Autorità Garante della Concorrenza e del Mercato

(UN-OFFICIAL TRANSLATION - ONLY THE ITALIAN TEXT IS AUTHENTIC)

THE ITALIAN COMPETITION AUTHORITY

AT ITS MEETING of 21 May 2024

HAVING HEARD the Rapporteur, Professor Elisabetta Iossa;

HAVING REGARD TO Article 101 of the Treaty on the Functioning of the European Union (TFEU);

HAVING REGARD TO Regulation (EC) No 1/2003 of the Council of the European Union of 16 December 2002;

HAVING REGARD TO Law No. 287 of 10 October 1990;

HAVING REGARD TO Presidential Decree No. 217 of 30 April 1998;

HAVING REGARD TO the Commission Notice on cooperation within the Network of Competition Authorities of 27 April 2004;

HAVING REGARD TO the Memorandum of Understanding between the Italian Antitrust Authority and the Italian Medicines Agency of 19 January 2017;

HAVING REGARD TO the complaint received on 11 November 2022, subsequently supplemented on 13 January 2023, 19 May 2023, 10 August 2023, 19 and 22 January 2024;

HAVING REGARD TO the documentation on file;

WHEREAS:

I. THE PARTIES CONCERNED

1. Samsung Bioepis Co. Ltd. (hereinafter also referred to as "Samsung Bioepis") is an Incheon, South Korea-based company active in the development of biosimilar drugs, including Byooviz (also referred to as "SB11"), based on the active ingredient *ranibizumab*. The company is a joint venture established in 2012 between Samsung BioLogics Co. Ltd. (a Samsung Group company) and Biogen Inc. Following a merger in 2022 sole control of Samsung Bioepis Co. Ltd. was acquired by Samsung BioLogics Co. Ltd.[1]. In 2022, Samsung Bioepis Co. Ltd., together with Biogen Inc., entered into an agreement with Genentech Inc. concerning Byooviz (see below section 26).

2. Secondly, Samsung Bioepis NL B.V. (hereinafter also "Samsung Bioepis NL") is a company incorporated under Dutch law, based in Delft, and is a subsidiary of Samsung Bioepis Co. Ltd. Samsung Bioepis NL B.V. also holds the Marketing Authorisation (hereinafter "MA") for the drug Byooviz issued by the *European Medicines Agency* (hereinafter "EMA") and valid at European level (see below section 31).

3. Biogen Inc. (hereinafter also referred to as "Biogen") is a biopharmaceutical corporation headquartered in Cambridge, Massachusetts, USA, active worldwide in the research, development and delivery of therapies for a range of neurological and neurodegenerative diseases. Biogen also markets biosimilars in Europe. After having concluded a commercialisation agreement with Samsung Bioepis in 2019 concerning, *inter alia*, Byooviz (see below section 26), in 2022, together with Samsung Bioepis Co. Ltd., it entered into an agreement with Genentech Inc. concerning the same Byooviz (see section 46).

4. Biogen Italia S.r.l. (hereinafter also "Biogen Italia") is the Italian subsidiary of the Biogen Group, headquartered in Milan. The shareholding of Biogen Italia is divided in equal shares between Biogen International GMBH and the parent company Biogen MA Inc.

5. Genentech Inc. (hereinafter also "Genentech"), a US corporation headquartered in San Francisco, active in the development and manufacture of biotechnology drugs, including Lucentis. Genentech is part of the Roche

[1] European Commission Decision of 4 April 2022, M10657 - *Samsung Biologics/Samsung Bioepis*.

Group, being a subsidiary of Hoffmann La Roche Inc. which, in turn, belongs to Roche Holdings AG. In 2022, Genentech Inc. signed an agreement with Samsung Bioepis Co. Ltd. and Biogen Inc. concerning Byooviz (see below section 46).

6. Novartis AG (hereinafter also referred to as "Novartis") is a public limited company under Swiss law with registered office in Basel, the operational head of the Swiss group of the same name, which is active worldwide in the manufacture and marketing of pharmaceuticals. Novartis is globally responsible for the licensing and collaboration agreement signed with Genentech in 2003 for Lucentis. Novartis is a public company listed on the Zurich and New York stock exchanges.

7. Novartis Europharm Ltd. (hereinafter also referred to as "Novartis Europharm"), headquartered in Dublin, Ireland, is the AIC holder of the drug Lucentis.

8. Novartis Farma S.p.A. (hereinafter also "Novartis Farma") is the Italian subsidiary of the Novartis group and has its registered office in Milan.

II. PREAMBLE

9. As of November 2022, the Authority received information from the Italian Medicines Agency (hereinafter also referred to as "AIFA" or "the Agency")[2] regarding the failure of the drug Byooviz, produced by Samsung Bioepis and marketed by Biogen, to enter the Italian market. Byooviz is the biosimilar of the highly profitable biotechnology drug Lucentis developed by Genentech (see Section V.a. below). In addition, public information was acquired by the Offices concerning a licensing agreement signed between Samsung Bioepis and Biogen, on the one hand, and Genentech, on the other, concerning the marketing of the aforementioned Byooviz (see Section V.b. below).

10. This agreement, by virtue of the reference also to countries in the world other than the United States of America, also affects Novartis, since the latter

[2] AIFA was established pursuant to Article 48 of Legislative Decree No. 269/2003, as converted, with amendments, by Law No. 326/2003, and is the national public body that regulates medicines for human use in Italy. AIFA governs pharmaceutical expenditure and monitors the lifecycle of a medicine to ensure its efficacy, safety and appropriateness as well as its access throughout the country.

has exclusive marketing rights to Lucentis in all other territories (see below section 73).

11. The motivation behind Samsung Bioepis' and Biogen's dilatory conduct, which was the subject of the information sent by AIFA, could therefore be found in the licence agreement for Byooviz entered into with Genentech in September 2021. As a result, Samsung Bioepis and Biogen would obtain early entry into the US market while committing to postpone entry into other markets (including Italy) well beyond the expiry of Lucentis' patent rights. For their part, Genentech and Novartis would have benefited from the maintenance of a monopoly condition even after the expiry of the patent rights (see below sections 73-74).

12. It follows from all the elements that will be better described below that such conduct could constitute an infringement of Article 101 TFEU.

III. THE REGULATORY FRAMEWORK

13. So-called "biosimilars" are obtained biologically from a living organism. These medicinal products are "similar" in quality, efficacy and safety to the originator or reference biological products already authorised in the European Union and no longer subject to patent coverage[3]. The development of biosimilars takes much longer than that required for equivalents or generics, as six to eight years are needed from development to marketing, as well as significantly higher initial investments than those required for generics. Furthermore, there is a risk of research and development failure in the development of biosimilars, so that the process is very similar to that of originators[4].

14. Regarding the authorisation process, while biological medicinal products can also be authorised only at national level, MA applications of biosimilar medicinal products are exclusively examined by the EMA through the centralised procedure. Consequently, the MA is then valid in all EU Member States[5]. It should be pointed out that any MA of a medicinal product lapses if

[3] According to the AIFA *Position Paper* on Biosimilar Medicines, 27 March 2018, p. 9, available via: *https://www.aifa.gov.it/sites/default/files/pp_biosimilari_27.03.2018.pdf* last accessed on 24 April 2024.

[4] European Commission Decision of 3 August 2010, M.5865 - *Teva/Ratiopharm*, section 29.

[5] Article 13 of Regulation (EC) No 726/2004 of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency.

it is not followed by actual marketing within three years after being granted (so-called *sunset clause*, Article 14(4), EU Regulation No. 726/2004. At national level, reference is made to Article 38(5) of Legislative Decree No. 219/2006.

15. Once a MA has been granted by the EMA, the marketing of the biosimilar medicinal product depends on the classification regime for supply purposes adopted by each Member State, i.e. whether it is paid for by the National Health Service (hereinafter "NHS") or by the patient.

16. Pricing and reimbursement schemes are also defined by individual Member States. In Italy, the pricing and reimbursement procedures provide, by analogy with the procedures for equivalent drugs, that the price of biosimilar products is determined through a negotiation between AIFA and the manufacturer (pursuant to the Decree of the Ministry of Health of 2 August 2019, which repealed the CIPE Resolution of 1 February 2001), at a price at least 20% lower than the price of the reference biological product, pursuant to Decree-Law No. 158/2012, as converted into Law No. 189/2012 (so-called Balduzzi Decree). Therefore, generics and biosimilars have an automatic price reduction mechanism and the guarantee of the same reimbursement classification as originators, where such price reductions are convenient for the SSN (Article 12(6) of the above-mentioned Decree-Law[6]).

17. In implementation of this rule, the Ministry of Health Decree of 4 April 2013, as later amended by the Ministry of Health Decree of 21 July 2022, defined the "*Criteria for the identification of tiers for the automatic negotiation of generics and biosimilars*"[7], thus identifying the "convenient" reductions for the NHS[8].

18. Pending the (possible) negotiation initiated at the initiative of the company concerned, Article 12(5) of the aforementioned Balduzzi Decree provides that drugs that have been granted a marketing authorisation are automatically

[6] Indeed, pursuant to Article 12(6) of the Balduzzi Decree, a generic or biosimilar medicinal product is "*automatically placed, without price negotiation, in the reimbursement class to which the reference medicinal product belongs if the holder company offers a sales price that is clearly advantageous for the National Health Service*. *This is considered to be the price which, compared to that of the reference medicinal product, shows a decrease at least equal to that established by a decree adopted by the Minister of Health, on a proposal by AIFA, in relation to the expected sales volumes.* [...]".

[7] Published in G.U.R.I. No. 131 of 6 June 2013.

[8] Based on the assumption that "*the current provisions do not allow applications for marketing authorisation of generic or biosimilar medicinal products to be conditioned by the date of expiry of the patent protection*" (considering the Ministry of Health Decree of 21 July 2022), the amendments made in 2022 to the Decree provide for the periodic publication by AIFA of the list of average annual NHS expenditure values recorded in the previous three years for active ingredients currently in the reimbursable class, whose patent rights will expire in the following year.

classified in a special section, called class C "non-negotiated" (hereinafter "C(nn)"), dedicated to drugs that have not yet been evaluated for reimbursability. Class C(nn) allows accessibility of the drug before the conclusion of the pricing and reimbursability process, with the cost to be borne in full by the patient or by the NHS for specific treatment needs of the patients taken care of and in the absence of available alternatives[9].

19. This class C(nn) differs from classes A, C and H already defined by Article 8(10) and (14) of Law no. 537/1993, as amended, in that it is a temporary classification that applies pending completion of the reimbursability procedure. In addition, again according to the aforementioned provision, before marketing begins, the MA holder is required to notify AIFA of the ex-factory price, the price to the public and the date when marketing of the medicinal product begins. The inclusion in Class C means that the prices of drugs are freely determined by the manufacturers and paid in full by the patient. In the event of non-marketing, the possibility of putting the medicinal product out to tender also ceases[10].

20. Moreover, reference is also made to Article 12(3) of the Balduzzi Decree, whereby in certain cases, which also include biosimilars, the application for classification as a drug payable by the NHS may also be submitted prior to the granting of the MA[11], i.e. immediately after the opinion of the Committee for Human Medicinal Products (hereinafter, "CHMP") of the EMA.

21. The subsequent subsection *5-ter* of the aforementioned Article 12 provides that, for such medicinal products, in the event of failure to submit an application for classification within thirty days of the granting of the MA, AIFA shall request the company holding the relevant MA to submit the application within the following thirty days. Once this deadline has expired without response, information is posted on AIFA's institutional website and the alignment to the lowest price within the fourth level of the *Anatomical Therapeutic Chemical* Classification System (hereinafter "ATC") is applied.

22. Lastly, Article 17 of Law No. 118/2022 provides that manufacturers of equivalent medicines may submit an application to AIFA for the issuance of a

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[9] Doc. 9.

[10] *Ibid.*

[11] Article 12(3) of Decree-Law No 158/2012, as converted into Law No 189/2012: "*Notwithstanding the provisions of subsection 2, the application concerning orphan drugs within the meaning of Regulation (EC) No 141/2000 of the European Parliament and of the Council of 16 December 1999, or other drugs of exceptional therapeutic and social importance provided for in a specific resolution of the AIFA, adopted on the proposal of the Technical and Scientific Advisory Commission, or concerning drugs that can be used exclusively in a hospital environment or in similar facilities, may be submitted prior to the granting of the marketing authorisation*".

MA, as well as an application for pricing and classification for the purposes of the reimbursability of the medicine, before the expiry of the patent or supplementary protection certificate (hereinafter "SPC"). In addition, it has been provided that equivalent medicines can be reimbursed by the NHS from the date of expiry of the patent or SPC on the active ingredient.

23. In this regard, a brief reference is made to the SPC legislation and, in particular, Regulation (EC) No 469/2009 of the European Parliament and of the Council concerning the supplementary protection certificate for medicinal products.

24. Based on the assumption that the period between the filing of a patent application for a new medicinal product and the granting of a marketing authorisation for that product reduces the effective protection conferred by the patent to a duration that is insufficient to amortise the investment made in research, thereby penalising pharmaceutical research, this regulation regulates a supplementary protection certificate for medicinal products whose marketing has been authorised. This certificate may be obtained by the patent holder for a maximum period of five years, in addition to the 20 years already recognised by the patent.

25. With regard to the effects of the SPC, Article 5 specifies that it confers the same rights as the basic patent and is subject to the same limitations and obligations, but that there are exceptions in the case, recently extended by Article 1(1)(2) of Regulation (EU) No. 2019/933. Indeed, by means of this derogatory regime, EU-based companies can produce their own generic and/or biosimilar products despite the CPC being in force, as long as they are intended for export outside the EU, in particular to territories where patent coverage has already expired or is not in force. In addition, during the last six months of the SPC's validity, storage for future release on the EU market is permitted, once the relevant protection also expires in that territory. In this way, the competing operator can be ready for marketing as early as the day after the CPC expires.

IV. THE FACTS UNDER INVESTIGATION

a. The drugs Byooviz and Lucentis

26. Byooviz (ATC: S01LA04; *ranibizumab-nuna*), a biotechnological medicinal product whose MA holder is Samsung Bioepis NL B.V., is the first drug approved by the EMA as a biosimilar of Lucentis[12], of which it has the same active ingredient (i.e. *ranibizumab*)[13]. On 6 November 2019, Bioepis and Biogen concluded a commercialisation agreement in Canada, Europe, Japan, Australia and the US for two biosimilar candidates in development: SB11*(id est* Byooviz) and SB15, biosimilar candidate of the drug aflibercept (EYLEA, registered trademark of Regeneron Pharmaceuticals). Under this agreement, Samsung Bioepis is responsible for product development, registration with regulatory authorities and production, while Biogen is responsible for marketing.

27. Lucentis, developed by Genentech Inc. and marketed in Europe by Novartis Europharm Ltd. (see below section 73), is an anti-VEGF antibody for intravitreal administration and is one of the most widely used products for the treatment of major retinal diseases, including age-related macular degeneration (hereafter "AMD'") and diabetic macular oedema (hereafter "DME"), which are widely spread diseases in the Italian population[14]. Lucentis' SPC expired on 23 July 2022, while the original patent, in turn, expired on 3 April 2018[15].

[12] Lucentis was the subject of proceeding I/760 - *Roche/Novartis*, Order No. 24823 of 27 February 2014, in Bulletin No. 11/2014. The current pricing regime for Lucentis is set by the AIFA Determination of 19 December 2022 (G.U.R.I. No. 1 of 2 January 2023), following Novartis Europharm Ltd.'s application of 22 September 2021, whereby the pack has (gross of statutory reductions) an ex-factory price of €742 and a retail price of €1,224.60 to which the mandatory discount to the NHS of 48.26% is applied. Therefore, net of discount and before statutory reductions Lucentis currently has an ex-factory price of €383.92 and a retail price of €633.61 (doc. 15). The agreement between AIFA and Novartis Europharm Ltd. concerning Lucentis was automatically renewed in January 2024 (doc. 16).

[13] Byooviz is administered by means of disposable vials (0.23 ml) for intravitreal use and is indicated in adults (recommended dose 0.05 ml) for the treatment of neovascular (exudative) age-related macular degeneration (AMD); the treatment of visual decrease caused by diabetic macular oedema (DME); the treatment of proliferative diabetic retinopathy (PDR); the treatment of visual decrease caused by macular oedema secondary to retinal venous occlusion (branch RVO or central RVO); and the treatment of visual decrease caused by choroidal neovascularisation (CNV); cf. doc. 3, annex 1.

[14] Doc. 1.

[15] Doc. 18. Source: Italian Patent and Trademark Office - Ministry of Economic Development and Made in Italy. The company that filed the patent and SPC applications is Genentech Inc.

b. The events reported

28. On 11 November 2022, AIFA informed the Authority of Samsung Bioepis NL and Biogen Italia's conduct such that the marketing of the biosimilar drug Byooviz[16] has not been allowed in Italy to date.
29. The transmission was subsequently supplemented by a series of replies to the requests for information made by the Offices[17] necessary to appreciate fully the complexity and extent of the conduct under investigation[18]. Furthermore, during the hearing with the Offices on 22 January 2024[19], the Agency further clarified that the conduct in question consisted in not having cultivated the process for the marketing of the biosimilar Byooviz for an extended period of time. In addition, the Agency provided due updates on the medicines concerned.
30. In order to understand the subject matter and context of the report, it is necessary to review the regulatory process of Byooviz, starting with the procedure initiated at European level.
31. In fact, following a specific request dated 10 September 2020, on 18 August 2021 Samsung Bioepis NL B.V. received, through a centralised procedure, the MA for Byooviz, as a biosimilar drug of Lucentis, by decision No. 6209 of the European Commission (subject to a positive opinion of the EMA), pursuant to Article 3.1. and point 1 of the Annex to Regulation (EU) No. 726/2004.
32. By means of this MA, Samsung Bioepis NL was therefore entitled to start marketing Byooviz in all EU Member States for the adult treatment of major retinal diseases, including AMD and DME. The authorisation is valid for five years from the notification of the decision by the Commission (Article 14 of Regulation (EU) No. 726/2004).
33. At the national level, at the meeting of the Technical-Scientific Committee (TSC) of the AIFA of 4-6 October 2021, Byooviz was classified for the purpose of supply as a hospital drug ("*Medicinal product subject to a restrictive medical prescription, to be used exclusively in a hospital environment or in a similar structure (OSP)*") and it was specified that "*the Determination can only be published after approval of the additional risk*

[16] Doc. 1.
[17] Precisely, on the dates: 13 December 2022, 7 February 2023, 12 April 2023 and 6 June 2023 (docs. 2, 5, 6 and 8).
[18] Replies were provided precisely on 13 January, 19 May and 10 August 2023, and 19 January 2024 (docs. 3, 7, 9 and 15). A final brief update was submitted on 13 May 2024 (doc. 25).
[19] Doc. 16.

minimisation measures by the Office of FV"[20].

34. Therefore, for the adoption of the Class C(nn) AIC determination, pending the reaching of a price agreement, the AIC holder, Samsung Bioepis NL, through its Italian representative Biogen Italia, was obliged to comply with the obligation to submit the informative material indicated in the additional risk minimisation measures, as requested by the Commission[21].

35. AIFA then repeatedly urged Biogen Italia (notably on the dates: 27 October 2021, 20 May 2022, 21 June 2022, 19 July 2022[22]) to transmit the necessary informative material to complete the Class C(nn) AIC procedure. It was not until 29 July 2022 that Biogen Italia replied to AIFA, stating that it did not have the documentation available and that "*with regard to the additional request concerning the formal submission of the application for admission for reimbursement, at this stage Biogen is unable to commit to a specific date* [...]"[23].

36. In the meantime, the European Commission, by Decision No. 7083 of 29 September 2022, authorised a new packaging of Byooviz, following an application by Samsung Bioepis NL itself[24].

37. The AIC change was then submitted to the STC for evaluation at its meeting of 7-9 November 2022, which approved the same hospital supply scheme[25].

38. It was not until 2 December 2022 that Biogen Italia transmitted the requested informative material. Following some revision requests, the final material was then completed at the end of January 2023[26]. The file was then approved on 1 February 2023 by AIFA's Risk Management Measures Office[27].

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[20] Doc. 3 annex 1. Authorised packages: EU/1/21/1572/001 AIC: 049689019/E In base 32: 1HDDFV 10 mg/ml - solution for injection - intravitreal use - vial (glass) 0.23 ml - 1 vial + 1 filter needle + 1 injection needle

[21] See Annex II of the EMA authorisation, p. 28: "*Prior to the launch of Byooviz in each Member State, the marketing authorisation holder must agree on the content and format of the informative material with the relevant national authorities. The purpose of the informative material is to provide adequate instructions to patients regarding the key signs and symptoms of potential adverse reactions and when to seek urgent medical advice, to ensure the rapid identification and treatment of such events".*

[22] Doc. 7 annex 2, doc. 7, doc. 1 annex 1.

[23] Doc. 1 annex 1.

[24] Decision published in the Official Journal of the European Union on 31 October 2022 (doc. 7 annex 1).

[25] Doc. 3 annex 2. Authorised packages: EU/1/21/1572/002 AIC: 049689021/E In base 32: 1HDDFX. 10 mg/ml - Solution for injection - Intravitreal use - Vial (glass) 0.23 ml - 1 vial

[26] Doc. 7.

[27] Doc. 7 annex 3.

39. On 18 April 2023, the Byooviz Classification Determination in C(nn) was published pursuant to Article 12(5) of Decree-Law No. 158/2012, as converted into Law No. 189/2012, published in G.U.R.I. No. 95 of 22 April 2023[28].

40. On 4 May 2023, AIFA's HTA and drug economics sector therefore urged Samsung to submit the negotiation request for the possible classification of the drug in the reimbursability Class[29].

41. However, Samsung Bioepis NL and Biogen Italia have since failed to respond to AIFA's reminders, nor is Byooviz still marketed in Italy as a class C(nn) drug[30].

42. This being the case, AIFA considers anomalous the conduct of the companies that, first of all, despite the proactivity of the Agency and only following the Agency's multiple requests, carried out the limited formalities necessary for the adoption of the Class C(nn) determination, pending the reaching of a price agreement. Once the resolution was published, however, Biogen Italia never submitted the necessary price application and, therefore, considering that the AIC issued by the EMA dates back to August 2021, it seems difficult for the Agency to explain the circumstance that this potentially highly profitable drug[31] has not yet entered the market in Italy, despite the long lapse of time since the issue of the MA and the expiry of Lucentis' SPC, and given that the *ranibizumab* molecule is highly profitable, Lucentis being worth almost €50 million in annual sales.

43. In support of the peculiarity of the conduct of the companies in question, AIFA points to the circumstance that in many cases the biosimilar companies made use of the possibility provided by the legislation to apply for reimbursability and to negotiate the price in advance of patent expiry (see above section 20), so as to enter the market as soon as possible. This therefore confirms the anomaly of the conduct of the *ranibizumab* biosimilar, which more than two years after EMA authorisation (August 2021) and after patent expiry (July 2022), is still not on the market in Italy[32].

44. Moreover, the Agency points out that, pursuant to the aforementioned Article 12(3) of Decree-Law No. 158/2012, for Byooviz it would have been possible to submit the application for classification as a medicinal product

[28] Doc. 7 annex 1.
[29] Doc. 9 annex 2.
[30] Doc. 9 annex 1.
[31] In 2022, total expenditure on *ranibizumab* amounted € [*40-50 million*] and, in general, expenditure on drugs authorised for the treatment of eye diseases due to ocular vascular disorders (including *aflibercept*, *brolucizumab* and *ranibizumab* but not also *bevacizumab*) amounted to €143,312,638 (doc. 9).
[32] Doc. 16.

payable by the NHS immediately after the opinion of the EMA CHMP, i.e. on 9 August 2021[33].

45. For AIFA, the behaviour appears without justification given the obvious interest that Samsung Bioepis NL and Biogen Italia should have shown in cultivating the procedure for the marketing of the drug[34]. Moreover, according to the Agency, a delay of three years has inevitable repercussions in terms of lost public expenditure, resulting in a potential saving of 33.30% of the total turnover of approximately €50 million[35].

c. The Licence Agreement

46. On 20 September 2021 Samsung Bioepis Co. Ltd. and Biogen Inc. issued a press release on the occasion of the approval of Byooviz by the US *Food and Drug Administration* ("FDA"), stating: "*Pursuant to a global licence agreement entered into with Genentech, Samsung Bioepis and Biogen will have freedom to market SB11 in the United States as of June 2022, i.e. before expiration of Genentech's applicable SPCs, and elsewhere in other territories after expiration of Genentech's SPCs".*

According to the press release, therefore, under a global licensing agreement with Genentech, Samsung Bioepis and Biogen, Byooviz will be allowed to be marketed in the US as of June 2022, i.e. before the US SPC expires, and in other territories after the expiry of the relevant Genentech SPC[36].

47. Between 21 and 23 September 2021, the news of a licensing agreement between Samsung Bioepis-Biogen and Genentech was commented on in a number of trade journals.

48. In particular, the *Daily Health Industry* reported on 21 September 2021 that "*According to what the two companies said in a joint statement* [ed. Samsung Bioepis and Biogen], *the newly approved biosimilar version can be marketed in the US from June 2022, as part of an agreement with Roche's Genentech unit. Lucentis, which already faces the competitor Novartis Beovu, is approved for the treatment of eye diseases such as age-related macular degeneration and had a turnover of $1.5 billion in 2020*"[37]. Already in the

[33] Doc. 7.
[34] Doc. 16.
[35] Doc. 16.
[36] Doc. 10 annex 1, *https://www.samsungbioepis.com/en/newsroom/newsroomView.do?idx=254*last accessed on 24 April 2024.
[37] Doc. 10 annex 2, *https://www.dailyhealthindustry.it/samsung-bioepis-biogen-fda-approva-biosimilare-di-lucentis-roche-ID22430.html*last accessed on 24 April 2024.

aftermath of the press release, *Pharmaceutical Technology* on 21 September 2021 observed: "*Estimates show that savings in the next five years from 2020 to 2024 due to the use of biosimilars are expected to cross $100bn in the US*"[38].

49. The news of the agreement is also reported on 23 September 2021 by *Korea Biomed*[39], highlighting, however, that it took place immediately after the EMA had issued the MA in Europe (18 August 2021) and giving rise to speculation that there may be a strategy to delay Byooviz's market entry: "*Industry watchers said Samsung Bioepis might have agreed with Genentech on when to release Byooviz in the U.S. and Europe as the two signed the licence agreement after Europe's marketing approval in August*. *Such speculation emerged because Samsung Bioepis suddenly disclosed the information about the licence agreement with Genentech. The Korean company used to be reluctant to comment on the original drug developer's patent strategy to delay the market entry of the biosimilar. Before Samsung Bioepis started selling Herceptin biosimilar Ontruzant (trastuzumab) in the U.S. in 2019, it ended the patent dispute with the developer of the original drug, Genentech, and entered a licence agreement. Samsung Bioepis refused to comment on the market release of Byooviz. However, the company said it can sell the biosimilar as of June 2022 before the expiration of Genentech's Supplementary Protection Certificate (SPC). In other regions, it can market the product after Genentech's SPC expires*".

50. An analysis of Samsung Bioepis and Biogen's press release entitled "*US Lucentis Competition Expectations Upended By Byooviz*"[40] is published in *Generics Bulletin* on 22 September 2021. The article expressed surprise at the indication of June 2022 as Byooviz's US market entry date, given that Roche (Genentech's parent company) had previously reported that the Lucentis biosimilar was instead expected in the second half of 2021. In addition, Genentech declined to comment on how expectations have changed with respect to Byooviz's entry into the US market already expected by the end of 2021, insisting instead that "*we have long-supported FDA's efforts to implement a science-based pathway for the approval of biosimilars and believe that they have a role in the healthcare system*". The same article states that for Byooviz "*Launch in Europe is expected in early 2022 as*

[38] Doc. 10 annex 3, *https://www.pharmaceutical-technology.com/news/samsung-bioepis-biogen-biosimilar-lucentis/* last accessed on 24 April 2024.

[39] Doc. 10 annex 4, *https://www.koreabiomed.com/news/articleView.html?idxno=12191* last accessed on 24 April 2024.

[40] Doc. 10 annex 5, *https://generics.citeline.com/GB151266/US-Lucentis-Competition-Expectations-Upended-By-Byooviz* last accessed on 24 April 2024.

supplementary protection certificates (SPCs) linked to the brand expire".

51. More recently, an article in *The Korea Herald* of 5 March 2023[41], in addition to stating that Byooviz had started to be marketed in Germany on 22 February, again refers to the fact that "*Bioepis plans to gradually bring SB11 to North American and European markets. Specific launch dates are different for each country according to the licensing contract that it co-signed with Genentech".*

V. ASSESSMENT

a. The relevant market

52. According to settled case law on restrictive practices, the definition of the relevant market is essentially aimed at identifying the characteristics of the economic and legal context in which the agreement or concerted practice takes place. This definition is, therefore, functional to delimiting the scope in which the cartel may restrict or distort the competitive mechanism and to deciphering its degree of offensiveness[42].

53. It should also be noted that on the basis of the established practice of the European Commission and the Authority, for the purposes of identifying the relevant product market in the pharmaceutical sector, the therapeutic classes, i.e. the chemical action and the therapeutic purpose of the medicinal product produced and/or marketed, are of relevance. These classes are identified using the *Anatomical Therapeutic Chemical Classification System* (hereafter "ATC"), according to which drugs are subdivided according to an alpha-numeric classification into five hierarchical levels.

54. In general, for the treatment of eye diseases due to ocular vascular disorders, at present, in addition to Novartis Europharm Ltd.'s Lucentis *(ranibizumab*), drugs based on other active ingredients, all included in the H/OSP reimbursement class, are also available on the market, such as: Beovu *(brolucizumab*), marketed by Novartis; Eylea *(aflibercept*), marketed by Bayer; Vabysmo *(faricimab*), marketed by Roche; Roche's Avastin and its biosimilars Abevmy, Alymsis, Mvasi and Oyavas (all *bevacizumab-based*), registered for non-ophthalmic therapeutic uses and non-intravitreal uses, but

[41] Doc. 10 annex 7, *https://www.koreaherald.com/view.php?ud=20230305000128*last accessed on 24 April 2024.

[42] See Council of State, Sec. VI, judgement of 3 June 2014, No. 2837 and, most recently, Council of State, Sec. VI, judgement of 15 April 2021, No. 3566.

administered off-label for the treatment of AMD and DME and therefore included in the so-called List pursuant to Law No. 648/1996[43].

55. The conduct at issue in the proceedings, consisting in a possible coordination between the holder of the marketing authorisation for the originator drug Lucentis and the holder of the marketing authorisation for its biosimilar Byooviz, primarily concerns the market for the same molecule that makes up both medicinal products, namely *ranibizumab*.

56. The absence of substitutability between medicines based on different active ingredients in the present case is confirmed by the consideration of the applicable rules on the purchase of biotechnological medicines by public establishments.

57. In particular, in terms of distribution, biotechnological drugs under analysis are purchased by hospitals and/or local health authorities through competitive supplier selection procedures. In this regard, Article 15, subsection *11-quater* of Decree-Law No. 95 of 6 July 2012, converted with amendments into Law No. 135 of 7 August 2012, is relevant insofar as it provides that "*In public purchasing procedures for biosimilar drugs, different active ingredients, even if having the same therapeutic indications, may not be put up for tender in the same lot*".

58. The above provision therefore excludes the possibility of tendering different active ingredients in the same lot, even if they have the same therapeutic indications. This, for the present case, would imply that the purchasing procedures for drugs used for the treatment of the main retinal diseases (AMD and DME) are structured on the basis of batches of drugs containing the same active ingredients.

59. It should also be borne in mind that, with specific reference to biosimilars, the European Commission, as part of its assessment of certain merger transactions, also conducted a market investigation which showed that the biosimilar competes only with the originator[44].

60. In view of this, the relevant market in the present case, as a first approximation, appears to be that for the active ingredient *ranibizumab* itself

[43] The assessment of therapeutic overlap between the above-mentioned drugs was carried out by AIFA. In fact, with Determination No. 1379 of 28 December 2020, published in the Official Gazette No. 323 of 31 December 2020 (the so-called Note 98), the Agency considered that *aflibercept, bevacizumab, brolucizumab* and *ranibizumab* can be regarded as substantially overlapping active ingredients for the therapeutic indication AMD; whereas *aflibercept*, *bevacizumab* and *ranibizumab* can be regarded as overlapping for the therapeutic indication DME in patients with *visus* no worse than 20/40 (i.e. at least 5/10).

[44] European Commission Decisions of 4 August 2015, M.7559 - *Pfizer/ Hospira*, section 21 and 20 November 2018 M.8955 - *Takeda/Shire*, section 47.

(ATC: S01LA04), a molecule electively intended for the treatment of the major retinal diseases AMD and DME, meaning the therapeutic subgroup of reference is ATC-5 (active ingredient).

61. With reference to the geographical dimension, the markets for the production and marketing of pharmaceuticals are usually considered national by both the Commission and the Authority[45]. This is because of differences in health policies in individual countries (i.e. regulation of prices, reimbursement modalities, classification of medicines, distribution channels) and different access regimes (i.e. patenting and marketing authorisation regimes). For these reasons, the product market identified above is limited in scope to the national territory.

62. The Italian market for *ranibizumab* therefore only includes Lucentis and its biosimilars, namely Byooviz, Ranivisio from Midas Pharma GMBH and Ximluci from Stada Arzneimittel AG.

63. Ranivisio, like Byooviz, is not on the market and is only classified in band C(nn) by virtue of AIFA Determination No. 1 of 9 January 2024[46], while Ximluci was admitted to class H reimbursability by AIFA Determination No. 749 of 11 December 2023. It should be noted that the price now charged to Ximluci is in accordance with the Staggers Decree, i.e. it is the result of applying the 33.3% discount to the last price charged to Lucentis (see above section 17)[47].

[45] See, *inter alia*, European Commission Decision M.7559 - *Pfizer/Hospira*, cited above, section 30; Order No. 24823 of 27 February 2014, I760-*Roche-Novartis/Avastin and Lucentis*drugs, cited above; Order No. 23194 of 11 January 2012 A431 - *Ratiopharm/Pfizer*, in Bulletin No. 2/2012.

[46] Published in G.U.R.I. No. 297 of 21 December 2023.

[47] On 13 May 2024, AIFA informed the Authority's Offices that, at the last meeting of the Agency's Board of Directors, the packaging of the medicinal product Ximluci was approved and that, following publication in a forthcoming edition of the Official Gazette of the Italian Republic, Ximluci will be available in Class H/OSP-Note 98 (Doc. 25).

b. The conduct concerned

64. From the available information, it could be inferred that there has been a coordination of commercial strategies between Samsung Bioepis and Biogen, on the one hand, and Genentech and Novartis, on the other, with regard to the market entry of Byooviz, at least since September 2021.

65. The coordination of the respective conduct would relate, in particular, to the non-marketing of Byooviz in Italy, even though the latter could have been available on the Italian market at least from 23 July 2022, i.e. from the expiry of Lucentis' patent rights.

66. In fact, it appears from Samsung Bioepis' press release of 20 September 2021 that Samsung Bioepis and Genentech entered into a global licensing agreement under which it was possible for Samsung Bioepis and Biogen to market Byooviz in the United States as of June 2022, i.e. before Genentech's CPC applicability in the United States expired. The wording of the press release suggests that the parties also agreed on the date of commercialisation of Byooviz in other countries after the expiry of Genentech's relevant SPCs ('*Specific launch dates are different for each country according to the licensing contract that it co-signed with Genentech*" - *Korea Herald*, 5 March 2023[48]).

67. Thus, while the licence agreement could be justified with regard to Byooviz's entry into the US market before the expiry of the relevant CPC, this does not apply to other countries. In this respect, it should be noted that, since the patent rights of the reference drug have expired, it is not necessary to enter into a licensing agreement with the originator to manufacture and market a biosimilar drug. Therefore, there is no need to address in a licence agreement the issue of the date of entry of the biosimilar into the other geographic markets at CPC of the expired originator.

68. As mentioned above, the drug Byooviz is not yet marketed in Italy. In this regard, it should be noted that the CPC of Lucentis expired on 23 July 2022. Therefore, considering that Byooviz already had an AIC (see above section 31), Samsung Bioepis NL - as from the day following that deadline - could potentially have been ready for the "*Day-1 launch*", i.e. the actual marketing in Italy, in the light of the derogatory hypothesis of the aforementioned Article 5 of Regulation (EC) No 469/2009 (see above section 25), which allows the generic or biosimilar medicine to be stored from six months before the expiry of the SPC.

[48] Doc. 10 annex 5.

69. In this respect, it must be pointed out that Samsung Bioepis NL and Biogen Italia could have already submitted to AIFA the application for classification of the drug to be charged to the SSN as from 9 August 2021 (date of the issue of the opinion of the EMA CHMP), pursuant to Article 12, subsection 3, of the Balduzzi Decree (see above section 20). However, not only did the companies fail to avail themselves of this possibility, but reminders from AIFA were necessary in order to deposit the informative material due for classification (at least in C(nn)). Moreover, the companies never followed up on the Agency's May 2023 request for reimbursement Class classification.

70. In addition, from the information gathered so far, it has not been possible to identify a specific justification for the fact that he biosimilar drug, which is related to a particularly lucrative market and in which investments have been made (see above section 13), has not yet entered the market in Italy. Furthermore, it transpired that repeated reminders from AIFA were necessary for Samsung Bioepis NL and Biogen Italia to deposit the informative material required for classification (at least in C(nn)). Finally, it appears that no price negotiations were initiated as a result of the classification. As pointed out by the Agency itself (see above sections 42-45) the behaviour of Samsung Bioepis NL and Biogen Italia, whereby almost two years after the expiry of the SPC Byooviz has still not been marketed in Italy, is anomalous both in view of the market value of the drug and in light of the practice of AIC holders of biosimilar drugs to enter the market as soon as possible, also in light of the current regulatory framework.

71. The interest of the Samsung Bioepis and Biogen groups in engaging in this dilatory conduct could therefore be found in an unlawful conspiracy, of which the licence agreement for Byooviz entered into with Genentech in September 2021 could be a manifestation, having as its object precisely the entry of the biosimilar by the Samsung Bioepis and Biogen groups into the various worldwide markets. As such, Samsung's Bioepis and Biogen groups would gain early entry into the US market while committing to postpone entry into other markets (including Italy) well beyond the expiry of Lucentis' patent rights.

72. With reference to the marketing of Lucentis, it should be recalled that Genentech is the pharmaceutical company wholly owned by the Roche Group that developed Lucentis, as well as the owner of the relevant patent rights in Italy, so much so that the patent application and the relevant SPC to the Italian Patent and Trademark Office was submitted by the latter and not by Novartis[49].

[49] Doc. 20.

73. Genentech had already entered into a marketing agreement with the Novartis group in 2003 granting the latter exclusive rights to Lucentis for the whole world (with the exception of only the United States of America for which Genentech retained these rights). Under this agreement, Genentech benefits not only from an upfront payment and a series of one-off payments, but also from royalties commensurate with sales of Lucentis outside the United States of America[50]. The holder of Lucentis' MA in Italy is Novartis Europharm Ltd., which is also responsible for pharmacovigilance and relations with regulatory authorities.

74. That being said, the hypothesised coordination between the Samsung Bioepis/Biogen and Genentech groups through the licensing agreement, by virtue of the reference also to countries in the world other than the United States of America, could also involve the Novartis group, at least with respect to its implementation. Novartis would also benefit from the continuation of its de facto monopoly on *ranibizumab* in the territories where it enjoys commercial exclusivity over Lucentis, including Italy.

75. The concerted action could, in fact, be ascribable to a strategy by Genentech (and, therefore, also by Novartis) to extract further monopoly rents from Lucentis even after the CPC has been exhausted. With respect to Genentech's interests in the distribution of Lucentis in Europe, it is recalled that, from its agreement with Novartis, Genentech derives royalties from the sale of the drug in Europe (see above section 73).

76. Such conduct, therefore, is capable of restricting Byooviz's entry into the Italian market, notwithstanding the exhaustion of Lucentis's patent rights and the validity of Byooviz's MA. Nor is it excluded that such restrictions may arise from further and different forms of interlocutions or coordination between the Parties.

77. These conducts, if confirmed, would reveal the existence of an alteration of competitive dynamics capable of artificially restricting competition on the merits for having the Parties having hindered the marketing in Italy of the biosimilar Byooviz, even though the Italian CPC of Lucentis had already expired on 23 July 2022.

78. Specifically in the pharmaceutical sector, such dilatory conduct in relation to the market entry of a biosimilar drug competing with the originator drug has negative repercussions on the possible savings for purchases at the expense of the NHS, as well as detrimental to patients and taxpayers in terms

[50] *Licence and Collaboration Agreement*- "*G N Agreement*", see Order No. 24823 of 27 February 2014, I/760, *Roche/Novartis*, cited above, sections 58-62.

of the breadth of supply and lower prices, given that biosimilar drugs tend to be marketed at a significantly lower price than their originator counterparts (see above sections 16-17).

79. This could be the result of a horizontal cartel, in the form of an agreement or concerted practice, aimed at preventing fair competition between operators in the market for the active ingredient *ranibizumab*.

c. *Effect on trade between Members States*

80. The concept of effect on trade between Members States must be interpreted taking into account the influence, direct or indirect, actual or potential, on trade flows between Member States.

81. In view of the fact that the conduct alleged against Samsung Bioepis co. Ltd., Samsung Bioepis NL B.V., Biogen Inc., Biogen Italia S.r.l., Genentech Inc., Novartis AG, Novartis Europharm Ltd. and Novartis Farma S.p.A. affects the national market, which constitutes a substantial part of the EU market, and appears likely to affect trading conditions between Member States[51].

82. In conclusion, the totality of the evidence in the file allows the existence of a possible agreement between the Parties aimed at restricting competition in the market for the active ingredient *ranibizumab* in violation of Article 101(1) TFEU.

CONSIDERING, therefore, that the conduct described above, carried out by Samsung Bioepis co. Ltd., Samsung Bioepis NL B.V., Biogen Inc., Biogen Italia S.r.l., Genentech Inc., Novartis AG, Novartis Europharm Ltd. and Novartis Farma S.p.A. Is likely to constitute an agreement restricting competition in violation of Article 101(1) TFEU;

[51] See, in the same sense, the Communication from the Commission, "*Guidelines on the concept of effect on trade between Member States*" (in OJEC C101/81 of 27 April 2004).

HAS ADOPTED THIS DECISION

a) to initiate an investigation, pursuant to Article 14 of Law No 287/1990, against the undertakings Samsung Bioepis co. Ltd, Samsung Bioepis NL B.V., Biogen Inc., Biogen Italia S.r.l., Genentech Inc., Novartis AG, Novartis Europharm Ltd. and Novartis Farma S.p.A., to ascertain the infringement of Article 101(1) TFEU;

b) to set a deadline of sixty days, starting from the notification of this decision, for the legal representatives of the Parties, or persons delegated by them, to exercise their right to be heard, specifying that the request for a hearing must reach the Cartels, Leniency and Whistleblowing Directorate of the Competition Department-1 of this Authority at least fifteen days before the expiry of the above-mentioned deadline;

c) that the person in charge of the procedure is Elisabetta Maria Lanza;

d) that the documents of the proceedings can be inspected at the Cartels, Leniency and Whistleblowing Directorate of the Competition Department-1 of this Authority by the legal representatives of the Parties, as well as by persons delegated by them;

(e) that the proceedings must be concluded by 30 September 2025.

This Decision will be notified to the Parties concerned and published in the Bulletin of the Authority.

THE SECRETARY GENERAL
Guido Stazi

THE PRESIDENT
Roberto Rustichelli