CLOSER LOOK

MEMORANDUM

Novartis 2Q17 - Sales flat YOY for DPP-4 inhibitor Galvus ($310 million) and Lucentis for DME/diabetic retinopathy ($477 million) - July 20, 2017

Executive Highlights

- Novartis recently reported earnings for 2Q17, a quarter best described as flat overall for the company's diabetes products. DPP-4 inhibitor Galvus posted $310 million in sales, which marks 1% YOY growth from a base of $306 million in 2Q16. Lucentis posted $477 million in sales vs. $475 million in 2Q16.
- There were no diabetes-relevant pipeline updates, nor was there any mention of the glucose-sensing contact lens project with Verily. We had hoped management might once again reiterate Novartis' commitment to NASH (an area of enormously high unmet need), as it did in 1Q17.

Novartis recently provided its 2Q17 update in a call led by CEO Mr. Joseph Jimenez (presentation slides here). We can best describe 2Q17 as a "flat quarter" for Novartis Diabetes, with no YOY change in sales (whether up or down) for either of the company's lead diabetes products - DPP-4 inhibitor Galvus and Lucentis for DME/diabetic retinopathy. There was little mention of diabetes during prepared remarks or Q&A.

In this report, we've compiled the most important takeaways on Novartis' diabetes products and pipeline. Read on for five detailed highlights and a pipeline summary table.

Top Five Highlights

1. DPP-4 inhibitor Galvus posted $310 million in 2Q17, continuing its trend of flat quarterly sales around ~$300 million. This represents 1% YOY growth as reported (3% in constant currencies) from a base of $306 million in 2Q16. Sequentially, revenue grew 8% from a base of $286 million in 1Q17.

2. Sales of Lucentis (intravitreal ranibizumab) were also flat YOY as reported in 2Q17 (but up 5% YOY in constant currencies), totaling $477 million vs. $475 million in 2Q16.

3. Management made no mention of Novartis' diabetes, obesity, or NASH pipeline. We're particularly excited about SGLT-1/2 dual inhibitor candidate LIK066 for NASH and obesity, given the company's recent doubling-down on its NASH investments.

4. As expected, there were no updates provided on the glucose-sensing contact lens that Novartis' ophthalmology division Alcon is said to be developing in partnership with Verily. Nor did we hear any mention of Novartis' diabetes and digital medicine partnerships with Parvus and Qualcomm, respectively.

5. Cardiovascular drug Entresto continues to soar, with sales more than tripling YOY and rising 31% sequentially to $110 million in 2Q17. Following presentation of a PARADIGM-HF sub-analysis in diabetes at ACC 2017, we're wondering (hoping!) if we'll see more application of Entresto for people with type 2 going forward.

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Top Five Highlights

1. DPP-4 INHIBITOR GALVUS SALES FLAT (ONCE AGAIN) AT $310 MILLION

DPP-4 inhibitor Galvus posted $310 million in 2Q17, continuing its trend of flat quarterly sales around ~$300 million. This represents 1% YOY growth as reported (3% in constant currencies) from a base of $306 million in 2Q16. Sequentially, Galvus (vildagliptin) revenue grew 8% from a base of $286 million in 1Q17. Sales for 1H17 now total $596 million, which the company's interim financial report lists as a 1% YOY increase from 1H16 (4% in constant currencies). We're somewhat disappointed that management has been quiet on the Galvus business for several consecutive earnings calls (though we understand this pharma giant has many, many products to talk about), since 3Q16, when we heard a specific, three-pronged strategy for marketing the DPP-4 inhibitor to (i) elderly patients, (ii) individuals with renal impairment, and (iii) all type 2 diabetes patients earlier in the course of disease. We interpreted this as a sign of Novartis' continued commitment to its DPP-4 inhibitor franchise, which was especially reassuring in the context of AZ de-prioritizing Onglyza (saxagliptin) in favor of SGLT-2 inhibitor Farxiga (dapagliflozin) and other signs of what could be perceived as wavering commitment to DPP-4 agents from other manufacturers. While some thought leaders - most recently, Drs. Jay Skyler and Steven Nissen at Keystone 2017 - have suggested that DPP-4 inhibitors should be used less frequently in diabetes care due to their lack of CV benefit and possible signal for heart failure hospitalization (in contrast to the demonstrated CV efficacy of some GLP-1 agonists and SGLT-2 inhibitors), others like Dr. Robert Ratner have defended the niche of DPP-4 inhibitors for key segments of the patient population. According to Dr. Ratner, this class has an important role to play in diabetes management for older patients and those with renal impairment, which aligns perfectly with Novartis' commercial strategy. Moreover, Dr. Ratner has pointed to the long history of safety/tolerability associated with DPP-4 inhibitors, making them highly-familiar therapies for HCPs to prescribe. We add that the convenient oral dosing of these agents makes them the preferred choice for some patients (as opposed to the injectable GLP-1 option). Novartis is the first major DPP-4 manufacturer to report 2Q17 sales, but we'll be back with a pooled class analysis after Merck, Takeda, AZ, and Lilly share 2Q17 revenue from Januvia (sitagliptin), Nesina (alogliptin), Onglyza (saxagliptin), and Tradjenta (linagliptin), respectively. In 1Q17, pooled revenue for the class declined 3% YOY to $2.2 billion, albeit from a high base of $2.3 billion in 1Q16. Galvus captured 13% of the market by value in 1Q17, while Merck's Januvia firmly held its frontrunner status with 61% of the market by value.

2. LUCENTIS SALES FLAT YOY AT $477 MILLION

Sales of Lucentis (intravitreal ranibizumab) were also flat YOY as reported in 2Q17 (but up 5% YOY in constant currencies), totaling $477 million vs. $475 million in 2Q16. Sequential growth was 8% from a base of $445 million in 1Q17. Novartis licenses intravitreal ranibizumab from Genentech and markets Lucentis ex-US, where it is indicated for the treatment of diabetic macular edema (DME) and diabetic retinopathy. Roche markets the product in the US, where the FDA approved an expanded indication for Lucentis to include diabetic retinopathy without DME in April 2017, though this won't impact Novartis' recorded revenue. Still, we look forward to Roche's 2Q17 update on July 27 to hear how Lucentis is faring in the US, and if it continues to face competitive pressure from Bayer/Regeneron's Eylea (intravitreal aflibercept) and Genentech's Avastin (bevacizumab). In the past, both Roche and Novartis have cited in-class competition from these other products as a reason for sluggish sales, and we note that Lucentis has a higher list price vs. Avastin which may be contributing to the lower uptake. Novartis' RAINBOW trial is ongoing to investigate Lucentis in infants with retinopathy of prematurity, with expected completion in 1Q18 - this was the only mention of the drug on the company's presentation slides, outside the context of diabetes.

3. NO UPDATES ON DIABETES-RELATED PHARMACOTHERAPY PIPELINE

Management made no mention of Novartis' diabetes, obesity, or NASH pipeline. We're particularly excited about SGLT-1/2 dual inhibitor candidate LIK066 for NASH and obesity, given the company's recent doubling-down on its NASH investments. In fact, commitment to NASH was a major theme of management's remarks during the 1Q17 earnings call - we were so pleased to hear this, given that NASH is an area of high unmet need with no FDA-approved therapies to-date. Novartis' recent partnerships with Allergan and Conatus Pharmaceuticals are also centered around NASH, and you'll find more details on each in the pipeline summary table below. This table reflects the latest updates on each diabetes-relevant product in Novartis' pipeline, to the best of our knowledge.

NOVARTIS DIABETES-RELATED PIPELINE SUMMARY

Candidate	Status	Timeline/Notes
ACZ885 (Anti-interleukin-1ß monoclonal antibody)	Phase 3	Being investigated for secondary CV prevention; Secondary endpoint includes time to new-onset diabetes in participants with prediabetes at baseline; Data to read out at ESC 2017
RLX033 (recombinant relaxin-2 hormone)	Phase 3/Undisclosed	In phase 3 for heart failure; Also being investigated for NASH with data expected in 2019
LIK066 (SGLT-1/2 dual inhibitor)	Phase 2	Being investigated for obesity and NASH
LJN452 (FXR agonist)	Phase 2	Phase 2 FLIGHT-FXR study expected to complete April 2018
Cenicriviroc (CVC)/FXR agonist	Phase 2	Through partnership with Allergan, Novartis will investigate CVC in combination with an FXR agonist for NASH; Phase 2 CENTAUR study of standalone CVC ongoing, expected to complete October 2017
Emricasan (oral pan-capase inhibitor)	Phase 2	Being developed for NASH in partnership with Conatus Pharmaceuticals; Conatus leading phase 2b studies; Novartis will be responsible for phase 3 development
LMB763 (FXR agonist)	Undisclosed	Data expected in 2018

4. NO WORD ON DIABETES PARTNERSHIPS WITH VERILY, PARVUS, OR QUALCOMM

As expected, there were no updates provided on the glucose-sensing contact lens that Novartis' ophthalmology division Alcon is said to be developing in partnership with Verily. We haven't heard anything concrete on this project since a Wall Street Journal article published in August 2015, reporting that the contact lens was meant to enter high-volume production and largescale clinical trials in 2016 (which has come and gone). Unfortunately, this persistent silence from Novartis and Verily could mean that the project has been pushed much further back on the docket (if it's still planned at all). On the other hand, we must acknowledge that both of these companies have a long list of portfolio and pipeline products to discuss on quarterly earnings calls - a glucose-sensing contact lens is an ambitious endeavor to be sure, and is perhaps taking more groundwork than Novartis/Verily initially anticipated before the partners can forge ahead, and before they have something tangible to discuss. Novartis reported $1.5 billion in sales from the Alcon division as a whole, up 1% YOY as reported (3% in constant currencies). Mr. Jimenez underscored at JPM 2017 that returning Alcon to a state of growth is a company priority, even though it's taken longer than expected, and we wonder if this return to growth must also precede forward progress on the glucose-sensing contact lens.

- **As of April 2017, Novartis is also partnered with Parvus to develop a nanotechnology-based type 1 diabetes treatment.** There was no mention of this collaboration on the call or in the company's presentation slides, but we're certainly excited to see where this goes. As per the agreement, Novartis has gained exclusive rights to Parvus' Navacim technology, nanoparticles that can bind and reprogram T cells into a regulatory T cell (Treg)-like state. These nanoparticles could thus work against the autoimmune attack in type 1 diabetes. With Parvus' advanced immunomodulatory technology and Novartis' expertise in clinical and commercial development, we can foresee this duo being very successful. Moreover, we're glad to see Novartis extend its activities into type 1 diabetes in addition to type 2.
- **Lastly, there were no remarks on Novartis' digital medicine partnership with Qualcomm.**

5. ENTRESTO SALES CLIMB 31% SEQUENTIALLY TO $110 MILLION; NO MENTION OF POSSIBLE INVESTIGATION IN DIABETES

Cardiovascular drug Entresto (sacubitril/valsartan) continues to soar, with sales more than tripling YOY and rising 31% sequentially to $110 million in 2Q17. Notably, this product is relatively new-to-market, so the YOY growth occurred from a very low base of $32 million in 2Q16 - 1Q16 was the first quarter with recorded Entresto revenue ($17 million). Following presentation of a PARADIGM-HF sub-analysis in diabetes at ACC 2017, we're wondering (hoping!) if we'll see more application of Entresto for people with type 2 going forward. This sub-analysis was highlighted on Novartis' 1Q17 presentation slides: From a baseline A1c of 7.4%, participants in PARADIGM-HF with diabetes (n=3,778) experienced a mean 0.4% A1c decline with three years of Entresto treatment vs. a mean 0.2% A1c decline with three years of enalapril treatment (p=0.001). Among patients with diabetes who were insulin-naïve at study start, Entresto was associated with a 29% relative risk reduction for new initiation of insulin therapy over three years (p=0.005). This post-hoc analysis can only be considered hypothesis-generating, but given the huge overlap between type 2 diabetes and CV disease, we can't help but be excited at the prospect of a CV drug that also offers glycemic benefits. We'll be watching closely for any movement on Entresto in diabetes.

-- by Payal Marathe and Kelly Close