Encapsulated Mesenchyme Stem Cells

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Current scientific evidence suggests that the therapeutic mechanism of action and therefore the therapeutic usefulness of mesenchyme stem cells ("MSC") is not derived from their ability to differentiate into their target tissue, but rather in their secretion of paracrine growth factors, cytokines and exosomes, known as the "secretome" [1]. The immunomodulatory effect of this protein milieu makes stem cells a potential "drug producer" with a promising beneficial effect in a variety of clinical conditions [2]. One of the reported therapeutic shortcomings observed in the use of these cells, whether from autologous or allogeneic sources, is that they do not survive and do not remain at the target area into which they have been administered for a sufficient duration to induce the desired effect for which they were administered - hence any effects are short lived requiring repeated dosing [3].

Tithon Biotech's collaboration with Austrianova has culminated in the development of a unique product that resolves the foregoing noted shortcoming observed in the therapeutic use of mesenchyme stem cells.

By using Austrianova's well tested cell encapsulation technology along with its experience in the area of encapsulation, in combination with Tithon's unique and proprietary immortalized adipose-derived mesenchyme stem cell product and Tithon's expertise and clinical experience in the stem cell industry, an off-the-shelf encapsulated stem cell product is in the works ("MSC-Encap(s)").

As currently envisioned by Tithon's science team, Tithon's immortalized MSC will be encapsulated with approved inert biomaterials utilizing Austrianova's encapsulation technology, into very small beads possessing pores of sufficient size to: (1) allow therapeutic quantities of their paracrine secretions to pass out of the MSC-Encap and (2) allow essential nutrients to pass into the MSC Encap to keep the encapsulated MSCs alive.

Tithon's researchers believe that the encapsulation of the MSC will also protect the encapsulated MSC from attack by the recipient's immune system, thereby allowing the use of Tithon's proprietary immortal MSC cell line, and eliminating the need for autologous sourced MSC.

Tithon will be starting preclinical work on this new MSC-Encap product. Our colleagues at the Faculty of Medicine, University of Thrace, a team specialized in Inflammatory Bowel Diseases research, will conduct in vitro work, using MSC-Encap in cultures of colonic epithelial cells and freshly isolated subepithelial myofibroblasts from gut mucosa of Chron's Disease patients in order to examine the immunomodulatory effect of MSC-Encap product in gut inflammation and fibrosis. In addition, they will conduct in vivo

research in animal models of experimental colitis, using MSC-Encap as an immunomodulatory mediators delivery method. Similar in vivo experiments in animal models will be conducted from our colleagues, specialized in the management of Idiopathic Pulmonary Fibrosis, at the Medical Scholl, University of Athens in Greece, as part of a continuation of our previous published trial work on autologous adipose-derived stem cells [4,5]. Tithon will also be continuing research conducted over the previous decade including extensive clinical work on the effect of MSC on aesthetics, such as facial rejuvenation and hair loss, utilizing the newly developed MSC-Encaps that will be tested in human trials to demonstrate their positive aesthetic effects.

As Idiopathic Pulmonary Fibrosis is considered a serious disease with a high unmet need by regulatory authorities in USA, Japan, South Korea and Europe the Tithon MSC-Encap cell therapy qualifies for the Regenerative medicine advanced therapy (RMAT) designation by the USA FDA, conditional marketing authorisation in Japan and South Korea, and for the Adaptive pathways program in the EU, upon a successful safety and efficacy human trial in those jurisdictions. Tithon Biotech believes it will be able to reach this goal in 18 months.

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