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EUROPEAN COMMISSION  
DG Competition

***Case M.7872 - NOVARTIS / GSK (OFATUMUMAB  
OUTOIMMUNE INDICATIONS)***

Only the English text is available and authentic.

**REGULATION (EC) No 139/2004  
MERGER PROCEDURE**

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Article 6(1)(b) NON-OPPOSITION  
Date: 18/12/2015

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## EUROPEAN COMMISSION

Brussels, 18.12.2015  
C(2015) 9710 final

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 Where possible the information omitted has been replaced by ranges of figures or a general description.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 Sir/Madam,

**Subject: Case M.7872 – Novartis / GlaxoSmithKline (*ofatumumab* autoimmune indications)  
Commission decision pursuant to Article 6(1)(b) of Council Regulation No 139/2004<sup>1</sup> and Article 57 of the Agreement on the European Economic Area<sup>2</sup>**

- (1) On 18 November 2015, the European Commission received notification of a proposed concentration pursuant to Article 4 of the Merger Regulation by which Novartis AG ("Novartis" or the "Notifying Party", Switzerland), acquires within the meaning of Article 3(1)(b) of the Merger Regulation control of the autoimmune indications of the pharmaceutical substance *ofatumumab* (the "Target") from GlaxoSmithKline plc ("GSK", United Kingdom) by way of purchase of assets, hereinafter "the Transaction".

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<sup>1</sup> 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.

<sup>2</sup> OJ L 1, 3.1.1994, p.3 ("the EEA Agreement").

- (2) Novartis and the Target are referred to as "the Parties".

## 1. THE PARTIES

- (3) **Novartis** is a Swiss healthcare company, active globally in the development, distribution and marketing of medical products. Its main areas of activity cover pharmaceuticals, eye care and generics.
- (4) **The Target** comprises the rights to the auto-immune indications of *ofatumumab* (an anti-CD20 monoclonal antibody), which are still in development. For one auto-immune indication in particular (pemphigus vulgaris), *ofatumumab* is currently in phase III trials.

## 2. THE OPERATION AND CONCENTRATION

### 2.1.1. The Oncology Transaction

- (5) *Ofatumumab* is an anti-CD20 monoclonal antibody developed both for auto-immune and oncology indications.<sup>3</sup> Novartis acquired the oncology indications of *ofatumumab* from GSK<sup>4</sup> as part of a broader, initial, transaction, which was authorised by the Commission subject to commitments with the Decision of 28 January 2015 in Case M.7275 – *Novartis / GlaxoSmithKline Oncology Business*, and closed on 2 March 2015 (the "*Oncology Transaction*").

### 2.1.2. The Transaction

- (6) GSK had retained the auto-immune indications business of *ofatumumab*, through a [...].<sup>5</sup> Under the terms of the Implementation and Transfer Agreement entered into between Novartis and GSK on 21 August 2015 (the "ITA"), Novartis will acquire from GSK the *ofatumumab* auto-immune indications business. The consideration for this business will be paid in a staggered form: Novartis will pay US\$ 300 million at closing. An additional US\$ 200 million will be payable when Novartis starts the Phase III study for the use of *ofatumumab* in multiple sclerosis. Novartis has also agreed to make additional payments of up to US\$ 764\* million to GSK in the future, if certain pre-determined milestones are achieved. Novartis has also agreed to pay to GSK royalties of up to 12% on any future net sales of the drug in the auto-immune indications.
- (7) The Target business is composed of the rights to develop, manufacture, promote and market *ofatumumab* for auto-immune indications, and tangible assets, such as biological materials and cells, product inventory, Investigational New Drug Applications granted by the US Food and Drug Administration, clinical trial data, as well as supply contracts.<sup>6</sup>

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<sup>3</sup> *Ofatumumab* is already marketed under the brand name Arzerra for oncology applications.

<sup>4</sup> GSK is a British pharmaceutical company active worldwide in the areas of pharmaceuticals, vaccines and consumer health products.

<sup>5</sup> See letters from Novartis' external counsel to the case team dated [...].

\* should read: US\$ 534 million

<sup>6</sup> More specifically, as per the ITA, tangible assets include [...].

### 2.1.3. *Notifiable concentration*

- (8) The Notifying Party has expressed the view that the Transaction does not constitute a concentration, because it does not involve the acquisition of an undertaking or part of an undertaking, for the purposes of the Merger Regulation. Novartis has in particular stated that the transaction involves the acquisition of rights for development or pipeline indications of which the future development and potential market entry is inherently uncertain and, even in the best case scenario, very far off in the future. Novartis asserts that it does not anticipate to launch *ofatumumab* for multiple sclerosis before [...]. The Notifying Party concluded that, at this stage, it is not possible to attribute any market turnover to these intangible assets that are being acquired and, consequently, the Transaction does not constitute a concentration for purposes of Article 3(1) of the Merger Regulation.
- (9) In this regard, the Commission observes that the Transaction at hand relates to the acquisition of sole control of the necessary intangible<sup>7</sup> and the core tangible assets for the development, manufacture and commercialisation of the resulting pharmaceutical products in question. For one auto-immune indication, relapsing remitting multiple sclerosis, the acquired *ofatumumab* assets have completed phase II trials [...]. But for another auto-immune indication, pemphigus vulgaris, currently the acquired *ofatumumab* assets are already in phase III clinical trials.<sup>8</sup> According to an internal assessment of the Notifying Party, based on [...], *ofatumumab* has a [...] probability (at [...]%) of successful launch.<sup>9</sup>
- (10) Moreover, Novartis has agreed to pay to GSK royalties of up to 12% on any future net sales of *ofatumumab* for auto-immune indications. This fact suggests that both Novartis and GSK expect that the timely entry of *ofatumumab* in the market for auto-immune indications is quite likely, including in particular the pemphigus vulgaris indication for which the drug is already in the advanced Phase III trials. Likewise, the fact that Novartis has agreed to pay to GSK US\$ 200 million following the start of phase III study in the use of *ofatumumab* for multiple sclerosis, on top of the US\$ 300 million payable at closing, suggests that both undertakings expect that the start of these phase III trials is quite likely and imminent. This is an additional factor supporting the conclusion that the business acquired by Novartis is reasonably expected to enter the market within a reasonable period of time.
- (11) The Commission therefore considers that the acquisition of the *ofatumumab* assets in question falls within the scope of the Merger Regulation because it involves the acquisition of the intangible and all core tangible assets that are expected to enable the acquirer to access the market, and therefore to produce a market turnover, within a reasonable timeframe. Indeed, in the context of this kind of industries with

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<sup>7</sup> As regards the intangible assets comprised in the Transaction, the ITA provides for [...].

<sup>8</sup> Phase III trials are commonly known as "confirmatory" trials, which aim to establish the final benefit-risk profile of the drug in a *well-characterised target population of relevance for clinical practice*. (EMA, *Guideline on the evaluation of anticancer medicinal products in man*, page 18.) The patients enrolled in these clinical trials should have the disease that the pharmaceutical company would like to obtain the indication for. Therefore, at the latest at the time of phase III trials, there will be clarity as to the relevant pharmaceutical market that will be addressed by the tested drug.

<sup>9</sup> See Novartis' internal document, [...].

important research and development projects, the acquisition of assets that are already in phase III clinical trials can be reasonably assumed to be capable of generating a turnover in the foreseeable future.<sup>10</sup>

- (12) The Transaction thus constitutes the acquisition of part of an undertaking within the meaning of Article 3(1)(b) of the Merger Regulation.

### **3. UNION DIMENSION**

- (13) Since the Transaction is a concentration taking place within a period of two years from the Oncology Transaction between the same undertakings, then, pursuant to Article 5(2), second sub-paragraph, of the Merger Regulation, the two transactions should be treated as one and the same concentration arising at the date of the last transaction for the purpose of calculating the turnover thresholds.

- (14) In this case, the undertakings concerned have a combined aggregate world-wide turnover of more than EUR 5 000 million.<sup>11</sup> Each of them has an EU-wide turnover in excess of EUR 250 million, but they do not 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.

### **4. MARKET DEFINITION AND COMPETITIVE ASSESSMENT**

- (15) The Transaction concerns the auto-immune indications of *ofatumumab* and the relevant markets for treatments of certain auto-immune diseases. As regards the markets affected by the Oncology Transaction, the Commission refers to the assessment in the Decision of 28 January 2015 in Case M.7275 – *Novartis / GlaxoSmithKline Oncology Business*.
- (16) The Transaction leads to an overlap with Novartis' activities only in the treatment of multiple sclerosis. There appear to be no overlaps or other competitively relevant relationships as to the other auto-immune indications for which *ofatumumab* is in clinical development, namely:<sup>12</sup>

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<sup>10</sup> Contrary to Novartis's assertions, the guidance provided by paragraph 24 of the Commission Consolidated Jurisdictional Notice under Council Regulation (EC) No 139/2004 on the control of concentrations between undertakings (OJ C95 of 16.04.2008) does not limit the Commission's jurisdiction to concentrations involving target undertakings or parts of undertakings with *current* market turnover. Paragraph 24 of the Commission Consolidated Jurisdictional Notice requires that the acquired *part of an undertaking* constitutes a clearly identifiable *business*, which can operate separately from the rest of the disposing undertaking, and is capable of producing a market turnover. As explained in paragraph 5 of the Commission Consolidated Jurisdictional Notice, the concepts of an *undertaking* and a *part of an undertaking* under Article 3 Merger Regulation are distinct and independent from the notion of *undertakings concerned* and the rules on the calculation of turnover set forth in Article 5 Merger Regulation.

<sup>11</sup> Turnover calculated in accordance with Article 5 of the Merger Regulation.

<sup>12</sup> For completeness, Novartis' subsidiary Sandoz offers a generic version of certain pharmaceuticals that may be prescribed off-label for the treatment of pemphigus vulgaris and neuromyelitis optica. However, these generic treatments are competing essentially against the originator and other generic versions of the same molecule.

- a. pemphigus vulgaris (a chronic autoimmune disease that causes blistering skin lesions and mucosal erosions), for which *ofatumumab* is currently in phase III clinical trials;<sup>13</sup>
  - b. neuromyelitis optica (a rare inflammatory and demyelinating autoimmune disorder that causes recurrent attacks of optic neuritis), [...].
- (17) It should also be noted that GSK terminated the development of *ofatumumab* for rheumatoid arthritis after [...]<sup>14</sup> and therefore this indication will not be further discussed in this decision.

#### 4.1. Market definition for multiple sclerosis ("MS")

##### 4.1.1. Product market

- (18) *Ofatumumab* is an anti CD-20 monoclonal antibody for subcutaneous injection which is currently developed for relapsing-remitting MS ("RRMS").
- (19) MS is an autoimmune disease in which the body immune system attacks the nerve fibres in the central nervous system – degenerating the myelin coating that insulates the nerves and helps the transmission of nerve impulses between the brain and other parts of the body. MS affects about 2.5 million people worldwide. As to the treatment architecture, there is no curative therapy for MS but only long term disease modifying therapies ("DMT") aimed at reducing the disease activity.
- (20) In previous decisions in which the Commission analysed the market for MS,<sup>15</sup> it concluded that it was not necessary to decide whether different attributes of DMT for MS (such as efficacy, side effects, route and frequency of administration) constitute relevant parameters for defining product markets. Also, the Commission did not consider a possible sub-segmentation by types of MS, such as RRMS.

##### *Notifying Party's views*

- (21) The Notifying Party submits that there are three forms of MS, reflecting the way that the disease evolves over time:
- i. RRMS, the most common form of MS, affecting around 85% of MS patients. It is characterised by clear episodes of inflammatory activity (relapses) alternated with periods in which the illness appears to fade or even disappear (remittances);
  - ii. secondary-progressive MS ("SPMS"), which is developed subsequently by two-thirds of RRMS patients and characterised by a progressive worsening of the conditions; and

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<sup>13</sup> Novartis had a pipeline compound, VAY736, a monoclonal antibody which completed phase II clinical trials for the treatment of PV. However, [...]. See Novartis' internal document, [...].

<sup>14</sup> [...].

<sup>15</sup> See for example cases M.5999 – *Sanofi-Zentiva/Genzyme* and M.4049 – *Novartis/Chiron*.

- iii. primary-progressive MS ("PPMS"), which only occurs for 10-15% of MS patients and characterised by a steadily worsening disease state from the outset, with no RRMS initial phase.
- (22) Within RRMS treatments, the Notifying Party submits that there are broadly three types of DMTs reflecting similar efficacy/safety profiles with different routes of administration:
- i. injectable therapies, which provide for moderate efficacy and have a good long-term safety profile (for example mild side effects);
  - ii. oral therapies, which offer improved efficacy but also lead to increased serious side effects and have been available to patient only over the last 5 years;
  - iii. monoclonal antibodies, which also deliver further improved efficacy but have significant increased risks of side effects.<sup>16</sup>
- (23) According to the Notifying Party, these types of therapies would broadly reflect lines of treatment for RRMS, injectables being the first line of treatment, followed by oral therapies and finally by monoclonal antibodies (if necessary).

*The Commission's assessment*

- (24) The market investigation broadly indicated that a distinction may be drawn by type of MS, distinguishing the relapsing-remitting form from progressive forms of MS (SPMS and PPMS). Indeed, a majority of responding practitioners in the field ("Key Opinion Leaders" or "KOL") considered that RRMS has specific clinical manifestations (clear relapses and periods of remission) and treatment architecture, with DMTs having beneficial effects essentially on RRMS. However, some KOLs highlighted that, as to clinical manifestations, there may be an overlap between RRMS and early stages of SPMS and, as to treatment, anti-inflammatory drugs used for RRMS may have little effect on progressive MS.<sup>17</sup>
- (25) The market investigation also broadly confirmed that DMTs for RRMS can be classified according to their modes of action and efficacy/safety profiles. *Interferon*-based drugs (which are mostly injectables) are generally considered as less efficient but safer than oral therapies and monoclonal antibodies, and tend to be used as first line of treatment. Monoclonal antibodies, namely *natalizumab* and *alemtuzumab*, are generally referred as high-efficacy drugs, used as second- or third-lines of treatment, after injectables and oral therapies.
- (26) However, whilst if the pipeline monoclonal antibodies *ofatumumab* and *ocrelizumab*<sup>18</sup> are usually referred to as high-efficacy drugs competing with the other monoclonal antibodies, respondents also highlighted that their safety profile

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<sup>16</sup> Two monoclonal antibodies are currently marketed: *natalizumab* by Biogen and *alemtuzumab* by Sanofi (both are administered by infusion).

<sup>17</sup> Minutes of a conference call with a competitor dated 2 December 2015; replies of Key Opinion Leaders to questions 3 and 4 of questionnaire Q1 – Multiple sclerosis.

<sup>18</sup> *Ocrelizumab* is a anti-CD20 monoclonal antibody currently undergoing a phase III clinical trial. It belongs to Roche.

could be better than existing treatments, thus opening the possibility to use them as earlier lines of treatment for RRMS, similarly to oral therapies or *interferon*-based drugs.<sup>19</sup>

- (27) As to the possible distinction by galenic form (such as injectable, oral and infusion), the market investigation revealed that galenic form has little effect on the treatment decision. While patients may prefer oral therapies as compared to injectables for instance, products in the same galenic form would not necessarily belong to the same market because of their different modes of action and efficacy/safety profiles.<sup>20</sup>
- (28) For the purpose of this case, it is not necessary to conclude on the exact product market definition, since, irrespective of the product market definition, the Transaction is unlikely to give rise to serious doubts as to its compatibility with the internal market for MS.

#### 4.1.2. *Geographic market*

- (29) In line with the findings of the Commission in past decisions regarding finished dose pharmaceuticals, the Notifying Party submits that the market for MS treatment is national in scope for marketed products<sup>21</sup> and at least EEA-wide in scope for pipeline products.<sup>22</sup>
- (30) For the purpose of this case, it is not necessary to conclude on the exact geographic market definition, since, irrespective of whether the market is defined at national or EEA level, the Transaction is unlikely to give rise to serious doubts as to its compatibility with the internal market for MS.

#### 4.2. **Competitive assessment for multiple sclerosis**

- (31) In its portfolio, Novartis owns the following drugs for the treatment for MS, which are all indicated (or intended to be) for RRMS:
- i. Marketed patented treatments:  *fingolimod* (Gilenya), an oral therapy, and  *interferon beta-1b* (Extavia), an injectable therapy;<sup>23</sup>
  - ii. Pipeline treatments:  *siponimod* (BAF312), an oral therapy in phase II clinical trials, and CJM112, a monoclonal antibody with phase II clinical trials not yet initiated.

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<sup>19</sup> Minutes of conference calls with competitors dated 25 November 2015, 26 November 2015, 27 November 2015 and 2 December 2015; replies of Key Opinion Leaders to questions 6 and 7 of questionnaire Q1 – Multiple sclerosis.

<sup>20</sup> Replies of Key Opinion Leaders to questions 8 of questionnaire Q1 – Multiple sclerosis.

<sup>21</sup> See for example cases M.7559 – Pfizer / Hospira, M.7379 – Mylan / Abbott EPD-DM, M.7276 – GlaxoSmithKline / Novartis Vaccines Business (excl. Influenza) / Novartis Consumer Health Business, M.7275 – Novartis / GlaxoSmithKline Oncology Business and M.5253 – Sanofi-Aventis / Zentiva.

<sup>22</sup> See for example cases M.7559 – Pfizer / Hospira, M.7480 – Actavis / Allergan and M.7275 – Novartis / GlaxoSmithKline Oncology Business.

<sup>23</sup> Novartis also markets in the US  *glatiramer acetate* generic (Glatopa), a generic version of Teva's Copaxone (injectable treatment), but [...].



- (32) In the market for all DMTs for RRMS, Novartis' market share derived from Gilenya and Extavia's sales was below 30% over the last three years in all EU countries where Novartis is active, except for Ireland in 2014 ([30-40]%). Novartis' main competitors are Biogen, leading the market with [20-30]% to [50-60]% market share in the EU countries where Novartis is active,<sup>24</sup> as well as Teva, Merck, Bayer and Sanofi-Genzyme.
- (33) In particular, Biogen has a wide portfolio of marketed drugs for RRMS including an injectable therapy (*interferon beta-1a*, Avonex), an oral therapy (*dimethyl fumarate*, Tecfidera) and a monoclonal antibody (*natalizumab*, Tysabri). On the narrowest possible segment, limited to monoclonal antibodies, Novartis does not have any marketed or pipeline product (with the exception of CJM112, discussed further below); only Sanofi (*alemtuzumab*) and Biogen (*natalizumab*) are currently active on this segment.

#### *Notifying Party's view*

- (34) The Notifying Party considers that the Transaction will mainly complement Novartis' existing portfolio of pharmaceuticals for the treatment of RRMS, given that *ofatumumab* has a different method of action, mode of administration and overall safety profile than its other marketed and pipeline drugs.
- (35) The Notifying Party also submits that numerous competitors, such as Biogen, Teva and Sanofi, will remain post-Transaction and that numerous compounds are, like *ofatumumab*, in development. In particular, the Notifying Party indicates that Roche's *ocrelizumab* is estimated to be the first anti-CD20 monoclonal antibody which will be approved in Europe, with an expected launch in 2017.

#### *Commission's assessment*

- (36) The market investigation revealed that, in the MS field, Novartis will continue to face strong competition from Teva, Bayer, Sanofi, as well as from Biogen which currently leads the market for RRMS treatment and has a similar sizeable portfolio of treatments as Novartis.<sup>25</sup>
- (37) The market investigation also confirmed that the Transaction will mostly complement Novartis' portfolio, with *ofatumumab* not being in close competition with other MS treatments of Novartis.<sup>26</sup> The product within Novartis' portfolio of pharmaceuticals for RRMS which would be closest to *ofatumumab* is its pipeline drug CJM112, an anti-IL17 monoclonal antibody. However, this pipeline does not have the same mechanism of action as *ofatumumab*. Moreover, it has [...].<sup>27</sup>

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<sup>24</sup> In particular, Biogen market share in 2014 was [30-40]% in Ireland, higher than Novartis'.

<sup>25</sup> Minutes of a conference call with a competitor dated 2 December 2015.

<sup>26</sup> See, in particular, replies to questions 11, 12, 16 and 17 of questionnaire Q1 – Multiple sclerosis.

<sup>27</sup> See Novartis' internal document, [...].

- (38) More importantly, the market investigation widely confirmed that *ofatumumab*'s closest future competitor is Roche's pipeline drug *ocrelizumab* which has the same mechanism of action (CD20 inhibitor).<sup>28</sup>
- (39) Given Novartis' limited overall market position for RRMS and the evidence indicating that *ofatumumab*'s closest future competitor is Roche's *ocrelizumab*, the Transaction is unlikely to raise serious doubts as to its compatibility with the internal market for MS.

## 5. CONCLUSION

- (40) For the above reasons, the European Commission has decided not to oppose the notified operation and to declare it compatible with the internal market and with the EEA Agreement. This decision is adopted in application of Article 6(1)(b) of the Merger Regulation and Article 57 of the EEA Agreement.

*For the Commission*

*(Signed)*  
*Margrethe VESTAGER*  
*Member of the Commission*

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<sup>28</sup> Minutes of conference calls with competitors dated 25 November 2015 and 2 December 2015; replies of Key Opinion Leaders to question 13 of questionnaire Q1 – Multiple sclerosis.