Closer Look

MEMORANDUM

Novartis 4Q13 Highlights - Galvus up 29% in 4Q13, 32% for full year; investing in secukinumab for early type 1 diabetes - January 29, 2013

Executive Highlights

- Galvus (vildagliptin) franchise sales rose 29% in 4Q13 to $328 million; full-year 2013 sales grew 32% to $1.2 billion, the franchise's first time reaching blockbuster status.
- Lucentis (ranibizumab) sales in 4Q13 were fairly flat ($630 million) YOY and rebounded 8% sequentially; the product continues to face pressure from Bayer's Eylea (aflibercept).
- Novartis' SGLT-1/2 dual inhibitor LIK066 remains in phase 2; notably, the company is investing its psoriasis drug secukinumab for beta cell preservation in recent onset type 1 diabetes.

This morning, Novartis CEO Joseph Jimenez presented the company's performance update for 4Q13 and the full-year 2013. Galvus (vildagliptin) continued its fairly robust performance from the first three quarters of 2013: in 4Q13, franchise sales rose 29% to $328 million from 4Q12, and rose 4% sequentially. Ironically, it was once a major disappointment that Galvus wasn't approved in the US; now, since major global weakness in the category is stemming from US weakness, it's actually a help to Novartis' DPP-4 inhibitor results. Full-year sales grew 32% to $1.2 billion, making the franchise a blockbuster (annual sales over $1 billion) for the first time. It was a relief to see a company where full-year results were on par with the fourth quarter; we're expecting 4Q13 results to be weaker than full-year results for a number of manufactures, especially those who are over weighted in DPP-4 inhibitors, a category that seems to be seeing more pricing competition than other classes - probably because this class is hard to differentiate, currently.

News was more mixed for Lucentis (intravitreal ranibizumab), Novartis' therapy for diabetic macular edema. Novartis achieved total sales for Lucentis in 4Q13 of $630 million, representing a 0.6% slide year-over-year (YOY) but and an 8% sequential rebound sequentially. The product continues to face competition from Bayer's Eylea (aflibercept).

Turning to Novartis' pipeline, we found a phase 2 trial on ClinicalTrials.gov investigating secukinumab (Novartis' drug for psoriasis) for beta cell preservation in recent onset type 1 diabetes (ClinicalTrials.gov Identifier: NCT02044848). LIK066, an SGLT-1/2 dual inhibitor, remains in phase 1; Novartis expects a possible regulatory filing no sooner than 2018. Included below are our top #5 highlights from the quarterly update, followed by selected Q&A.

1. The Galvus (vildagliptin) franchise continued its fairly robust growth in 4Q13, and hit blockbuster status (annual sales over $1 billion) for the first time. In 4Q13, Galvus franchise revenue rose 29% as reported from 4Q12 (37% in constant currencies) to $328 million. Sequentially, 4Q13 sales increased 4% (compared with 9% sequential growth in 3Q13, 8% in 2Q13, and 5% in 1Q13). Full-year 2013 sales grew 32% (40% in constant currencies) to $1.2 billion, building on 34% growth as reported in 2012 (of course, 2013's growth is from a higher base of $910 million compared to $677 million). As a reminder, Novartis' DPP-4 inhibitor is only marketed outside the US. During today's presentation, management attributed the franchise's growth to "strong performance"(we assume patient gains) and new indications in the EU, including as an add-on to insulin and as triple therapy. Management also noted that Galvus has the largest DPP-4 inhibitor market share in over 11 countries, despite being second or third to market in most geographies. As noted, the fact that it is not available in the US means it is not experiencing the more marked US weakness that other manufacturers are.

- **BMS/AZ's Onglyza (saxagliptin), the only other major DPP-4 inhibitor for which we have 4Q13 figures, had a weaker performance in 4Q13, particularly in the US.** Worldwide Onglyza franchise sales rose 13% as reported from 4Q12 to $224 million, representing the franchise's lowest quarterly growth to date. Onglyza franchise sales grew 24% in the full-year 2013 to $877 million. A clue to the differing performance comes from looking at the geographic breakdown of Onglyza's and Galvus' performances: domestic Onglyza sales grew 4% in 4Q13, while ex-US sales increased 34% (Galvus is only marketed ex-US, as noted above). Galvus' global growth was 32% globally and didn't have weak US numbers to pull down the global result. In recent quarters, we have seen signs of a gradual domestic slowing in the DPP-4 inhibitor class, probably due to a combination of factors:
    - the introduction of SGLT-2 inhibitors;
    - lingering pancreatitis fears (doctors may be more worried about litigation in the US);
    - the drying-up of patient flow from TZDs (which had been more prevalent in the US); and
    - pricing pressure intensified by payers who are making it challenging for manufacturers to differentiate their products (arguably, DPP-4 inhibitors are more similar to each other than drugs in other classes).

  Perhaps, by eschewing the US market (although certainly not by choice originally), Novartis and Galvus have avoided the "bullet" of a DPP-4 inhibitor class slowdown in the US.

- **During Novartis' 3Q13 update, management suggested that Galvus might be withdrawn from Germany due to a ruling from the German Federal Joint Committee (G-BA) mandating effectively generic-level pricing of the drug.** We have not heard news on whether Novartis will indeed withdrawing the drug and it is hard to speculate on the specific effect of the German decision, as Novartis does not break out Galvus sales by country; however, we certainly know Galvus' sales would suffer as a result of this development, both directly as well as indirectly, since this could set a quite unfavorable precedent (see #5).

2. On a surprise note (this was not discussed in the call), we found a Novartis-sponsored phase 2 trial on ClinicalTrials.gov investigating the ability of secukinumab (Novartis' drug for psoriasis) to preserve beta cells in newly diagnosed type 1 diabetes patients. The study (registered on ClinicalTrials.gov a week ago) has an estimated enrollment of 100 patients, and a forecasted primary completion date in 2019 (Identifier: NCT02044848). The reason for the long wait appears to be in the intensity of the safety analysis - one of the primary outcomes is the number of patients with adverse events over the course of three years (including a one-year treatment period). Given that safety has been a key concern for prior type 1 diabetes candidates, we are not surprised about the prioritization on robustly proving safety and are interested in following this study.

3. The presentation's supplementary slides indicated that Novartis expects a regulatory submission of its phase 2 SGLT-1/SGLT-2 dual inhibitor LIK066 no sooner than 2018. We would have hoped for sooner, but can understand that extra time and diligence may be needed given the relative novelty of the SGLT-1/2 dual inhibitor class. A 12-week dose finding study of LIK066 is still listed as not yet recruiting on ClinicalTrials.gov (Identifier: NCT01824264); however, a newer study testing the candidate's effect on gut glucose absorption is now recruiting (ClinicalTrials.gov Identifier: NCT01915849). Both trials are beyond their expected primary completion dates listed on ClinicalTrials.gov. For context, Lexicon is currently in partnership discussions for its SGLT-1/SGLT-2 dual inhibitor LX4211, which has completed phase 2 testing for type 2 diabetes and is in the middle of phase 2 testing for type 1 diabetes (for more details on LX4211, please see our JP Morgan Day #3 Report).

- **Novartis appears to have completed a phase 2 trial for an unspecified oral once-daily treatment for type 2 diabetes, LEZ763 (ClinicalTrials.gov Identifier: NCT01619332).**

4. Lucentis (intravitreal ranibizumab), a therapy for ocular disorders, including diabetic macular edema, continued its somewhat sluggish performance. In 4Q13, sales fell 0.6% YOY as

reported and rose 1% in constant currencies to $630 million. Sequentially, 4Q13 sales were up 8% following poor sequential results in the first three quarters of 2013 (down 6%, down 3%, and up 1%, chronologically). Full-year 2013 sales fell 0.6% (up 1% in constant currencies) to $2.4 billion, compared with 17% growth as reported in 2012.

- **Novartis characterized these results as only "okay."** Mr. David Epstein, head of Novartis Pharmaceuticals, acknowledged that Bayer's Eylea (aflibercept) had dampened sales in markets where the agent has launched (Australia and Japan were mentioned by name). However, he stated that the company has seen sales stabilize and resume growth in 4Q13 (Lucentis' relatively strong sequential performance in 4Q13 could evince this rebound).
- **Mr. Epstein also attributed some of Lucentis' sluggishness in 2013 to one-time price decreases to gain reimbursement for new indications.** The presentation slides indicated that the percentage of Lucentis' sales due to the three newest indications (diabetic macular edema, retinal vein occlusion, and choroidal neovascularization secondary to pathologic myopia) rose from 11% in 2012 to 24% in 2013.
- **Novartis's pre-filled syringe for the product has been approved in Europe and Australia,** and will be launched in 1Q14. Management commented that this new delivery product will help defend the ocular business against Eylea, and potentially even win back some of its lost business.
- **During Q&A, Novartis guided for low-single-digit growth for Lucentis in 2014.** Although the pricing reductions needed to secure reimbursement for new indications will end, Bayer's Eylea will likely be launched in France, Canada, and the UK. We also learned that Novartis is "ramping up" the cooperation between Novartis Pharmaceuticals and Alcon (Novartis' eye care division) to jointly market Lucentis and Jetrea (a therapy for vitreomacular adhesion). Novartis expects possible regulatory approval of Lucentis for diabetic macular edema in Japan in 1H14. Unfortunately, we did not hear management's forecast for the Galvus DPP-4 inhibitor franchise.

5. Novartis CEO Joseph Jimenez stated that cost containment is "here to stay" and that the pharmaceutical industry is entering a "new phase of innovation." During this era, Mr. Jimenez sees innovation being driven by a wealth of data that enables companies to target diseases in new ways. On the cost side, Mr. Jimenez expects a bifurcation in the industry ostensibly between companies who can innovate and stay ahead, and those that cannot develop innovative new therapies and become increasingly subject to strangling pricing pressure. We would agree that innovation is the way to stay ahead, although we wish that the current environment were more forgiving in terms of reimbursement - access for patients must improve and we would like to see an environment much more focused on making consistently optimal care a higher priority for patients - this of course will help the diabetes care arena longer-term.

Questions & Answers

Q: For Lucentis, you highlighted double-digit volume growth last year but flat sales. The price reductions should normalize this year, so should we be forecasting double-digit revenue growth in 2014?

A: The dynamic for Lucentis will be a bit different this year. We will start eventually in the second half of the year to wrap up the pricing decreases. However, we will see Eylea entering the market in France, the UK, and Canada. I would dampen your expectations more towards low-single-digit growth, if I had to give you an idea of where the product to be. After 2014, we would expect growth to become more dynamic.

Comment: I would say we're ramping up our organizations' [Alcon and Novartis Pharmaceuticals] ability to jointly sell Lucentis and Jetrea, which gives us firepower in the marketplace.

-- by Manu Venkat, Hannah Deming, and Kelly Close