EN

Case No COMP/M.7275 - NOVARTIS/ GLAXOSMITHKLINE ONCOLOGY BUSINESS

Only the English text is available and authentic.

REGULATION (EC) No 139/2004
MERGER PROCEDURE

Article 6(1)(b) in conjunction with Art 6(2)
Date: 28/01/2015

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Brussels, 28.1.2015
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In the published version of this decision, some information has been omitted pursuant to Article 17(2) of Council Regulation (EC) No 139/2004 concerning non-disclosure of business secrets and other confidential information. The omissions are shown thus […]. Where possible the information omitted has been replaced by ranges of figures or a general description.

PUBLIC VERSION

MERGER PROCEDURE

To the notifying party:

Dear Madam(s) and/or Sir(s),

Subject: **Case M.7275 – NOVARTIS/ GLAXOSMITHKLINE ONCOLOGY BUSINESS**
Commission decision pursuant to Article 6(1)(b) in conjunction with Article 6(2) of Council Regulation No 139/2004[1]

(1) On 28 November 2014, the Commission received a notification of a proposed concentration pursuant to Article 4 of Council Regulation (EC) No 139/2004 by which Novartis AG ("Novartis", Switzerland), acquires a portfolio of oncology products (excluding manufacturing assets) from GlaxoSmithKline plc. ("GSK", United Kingdom) (the "GSK Oncology Business"), by way of purchase of assets (the "Transaction" or "the proposed transaction").[2] GSK and Novartis are jointly referred to as "the Parties". Novartis is also referred to as "the Notifying Party".

(2) The proposed transaction forms part of a three-part inter-conditional transaction whereby GSK has agreed to acquire sole control over Novartis' vaccine business (excluding the influenza business) and GSK and Novartis have agreed to combine their consumer health businesses into a new venture. These parts of the overall transaction have been notified on 28 November 2014 as case M.7276.

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1 OJ L 24, 29.1.2004, p. 1 ('the Merger Regulation'). With effect from 1 December 2009, the Treaty on the Functioning of the European Union ('TFEU') has introduced certain changes, such as the replacement of 'Community' by 'Union' and 'common market' by 'internal market'. The terminology of the TFEU will be used throughout this decision.

2 Publication in the Official Journal of the European Union No C 436, 5.12.2014, p. 11.

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I. THE PARTIES

(3) Novartis is a healthcare company headquartered in Basel (Switzerland), active globally in the development, distribution and marketing of medical products. Its main areas of activity cover: pharmaceuticals; eye care; generics; over-the-counter products and vaccines.

(4) GSK is healthcare company headquartered in Brentford (United Kingdom), active globally in three main areas: pharmaceuticals, vaccines and consumer healthcare products. GSK develops, distributes and markets globally medical products including respiratory, oncology, vaccines, HIV, and consumer health medicines. The GSK oncology business consists in research, development and marketing of oncology products for various indications worldwide.

II. THE OPERATION

(5) On 22 April 2014, the Parties signed a Share Purchase Agreement based on which Novartis will acquire sole control over GSK's portfolio of oncology pharmaceutical products composed of 10 marketed products and 2 pipeline products.[3] These products are marketed or are in clinical development for the treatment of advanced cancers. The acquired business consists in transfer of rights, licences, marketing authorisations and employees necessary for commercialisation and R&D in respect of the oncology pharmaceuticals concerned.[4]

(6) The Commission concludes that the Transaction constitutes a concentration within the meaning of Article 3(1)(b) of the Merger Regulation.

III. EU DIMENSION

(7) The undertakings concerned have a combined aggregate world-wide turnover of more than EUR 5 000 million (Novartis: EUR 43 609 million, GSK Oncology Business: EUR […] million).[5] Each of them has an EU-wide turnover in excess of EUR 250 million (Novartis: EUR [13 000 – 16 000] million, GSK Oncology Business: EUR […] million). None of these undertakings achieve more than two-thirds of their aggregate EU-wide turnover within one and the same Member State. The notified operation therefore has a Union dimension according to Article 1(2) of the Merger Regulation.

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3 The agreement was subsequently amended on […] and […].

4 The Transaction does not foresee transfer of manufacturing assets; however Novartis will enter in a Manufacturing and Supply Agreement with GSK for an initial period of […]. GSK will also retain its R&D activities. In addition, under the terms of the Transaction, Novartis will have certain opt-in rights to GSK's current and future oncology R&D pipelines for duration of […] from completion of the proposed transaction.

5 Turnover calculated in accordance with Article 5(1) of the Merger Regulation and the Commission Consolidated Jurisdictional Notice (OJ C95, 16.04.2008, p1).

IV. TARGETED THERAPIES

IV.1. Introduction on cancer therapies

(8) Cancers are diseases where certain cells (malignant cells) mutate and undergo uncontrolled cell growth. Cancers are usually classified according to the part of the body where they originate.[6]

(9) Traditional forms of therapies such as surgery, radiation therapy, chemotherapy, have been joined over the last two decades by targeted therapies and immunotherapies.[7]

(10) Targeted therapies are drugs or other substances that work at the cellular level by interfering with specific molecules involved in tumour growth and progression. They are used primarily at advanced stages of the tumour, when surgery is not an option any longer or when the cancer has spread to other parts of the body. Their goal is to slow down the cancer progression, and their success is often measured in terms of additional months of survival.

(11) Two classes of targeted therapies are of specific interest for the assessment of the Transaction: (i) targeted therapies that inhibit specific proteins carrying the signal for the cell to reproduce, such as B-Raf, MEK and mToR inhibitors[8]; (ii) targeted therapies that inhibit proteins responsible for the creation of new blood vessels in tumours ("VEGF inhibitors"). The figure below illustrates the chain of the main proteins (RAS, RAF, MEK, ERK in the MAPK/ERK signalling pathway; and PI3K, AKT, mTOR in the PI3K/AKT/mTOR signalling pathway) that are relevant to the case at hand:

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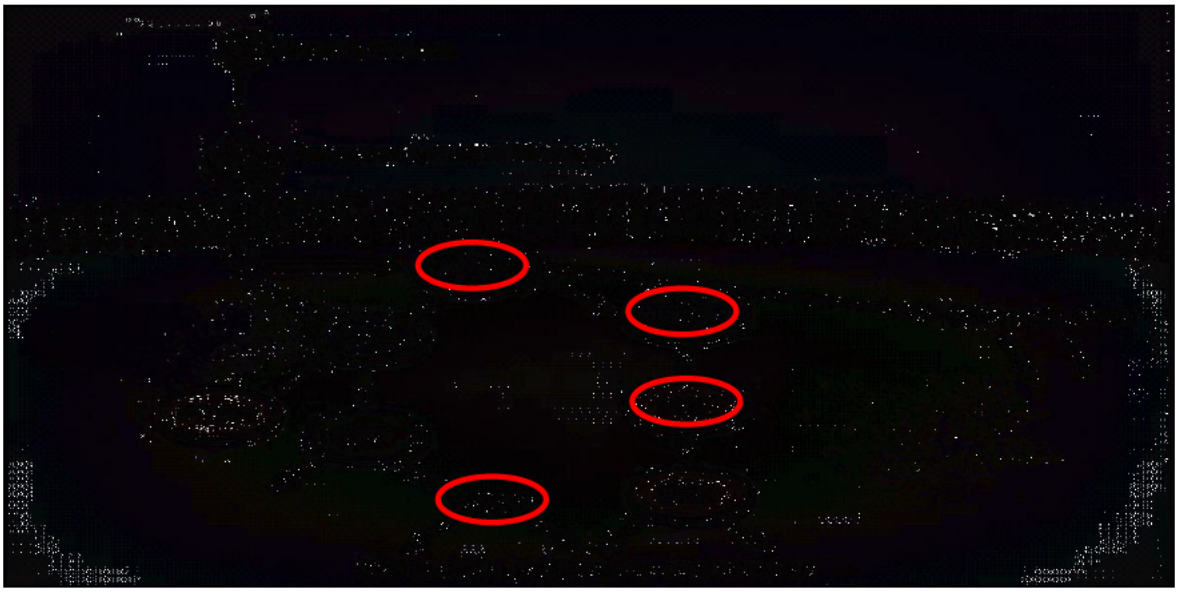
6 Cancer is the second most common cause of death in the EU (29% of deaths for men, 23% of deaths for women); a figure expected to rise due to the ageing European population. In its Communication on Action against Cancer, the Commission has set a goal to reduce cancer incidence by 15% by 2020, see Communication from the Commission to the European Parliament, the Council, the European Economic and Social Committee and the Committee of the Regions on Action Against Cancer: European Partnership, COM(2009) 291/4.

7 Immunotherapies are a relatively new type of cancer treatment designed to enhance the body's natural mechanisms to fight cancer. Immunotherapies work by helping the immune system to increase its natural ability to eliminate cancer cells.

8 Genetic mutations can cause these proteins to over-express and thus lead to uncontrolled cell growth that characterise tumours.



Source: Form CO

IV.2. MEK and B-Raf inhibitors

(12) B-Raf and MEK inhibitors are targeted therapies that block cell proliferation by inhibiting the over-expression of the B-Raf (a member of the RAF class) and MEK proteins responsible for tumour growth and progression. They are currently being developed and researched for the treatment of a number of different cancer types (such as advanced melanoma, ovarian cancer, colorectal cancer and lung cancer).

(13) Following successful clinical trials, a developing pharmaceutical company can file for authorisation to market a product for a certain type of cancer (indication), line of treatment, following specific prior therapy, etc. Such approval is decisive for reimbursement of the costs of the drug by national social security systems. Therefore, MEK and B-Raf inhibitors will be assessed with respect to each cancer type for which they are undergoing clinical trials.

IV.2.1. Advanced melanoma

(14) Melanoma is the most serious form of skin cancer, accounting for the eleventh most common cancer in Western Europe in 2013.

(15) Melanoma is traditionally classified in five stages (I-V), according to the severity of the disease and whether it has metastasised beyond the primary tumour. Treatments can vary across the different stages. Surgery is the main treatment for early stages (I-III). When the tumour has metastasised (IV-V), surgery is no longer feasible and targeted therapies, immunotherapies and chemotherapies are primary means of treatment.

(16) MEK and B-Raf inhibitors are considered particularly promising to treat advanced melanoma (as of stage IV). Both MEK and B-Raf inhibitors are relevant for B-Raf mutated melanoma, which represents 50% of all melanoma patients, whereas only

MEK inhibitors are currently expected to be relevant for N-Ras mutated melanoma, which accounts for 15% of patients.[9]

IV.2.1.1. *Market definition*

The Parties' views

(17) The Parties concur with the Commission's finding in previous decisions[10] relating to oncology pipeline pharmaceuticals and submits that the type of cancer for which a pipeline oncology pharmaceutical is being developed is an appropriate starting point for market definition.

(18) The Parties also note that the future use of oncology pipeline pharmaceuticals, particularly targeted therapies, is likely to be determined by the indication for which they are undergoing Phase III clinical trials.

(19) A segmentation of pharmaceuticals for the treatment of advanced melanoma by line of treatment would be artificial, as sequencing of targeted therapies in advanced melanoma is not established yet. Likewise, partitioning the market by mechanism of action or by oncogenic driver would artificially separate pharmaceuticals treating the same disease although with different mechanism of action or irrespective of the mutation status.[11]

(20) Accordingly, the Parties claim that the relevant product market for pipeline targeted therapies should encompass all targeted therapies, including pipeline targeted therapies, and immunotherapies, including pipeline immunotherapies, for the treatment of advanced melanoma.

(21) As regards the geographic scope of the market, the Parties concur with the Commission's previous conclusions that the geographic scope of the market for pipeline pharmaceuticals is at least EEA-wide.

(22) However, the Parties claim that it is not necessary to reach a final conclusion on the precise scope of the relevant product and geographic markets, as the Transaction would not raise any competition concerns under any possible market definition.

Commission's assessment

(23) The Commission has not previously considered the relevant product market definition for pharmaceuticals treating melanoma.

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9 Kantar Health, *"Future Trends and Insights Western Europe Melanoma, 2014"*, March 2014, page 2.

10 Commission decision of 22 May 2000 in case M.1878 – *Pfizer/Warner Lambert*, paragraph 42 and following, Commission decision of 04 February 1998 in Case M.737 – *Ciba-Geigy/Sandoz*, paragraph 42 and following, Commission decision of 29 July 2011 in case M. 6278 – *Takeda/Nycomed*, paragraph 10 to13, and Commission decision of 8 May 2000 in Case M.1846 – *Glaxo Wellcome/Smithkline Beecham*, paragraph 70 to 72.

11 Novartis' response to question 21 and question 30 of Commission request for information dated 9 September 2014.

(24) In its previous practice, the Commission assessed the potential competitive constraint likely to be exerted by products in Research & Development ("R&D") on existing product markets as well on possible future markets.[12]

(25) In particular, the Commission concluded that the potential for these products to enter into competition with other products which are either on the market or at the development stage should be assessed by reference to their characteristics and intended therapeutic use.[13]

(26) In line with its previous decisions,[14] in this case the Commission considers that when research and development ("R&D") activities are assessed in terms of importance for future markets, the product market definition can be left open, reflecting the intrinsic uncertainty in analysing products that do not exist as yet.

(27) In particular, the Commission considers that the product market definition for pipeline pharmaceuticals can be guided primarily by the characteristics of future products as well as by the indications to which they are to be applied.[15]

(28) The Commission has taken these principles into account in its assessment of the relevant product market encompassing the B-Raf and MEK inhibitors targeted therapies, and in particular whether immunotherapies belong to the same product market.

(29) The responses received in the market investigation indicated that new generation immunotherapies, such as anti-programmed cell death protein 1 ("Anti-PD-1s"),[16] are complementary rather than alternative to B-Raf and MEK inhibitors[17], because immunotherapies and targeted therapies would be used in different lines of treatment according to the mutation status, tumour's load[18] and progression. Immunotherapies would likely be used as first line treatment for wild-type (i.e. not linked to a specific

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12 Commission decision of 22 May 2000 in case M.1878 – *Pfizer/Warner Lambert*, paragraph 42 and following, Commission decision of 04 February 1998 in Case M.737 – *Ciba-Geigy/Sandoz*, paragraph 42 and following, Commission decision of 29 July 2011 in case M. 6278 – *Takeda/Nycomed*, paragraph 10 to13, and Commission decision of 8 May 2000 in Case M.1846 – *Glaxo Wellcome/Smithkline Beecham*, paragraph 70 to 72.

13 Commission decision of 17 July 2009 in case M. 5476 – *Pfizer/Wyeth*, paragraphs 15 to 16, Commission decision of 8 May 2000 in Case M.1846 – *Glaxo Wellcome/Smithkline Beecham*, paragraphs 70 to 72.

14 Commission decision of 22 May 2000 in case M.1878 – *Pfizer/Warner Lambert*, paragraph 44, Commission decision of 04 February 1998 in Case M.737 – *Ciba-Geigy/Sandoz*, paragraph 44, and Commission decision of 8 May 2000 in Case M.1846 – *Glaxo Wellcome/Smithkline Beecham*, paragraph 72.

15 Commission decision of 8 May 2000 in Case M.1846 – *Glaxo Wellcome/Smithkline Beecham*, paragraph 70 to 72.

16 Immunotherapy is a type of cancer treatment designed to enhance the body's natural mechanisms to fight cancer. Anti-PD-1's are checkpoint inhibitors, a new generation of immunotherapies drugs, which stimulate or prevent the inhibition of a patient's immune system when faced with cancer. Merck's PD-1 inhibitor, Keytruda (pembrolizumab), and BMS's PD-1 inhibitor, Nivolumab, are expected to have significant impact on the treatment of several types of cancer, including melanoma. Pembrolizumab and Nivolumab are likely to be approved in the EEA in 2015. *"Immunotherapies",* Decision Resources, June 2014, page 68.

17 Non-confidential minutes of a conference call with a Key Opinion Leader, 23 October 2014.

18 It refers to the number of cancer cells, the size of a tumour, or the amount of cancer in the body.

genetic mutation) melanoma or for B-Raf mutated melanoma with low tumour load and/or progression. Conversely, targeted therapies would be used as first line treatment for B-Raf mutated melanoma or for wild-type melanoma with extensive tumour load and/or rapid progression.[19] Therefore, as targeted therapies and immunotherapies are and will be prescribed in different settings, they cannot be considered as substitutable.

(30) Likewise, physicians consider chemotherapies as inferior treatment compared to targeted therapies and therefore believe they cannot be considered as suitable alternative treatments.[20]

(31) Based on the above elements, the Commission considers that for the purposes of this Transaction the relevant product market is the market for targeted therapies for the treatment of advanced melanoma. It can be left open whether targeted therapies for the treatment of advanced melanoma could be further segmented according to lines of treatment, mechanism of action or oncogenic driver, as, as set out below, the Transaction raises serious doubts as to its compatibility with the internal market irrespective of any further market segmentation.

(32) As regards the geographic dimension of pipeline pharmaceuticals, in line with its previous practice, the Commission considers that since pipeline products need to be assessed with reference to the R&D in a given area and to the extent that R&D for the relevant products is normally global, the geographic scope of the market should global or at least be EEA-wide.[21]

Conclusion

(33) In light of the above and all available evidence, in this case the relevant product and geographic market is the global or at least EEA-wide market for pipeline targeted therapies for the treatment of advanced melanoma. The Commission considers that it is not necessary to reach a conclusion on possible further delineations of this market by lines of treatment, mechanism of action and/or oncogenic driver, since, as set out below, the Transaction raises serious doubts as to its compatibility with the internal market irrespective of any possible further segmentation of the market.

IV.2.1.2. *Competitive assessment*

(34) The activities of the Parties overlap in the market for B-Raf and MEK inhibitors used alone or in combination for the treatment of advanced melanoma.

(35) Novartis' B-Raf inhibitor, LGX818 (*encorafenib*), is undergoing a Phase III clinical trial assessing LGX818 as monotherapy for the treatment of B-Raf mutated advanced melanoma.

(36) Novartis' MEK inhibitor, MEK162 (*binimetinib*), is undergoing Phase III clinical trial for advanced melanoma patients with an N-Ras mutation (the "NEMO study"). If trials are successful, MEK162 is expected to be approved for the treatment of melanoma patients with an N-Ras mutation in […] in the EEA.

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19 Replies to questions 5 and 16 of Q3 – Questionnaire on MEK and B-Raf inhibitors to Physicians.

20 Replies to question 17 of Q3 – Questionnaire on MEK and B-Raf inhibitors to Physicians.

21 Commission decision of 17 July 1996 in Case M. 737 – *Ciba-Geigy/Sandoz*, paragraph 51.

(37) LGX818 and MEK162 are also in Phase III study trialling LGX818 and MEK162 in combination for the treatment of B-Raf advanced melanoma (the "Columbus Study"). The Columbus Study started in September 2013 and is not due for completion before […]. Should the Columbus study be successful, Novartis estimates to file for market authorisation for its B-Raf-MEK combination in […].[22]

(38) GSK's B-Raf inhibitor, Tafinlar (*dabrafenib*), was approved as monotherapy for the treatment of unresectable or metastatic melanoma with a B-Raf V600 mutation in September 2013.

(39) GSK's MEK inhibitor, Mekinist (*trametinib*), was approved as monotherapy for the treatment of advanced melanoma with a B-Raf mutation in July 2014.[23]

(40) GSK's Tafinlar and Mekinist are undergoing Phase III clinical trials for use in combination for the treatment of advanced melanoma with a B-Raf mutation and are expected to enter the market in the EEA in […].[24]

(41) Therefore, in the treatment of advanced melanoma, the Transaction would create horizontal overlaps in the market for (i) B-Raf and MEK inhibitors used as single agent as well as in the market for (ii) B-Raf and MEK for use in combination, as summarised in the Table below.

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22 Novartis has also other compounds in earlier-stage trials for the treatment of advanced melanoma, such as BGJ398, BKM120, INC280 and LEE011, which are in Phase II trials for use in combination with LGX818 and LGX818 in combination with MEK162 for the treatment of melanoma with a B-Raf mutation; non-confidential minutes of a conference call with a Key Opinion Leader, 5 September 2014.

23 After conducting a Phase I clinical study exploring the potential of Mekinist to treat melanoma with several mutations, including N-Ras mutation, GSK decided that […]. See Novartis' response to question 20 of Commission request for information dated 9 September 2014.

24 The use in combination of GSK's Tafinlar and Mekinist in advanced melanoma has been approved in the United States. GSK withdrew its approval application for the use in combination of the two compounds in the EEA in March 2014, pending additional data from the Phase III programme (See http://www.gsk.com/en-gb/media/press-releases/2014/regulatory-update-combined-use-of-mekinist-trametinib-and-tafinlar-dabrafenib-in-europe/. Recently, GSK has announced that one set of its Phase III combination clinical trials for Tafinlar and Mekinist (the "COMBI-V" study) was terminated early, as the combination of Tafinlar and Mekinist demonstrated sufficiently superior efficacy compared to Roche's B-Raf inhibitor Zelboraf (See http://www.gsk.com/en-gb/media/press-releases/2014/trametinib-mekinist-and-dabrafenib-tafinlar-combination-demonstrated-overall-survival-benefit-compared-to-vemurafenib-phase-iii-braf-v600-mutant-metastatic-melanoma-study-stopped-early/). On 24 January 2014 GSK announced that the other set of its Phase III combination study for Tafinlar and Mekinist (the "COMBI-D" study) met its primary end point of progression free survival and that patients would be followed to assess overall survival. See http://us.gsk.com/en-us/media/press-releases/2014/gsk-announces-headline-results-for-phase-iii-study-of-the-combination-of-tafinlar-dabrafenib-and-mekinist-trametinib-in-metastatic-melanoma/.

Table 1 – Parties' B-Raf and MEK inhibitors for the treatment of advanced melanoma

	B-Raf inhibitor	MEK inhibitor	B-Raf / MEK combination
Novartis	LGX 818 B-Raf mutated melanoma (Phase III)	MEK162 N-Ras mutated melanoma (Phase III)	LGX818 and MEK162 B-Raf mutated melanoma (Phase III)
GSK	Tafinlar B-Raf mutated melanoma (Approved)	Mekinist B-Raf mutated melanoma (Approved)	Tafinalr and Mekinist B-Raf mutated melanoma (Phase III)

Source: Form CO.

The Parties' view

(42) The Parties submit that the Transaction does not raise serious doubts as regards the market for targeted therapies for the treatment of advance melanoma for the following reasons.

(43) First, the Parties have a negligible presence in the treatment of melanoma, as Novartis has only pipeline products and GSK has only recently entered the market, which is currently dominated by Roche's B-Raf inhibitor, Zelboraf (*vemurafenib*), and BMS' checkpoint inhibitor, Yervoy (*ipilimumab*).

(44) Second, there would be no overlap between the Parties MEK and B-Raf inhibitors: Mekinist and MEK162 are approved or likely to be approved to treat different mutations of advanced melanoma (B-Raf and N-Ras respectively), and [Parties' comparison between LGX818 and Tafinlar]. In addition, as Novartis' LGX818 is currently in Phase III studies, there is uncertainty over whether it would eventually reach the market. If Novartis' MEK and B-Raf eventually enter the market, the Parties' MEK and B-Raf inhibitors would not be closer competitors to each other.

(45) Third, the treatment of advanced melanoma is a "crowded space", where the Parties' targeted therapies would face strong competition from currently marketed and pipeline pharmaceuticals, including immunotherapies and chemotherapies. In particular, the Parties claim that new immunotherapies drugs, such as Anti-PD-1s, would completely change the landscape for the treatment of advanced melanoma, significantly constraining the Parties' molecular targeted therapies.

(46) Finally, the Parties claim that pursuant to the Transaction Novartis will continue developing B-Raf and MEK to bring them to market, as there is an unmet need for the treatment of advanced melanoma and thus potential for new products to find a space in this market.

Commission's assessment

(47) The Transaction creates potential overlaps in the following markets for the treatment of advanced melanoma: (i) B-Raf and MEK inhibitors used as monotherapy, where GSK's Tafinlar and Mekinist are already on the market, whereas Novartis' LGX818 and MEK162 are undergoing Phase III clinical studies ("affected market-to-pipeline"); and (ii) B-Raf and MEK inhibitors used in combination, where both GSK

and Novartis have pipeline products in Phase III clinical studies ("pipeline-to-pipeline").

(48) Before the approval of GSK's Tafinlar and Mekinist[25] as single agents, the standard of treatment for advanced melanoma consisted of Bristol Myers Squibb's ("BMS") immunotherapy Yervoy, a checkpoint inhibitor approved in 2011, and Roche's B-Raf inhibitor, Zelboraf, approved in 2012.

(49) The respondents to the market investigation overwhelmingly indicated that in the near future B-Raf and MEK inhibitors would become the standard of care in the treatment of advanced melanoma[26], particularly for use in combination.[27]

(50) The positive results of GSK's COMBI-v and COMBI-d studies,[28] trialling Tafinlar and Mekinist in combination against Zelboraf and Tafinlar as single agents respectively, confirm the superiority of the combination of B-Raf and MEK inhibitors over B-Raf inhibitors used as monotherapies.[29]

(51) The market investigation indicated that there are only three companies holding B-Raf and MEK inhibitors marketed or in phase III clinical trials for the treatment of advanced melanoma: Roche, GSK and Novartis.[30]

(52) Therefore Roche is the only competitor of the Parties in the market for B-Raf and MEK inhibitors in advanced melanoma. Roche's B-Raf inhibitor, Zelboraf, entered the market in 2012, while Roche's MEK inhibitor, Cobimetinib, successfully completed Phase III clinical studies for use in combination with Zelboraf. Roche's B-Raf and MEK combination is likely to be approved in the EEA in 2015.[31]

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25 GSK's Mekinist was the first MEK inhibitor to obtain market approval in the EEA for the treatment of advanced melanoma in July 2014.

26 Replies to questions 4 of Q3 – Questionnaire on MEK and B-Raf inhibitors to Physicians.

27 Replies to question 15 of Q3 – Questionnaire on MEK and B-Raf inhibitors to Physicians and question 9 of Q1 – Questionnaire to competitors; non-confidential minutes of a conference call with a competitor, 20 October 2014: *" The combination MEK and B-Raf inhibitors is very promising in advanced melanoma with B-Raf/N-Ras mutation, due to the unique biology of these diseases";* non-confidential minutes of a conference call with a Key Opinion Leader, 03 September 2014: "*Compared to a MEK or B-Raf inhibitor alone, the combination appears superior both in potency terms shown by the pre-clinical studies and side-effects. B-Raf inhibitors alone can be used in niche applications, for example for patients with ocular problems for which MEK inhibitors are not recommended. Nevertheless the combination MEK/B-Raf will become the standard of care*"; non-confidential minutes of a conference call with a Key Opinion Leader, 05 September 2014*: "[..]There have been important confirmation of the superiority of combined therapy with respect to monotherapy in Phase III trials: two phase III trials demonstrated superiority of dabrafenib/trametinib over drabrafenib alone or vemurafenib alone; and a phase III trials demonstrating superiority of vemurafenib/cobimetinib over vemurafenib alone. Additionally, the combined therapy showed better results in terms of efficacy (safety grounds) than stand-alone therapies".*

28 See footnote above and the referenced links to GSK's announcements on the positive results of these trials.

29 Upon completion of […] studies, […]. Tafinlar and Mekinist are likely to be launched in the […] in […] on the basis of data from […].

30 Replies to question 4 of Q1 – Questionnaire to competitors.

31 See http://www.fiercebiotech.com/story/roche-and-exelixis-herald-phase-iii-victory-their-cancer-combo/2014-07-14

(53) As a consequence, in the near future the market for B-Raf and MEK inhibitors would be characterised by the presence of Roche's Zelboraf in combination with Cobimetinib, which is expected to obtain a market authorisation in the first half of 2015, GSK's Tafinlar in combination with Mekinist, which would likely enter the market in […][32] and Novartis' LGX818 in combination with MEK162 which would likely to enter the market by […].

(54) Notwithstanding the fact that Novartis' B-Raf and MEK combination is expected to enter the market […], according to the respondents to the market investigation, Novartis', GSK's and Roche's B-Raf and MEK inhibitors, used alone or in combination, are close competitors to each other's.[33]

(55) In addition, the Parties' MEK and B-Raf inhibitors are not constrained by other MEK and B-Raf inhibitors which are at earlier stages of development.[34]

(56) The replies received in the market investigation further revealed that the Transaction is likely to reduce Novartis' incentives to launch LGX818 and MEK162, to the benefit of Tafinlar and Mekinist, which are at a more advanced stage in the Phase III trials for the treatment of advanced melanoma.[35]

(57) Therefore, the Transaction would lead to a reduction of potential competition on the market for B-Raf and MEK inhibitors used in combination for the treatment of advanced melanoma, as well as on the market for B-Raf and MEK inhibitors used as single agents, by reducing the number of available B-Raf and MEK inhibitors from 3 to 2.[36] Furthermore, the Transaction would likely lead to the abandonment of current efforts to launch Novartis' combination of B-Raf and MEK, to the benefit of GSK's B-Raf and MEK combination.

Conclusion

(58) Absent the Transaction, Novartis and GSK's B-Raf and MEK inhibitors would likely have constrained each other in the market for targeted therapies for advanced melanoma. Based on the above, the Commission considers that the likely elimination of Novartis' pipeline B-Raf and MEK inhibitors following the Transaction will result in

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32 GSK, *'[…] Brand Plan Tafinlar […]*, dated […].

33 Replies to questions 20 and 21 of Q3 – Questionnaire on MEK and B-Raf inhibitors to Physicians.

34 Other B-Raf inhibitors are: Teva's CEP-32496, in Phase II trials and Takeda's MLN2480 in Phase I trial. In addition, six B-Raf inhibitors are in pre-clinical development: Roche's PLX3603, Eternity Bioscience's EB1967/EB1945, Plexxikon's PLX4720/PLX8394, Pfizer's PF 04880594, Millennium's BIIB624 and Amgen's and Lilly/Deciphera's pre-clinical programme. Other MEK inhibitors are: AstraZeneca's Selumetinib, in Phase III trials as single agent for the treatment of N-Ras mutated advanced melanoma (like Novartis' MEK162), and other compounds in earlier stage of development, such as Merck's Pimasertib, Bayer's Refametinib, Pfizer's PD-325901, Takeda's TAK-733 and Wilex AG's WX-554.

35 Replies to question 58 of Q3 – Questionnaire on MEK and B-Raf inhibitors to Physicians; non-confidential minutes of a conference call with a Key Opinion Leader, 24 September 2014.

36 This would represent a significant loss of competition, as Novartis' B-Raf inhibitor used alone or in combination with Novartis' MEK inhibitor seems to be particularly promising. A Key Opinion Leader reported: "[…] *from the phase I trial (Kefford et al. ASCO, 2013) MEK162 and LGX818 seem to be the most interesting combination. By itself LGX818 seems to be the most potent B-Raf inhibitor with the least adverse effects, and the combination appears to have the best safety profile"* - non-confidential minutes of a conference call with a Key Opinion Leader, 03 September 2014.

the loss of a credible competitor. Furthermore, the Commission considers that the only other player that is currently on the market, Roche, would not exert sufficient competitive pressure on the merged entity post-Transaction.

(59) In light of the above and of all available evidence, the Commission concludes that the Transaction raises serious doubts as to its compatibility with the internal market as regards targeted therapies for the treatment of advanced melanoma because it would enable the merged entity to restrict competition through non-coordinated effects.

IV.2.2. Ovarian cancer

(60) Ovarian cancer is the fourth most common cause of cancer death in women. It forms in the tissue of the ovary, arising either from the cells on the surface of the ovary ("epithelial ovarian cancer"), which account for 90% of cases, or from other tissues within the ovary ("non-epithelial ovarian cancer").[37]

(61) Ovarian cancer is typically treated with surgery and platinum based-chemotherapy (such cisplatin or carboplatin) in combination with a taxane (like paclitaxel or docetaxel). The treatment of the patients is determined mainly according to the stage of the cancer and the grade of the tumour.[38]

(62) Novartis' MEK162 and GSK's Mekinist are currently in Phase III clinical studies for the treatment of low-grade serous carcinoma ("LGSC"), a rare type of ovarian cancer, which occurs in 10% of all ovarian patients.[39]

(63) In addition, GSK has another targeted therapy, Afuresertib (an AKT inhibitor), in Phase I/II clinical studies in combination with chemotherapy for the treatment of recurrent platinum-resistant ovarian cancer.

IV.2.2.1. *Market definition*

The Parties' views

(64) The Parties submit that the type of cancer for which a pipeline oncology pharmaceutical is being developed is an appropriate starting point for market definition. Other factors such as mechanism of action, intended line of treatment and the characteristics of the patient can also be relevant in assessing whether two products are substitutable and thus compete against each other. In particular, the Parties claim that targeted therapies used for treatment of a specific form of ovarian cancer may not prove effective in the treatment of LGSC (and vice versa) and may therefore not belong to the same product market.

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37 European Society for Medical Oncology, Clinical Practice Guidelines, "Ovarian Cancer: a guide for patients. Patient information based on ESMO clinical practice guidelines", page 3.

38 The current standard of care is represented by Roche's targeted therapy Avastin (*bevacizumab*) used either as a monotherapy in the maintenance setting or in combination with chemotherapy agents (carboplatin and paclitaxel) as second-line treatment for platinum-sensitive patients.

39 European Society for Medical Oncology, Clinical Practice Guidelines, "Newly diagnosed and relapsed epithelial ovarian carcinoma: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up", page 1.

(65) The Parties conclude that in this case it is not necessary to reach a clear view on market definition for targeted therapies for the treatment of ovarian cancer, as the Transaction would not raise any serious doubts as to its compatibility with the internal market.

Commission's assessment

(66) The Commission has not previously considered the relevant product market definition for pharmaceuticals treating ovarian cancer.

(67) In line with its previous practice and similarly to the assessment performed with reference to targeted therapies for the treatment of advanced melanoma (see Section IV.2.1), the Commission considers that the potential for pipeline pharmaceuticals to enter into competition with other products which are either on the market or at the development stage should be assessed by reference to their characteristics and intended therapeutic use.[40]

(68) As long as R&D is assessed in terms of importance not only for existing, but also for future markets, the relevant product market can, by their very nature, be left open. In particular, the Commission considers that the product market definition for pipeline pharmaceuticals can be guided primarily by the characteristics of future products as well as by the indications to which they are to be applied.[41]

(69) A Key Opinion Leader indicated that low-grade serous ovarian cancer is morphologically different from high-grade serous ovarian cancer ("HGSC"). The biology of the disease is routinely tested with immunohistochemistry.[42]

(70) The Commission considers that it is not necessary to reach a definite conclusion on whether ovarian cancer should be further segmented and whether LGSC and HGSC belong to the same market, as the Transaction raises serious doubts as to its compatibility with the internal market irrespective of any possible market definition.

(71) As regards the geographic dimension of pipeline pharmaceuticals, in line with its previous practice, the Commission considers that since pipeline products need to be assessed with reference to the R&D in a given area and, to the extent R&D is normally global, the geographic scope of the market should be global or at least EEA-wide.[43]

Conclusion

(72) In light of the above and all available evidence, in this case, the Commission will carry out its competitive assessment assuming that the relevant product and geographic market is the global or at least EEA-wide market for targeted therapies for the treatment of ovarian cancer.

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40 Commission decision of 17 July 2009 in case M. 5476 – *Pfizer/Wyeth*, paragraphs 15 to 16, Commission decision of 8 May 2000 in Case M.1846 – *Glaxo Wellcome/Smithkline Beecham*, paragraph 70 to 72.

41 Commission decision of 8 May 2000 in Case M.1846 – *Glaxo Wellcome/Smithkline Beecham*, paragraph 70 to 72.

42 Non-confidential minutes of a conference call with a Key Opinion Leader, 4 September 2014.

43 Commission decision of 17 July 1996 in Case M. 737 – *Ciba-Geigy/Sandoz*, paragraph 51.

IV.2.2.2. *Competitive assessment*

The Parties' views

(73) The Parties submit that GSK's Mekinist, which is undergoing Phase III clinical trials for the treatment of LGSC, should not be considered for the assessment of this Transaction, because Mekinist is trialled in an Investigator Sponsored Study ("ISS") sponsored by the National Cancer Institute ("NCI"), which is part of a US government agency.[44] An ISS is led by an external investigator, research institution or network, as opposed to clinical trial sponsored by a commercial entity, such as a pharmaceutical or a biotech company. In the ISS trialling Mekinist for LGSC, the external sponsor, not GSK, is accountable for all aspects of the study. As a consequence, the Parties did not provide any assessment between the potential overlap between the Parties' MEK inhibitors in the treatment of LGSC.

(74) Novartis further claims that the Transaction does not raise any serious doubts with respect to the targeted therapies for the treatment of ovarian cancer, since even if Novartis' and GSK's pipeline pharmaceuticals were to reach the market, they would not be substitutable, as Novartis' MEK162 […], while GSK's Afuresertib […].

(75) Finally, Novartis' and GSK's targeted therapies would face competition from existing products (such as Roche's Avastin) as well as from other pipeline pharmaceuticals which are in more advanced stages of development than the Parties' products.

Commission's assessment

(76) The Transaction creates a potential overlap in the market for targeted therapies in the treatment of LGSC, where Novartis' MEK162[45] and GSK's Mekinist are undergoing Phase III clinical study ("pipeline-to-pipeline").[46]

(77) The Commission considers the Mekinist ISS as relevant for the assessment of the Transaction, as, if the results of the Mekinist ISS were positive and the trial had been conducted and data collected by the NCI in compliance with the European Medecines Agency ("EMA") requirements to file for registration, GSK could enter into discussion with EMA in order to obtain market authorisation in the EEA on the basis of the ISS data. As a result, Mekinist could enter the market and compete with MEK162 as an alternative treatment for LGSC.

(78) The only competitor of the Parties for the treatment of LGSC is AstraZeneca, whose MEK inhibitor Selumetinib is in Phase II clinical studies.[47]

(79) The market investigation indicated that Novartis', GSK's and AstraZeneca's MEK inhibitors might play a significant role in the treatment of LGSC.[48]

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44 Novartis' response to question 40 of Commission request for information dated 9 September 2014.

45 The Phase III clinical study trialling MEK162 for LGSC ("MILO") is sponsored by Array Biopharmaceutical, Inc.

46 As regards MEK162 and GSK's Afuresertib, the Commission considers that the two products […] and […]. Therefore they would not this potential overlap would not discussed further.

47 https://clinicaltrials.gov/ct2/show/NCT00551070?term=selumetinib+ovarian&rank=1

48 Replies to question 39 of Q3 – Questionnaire on MEK and B-Raf inhibitors to Physicians.

(80) In addition, a Key Opinion Leader stated that "*compared to chemotherapy, MEK inhibitors and in particular MEK162 and trametinib (Mekinist, ndr) represent a promising treatment for LGSC*", as the use of Avastin is not a mainstream option for the treatment of LGSC, although Avastin could be prescribed also for this indication.[49]

(81) Therefore, the Transaction might lead to the reduction of available treatments for LGSC from 3 to 2 and remove the potential competitive constraint that MEK162 can exert on Mekinist, as Novartis would have reduced incentives to run significant costs to launch two products with similar characteristics.

Conclusion

(82) Absent the Transaction, Novartis and GSK's MEK inhibitors would likely have constrained each other in the potential market for targeted therapies for ovarian cancer. Based on the above, the Commission considers that the likely elimination of Novartis' pipeline MEK inhibitor following the Transaction will result in the loss of a credible competitor. Furthermore, there would not be any other player that would exert any competitive pressure on the merged entity post-Transaction.

(83) In light of the above and of all available evidence, the Commission concludes that the Transaction raises serious doubts as to its compatibility with the internal market as regards targeted therapies for the treatment of ovarian cancer because it would enable the merged entity to restrict competition through non-coordinated effects. .

IV.2.3. Innovation in the MEK and B-Raf inhibitors

(84) Both GSK and Novartis have ongoing Phase I and Phase II clinical trials to investigate the potential use of their MEK and B-Raf inhibitors, either as monotherapies or in combination, in a number of other types of cancer, notably colorectal cancer, non-small-cell lung cancer (NSCLC) and advanced melanoma brain metastases. Novartis also has an on-going Phase III clinical trial for the use of its MEK inhibitor in uveal melanoma.

IV.2.3.1. *Market definition*

The Parties' view

(85) The Parties submit that compounds in Phase I or Phase II clinical trials do not provide a reliable indicator of likely future market situations as it is extremely uncertain as to whether they will enter the market at all, and there is not necessarily clarity as to the indications or the lines of treatment for which the compounds would ultimately be approved.

(86) According to the Parties, uncertainty on the outcome of clinical research increases with the complexity of the drugs concerned. The lowest probability of success would be achieved by the category relating to “new molecular entities” which encompass cytokines, growth factors, enzymes, gene therapies and cell therapies. MEK and B-Raf inhibitors fall into this category.

(87) Similarly, the Parties submit that there is inherently likely to be a lower probability of success for those cancers that express a significant number of different mutations.

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49 Non-confidential minutes of a conference call with a Key Opinion Leader, 4 September 2014.

This is the case in cancers for which MEK and B-Raf inhibitors are currently being investigated, including colorectal cancer, non-small cell lung cancer, uveal melanoma and advanced melanoma brain metastases.

(88) The Parties claim that it is therefore not relevant to assess products at an earlier stage of development than Phase III of clinical trials, as these do not provide a reliable indicator of likely future market situations, given that it remains extremely uncertain whether they will enter the market at all.

Commission's assessment

(89) As preliminary remark, the Commission considers that a concentration may not only affect competition in existing markets, but also competition in innovation and new product markets.[50] This may be the case when a concentration concerns entities currently developing new products or technologies which either may one day replace existing ones or which are being developed for a new intended use and will therefore not replace existing products but create a completely new demand.[51] In principle, the effects of a concentration on competition in innovation in this type of situation may not be sufficiently assessed by restricting the assessment to actual or potential competition in existing product markets.[52]

(90) In the pharmaceutical industry, the process of innovation is structured in such a way that it is typically possible at an early stage to identify competing clinical research programs. Competing clinical research programs can be defined as R&D efforts aimed at developing substitutable products and having similar timing. The potential for such clinical research programs to deliver substitutable products should be assessed by reference to the products' characteristics and intended therapeutic use, in particular by reference to their mechanism of action and to the cancer types for which they are being investigated. For the purposes of this case, the timing of the clinical research programs should be assessed by reference to the Phases of the ongoing clinical trials.

(91) The Proposed Transaction would result in the Notifying Party retaining two pairs of MEK and B-Raf inhibitors, namely GSK' Mekinist and Tafinlar on the one hand and Novartis' MEK162 and LGX818 on the other hand. Evidence from the market investigation indicates that the Parties' clinical research programs with MEK and B-Raf inhibitors are based on the same mechanisms of action, are expected to address similar unmet medical needs and are at similar stages of clinical development. Although there can be no certainty of this until the products reach the final stages of research, products resulting from such clinical research programs are likely to be substitutes to

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50 The "Guidelines on the assessment of horizontal mergers under the Council Regulation on the control of concentrations between undertakings" (HMG) state in paragraph 8 that through its control of mergers, the Commission prevents mergers that would be likely to deprive costumers from the benefits of competition, and expressly includes diminished innovation as one of the negative consequences of increased market power, together with higher prices, reduced output and lower quality and choice. (http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52004XC0205(02)&from=EN)

51 The HMG also state in paragraph 38 that effective competition may be significantly impeded by a merger between two important innovators.

52 "Guidelines on the applicability of Article 101 of the TFEU to horizontal co-operation agreements", paragraphs 119 to 122. Generally, this approach can be equally well applied to the case at hand. (http://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=OJ:C:2011:011:FULL&from=EN)

each other,. As explained by a Key Opinion Leader, *"GSK's and Novartis' B-RAF and MEK inhibitors seem very comparable."*[53] Moreover, clinical research programs are very likely to identify the same cancer types and same applications as promising areas of research and development. It can therefore be concluded that GSK's and Novartis' MEK and B-Raf research programs are competing clinical research programs at least in colorectal cancer, NSCLC and advanced melanoma brain metastases.

(92) Targeted molecular therapies, and in particular MEK and B-Raf inhibitors, are not the only mechanisms of action currently being trialled for their potential use in colorectal cancer, NSCLC, advanced melanoma brain metastases and uveal melanoma. Immunotherapies are also the object of intense clinical research efforts. Submissions received in the market investigation indicated that immunotherapies are mostly seen as complementary to targeted molecular therapies.[54] A competitor submitted that *"immunotherapy will more likely complement rather than substitute targeted therapies. More likely, initially targeted therapies and immunotherapies will be administered sequentially."*[55]A Key Opinion Leader explained that *"Anti-PD-1 [immunotherapies] and targeted therapies with small molecules will most likely be complementary: the checkpoint inhibitors ensure a long term disease control whereas targeted treatments are effective in shrinking the tumour"*, and expected *"the development of combination therapies with non-immunosuppressant targeted therapies and immunotherapies."*[56] On the basis of this evidence, the Commission concludes that clinical research programs involving MEK and B-Raf inhibitors are not competing with clinical research programs based on immunotherapies, and that they rather constitute complementary clinical research.

(93) As regards the geographic dimension of clinical research, in line with its previous practice, the Commission considers that since pipeline products need to be assessed with reference to the R&D in a given area and R&D is normally global, the geographic scope of the assessment of competition in innovation should at least be EEA-wide.[57]

Conclusion

(94) In light of the above, the Commission considers that the relevant competing clinical research programs in this case should be identified by reference to the mechanism of action of the pipeline products concerned, the cancer type for which the pipeline products are being trialled in clinical studies and the Phase of these clinical trials. Therefore, the competitive assessment will focus on competition in innovation concerning the development of MEK and B-Raf inhibitors for the treatment of colorectal cancer, NSCLC and advanced melanoma brain metastases.

IV.2.3.2. *Competitive assessment*

(95) The Parties are active in clinical research involving MEK and B-Raf inhibitors in at least four types of cancer, in addition to advanced melanoma and ovarian cancer.

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53 Non-confidential minutes of a conference call with a Key Opinion Leader, 6 October 2014.

54 Replies to question 15 of Q1 – Questionnaire on targeted therapies to Competitors.

55 Non-confidential minutes of a conference call with a competitor, 20 October 2014.

56 Non-confidential minutes of a conference call with a Key Opinion Leader, 23 October 2014.

57 Commission decision of 17 July 1996 in Case M. 737 – *Ciba-Geigy/Sandoz*, paragraph 51.

(96) Novartis' MEK inhibitor, MEK162, is undergoing clinical trials as monotherapy in colorectal cancer (Phase I/II), NSCLC (Phase II) and uveal melanoma (Phase III). Novartis' B-Raf inhibitor, LGX818, is undergoing clinical trials as monotherapy in colorectal cancer (Phase I/II) and NSCLC (Phase II). MEK162 and LGX818 are undergoing clinical trials as combination therapy in NSCLC (Phase II) and advanced melanoma brain metastases (Phase II).

(97) GSK's B-Raf inhibitor, Tafinlar, is undergoing clinical trials as monotherapy in colorectal cancer (Phase II), NSCLC (Phase II) and advanced melanoma brain metastases (Phase II). GSK's MEK inhibitor, Mekinist, is undergoing clinical trials in combination with Tafinlar in colorectal cancer (Phase II), NSCLC (Phase II) and advanced melanoma brain metastases (Phase II).

Table 2 – Competitive landscape for B-Raf and MEK clinical trials programs

	B-Raf inhibitor	**MEK inhibitor**	**B-Raf / MEK combination**
Colorectal cancer			
Novartis	Phase I/II	Phase I/II	
GSK			Phase II
NSCLC (lung cancer)			
Novartis	Phase II	Phase II	Phase II
GSK	Phase II		Phase II
Melanoma brain metastases			
Novartis			Phase II
GSK	Phase II		Phase II
Uveal melanoma			
Novartis		Phase III	

Source: Form CO.

(98) Therefore, the Transaction brings together clinical research programs currently pursued independently by GSK and Novartis and which involve products based on the very same mechanisms of action that are currently being trialled for use in the same types of cancer.

The Parties' view

(99) In the Parties' view, pipeline pharmaceuticals at such an early stage of development as Phase I and Phase II face considerable uncertainty as to their future clinical use and are not close to entering the market. The efficacy and safety of each product remains to be established. It is therefore difficult to predict in which disease or setting a pharmaceutical may ultimately be successful and it is far from certain whether the pharmaceuticals will achieve the clinical results necessary to obtain marketing authorisation in the EEA.

(100) On the basis of such uncertainty, the Parties conclude that the Transaction does not give rise to anti-competitive concerns in respect of pharmaceuticals for the treatment of colorectal cancer, NSCLC, advanced melanoma breast metastases or uveal melanoma.

Commission's assessment

(101) In a concentration involving pharmaceutical companies with competing clinical research programs, it must be analysed whether after the Transaction there will be a sufficient number of remaining clinical research programs.

(102) There is currently limited research capacity elsewhere that could deliver similar outcomes to the Parties' clinical research on MEK and B-Raf inhibitors. As the market investigation confirmed, only Roche has a pair of MEK and B-Raf inhibitors that could compete with the Parties' pairs of MEK and B-Raf inhibitors as combined therapies in these types of cancer. This is relevant because, as stated by a competitor, *"currently competition is more for BRAF and MEK inhibitors combined together than for BRAF inhibitors as monotherapies"*.[58]

(103) Roche is currently conducting only a Phase II clinical trial for its B-Raf inhibitor, Zelboraf, as monotherapy in colorectal cancer. No other clinical trial is being conducted involving Roche's MEK and B-Raf inhibitors, either as monotherapies or as combination therapy, in colorectal cancer, NSCLC, advanced melanoma brain metastases and uveal melanoma.

(104) Therefore, the transaction brings together under the Notifying Party's ownership two among the only three competing clinical research programs based on the MEK and B-Raf inhibitors and pursuing to serve the same unmet medical needs. This is likely to diminish competition in innovation by curtailing the Notifying Parties' R&D efforts. Pre-transaction each party's incentive to invest in its clinical research program was driven by the future sales that the programme was expected to generate, without consideration of the fact that it could also be expected to reduce future sales of competing clinical research programs. Post-transaction, the Notifying Party will internalise that investing in one of the clinical research programs can be expected to cannibalise future sales of its other clinical research program. In light of the few competing research programs in this area, the transaction is likely to significantly reduce the Notifying Party's incentive to continue investing substantial amounts in R&D on both MEK and B-Raf clinical research programs in parallel.[59]

(105) Pharmaceutical products based on different active principal ingredients are typically characterised by some degree of differentiation, for instance in terms of tolerability and safety profile for certain segments of patients. A common practice in oncology clinical research is to design late-stage clinical trials in order to obtain clinical evidence to support such differentiation and strategically position a product vis-à-vis its likely competitors in the market. Pre-transaction each party had an incentive to invest in this type of differentiation strategy to the extent that it was expected to provide some competitive advantage over its competitors, either regarding the entire potential patient population or regarding a specific segment of patients. Post-transaction, the Notifying Party could still have some incentive to develop two competing clinical research programs in parallel, provided that through differentiation it

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58 Non-confidential minutes of a conference call with a competitor, 17 October 2014.

59 The cannibalisation effect on expected sales in competition in innovation is very similar to the mechanism by which internalisation of cannibalisation effects on sales lead merging firms to unilaterally increase prices on existing products. Here firms internalise an expected effect on sales that will materialise in the future, and modify their conduct today by reducing R&D investments instead of raising prices.

could expect to attain additional overall sales to compensate and reward the incremental cost of running the second clinical research program. However, such incentives will be undermined compared to the pre-transaction situation by the internalisation of the expected sales-cannibalisation effect between the two competing clinical research programs. Hence, the transaction is also likely to significantly reduce the Notifying Party's incentive to continue investing substantially in R&D to pursue and differentiate the two MEK and B-Raf clinical research program in parallel.

(106) Given the more advanced stage of development of GSK's Mekinist and Tafinlar combination therapy for the treatment of advanced melanoma, the Notifying Party is likely to prioritise the development of a clinical research program for this pair of MEK and B-Raf inhibitors also in other types of cancer, either as monotherapies or as combination therapies. The competing clinical research program for Novartis' MEK162 and LGX818 is instead likely to be deprioritised by the Notifying Party, resulting either in the abandonment or at least in a significant reduction of its current R&D efforts.

(107) Respondents in the market investigation submitted that the incentives to pursue current clinical research efforts would be significantly reduced post-transaction, potentially leading to the abandonment of the clinical research for Novartis' MEK162 and LGX818. A Key Opinion Leader indicated that *"there is now little interest for Novartis to pursue research into their own B-RAF and MEK inhibitors"*, already envisaging that *"Novartis will simplify its pipeline"*, even *"terminating the program with its own B-RAF and MEK inhibitors"*.[60] [Description of further elements of the Commission's investigation supporting the Key Opinion Leader's statement.]

(108) Pipeline products at early stages of clinical development face higher uncertainty as to their future clinical use than pipeline products at advanced stages of development. However, the uncertainty about the outcome of on-going clinical research does not preclude an assessment of the likely effects of the Proposed Transaction on the development of such pipeline products. Whatever the level of uncertainty might be, a reduction in the efforts invested to bring forward a clinical research program can reasonably be expected to reduce its probability of success. Ultimately, the abandonment of an entire clinical research program for a certain product or products would have as necessary consequence the failure in bringing such products to the market.

(109) Respondents in the market investigation indicated that, despite the uncertainty on the future outcomes of on-going clinical trials, there are evidence-based expectations among the scientific community that MEK and B-Raf inhibitors will have a significant role in a number of cancer types in the next years. Most competitors in the oncology area indicated that MEK and B-Raf inhibitors are expected to play a role in a number of cancers, including colorectal cancer and NSCLC.[61] The same view is shared by most physicians surveyed in the context of the market investigation.[62] A Key Opinion Leader explained that *"already at this stage of the clinical studies, it is possible to say that treating CRC [colorectal cancer] patients with a B-RAF inhibitor alone is not as effective as treating them with B-RAF and MEK inhibitors combined, or B-RAF inhibitors plus EGFR inhibitors."*[63] Firms' incentives to further in-

60 Non-confidential minutes of a conference call with a Key Opinion Leader, 24 September 2014.

61 Replies to questions 16 of Q1 – Questionnaire on targeted therapies to Competitors.

62 Replies to questions 48 and 55 of Q3 – Questionnaire on MEK and B-Raf inhibitors to Physicians.

63 Non-confidential minutes of a conference call with a Key Opinion Leader, 6 October 2014.

vest in clinical research programs are grounded on these evidence-based expectations, taking also into account the uncertainty inherent to clinical research. The Proposed Transaction is likely to reduce the Notifying Party's incentives to further invest in clinical research for MEK162 and LGX818 due to its potential to cannibalise Mekinist and Tafinlar sales, not due to a change on the expectations about MEK162 and LGX818 clinical success.

(110) Reduced competition in innovation is likely to reduce the number of new products that will be developed for the same product market. This has two main consequences, both negative for patients and healthcare providers. First, as these products are expected to be demand substitutes to a significant extent, reduced competition in innovation is likely to result in a lessening of competition in future product markets and higher prices for patients and healthcare systems. Second, a lower expected number of differentiated products in future markets means reduced variety available to physicians and patients, for example in terms of tolerability and safety profile. Hence, some patients are likely to lose access to products better suited to their medical needs. Both negative effects are likely to be observed post-transaction, as the Notifying Party is likely to have reduced incentives to bring forward broad clinical research programs for the two pairs of MEK and B-Raf inhibitors in parallel.

(111) Moreover, the abandonment of a clinical research program for MEK162 and LGX818 would most likely have a negative impact on areas where GSK's and Novartis' clinical research programs do not currently compete. In uveal melanoma, for instance, Novartis currently sponsors a Phase III clinical trial for MEK162, while GSK has no on-going clinical trial. Although the Notifying Party could have an incentive to bring forward the clinical research in uveal melanoma, it is unlikely that the expected returns from the use of MEK162 in uveal melanoma could justify on their own the launch of the product. As noted by a Key Opinion Leader, *"as the disease is very rare, I do not expect many therapies to be developed in parallel since very few patients are available for clinical trials. Many companies also hesitate to pursue trials because there are few expected commercial benefits"*[64] from uveal melanoma. If post-Transaction the Notifying Party had instead an incentive to launch a clinical research line for Mekinist in uveal melanoma, this would anyway imply a substantial delay of several years, given the time that would be required to design and complete new clinical trials.

(112) The proposed concentration would hinder innovation by significantly reducing the Notifying Party's incentive to develop the broader clinical research program for LGX818 and MEK162, either as monotherapies or as combination therapies, for the various cancer types for which they are currently at early stages of clinical development and for potential further indications. Such cancer types include in particular colorectal cancer, NSCLC, advanced melanoma brain metastases and uveal melanoma.

(113) The reduced incentives that the Notifying Party would have post-Transaction to bring forward its current clinical research program for MEK162 and LGX818 would therefore result in a lower expected number of different MEK and B-Raf inhibitors being available to patients in a number of cancer types, notably colorectal cancer, NSCLC, advanced melanoma brain metastases and uveal melanoma. In most cases this would likely result in a restriction of the variety of MEK and B-Raf therapies

64 Non-confidential minutes of a conference call with a Key Opinion Leader, 24 October 2014.

available to physicians and patients, and in a lessening of competition in the concerned future markets. For some types of cancer, this could even result in a complete lack of available MEK and B-Raf therapies (e.g. uveal melanoma).

Conclusion

(114) In light of the above and of all available evidence, the Commission concludes that the Transaction raises serious doubts as to its compatibility with the internal market as regards the clinical development of B-Raf and MEK inhibitors for the treatment of colorectal cancer, NSCLC, advanced melanoma brain metastases and uveal melanoma because it would enable the merged entity to restrict competition through non-coordinated effects. .

IV.3. Other overlaps

(115) In addition to the B-Raf and MEK inhibitors, the Parties' activities overlap with regard to a number of cancer types:[65]

(a) Advanced renal cell carcinoma ("aRCC"): marketed / marketed overlap;

(b) Neuroendrocrine tumors of pancreatic origin ("pNET"): marketed / […] pipeline overlap;

(c) Breast cancer: marketed / phase III pipeline overlap;

(d) Leukaemia: marketed / phase III pipeline overlap;

(e) Multiple myeloma; phase III pipeline / phase II pipeline overlap.

IV.3.1. Product market definition

IV.3.1.1. *Advanced Renal Cell Carcinoma ("aRCC")*

Commission's precedents

(116) In its precedent decision,[66] the Commission considered the relevant product market to encompass the products used in all lines of treatment, based on the treatment of metastatic advanced renal cell carcinoma as a whole. Ultimately, however, the Commission concluded that the exact market definition could be left open.

The Parties' view

(117) The Parties consider that the treatment regimen for aRCC has considerably evolved since the Commission's investigation in 2009. Since then, an increased number of targeted therapies became available for the treatment of aRCC which has led to further product differentiation increasing the importance of lines of treatment and the mechanism of action. The results of clinical trials have influenced the specific clinical setting of each targeted therapy.

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65 The Parties have identified the treatment areas where one Party has a marketed or phase III pipeline oncology pharmaceutical and the other has at least a pipeline pharmaceutical in Phase I/II clinical trials.

66 Commission decision of 17 July 2009 in Case M.5476– *Pfizer/Wyeth*, paragraphs 24 to 26.

(118) The Parties submit that in most circumstances a physician would not consider a chemotherapy agent to be substitutable with a molecular targeted therapy.

(119) On the contrary, the Parties state that immunotherapies pharmaceuticals are likely to be substitutable with targeted therapies. Therefore it should not be differentiated between targeted therapies and immunotherapies for the treatment of aRCC.

Commission's assessment

(120) It can be derived from the results of the market investigation that prescribers distinguish between chemotherapy and targeted therapy for the treatment of aRCC.[67]

(121) Respondents in the market investigation also indicated[68] that prescribers distinguish between different lines of treatment for targeted therapies in aRCC and they generally follow the recommendation of the corresponding European clinical guidelines.[69] The lines of treatment for aRCC evolve over time, as new treatment methods are developed and the ways to use chemotherapy have shifted.

(122) Additionally, and contrary to what was submitted by the Parties, it can be derived from both physicians' and competitors' statements during the market investigation that the more novel immunotherapies are considered by a majority of prescribers and competitors as being complementary rather than substitutable to targeted treatments for aRCC.[70]

(123) Finally, it can also be derived from the results of the market investigation that national registration and national reimbursement rules for oncology drugs strongly in-

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67 Replies to question 14 of Q2 – Questionnaire on aRCC and NET: *"There is no chemotherpeutic agent available providing results comparable to tki in clearcell RCC."*; *"Totally different philosophy, mechanism of action and pattern of toxicity."; "So the therapies are not comparable in their management and side-effects."*; *"Multiple tumor and patient characteristics make it impossible to regard chemo- and targeted therapies as comparable."*

68 Published in 2014, Annals of Oncology 25 (Supplement 3): iii49–iii56.

69 Non-confidential minutes of a conference call with a Key Opinion Leader, 04 September 2014: *"There are several new agents for aRCC treatment that are already marketed. The first line of treatment comprises: Votrient (pazopanib) by GSK, Sutent (sunitinib) by Pfizer and Torisel (temsirolimus) also by Pfizer. Sunitinib and pazopanib are prescribed for good and intermediate condition patients whilst temsirolimus is for patients with a poorer condition (5-10% of the patients). These three agents have different side effects profiles. (3)The second line of treatment comprises: Afinitor (everolimus) by Novartis, Inlyta (axitinib) by Pfizer and Nexavar (sorafenib) by Bayer. Axitinib is registered with the EMA only following sunitinib as first-line treatment (this is how the trial was designed). In the UK, NICE went beyond and allowed axitinib second-line regardless of the first-line treatment, but the product was used for limited number of patients (only 26 in the UK). Everolimus has been authorised and used since 2007."* Non-confidential minutes of a conference call with a Key Opinion Leader, 5 November 2014: *"Il existe différentes lignes de traitement pour le cancer du rein."*

70 Non-confidential minutes of a conference call with a competitor, 20 October 2014: "*Immunotherapy will more likely complement rather than substitute targeted therapies.*", and non-confidential minutes of a conference call with a Key Opinion Leader, 23 October 2014: *"Anti-PD-1 and small molecules will most likely be complementary."*

fluences the prescription behaviour. For instance, the use of Afinitor (*everolimus*) in first line is not possible in Poland due to the national Polish label of this product.[71]

Conclusion

(124) In the present case, the exact definition of the product market regarding targeted therapies for aRCC, and in particular whether a distinction should be made according to the lines of treatment and whether immunotherapies should be included in this market, can be left open as the Transaction, as set out in [the competitive assessment part], does not raise serious doubts as to its compatibility with the internal market under any plausible market definition.

IV.3.1.2. *Neuroendrocrine Tumors of pancreatic origin ("pNET")*

Commission's precedents

(125) The Commission has so far neither assessed the treatment of Neuroendrocrine Tumors of pancreatic origin nor of any other neuroendocrine tumors ("other NET").

The Parties' view

(126) The Parties propose to base the product market definition on the relevant cancer type.[72] In addition, they consider that for defining the product market for the current generation of oncology pharmaceuticals and pipeline pharmaceuticals factors such as line of treatment, form of administration and mechanism of action have to be taken into account, which can have a greater or lesser bearing in each instance.[73]

(127) The Parties submit that in most circumstances a physician would not consider a chemotherapy agent to be substitutable with a molecular targeted therapy.

(128) Due to the small incidence of pNET and the relatively few targeted therapies presently approved, the Parties state that there is currently no distinction between lines of treatment for pNET. The Parties consider that, as more pharmaceuticals are approved and more clinical trials are conducted with respect to the treatment of pNET, the most efficacious sequencing patterns will be identified. Ultimately, the Parties submit that the market for the treatment of pNET does not need to be defined for this case, as no competition concerns arise.

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71 Replies from several Key Opinion Leaders to questions 4.1, 5, and 7 of Q2 - Questionnaire on aRCC and NET: "*We do not use some therapies for certain categories of patients. We have to use drugs according to registration in our country afinitor not possible as first line in PL (not allowed, although medically possible for certain patients)*"; "*None of my patients is treated with pazobanib third (or subsequent) line since it is not allowed by the IT label of the drug (not to take into account the lack of data in these settings).*"; "*Our choice depend on the reimbursement policy in BE and we would like to have more choice between drugs undistinguishing the line but how patient would respond or tolerate it.*"

72 Commission decision of 17 July 2009 in Case M.5476– *Pfizer/Wyeth*, paragraphs 24 to 26.

73 Commission decision of 8 May 2000 in Case M.1846 - *Glaxo Wellcome/Smithkline Beecham*, paragraph 212 to 213.

Commission's assessment

(129) It can be derived from the responses in the market investigation that prescribers distinguish between chemotherapy and targeted therapy for the treatment of pNET and other NET.[74]

(130) Furthermore, the replies to the market investigation indicate that, contrary to the Parties' view, prescribers distinguish between different lines of treatment for targeted therapies in pNET,[75] in line with the clinical guidelines.

(131) The replies of the competitors support the importance of both guidelines and clinical studies for oncologists active in pNET treatment. Prescribers expect to use Afinitor and Votrient (*pazopanib*) […].[76]

(132) The responses in the market investigation from both competitors[77] and prescribers indicate that for other NET, since there are currently no targeted therapies marketed, prescribers use – off-label – the targeted treatments, in the same way as they do for the treatment of pNET, basing themselves on the results of clinical trials (such as RADIANT 4, SUNLAND, BETER, LUNA studies).[78]

Conclusion

(133) In the present case, the exact definition of the product market for the treatment of pNET and other NET, and in particular whether a distinction should be made according to the lines of treatment, can be left open as the proposed transaction does not raise serious doubts as to its compatibility with the internal market under any plausible market definition, as set out below.

IV.3.1.3. *Breast Cancer*

The Parties' view

(134) Breast cancer is the most common tumour type diagnosed in women in the EU, remaining the second-leading cause of cancer-related death. The Commission has not previously considered the appropriate market definition for pharmaceuticals treating breast cancer.

(135) The Parties first note that the generic term "breast cancer" covers a number of specific types of cancer that affect the breast. For the purposes of treatment by molecular targeted therapies, breast cancers can be broadly categorised as follows:

(a) breast cancers that over-express the protein human epidermal growth factor receptor 2 ("**HER2+**", HER2 positive) and those that do not ("**HER2-**", HER2 negative);

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74 Replies to question 14 of Q2 – Questionnaire on aRCC and NET: "*Because we don´t have any study that compare chemotherapy vs targeted therapies in this setting (advanced pNETs)*"; "*Chemotherapy has little impact on RCC and NET.*"; "*Chemotherapy is highly toxic and marginally effective in well-differentiated NET.*"

75 Replies to question 9 of Q2 – Questionnaire on aRCC and NET to prescribers.

76 Non-confidential minutes of a conference call with a Key Opinion Leader, 23 October 2014.

77 Replies to question 38 of Q1 – Questionnaire on Competitors targeted therapies.

78 Replies to questions 12 and 13 of Q2 – Questionnaire on aRCC and NET.

(b) breast cancers that over-express hormone receptors ("**HR+**") and those that do not ("**HR-**").

(136) The Parties are not aware of the precise proportional split in the EEA for each of these types of breast cancer. Data is, however, available in the United States at this level of granularity and the Parties consider that this US data represents an accurate proxy for the EEA:

Table 3: Breast cancer type at the time of diagnosis in the US

Type	Proportion of overall breast cancer patients
HR+ / HER2+	10%
HR+ / HER2-	73%
HR- / HER2+	5%
Triple negative (HR- / HER2-)	12%
Unknown	12%

Source: Form CO.

(137) The Parties submit that a product market definition encompassing all "breast cancer" pharmaceuticals would not be appropriate for either existing markets or future market situations, since pharmaceutical indications and clinical guidelines segment breast cancer patients by whether patients are: (i) HER2+ or HER2-; and/or (ii) hormone receptor positive (HR+) or negative (HR-); or (iii) neither HER2+ nor HR+.

(138) The Parties further submit that the relevant market definition for the treatment of advanced HER2+ breast cancer can be further delineated by line of treatment, since the treatment regimen for advanced HER2+ breast cancer is highly developed with indications and clinical guidelines for pharmaceuticals treating advanced HER2+ breast cancer generally specifying the particular clinical setting in which pharmaceuticals should be used distinguishing between, stage, line of treatment and, in certain cases, the sequencing and combinations of different targeted therapies.

(139) The Parties' activities concern two situations:

(a) first, GSK's Tyverb is indicated and Novartis' Afinitor is in Phase III clinical trials for advanced HER2+ breast cancer;

(b) second, Novartis' Afinitor is also indicated for advanced HER2-/HR+ breast cancer.

Commission's assessment

(140) The current European clinical guidelines on advanced breast cancer distinguish between treatment for advanced HER2+ breast cancer on the one hand, and advanced HER2-/HR+ breast cancer on the other hand, highlighting in particular that: "*treatment choice should take into account at least these factors: HR and HER-2 status […]*".[79]

79 These Guidelines were developed by the European School of Oncology "ESO" and by the European Society for Medical Oncology "ESMO" and are published simultaneously in The Breast (The Breast 2014, http://dx.doi.org/10.1016/j.breast.2014.08.009) and Annals of Oncology (Ann Oncol 2014;25: http://dx.doi.org/10.1093/annonc/mdu385).

(141) This is confirmed by Key Opinion Leaders in advanced breast cancer. One indicated that "*there are 4 types of breast cancer: HER2+ / HR+, HER2+ / HR-, HER2- / HR+, HER2- / HR- (triple negative)*"[80] and that "*for HER2+, it is not usual to make a distinction between HR+ and HR- so far*",[81] while another further specified that "*this is relevant as regards treatment*".[82]

(142) Finally, the indications for the Parties' compounds respect this segmentation. Indeed, Afinitor is indicated for "the treatment of hormone-receptor-positive, HER2/neu-negative[83] advanced breast cancer, in combination with exemestane, in post-menopausal women without symptomatic visceral disease after recurrence or progression following a non-steroidal aromatase inhibitor" (emphasis added), while Tyverb is indicated for "*the treatment of patients with breast cancer, whose tumours overexpress HER2*" (emphasis added).

Conclusion

(143) In light of the above, the Commission takes the view that, for the purpose of market definition regarding targeted therapies, a distinction should be made between advanced HER2+ breast cancer and advanced HER2-/HR+ breast cancer. In the present case, the exact definition of the product market, and in particular the need to distinguish between lines of treatment, can be left open as the proposed transaction does not raise serious doubts as to its compatibility with the internal market under any plausible market definition.

IV.3.1.4. *Leukaemia*

The Parties' view

(144) Leukaemias are a heterogeneous group of disorders relating to the precursor cells in the bone marrow that eventually become blood cells. Leukaemias can be classified into lymphocytic leukaemias which relate to the precursor cells to lymphocytes (also known as "white blood cells"); and myelogenous leukaemias which relate to the precursor cells to the other blood cells (e.g. "red blood cells"). Each of the lymphocytic leukaemias and myelogenous leukaemias has different subtypes of chronic and acute leukaemia, with different levels of cell development. On this basis, from a medical perspective, it is possible to identify four broad categories of leukaemias:[84]

(a) acute myeloid leukaemia ("**AML**");

(b) acute lymphoblastic leukaemia ("**ALL**");

(c) chronic myelogenous leukaemia ("**CML**"); and

(d) chronic lymphocytic leukaemia ("**CLL**").

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80 Non-confidential minutes of a conference call with a Key Opinion Leader, 11 September 2014.

81 Non-confidential minutes of a conference call with a Key Opinion Leader, 11 September 2014.

82 Non-confidential minutes of a conference call with a Key Opinion Leader, 3 September 2014.

83 The protein HER2 is also referred to as HER2/neu.

84 In case M.5999 – *Sanofi/Genzyme*, the Commission has previously considered market definitions for pharmaceuticals used for the treatment of leukaemia. It examined the markets for the treatment of leukaemia, the treatment by type of leukaemia, or by therapeutic class, while ultimately leaving the exact product market definition open.

(145) The Parties submit that the appropriate market definition should, at least, distinguish between pharmaceuticals for the treatment of ALL, CLL, AML and CML, given that a physician's first step is to categorise the leukaemia of the patient in question as one of AML, ALL, CML or CLL (or indeed a subtype of one of them).

(146) The Parties further claim that their respective pharmaceuticals (marketed or pipeline) for the treatment of leukaemia are indicated to treat different types of leukaemias.

Commission's assessment

(147) There are three current European clinical guidelines on leukaemias: one for AML,[85] one for CLL[86] and one CML[87] (the guidelines do not cover ALL).

(148) The indications for the Parties' compounds respect this segmentation. Indeed, GSK's Arzerra is indicated for the treatment of "*chronic lymphocytic leukaemia (CLL) in patients who are refractory to fludarabine and alemtuzumab*" (emphasis added), while Novartis' Glivec is indicated for various types of CML and ALL[88] and Novartis' Tasigna is indicated for "*adult patients with newly diagnosed Philadelphia-chromosome-positive chronic myelogenous leukaemia (CML) in the chronic phase*" (emphasis added).

(149) This is confirmed by a competitor, which provides "*market shares for [the competitor's targeted therapy] MabThera and [GSK's targeted therapy] Arzerra for the treatment of CLL in Europe*".[89]

Conclusion

(150) In light of the above, the Commission takes the view that, for the purpose of market definition regarding targeted therapies, a distinction should be made between the four types of leukaemias (AML, ALL, CML, CLL). In the present case, the exact definition of such product markets, and in particular the need to distinguish between lines of treatment, can be left open as the proposed transaction does not raise serious doubts as to its compatibility with the internal market under any plausible market definition.

IV.3.1.5. *Multiple myeloma*

The Parties' view

(151) Multiple myeloma is a cancer of the plasma cell characterised by excessive numbers of abnormal plasma cells in the bone marrow. The Parties submit that multiple mye-

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85 Published in 2013 – Ann Oncol 2013; 24 (Suppl 6): vi138-vi143.

86 Published in 2011 – Ann Oncol 2011; 22 (Suppl 6): vi50-vi54.

87 Published in 2012 – Ann Oncol 2012; 23 (Suppl 7): vii72-vii77.

88 Glivec is indicated for, *inter alia*, the treatment of "*adult and paediatric patients with newly diagnosed Philadelphia-chromosome (bcr-abl)-positive (Ph+) chronic myeloid leukaemia (CML) for whom bone-marrow transplantation is not considered as the first line of treatment; adult and paediatric patients with Ph+ CML in chronic phase after failure of interferon-alpha therapy, or in accelerated phase or blast crisis; adult and paediatric patients with newly diagnosed Philadelphia-chromosome-positive acute lymphoblastic leukaemia (Ph+ ALL) integrated with chemotherapy; adult patients with relapsed or refractory Ph+ ALL as monotherapy*" (emphasis added).

89 Non-confidential minutes of a conference call with a competitor, 17 October 2014.

loma is divided into asymptomatic multiple myeloma and symptomatic multiple myeloma. For asymptomatic multiple myeloma, no treatment is currently recommended. Symptomatic multiple myeloma appears when the patient starts to develop symptoms, and the patient's treatment will vary depending on eligibility for stem cell transplantation ("SCT").

Commission's assessment

(152) In the present case, regarding targeted therapies for multiple myeloma, the exact definition of the product market, and in particular the need to distinguish between subtypes of multiple myeloma and/or lines of treatment, can be left open as the proposed transaction does not raise serious doubts as to its compatibility with the internal market under any plausible market definition.

IV.3.2. Geographic market definition

(153) The Commission has previously found that the relevant geographic market for marketed originator pharmaceuticals is national in scope.[90] The Notifying Party does not contest this.

(154) In the present case, the exact definition of the geographic market for targeted therapies for advanced renal cell carcinoma, neuroendocrine tumours of pancreatic origin, breast cancer, leukaemia and multiple myeloma can be left open as the proposed transaction does not raise any competitive concern under any plausible geographic market definition.

IV.3.3. Competitive assessment

IV.3.3.1. *Advanced Renal Cell Carcinoma ("aRCC")*

(155) Both Parties, along with Pfizer, Roche and Bayer, market targeted therapy drugs for the treatment of aRCC. GSK's Votrient is approved for the first line of treatment and Novartis' Afinitor is approved for the second or later lines of treatment:

Table 4 - Marketed targeted therapies for the treatment of aRCC

Line of treatment	Company	Product
First	**GSK**	Votrient (*pazopanib*)
	Pfizer	Sutent (*sunitinib*) Torisel (*temsirolimus*)
	Roche	Avastin (*bevacizumab*)
Second/later	**Novartis**	Afinitor (*everolimus*)
	Pfizer	Inlyta (*axitinib*)
	Bayer	Nexavar (*sorafenib*)

Source: Form CO.

The Parties' view

90 Commission decision of 19 December 2008 in Case M.5295 – *Teva/Barr*, paragraph 19.

(156) The Parties submit that their products are authorised for use in different lines of treatment. Votrient is indicated in the EEA for first-line treatment of aRCC, while Afinitor is only approved for second- or later-line treatment.[91] This position is also reflected in Afinitor's Summary of Product Characteristic published by the EMA.

(157) Overall, the Parties submit that Afinitor and Votrient are not substitutable for the treatment of aRCC.

Commission's assessment

(158) Both the physicians and the competitors stated that Votrient and Afinitor are prescribed in different lines of treatment and are therefore not considered to be substitutable.

(159) In their replies to the market investigation, the physicians pointed out that negative results of clinical studies, such as the RECORD-3 study with regard to Afinitor used in first line of treatment or the lack of scientific data with regard to use Votrient in second line of treatment confirm that the two drugs are to be used in different lines.[92] The physicians mention in their replies that a very limited number of patients (up to 5%) receive Votrient after having received Sutent. Such a sequence is caused by toxicity problems of patients with Sutent and not by cancer progression.[93]

(160) Derived from the considerations above, it can be concluded that, if the market were to be defined along lines of treatment, no competition concerns arise, because Afinitor and Votrient are used in different lines for the treatment of aRCC.

(161) Turning to the possible market including all marketed therapies for the treatment of aRCC, it can be derived from the results of the market investigation that for the market of targeted treatments for aRCC, the notified transaction would reduce the number of major competitors from three to two. Novartis, GSK and Pfizer represent together almost the entirety of the market. Indeed, the most prescribed treatments are Votrient and Sutent in first line, and Afinitor and Inlyta (a*xitinib*) in second/later lines, with Avastin (*bevacizumab*), Torisel (*temsirolimus*) and Nexavar (*sorafenib*) having much smaller market shares.

(162) The Parties have provided market share data (volume) of 2013 for the five main national EEA markets. While market share data from other EEA countries was not

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91 After the use of a VEGF-targeted therapy such as Votrient.

92 Replies to questions 5 and 6 of Q2– Questionnaire on aRCC and NET: "*None of my patients is treated with everolimus first line, especially after neg. results of RECORD-3 study. None of my patients is treated with pazobanib second line due to lack of scientific data, even though in IT is it theoretically possibly for patients intolerant to first line sunitinib*"; non-confidential minutes of a conference call with Key Opinion Leader, 4 September 2014: "*Votrient (pazopanib) and Afinitor (everolimus) can be considered for the same patient in different lines of treatment, but these options are not exhaustive.*"; Non-confidential minutes of a conference call with Key Opinion Leader, 23 October 2014: "*Pazopanib or sunitinib (first line) and everolimus or axitinib (second line) are the options for this type of cancer.*"

93 Replies to question 6 of Q2– Questionnaire on aRCC and NET: "*I never use pazobanib as second line except of a switch from sunitinib for toxicity, ca 5% of patients.*"; non-confidential minutes of a conference call with a Key Opinion Leader, 5 November 2014: "*Il est également possible d'administrer Votrient avant Afinitor, mais uniquement en cas d'effets secondaires trop importants dus à la toxicité de Sutent (il ne s'agit donc pas d'un traitement de deuxième ligne à proprement parler).*"

available, the data presented represents together [a majority] of the Parties' sales for the treatment of aRCC.[94]

Table 4 – Market shares by volume of the Parties in value for targeted therapies for the treatment of aRCC in the five main national countries, 2013

	Afinitor (*everolimus*) **Novartis**	Votrient (*pazopanib*) **GSK**	**Combined share**
France	[0-5]%	[0-5]%	[0-5]%
Germany	[15-20]%	[25-30]%	[40-45]%
Italy	[15-20]%	[30-35]%	[45-50]%
Spain	[5-10]%	[30-35]%	[40-45]%
UK	[5-10]%	[45-50]%	[55-60]%

Source: Form CO.

(163) While in four out of five EEA countries the combined market shares of the Parties are high, neither the physicians nor the competitors stated in their replies to the market investigation that Votrient and Afinitor are considered being closest competitors.

(164) It can be derived from the responses received in the market investigation that the competive pressure between Afinitor and Votrient is very limited. Competitors consider Sutent as the main competitor of Votrient in the first line and Inlyta and Nexavar as main competitors of Afinitor in the second or later lines of treatment.

(165) As submitted by the Parties,[95] Afinitor failed its Phase II "RECORD-2" and "RECORD-3" clinical trials as the first line treatment for aRCC. Accordingly, Novartis stopped to develop Afinitor as a first line aRCC treatment. The use of Afinitor as a first line of treatment would therefore be inconsistent with Afinitor's approved indication and clinical trial results.

(166) In addition, entry into the market for the treatment of aRCC requires approximately 10 years of development time until a marketing authorisation can be achieved. Nevertheless, several products received market authorisation in the last years: Nexavar (2006), Sutent and Torisel (2007), Afinitor (2009), Votrient (2010) and Inlyta (2012). After its market entry, Votrient constrained Sutent, because its market share increased while Sutent's decreased in [certain EEA markets] during that period. Furthermore, after its market entry Inlyta started to constrain Afinitor and increased its market shares while Afinitor's decreased.

(167) The Parties submit that this sequence of new products entering the relatively small market for the treatment of aRCC, which is considered a rarer cancer type, is an indicator of strong competition in this market. In addition, the Parties state that Inlyta was specifically brought to the market by Pfizer in order to compete with Afinitor in the second or later lines of treatment.

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94 In addition, the Parties submit that the market shares in the other EEA countries are of the same magnitude. In any event, even if this point was not verified, it would not materially alter the Commission's assessment, because, as laid out in this section, Votrient and Afinitor do not overlap with regard to the treatment of aRCC.

95 Reply of the Parties to question 14 of the request for information dated 9th September 2014.

(168) Finally, both Afinitor and Votrient are already approved for several other significantly larger cancer indications, where they do not overlap. When negotiating reimbursement conditions with national health authorities, it is not possible to price discriminate across indications. Accordingly, Novartis will have no ability or incentive to increase the price of Afinitor or Votrient with respect to aRCC.

Conclusion

(169) In light of the above and of all available evidence, the Commission concludes that the Transaction does not raise serious doubts as to its compatibility with the internal market as regards targeted therapies for the treatment of aRCC.

IV.3.3.2. *Neuroendrocrine Tumors of pancreatic origin ("pNET")*

(170) Novartis currently markets Afinitor in the EEA which is indicated for the treatment of advanced pNET when the cancer cells are well or moderately differentiated (i.e. they have a similar appearance to normal pancreatic cells) and the cancer is progressing. Afinitor is indicated for use when the cancer is metastatic or when it cannot be surgically removed.

(171) GSK does not currently market any pharmaceuticals indicated for the treatment of pNET in the EEA. GSK's Votrient was placed in Phase II trials for the treatment of advanced pNET, […].

(172) For the treatment of pNET, Novartis currently has one marketed product, Afinitor. As was confirmed by the replies from the competitors to the market investigation,[96] next to Afinitor the only other targeted treatment which is marketed for the treatment of pNET is Pfizer's Sutent.

(173) GSK's Votrient is still undergoing clinical trials. It is currently in Phase II […]. In addition to GSK, other competitors have initiated clinical trials with their targeted therapies for the treatment of pNET. All these trials are currently no further than Phase II: Novartis with BKM120, Roche with Avastin, Bayer/Onyx with Nexavar and Pfizer with Torisel.

(174) The Parties submit that the potential entry into the market of Votrient remains inherently uncertain given the current state of clinical development. […]

(175) Even if Votrient will eventually obtain its market authorisation, it is likely that the competitive pressure between Afinitor and Votrient for the treatment of pNET would be limited, because [prescribers responding to the Commission's market investigation expect that Afinitor and Votrient will be used in different lines]. The responses received in the market investigation indicated that since Votrient is non-inferior but probably also not superior to Afinitor or Sutent, it was more risky for GSK to seek a broader approval (for which superiority against the existing standard of care would have to be proven) than pursuing an indication for later lines of treatment (where proof of efficacy will be sufficient).[97]

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96 Replies to question 35 of Q1 – Questionnaire Competitors targeted therapies.

97 Non-confidential minutes of a conference call with a Key Opinion Leader, 23 October 2014.

(176) With regard to a possible competition constraint posed to targeted therapies by immunotherapies, the majority of competitors stated in the market investigation that the position of immunotherapies for the treatment of pNET is still unclear.[98]

(177) For the treatment of other NETs**,** there are no targeted therapies marketed. Afinitor is in phase III clinical trials (RADIANT-4), while Votrient is in investigator sponsored phase II clinical trials.[99] […]

(178) In addition, both Afinitor and Votrient are already approved for several other, significantly larger cancer indications, where they do not overlap. When negotiating reimbursement conditions with national health authorities, it is not possible to price discriminate across indications. Accordingly, Novartis will have no ability or incentive to increase the price of Afinitor or Votrient with respect to pNETs (or other NET).

Conclusion

(179) In light of the above and of all available evidence, the Commission concludes that the Transaction does not raise serious doubts as to its compatibility with the internal market as regards targeted therapies for the treatment of pNET and other NETs.

IV.3.3.3. *Breast Cancer*

The Parties' view

(180) The Parties submit that the only potential overlap arises regarding targeted therapies for HER2+ breast cancer, where:

(a) GSK's Tyverb is approved for second or later lines of treatment;

(b) Novartis' Afinitor is in two phase III clinical trials (Bolero 1 for first line of treatment and Bolero 3 for second or later lines of treatment).

(181) During the investigation, Novartis indicated to the Commission that based on recent negative results stemming from Bolero 1 and Bolero 3 […].[100]

98 Replies to question 41 of Q1 - Questionnaire Competitors targeted therapies.

99 Investigator sponsored trials are trials, where the Sponsor is not a privately owned cooperation, but a physical person (physician, nurse, dentist, or other health professional) or a "not-for-profit organization", which can be a governmental body (for example, the National Institute of Health), a public institution (hospital, University, a trust), or a research group.

100 Email of [Novartis' external counsel] to the case team, 15 December 2014.

Commission's assessment

(182) In light of […] regarding Bolero 1 and Bolero 3 clinical trials, it is very unlikely that Afinitor would be […] approved in Europe, for the treatment of HER2+ advanced breast cancer.

(183) The lack of relevance of Afinitor regarding HER2+ advanced breast cancer was confirmed by Key Opinion Leaders. Regarding the Bolero 3 clinical trial, one indicated that "*data are weak, and do not seem to lead to a major advance in the treatment of HER2+ patients*",[101] while another suggested that "*more randomized studies would be needed to support a change in the standard treatment*".[102] Finally, another confirmed that "*by now, everolimus [Afinitor] has no role as standard treatment of metastatic HER2+ breast cancer*".[103]

(184) In light of the above, the Commission takes the view that the Parties' activities are not materially overlapping regarding targeted therapies for the treatment of advanced HER2+ breast cancer.

Conclusion

(185) In light of the above and of all available evidence, the Commission concludes that the Transaction does not raise serious doubts as to its compatibility with the internal market as regards targeted therapies for the treatment of breast cancer.

IV.3.3.4. *Leukaemia*

The Parties' view

(186) The Parties submit that their activities do not overlap since their respective pharmaceuticals (marketed or pipeline) for the treatment of leukaemia are indicated to treat different types of leukaemia.

(187) Nonetheless, the Parties list the following molecular targeted therapies for the treatment of CLL:

101 Non-confidential minutes of a conference call with a Key Opinion Leader, 5 September 2014.

102 Non-confidential minutes of a conference call with a Key Opinion Leader, 11 September 2014.

103 Non-confidential minutes of a conference call with a Key Opinion Leader, 3 September 2014.

Table 5 – Marketed and late stage pipeline molecular targeted therapies for the treatment of CLL

Product	Manufacturer	Status
MabThera (*rituximab*)	Roche	Approved
Arzerra	GSK	Approved
Gazyvaro	Roche	Approved
Zydelig	Gilead	Approved
Imbruvica	Johnson & Johnson	Approved
RG7601/ABT-199	Roche	Phase III
***Rituximab* biosimilars**[104]		
Rituximab	Pfizer	Phase III
	Boehringer Ingelheim	
	Celltrion	
	Amgen	
	Novartis[105]	

Source: Form CO.

(188) A potential overlap might arise regarding targeted therapies for the treatment of CLL between GSK's Arzerra and Novartis' biosimilar *rituximab*. The Parties claim that, as a biosimilar version of MabThera, Novartis' biosimilar will, if approved, be MabThera's closest competitor along with the other *rituximab* biosimilars in development. Indeed, it is expected that Roche's MabThera and the *rituximab* biosimilars will share the same clinical attributes and so should be wholly interchangeable from a clinical perspective.

Commission's assessment

(189) GSK's Arzerra is used infrequently for the treatment of CLL, with 2013 national shares below [10-15]% expect for Austria ([10-15]%), Denmark ([10-15]%) and Greece ([15-20]%). This is confirmed by Roche, which indicates that for the treatment of CLL in "*region Europe (22/28 countries)*", MabThera had a [95-100]% market share in 2013 and [95-100]% in H1 2014, and Arzerra had a [0-5]% market share in 2013 and [0-5]% in H1 2014. A Key Opinion Leader also stated that "*MabThera has a much stronger position than Arzerra and Gadzyva. […] MabThera is a success story and it is difficult for other drugs such as Arzerra or Gadzyva to replace it*".[106]

(190) Furthermore, the market investigation confirmed that Arzerra and Novartis' pipeline biosimilar *rituximab* are not the closest competitors:

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104 According to the Parties, MabThera's exclusivity is reported to have expired in late 2013 in the EU, and a number of pharmaceutical companies are working on a biosimilar (generic) version of MabThera (*rituximab*).

105 Through its subsidiary Sandoz.

106 Non-confidential minutes of a conference call with a Key Opinion Leader, 16 October 2014.

(a) […];[107]

(b) a Key Opinion Leader stated that "*MabThera's patent is expiring in the EU. Biosimilars are expected to penetrate the market and will constitute alternatives treatments to MabThera*";[108]

(c) the EMA indicated that "*for CLL, the majority of established combination regimens for first-line therapy include MabThera (rituximab) produced by Roche. Up to EMA's knowledge, there are around 16 companies currently developing rituximab biosimilars*".[109]

(191) If approved, Novartis' biosimilar *rituximab* is therefore likely to be a closer competitor to Roche's MabThera than to GSK's Arzerra.

(192) Therefore, the Commission takes the view that, even though Novartis' biosimilar *rituximab* and GSK's Arzerra would be both targeting CLL, they are not close competitors.

Conclusion

(193) In light of the above and of all available evidence, the Commission concludes that the Transaction does not raise serious doubts as to its compatibility with the internal market as regards targeted therapies for the treatment of leukaemia.

IV.3.3.5. *Multiple myeloma*

The Parties' view

(194) The Parties list the following molecular targeted therapies currently approved, in phase III or phase II clinical trials for the treatment of multiple myeloma:

Table 6 – Marketed and pipeline molecular targeted therapies for the treatment of multiple myeloma

Product	Manufacturer	Status
Velcade	Takeda	Approved
LBH589	Novartis	Phase III
HuLuc63	BMS	Phase III
HuMax-CD3	Janssen	Phase III
Zelboraf	Roche	Phase II
GSK2110183	GSK	Phase II

(195) The Parties submit that, while Novartis' LBH589 is in phase III clinical trials, GSK's GSK2110183 is only in phase II trials to investigate safety and clinical activity. Furthermore, should some or all of the Parties' pipeline pharmaceuticals ultimately

107 Novartis' internal document, […], 13 May 2014. Annex 26 to the Form CO.

108 Non-confidential minutes of a conference call with a Key Opinion Leader, 16 October 2014.

109 Non-confidential minutes of a conference call with the EMA, 9 October 2014.

reach the market, the Parties argue that they would not be considered substitutable as they have very different mechanism of actions and will likely be used in different lines of treatment.[110]

Commission's assessment

(196) Regarding LBH589, Novartis announced on 6 November 2014 that "*the US Food and Drug Administration's (FDA) Oncologic Drugs Advisory Committee (ODAC) did not recommend the investigational compound LBH589 (panobinostat), […] for patients with previously treated multiple myeloma*". This announcement increases the uncertainty regarding a potential approval of LBH589 for multiple myeloma in the US, and consequently in the EEA. Furthermore, a Key Opinion Leader stated that "*in the field of multiple myeloma Novartis and GSK have different portfolios and the transaction does not present any negative impact on competition*".[111]

Conclusion

(197) In light of the above and of all available evidence, the Commission concludes that the Transaction does not raise serious doubts as to its compatibility with the internal market as regards targeted therapies for the treatment of multiple myeloma.

IV.4. Conclusion on competitive assessment on targeted therapies

(198) In light of the above, the Commission concludes that the Transaction raises serious doubts as to its compatibility with the internal market with respect to targeted therapies, namely B-Raf and MEK inhibitors for the treatment of advanced melanoma, ovarian cancer, and other types of cancer.[112]

V. CHEMOTHERAPIES

(199) The Transaction creates horizontal overlaps on the market for mature oncology products used in the chemotherapy treatment, where both GSK and Novartis, *via* its generic division – Sandoz – are active.

(200) The Parties' activities overlap with respect to the following molecules:

(a) GSK commercialises the originator drug based on the *topotecan* molecule under the brand name of *Hycamtin* in the EEA. Sandoz commercializes a generic version of *topotecan*. *Topotecan* is a chemotherapeutic agent primarily used in the treatment of metastatic ovarian cancer as a monotherapy, small lung cancer as a monotherapy and in cervical cancer as a combination therapy together with *cisplatin*;

(b) GSK commercialises the originator drug based on the *nelarabine* molecule under the brand name of *Atriance* in the EEA. In the EEA, *Atriance* is approved for the treatment of patients with T-cell acute lymphoblastic leukaemia (T-ALL) and T-cell lymphoblastic lymphoma (T-LBL). Sandoz markets

110 GSK2110183 is an AKT inhibitor, whereas LBH589 is an HDAC inhibitor.

111 Non-confidential minutes of a conference call with a Key Opinion Leader, 30 October 2014.

112 Notably colorectal cancer, non-small-cell lung cancer, uveal melanoma and advanced melanoma brain metastases.

generic versions of treatments indicated for the treatment of T-ALL such as *methotrexate*, *cytarabine*, *doxorubicin* and *vincristine*;

(c) GSK commercialises the originator drug based on the *ondansetron* molecule under the brand name of *Zofran*, *Zydis*, *Zophren* or *Avessaron*, depending on the EEA country. Sandoz commercializes a generic version of *ondansetron*. *Ondansetron* is a serotonin antagonist used in the treatment of nausea and vomiting caused by chemotherapy, radiotherapy and surgery.

V.1. Market definition

V.1.1. Product market

(201) In its past merger decisions in the pharmaceutical sector, the Commission has referred to the third level (ATC3) of the European Pharmaceutical Market Research Association ("EphMRA") classification as the starting point for defining the relevant product market.[113] However, in a number of cases, the Commission found that the ATC3 level classification did not yield the appropriate market definition within the meaning of the Commission Notice on the Definition of the Relevant Market. As a result, where appropriate and based on the factual evidence collected during the market investigation, the Commission has defined the relevant product market at the ATC4 level or at a level of molecule or a group of molecules that are considered interchangeable so as to exercise competitive pressure on one another. The overlap in therapeutic uses does not necessarily imply any particular economic substitution patterns between products.

(202) The Parties submit that for the mature oncology pharmaceuticals, such as chemotherapy products, a market definition based on an ATC3 level would not be appropriate, and that the market should be analysed at ATC4 or molecule level. The Parties further submit that for generic oncology products the market should not be defined by cancer type and line of treatment.

V.1.1.1. *Topotecan*

(203) *Topotecan* belongs to ATC3 class L1C (vinca alkaloids and other plant products), which is not further subdivided at ATC4 level.

(204) The Commission concluded, in a previous decision, that molecules *paclitaxel* and *docetaxel* are part of a separate market within L1C since hospitals which procure these products for chemotherapy treatment would not switch from one molecule to another in case of price increase.[114]

The Parties' views

(205) The Parties submit that each molecule within L1C belongs to a separate product market, and that none of the molecules belonging to L1C is substitutable to *topotecan*, even when some molecules may partially have the same indications.

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113 Commission decision of 4 February 2009 in Case No M.5253 – *Sanofi-Aventis/Zentiva*, paragraph 12.

114 Commission decision of 12 December 2008 in Case No M.5295 – *Teva/Barr*, paragraph 14 to 15.

Commission's assessment

(206) During the market investigation, competitors identified the molecule level as the appropriate one.[115] A competitor pointed out that competition could also take place at "*a group of molecules having the same therapeutic indication.*"[116] Hospital pharmacies also confirmed that they procure generic products, such as *topotecan*, via tender procedure and lots are typically structured per molecule. Only a few hospitals mentioned that they procure *topotecan* as part of a group of molecules.[117]

(207) In light of the above, it follows that the relevant product market is narrower than the ATC3 class L1C, and is likely to encompass all chemotherapy drugs based on the *topotecan* molecule. Nevertheless, the precise scope could be left open, since the Transaction does not give rise to serious doubts as to its compatibility with the internal market under any alternative product market definition.

V.1.1.2. *Nelarabine*

(208) The Commission has previously analysed the market definitions for finished dose pharmaceuticals used in leukaemia treatments and noted that the ATC3 level was not the appropriate level to look at this market, since it comprises a large range of drugs whose indication and mechanism of action differ substantially and could not be regarded as substitutable.[118] Further, in cases involving originator oncology drugs, the Commission considered the possibility of defining the market based on the type and stage of cancer, whereas for generic products the Commission typically defined the market at molecule level.[119]

The Parties' view

(209) The Parties consider that Atriance *(nelarabine)* is a mature chemotherapy product, thus a market definition based on the specific molecule is the appropriate way to analyse this market. While Atriance remains under Regulatory Data Protection, the Parties submit that the majority of chemotherapies for the treatment of ALL are off-patent and genericised, and thus an analysis on a molecular basis remains relevant. Nevertheless, the Parties provided an alternative analysis based on the type and stage of cancer.

Commission's assessment

(210) Responses in the market investigation confirmed that the ATC3 level is too wide to be considered as the relevant product market. Some competitors indicated that *nelarabine* is substitutable to some molecules which belong to the same ATC3 class (L1B) namely: *methotrexate*, *cytarabine*, *fludarabine*, *mercaptopurine*, *tioguanine*,

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115 Replies to question 10 of Q5 – Questionnaire to competitors – Chemotherapies.

116 Replies to question 10 of Q5 – Questionnaire to competitors – Chemotherapies.

117 Replies to questions 8 and 9 of Q4 – Questionnaire to Hospitals.

118 Commission decision of 23 July 2012 in Case No M.5999 – *Sanofi-Aventis/Genzyme*, paragraphs 47-55.

119 Commission decision of 26 April 2004 in Case No M.3354-*Sanofi-Synthélabo/Aventis*, paragraphs 55-58; Commission decision of 17 July 2009 in Case No M.5476 - *Pfizer/Wyeth* – Metastatic renal cell carcinoma, paragraphs 21 to 26.

since they have the same therapeutic indication for the treatment of ALL.[120] A competitor pointed out that while several other drugs part of ATC3 class (L1B) can be used in the treatment of ALL, only *nelarabine* is relevant for the treatment of T-cell acute lymphoblastic leukaemia (T-ALL) and T-cell lymphoblastic lymphoma (T-LBL).[121]

(211) Nevertheless, the precise scope of the product market definition can be left open, since the Transaction does not give rise to serious doubts as to its compatibility with the internal market under any alternative product market definition.

V.1.1.3. *Ondansetron*

(212) The Commission has previously analysed the product market for *ondansetron*, which belongs to ATC3 class A4A (Antiemetics and antinauseants), as part of a product market composed of ATC4 class A4A1 (Serotonin antagonist antiemetics/antinauseants), and also at molecule level.[122] The Commission has also found that the market for products indicated against chemotherapy and surgery side effects could be limited to serotonin antagonists.[123] This category includes the following molecules: *ondansetron*, *granisetron*, *tropisetron*, *dolasetron* and *palonosetron*.

The Parties' view

(213) The Parties submit that *ondansetron*, *granisetron*, and *tropisetron* are considered to be first-generation drugs, whereas *palonosetron* is a second generation drug with a different half-life, binding capacity and mechanism of action. The Parties further consider that all first-generation serotonin antagonists included in the A4A1 class are substitutable from a demand-side perspective and should be analysed as part of the same market.

Commission's assessment

(214) Responses received in the market investigation indicated that from the supply-side perspective, *ondansetron* is substitutable to other drugs which belong to the A4A1 class and have the same mechanism of action, namely *granisetron*, *palonosetron*, and *tropisetron*, without distinction about the product generation.[124] A competitor pointed out that "*ondansetron is a product of first choice and efficacy level may not be reached to the expectation of the therapy response required with other drugs*". Competitors identify *granisetron* and *tropisetron* as the closest substitute to *ondansetron*.

(215) From a demand-side perspective, the vast majority of prescribers also confirmed that they prescribe *ondansetron* amongst other serotonin antagonists.[125] Hospital pharma-

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120 Replies to question 5 of Q5 – Questionnaire to competitors – Chemotherapies.

121 Replies to question 5 of Q5 – Questionnaire to competitors – Chemotherapies.

122 Commission decision of 12 December 2008 in Case No M.5295 – *Teva/Barr*, paragraph 18, Commission decision of 3 August 2010 in Case No M.5865 – *Teva/Radiopharm*, paragraph 14, Commission decision of 4 February 2009 in Case No M.5253 – *Sanofi-Aventis/Zentiva*, paragraphs 43 to 46.

123 Commission decision of 8 May 2000 in Case No. M.1846 – *Glaxo Wellcome/SmithKline Beechman*, paragraph 34.

124 Replies to question 14 of Q5 – Questionnaire to competitors – Chemotherapies.

125 Replies to question 15 of Q2 - Questionnaire to physicians – aRCC and NET.

cies also typically procure *onsansetron*, but do consider other drugs addressing the same medical need as *ondansetron* in the context of their tender process.[126]

(216) In light of the above, it follows that the relevant product market is narrower than the ATC3 class A4A, and is likely to encompass all serotonin antagonists part of the A4A1 class, if not all products based on the *ondansetron* molecule. Nevertheless, the precise scope could be left open, since the Transaction does not give rise to serious doubts as to its compatibility with the internal market under any alternative product market definition.

V.1.2. Geographic market

(217) The Commission has consistently considered that the geographic market for pharmaceutical products, including generics, is national in scope, as competition between pharmaceutical companies still predominantly takes place at national level. The results of the market investigation supported this finding. From a supply-side perspective, competitors typically market chemotherapy drugs and conclude contracts with customers at national level.[127] From a demand-side perspective customers also confirmed that they purchase chemotherapy drugs via open tender procedure organised at national level or on a bilateral basis with suppliers active in their country.[128]

(218) In any event, for the purposes of the present decision, it is not necessary to conclude on the exact scope of the geographic market definition for various chemotherapy drugs, because the proposed transaction does not give rise to serious doubts as to its compatibility with the internal market even at narrowest (national) level.

V.2. Competitive assessment

V.2.1. Topotecan

(219) The proposed transaction creates horizontal overlaps resulting into affected markets at molecule level in Germany, Romania and Hungary:

Table 7 – Total market shares of the Parties in value in EEA affected countries in the market for *topotecan*, 2013

Country	Novartis (Sandoz)	GSK Oncology Business	Combined
Germany	[0-5]%	[40-45]%	**[40-45]%**
Hungary[129]	-	[40-45]%	**[40-45]%**
Romania	[0-5]%	[70-75]%	**[70-75]%**

Source: Form CO.

(220) Responses received during the market investigation revealed that market for *topotecan* is mature and significant number of pharmaceutical companies offer generic version of *topotecan* among which Teva, Hospira and Actavis.[130] There will be at

126 Replies to questions 17 and 17.1 of Q4 – Questionnaire to Hospitals.

127 Replies to question 3 and 4 of Q5 – Questionnaire to competitors – Chemotherapies.

128 Replies to questions of 11 and 12 Q4 – Questionnaire to Hospitals.

129 Sandoz started selling *topotecan* in Hungary in April 2014 but sales remain low as shown hereafter. For the period January-August 2014, Novartis/Sandoz' share was [0-5]%, while GSK's share was [30-40]%.

130 Replies to question 12.1 of Q5 – Questionnaire to competitors – Chemotherapies.

least three alternative suppliers having a market share higher than the increment in each of the countries concerned (in Germany and Hungary suppliers will be at least seven).

(221) Ultimately, the overwhelming majority of the customers do consider that there will be a sufficient number of reliable suppliers for *topotecan* post-transaction.[131]

(222) In light of the above, the Commission concludes that the proposed transaction does not raise serious doubts as to its compatibility with the internal market with respect to the plausible markets for *topotecan*.

V.2.2. Nelarabine

(223) *Nelarabine* belongs to the ATC3 class L1B – Antimetabolites. The Transaction leads to a horizontal overlap at ATC3 level, since Sandoz' generic molecules *methotrexate*, *fludarabine*, *cytarabine*, *capecitabine*, *gemcitabine* and *5-fluorouracil* fall into the L1B class. The Transaction also leads to an overlap with respect to a potential market comprising chemotherapy agents used for the treatment of ALL and LBL (or the narrower subtypes T-ALL and T-LBL).

The Parties' view

(224) The Parties submit that, while the line of treatment is generally not relevant to the assessment of chemotherapy agents used in the treatment of T-ALL, Atriance is only approved for a specific subtype of ALL and a specific line of treatment,[132] whereas Sandoz products are indicated in the first two lines of treatment. The Parties further submit that Atriance is a niche product due to the limited number of patients suitable for this treatment and sales in the EEA amount to less than EUR […] million, which represent around […]% of GSK EEA-wide sales across its oncology portfolio.

Commission's assessment

(225) There is no overlap at molecule level since Sandoz neither manufactures nor sells *nelarabine*.

(226) At ATC3 (L1B) level, the Transaction does not result into any affected market: in all countries where the Parties' activities would overlap, their combined share would not exceed [10-15]%.

(227) In relation to a potential market comprising chemotherapy agents used for the treatment of ALL and LBL, the indication for Atriance as approved by the EMA confirms it is used in a third-line setting for T-ALL and T-LBL: "*nelarabine is indicated for the treatment of patients with T-cell acute lymphoblastic leukaemia (T-ALL) and T-cell lymphoblastic lymphoma (T-LBL) whose disease has not responded to or has relapsed following treatment with at least two chemotherapy regimens*". The indication further mentions that: "*due to the small patient populations in these disease settings, the information to support these indications is based on limited data*". Therefore, the Commission takes the view that Atriance is not a close competitor of chemotherapies indicated for the treatment of ALL or LBL more generally.

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131 Replies to question 13 of Q4 – Questionnaire to Hospitals.

132 Atriance is only indicated in a third line of treatment after the failure of two previous chemotherapy regimens for the treatment of T-ALL and T-LBL.

(228) Finally, in relation to the narrowest possible market, limited to pharmaceuticals indicated for the third-line treatment of T-ALL and T-LBL, respectively, Atriance would currently be the only pharmaceutical in the market.

(229) From a demand-side perspective, responses in the market investigation confirmed that Atriance is a niche market and very few customers purchase this product (essentially on a basis of bilateral negotiations).[133] Furthermore, the majority of chemotherapies for the treatment of ALL are off-patent and genericised.

(230) As to the supply-side, competitors generally do not perceive Sandoz and GSK as close competitors. The closest substitute to *nelarabine* appears to be *cyclophosphamide* manufactured by Baxter, followed by *cytarabine* manufactured by Hospira, Fresenius Kabi and Accord.[134] Lastly, an overwhelming majority of the respondents to the market investigation consider that the Transaction would not have any impact regarding the commercialisation of *nelarabine* in the EEA.[135]

(231) In light of the above, the Commission concludes that the Transaction does not raise serious doubts as to its compatibility with the internal market with respect to the plausible markets for *nelarabine*.

V.2.3. Ondansetron

(232) The transaction creates horizontally affected market both at ATC4 level and at molecule level. At molecule level the Transaction results into five affected markets in Belgium, Czech Republic, Germany, Ireland and Sweden:

Table 8: Total market shares in value of the Parties in value in EEA affected countries in the market for *ondansetron*, 2013

Country	Novartis (Sandoz)	GSK Oncology Business	Combined
Belgium	[0-5]%	[80-85]%	**[80-85]%**
Czech Rep.	[0-5]%	[70-75]%	**[70-75]%**
Germany	[15-20]%	[35-40]%	**[50-55]%**
Ireland	[5-10]% [136]	[60-65]%	**[65-70]%**
Sweden	[5-10]%	[30-35]%	**[35-40]%**

Source: Form CO.

(233) At ATC4 (A4A1) level, in addition to the above mentioned countries, the only affected market is Italy where the combined share is [30-35]% with an increment of [0-5]%. Due to the moderate market share and the limited increment, the Italian market will be not further analysed:

133 Replies to question 5 of Q4 – Questionnaire to Hospitals.

134 Replies to question 6 of Q5 – Questionnaire to competitors – Chemotherapies.

135 Replies to question 9 of Q5 – Questionnaire to competitors – Chemotherapies.

136 Sandoz's ondansetron is sold in Ireland by Rowex Ltd ("Rowex"), a […] joint venture established in 1994 between Hexal (a company acquired by Novartis in 2005 and integrated into Sandoz) and Rowa Wagner. The market share of Rowex is [10-15]%, and the Parties submit IMS allocates it […] between Sandoz and Rowa Wagner.

Table 9: Total market shares in value of the Parties in value in EEA affected countries in the market for serotonin antagonists (ATC4 class: A4A1), 2013[137]

Country	Novartis (Sandoz)	GSK Oncology Business	Combined
Belgium	[0-5]%	[55-60]%	**[55-60]%**
Czech Rep.	[0-5]%	[20-25]%	**[20-25]%**
Germany	[10-15]%	[20-25]%	**[30-35]%**
Ireland	[5-10]% [138]	[50-55]%	**[55-60]%**
Sweden	[5-10]%	[25-30]%	**[30-35]%**

Source: Form CO.

Belgium

(234) In Belgium, GSK supplies *ondansetron* under the form of tablets, injectable solutions and suppository. Sandoz supplies *ondansetron* under the form of injectable solutions and tablets.

(235) First, the relatively high combined market share is almost entirely due to GSK specific position as originator of the drug, now genericised. The increment brought by Novartis' Sandoz as one of many generic producers is very small, and the merged entity will continue to face competitive constraints from other generic suppliers among which Mylan (market share of [10-15]% at molecule level and [5-10]% at ATC4 level) and Stada (market share of [5-10]% at molecule level and [0-5]% at ATC4 level).

(236) Second, the Parties submit that GSK expects its *ondansetron* share to […] due to regulatory change in the Belgium reimbursement system, which occurred in 2014. […]

(237) Third, a number of generic suppliers exert significant competitive pressure, since the customers' purchasing pattern is essentially price driven[139] and there are no particular obstacles for customers to switch *ondansetron* suppliers, especially so amongst generic producers. Regarding the latter aspect, the contractual duration for supply of ondansetron is less than 3 years and contracts generally do not contain commitments to purchase certain minimum quantities for a given period of time.[140]

(238) Fourth, the market investigation highlighted that the Parties are not the closest competitors. Novartis' Sandoz is one of the several generic producers present on the market, and achieved a limited penetration. Customers generally perceive Mylan as the closest competitor to GSK in Belgium in the market for *ondansetron*.[141] In a wider

137 Italy is not covered, in accordance with the main text of the Decision.

138 Sandoz's ondansetron is sold in Ireland by Rowex Ltd ("Rowex"), a […] joint venture established in 1994 between Hexal (a company acquired by Novartis in 2005 and integrated into Sandoz) and Rowa Wagner. The market share of Rowex is [10-15]%, and the Parties submit IMS allocates it […] between Sandoz and Rowa Wagner.

139 Replies to question 18 of Q4 – Questionnaire to Hospitals.

140 Replies to question 18.5 of Q4 – Questionnaire to Hospitals.

141 Replies to question 16 of Q4 – Questionnaire to Hospitals.

market comprising group of molecules, customers generally purchaser *ondansetron* or *granisetron* which they consider as closely competing products.[142]

(239) Fifth, two pharmaceutical companies entered the Belgium market with an *ondansetron* product in the last three years: Accord Healthcare (Infas Group) entered in 2012 and Norgine in 2013.

(240) Finally, the investigation revealed that customers in Belgium consider having sufficient number of alternative suppliers post-transaction.[143]

(241) In the light of the above, the Commission considers that the Transaction does not raise serious doubts as to its compatibility with the internal market with respect to the plausible markets for *ondansetron* in Belgium.

Czech Republic

(242) In the Czech Republic, GSK supplies hospitals and retail pharmacies with three forms of *ondansetron*: injection, orally disintegrating tablets and suppositories film coasted tablets. Sandoz sells *ondansetron* under the form of film coated tablets and since 2013 it stopped supplying *granisetron*.

(243) In a hypothetical market limited to *ondansetron*, several alternative generic suppliers have a market share higher than the increment, namely Teva ([15-20]%), Fresenius ([0-5]%) and Ardez Pharma ([0-5]%).

(244) The Parties submit that both Sandoz's and GSK's presence decreased in the last three years. Sandoz's *ondansetron* share decreased […] from [15-20]% in 2011 to [5-10]% in 2012 and only [0-5]% in 2013. GSK's *ondansetron* share decreased from [70-75]% in 2012 to [65-70]% in 2013. At the same time, the abovementioned competitors increased their share.

(245) On an ATC4 market, in the Czech Republic the Parties combined share is [20-25]% with an increment lower than [0-5]%. In addition to generic companies, the combined entity would face significant competitive constraints from alternative suppliers offering originator products such as Roche ([20-25]%) and Angelini ([25-30]%; sales of *palonosetron*), the later remaining the market leader post-transaction.

(246) Ultimately, neither customers nor competitors active in the Czech Republic expressed competition concerns due to the Transaction regarding the market for *ondansetron* or a wider market following the ATC4 class.

(247) In the light of the above, the Commission considers that the Transaction does not raise serious doubts as to its compatibility with the internal market with respect to the plausible markets for *ondansetron* in the Czech Republic.

Germany

(248) GSK supplies *ondansetron* as injectables, film-coated tablets, orally disintegrating tablets and syrup. Sandoz sells *ondansetron* as orally disintegrating tablets, film-coated tablets and injections. Sandoz also sells *granisetron* in Germany.

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142 Replies to question 17 of Q4 – Questionnaire to Hospitals.

143 Replies to question 19 of Q4 – Questionnaire to Hospitals.

(249) On the narrowest market (molecule-level), the Parties submit that Sandoz's share decreased from [15-20]% in 2012 to [15-20]% in 2013. GSK's share also […] decreased.

(250) Generic companies exert significant competitive constraints on the German market. Post-transaction the merged entity will be a market leader in all plausible product markets; however it will face significant competitive constraints from numerous generic suppliers among which Teva ([15-20]% at ATC4 level, [15-20]% at molecule level), and Aristo Pharma ([5-10]% at ATC4 level, [10-15]% at molecule level), Stada ([0-5]% at ATC4 level, [5-10]% at molecule level).

(251) The Parties submit that the German market is one of the most developed generic markets in the EEA, in part due to the system according to which the pharmacist can substitute the drug with a lower-priced identical molecule unless the physician has specifically prohibited it.

(252) The market investigation confirmed that in Germany the originator *ondansetron* is facing significant price pressure from its generic versions. It also faces significant constraints from superior drugs within in its own class.[144] For instance, GSK's branded *ondansetron* is competing closely with Roch's branded *granisetron*.[145] Customers also consider that following the Transaction they will still have enough alternative suppliers of *ondansetron*.[146]

(253) Lastly, several companies entered the German market with *ondansetron*-based products in the recent years, namely Mylan (2010), Bluefish (2011), Norgine and Intas (both in 2013).

(254) In the light of the above elements, the Commission considers that the Transaction does not raise serious doubts as to its compatibility with the internal market with respect to the plausible markets for *ondansetron* in Germany.

Ireland

(255) In Ireland, GSK supplies orally disintegrating tablets, injections, film-coated tablets, syrups and suppositories. Sandoz sells *ondansetron* in Ireland under the form of tablets and injection via a […] joint venture Rowex Ltd. ("Rowex") between Novartis and Rowa Wagner. Rowex distributes *ondansetron* […] with no reference to Sandoz in the packaging. Rowex is also the holder of the marketing authorization in Ireland.

(256) The Parties consider that Rowex's sales of *ondansetron* in Ireland should not be attributed to Sandoz. In this hypothesis the Transaction does not create an overlap in Ireland.

(257) Alternatively should a fraction of the sales be attributed to Sandoz, as it is reflected in the IMS data (which attributes [a fraction] of Rowex's sales), the Parties will still face significant competitive constraints from numerous generic suppliers such as Wockhardt and Teva at molecule level. In a wider ATC4 market the Parties also compete with Wockhardt, Roche and Sinclair Pharma.

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144 Replies to question 17.1 of Q5 – Questionnaire to competitors – Chemotherapies.

145 Replies to question 15 of Q5 – Questionnaire to competitors – Chemotherapies.

146 Replies to question 19 of Q4 – Questionnaire to Hospitals.

(258) Generic penetration is relatively low in Ireland and remains below 20% in value. However in 2013, the local authorities undertook measures to encourage generic sales. The Health Act 2013 introduced a system of generic substitution based on which pharmacists are allowed to substitute originator medicines with a generic. Therefore, the Irish generics market is set to grow and allows for increased competition.

(259) In Ireland, the price for all pharmaceuticals (including generics) is settled at the ex-factory level through agreements between the State, *i.e.* the Department of Health (DOH) and/or the Health Services Executive (HSE), and representative bodies of different segments of the pharmaceutical manufacturing industry. These arrangements establish a single maximum ex-factory price to be charged to hospitals and retail pharmacies. The State pharmaceutical reimbursement scheme uses the agreed ex-factory price for the reimbursement purpose. Therefore, despite a relatively high market share, the merged entity would not have the ability to raise unilaterally the price for *ondansetron* in Ireland.

(260) In the light of the above, the Commission considers that the Transaction does not raise serious doubts as to its compatibility with the internal market with respect to the plausible markets for *ondansetron* in Ireland.

Sweden

(261) In Sweden, GSK supplies *ondansetron* as injectables, film-coated tablets, orally soluble tablets and syrup. Sandoz sells *ondansetron* as injectables.

(262) There is significant number of competitors active at both molecule and ATC4 level in Sweden, among which Bluefish ([10-15]% at ATC4 level, [10-15]% at molecule level), Fresenius ([10-15]% at ATC4 level, [10-15]% at molecule level), Teva ([5-10]% at ATC4 level, [5-10]% at molecule level), Stada ([5-10]% at ATC4 level, [5-10]% at molecule level) and several other smaller players.

(263) The Parties submit that although GSK was the leader on the *ondansetron* market in 2013, its share decreased from [50-60]% in 2011 to [30-40]% in 2013. GSK notes that […]. At the same time, Teva increased its market share from below [0-5]% in 2011 to [5-10]% in 2013, and Stada increased its market share from less than [0-5]% in 2011 to almost [5-10]% in 2013.

(264) The Parties further that other recent entrants have gained significant share, e.g. 2Care4 entered in 2013 and reached a market share of almost [0-5]% in that year. Bluefish, an existing player, introduced a new product in 2010 which increased its overall share from [10-15]% in 2011 to [10-15]% in 2013. In addition, two pharmaceutical companies (Aurobindo and Intas) entered the Swedish market with *ondansetron*-based products respectively in 2013 and 2014.

(265) Finally, neither customers nor competitors raised competition concerns regarding the impact of the Transaction in Sweden.

(266) In the light of the above, the Commission considers that the Transaction does not raise serious doubts as to its compatibility with the internal market with respect to the plausible markets for *ondansetron* in Sweden.

VI. COMMITMENTS

VI.1. Commitments submitted by the Parties

VI.1.1. Procedure

(267) To address the serious doubts raised by the Transaction on potential and innovation competition in the area of B-Raf and MEK inhibitors and render the concentration compatible with the internal market, Novartis has modified the notified Transaction by entering into the following commitments, whose final version is annexed to this decision and form an integral part thereof.

(268) On 26 November 2014, Novartis informed the Commission that it had entered into a termination and asset transfer agreement with Array BioPharma Inc. ("Array") for the return of MEK162.[147]

(269) On 7 January 2015, Novartis lodged two alternative sets of formal commitments (the "**Commitments Option One**" and "**Commitments Option Two**", respectively). On 9 January 2015 Novartis submitted a revised version of both sets of Commitments.

(270) The revised commitments of 9 January contained, as regards Commitments Option One, (i) improved Purchaser criteria (modelled after those offered in Commitments Option Two), and (ii) a more complete list of assets, rights and personnel relating to LGX818 to be transferred; as regards Commitments Option Two, they introduced (i) a clear deadline for Array to find a suitable partner, (ii) the commitment of Novartis to return MEK162 and divest LGX818 to Array within […] from the adoption of this Decision, (iii) Novartis' obligation, as of the adoption of this Decision, to give Array access to all relevant information relating to the MEK162 and LGX818 divestment business, [description of other improved aspects of the Commitments].

(271) The market test for the two alternative remedy packages was launched on the same day, with a deadline for reply on 14 January 2015.

(272) On 19 January 2015, Novartis informed the Commission that it had entered into an agreement with Array for the divestiture of LGX818, and announced its intention to proceed with Commitments Option Two. On 20 January 2015, Novartis provided a revised version of Commitments Option Two on 20 January 2015, incorporating the executed agreements with Array for the divestiture of LGX818.

(273) On 22 January 2015, Novartis lodged a revised version of the Commitments Option Two, with minor amendments compared to the version of 20 January 2015, mainly aimed at ensuring consistency between the final Commitments and the executed agreements with Array in respect to the divestiture of LGX818.

(274) On 27 January 2015, Novartis submitted a further revised version of Commitments Option Two (the "final Commitments").

(275) The final Commitments include some revisions concerning (i) the time period by which Novartis shall be deemed to have complied with the Commitments, and (ii)

147 The termination and asset transfer agreement was further amended on 19 January 2015.

the review clause as well as additional commitments from Novartis as regards Array's suitability as a buyer of LGX818.[148]

(276) After the market test, Array submitted [Array's confidential information about its collaboration with a third party].[149]

(277) Array clearly committed to Novartis that [Array's confidential information about its collaboration with a third party].

(278) Consequently, for the purpose of accepting Array as a suitable buyer of LGX818, in the final Commitments Novartis commits that (i) [Array's position as regards its cooperation with a third party]; and that (ii) [Array's position as regards its cooperation with a third party].

VI.1.2. Description of the Commitments

Commitments Option One

(279) Commitments Option One is an up-front buyer solution consisting in: (i) the return of MEK162, Novartis' MEK inhibitor, to its owner Array;[150] and (ii) the divestiture of LGX818, Novartis' B-Raf inhibitor, to a Suitable Purchaser, provided such purchaser enters into a binding agreement with Array for the worldwide development and EEA commercialization of LGX818 and MEK162 in combination.

(280) In this structure, LGX818 and MEK162 are owned by two different entities, which have to find an agreement to cooperate regarding the two compounds in combination. The obligation to find a suitable purchaser lies with Novartis, which otherwise cannot close the Transaction.

Commitments Option Two

(281) Commitments Option Two is a post-closing remedy consisting in both the return of MEK162 and the divestiture of LGX818 to Array, under the condition that Array enters into a binding agreement with a suitable partner to jointly develop worldwide and commercialise in the EEA LGX818 and MEK162, within […] from the adoption of the Commission's Decision.

(282) Should Array be unable to enter into such binding agreement in the prescribed deadline, a non-exclusive licence to develop worldwide and an exclusive licence to commercialize in the EEA both LGX818 and MEK162 would be assigned to a divestiture trustee for sale […].

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148 After the market test, Array submitted [Array's confidential information about its cooperation with a third party]. Array represented to the Commission that it has reasonable grounds to believe that [Array's confidential information about its cooperation with a third party] would not affect the viability and implementation of the Commitments. In addition, the Commitments Option Two of 22 January 2015 envisioned an agreement between Array and Novartis to […].

149 Array represented to the Commission that [Array's confidential information about its cooperation with a third party] would not affect the viability and implementation of the final Commitments. In addition, the Commitments Option Two of 22 January 2015 envisioned an agreement between Array and Novartis to […].

150 Array had licenced MEK162 exclusively to Novartis pursuant to the Licence Agreement of 19 April 2010.

The final Commitments

(283) The final Commitments are an up-dated version of Commitments Option Two of 9 and 20 January 2015, introducing (i) a reference to the executed agreement between Novartis and Array for the divestiture of LGX818 as well as (ii) additional commitments from Novartis for the purpose of accepting Array as a suitable purchaser of LGX818.

(284) The final Commitments thus consist in the following.

(285) Novartis commits to returning MEK162[151] and divesting LGX818[152] to Array (together, the "**Divestment Business**") within […] after the adoption of this Decision ("Effective Date").

(286) Under the final Commitments, Novartis shall divest LGX818 to Array provided that (i) Array [Array's position as regards its cooperation with a third party]; and (ii) [Array's position as regards its cooperation with a third party.[153]

(287) The Divestment Business essentially consists of all rights, title, interests and assets necessary to continue developing and, if development is successful, commercialise MEK162 and LGX818, including:

(a) all patent rights and all know-how, including manufacturing technology, to the extent related to LGX818 or MEK162;

(b) the rights to conduct the clinical trials sponsored by Novartis and related to LGX818 and MEK162;

(c) all product development reports, clinical trial and safety data, databases and analyses to the extent related to MEK162 or LGX818;

(d) all regulatory filings, correspondence and registrations, to the extent related to MEK162 or LGX818;

(e) employees on Novartis' Core Global Program Team, Core International Clinical Team, and Core Clinical Team, that have participated in any material respect in Novartis' activities regarding MEK162 or LGX818;

(f) all third party agreements related to MEK162 and LGX818, including agreements related to manufacturing technology and on-going investigator-initiated clinical trials involving MEK162 and LGX818;

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151 In addition to the termination and asset transfer agreement with Array dated 26 November 2014, amended on 19 January 2015, Novartis has entered into, or commits to enter into, various subordinate collaboration and license agreements with Array relating to MEK162. All these agreements are conditional upon closing of the Transaction.

152 Novartis has entered into an asset transfer agreement with Array dated 19 January 2015. Novartis also has entered into, or commits to enter into, various subordinate collaboration and license agreements with Array relating to LGX818. All these agreements are conditional upon closing of the Transaction.

153 Capitalized terms used herein but not defined herein have the meaning ascribed to them in the final Commitments attached to this Decision.

(g) during a transition period, Novartis will provide assistance with the technical transfer, support and funding for all clinical trials involving LGX818 and MEK162,[154] and interim supply of both compounds.

(288) The divestment of the Divestment Business will oblige Array to negotiate, within […] after the adoption of this Decision, appropriate agreements to partner with a suitable company (the "**Suitable Partner**"), which shall have the ability and incentive to develop worldwide and commercialise in the EEA MEK162 and LGX818.

(289) The Commission will have to approve the Suitable Partner and the final binding agreements entered into between it and Array, and will verify, among others, that:[155]

(a) the Suitable Partner shall have the ability and incentive to develop worldwide and commercialize in the EEA MEK162 and LGX818, on the basis of a co-operation with Array laid down in point (b) below;

(b) the Suitable Partner shall reach an agreement with Array which shall enable and incentivise Array and the Suitable Partner to develop worldwide and commercialise in the EEA MEK162 and LGX818 under the terms of the agreements, subject to the results of the clinical trials;

(c) the Suitable Partner shall have the financial resources, proven expertise, ability and incentive to maintain and develop MEK162 and LGX818 as a viable and active competitive force in competition with the Notifying Party and other competitors, together with Array under the terms of their agreements.

(290) If Array is unable to obtain the Commission's approval for its binding agreements with a Suitable Partner within the First Divestiture Period, the Conditional Licence, granting non-exclusive rights to develop worldwide and exclusive rights to commercialize in the EEA both LGX818 and MEK162 would be assigned to a divestiture trustee for sale […].

(291) On 19 January 2015, Array and Novartis entered into the Conditional Licence Agreement, whose main terms are reflected in Annex 1 to the final Commitments. The Conditional Licence will take effect as of closing of the Transaction. The exercise of any right under the Conditional Licence is conditional upon Array not obtaining the Commission's approval within the First Divestiture Period. If that condition is fulfilled, Novartis will have the right and the obligation to immediately assign the Conditional Licence to a Divestiture Trustee, which will have an exclusive mandate to sell it […] to a Suitable Purchaser. Novartis cannot derive any other rights from the Conditional Licence.

(292) The Conditional Licence include, among others, a licence to cross-reference, file or incorporate any study data and data included or referenced in any regulatory approv-

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154 Including but not limited to, Columbus Study, where LGX818 and MEK162 are phase III trial in combination for advanced melanoma. More generally, during the transition period, Novartis will continue to sponsor the standalone clinical trials involving either LGX818 or MEK162 as a monotherapy, the combination studies involving LGX818 and MEK162; the combination studies involving either LGX818 or MEK162 and one or more other Novartis compounds; the combination studies involving LGX818, MEK162 and one or more other Novartis compounds. The strategic decisions relating to the existing trials would be adopted by unanimity by Novartis and Array.

155 In addition to the standard criteria, such as for instance the independence from Novartis.

als for the trials in order to support regulatory approvals to market MEK162 and LGX818 in the respective territory of each party of the agreement. In addition, the Conditional Licence governs the cooperation of Array and the Suitable Purchaser with respect to existing and new clinical trials.

(293) The Suitable Purchaser, together with the agreements intended to give effect to the sale of the Conditional Licence, shall be approved by the Commission on the basis of specific criteria which substantially mirror the ones required for the Suitable Partner.

VI.2. Assessment of the proposed remedies

VI.2.1. The Parties' view

(294) The Parties claim that both Commitments Option One and Option Two address the Commission's preliminary competition concerns in relation not only to the potential overlap between the Parties' marketed and pipeline MEK and B-Raf inhibitors for the treatment of advanced melanoma but also for other potential future indications for which they are currently undergoing in phase III and earlier stages clinical trials.

VI.2.2. The results of the market test and the Commission's assessment

(295) The specificity of remedies in this case consists in the involvement of a third party to the Transaction, Array, which owns MEK162.

(296) The return of MEK162 to Array[156] is the starting point of both Commitments Option One and Option Two, which constitute two different ways to achieve the same outcome: (a) on the one hand, removing the overlap caused by the Transaction between B-Raf and MEK inhibitors (both alone and in combination) for the treatment of advanced melanoma; and (b) on the other hand, ensuring that the broader clinical trial programme of LGX818 and MEK162 will continue to be developed, and if successful, brought to the EEA market, through the joint cooperation between Array and the Suitable Purchaser of LGX818 (in Option One) or between Array and its Suitable Partner (in Option Two).[157]

(297) Therefore, both Commitments Option One and Option Two could remove the serious doubts identified and for that reason have been both market tested.

(298) On 19 January Novartis entered into an agreement with Array for the divestiture of LGX818[158]. Therefore, Commitments Option One no longer stands and will not be assessed further.

(299) The final Commitments consist in an updated version of Commitments Option Two, reflecting the executed agreements between Novartis and Array as regards the di-

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156 Pursuant to the licence agreement between Novartis and Array dated 19 April 2010, [Novartis' and Array's contractual arrangements as regards MEK162]. […], on […], Novartis terminated the licence agreement and returned back MEK162 to Array.

157 As stated above in footnote 160, Novartis and Array entered into transitional agreements in order to ensure that existing clinical trials (such as the Columbus Study) will be continued and be smoothly transitioned to Array. Therefore, for a transitional period, which varies according to the specific trials, Novartis and Array will cooperate to continue developing the trials and, subject to positive results from the trials, bring to the market MEK162 and LGX818, used as monotherapies or in combination.

158 The transfer and asset agreement for LGX818 is conditional upon closing of the Transaction.

vestiture of LGX818 as well as introducing additional commitments from Novartis for the purpose of accepting Array as a suitable purchaser of LGX818.

(300) The final Commitments, thus, do not materially differ from Commitments Option Two which has been market tested. Consequently, the views of the market participants on Commitments Option Two are deemed to be referring to the final Commitments.

(301) The majority of the respondents to the market test indicated that the Divestment Business is viable, as MEK162 and LGX818 are (owned) and developed together. In particular, a competitor highlighted that: "*if the two molecules and their businesses are sold and developed together there is a greater likelihood of them being viable*".[159]

(302) The majority of respondents further indicated that the final Commitments are sufficiently attractive for a Suitable Partner to enter into a cooperation agreement with Array to develop worldwide and commercialise in the EEA both MEK162 and LGX818.[160] At least one respondent mentioned a (non-binding) interest in becoming such partner, further specifying that it "*satisfies the criteria for a Suitable Partner as outlined in […] the Commitments Option Two*".[161]

(303) The majority of participants to the market test who expressed an opinion, stated that the requirements identified in the final Commitments for a Suitable Partner allow the Suitable Partner, in cooperation with Array, to exert sufficient competition constraint on Novartis post-Transaction. In particular, one competitor mentioned that "*if the partner has adequate resources and expertise to develop the assets and compete in the marketplace with Novartis, then we did not see any "show stoppers" in the proposals that would unduly hinder the ability of such a purchaser, reasonably skilled in the area of oncology drug development and commercialization, to generate value from these assets*",[162] while another submitted that "*the success of the development will depend critically on who the Suitable Partner is and their skillset, experience in developing oncology products, motivation, financial know-how and market presence*".[163]

(304) As regards the Conditional Licence, the majority of respondents to the market test declared that no other assets, contracts, rights and/or personnel that would be important for the viability and competitiveness of the Conditional Licence.[164]

(305) A competitor raised some doubts as regards the viability and effectiveness of the final Commitments. In particular, it questioned how the Commission would ensure that Array would enter into cooperation agreements with the Suitable Partner. Second, it stated that the final Commitments should have expressly indicated the terms and conditions of the cooperation agreement between Array and the Suitable Partner. Third, it claimed that Array's ownership of both MEK162 and LGX818 would hinder the Suitable Partner from accessing all relevant information relating to the Di-

159 Replies to question 9 of R1 – Market test of the Commitments.

160 Replies to question 10 of R1 – Market test of the Commitments.

161 Replies to question 11 of R1 – Market test of the Commitments.

162 Replies to question 12 of R1 – Market test of the Commitments.

163 Replies to question 12 of R1 – Market test of the Commitments.

164 Replies to question 13 of R1 – Market test of the Commitments.

vestment Business. Forth, Annex 1 to the final Commitments would not guarantee that new trials would be co-developed, as the Suitable Purchaser would be a licensee with commercialisation rights in the EEA and no decision-making powers and either party (Array or the Suitable Purchaser) would be entitled to object to any proposed new trials under vague circumstances. Finally, this competitor also raised some doubts as to whether the final Commitments would ensure that the Columbus trials and other existing trials could be completed and the products launched, also in light of the fact that Novartis will conduct the trials during a transitional period.

(306) The Commission considers that all these doubts expressed during the market test should be dismissed for the following reasons.

(307) In the final Commitments, Array would be the owner of both MEK162 and LGX818, which have been considered by the overwhelming majority of the market participants as a viable and attractive Divestment Business. Therefore, Array will have all the incentives to find a pharmaceutical company to cooperate with in order to maximise the value of both drugs, used alone or in combination. In addition, the divestiture of the Conditional Licence by the Divestiture Trustee is meant to further incentivise Array to find a partner within the First Divestiture Period […]. Furthermore, to render Array's obligations under the final Commitments enforceable between the Novartis and Array, on 19 January 2015 Novartis and Array entered into an agreement, whereby Array assumed vis-à-vis Novartis obligations to respect the final Commitments. This agreement, which is attached to the final Commitments, envisions [terms of the agreement between Novartis and Array].

(308) The final Commitments do not detail the terms and conditions of the cooperation agreement to be entered into Array and the Suitable Partner because the Commission considered not appropriate to let Novartis and Array solely decide on those elements. However, the final Commitments envision the overarching goal of these agreements which "*shall enable and incentivise Array and the Suitable Partner to develop worldwide and commercialise in the EEA MEK162 and LGX818*". The Commission will assess the suitability of the Suitable Partner also against this important requirement, in a separate decision.

(309) As indicated by some market participants, the common ownership of MEK162 and LGX818 is not a barrier. To the contrary, some competitors highlighted that it facilitates the workability of the remedies, as it better ensures that MEK162 and LGX818 will be jointly developed and, if trials are successful, brought to the market. Novartis commits to give Array access to all relevant information relating to the Divestment Business as of adoption of this Decision, and Array will have all the incentives to share this information with the Suitable Partner, in order to engage in meaningful negotiations and reach final agreements for the development of the two compounds.

(310) As regards Annex 1 to the final Commitments, which contains the main elements of the Conditional Licence, the Commission notes that (i) Array and the Suitable Purchaser will be able to adopt by unanimity all […] [165]; (ii) the circumstances under which either party can block the other party proceeding with a new clinical trial are […]" and thus would not constitute a barrier to the commencement of (joint) new clinical trials; and (iii) Annex 1 (as well as the Conditional Licence) sets out some rules to facilitate the co-development of new trials by the Suitable Purchaser and Ar-

165 Section 2.3 of Annex 1 to the final Commitments.

ray, such as the obligation of each party to invite the other party to co-develop new trials involving MEK162 and LGX818, as well as […].

(311) As regards the concerns regarding the continuation of the promising Columbus trials and the other existing clinical trials at earlier stages of development, at closing of the Transaction, Array and Novartis will enter into transitional agreements and clinical trials agreements, whose main terms and conditions have already been agreed in the final form upon Novartis and Array and have been attached to the final Commitments. These agreements ensure the continuation of the Columbus trials and other clinical trials involving MEK162 and LGX818 alone, in combination and/or in combination with other compounds by Novartis and Array, under the supervision of the Monitoring trustee.

(312) In conclusion, the Commission considers that, provided all conditions laid down in the final Commitments are fulfilled, Array is a suitable purchaser of LGX818. The final Commitments further ensure that, together with the Suitable Partner or the Suitable Purchaser (as applicable), Array will have the ability and the incentive to develop worldwide and commercialise in the EEA MEK162 and LGX818, subject to the results of the clinical trials.

(313) Therefore, the Commission considers that the final Commitments are sufficient to remove all serious doubts identified with respect to targeted therapies for the treatment of advanced melanoma and other cancers types, as, on the one hand, they remove the overlap between MEK and B-Raf inhibitors and, on the other hand, they ensure that the broader clinical trial programme of LGX818 and MEK162 will continue to be developed, and if successful, brought to the EEA market.

VI.3. Overall conclusion on the Commitments

(314) In light of the above, the Commission concludes that the final Commitments are sufficient to eliminate all serious doubts identified in the competition analysis as regards targeted therapies for the treatment of advanced melanoma and other cancer types (such as ovarian, colorectal and lung cancer).

VI.4. Conditions and obligations

(315) Under the first sentence of the second subparagraph of Article 6(2) of the Merger Regulation, the Commission may attach to its Decision conditions and obligations intended to ensure that the undertakings concerned comply with the commitments they have entered into *vis-à-vis* the Commission with a view to rendering a notified concentration compatible with the internal market.

(316) The achievement of the measure that gives rise to the structural change of the market is a condition, whereas the implementing steps which are necessary to achieve this result are generally obligations on the Parties. Where a condition is not fulfilled, the Commission's decision declaring the concentration compatible with the internal market no longer stands. Where the undertakings concerned commit a breach of an obligation, the Commission may revoke the clearance decision in accordance with Article 8(6) of the Merger Regulation. The undertakings concerned may also be subject to fines and periodic penalty payments under Articles 14(2) and 15(1) of the Merger Regulation.

(317) In accordance with the distinction described above, the Decision in this case is conditioned on the full compliance with the requirements set out in section B of the final

Commitments (conditions), whereas sections C and E of the final Commitments constitute obligations on Novartis.

(318) The detailed text of the final Commitments is annexed to the present Decision. The full text of the final Commitments forms an integral part to this Decision.

VII. CONCLUSION

(319) For the above reasons, the Commission has decided not to oppose the notified operation as modified by the commitments and to declare it compatible with the internal market and with the functioning of the EEA Agreement, subject to full compliance with the conditions in section B of the commitments annexed to the present decision and with the obligations contained in the other sections of said commitments. This decision is adopted in application of Article 6(1)(b) in conjunction with Article 6(2) of the Merger Regulation.

For the Commission

(Signed)

Margrethe VESTAGER

Member of the Commission

Dated 27 January 2014

Novartis AG

CASE NO. COMP/M.7275 – NOVARTIS / GLAXOSMITHKLINE ONCOLOGY BUSINESS

Commitments to the European Commission – Option 2

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CASE NO. COMP/M.7275 – NOVARTIS / GLAXOSMITHKLINE ONCOLOGY BUSINESS

Commitments to the European Commission

Pursuant to Article 6(2) of Council Regulation (EC) No. 139/2004 (the "**Merger Regulation**"), Novartis AG (the "**Notifying Party**") hereby enters into the following Commitments (the "**Commitments**") vis-à-vis the European Commission (the "**Commission**") with a view to rendering the Notifying Party's acquisition of GlaxoSmithKline's oncology business (the "**Concentration**") compatible with the internal market and the functioning of the EEA Agreement.

This text shall be interpreted in the light of the Commission's decision pursuant to Article 6(1)(b) of the Merger Regulation to declare the Concentration compatible with the internal market and the functioning of the EEA Agreement (the "**Decision**"), in the general framework of European Union law, in particular in the light of the Merger Regulation, and by reference to the Commission Notice on remedies acceptable under Council Regulation (EC) No 139/2004 and under the Commission Regulation (EC) No 802/2004 (the "**Remedies Notice**").

Section A. Definitions

1. For the purpose of the Commitments, the following terms shall have the following meaning:

Affiliated Undertakings: undertakings controlled by the Parties and/or by the ultimate parents of the Parties whereby the notion of control shall be interpreted pursuant to Article 3 of the Merger Regulation and in the light of the Commission Consolidated Jurisdictional Notice under Council Regulation (EC) No 139/2004 on the control of concentrations between undertakings (the "**Consolidated Jurisdictional Notice**").

Assets: the assets that contribute to the current operation or are necessary to ensure the viability and competitiveness of the Divestment Business as indicated in Section B, and described more in detail in the Schedule.

Array: Array BioPharma Inc.

Array Termination agreements: collectively, the MEK License Termination Agreement and the MEK Subordinate Agreements.

Closing: the transfer of the legal title of the Divestment Business to Array.

Conditional License: a perpetual and irrevocable license, granted by Array to Novartis, conferring Development Rights with respect to MEK162 and LGX818 and exclusive rights

to commercialise MEK162 and LGX818 in the EEA, and such other rights as set forth in Annex 1.

Confidential Information: any business secrets, know-how, commercial information, or any other information of a proprietary nature that is not in the public domain.

Conflict of Interest: any conflict of interest that impairs the Trustee's objectivity and independence in discharging its duties under the Commitments.

Development Rights: means the rights conferred on the Suitable Purchaser as set forth in Annex 1.

Divestment Agreements: means the Alliance Agreements or the Trustee Divestment Agreement and any other agreements intended to give effect to the Commitments (subject to agreement between the relevant parties and subsequent approval by the Commission in accordance with these Commitments).

Divestment Business: the LGX Divestment Business and the MEK Divestment Business.

Divestiture Trustee: one or more natural or legal person(s) who is/are approved by the Commission and appointed by Novartis and who has/have received from Novartis the exclusive Trustee Mandate to sell the Conditional Licence to a Suitable Purchaser at no minimum price.

Effective Date: the date of adoption of the Decision.

EMA: European Medicines Agency.

First Divestiture Period: the time period of [...] from the Effective Date.

GlaxoSmithKline Oncology Business: the business relating to a portfolio of oncology products (excluding manufacturing) of GlaxoSmithKline Plc to be acquired by Novartis.

Initial Divestment Agreements: (i) a licence termination agreement pursuant to which Novartis would return MEK162 to Array, (ii) an asset purchase agreement pursuant to which Novartis would divest LGX818 to Array and (iii) any additional agreement entered into in relation to (i) and (ii).

LGX Divestment Business: the business relating to LGX818 as defined in Section B and in the Schedule which the Notifying Party commits to divest.

LGX Key Personnel: all personnel necessary to maintain the viability and competitiveness of the LGX Divestment Business.

LGX Transfer Agreements: collectively the LGX Asset Transfer Agreement and the LGX Subordinate Agreements.

MEK Divestment Business: the business relating to MEK162 as defined in Section B and in the Schedule which the Notifying Party commits to divest.

MEK Key Personnel: all personnel necessary to maintain the viability and competitiveness of the MEK Divestment Business, as listed in the Schedule.

Monitoring Trustee: one or more natural or legal person(s), who is/are approved by the Commission and appointed by Novartis, with prior advice and consent of Array (such consent not to be unreasonably withheld, delayed or conditioned) and who has/have the duty

to monitor Novartis's and Array's compliance with the conditions and obligations attached to the Decision.

Novartis: Novartis AG, incorporated under the laws of Switzerland, with its registered office at Lichtstrasse 35, 4056 Basel, Switzerland and registered with the Commercial/Company Register of Canton Basel-City under number CHE-103.867.266.

Parties: the Notifying Party and the undertaking that is the target of the concentration.

Partner Criteria: the criteria laid down in paragraph 13 of these Commitments that the Suitable Partner must fulfil in order to be approved by the Commission.

Personnel: the MEK Key Personnel and the LGX Key Personnel.

Purchaser Criteria: the criteria laid down in paragraph 14 of these Commitments that the Suitable Purchaser must fulfil in order to be approved by the Commission.

Schedule: the schedule to these Commitments describing more in detail the Divestment Business.

Suitable Partner: the entity approved by the Commission as counterparty to the Alliance Agreements in accordance with the criteria set out in Section D.

Suitable Purchaser: if applicable, an entity approved by the Commission to which the Divestiture Trustee sells the Conditional License in accordance with the criteria set out in Section D.

Trustee: the Monitoring Trustee and/or the Divestiture Trustee as the case may be.

Trustee Divestiture Period: the period of [...] from the end of the First Divestiture Period.

Trustee Divestment Agreements: means the agreements intended to give effect to the sale by the Divestiture Trustee of the Conditional License and the Commitments (subject to agreement between the relevant parties and subsequent approval by the Commission in accordance with these Commitments).

Section B. The commitment to divest and the Divestment Business

Commitment to divest

2. In order to maintain effective competition, Novartis

(a) has entered into a termination and asset transfer agreement with Array dated 26 November 2014 pursuant to which Array will obtain all relevant rights, title and interest in MEK162 worldwide (the "**MEK License Termination Agreement**"). Novartis has also entered into, or commits to enter into, various subordinate collaboration and license agreements with Array (the "**MEK Subordinate Agreements**"), (collectively, the "**Array Termination agreements**"). A list of the MEK Subordinate Agreements is provided at Annex 6;

(b) has entered into an asset transfer agreement with Array dated 19 January 2015 pursuant to which Array will obtain all relevant rights, title and interest in LGX818 worldwide (the "**LGX Asset Transfer Agreement**"). Novartis has also entered into, or commits to enter into, various subordinate collaboration and license agreements

with Array (the "**LGX Subordinate Agreements**"), (collectively, the "**LGX Transfer Agreements**"). A list of the LGX Subordinate Agreements is provided at Annex 7;

(c) commits to divest, or procure the divestiture of the Divestment Business to Array. To effect the foregoing commitment, Novartis will divest the Divestment Business to Array within [...] after the Effective Date. The divestment of the Divestment Business to Array will oblige Array to negotiate, within the First Divestiture Period, appropriate agreements to partner with a Suitable Partner (collectively, the "**Alliance Agreements**"), that has the ability and incentive to develop and commercialise MEK162 and LGX818 ("**Divestment Business**") in the EEA. Pursuant to the Initial Divestment Agreements, Array will grant Novartis the Conditional License. Exercise of any and all rights under the Conditional License will be subject to the condition that Array has been unable to obtain final approval from the Commission for execution of the Alliance Agreements at the end of the First Divestiture Period. If that condition is fulfilled, Novartis shall immediately assign the Conditional License to the Divestiture Trustee. Novartis would have no other rights or obligations under the Conditional License. The Divestiture Trustee shall have an exclusive mandate to sell the Conditional Licence to a Suitable Purchaser in accordance with the procedure described in paragraphs 27 and 28 in the Trustee Divestiture Period;

(d) As soon as practicable following the Effective Date, Novartis would cooperate with Array to provide the relevant information regarding the Divestment Business in order to facilitate Array finding a Suitable Partner, subject to appropriate confidentiality safeguards.

3. [...]

4. Novartis shall be deemed to have complied with this commitment if, by the end of the First Divestiture Period, Array has entered into final binding Alliance Agreements (as well as ancillary agreements) or, by the end of the Trustee Divestiture Period, the Divestiture Trustee has entered into final binding Trustee Divestment Agreements (as well as ancillary agreements) (as applicable) and the Commission approves the proposed Suitable Partner or Suitable Purchaser (as applicable) and the terms of sale as being consistent with the Commitments in accordance with the procedure described in paragraph 13 or 14 (as applicable) and if the closing of the final binding Alliance Agreements or the final binding Trustee Divestment Agreements takes place within a period not exceeding [...] after the approval of the Suitable Partner or Suitable Purchaser and the terms of the agreements by the Commission.

5. In order to maintain the structural effect of the Commitments, the Notifying Party shall, for a period of 10 years after Closing, not acquire, whether directly or indirectly, the possibility of exercising influence (as defined in paragraph 43 of the Remedies Notice, footnote 3) over the whole or part of the Divestment, unless, following the submission of a reasoned request from the Notifying Party showing good cause and accompanied by a report from the Monitoring Trustee (as provided in paragraph 42 of these Commitments), the Commission finds that the structure of the market and the competitive conditions have changed to such an extent that the absence of influence over the Divestment Business is no longer necessary to render the proposed concentration compatible with the internal market.

Structure and definition of the Divestment Businesses

6. The Divestment Businesses consist of all relevant rights, title and interest in LGX818 and MEK162 worldwide as well as certain ancillary assets and the rights to or licences for certain technologies needed to successfully develop MEK162 and LGX818, respectively. The legal and functional structure of the Divestment Business as operated to date is described in the Schedule. The Divestment Business, described in more detail in the Schedule, includes all assets and rights that are necessary to ensure the viability and competitiveness of the Divestment Business.

7. In addition, the Divestment Business includes the benefit, for a transitional period after Closing and on terms and conditions equivalent to those at present afforded to the Divestment Business and as set out in the Array Termination Agreements and the LGX Transfer Agreements, of all current arrangements under which Novartis or its Affiliated Undertakings supply products or services to the Divestment Business as detailed in the Schedule. Strict firewall procedures will be adopted so as to ensure that any competitively sensitive information related to, or arising from such arrangements is protected in accordance with the confidentiality provisions set out in the Initial Divestment Agreements and the Divestment Agreements and paragraph 9 of these Commitments.

Section C. Related Commitments

Preservation of viability, marketability and competitiveness

8. From the Effective Date until Closing, the Notifying Party shall preserve or procure the preservation of the economic viability, marketability and competitiveness of the Divestment Business, in accordance with good business practice, and shall minimise as far as possible any risk of loss of competitive potential of the Divestment Business. In particular Novartis undertakes:

(a) not to carry out any action that might have a significant adverse impact on the value, management or competitiveness of the Divestment Business or that might alter the nature and scope of activity, or the industrial or commercial strategy or the investment policy of the Divestment Business;

(b) to make available, or procure to make available, sufficient resources for the development of the Divestment Business, on the basis and continuation of the existing business plans; and

(c) to take all reasonable steps, or procure that all reasonable steps are being taken, including appropriate incentive schemes (based on industry practice), to encourage all Personnel to remain with the Divestment Business (as applicable), and not to solicit or move any Personnel to Novartis' remaining business.

Ring-fencing

9. Novartis shall implement, or procure to implement, all necessary measures to ensure that it does not, after the Effective Date, obtain any Confidential Information relating to the Divestment Business and that any such Confidential Information obtained by Novartis before the Effective Date will be eliminated and not be used by Novartis (except to the extent this is permitted under the Initial Divestment Agreements). Novartis may obtain or keep infor-

mation relating to the Divestment Business which is reasonably necessary for the divestiture of the Divestment Business or the disclosure of which to Novartis is required by law.

Non-solicitation clause

10. Novartis undertakes, subject to customary limitations, not to solicit, and to procure that Affiliated Undertakings do not solicit, the Personnel transferred in accordance with the Initial Divestment Agreements for a period of [...] after Closing.

Due diligence

11. In order to facilitate Array finding a suitable purchaser, as soon as practicable following the Effective Date, Novartis shall, subject to customary confidentiality assurances and dependent on the stage of the divestiture process:

(a) provide to Array sufficient information as regards the Divestment Business; and

(b) provide to Array sufficient information relating to the Personnel that have participated in Novartis' activities regarding MEK162 and LGX818.

Reporting

12. The Initial Divestment Agreements shall provide the following: the Monitoring Trustee shall submit written reports in English on potential purchasers for the Alliance Agreements and developments in the negotiations with such potential purchasers to the Commission no later than 10 days after the end of every month following the Effective Date (or otherwise at the Commission's request). The Monitoring Trustee shall submit a list of all potential purchasers having expressed interest in entering into the Alliance Agreements to the Commission at each and every stage of the divestiture process, as well as a copy of all the offers made by potential purchasers within five days of their receipt.

Section D. The Purchaser

13. In order to be approved by the Commission, the Suitable Partner must fulfil the following criteria:

(a) The Suitable Partner shall be independent of and unconnected to the Notifying Party and its Affiliated Undertakings.

(b) The Suitable Partner shall have the ability and incentive to develop worldwide and commercialize in the EEA MEK162 and LGX818, on the basis of a cooperation with Array foreseen under point (c) below.

(c) The Suitable Partner shall reach Alliance Agreements with Array which shall enable and incentivize Array and the Suitable Partner to develop worldwide and commercialize in the EEA MEK162 and LGX818 under the terms of the Alliance Agreements, subject to the results of the clinical trials.

(d) The Suitable Partner shall have the financial resources, proven expertise, ability and incentive to maintain and develop MEK162 and LGX818 as a viable and active competitive force in competition with the Notifying Party and other competitors, together with Array under the terms of the Alliance Agreements.

(e) The Alliance Agreements must neither be likely to create, in light of the information available to the Commission, prima facie competition concerns nor give rise to a risk that the implementation of the Commitments will be delayed. In particular, the Suitable Partner must reasonably be expected to obtain all necessary approvals from the relevant regulatory authorities for the implementation of the Alliance Agreements.

14. In order to be approved by the Commission, the Suitable Purchaser must fulfil the following criteria:

(a) The Suitable Purchaser shall be independent of and unconnected to the Notifying Party and its Affiliated Undertakings;

(b) The Suitable Purchaser shall have the financial resources, proven expertise, ability and incentive to maintain and develop the Divestment Business as a viable and active competitive force in competition with the Notifying Party and other competitors;

(c) The Suitable Purchaser shall have the ability and incentive to develop worldwide and to commercialize in the EEA the Divestment Business, subject to the results of the clinical trials; and

(d) The acquisition of the Divestment Business by the Suitable Purchaser must neither be likely to create, in light of the information available to the Commission, prima facie competition concerns nor give rise to a risk that the implementation of the Commitments will be delayed. In particular, the Suitable Purchaser must reasonably be expected to obtain all necessary approvals from the relevant regulatory authorities for the acquisition of the Divestment Business.

15. The Initial Divestment Agreements shall include the following provisions:

(i) The final binding Alliance Agreements (as well as ancillary agreements) shall be conditional on the Commission's approval. When Array has reached an agreement with a Suitable Partner, it shall submit a fully documented and reasoned proposal, including a copy of the final Alliance Agreements (as well as ancillary agreements), within one week to the Commission and the Monitoring Trustee. Array must be able to demonstrate to the Commission that the partner fulfils the Partner Criteria and that the Alliance Agreements are being designed in a manner consistent with the Commission's Decision and the Commitments. For the approval, the Commission shall verify that the partner fulfils the Partner Criteria and that the Alliance Agreements are being entered into in a manner consistent with the Commitments including their objective to bring about a lasting structural change in the market.

(ii) The final binding Trustee Divestment Agreements (as well as ancillary agreements) shall be conditional on the Commission's approval. When the Divestiture Trustee has reached an agreement with a Suitable Purchaser, it shall submit a fully documented and reasoned proposal, including a copy of the final agreement(s), within one week to the Commission. The Divestiture Trustee must be able to demonstrate to the Commission that the purchaser fulfils the Purchaser Criteria and that the Divestment Business is being sold in a manner consistent with the Commission's Decision and the Commitments. For the approval, the Commission shall verify that the purchaser fulfils the Purchaser Criteria and that the Divestment Business is being

sold in a manner consistent with the Commitments including their objective to bring about a lasting structural change in the market.

(iii) The Monitoring Trustee shall act as a contact point for any question Novartis or Array might have relating to the sale of the Divestment Business, while keeping confidential any business secrets of either Novartis and Array.

Section E. Trustee

I. Appointment procedure

16. Novartis shall appoint a Monitoring Trustee, with prior advice and consent of Array (such consent not to be unreasonably withheld, delayed or conditioned), to carry out the functions specified in these Commitments for a Monitoring Trustee within two weeks of the Effective Date. The Notifying Party commits not to close the Concentration before the appointment of a Monitoring Trustee.

17. If Array has not entered into the Alliance Agreements one month before the end of the First Divestiture Period or if the Commission has rejected a purchaser proposed by Array at that time or thereafter, Novartis shall appoint a Divestiture Trustee. The appointment of the Divestiture Trustee shall take effect upon the commencement of the Trustee Divestiture Period.

18. The Trustee shall:

(a) at the time of appointment, be independent of the Notifying Party and its Affiliated Undertakings;

(b) possess the necessary qualifications to carry out its mandate, for example have sufficient relevant experience as an investment banker or consultant or auditor; and

(c) neither have nor become exposed to a Conflict of Interest.

19. The Trustee shall be remunerated by Novartis in a way that does not impede the independent and effective fulfilment of its mandate. In particular, where the remuneration package of a Divestiture Trustee includes a success premium linked to the final sale value of the Divestment Business, such success premium may only be earned if the divestiture takes place within the Trustee Divestiture Period.

Proposal by Novartis

20. No later than two weeks after the Effective Date, Novartis shall submit the name or names of one or more natural or legal persons whom Novartis, proposes to appoint as the Monitoring Trustee to the Commission for approval. No later than one month before the end of the First Divestiture Period or on request by the Commission, Novartis shall submit a list of one or more persons whom Novartis proposes to appoint as Divestiture Trustee to the Commission for approval. The proposal shall contain sufficient information for the Commission to verify that the person or persons proposed as Trustee fulfil the requirements set out in paragraph 18 and shall include:

(a) the full terms of the proposed mandate, which shall include all provisions necessary to enable the Trustee to fulfil its duties under these Commitments;

(b) the outline of a work plan which describes how the Trustee intends to carry out its assigned tasks.

(c) an indication whether the proposed Trustee is to act as both Monitoring Trustee and Divestiture Trustee or whether different trustees are proposed for the two functions.

Approval or rejection by the Commission

21. The Commission shall have the discretion to approve or reject the proposed Trustee(s) and to approve the proposed mandate subject to any modifications it deems necessary for the Trustee to fulfil its obligations. If only one name is approved, Novartis shall appoint or cause to be appointed the person or persons concerned as Trustee, in accordance with the mandate approved by the Commission. If more than one name is approved, Novartis shall be free to choose the Trustee to be appointed from among the names approved. The Trustee shall be appointed within one week of the Commission's approval, in accordance with the mandate approved by the Commission.

New proposal by Novartis

22. If all the proposed Trustees are rejected, Novartis shall submit the names of at least two more natural or legal persons within one week of being informed of the rejection, in accordance with paragraphs 16 and 21 of these Commitments.

Trustee Nominated by the Commission

23. If further proposed Trustees are rejected by the Commission, the Commission shall nominate a Trustee, whom Novartis shall appoint, or cause to be appointed, in accordance with a trustee mandate approved by the Commission.

II. Functions of the Trustee

24. The Trustee shall assume its specified duties and obligations in order to ensure compliance with the Commitments. The Commission may, on its own initiative or at the request of the Trustee or Novartis, give any orders or instructions to the Trustee in order to ensure compliance with the conditions and obligations attached to the Decision.

Duties and obligations of the Monitoring Trustee

25. The Monitoring Trustee shall:

(i) propose in its first report to the Commission a detailed work plan describing how it intends to monitor compliance with the obligations and conditions attached to the Decision.

(ii) Oversee the continuation of the on-going clinical trials of the Divestment Business with a view to ensuring that appropriate decisions are taken to maintain the economic viability, marketability and competitiveness and monitor compliance by Novartis with the conditions and obligations attached to the Decision. To that end the Monitoring Trustee shall:

(a) monitor the preservation of the economic viability, marketability and competitiveness of the Divestment Business in accordance with paragraph 8 of these Commitments;

(b) supervise the management of the Divestment Business;

(c) with respect to Confidential Information:

- determine all necessary measures to ensure that Novartis does not after the Effective Date obtain any Confidential Information relating to the Divestment Business (except as permitted under the Initial Divestment Agreements),
- make sure that any Confidential Information relating to the Divestment Business obtained by Novartis before the Effective Date is eliminated and will not be used by Novartis (except as permitted under the Initial Divestment Agreements); and
- decide whether such information may be disclosed to or kept by Novartis as the disclosure is reasonably necessary to allow Novartis to carry out the Commitments or as the disclosure is required by law;

(d) monitor the splitting of assets between the Divestment Business and Novartis or Affiliated Undertakings;

(iii) ensure that Novartis makes full and timely disclosure of all information relating to MEK162 and LGX818, so that Array has a prompt and effective opportunity to find and negotiate appropriate Alliance Agreements with a Suitable Partner;

(iv) propose to each of Novartis and Array such measures as the Monitoring Trustee considers necessary to ensure compliance with the conditions and obligations attached to the Decision, in particular the maintenance of the full economic viability, marketability or competitiveness of the Divestment Business and the non-disclosure of competitively sensitive information;

(v) review and assess potential purchasers as well as the progress of the divestiture process and verify that, dependent on the stage of the divestiture process:

(a) potential purchasers receive sufficient and correct information relating to the Divestment Business in particular by reviewing, if available, the data room documentation, the information memorandum and the due diligence process, and

(b) potential purchasers are granted reasonable access to the Personnel;

(vi) act as a contact point for any requests by third parties, in particular potential purchasers, in relation to the Commitments;

(vii) provide to the Commission, sending Novartis a non-confidential copy at the same time, a written report within 15 days after the end of every month that shall cover the operation and management of the Divestment Business as well as the splitting of assets and the allocation of Personnel so that the Commission can assess whether the business is held in a manner consistent with the Commitments and the progress of the divestiture process as well as potential purchasers;

(viii) report to the Commission and to Array (but not to Novartis) on the progress of efforts to find a Suitable Partner and negotiate the Alliance Agreements, and progress on any subsequent sale of the Divestment Business by the Divestiture Trustee;

(ix) promptly report in writing to the Commission, sending Novartis and Array a non-confidential copy at the same time, if it concludes on reasonable grounds that Novartis or Array is failing to comply with these Commitments;

(x) within one week after receipt of the documented proposal referred to in paragraph 15(ii) of these Commitments, submit to the Commission, sending Array a non-confidential copy at the same time, a reasoned opinion as to the suitability and independence of the proposed Suitable Partner and the viability of the Divestment Business after the arrangements are implemented in a manner consistent with the conditions and obligations attached to the Decision;

(xi) in case of disagreement between any of Novartis, Array and/or third parties in relation to matters dealt with by the commitments, discuss those matters with both sides and report to the Commission; and

(xii) assume the other functions assigned to the Monitoring Trustee under the conditions and obligations attached to the Decision.

In carrying out its role, the Monitoring Trustee will keep confidential any business secrets of the parties and third parties.

26. If the Monitoring and Divestiture Trustee are not the same legal or natural persons, the Monitoring Trustee and the Divestiture Trustee shall cooperate closely with each other during and for the purpose of the preparation of the Trustee Divestiture Period in order to facilitate each other's tasks.

Duties and obligations of the Divestiture Trustee

27. Within the Trustee Divestiture Period, the Divestiture Trustee shall sell at no minimum price the Conditional Licence to a Suitable Purchaser, provided that the Commission has approved both the purchaser and the final binding agreement (and ancillary agreements) as in line with the Commission's Decision and the Commitments in accordance with paragraphs 14 and 15(ii) of these Commitments. The Divestiture Trustee shall include in the agreement (as well as in any ancillary agreements) such terms and conditions as it considers appropriate for an expedient sale of the Conditional License in the Trustee Divestiture Period. In particular, the Divestiture Trustee may include in the agreement such customary representations and warranties and indemnities as are reasonably required to effect the sale. The Divestiture Trustee shall protect the legitimate financial interests of Array, subject to the Divestiture Trustee's obligation to divest at no minimum price in the Trustee Divestiture Period.

28. In the Trustee Divestiture Period (or otherwise at the Commission's request), the Divestiture Trustee shall provide the Commission with a comprehensive monthly report written in English on the progress of the divestiture process. Such reports shall be submitted within 15 days after the end of every month with a simultaneous copy to the Monitoring Trustee and a non-confidential copy to the Notifying Party and Array.

III. Duties and obligations of the Parties

29. Novartis and Array shall provide and shall cause their respective advisors to provide the Trustee with all such co-operation, assistance and information as the Trustee may reasonably require to perform its tasks. The Trustee shall have full and complete access to any of Novartis' or Array's or the Divestment Business' books, records, documents, management or other personnel, facilities, sites and technical information necessary for fulfilling its duties under the Commitments and Novartis and Array and the Divestment Business shall provide the Trustee upon request with copies of any document. If necessary, Novartis and Array and the Divestment Business shall make available to the Trustee one or more offices on their premises and shall be available for meetings in order to provide the Trustee with all information necessary for the performance of its tasks.

30. Novartis and Array shall provide the Monitoring Trustee with all managerial and administrative support that it may reasonably request on behalf of the management of the Divestment Business. This shall include all administrative support functions relating to the Divestment Business which are currently carried out at headquarters level. Novartis and Array shall provide and shall cause their respective advisors to provide the Monitoring Trustee, on request, with the information submitted to potential purchasers, in particular give the Monitoring Trustee access to the data room documentation and all other information granted to potential purchasers in the due diligence procedure. Array shall inform the Monitoring Trustee on possible purchasers, submit lists of potential purchasers at each stage of the selection process, including the offers made by potential purchasers at those stages, and keep the Monitoring Trustee informed of all developments in the divestiture process.

31. Array shall grant or procure Affiliated Undertakings to grant comprehensive powers of attorney, duly executed, to the Divestiture Trustee to effect the sale (including ancillary agreements), the Closing and all actions and declarations which the Divestiture Trustee considers necessary or appropriate to achieve the sale and the Closing, including the appointment of advisors to assist with the sale process. Upon request of the Divestiture Trustee, Array shall cause the documents required for effecting the sale and the Closing to be duly executed.

32. Novartis shall indemnify the Trustee and its employees and agents (each an "**Indemnified Party**") and hold each Indemnified Party harmless against, and hereby agrees that an Indemnified Party shall have no liability to Novartis for, any liabilities arising out of the performance of the Trustee's duties under the Commitments, except to the extent that such liabilities result from the wilful default, recklessness, gross negligence or bad faith of the Trustee, its employees, agents or advisors. Array shall indemnify each Indemnified Party and hold each Indemnified Party harmless against, and hereby agrees that an Indemnified Party shall have no liability to Array for, any liabilities arising out of the performance of the Trustee's duties under the Commitments, except to the extent that such liabilities result from the wilful default, recklessness, gross negligence or bad faith of the Trustee, its employees, agents or advisors.

33. At the expense of Novartis, the Trustee may appoint advisors (including for corporate finance, legal advice or oncology expertise), subject to Novartis' approval (this approval not to be unreasonably withheld or delayed) if the Trustee considers the appointment of such advisors necessary or appropriate for the performance of its duties and obligations under the Mandate, provided that any fees and other expenses incurred by the Trustee are reasonable. Should Novartis refuse to approve the advisors proposed by the Trustee the

Commission may approve the appointment of such advisors instead, after having heard Novartis. Only the Trustee shall be entitled to issue instructions to the advisors. Paragraph 32 of these Commitments shall apply mutatis mutandis. In the Trustee Divestiture Period, the Divestiture Trustee may use advisors who served Novartis or Array during the Divestiture Period if the Divestiture Trustee considers this in the best interest of an expedient sale.

34. Novartis agrees that the Commission may share Confidential Information proprietary to Novartis with the Trustee, and Array agrees that the Commission may share Confidential Information proprietary to Array with the Trustee. The Trustee shall not disclose such information and the principles contained in Article 17 (1) and (2) of the Merger Regulation apply mutatis mutandis.

35. The Notifying Party and Array each agree that the contact details of the Monitoring Trustee are published on the website of the Commission's Directorate-General for Competition and they shall inform interested third parties, in particular any potential purchasers, of the identity and the tasks of the Monitoring Trustee.

36. For a period of 10 years from the Effective Date the Commission may request all information from the Parties and Array that is reasonably necessary to monitor the effective implementation of these Commitments.

37. The Initial Divestment Agreements will, *inter alia*, confer on Array the rights and obligations entailed in compliance with the Commitments.

IV. Replacement, discharge and reappointment of the Trustee

38. If the Trustee ceases to perform its functions under the Commitments or for any other good cause, including the exposure of the Trustee to a Conflict of Interest:

(a) the Commission may, after hearing the Trustee, Novartis and Array, require Novartis to replace the Trustee; or

(b) Novartis may, with the advice and consent of Array (which shall not be unreasonably withheld, delayed or conditioned), and with the prior approval of the Commission, replace the Trustee.

39. If the Trustee is removed according to paragraph 38 of these Commitments, the Trustee may be required to continue in its function until a new Trustee is in place to whom the Trustee has effected a full hand over of all relevant information. The new Trustee shall be appointed in accordance with the procedure referred to in paragraphs 16 - 23 of these Commitments.

40. Unless removed according to paragraph 38 of these Commitments, the Trustee shall cease to act as Trustee only after the Commission has discharged it from its duties after all the Commitments with which the Trustee has been entrusted have been implemented. However, the Commission may at any time require the reappointment of the Monitoring Trustee if it subsequently appears that the relevant remedies might not have been fully and properly implemented.

Section F The review clause

41. The Commission may extend the time periods foreseen in the Commitments in response to a reasoned request from either Novartis or Array or, in appropriate cases, on its own initia-

tive. Novartis or Array shall submit such reasoned request to the Commission no later than one month before the expiry of that period, showing good cause. This request shall be accompanied by a report from the Monitoring Trustee, who shall, at the same time send a non-confidential copy of the report to the Notifying Party. Only in exceptional circumstances shall Novartis or Array be entitled to request an extension within the last month of any period.

42. The Commission may further, in response to a reasoned request from the Notifying Party showing good cause waive, modify or substitute, in exceptional circumstances, one or more of the undertakings in these Commitments. This request shall be accompanied by a report from the Monitoring Trustee, who shall, at the same time send a non-confidential copy of the report to the Notifying Party. The request shall not have the effect of suspending the application of the undertaking and, in particular, of suspending the expiry of any time period in which the undertaking has to be complied with.

Section G. Entry into force

43. The Commitments shall take effect upon the date of adoption of the Decision.

(Signed)

Brussels, 27 January 2015

Duly authorised for and on behalf of Novartis AG

Schedule

1. The Divestment Business is currently operated by Novartis and consists of two pipeline compounds (MEK162 and LGX818) undergoing a variety of clinical trials. The Divestment Business essentially consist of all rights necessary to continue developing and, if development is successful, commercialise MEK162 and LGX818 (including continuation of the existing clinical trials).

2. In accordance with Section B of these Commitments, the Divestment Business encompasses:

(a) the following main tangible assets:

(i) existing inventory of MEK162 and LGX818 drug substance and drug product;

(ii) all documents including books, records and files to the extent related to MEK162 or LGX818.

(b) the following main intangible assets:

(i) all patent rights as listed in Annex 2, and all know-how, including manufacturing technology, to the extent related to MEK162 or LGX818;

(ii) the rights to conduct the clinical trials sponsored by Novartis and related to MEK162 as further detailed in Annex 3;

(iii) the rights to conduct the clinical trials related to LGX818 as further detailed in Annex 4;

(iv) the trademarks and domain names ([...]) for MEK162. A list of these is provided in Annex 5; and

(v) the domain names [...].

(c) the following main licences, permits and authorisations:

(i) all regulatory filings, correspondence and registrations (including, but not limited to, those between Novartis and the Food and Drug Administration and any other regulatory agencies) to the extent related to MEK162 or LGX818.

(d) the following main contracts, agreements, leases, commitments and understandings:

(i) all third party agreements primarily related to MEK162 and LGX818, including agreements related to manufacturing technology and ongoing investigator-initiated clinical trials involving MEK162 or LGX818.

(e) the following customer, credit and other records:

(i) all documentation related to product marketing to the extent specifically related to MEK162 and/or LGX818;

(ii) all product development reports to the extent related to MEK162 and/or LGX818; and

(iii) all clinical trial and safety data, databases and analyses (including the MEK162 safety database) to the extent related to MEK162 and/or LGX818.

(f) the following Key Personnel:

(i) [...]. For a period of [...] after Closing, Array shall have the opportunity to interview such employees and enter into employment contracts with employees (should Array wish to do so).

(g) the arrangements for the supply with the following products or services for a transitional period after Closing:

(i) During the transition period Novartis will supply Array with both MEK162 and LGX818.

3. The Divestment Business shall not include:

(a) any right, title or interest in or to any of the assets of Novartis or Affiliated Undertakings other than those specified in paragraph 2 of this Schedule and, for the avoidance of doubt will not include:

(i) the name “Novartis”, together with all variations thereof and all trademarks, service marks, domain names, trade names, trade dress, corporate names, logos and other identifiers of source containing, incorporating or associated with any of the foregoing, save as provided for in paragraph 2 of this Schedule;

(ii) any compounds other than MEK162 (or any other Array compound) and LGX818 and related submissions to a regulatory authority of any appropriate regulatory application together with any related correspondence and documentation (including any submission to a regulatory advisory board, marketing authorisation application, and any supplement or amendment thereto);

(iii) accounts receivable, pre-paid expenses and any cash or cash equivalents of Novartis or Affiliated Undertakings; and

(iv) any plant, tangible property, equipment or employees of Novartis or Affiliated Undertakings, save as provided for in paragraph 2 of this Schedule.

Annex 1

Ongoing Conditional Licence Provisions

The Conditional Licence Agreement, agreed between Novartis and Array on 19 January 2015, includes, *inter alia*, the following provisions regarding the Products:

1 Rights

1.1 The Suitable Purchaser would have the exclusive right to seek regulatory approvals and Commercialize in the EEA and the right to conduct clinical trials and other Development activities for that purpose.

1.2 Array would have the exclusive right to seek regulatory approvals and Commercialize in the US and RoW and the right to conduct clinical trials and other Development activities for that purpose.

1.3 There would be no restriction on where either party could conduct trials.

For purposes of these rights: "Commercialize" means to pursue regulatory approvals, market, manufacture, promote, distribute, import, export, offer to sell and/or sell a product and/or conduct related commercialization activities, including activities relating to pursuit of regulatory approvals, marketing, manufacturing, promoting, distributing, importing, exporting, offering for sale or selling such product; and "Development" means drug development activities, including preclinical and clinical activities, test method development and stability testing, assay development and audit development, toxicology, formulation, manufacturing and distribution of compounds and products for use in clinical trials including placebos and comparators as the case may be, development activities with respect to a diagnostic product, quality assurance/quality control development, statistical analysis, clinical studies, packaging development, and regulatory affairs.

2 Existing Trials

2.1 Array would remain responsible for all existing trials and responsible for contracting with and managing any contract research organization(s) (CRO) that may be involved with such trials.

2.2 Each party would have the right to cross-reference, file or incorporate by reference any study data and data included or referenced in any regulatory approvals for the trials in order to support regulatory approvals to market the Products in its territory.

2.3 There would be a Joint Steering Committee ("**JSC**") responsible for the overall coordination and oversight of the trials, including (i) providing general oversight, (ii) discussing and reviewing the conduct of the trials, (iii) discussing and reviewing any submissions to any regulatory authority in connection with any regulatory approvals for or with respect to the trials, (iv) discussing and reviewing any amendments to the clinical plans, (v) discussing and reviewing the results of the trials, and (vi) overseeing data analysis and study completion activities.

2.4 The Suitable Purchaser would have the right to require that:

Array implement modifications to on-going clinical trials that are reasonably requested by the EMA, provided that such modifications do not prejudice Array as regards safety or reputational issues or material delay in on-going clinical trials or planned clinical trials that have a completed protocol and, provided further, that the Suitable Purchaser agrees to reimburse Array for all costs and expenses in connection with such modification; and

2.4.1 Array does not implement modifications to on-going clinical trials for any Products (or products incorporating MEK162 and/or LGX818) that would prejudice the Suitable Purchaser or its intended objectives for such clinical trial, and, provided further, that Array agrees to reimburse the Suitable Purchaser for all costs and expenses in connection with such modifications;

Any disputes would be escalated and ultimately resolved by a third party under a dispute resolution procedure.

3 New Trials

3.1 ***Responsibility.*** The Suitable Purchaser would be responsible, at its expense, for the development of the Products for approval in the EEA, and Array would be responsible, at its expense, for the development of the Products for approval in the US/RoW. Other than for joint development activities (described below), neither Party would have the right to access or use the results of any clinical trials or other development activities.

3.2 ***Development Plans.*** The development of Products would be governed by development plans that describe the proposed program of development for the Products in each territory. Each party would be responsible for preparing and implementing the development plan for its territory, provided, that the development plans would be reviewed by the JSC and each party would give due consideration to any comments of the other party.

3.3 ***Clinical Trials.*** Prior to commencing any clinical trial, the Party that proposes to conduct such clinical trial would first submit to the JSC the proposed protocol for such proposed clinical trial. Neither Party would be permitted to proceed with such clinical trial if the other Party reasonably determines that the clinical trial is reasonably likely to have a material adverse impact, by reason of safety or reputational issues or material delay in on-going clinical trials or planned clinical trials that have a completed protocol, on the development and/or commercialization of Products in its territory. Any disputes would be escalated and ultimately resolved by a third party under a dispute resolution procedure.

3.4 ***Joint Development Activities.*** Either party shall propose to collaborate with the other Party to conduct clinical trials with respect to Products. If the other Party elects to participate, the parties would cooperate with respect to the conduct of the clinical trial and share the costs. If the other party declines to participate, then the party proposing the trial could proceed (and the other party would have no right to access or use the results of the clinical trial), except where the other Party reasonably determines that the clinical trial is reasonably likely to have a material adverse impact, by reason of safety or reputational issues or material delay in on-going clinical trials or planned clinical trials that have a completed protocol, on the development and/or commercialization of Products in its territory as described above.

Annex 2

MEK162 Patent Rights

[...]

LGX818 Patent Rights

[...]

Annex 3: Novartis Sponsored Clinical Trials for MEK162

[...]

Annex 4: Novartis Sponsored Clinical Trials for LGX818

[...]

Annex 5

MEK162 Trademarks and Domain Names

1 Trademarks

[...]

2 Domain Names

[...]

Annex 6

MEK Subordinate Agreements

[...]

Annex 7

LGX Subordinate Agreements

[...]