CLOSER LOOK

MEMORANDUM

FDA grants full approval to Sanofi's Admelog, first-to-market biosimilar mealtime insulin - December 12, 2017

Executive Highlights

- **The FDA has approved Sanofi's biosimilar mealtime insulin Admelog (biosimilar lispro).** This full approval comes ~three months after FDA granted tentative approval to the first-to-market biosimilar rapid-acting insulin. Lilly announced during its 3Q17 update that it would not pursue a patent infringement lawsuit over Humalog (insulin lispro), and Sanofi management then shared that full approval was imminent.
- **No details were announced on US launch timing or pricing.** Due to timing of the payer contracting cycle, Sanofi expects Admelog to be more of a growth opportunity in 2019 rather than 2018. To be sure, the new product could help revitalize the company's diabetes business, which has posted relatively weaker sales in 2017. Sanofi's most recent financial guidance suggests 6%-8% annual loss in diabetes revenue between 2015-2018, but this doesn't include the possible favorable sales spike to come from Admelog in 2019. We imagine reimbursement will be critical for Admelog's commercial success, especially since payer contracts are said to be more exclusive in the rapid-acting insulin category vs. any other diabetes drug class.
- **Notably, the FDA press release positions Admelog as a key piece in the agency's efforts to facilitate generic drug approvals**, a movement championed by Commissioner Dr. Scott Gottlieb.
- **Sanofi's biosimilar was EMA-approved in July** under brand name Insulin lispro Sanofi. Both the US and EU approvals were based on phase 3 SORELLA studies demonstrating comparable safety/efficacy of Sanofi's biosimilar formulation vs. Lilly's Humalog.

Yesterday, Sanofi announced full FDA approval of Admelog (biosimilar insulin lispro), the first-to-market biosimilar mealtime insulin in the US. This decision follows FDA's tentative approval of Admelog in September (indicating that the candidate had fulfilled all regulatory requirements, but that it couldn't be launched until all patent disputes were settled), after which Lilly announced that it would not pursue a patent infringement lawsuit over Humalog (insulin lispro).

Sanofi management has been positive about prospects for US approval by year-end. However, given the timing of the payer contracting cycle, management anticipates that Admelog will be more of a growth opportunity in 2019 rather than 2018. Thus, although the company announcement contained no information about US launch timing, we expect the new product to hit pharmacy shelves sometime next year, with a gradual increase in marketing activities.

Formulary positioning has been a significant influence on the basal insulin market: Lilly/BI's Basaglar (biosimilar insulin glargine) was preferred on the CVS Health and UnitedHealthcare formularies over Sanofi's Lantus (insulin glargine) in 2017 (and this will continue into 2018), which has been a major tailwind for the biosimilar, a major headwind for Sanofi's flagship product. Similarly, we imagine reimbursement will be critical for Admelog's commercial success, especially as providers build familiarity with the concept of a biosimilar rapid-acting insulin, and are convinced of its equivalent efficacy and strong safety. We've heard that payer contracts are more challenging and more exclusive in the rapid-acting insulin category vs. any other diabetes drug class, and Sanofi's EVP of Diabetes & Cardiovascular Mr. Stefan Oelrich elaborated, "it's because products are seen as largely interchangeable by the payer." Provided safety/efficacy are established,

biosimilars promise 15%-20% discounts in list price to the originator product (in this case, Lilly's Humalog), which implies wider access. That said, Sanofi has not disclosed any specific details on pricing strategy around Admelog, so we'll have to wait and see.

Admelog could help revitalize Sanofi's diabetes business, which has posted sluggish sales in recent quarters, falling 11% YOY in 2Q17 and 14% YOY in 3Q17 (to $1.8 billion). Declining revenue from Lantus, largely due to the CVS Health and UnitedHealthcare exclusions, has driven this drop in sales for the whole portfolio, and Sanofi's own rapid-acting insulin product Apirda (insulin glulisine) has never quite taken off commercially, capturing 6% of the $1.6 billion market in 3Q17 (while Novo Nordisk's NovoLog and Lilly's Humalog dominate). Sanofi's most recent financial guidance suggests 6%-8% annual loss in the diabetes business between 2015-2018 - notably, this doesn't include the possible favorable sales spike to come from Admelog in 2019.

Given Sanofi's long history of insulin manufacturing and extensive expertise in marketing insulin products, we certainly see potential for Admelog to help return the company's insulin business to growth over the next several years, alongside next-generation basal insulin Toujeo (insulin glargine U300). We'll be curious to see how Sanofi prioritizes Admelog relative to Toujeo, Apidra, and Lantus going forward - we suspect the first two will receive the bulk of commercial resources.

Table of Contents

FDA Commitment to Generics

- **Notably, the FDA press release positions Admelog as a key piece in the agency's efforts to facilitate generic drug approvals and to support the market entry of lower-cost alternatives, a movement championed by Commissioner Dr. Scott Gottlieb.** In a recent blog post, Dr. Gottlieb outlined his stance: Although FDA doesn't specifically control pricing, he can enact policies to spur commercial competition and thereby expand patient access. In October, FDA issued two draft guidances to support generic manufacturers looking to submit an Abbreviated New Drug Application (ANDA), (i) encouraging applicants to set up earlier meetings with the agency and (ii) helping applicants determine when it's appropriate to submit an ANDA for a peptide-based complex product. These guidances wouldn't have affected Sanofi's filing of biosimilar insulin lispro (a submission that went largely under-the-radar until news of the tentative approval in September), but it's still noteworthy that FDA is emphasizing biosimilar insulin as an important new generic option for patients. We wonder if this will impact the agency's approach to Mylan/Biocon's NDA for their biosimilar basal insulin glargine candidate (this was submitted by Mylan in 3Q17, triggering a patent infringement lawsuit from Sanofi over Lantus).

Clinical and Regulatory Milestones

- **Sanofi's biosimilar was EMA-approved in July under brand name Insulin lispro Sanofi.** At EASD, the company promoted this first-to-market biosimilar prandial insulin as "everything you'd expect from a mealtime insulin, without the brand name," also highlighting the familiar SoloStar pens. Both the US and EU approvals were based on phase 3 SORELLA studies demonstrating comparable safety/efficacy of Sanofi's biosimilar formulation vs. Lilly's Humalog. Results from SORELLA 1 in type 1 diabetes and SORELLA 2 in type 2 showed non-inferiority on A1c, postprandial glucose excursions, and total insulin dose as well as similar frequency of hypoglycemia with both treatments.

Competitive Landscape

- **The rapid-acting insulin class could see several changes in 2018, including the market entry of Admelog (the first biosimilar) and Novo Nordisk's Fiasp (the first next-gen mealtime insulin).** Moreover, MannKind's inhaled insulin Afrezza recently received an ultra-rapid-acting label claim, which will continue to be rolled out in 2018. Both Fiasp and Afrezza promise faster-acting boluses, presumably lowering hypoglycemia risk and reducing uncertainty around meals. Meanwhile, Admelog promises similar safety/efficacy to a current leading prandial insulin, at a substantially reduced cost. That said, we imagine these products will still face the major commercial challenges affecting the rapid-acting insulin market - namely, a competitive pricing environment in the US and growing competition from GLP-1 agonists and SGLT-2 inhibitors (advanced therapy classes that address postprandial excursions without any hypoglycemia risk). The rapid-acting class has fluctuated around ~$1.6 billion for a couple years, which was matched by GLP-1 agonists in 2Q17 and 3Q17.

-- by Payal Marathe and Kelly Close