REGENEUS FOCUSED ON DEVELOPING ADIPOSE - DERIVED ALLOGENEIC MSC PRODUCT W/ ADDED SECRETIONS

Searching for Domestic Commercialisation Partner with their JV Partner AGC Asahi Glass

Original article published by Nikkei Business Publication Inc., Japan in Nikkei Biotech ONLINE (July 21, 2017).
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English Version

Regeneus is a firm that conducts research and development in adipose-derived cellular therapies for both human and veterinary use. In December 2016 the firm out-licensed the exclusive Japanese manufacturing rights for their adipose-derived allogeneic mesenchymal stem cell (MSC) product, Progenza, to AGC Asahi Glass. In line with this development, the two firms established a joint-venture, Regeneus Japan, in Shibuya, to assist in their search for a commercialisation partner for Progenza in Japan.
On June 9, 2017 Regeneus' CEO, Mr. John Martin, and the firm's Head of Licensing and Alliances, Dr. Duncan Thomson, answered some of this newspaper's questions on their plans for Japan.

QUESTION #1: We understand that Progenza is an allogeneic adipose-derived stem cell product with secretions being part of the final product. Could you please provide us with the current status of development for this product?

ANSWER #1*: (Mr. Martin)* We've just finished our Phase I trial for osteoarthritis (OA) in Australia. The primary endpoints for this trial were safety and tolerability. The secondary endpoints included more efficacy focused items such as the WOMAC score, which we used to rate the participants level pain associated with their OA. We had a placebo cohort as part of the trial as well, and were able to see a significant reduction in pain when comparing the active cohorts to the placebo cohort. Furthermore, we also looked at MRI data to check the total volume of the lateral tibial cartilage of the participants. It is generally said that OA patients lose about 5% of their lateral tibial cartilage volume year on year, but the active cohorts showed a stable amount of cartilage volume even one year after administration.

QUESTION #2: You've signed an exclusive manufacturing license agreement with AGC Asahi Glass here in Japan, and received USD5.5m as an upfront payment, with another anticipated USD11.0m in subsequent milestone payments. We also understand that you've established a 50/50 joint-venture (JV) between the two companies?

ANSWER #2: *(Mr. Martin)* Regeneus Japan is a special purpose company established specifically to manage the Japan-specific development and commercialisation licenses of Progenza, and license those out to a commercialisation partner. Both AGC Asahi Glass and Regeneus will receive a portion of any milestone payments and royalties that are born out of payments from the commercialisation partner to Regeneus Japan. At the moment we are in the process of transferring the necessary technology to AGC Asahi Glass regarding the manufacturing of Progenza. We believe that it will take anywhere from 1.5 years to 2 years before we will have GMP level investigational product ready. In the meantime we are focused on finding a commercialisation partner here in Japan, and would like have this partner in place to allow for us to commence the Phase II clinical trail in Japan soon after the aforementioned GMP level investigational product is ready to go.

QUESTION #3: What sort of characterisations do you envision your cellular therapy to have?

ANSWER #3: *(Dr. Thomson)* While we are working on the exact characterisations and as such they are yet to be finalised, you already know that we add secretions to adipose-derived stems cells to create our product. The secretions are a mixture that includes items such as cytokines and growth factors, etc. Currently we envision that there will be specific values of specific components of the secretions that need to be cleared for the product to be slated for release. We will of course work closely with the Japanese regulator, the PMDA, to finalise this matter.

QUESTION #4: What are the merits of using adipose tissue as the source of your stem cells?

ANSWER #4: *(Dr. Thomson)* While you can obtain MSCs from a plethora of different tissue types (e.g. bone marrow, placenta), the number of MSCs per cubic-centimetre of adipose tissue exceeds the amount you can obtain from other tissue types. As such, one of the largest merits of using adipose tissue is this advantage in starting material.
(Mr. Martin) Currently, we are able to manufacture tens of millions of doses from a single adipose-tissue donor, with each dose being between 5 and 10 million cells. Furthermore, as our cells require no genetic manipulation or differentiation (like iPSCs or ESCs), we also believe that establishing the safety of our cells will be easier.

QUESTION #5: Why do you add the secretions to your MSCs?

ANSWER #5: *(Mr. Martin)* We look to utilise Progenza's anti-inflammatory effect on OA. One of the main mechanisms of action for MSCs is their ability to secrete things such as cytokines. One of the effects of adding back in the secretions to the MSCs is that the secretions assists those MSCs in their ability to secrete post-thaw. Regenerative medicine therapies will be a boom for the regenerative medicine markets of both countries.