CLOSER LOOK

MEMORANDUM

ViaCyte launches first clinical trial of PEC-Direct for type 1 diabetes - October 5, 2017

Executive Highlights

- ViaCyte recently announced that the first clinical trial of PEC-Direct is officially underway, investigating the islet cell replacement therapy for type 1 diabetes. The first patients were implanted with the product candidate by the beginning of August, slightly delayed from the projected 1H17 timeline.
- This first cohort of participants received multiple smaller cell-filled devices that will be removed on pre-specified dates to evaluate implant engraftment (are the implanted cells healthy and showing evidence of maturation into pancreatic islets including insulin-producing beta cells?). A second cohort of up to 40 participants will undergo the implantation procedure starting later this year, with a primary endpoint of C-peptide levels as a proxy for insulin production. According to ClinicalTrials.gov, the study is expected to complete in December 2020.
- Shortly after the launch of this clinical trial, ViaCyte was awarded a $20 million grant from the California Institute for Regenerative Medicine (CIRM) to further support the development of PEC-Direct. And, the product candidate was named a top three finalist in the clinical-stage life science technologies category for the 30th annual Most Innovative New Product Awards, run by CONNECT (a company accelerator).

*ViaCyte recently announced that the f*irst clinical trial of PEC-Direct is officially underway, investigating the islet cell replacement therapy for high-risk type 1 diabetes. The first patients were implanted with the product candidate by the beginning of August, slightly delayed from the projected 1H17 timeline for clinical trials to commence. According to the company announcement, the first participants were treated at the University of Alberta and UC San Diego (the University of Minnesota is now actively enrolling patients as well). In this first cohort, individuals received multiple smaller cell-filled devices that will be removed at specific time points to evaluate implant engraftment, the key question being, are these cells healthy and showing signs of maturation into pancreatic islet cells including insulin-secreting beta cells? A second cohort of up to 40 patients will start enrollment later this year (at the three active study sites, plus other locations across the US and Canada) to evaluate efficacy. The company expects enrollment to be fully complete in 2H18, with efficacy results ~six months later. ClinicalTrials.gov lists an expected completion date of December 2020 for the phase 1/2 study. The primary efficacy endpoint is clinically-relevant insulin production, as measured by C-peptide levels six months post-implantation. Injectable insulin doses and hypoglycemia rates will also be evaluated as secondary endpoints. *We're very happy to note this forward progress - with this move, ViaCyte has advanced PEC-Direct from the preclinical stages to clinical development, and we can't wait to follow this trial closely.*

We've noticed that ViaCyte has been de-prioritizing its phase 1/2 PEC-Encap candidate relative to PEC-Direct for some time now. This was further solidified when the open-label PEC-Direct clinical trial program received a greenlight from FDA and Health Canada in May, and with this recent news of study start. ViaCyte management has even suggested that PEC-Direct is positioned to reach the market sooner than PEC-Encap, despite it being second to the clinic. From a technical perspective, PEC-Direct is somewhat less challenging than PEC-Encap, which fully encapsulates progenitor cells and is meant to completely eliminate the need for chronic immunosuppression. Unfortunately, PEC-Encap engraftment has not been as sufficiently robust and reproducible as would be desired, apparently related to foreign body response to the

implant. In contrast, PEC-Direct allows for direct vascularization of the implanted progenitor cells, avoiding impact of foreign body response and thus leading to better engraftment and cell growth, though patients would be required to take concomitant immunosuppressive therapy as a tradeoff. As such, PEC-Direct is aimed at a smaller, higher-risk subset of the type 1 diabetes population and is unlikely to be a general "cure." We're hopeful that the results from this PEC-Direct trial will inform modifications to the more widely applicable PEC-Encap approach, ultimately leaving ViaCyte with two high-potential therapeutic candidates. See our type 1 diabetes cure and prevention competitive landscape for an overview of efforts in this area.

- **Shortly after the launch of this clinical trial, ViaCyte was awarded a $20 million grant from the California Institute for Regenerative Medicine (CIRM) to further support development of PEC-Direct.** This represents a strong vote of confidence in ViaCyte's technology and we imagine that this significant grant will be instrumental in propelling PEC-Direct through phase 1/2 into further development, should the ongoing study prove a success. CIRM is an increasingly influential funder in the type 1 diabetes cure and prevention arena, also funding Caladrius Biosciences' CLBS03 regulatory T-cell based type 1 diabetes therapy (now in phase 2) to the tune of $12.2 million. In contrast to stem cell-based PEC-Direct, CLBS03 involves the administration of regulatory T-cells intended to boost the immune system's natural response. It is geared toward recent-onset type 1 diabetes, whereas ViaCyte's PEC-Direct is targeted toward people with established type 1 diabetes at high-risk of complications or recurring severe hypoglycemia.
- **In more good news for ViaCyte, San Diego-based CONNECT (a company accelerator) recently announced PEC-Direct as one of three finalists for its 30th annual Most Innovative New Product Awards in the category of clinical-stage life science technologies.** A winner will be announced on November 30. We are pleased to see this additional momentum for ViaCyte and visibility for type 1 diabetes cures and prevention therapies more broadly.

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