CLOSER LOOK

MEMORANDUM

FDA accepts Merck's New Drug Application for its "biosimilar" insulin glargine MK-1293 - August 5, 2016

Executive Highlights

- This morning, Merck announced that the FDA has accepted a New Drug Application (NDA) for its "biosimilar" insulin glargine MK-1293. Assuming a standard 10-month review, a decision is expected in early June 2017.
- If approved, MK-1293 will be the third-to-market product in the increasingly competitive basal insulin arena, after the originator (Sanofi's glargine [Lantus]) and Lilly/BI's Basaglar.

This morning, Merck announced that the FDA has accepted the New Drug Application (NDA) for its Samsung Bioepis-partnered investigational follow-on insulin glargine candidate MK-1293. A follow-on biologic is a similar, but not identical, US version of an approved reference product, in this case Lantus. Follow-on insulins, such as MK-1293, are reviewed in the US under a different regulatory pathway than biosimilars. In other countries, a follow-on insulin is known as a biosimilar insulin. Assuming a standard 12-month review, a decision is expected in 2Q17 - if all goes well, in time for EASD 2017. MK-1293 marks the further expansion of Merck's diabetes portfolio into the insulin market - the company also has smart (or glucose-responsive) insulin in development after buying JDRF-funded SmartCells in 2010.

The NDA submission includes the results of two phase 3 studies presented at this year's ADA conference in which MK-1293 demonstrated non-inferiority to Lantus in both type 1 (n=506) and type 2 (n=531) diabetes patients. The two insulin products exhibited highly similar therapeutic profiles in terms of A1c, fasting plasma glucose reduction, and hypoglycemia. MK-1293's NDA submission in the US comes a few months behind its submission of a Marketing Authorization Application in Europe in December 2015. If approved, Merck's product will be the third-to-market product in the increasingly competitive basal insulin arena (after Sanofi's Lantus [insulin glargine] and Lilly/BI's Basaglar biosimilar). This makes Merck's product the likely second-to-market biosimilar insulin glargine; Biocon/Mylan's biosimilar insulin glargine is expected to be submitted in the US and EU in the second half of 2016. While the insulin arena is challenging, given ongoing woes with insulin pricing and competition - as illustrated in our pooled basal insulin market analysis here - it is also an area with enormous opportunity. This is especially true given that many more patients may go on or stay on basal insulin if the price were even slightly lower. Furthermore, we believe that many doctors have traditionally had "insulin resistance" that would decline with more companies in the field characterizing the unmet need. We will be interested to see how MK-1293 fares in this competitive arena - we expect it could grow quite significantly, at least by volume.

- **Merck chose not to seek an interchangeable designation for MK-1293, which, according to recently-modified FDA guidelines, would allow pharmacists to switch Lantus or Basaglar for MK-1293 without consulting the prescriber.** The two studies Merck included in its ADA submission establish MK-1293's comparability to Lantus in terms of efficacy and safety, but were not designed to demonstrate any of the additional requirements the FDA has established as prerequisites for interchangeability. In a conversation with Dr. Charles Alexander, former Global Medical Director for Diabetes at Merck, we learned that the FDA has not yet released information on what standards a product must meet to be deemed interchangeable, making Merck's decision to forgo this designation quite understandable.
- **Dr. Peter Stein, VP of Late Stage Development for Diabetes and Endocrinology at Merck, shared with us that MK-1293 marks Merck's entrance into the type 1 diabetes arena.** Noting the steadily rising rates of type 1 diabetes, he highlighted the importance of

developing a better insulin to help these patients in addition to the type 2 patients to whom Merck's diabetes portfolio has previously been targeted. We are excited to hear this clear commitment to making type 1 diabetes a priority.

- **With the advancement of this new insulin product, Merck now envisions its diabetes franchise as a "portfolio of options to help physicians treat their diabetes patients."** With its DPP-4 inhibitor Januvia (sitagliptin), upcoming Pfizer-partnered SGLT-2 inhibitor ertugliflozin, and now biosimilar insulin glargine MK-1293, Merck now holds (or hopes to soon hold) market share for three main classes of antiglycemic agents. Dr. Stein emphasized the different needs of different patients, and how Merck's suite of diabetes drugs should promote more personalized diabetes therapy.

Close Concerns Questions

Q: Will US managed care instruct their health care providers to only use the contracted basal insulin regardless of the FDA's decision on interchangeability? How much of a discount will payers be seeking from the basal insulin companies?

Q: How will Merck position its DPP-4 inhibitor Januvia (sitagliptin), MK-1293, and the upcoming Pfizer/ Merck SGLT-2 inhibitor ertugliflozin franchise relative to each other within its expanding diabetes portfolio? To what degree will combination approaches be used?

Q: Is there a specific strategy in the patients Merck is seeking to target with its diabetes offerings?

Q: How will Merck fare against the three insulin giants (Novo Nordisk, Sanofi, and Lilly) who have been marketing insulin for decades?

Q: What might a typical US formulary look like with multiple basal insulins on the market?

Q: How do you think the new FDA rules on interchangeability (where new biosimilars must meet standards for being equally effective as the reference product) will impact pricing for biosimilars?

Q: The FDA rules on interchangeability stress that biosimilars must be similar in efficacy and safety compared to their reference products - what would happen if a biosimilar went beyond showing non-inferiority and showed superiority to its reference in a clinical trial?

-- by Abigail Dove, Helen Gao, and Kelly Close