose on any plausible basis, and submitted that the same applies for the current case.
146. With regard to the supply of Hem A treatments, including those for Hem A prophylaxis, the CMA acknowledges that certain competitive parameters relevant to pipeline treatments, such as product quality and innovation, are likely to be set on a global basis. However, the CMA nevertheless considers that the relevant geographic frame of reference should be national in scope, on the basis of national regulatory schemes for authorising and reimbursing treatments, prescribing practices, pricing policies and marketing strategies used by pharmaceutical firms which differ across jurisdictions. In particular, Spark's internal documents indicate that firms undertake detailed evaluations of different countries to inform launch priorities.¹⁵¹
147. The CMA has therefore considered the impact of the Merger in the supply of Hem A prophylaxis in the UK. However, the CMA has been able to leave open the exact geographic frame of reference since, as set out below, the CMA considers the Merger does not give rise to a realistic prospect of an SLC.

Conclusion on frame of reference

148. For the reasons set out above, the CMA has considered the impact of the Merger in the supply of all Hem A prophylactic treatments in the UK, including traditional and novel non-GT and GT treatments.

COMPETITIVE ASSESSMENT

Horizontal unilateral effects

149. Horizontal unilateral effects may arise when one firm merges with a competitor that previously provided a competitive constraint, allowing the

¹⁵⁰ Final Merger Notice, paragraphs 117-119.

¹⁵¹ Spark response to section 109 notice dated 8 July 2019, [redacted].

merged firm to profitably raise prices or degrade quality on its own and without needing to coordinate with its rivals.¹⁵² Horizontal unilateral effects are more likely when the merging parties are close competitors.

150. The CMA has assessed whether it is or may be the case that the Merger may be expected to result in a loss of actual potential competition in the supply of Hem A treatments in the UK, thus, giving rise to a realistic prospect of an SLC. In particular, the CMA has focused on the likely impact of the Merger with regard to the following competitive parameters:

- (a) **Innovation:** the CMA has considered whether the merged entity could reduce investment in developing Spark's SPK-8011 and SPK-8016 GT compounds (or refocus its innovation efforts towards therapeutic areas other than Hem A which complement Roche's product portfolio or R&D efforts), ultimately leading to delayed entry of Spark's GT products into the market globally and in the UK.
- (b) **Price:** as discussed above, price plays an important role in the NHS reimbursement and procurement regimes. To be reimbursed and prescribed in the UK, new Hem A non-GT and GT treatments are expected to go through this procurement process, which may place certain limitations on their price. For instance, the price of new Hem A treatments may be compared with the average price of existing treatments, and generally only treatments which can offer a cost-neutral price may be reimbursed by the NHS.¹⁵³ The CMA considers that this may constrain the pricing of new treatments to some extent but that scope for price competition between different Hem A treatments (ie to below the level of cost neutrality) will remain. Consequently, any relative price cap that is implied by cost neutrality may not be a binding constraint on price once new competing treatments have entered the market. Hem A treatments are likely to continue to be purchased via NHS tender frameworks and pharmaceutical companies, including the Parties, will be able to adjust their prices depending on the degree of competition under these frameworks.¹⁵⁴
- (c) **Product quality and marketing expenditure:** while price may be the main competitive parameter for marketed Hem A treatments, the Parties nevertheless compete on other parameters, such as additional investments in improving product quality and investment in marketing expenditure in order to educate patients and prescribers of the benefits of

¹⁵² [Merger Assessment Guidelines](#), from paragraph 5.4.1.

¹⁵³ Note of call with NHS England Commercial Medicines Directorate, 11 September 2019.

¹⁵⁴ NHS England confirmed that Hemlibra and FVIII will be purchased as part of the same tendering framework. NHS Commissioning Board response to CMA section 109 notice dated 13 September 2019. Third parties believed that NHS England has not yet agreed a specific process for procuring GT treatments. [REDACTED].

their product. In addition, pharmaceutical companies may continue to invest in extending the treatment to patients not yet covered by their marketing authorisations as a means of improving product quality.

151. In its assessment, the CMA has also considered the distinctive characteristics of prescription-only medicines such as Hem A treatments which affect customer decision-making (ie the prescribing decisions of healthcare professionals) in practice and influence the significance of different competitive parameters. In particular:
- (a) Substitution decisions occur at the time of prescription where different treatment options are weighed against each other. The healthcare professionals typically select which treatment to prescribe,¹⁵⁵ primarily based on what is therapeutically most appropriate and effective for a particular patient.
 - (b) It is the NHS, rather than the patient or prescriber, who pays for the treatment. The prescribers' choice is therefore limited to the treatments approved and reimbursed by the NHS. In contrast to patients and prescribers, the NHS puts significant weight on the treatment's price and may choose to reimburse and procure only the most cost-effective treatments.

Framework for assessment

152. As noted above, the CMA considers that the share of supply test is or may be met on the basis of the Parties' overlap in the supply of novel non-GT and GT Hem A treatments in the UK (including commercialised products and pipeline treatments which are at least at the Phase II stage of clinical development). The CMA considers this properly reflects the commercial realities of the Merger and the intention of the Act for the share of supply test to be a key gateway to providing the CMA with the power to intervene in transactions that may raise competition concerns that could impact UK consumers. This is not an economic assessment of the type used in the CMA's substantive assessment and, in this case, has not been based on a relevant economic market.
153. For the purpose of the CMA's substantive analysis of the Merger, the CMA has applied an economic assessment of the type envisaged in its Merger Assessment Guidelines¹⁵⁶ – ie to consider the competitive interaction between

¹⁵⁵ These decisions are ultimately made by prescribers, although patients may be able to express a preference for a particular treatment.

¹⁵⁶ [Merger Assessment Guidelines](#)

the Parties within the framework of actual potential competition (on the basis that Spark's products are not currently marketed to patients in the UK).

154. Consistent with these guidelines,¹⁵⁷ in assessing a loss of actual potential competition, the CMA considered:
- (a) Whether Spark would be likely to enter and expand in the absence of the Merger; and
 - (b) Whether such entry would lead to greater competition (ie whether the loss of constraint posed by Spark would lead to a realistic prospect of an SLC), taking into account other potential entrants as part of its assessment.
155. The CMA has therefore considered whether the loss of Spark as an entrant would lead to horizontal unilateral effects.
156. The CMA has assessed the likelihood of Spark expanding its current activities to commercialising its product in this context by reference to evidence gathered on Spark's ability and incentive to obtain marketing authorisation, thereby enabling its GT product to be included in an NHS framework and prescribed by clinicians.
157. The CMA has also assessed whether such entry and expansion by Spark would lead to greater competition (ie whether the loss of constraint posed by Spark would lead to a realistic prospect of an SLC), in the supply of Hem A treatments in the UK by reference to evidence on:
- (a) the competitive strength of Roche's Hemlibra;
 - (b) the strength of the constraint posed on Roche by Spark, relative to the constraint posed by other GT treatments; and
 - (c) the strength of the constraint posed on Roche by non-GT treatments (including both novel non-GT treatments and traditional FVIII treatments) in addition to other GT treatments.
158. As part of its assessment, the CMA has considered a range of sources of evidence. Given the importance of R&D and innovation in this market, the unfolding nature of the competitive conditions created by such R&D developments, and the expected launch of novel treatments, the CMA has placed more weight on up-to-date forward-looking evidence than on evidence reflecting the Parties' and third parties' historical performance. As a result, when considering [X], the CMA has taken into account, where relevant to the issue under consideration, the fact that certain internal documents contain

¹⁵⁷ [Merger Assessment Guidelines](#), paragraphs 5.4.13 to 5.4.15.

information based on [REDACTED]. When considering third-party views, the CMA has also taken into account, where appropriate, their unfamiliarity with [REDACTED]. Accordingly, the CMA has focused on [REDACTED] and more reliable future projections provided by the Parties, third parties and relevant regulatory authorities.

Likelihood of Spark's entry

The Parties' submissions

159. The Parties submitted that [REDACTED].¹⁵⁸ The Parties have not, however, proposed that Spark would not commercialise its product in the UK at all absent the Merger [REDACTED].¹⁵⁹
160. Specifically, the Parties suggested that the earliest Spark could bring its Hem A GT treatment to market in the US is [REDACTED], with expected entry into the UK about [REDACTED] later,¹⁶⁰ [REDACTED].¹⁶¹ The Parties emphasised particular concerns [REDACTED]¹⁶² [REDACTED].¹⁶³ [REDACTED].¹⁶⁴
161. The Parties also submitted that [REDACTED] the pool of eligible Hem A patients is small and other GT manufacturers are competing for the same trial patients, [REDACTED].¹⁶⁵
162. In addition, the Parties stated that [REDACTED].¹⁶⁶ Further, the Parties submitted that [REDACTED].¹⁶⁷
163. The Parties also submitted analyses purporting to show that the merged entity will neither have an incentive to delay Spark's entry into the market nor to raise either Hemlibra's or Spark's GT product's prices post-Merger.¹⁶⁸ The analyses attempt to project how the market may develop in future by considering several different parameters, such as the Parties' shares of supply, the expected uptake of GT treatments and substitution patterns between different treatment types. The analyses then consider several different scenarios which purport to support the Parties' position on the merged entity's incentives post-Merger. The CMA has addressed the Parties' submission on these points at paragraph 177.

¹⁵⁸ [REDACTED].

¹⁵⁹ [REDACTED].

¹⁶⁰ Final Merger Notice, paragraph 110. Several third parties also gave feedback that it can take about two years following FDA approval to obtain the necessary regulatory approvals for a launch in the UK. [REDACTED].

¹⁶¹ Final Merger Notice, paragraph 14(b).

¹⁶² [REDACTED].

¹⁶³ Final Merger Notice, paragraphs 27 and 142.

¹⁶⁴ Final Merger Notice, paragraph 136 and 141. [REDACTED].

¹⁶⁵ The Parties submitted that [REDACTED].

¹⁶⁶ The Parties submitted that, [REDACTED].

¹⁶⁷ [REDACTED].

¹⁶⁸ Final Merger Notice, Annex 001(f) - [REDACTED] and annexes to Roche response of CMA RFI 3, question 17.

164. In addition to assessing the Parties' submissions on [REDACTED], the CMA has considered evidence from the Parties' internal documents and from third parties when assessing the likelihood of Spark's entry.

Steps towards entry

165. Spark has already taken clear concrete steps towards commercialisation of its Hem A GT products in the UK. Spark's compounds are already at the clinical development stage of supply (with Spark's SPK-8011 compound being at a more advanced stage of development at Phase II). As set out paragraphs [79] and following, and further below in this section, Spark has already invested significant resources not only in developing its products, but also through pre-emptive marketing ahead of commercialisation. This includes efforts to target UK customers, in particular through the outreach efforts of UK-based staff.¹⁶⁹

The Parties' internal documents

166. Spark's internal documents also broadly demonstrate a clear intention to commercialise [REDACTED]. Spark's internal documents reveal a strong focus on marketing strategies aimed at [REDACTED] against competing Hem A treatments [REDACTED].¹⁷⁰ They also indicate that Spark has undertaken [REDACTED] market research, whether internally or obtained by a third party, of the potential markets in which it is considering commercialising a Hem A GT product.¹⁷¹ Several of Spark's internal documents from early 2019 focus on access to the UK market [REDACTED].¹⁷²

167. Roche's internal documents also indicate a strong degree of confidence that Spark will commercialise a Hem A GT product, including in the UK. Roche's confidence in Spark's ability to commercialise its GT product is further evidenced by its internal documents assessing the expected timeline of, and threat posed by, the launch of Hem A products being developed, including SPK-8011 (see also paragraph 210).¹⁷³

Third party evidence

168. Third parties also generally considered Spark to be a key player in the field of Hem A GT treatments and indicated that they considered Spark was likely to commercialise its GT product (whilst noting the speculative nature of such

¹⁶⁹ As set out above in paragraph 44.

¹⁷⁰ Spark response to section 109 notice dated 8 July 2019, [REDACTED].

¹⁷¹ See for example Spark response to section 109 notice dated 8 July 2019, [REDACTED].

¹⁷² See for example Spark response to section 109 notice dated 8 July 2019, [REDACTED].

¹⁷³ Final Merger Notice, [REDACTED].

comments given the limited clinical trial data available).¹⁷⁴ Further, despite uncertainty around the timing of commercialisation and NHS pricing and reimbursement policies, most third parties considered that GT treatments in general will be made available to Hem A patients in the UK.¹⁷⁵ Third party evidence discussed in the following sections also demonstrate a general confidence that Spark will obtain marketing authorisation.

[REDACTED]

169. The CMA notes that [REDACTED].¹⁷⁶ The CMA also notes, however, that [REDACTED].¹⁷⁷

170. The CMA further notes that [REDACTED].¹⁷⁸

171. This is consistent with feedback on Spark's clinical trials from the EMA. [REDACTED].¹⁷⁹

172. Finally, as explained in paragraphs 21 and 22, the CMA considers Roche's valuation of Spark's Hem A GT asset at \$[REDACTED] evidences the confidence that Roche places in the future commercial success of the Spark Hem A business. The CMA acknowledges that this valuation was based on [REDACTED]. The CMA therefore considers that Roche [REDACTED] a degree of confidence that Spark will obtain marketing authorisation globally (including the UK), [REDACTED].

[REDACTED]

173. [REDACTED], the CMA notes that Spark has previously been able to rely on third parties to bring its products to market through manufacturing or licensing agreements, for example in relation to its marketed GT product, Luxturna, and for its pipeline GT product for Haemophilia B.¹⁸⁰ [REDACTED].¹⁸¹ Further, evidence received from third parties [REDACTED]. One third party considered Spark's

¹⁷⁴ [REDACTED].

¹⁷⁵ [REDACTED].

¹⁷⁶ Final Merger Notice, paragraph 102(b).

¹⁷⁷ Note of call with Dr Katherine High, 3 September 2019; Spark response to RFI 1, [REDACTED].

¹⁷⁸ See articles *BioMarin Announces Plans to Progress Both the 6e13vg/kg and 4e13 vg/kg Doses of BMN 270, its Investigational Gene Therapy for Hemophilia A, into Phase 3 Studies*, dated 2 August 2017, <https://investors.biopharm.com/2017-08-02-BioMarin-Announces-Plans-to-Progress-Both-the-6e13vg/kg-and-4e13-vg/kg-Doses-of-BMN-270-its-Investigational-Gene-Therapy-for-Hemophilia-A-into-Phase-3-Studies> and *Sangamo and Pfizer Announce Updated Phase 1/2 Results for SB-525 Investigational Hemophilia A Gene Therapy Showing Sustained Increased Factor VIII Levels*, dated 5 July 2019, <https://investor.sangamo.com/news-releases/news-release-details/sangamo-and-pfizer-announce-updated-phase-12-results-sb-525>. [REDACTED].

¹⁷⁹ [REDACTED].

¹⁸⁰ Spark contracts with a third party for filling and packaging Luxturna. Another third party, Novartis, commercialises Luxturna outside the US under a licence agreement with Spark. Spark has also partnered with Pfizer in the development and ultimate commercialisation of its GT product for Haemophilia B. Final Merger Notice, paragraphs 26, 53 and 55.

¹⁸¹ Final Merger Notice, paragraph 34 and Roche Annex 9-004-[REDACTED].

manufacturing capabilities (notwithstanding the fact that it does not have its own facilities) to be a valuable asset.¹⁸²

174. With regard to the [REDACTED].¹⁸³ However, the available evidence does not suggest that [REDACTED] would necessarily prevent Spark from commercialising its Hem A products in the UK.
175. [REDACTED].¹⁸⁴ While the Merger would provide Spark with the funds necessary to continue developing its GT treatments, it may also have been possible for Spark to achieve this through a sale to an alternative purchaser or as part of a collaboration with other suppliers – [REDACTED].¹⁸⁵ [REDACTED].
176. On the basis of the evidence set out above, taken in the round, the CMA considers that [REDACTED] will not prevent Spark from [REDACTED].

Analyses on merged entity's incentives

177. The CMA has assessed but not given weight to the Parties' analyses on whether the merged entity would have incentives to delay Spark's entry or to raise prices post-Merger, referred to at paragraph 163 above.¹⁸⁶
- (a) The analyses are based on a number of assumptions which are inconsistent with the Parties' statements and the evidence collected from third party sources (eg the analyses assume [REDACTED]).
- (b) The CMA also found that the analyses attempt to project how the market may develop in future by considering several different parameters, such as the Parties' shares of supply, the expected uptake of GT treatments and substitution patterns between different treatment types. Several different scenarios are then discussed which, according to the Parties, demonstrate that the merged entity will neither have an incentive to delay Spark's entry into the market nor to raise either Hemlibra's or Spark's GT product's prices post-Merger. While these outcomes may hold under specific scenarios, such as those outlined by the Parties, it nevertheless remains possible that there may be circumstances (eg where Hemlibra has gained a high share of supply and the uptake of first to market GT treatments has been less rapid) under which the merged entity could find it profitable to delay Spark's entry or raise the prices of Hemlibra or Spark's GT products.¹⁸⁷

¹⁸² [REDACTED].

¹⁸³ For example, see Spark response to section 109 notice dated 8 July 2019, [REDACTED].

¹⁸⁴ [REDACTED].

¹⁸⁵ [REDACTED].

¹⁸⁶ Final Merger Notice, Annex 001(f) - [REDACTED] and annexes to Roche response of CMA RFI 3, question 17.

¹⁸⁷ This has also been recognised by the Parties themselves, eg [REDACTED], see Final Merger Notice, Annex 001(f) - [REDACTED].

Conclusion on likelihood of Spark's entry

178. Based on a consideration of evidence in the round, the CMA believes that absent the Merger, there is a realistic prospect that Spark would have succeeded in progressing through its R&D phase to achieve marketing authorisation within the foreseeable future, [REDACTED] in relation to SPK-8011.

Impact of entry on competitive conditions

179. The CMA has considered whether Spark's entry into the market for Hem A treatments in the UK would likely lead to greater competition (ie whether the loss of the constraint posed by Spark would give rise to a realistic prospect of an SLC). The CMA has assessed the effect of Spark's entry on competition by reference to the following factors:

- (a) Roche's competitive strength;
- (b) The constraint posed by Spark and other GT treatments on Roche; and
- (c) The constraint from non-GT treatments (including both novel non-GT treatments and traditional FVIII treatments) on Roche.

180. Each of these factors are discussed in more detail below.

Roche's competitive strength

181. The Parties submitted that Hemlibra had only a *de minimis* share by patients diagnosed with Hem A of less than [0-5]% for the supply of products issued to treat UK patients with Hem A in 2017/2018. The Parties estimated this share would reach [0-5]% in 2018/2019.¹⁸⁸

182. The CMA considers that the Parties' estimated shares of supply do not accurately reflect the strength of Hemlibra in the UK or the fact that, taking a forward-looking view, Roche's market position is expected to grow significantly in future, given the rapid uptake of Hemlibra seen to date (both in the UK and US) and high growth expectations.

183. First, the CMA considers that Roche's estimated <[0-5]% share of supply for Hemlibra for 2017/18 may understate Roche's actual share as a result of the categorisation of UKHCDO data on which the estimates are based. The UKHCDO provides data on both on-demand and prophylactic treatments (see paragraph 46 and following for further explanation of these treatment types) received by all patients, regardless of age or whether they have mild,

¹⁸⁸ Final Merger Notice, paragraph 57(e) and Roche response to RFI 1, question 38.

moderate or severe Hem A. First, the CMA considers this to be an overly broad competitor set. The CMA has excluded on-demand treatments from the frame of reference in this case. Second, the CMA considers that data does not reflect Hemlibra's current market position. Hemlibra has only been reimbursed for use in inhibitor patients in the UK since 6 July 2018. These patients account for only 6% of all treated Hem A patients in the UK.¹⁸⁹ The reimbursement for all severe Hem A patients without FVIII inhibitors, which account for 53% of all treated Hem A patients, was only agreed on 21 August 2019 and therefore the UKHCDO data and thus Hemlibra's share of supply does not reflect treatment provided to this patient group.¹⁹⁰ Accordingly, the CMA considers that in the light of the facts in this case, a static market share analysis based on the prior year's sales data is an unreliable indicator of market strength.

184. Third party feedback from the market test the CMA has conducted as part of its investigation also suggests that the use of Hemlibra has grown rapidly since its launch in the UK, with some clinicians estimating that the majority of eligible patients with persistent FVIII inhibitors have already switched to Hemlibra since July 2018.¹⁹¹ The NHS predicts that around 30% of severe Hem A patients without inhibitors will switch to Hemlibra in the first year following its entry, reaching around 60% by year five.¹⁹² Data provided by the Parties also demonstrate that, since Hemlibra's entry into the US in November 2017, its share of treatment of all Hem A patients has grown steadily, reaching approximately [10-20]% in June 2019.¹⁹³
185. Similarly, the Parties' internal documents demonstrate that both Roche and Spark expect the uptake of Hemlibra to rise significantly in the short term.¹⁹⁴ Some of the Parties' competitors also had similarly high growth expectations for Hemlibra in the short term.¹⁹⁵

¹⁸⁹ CMA analysis using as a proxy the number of patients that had inhibitors reported in the previous year in the UKHCDO 2018 Annual Report.

¹⁹⁰ CMA analysis based on UKHCDO 2018 Annual Report.

¹⁹¹ [REDACTED].

¹⁹² Note of call with Lead Commissioner for Specialised Blood Disorders, 9 August 2019; NHS Commissioning Board response to CMA section 109 notice dated 13 September 2019, question 2.

¹⁹³ These figures are based on Hem A patients of all severities and patients receiving both prophylactic and on demand treatment. Therefore, these figures necessarily understate Roche's share of supply with regard to patients for which Hemlibra is currently licensed, ie severe Hem A patients without FVIII inhibitors or patients with persistent FVIII inhibitors. Roche response to RFI 4, question 25.

¹⁹⁴ Final Merger Notice, Annex 5-001 - [REDACTED]; Annex 9-015 - [REDACTED]. Spark response to section 109 notice dated 8 July 2019, [REDACTED].

¹⁹⁵ [REDACTED].

Conclusion on Roche's competitive strength

186. Based on the above, the CMA therefore believes that it is likely that Hemlibra will have gained a significant share of treatment of severe Hem A non-inhibitor patients in the UK by the time GT treatments (including Spark's GT treatment) come to be commercialised in the UK. This indicates that Hemlibra is a strong competitor that is likely to come to hold a strong market position within the supply of Hem A prophylactic treatments.

Constraint posed by Spark and other GT treatments on Roche

187. The Parties submitted that Spark's Hem A GT product does not exert a close or unique competitive constraint on Hemlibra, relative to those being developed by BioMarin and Sangamo.¹⁹⁶ As outlined above, the Parties positioned Spark as [REDACTED].¹⁹⁷ The Parties submitted that [REDACTED], BioMarin and Sangamo would impose a [REDACTED] constraint on Hemlibra by virtue of having access to the necessary manufacturing facilities and making strong progress with their Hem A GT product developments, which are exhibiting positive clinical profiles.¹⁹⁸
188. The Parties also stated that Roche had not taken any actions to address the potential entry of Hem A GT treatments but that it simply monitors and undertakes market research in relation to pipeline developments across non-GT and GT Hem A treatments as part of its ordinary business operations.¹⁹⁹
189. Unilateral effects are more likely where customers (in this case, the NHS, patients and/or prescribers) have little choice of alternative supplier. The CMA has identified BioMarin and Sangamo as being at a relatively advanced stage of developing GT treatments. Taking a forward-looking approach, the CMA has therefore considered the constraint posed by Spark on Roche (relative to that which would be posed by BioMarin and Sangamo), as well as considering the constraint that GT treatments would be expected to impose as a whole on the merged entity.
190. As explained above, [REDACTED] Spark's products [REDACTED] have [REDACTED], the available evidence does not indicate that [REDACTED]. The CMA has therefore considered the relative strength of the constraint posed by Spark having regard to:
- (a) A comparison of the respective clinical profiles of Spark, BioMarin and Sangamo;

¹⁹⁶ Final Merger Notice, paragraph 131.

¹⁹⁷ The Parties' arguments and CMA assessment in this respect were considered from paragraph 159.

¹⁹⁸ Final Merger Notice, paragraphs 131, 145-152.

¹⁹⁹ Roche response to section 109 notice dated 8 July 2019, paragraph 3.2.

- (b) The target patient groups of GT treatments;
- (c) Evidence of whether being first to market is likely to influence the competitive strength of different GT treatments following their commercialisation;
- (d) The Parties' internal documents; and
- (e) Evidence from third parties.

Clinical profiles

191. To assess whether Spark's product is likely to display any material clinical advantages relative to those of Roche, BioMarin and Sangamo, the CMA has considered evidence on the clinical profiles of these GT products by reference to the clinical parameters outlined above at paragraph 65, namely: (i) efficacy; (ii) variability/predictability; (iii) durability; (iv) safety; and (v) immunogenicity.²⁰⁰ In doing so, the CMA has considered the most recent clinical trial results and future projections provided by the Parties, third parties and relevant regulatory authorities (whilst noting the inherent assumptions and uncertainties that such forward-looking evidence may entail).
192. Broadly speaking, the evidence does not appear to suggest that Spark's GT products will [REDACTED] relative to those of BioMarin and Sangamo. More specifically:
- (a) With regard to treatment efficacy, the CMA understands the latest clinical trial results available indicate that Spark, BioMarin and Sangamo's GT products are [REDACTED]²⁰¹ and that FVIII expression levels may, therefore, be a more important differentiator. Although the CMA received mixed feedback on what FVIII levels could be considered optimal for Hem A GT

²⁰⁰ Several third parties contacted by the CMA in its market investigation confirmed these parameters to be important differentiators when assessing clinical profiles. The CMA also notes that aside from Spark, BioMarin and Sangamo, a number of other players are also developing GT treatments which are currently in relatively early stages of the supply cycle, including pre-clinical stages (for example, Takeda, Bayer and UCL have AAV-based GT products in Phase 1 clinical trials, and next generation non-AAV based GT and gene editing are in preclinical stage; see Spark response to section 109 notice dated 8 July 2019, [REDACTED] and <https://www.takeda.com/what-we-do/research-and-development/our-pipeline/>; <https://clinicaltrials.gov/ct2/show/NCT03588299>; <https://academic.oup.com/hmg/article/28/R1/R95/5537029>). Given the early stage of development and the lack of sufficient evidence for the CMA to meaningfully assess their clinical profiles or likelihood of commercialisation in the UK, the CMA has therefore not examined their potential competitive strength or placed as much weight on the potential constraint from these players.

²⁰¹ Spark response to RFI 5, question 1; see press releases: *BioMarin Provides 3 Years of Clinical Data from Ongoing Phase 1/2 Study of Valoctocogene Roxaparvovec Gene Therapy for Severe Hemophilia*, dated 28 May 2019, <https://investors.biomin.com/2019-05-28-BioMarin-Provides-3-Years-of-Clinical-Data-from-Ongoing-Phase-1-2-Study-of-Valoctocogene-Roxaparvovec-Gene-Therapy-for-Severe-Hemophilia-A>; *Sangamo and Pfizer Announce Updated Phase 1/2 Results Showing Sustained Increased Factor VIII Activity Through 44 Weeks Following SB-525 Gene Therapy Treatment*, dated 7 December 2019, <https://investor.sangamo.com/news-releases/news-release-details/sangamo-and-pfizer-announce-updated-phase-12-results-showing>.

treatments, third parties concurred that higher FVIII levels (ie between 50% and 150%) could be viewed as advantageous as they would remove the need for on-demand treatment.²⁰² In this regard, Spark's products [REDACTED] relative to those being developed by BioMarin and Sangamo. [REDACTED], clinical trial results confirm that [REDACTED], whereas the majority of patients on both BioMarin's and Sangamo's products are achieving [REDACTED] therapeutic FVIII levels.²⁰³

- (b) With regard to variability, [REDACTED], the implications of this for Spark's relative constraint on Roche compared to BioMarin and Sangamo is unclear.²⁰⁴ [REDACTED].²⁰⁵
- (c) With regard to the safety of particular GT products, the CMA understands from the Parties and third parties that, to date, [REDACTED] have seen some patients develop an immune response to their products. [REDACTED] BioMarin and Sangamo have been able to effectively manage these issues using steroids, which has allowed their patients to maintain FVIII expression levels, [REDACTED].²⁰⁶
- (d) Finally, the CMA considered evidence on the differences in eligible patient populations (also known as immunogenicity profiles) of each product developed by Spark, BioMarin and Sangamo.²⁰⁷ The importance of immunogenicity for the likely competitive strength of GT products is unclear; while some third parties indicated that GT products with a higher pool of eligible patients may be more likely to be reimbursed, internal evidence suggests that the importance of having a lower immunogenicity profile remains uncertain.²⁰⁸ In any event, the evidence does not suggest that Spark [REDACTED]. The CMA received evidence indicating [REDACTED] in terms of the

²⁰² Spark's document: [REDACTED], Note of call with Consultant in Paediatric Haemostasis and Thrombosis, 12 August 2019; Note of call with Consultant Haematologist, 16 August 2019.

²⁰³ CMA analysis based on third party responses. BioMarin, Sangamo and Pfizer response to CMA questionnaire dated 27 September 2019, question 1.

²⁰⁴ Spark response to RFI 5, question 1; [REDACTED].

²⁰⁵ While the CMA observed some concerns over the durability of BioMarin's GT product, BioMarin confirmed that, based on its projections, its GT product is expected to maintain expression levels for at least [REDACTED] years, which they considered to be likely to be considered sufficient for first generation GT treatments. Spark response to RFI 5, question 1; BioMarin response to CMA questionnaire dated 27 September 2019, question 1; [REDACTED].

²⁰⁶ [REDACTED]; Note of call with Sangamo, 21 August 2019.

²⁰⁷ Ie the specific AAV vector used to manufacture a first-generation GT product is directly related to the proportion of patients that can be treated with that particular GT product. The Parties and third parties tend to differentiate between (i) the patents with pre-existing antibodies to a particular GT product (discussed in this paragraph) and (ii) patients which have developed antibodies following a GT treatment. The CMA understands that each GT product may have slightly different eligible patient populations which are influenced by the number of patients with pre-existing antibodies (ie those in category (i)). However, once a patient has received a first-generation GT treatment, s/he will develop antibodies to that treatment and will not be able to repeat GT treatment by either the same or a different GT manufacturer.

²⁰⁸ See eg Spark's documents: [REDACTED]. [REDACTED].

percentages of its patients that had developed antibodies to their GT products.²⁰⁹ [REDACTED], it appears that Spark is [REDACTED].

193. Based on the available evidence, the CMA therefore did not find that any one GT product was likely to be a materially stronger competitive constraint on Roche than another in light of its clinical profile. Some of the available evidence indicates that BioMarin's GT product may [REDACTED] relative to those of Spark and Sangamo [REDACTED]. However, the CMA has placed limited weight on this evidence given the potential for this profile to change as clinical trials progress.²¹⁰ This assessment is consistent with third parties who generally indicated that it was too early to provide a view on which product may display the greatest clinical advantage.
194. The CMA also considered whether GT manufacturers, in particular Spark, may be able to improve their first-generation GT products to develop GT products that would expand their eligible patient population (eg to include inhibitor or children) or enable re-dosing, thereby conferring a competitive advantage relative to other GT products. However, the CMA did not receive any conclusive evidence to suggest that – even in a hypothetical scenario in which GT product eligibility were extended to children, patients with inhibitors, and/or re-dosing was possible – Spark would be the only GT manufacturer to achieve these product improvements. More specifically:
- (a) Although Spark's internal documents and Roche's valuation of Spark indicate that [REDACTED],²¹¹ Spark acknowledges that [REDACTED].²¹²
 - (b) While some of Spark's internal documents suggest that Spark has some confidence that re-dosing will be possible,²¹³ third parties were generally of the view that it was highly unlikely that patients could repeatedly take first generation GT products (either by the same or different GT manufacturers).²¹⁴ In addition, Spark's GT competitors are also interested in achieving similar future product developments and BioMarin is currently

²⁰⁹ Spark estimated that around [REDACTED]. BioMarin estimated that around 31% of the global Hem A population has antibodies to BioMarin's GT product and Sangamo submitted that [40-50]% out of the first [REDACTED] patients screened had antibodies to its GT product. BioMarin and Sangamo response to CMA questionnaire dated 27 September 2019, question 1.

²¹⁰ For example, one third party explained that with every data release the industry can see one GT program leap-frogging another and it is difficult to say which product is the leader. Note of call with BioMarin, 22 August 2019.

²¹¹ Re-dosing is sometimes referred to as expansion into AAV+ patient population, ie patients with pre-existing antibodies to the AAV based GT treatments currently in development.

²¹² Spark response to RFI 1, question 19.

²¹³ Spark response to section 109 notice dated 8 July 2019, [REDACTED].

²¹⁴ For instance, one competitor estimated [REDACTED]. See Spark response to RFI 5, question 2; [REDACTED].

exploring re-dosing, although the likely success of it or the possibility of re-dosing, in general, is as yet unclear.²¹⁵

Target patient groups

195. The CMA notes that the overlap between Roche's Hemlibra's target population and GT products in general is limited in scope. Roche's Hemlibra is currently indicated for the treatment of Hem A patients with persistent FVIII inhibitors and all severe Hem A patients without inhibitors. By contrast, all first-generation GT treatments will, at least initially, only be indicated for the treatment of severe adult Hem A patients without FVIII inhibitors. The extent of the overlap between Roche's Hemlibra on the one hand and the GT products of Spark, BioMarin and Sangamo on the other is therefore likely to be limited to this patient group only – a group that represents at most 37% of all treated Hem A patients in the UK.²¹⁶ The CMA estimates that only about [X%] of Hemlibra's eligible patient population is likely to be eligible for Spark's GT product, leaving [X%] who could not be recaptured by GT products following a potential increase in the price of Hemlibra.²¹⁷
196. Moreover, the CMA considers that the potential for switching between Hemlibra and GT products would be further reduced by the fact that not all Hemlibra patients that are eligible for GT treatments would switch to them. In practice, lower levels of diversion might be expected because of patient resistance to switching and the anticipated availability of alternative novel non-GT treatments (which, as described further below, are likely to be closer alternatives to Hemlibra than GT treatments).

First mover advantage

197. To further assess the relative strengths of Spark in comparison to BioMarin and Sangamo, the CMA has also considered whether a competitive advantage would be gained by the first GT product to be commercialised in the UK and, more generally, the extent to which this would influence its competitive strength. The CMA has also considered the potential impact of an

²¹⁵ BioMarin response to CMA questionnaire dated 27 September 2019, question 2, 4; Note of call with Pfizer, 22 August 2019.

²¹⁶ CMA's calculations based on UKHCDO 2018 Annual Report. The 37% includes all severe adult Hem A patients and may also include some patients with FVIII inhibitors, thus overestimating the true size of this patient group relative to all treated Hem A patients.

²¹⁷ CMA's calculations based on UKHCDO 2018 Annual Report. The proportion of Roche's patients who may be eligible for Spark's GT product is based on the number of severe adult Hem A patients adjusted for the [X%]. The [X%] figure may therefore slightly overestimate the proportion of Roche's patients eligible for Spark's GT as the UKHCDO report does not allow for the splitting of patients by both age and presence of inhibitors. The [X%] figure includes severe children and adolescent patients, mild and moderate patients with FVIII inhibitors and patients with pre-existing antibodies to Spark's GT product, which are eligible for Hemlibra, but not for Spark's GT. Spark estimates that around [X%] UK Hem A patients would be eligible for its GT products ([X%]). Spark response to RFI 1, question 19.

orphan drug designation on a GT product's competitive strength. The impact of each of these factors on competitive assessment is described below.

- *First to commercialisation*

198. The Parties submitted that [X] gain a significant first mover advantage by having the first and only GT product in the market. They further submitted that [X].
199. In addition, the Parties also submitted that Roche does not have an incentive to delay the launch of Spark's Hem A GT treatment in light of the expected rapid earlier uptake by eligible patients of rival GT treatments or novel non-GT treatments and the current inability to re-dose patients.²¹⁸
200. The CMA acknowledges that the available evidence indicates that BioMarin is currently likely to be the first to commercialise its Hem A GT treatments (both globally and in the UK), having publicly announced its plans to submit applications to both the FDA and the EMA to obtain marketing authorisations in late 2019.²¹⁹ BioMarin has also confirmed that it expects to enter the UK market in [X].²²⁰
201. The CMA further notes that Sangamo is likely to commercialise its product after BioMarin [X]. This is on the basis that Phase III clinical trials for Sangamo's GT product are expected to start in 2020, [X] the timing for Spark's product is [X].²²¹
202. However, the evidence as to the potential benefits of being the first GT product to commercialisation is mixed. On one hand, absent the possibility to re-dose first generation GT treatments (which, as discussed above, is currently unlikely (but may be more likely for next generation GT products), being first to market may represent significant advantages for manufacturers. This will likely be the case in particular if the rate of uptake of that particular GT product is expected to be rapid (for example, due to a favourable clinical product profile as perceived by prescribers) and the development of other GT products are significantly further behind.

²¹⁸ Final Merger Notice, paragraph 14.

²¹⁹ See press release *BioMarin Plans Regulatory Submissions for Marketing Authorization of Valoctocogene Roxaparovec to Treat Severe Hemophilia A in 4Q 2019 in both U.S. and Europe*, dated 8 July 2019, <https://investors.biomin.com/2019-07-08-BioMarin-Plans-Regulatory-Submissions-for-Marketing-Authorization-of-Valoctocogene-Roxaparovec-to-Treat-Severe-Hemophilia-A-in-4Q-2019-in-both-U-S-and-Europe>.

²²⁰ Entry in the US expected in 2020. BioMarin response to CMA questionnaire dated 27 September 2019, question 1.

²²¹ Spark response to RFI 1, question 2; Sangamo response to CMA questionnaire dated 27 September 2019 question 1.

203. The Parties estimated that approximately [REDACTED]% of Hem A patients were likely to be ‘early adopters’ switching to the first available GT treatment within the first year of commercialisation, and that the proportion of patients switching to GT was expected to grow to [REDACTED]% of the eligible patient population over the first five years following commercialisation.²²² Third parties were unable to provide a clear picture on the expected uptake of GT, with very few attempting to estimate a figure. However, the majority of third parties expected the GT uptake to be slow over the first five years following GT entry.²²³ This suggests that even if Spark launches a GT product after BioMarin and Sangamo, a material proportion of the GT eligible patient population would remain for which Spark could pose a constraint.
204. On the other hand, the effects of being first to commercialisation appear likely to be closely related to the clinical profiles of different GT products. Given that first generation GT treatments will only be administered once, it is possible that patients and prescribers may seek more data on the clinical profile of a particular treatment and may choose to wait for the treatment with the most advantageous clinical profile.²²⁴ This would reduce any first mover advantage. However, to the extent a material proportion of patients may prefer not to wait for a product with the most beneficial clinical profile, the CMA believes there remains some potential for a first mover advantage.
205. Third parties generally provided a positive view on the importance of being the first player to bring a Hem A GT product to market. Some third parties indicated that, given the shrinking patient population resulting from the inability to re-dose first generation GT treatments, being the first to market was vital and that accordingly there is significant competition between the pipeline Hem A GT products.²²⁵ In addition, some noted that having the first treatment in the market would by definition confer an advantage on its manufacturer due to a larger pool of data on treatment durability and safety, an important factor for prescribers. It was also suggested that first movers may also benefit from a price-setting advantage and negotiations with payers.²²⁶
206. Overall, the CMA believes that the precise extent of the competitive advantages afforded by being first to commercialisation are unclear. The CMA

²²² Teach-in with the Parties, 24 July 2019. Spark response to section 109 notice dated 8 July 2019, [REDACTED]; [REDACTED].

²²³ For instance, one third party estimated that by 2024 all GTs will account for 14.2% of revenue received from sales to all Hem A patients (including both on-demand and prophylaxis treatments); another estimated that 6% of patients globally (and 8% in the UK) will be using GT treatments within the next five years; another estimated that GTs will account for less than 5% of non-inhibitor patients, while one third party did not provide an estimate but considered that the share of GT in the next five years will be very low and that the share within the next five to ten years will be dependent on pricing and reimbursement models. [REDACTED].

²²⁴ Based on third party feedback [REDACTED].

²²⁵ [REDACTED].

²²⁶ Note of call with Pfizer, 22 August 2019; [REDACTED].

nevertheless considers that the GT product that is first to market is likely to gain at least some advantage (in particular from the absence of redosing possibilities for first generation GT treatments and having longer clinical data). The CMA therefore considers it likely that BioMarin will gain some advantage in this regard, albeit the extent of this advantage will depend on future factors such as the final clinical profiles of the GT products of Spark and Sangamo.

- *Orphan drug designation*

207. As explained previously at paragraph 39, orphan designation prevents the authorities from granting a marketing authorisation or extension of existing marketing authorisations for the same therapeutic indication for any medicinal product considered similar to the one with an orphan designation (although there is scope in limited circumstances for similar medicinal products to obtain marketing authorisation regardless). The assessment of similarity between medicinal products is only undertaken by the relevant authority upon application for a marketing authorisation.
208. Spark, BioMarin and Sangamo have each been granted an orphan drug designation for their Hem A GT products in the US and the EU. However, the exclusivity period does not commence until they obtain a marketing authorisation. The Parties submitted that [REDACTED].²²⁷ With regard to this concern, the EMA confirmed to the CMA that it was currently too early to determine whether BioMarin, Sangamo and Spark's GT products would be considered 'similar' for orphan exclusivity purposes.²²⁸
209. While the CMA acknowledges that it is possible that the first commercialised GT product may benefit from a ten-year period of exclusivity following entry, it has not placed significant weight on this likelihood, given the lack of clarity over how the relevant authorities will assess the similarity of the various first generation Hem A GT products.

Internal documents

210. Roche's internal documents indicate that it views the collective entry of first generation Hem A GT treatments as a [REDACTED] threat to Hemlibra's competitive position. However, [REDACTED], Roche's internal documents refer to the collective constraint of GT products and [REDACTED].²²⁹ For example, [REDACTED].²³⁰

²²⁷ Spark response to RFI 1, question 2; RFI 2, question 8 and RFI 3, question 10.

²²⁸ EMA response to CMA questionnaire dated 1 October 2019, question 11.

²²⁹ Roche internal documents received from FTC: [REDACTED]. See also the discussion of Roche's internal documents in the section on 'Constraint posed by Spark and other GT treatments on Roche'.

²³⁰ Roche internal documents received from FTC: [REDACTED].

211. Spark's internal documents suggest that it views Roche as a key competitor.²³¹ [REDACTED]²³² [REDACTED].²³³
212. Spark's internal documents also suggest that with regard to other GT treatments, Spark considers that – [REDACTED],²³⁴ [REDACTED] – BioMarin's GT product will represent [REDACTED] competitive threat to Spark. [REDACTED].²³⁵ Spark's internal documents further suggested that it perceived Sangamo [REDACTED] to also be a constraint. However, the CMA notes that Spark's assessment of Sangamo [REDACTED] and has therefore placed limited weight on its evidentiary value.²³⁶

Third party evidence

213. Third party responses suggested that it was too early to judge whether Spark's product was likely to become the most competitive Hem A GT product relative to other GT products from BioMarin and Sangamo.²³⁷ Third parties generally indicated, however, that in comparison to other non-GT treatments, Roche's Hemlibra is likely to present the most significant constraint on GT treatments (including Spark's).

Conclusion on constraint posed by Spark and other GT treatments

214. The CMA considers that in the round, the evidence indicates that Spark's, BioMarin's and Sangamo's GT products will, collectively, be an important competitive constraint on Roche but that the constraint posed by Spark is unlikely to exceed that posed by BioMarin and Sangamo. In particular:
- (a) While the CMA has placed little weight on [REDACTED]: (i) there are tentative indications that BioMarin's product [REDACTED]; (ii) Sangamo's product is likely to be commercialised [REDACTED]; and (iii) BioMarin's product in particular is likely [REDACTED] to gain at least some first-mover advantage [REDACTED];
 - (b) While collectively, GT treatments will be an important competitive constraint on Roche (a point reflected in the Parties' internal documents and third party feedback), this constraint will be limited to a minority

²³¹ Spark response to section 109 notice dated 8 July 2019, [REDACTED].

²³² Spark response to section 109 notice dated 8 July 2019, [REDACTED].

²³³ Spark response to section 109 notice dated 8 July 2019, [REDACTED].

²³⁴ See press releases which indicate BioMarin's product has positive indications for success: *BioMarin Provides 3 Years of Clinical Data from Ongoing Phase 1/2 Study of Valoctocogene Roxaparvovec Gene Therapy for Severe Hemophilia*, dated 28 May 2019, <https://investors.biomarin.com/2019-05-28-BioMarin-Provides-3-Years-of-Clinical-Data-from-Ongoing-Phase-1-2-Study-of-Valoctocogene-Roxaparvovec-Gene-Therapy-for-Severe-Hemophilia-A; BioMarin Plans Regulatory Submissions for Marketing Authorization of Valoctocogene Roxaparvovec to Treat Severe Hemophilia A in 4Q 2019 in both U.S. and Europe>, dated 8 July 2019, <https://investors.biomarin.com/2019-07-08-BioMarin-Plans-Regulatory-Submissions-for-Marketing-Authorization-of-Valoctocogene-Roxaparvovec-to-Treat-Severe-Hemophilia-A-in-4Q-2019-in-both-U-S-and-Europe>.

²³⁵ Spark response to section 109 notice dated 8 July 2019, [REDACTED].

²³⁶ Spark response to section 109 notice dated 8 July 2019, [REDACTED].

²³⁷ [REDACTED].

portion of Hemlibra's overall eligible patient population (severe adult Hem A patients without FVIII inhibitors). The narrower scale of GT products' target patient group will therefore limit at least the initial scale of customer overlap between Roche's and Spark's products, and between Roche's and GT products more generally.

Constraint from non-GT treatments on Roche

215. The CMA has also considered the competitive constraint posed by non-GT treatments on the Parties, namely novel non-GT treatments and traditional FVIII treatments. The CMA has, with regard to novel pipeline non-GT treatments, focused primarily on a small number of products that are at least at a relatively advanced Phase II stage of development and therefore have a realistic potential of being commercialised within the foreseeable future.
216. The Parties submitted that Roche's Hemlibra currently faces strong competition from several marketed Hem A treatments and will continue to face competition from pipeline non-GT treatments expected to enter the market in the coming years.²³⁸
217. As discussed in more detail below, the CMA believes that novel non-GT treatments will continue to pose a strong constraint on the merged entity post-Merger. However, the constraint from traditional non-GT treatments is likely to be weak.
218. With regard to the constraint from novel non-GT treatments, the CMA notes that while Hemlibra is the only marketed novel non-GT treatment at present, a number of similar treatments are currently in development. These include treatments by Sanofi (Fitusiran), Novo Nordisk (concizumab) and Pfizer (PF-06741086), all of which are expected to be commercialised within the next [X] years.²³⁹ Unlike traditional treatments, novel non-GT treatments offer similar or potentially greater advantages than Hemlibra over traditional FVIII treatments with regard to the frequency, mode of application and/or dosing.²⁴⁰ Hemlibra, which is administered subcutaneously once a week or as rarely as once every four weeks, differentiates itself from other marketed non-GT products such as traditional FVIII treatments (which require frequent injections

²³⁸ Final Merger Notice, paragraph 14(a).

²³⁹ Fitusiran is expected to be marketed in [X]. Concizumab is expected to be marketed in [X] for the UK. PF-06741086 is expected to be marketed in the EU in 2024. See Sanofi response to CMA questionnaire dated 27 September 2019, question 4; Novo Nordisk response to CMA questionnaire dated 27 September 2019, question 4; Pfizer response to CMA questionnaire dated 27 September 2019, question 1; [X].

²⁴⁰ For instance, Fitusiran and concizumab will both be administered subcutaneously and either less frequently or using a [X] and [X] method of administration. Sanofi response CMA questionnaire dated 27 September 2019, question 4; Novo Nordisk response to CMA questionnaire dated 27 September 2019, question 4. Further, the CMA understands that Roche [X]. Roche response to RFI 4, question 2.

three to four times a week) by offering a less frequent and more convenient mode of administration. Novel non-GT products in development are expected to bring improvements in dosing frequency and/or treatment administration that will make them more similar to Hemlibra (than either traditional FVIII treatments or GT products).²⁴¹ Given the similarities between novel non-GT treatments with regard to frequency and mode of administration, the CMA considers it likely that such treatments would represent patients' closest alternative to Hemlibra and will also represent a similarly close competitive constraint on Spark's GT product, albeit less so than competing GT treatments in development.

219. While traditional FVIII treatments will continue to pose a constraint to a limited extent, these are perceived as inferior to the Parties' products (primarily due to the necessity of more frequent administration). As these are well-established treatments, it is possible that some patients will be resistant to switch away from these treatments to Hemlibra and other novel treatments such as GT, at least until more clinical data becomes available.²⁴² Some third party evidence and evidence from the Parties' internal documents indicates that patients on a well-managed FVIII replacement therapy may be less inclined to switch to another treatment.²⁴³
220. A number of pharmaceutical companies are developing new enhanced half-life FVIII products which are expected to bring improvements to the frequency of treatment administration and FVIII levels achieved.²⁴⁴ However, notwithstanding these incremental improvements, it is clear that traditional FVIII treatments will represent a much more limited constraint on the merged entity relative to both novel GT and non-GT products.
221. While both Parties monitor non-GT treatments and recognise that they will continue to exert a competitive constraint, the Parties' internal documents also indicate that these are - in particular, [REDACTED] - currently viewed as a [REDACTED] threat to both Roche and Spark than GT treatments.²⁴⁵

²⁴¹ Spark's GT product is, like other GT products, intended to be dosed once in a patient's lifetime. In this respect, GT products are also likely to compete more closely with Hemlibra than as against other FVIII treatments (although to a lesser degree than novel non-GT products).

²⁴² Hemlibra also has clear clinical advantages over BPAs in reducing bleed rates, which has been reflected in Hemlibra's quick growth in this segment. Although it remains unclear whether Hemlibra has any clinical advantages in severe Hem A patients without persistent FVIII inhibitors, it is nevertheless expected that Hemlibra will achieve a high uptake in this patient segment. Note of call with Consultant Haematologist, 16 August 2019.

²⁴³ [REDACTED]. Spark response to section 109 notice dated 8 July 2019, [REDACTED].

²⁴⁴ Sanofi and Sobi have partnered in the development of BIVV001 (requiring weekly IV administration) which is expected to launch in [REDACTED], Octapharma's treatment is expected to launch in the US in [REDACTED] and the UK in [REDACTED]. Sanofi and Octapharma responses to CMA questionnaire dated 27 September 2019, question 4.

²⁴⁵ Eg, [REDACTED], see [REDACTED]. [REDACTED]. Spark response to section 109 notice dated 8 July 2019, [REDACTED].

222. Third party views as to the expected constraint from novel non-GT and traditional FVIII treatments were mixed.
- (a) A few competitors estimated the proportion of patients that they expected to be treated by novel non-GT treatments over the next five years.²⁴⁶ Some third parties suggested that Roche's Hemlibra was likely to benefit from a significant first mover advantage relative to other novel non-GT treatments, unless it could be shown that these alternative treatments can achieve better results than Hemlibra. At the same time, novel non-GT treatments were mentioned as some of the closest competitors to Hemlibra, aside from other half-life and traditional FVIII treatments and GT treatments.²⁴⁷
- (b) Overall, third parties indicated that they expected FVIII treatments to continue to maintain a role for Hem A patients, although some also indicated that their position was expected to be the strongest with regard to on-demand treatments and less so for Hem A prophylaxis.²⁴⁸
223. Based on the available evidence, the CMA believes that novel non-GT treatments will continue to impose a substantial competitive constraint, in particular on Hemlibra. As explained in paragraph 53, GT treatments will only be indicated for the treatment of severe adult Hem A patients without FVIII inhibitors. This means that if the merged entity were to increase the price of Hemlibra or otherwise worsen its offering, it would have to do so for all eligible patients as it is not currently possible to price discriminate between different patient groups under NHS procurement regimes. As such, the merged entity would risk that around 60% of its eligible patients would switch to other non-GT treatments.²⁴⁹

²⁴⁶ These estimates ranged from [0.5]% to [10]%; however, these were not calculated by players on an entirely consistent basis. BioMarin estimates that by 2024 patients using both Hemlibra and other novel Hem A treatments will still have a combined share of supply of [30-40]% of on-demand and prophylaxis Hem A treatments; [REDACTED] estimated that [0-5]% of patients globally (and [0-5]% in the UK) would be using other novel non-GT treatments within the next five years; Bayer estimates that novel non-GT treatments will be the second most commonly-used treatment (after traditional FVIII treatments) for non-inhibitor patients, and Octapharma submitted that the uptake of new non-GT treatments will depend on clinical advantages over Hemlibra which are yet to be proven to patients. See BioMarin, [REDACTED], Bayer and Octapharma responses to CMA questionnaire dated 27 September 2019.

²⁴⁷ [REDACTED].

²⁴⁸ BioMarin estimates that by 2024 FVIII and BPA treatments will still have a combined share of supply of [50-60]% of on-demand and prophylaxis Hem A treatments; [REDACTED] estimated that [60-70]% of patients globally (and [50-60]% in the UK) would continue to be using traditional Hem A treatments within the next five years; Bayer estimates that FVIII treatments will account for the majority of non-inhibitor patients, and Octapharma between [10-20]% to [60-70]% of prophylactic patients will continue using FVIII and BPA treatments. See BioMarin, [REDACTED], Bayer and Octapharma responses to CMA questionnaire dated 27 September 2019. [REDACTED].

²⁴⁹ ie children as well as patients with FVIII inhibitor and pre-existing antibodies which are ineligible for GT, see paragraph 194.

Conclusion on constraint from non-GT treatments

224. The CMA considers that while the constraint from novel non-GT and, in particular, traditional non-GT treatments for Hem A will be more limited than that of GT treatments, collectively non-GT treatments will nevertheless exert a significant competitive constraint on the merged entity. In particular, as a result of their similarity in terms of product characteristics, other novel non-GT treatments are likely to represent the closest alternative to Hemlibra and exert a strong competitive constraint on Roche.

Conclusion on horizontal unilateral effects

225. For the reasons set out above, the CMA believes that Spark would be likely to commercialise its products within the foreseeable future. [REDACTED]. The CMA also believes that Roche's Hemlibra is already a significant competitor and is likely to develop a strong market position by the time Spark's GT product comes to be commercialised in the UK.
226. However, the CMA has found that entry by Spark, absent the Merger, would not have led to greater competition, or that the loss of the constraint posed by Spark would lead to a realistic prospect of an SLC, in the supply of Hem A prophylactic treatments in the UK. This is on the basis that:
- (a) Although GT products will collectively be an important competitive constraint on Roche, the evidence does not suggest that Spark's GT product will have [REDACTED]. BioMarin and Sangamo will continue to constrain Roche post-Merger, [REDACTED] (with BioMarin being likely to gain at least some first mover advantage).
 - (b) The constraint posed by GT treatments will be restricted to a limited proportion (about 40%) of Hemlibra's overall eligible patient population (severe adult Hem A patients without FVIII inhibitors); and
 - (c) There are several novel non-GT products which are likely to have common characteristics with Hemlibra and thus represent the closest alternative for the c.60% of Hemlibra's patients who are ineligible for GT treatments.
227. The available evidence therefore does not suggest that Spark would be a particularly close or significant constraint on Roche (as compared to other GT treatments and novel non-GT treatments). The CMA therefore considers remaining competitors whose products have a realistic potential of being commercialised will pose a strong constraint on the merged entity post-Merger which will, as a consequence, retain incentives to invest in

commercialising Spark's GT products and compete on pricing, improvements in product quality and marketing activities post-Merger.

228. Accordingly, the CMA found that these constraints, taken together, are sufficient to ensure that the Merger does not give rise to a realistic prospect of an SLC as a result of horizontal unilateral effects in relation to the supply of Hem A prophylactic treatments in the UK.

BARRIERS TO ENTRY AND EXPANSION

229. Entry, or expansion of existing firms, can mitigate the initial effect of a merger on competition, and in some cases may mean that there is no SLC. In assessing whether entry or expansion might prevent an SLC, the CMA considers whether such entry or expansion would be timely, likely and sufficient.²⁵⁰
230. In the context of a relatively dynamic market considered such as in the present case, the CMA has taken entry and expansion into account in the competitive assessment above. In any event, the CMA has not had to conclude on barriers to entry or expansion as the Merger does not give rise to a realistic prospect of an SLC.

THIRD PARTY VIEWS

231. The CMA contacted competitors of the Parties, clinical experts in haematology, the NHS and the EMA. Several third parties considered that the market for prophylactic Hem A treatments is increasingly competitive and that there will continue to be a number of Hem A treatments available in the UK that will pose a competitive constraint on the merged entity.²⁵¹
232. A minority of third parties, including competitors, raised concerns in the event of a hypothetical scenario arising in which Spark's product would be the leading or sole GT available on the market.²⁵² However, no third parties provided any substantiated submissions as to the likelihood of such a hypothetical scenario arising.
233. Third party comments have been taken into account where appropriate in the competitive assessment above.

²⁵⁰ [Merger Assessment Guidelines](#), from paragraph 5.8.1.

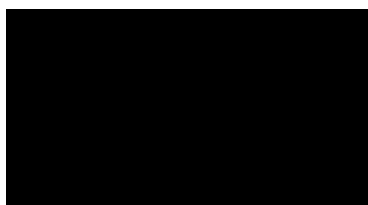
²⁵¹ [REDACTED].

²⁵² [REDACTED].

DECISION

234. Consequently, the CMA does not believe that it is or may be the case that the Merger may be expected to result in an SLC within a market or markets in the United Kingdom.

235. The Merger will therefore not be referred under section 33(1) of the Act.



Alex Olive
Director, Mergers
Competition and Markets Authority
16 December 2019

Glossary

AAV vector	Adeno-associated viral vector
BPA	Bypassing agent
CPAG	Clinical Priority Advisory Group
DMC	Data Monitoring Committee
EMA	European Medicines Agency
EPO	European Patent Office
FDA	US Food and Drug Administration
FVIII	Factor VIII
Final Merger Notice	Final merger notice submitted by the Parties on 18 October 2019
FTC	US Federal Trade Commission
GT	Gene therapy
Hem A	Congenital haemophilia A
ITI	Immune Tolerance Induction
IP	Intellectual property
Jurisdiction Paper	Paper submitted by the Parties on 4 November 2019
MHRA	Medicines and Health Regulatory Agency
NHS	National Health Service
Novel non-GT	Novel non-factor based non-GT
R&D	Research and development
Parties	Roche and Spark
SPK-8011	Spark's SPK-8011 Hem A GT compound
SPK-8016	Spark's SPK-8016 Hem A GT compound

UKHCDO

UK Haemophilia Centres Doctors'
Organisation

UKIPO

UK Intellectual Property Office

White paper

Paper on [X] of Spark's Hem A GT program
submitted to the FTC on 3 September 2019
