Closer Look

MEMORANDUM

Novartis 1Q14 - Galvus up 15% as reported to $308 million - May 2, 2014

Executive Highlights

- Sales of Novartis' DPP-4 inhibitor Galvus (vildagliptin) rose 15% year-over-year as reported (20% in constant currencies) to $308 million.
- Lucentis (ranibizumab), indicated for a number of ocular disorders (including diabetic macular edema), grew 4% as reported (6% in constant currencies) to $620 million.
- The company recently withdrew a phase 2 dose-finding study of the SGLT-1/2 dual inhibitor LIK066; the candidate still appears on the company's pipeline slide.

Novartis CEO Mr. Joseph Jimenez led the company's 1Q14 financial update last week - the call was somewhat light on diabetes discussion, in keeping with most Novartis calls. Galvus (vildagliptin) franchise sales rose 15% as reported and 20% in constant currencies to $308 million in 1Q14. Although these results were slightly weaker than in the previous few quarters, Galvus continues to weather the class-wide DPP-4 inhibitor slowdown relatively well, perhaps due to the fact that it is shielded from the particularly sharp slowdown in the US (Galvus is only marketed ex-US). We learned in early April that Novartis is suing Biocon regarding the latter company's generic vildagliptin, although we have not yet heard much in the way of specifics on the case.

Lucentis (intravitreal ranibizumab), an anti-VEGF therapy for diabetic macular edema (and other conditions), grew 4% in 1Q14 as reported (6% in constant currencies) to $620 million, a slight rebound following a tough 2013 (due to competition from Bayer's Eylea [aflibercept]). On the pipeline front, we noticed that a 12-week phase 2 dose-finding study on Novartis' SGLT-1/2 dual inhibitor LIK066 was withdrawn in early April, raising questions about the candidate's future, although LIK066 still appeared on the company's pipeline slide.

Read on below for our top five highlights from the presentation.

TOP FIVE HIGHLIGHTS

1. Global sales of the Galvus (vildagliptin) DPP-4 inhibitor franchise rose 15% year-over-year as reported and 20% in constant currencies in 1Q14 to $308 million. Year-over-year reported growth for the franchise in the four quarters of 2013 ranged from 29-33%, so 1Q14's results actually represented a slight slowdown (from a higher base). Sequentially, Galvus sales fell 6% as reported, making 1Q14 the first quarter of negative sequential results for the franchise in many years.

- **Relative to other DPP-4 inhibitors, Galvus still appears to be pretty strong in the face of a class-wide slowdown.** Merck's market-leading Januvia grew only 3% in 1Q14, albeit from a much higher base (~$1.3 billion quarterly) - read our Merck 1Q14 Report for more details. Galvus' sole ex-US marketing is, of course, largely responsible for its relative success, as the class-wide DPP-4 inhibitor slowdown appears to due in large part to US weakness. Januvia grew 5% ex-US but fell 2% in the US for the full year 2013. In 2013, the DPP-4 inhibitor class grew 10% globally, with 3% growth in the US and 15% international growth. This contrasted with 2012 and 2011, when global growth was 31% and 53% respectively, US growth was 23% and 27% respectively, and international growth was 39% and 90% respectively.
- **See our 4Q13 Industry Roundup for a big-picture look at the DPP-4 inhibitor class -** during 4Q13, Galvus held a ~23% share of the ex-US DPP-4 inhibitor market. This was down from

26% in 3Q13, but up from the company's 21% ex-US share for the full-year 2012. The franchise also hit blockbuster status (annual sales >$1 billion) for the first time last year.

- **We learned in early April that Novartis is suing India-based Biocon for infringing on its patent on Galvus.** We do not yet know the scope, scale, or timing of this suit, and we have not heard many details since on the progress of the litigation. The generics situation in many countries, particularly India, continues to be a convoluted one. The size of the diabetes patient population in the country is enormous and growing, though most cannot afford to pay high premiums for diabetes medications. Certainly, in both the developing and the developed world, major pharmaceutical companies in diabetes will face increasing pressure from generics.
- **During Novartis' 3Q13 update, management suggested that Galvus might be withdrawn from the German market due to a ruling from the German Federal Joint Committee (G-BA).** The ruling, which stated that Galvus shows "no additional benefit" over sulfonylureas, effectively mandates generic-level pricing for the drug. We have not yet heard news on any sort of appeals process or on any final decision to withdraw the drug. A number of other companies have been hit with similar G-BA rulings and have been stripped of the right to pricing premiums - read our report on AZ's withdrawal of its SGLT-2 inhibitor Forxiga (dapagliflozin) for more details on the issue. The issue is particularly frustrating because the G-BA's decisions are often due to technicalities (such as the use of a comparator therapy not specified by the G-BA) in manufacturers' clinical trial programs.

2. There were no updates on the company's diabetes pipeline. However, we did learn some things about the pipeline from ClinicalTrials.gov.

- **LIK066, an SGLT-1/2 dual inhibitor, remains in phase 2;** according to the company's 1Q14 pipeline, a regulatory filing is not expected before 2018. We did see that a 12-week phase 2 dose-finding trial comparing LIK066 to sitagliptin (ClinicalTrials.gov Identifier: NCT01824264) was withdrawn in early April, although no reason was given. A phase 2 study on LIK066's effect on glucose absorption was completed in January. The fact that the dose-finding study was discontinued raises questions about the candidate's future, although LIK066 was still listed on the company's pipeline slide (which guided for a potential filing in 2018 or beyond). The most advanced SGLT-1/2 dual inhibitor under development is Lexicon's LX4211, which is in phase 2 (see our JP Morgan 2014 Report for data and commentary on that candidate).

3. Sales of Lucentis (intravitreal ranibizumab), Novartis' anti-VEGF therapy for ocular conditions (including diabetic macular edema, a leading cause of blindness in diabetes patients) rose 4% as reported and 6% in constant currencies to $620 million in 1Q14. This marked the drug's first quarter of positive reported growth following three consecutive quarters of decline. Sequentially, sales fell 2% in 1Q14. As background, Novartis markets Lucentis ex-US; Roche/Genentech also market the drug. The product experienced a sluggish 2013 (sales fell 0.6%) due to competition from Bayer's Eylea (aflibercept).

- **Management highlighted that Japanese regulatory authorities approved an expanded diabetic macular edema indication for Lucentis in 1Q14 - read our report on that news.** This approval made Lucentis the first anti-VEGF therapy to be approved for diabetic macular edema in Japan. Japanese authorities also approved the Lucentis pre-filled syringe. The company launched the pre-filled syringe in Germany as well, and has apparently received encouraging feedback from physicians there.

4. Earlier this year, we noticed a Novartis-sponsored study investigating the company's psoriasis drug secukinumab (an anti-IL-17A mAB) as a way to preserve beta cells in newly-diagnosed type 1 diabetes patients. The study (ClinicalTrials.gov Identifier: NCT02044848) has an estimated enrollment of 100 patients and a forecasted primary completion date in late 2019; 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).

5. At last month's Genomics Institute of the Novartis Research Foundation (GNF)-JDRF Diabetes Research Symposium, GNF's Dr. Byran Laffitte described how GNF has the potential to identify the first disease altering therapy for type 1 diabetes. GNF has identified the first highly effective low molecular weight regulators of beta cell proliferation (two of which he revealed to be called GNF4156 and GNF4877). These preclinical agents have been found cause an expansion of human islet mass with the retention of function. These agents' key mechanism of action is the inhibition of Dyrk1a, which is thought to be help regulate cell proliferation.

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