CLOSER LOOK

MEMORANDUM

Novo Nordisk announces collaborations with UCSF and Cornell for development of encapsulated beta cell therapy for type 1 diabetes - May 16, 2018

Executive Highlights

- **Novo Nordisk has strengthened its commitment to stem cell therapy for type 1 diabetes, with a goal to advance encapsualted beta cells into clinical trials "within the next few years."** This effort involves strategic industry-academia partnerships with UCSF and Cornell. From UCSF, Novo Nordisk has licensed technology to generate human embryonic stem cell lines. The company also founded a Good Manufacturing Practice (GMP) laboratory where UCSF and Novo Nordisk scientists are collaborating to develop the high quality stem cell lines. With Cornell, Novo Nordisk has made headway on developing an encapsulation device that can house these stem cell-derived beta cells and protect them from foreign body response.
- **In a call with our team, Novo Nordisk CSO Dr. Mads Thomsen discussed the company's approach to a type 1 "cure" and the major challenges in this area of R&D.** Encapsulation is a notable hurdle, and Dr. Thomsen also emphasized that stem cell-derived beta cells must produce a sufficient amount of insulin; he explained that earlier attempts secreted too little, which meant that far too many cells had to be implanted for a therapy to work. Read much more from Dr. Thomsen below.

Earlier today, Novo Nordisk announced an increased commitment to stem cell-based therapy for type 1 diabetes. Through strategic collaborations with UCSF and Cornell, the company plans to advance encapsulated beta cells into clinical trials "within the next few years."

From UCSF, Novo Nordisk has licensed technology to generate human embryonic stem cell lines. The company also founded a GMP laboratory where UCSF and Novo Nordisk scientists are collaborating to develop the high quality stem cell lines. In a call with our team, CSO Dr. Mads Thomsen elaborated on this ambition to create stem cell lines that define a new quality standard: He acknowledged the importance of satisfying FDA and regulatory requirements so that this therapy can move forward without hindrance into clinical trials.

According to Dr. Thomsen, an industry-academia partnership on a stem cell project is mutually beneficial. "We're combining the best of two worlds - expertise in stem cell generation and subsequent differentiation to target cells, with industrial scale and quality manufacturing," he said, adding that this approach will also help to "satisfy regulators as we move toward clinical trials."

He also cited preclinical studies in a mouse model of type 1 diabetes, in which these stem cell-derived beta cells "worked wonderfully."

With a Cornell team led by Professor Minglin Ma, Novo Nordisk has made headway on developing an encapsulation device that can house these stem cell-derived beta cells and protect them from foreign body response. To be sure, there is no shortage of challenges in designing a viable cell replacement therapy for patients, and proper encapsulation tops this list; the system must allow glucose to enter and insulin to exit, while simultaneously protecting the implanted cells from immune attack.

But Dr. Thomsen listed a range of notable challenges in this effort toward a type 1 "cure." (i) The stem cells must be differentiated into true beta cells, so they don't secrete glucagon or somatostatin. (ii) The cells must

produce enough insulin - Dr. Thomsen explained that earlier attempts at stem cell-derived beta cells secreted only a small amount of insulin, which meant that far too many cells were needed in an implant for the treatment to work. (iii) He highlighted encapsulation as a hurdle as well.

"All of these things have to come together, so it's taken a long time," Dr. Thomsen stated.

Competitive Landscape

- **There's been movement from major diabetes manufacturers on early-stage type 1 research of late.** In early April, Lilly announced a new partnership with Sigilon to develop its own beta cell encapsulation therapy for type 1 diabetes. The beta cell encapsulation competitive landscape also includes ViaCyte's phase 1/2 PEC-Encap/VC-01 and PEC-Direct/VC-02, Sernova's phase 1/2 Cell Pouch System, and Semma/Defymed's preclinical MAILPAN macroencapsulation system (expected to enter phase 1 in 2020). Investment from Novo Nordisk and Lilly could shake up this R&D field, and in our view, represents a vote of confidence for the plausibility of beta cell encapsulation techniques.

Next Steps for Novo Nordisk's Beta Cell Encapsulation Therapy

- **This is the first R&D news on a type 1 "cure" that we've heard from Novo Nordisk in quite some time, but Dr. Thomsen emphasized that this has been a two decade-long effort at least** (i.e. Novo Nordisk biologists were working on stem cell-derived beta cells in the 1990s). The company is now scaling up this research program, and it's noteworthy that management is reaffirming its commitment to this effort. Dr. Thomsen suggested that the beta cell encapsulation device will soon be tested in larger animal models ahead of in-human clinical studies.
- **Although this news marks Novo Nordisk's official entry into the stem cell arena, the company has already dipped its toes in the water when it comes to non-insulin type 1 therapy with an anti-IL 21/liraglutide combination.** This candidate is in phase 2 for beta cell preservation in the newly-diagnosed. It was granted FDA Orphan Drug Designation in January 2017, and an ongoing phase 2 trial is expected to complete in March 2019. Dr. Thomsen clarified that anti-IL 21/liraglutide is targeting patients who still have some insulin producing capacity. Say 10%-15% of their beta cells are still making physiologic insulin - anti-IL 21/liraglutide could protect and preserve those islets. In contrast, this stem cell-based therapy aims to give people new functioning beta cells, and it targets type 1s with longer duration of diabetes/without residual insulin production.
- **Novo Nordisk's press release further alludes to future stem cell collaborations with Swedish biotech Biolamina for Parkinson's disease (with Lund University) as well as chronic heart failure and age-related macular degeneration (with Duke University).**

-- by Abigail Dove, Payal Marathe, and Kelly Close