CLOSER LOOK

MEMORANDUM

Merck Will Not Commercialize Lusduna (Biosimilar Insulin Glargine), Terminates Part of Deal with Samsung Bioepis - October 15, 2018

Executive Highlights

- **Merck and Samsung Bioepis have jointly ended their partnership for the worldwide commercialization of Lusduna (biosimilar insulin glargine).** According to a prepared statement from Merck to our team, the agreement's termination was based on an assessment of anticipated pricing and cost of production for Lusduna. Merck will reportedly pay Samsung Bioepis a ~$155 million termination fee.
- **Lusduna's termination is a major disappointment for patients and the healthcare system, particularly for providers who are constantly searching for more affordable medicines for patients.** We continually hear that at least two (and potentially more) biosimilars will be required to truly drive down insulin prices and patient costs, and Lusduna was notably close to market (already approved in the EU; full FDA approval pending patent infringement lawsuit settlement). Mylan/Biocon's Semglee now represents the next closest candidate to market, set for 2H18 and 2020 launches in Europe and the US, respectively. We have far less confidence in Mylan than in Merck for a biosimilar.
- **With Lusduna's discontinuation, Merck's pipeline contains no diabetes products in current development that we're aware of.** Only phase 2 GLP-1/glucagon co-agonist MK-8521 remains listed, and notably, its development has been paused. Given this dearth of diabetes candidates (along with a muted rollout for Steglatro and patent expiries in several years for DPP-4 inhibitor Januvia), some have wondered if the decision to discontinue Lusduna at all fits into a larger plan for Merck to leave the diabetes arena altogether. However, a Merck representative confirmed to our team that the company remains committed to investing in its early-stage diabetes pipeline, including co-agonists, novel insulins, and other novel molecules. Merck has shown incredible commitment to date to people with diabetes, including the among the very best patient access programs (see diaTribe's "How To Get Diabetes Drugs for Free."

Merck just announced that Merck and Samsung Bioepis have jointly ended their partnership to commercialize biosimilar insulin glargine Lusduna Nexvue (both vial and pen). Merck clarified to us via prepared statement that the agreement's termination was based on an assessment of anticipated pricing and cost of production for Lusduna; that is, Merck has chosen not to commercialize Lusduna due to anticipated costs. Notably, the termination applies worldwide - not just in the US, where pricing pressure in the basal insulin market is most intense. According to a Korean stock exchange disclosure form, Merck will pay Samsung Bioepis a termination fee of ~$155 million; the same form states that Samsung Bioepis has invested ~$91 million in the drug, meaning that the company has received a net profit of ~$64 million from the agreement termination.

We are extremely disheartened by this news. Lusduna was one of only three biosimilar basal insulins near or on the market. Lilly/BI's Basaglar was launched in Europe and the US in 2015 and 2016, respectively, and Mylan/Biocon's Semglee is set for 2H18 and 2020 launches in Europe and the US, respectively. Lusduna was already approved in the EU (though not yet launched, to our knowledge) and received tentative FDA approval in July 2017, with full approval contingent on the settlement of a patent infringement lawsuit from Sanofi over Lusduna's originator insulin Lantus. That's a lot of work to go to for this change in mind. On balance, this is welcome news for Sanofi as well as Lilly. Novo Nordisk does not have a biosimilar and we view the news as more neutral for them though patients who have fewer funds to pay may be more likely to get Novo Nordisk's human insulin as a result (this is lower margin though still profitable).

Soaring insulin prices have certainly led to negative consequences for both patients and the healthcare system (e.g., insulin glargine was the second largest of all Medicare expenditures in 2015), and biosimilars are theorized to bring down prices by coming in at a 15%-20% discount vs. the originator product. However, it is unclear whether patients are realizing the promised discount on Basaglar vs. Lantus as of yet, and we continually hear that at least two (and potentially more) biosimilars will be required to truly drive down prices. As such, the discontinuation of Lusduna, a product so close to market, is certainly a blow for patients and the entire healthcare system.

Full FDA approval of Lusduna could have been achieved in one of three ways: (i) Sanofi/Merck reach an agreement, like Sanofi did with Lilly/BI over a similar patent dispute regarding Basaglar; (ii) a court decides in favor of Merck; or (iii) 30 months elapse since Sanofi filed the lawsuits (September 2016 for the pen and August 2017 for the vial), which would have delayed launch of the pen to March 2019 and the vial to February 2020. We think it speaks volumes to the current state of diabetes drug development that, instead of waiting for March 2019 to roll out Lusduna, the company chose to cancel the product's development (more on this below).

- **With Lusduna's discontinuation, Merck's pipeline contains no diabetes products currently under development.** However, this pipeline only includes candidates in phase 2 or later, meaning that Merck may well have phase 1 and preclinical candidates that are not publicly disclosed. Indeed, a Merck representative confirmed to our team that the company remains committed to investing in its early-stage diabetes pipeline, including co-agonists, novel insulins, and other novel molecules. Only phase 2 GLP-1/glucagon co-agonist MK-8521 remains listed on Merck's online pipeline, though its development has been paused. In particular, we are glad to hear that Merck is apparently still pursuing glucose-responsive insulin following the termination of MK-2640 (due to insufficient efficacy) in phase 1. Most recently on this front, we heard from Dr. J Hans DeVries at IDF 2017 that phase 1 studies for a new GRI are underway and expected to report in 2018 (preclinical data was presented at ADA 2017).
- **Merck's prepared statement was quick to defend biosimilars' potential to bring down pricing.** "We believe that biosimilars can present significant opportunities for cost savings through competition and improved patient access to therapies. This decision does not affect the other biosimilar assets currently in development with Samsung Bioepis." There was not any corresponding statement that this did not affect Merck's diabetes franchise.
- **While it is disappointing that Merck does not see it as commercially wise to continue development of Lusduna, it is perhaps not too surprising;** indeed, in the last several years, multiple companies (including BMS, Amgen, Gilead, Takeda, GSK and Novartis) have left diabetes drug development, and multiple companies (e.g. J&J and other smaller companies) no longer appear to be investing in their franchises. While some may say that it is disappointing that a company doesn't see value in bringing a new insulin to market, it is certainly true that US margins are far lower than they used to be.
- **To date, Merck has employed a restrained rollout strategy for their Pfizer-partnered SGLT-2 inhibitor Steglatro (ertugliflozin) - we have assumed this is smart until they get all the coverage they are after.** While Merck has failed to mention or report sales for Steglatro on its past two earnings calls (1Q18 and 2Q18), this is perhaps unsurprising for a fourth to market compound (after Invokana, Jaridance, and Farxiga). As background, the SGLT-2 franchise brought in an impressive $3.5 billion in 2017, up 24% year-over-year; in the first half of 2018, SGLT-2s rose approximately 30% with approximately $1.0 billion in sales each quarter. Moreover, with important patents for blockbuster DPP-4 inhibitor Januvia set to expire in 2022/2023 and anticipated competition from generics thereafter, Merck's diabetes portfolio will face increasing pressures in the near future. We surely hope that Merck maintains an innovative presence in diabetes - the company has been such a positive force, including, as noted, in leading the way with a patient access program that diaTribe.org has ranked one of the very best in the field. Given the incredible strength of Merck leadership, with one of the best CEOs in the Fortune 100, and given

Merck's unbelievable leadership with primary care doctors globally and particularly in the US, we hope to see even more focus on diabetes in the years and decades ahead. Merck was among the very first to bring diabetes glycemic-dependent therapy for people with type 2 diabetes - we look forward to seeing even more innovation in the future, particularly innovation on the care delivery front.

Close Concerns Questions

How does Lusduna's discontinuation bode for future biosimilar development? If players like Merck and Samsung with their impressive production capabilities do not see biosimilar basal insulins as commercially viable, then is it possible for other players to come into the international market? Not only is production set up expensive (and Merck/Samsung have already done that) but maintenance, quality control, registration expenses in multiple jurisdictions, marketing/sales expenses, uncertainty in negotiations with payers, and the prospect of every declining prices must make biosimilar development and commercialization a daunting task.

How does Merck's divestment from diabetes bode for the general diabetes pharmaceutical space? From a profit standpoint, new drugs will have to be more than incrementally more effective than current treatments, and the bar is ever higher given the impressive A1c lowering achieved with currently available drugs (GLP-1 RA and SGLT2 inhibitors).

--by Peter Rentzepis, Martin Kurian, Ann Carracher, and Kelly Close