Stempeutron®: A novel, point of care Medical Device for addressing major unmet medical needs

About Stempeutics:

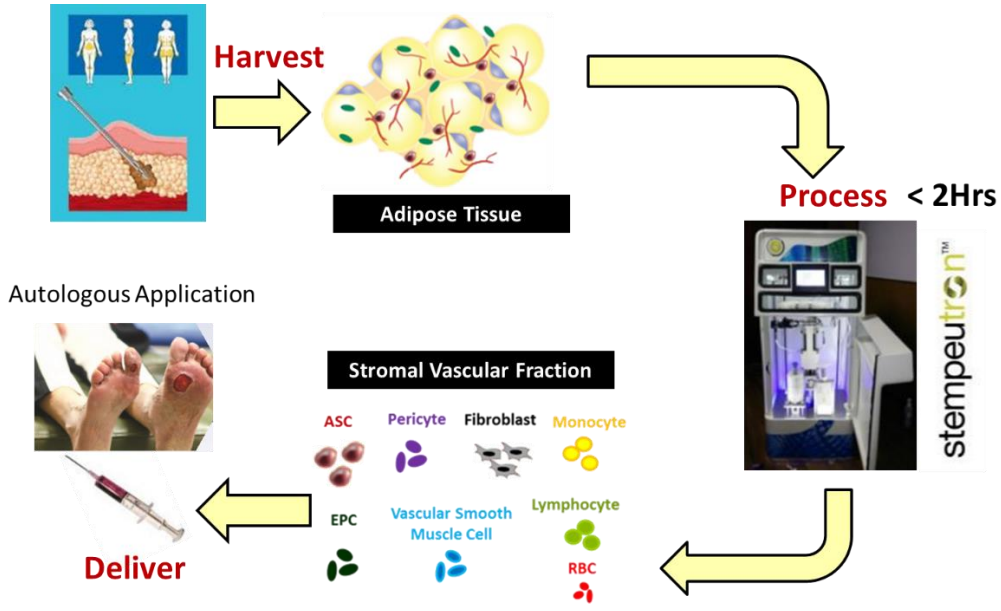
Stempeutics Research Bangalore is a late stage life science company focused on developing and commercializing novel therapeutics based on adult stem cells. It was incorporated by the Manipal Education & Medical Group in Jan 2006. Stempeutics strength lies in developing innovative stem cell based products by nurturing cutting edge research and clinical applications through dedicated efforts of its highly qualified team. Currently it is focusing on the following innovative product:

About Stempeutron® Medical Device:

Stempeutron® is an automated medical device for point-of-care isolation of therapeutic stem and stromal cells from aspirated fat/adipose tissue. Adipose tissue stroma is a rich source of mesenchymal stem cells and endothelial progenitor cells, as well as other tissue-building cells such as vascular smooth muscle cells, pericytes, pre-adipocytes and fibroblasts. This cell cocktail, called the stromal vascular fraction (SVF), can give rise to new blood vessels, bone, cartilage, fat and muscle among others. In recent years, researchers have established that SVF derived from fat tissue have clinical utility in the broad field of cell therapy and regenerative medicine for repair of diseased organs.

Stempeutron® provides a unique opportunity to isolate and concentrate SVF cells from a given volume of fat at the doctor's clinic in a matter of hours for personalized therapeutic application. Stempeutics has successfully completed the proof-of-concept phase, and is presently in the beta phase of development. Stempeutron™ is proposed to enter the market in 2021.

Concept Diagram:



Stromal Vascular Fraction (SVF) Cells: Clinical Applications:

Several clinical trials using autologous fat tissue derived SVF have been conducted worldwide, and have shown promising results in a wide variety of regenerative cell therapy applications such as diabetic foot ulcer, skeletal regeneration, cartilage regeneration, cardiovascular and peripheral vascular diseases, as well as autoimmune disorders. Owing to the encouraging outcomes reported, SVF based therapeutics is very close to becoming accepted clinical practice in the very near future. But the challenge is availability of SVF at the point of care and at an affordable cost

Need for an automated point-of-care medical device:

Availability of SVF at the point of medical care within few hours and with simple operations will help suffering patients a lot. Patients need not travel to Metros to get Stem Cell based treatment. Instead it can be made available at the point of care even in clinics in villages with simple infrastructure. Also it can be made available in a cost effective manner.

Isolation of SVF requires the fat to be harvested by liposuction, washed, enzymatically digested and centrifuged to recover the cells. Manual processing has been in practice for some time, but requires skilled technicians, expensive infrastructure and laboratory with GMP and GCP compliance, which are not available with most healthcare units. Isolation in a certified external laboratory entails storage, handling and transportation of fat and cells from and to the clinic, and multiple patient visits. These challenges are largely overcome by the development of a fully automated, point-of-care device like Stempeutron® for SVF isolation in a highly quality controlled and consistent manner.

Stempeutron® Technology:

Stempeutron® is a medical device intended for automated isolation of SVF cells from the patient's own fat tissue at the point-of-care, with minimal manipulation and human intervention. The device will comprise of a hermetically sealed enclosure housing the mechanical and electronic components, within which the tissue processing will be carried out using sterile single-use disposables. Stempeutron® is designed to operate on a proprietary process and technology. The innovation in Stempeutron® lies in the concentration of clinical grade SVF cells without the use of a centrifuge, which is the conventional process for recovering the cells. This is achieved by using a proprietary filtration system. By eliminating centrifugation, the isolation becomes gentle, and the cost and footprint of the device is reduced.

Stempeutron® is under development as a fully automatic, embedded controlled, robotics technology based device. It is under development as a trolley mounted device, with a TFT display for the user interface. It will be enabled with tightly interlocked sensor based controls for safe and

sequence based operations. The device will have inbuilt remote monitoring enablers which when put on ethernet backbone will facilitate monitoring and control from a central server.

Stempeutron® is being designed with easy to install interfaces for the consumables, which are meant for single use. A pre-programmed robotic arm is designed to move in a predefined path. Each movement will be sensed, acknowledged and controlled by a set of sensors with level-II safety interlocks. The robotic arm and synchronized valves will manage the transfer of tissue and other reagents into the digestion chamber. In line with specific kinematic equations, the robotic arm effects movements to manage the washing and digestion processes. At defined intervals the robotic arm will move to a particular location to discharge waste generated during the wash cycle. At the end of the digestion process, a defined quantity of the digested tissue is to be transferred to the filtration unit. The filtration process to concentrate the SVF will also be driven by the embedded controls.

At the end of the filtration process, the robotic arm is expected to facilitate transfer of the SVF into a designated syringe and deliver the same to a surgeon. This delivery mechanism is to be managed and controlled by a defined algorithm and set of safety sensors.

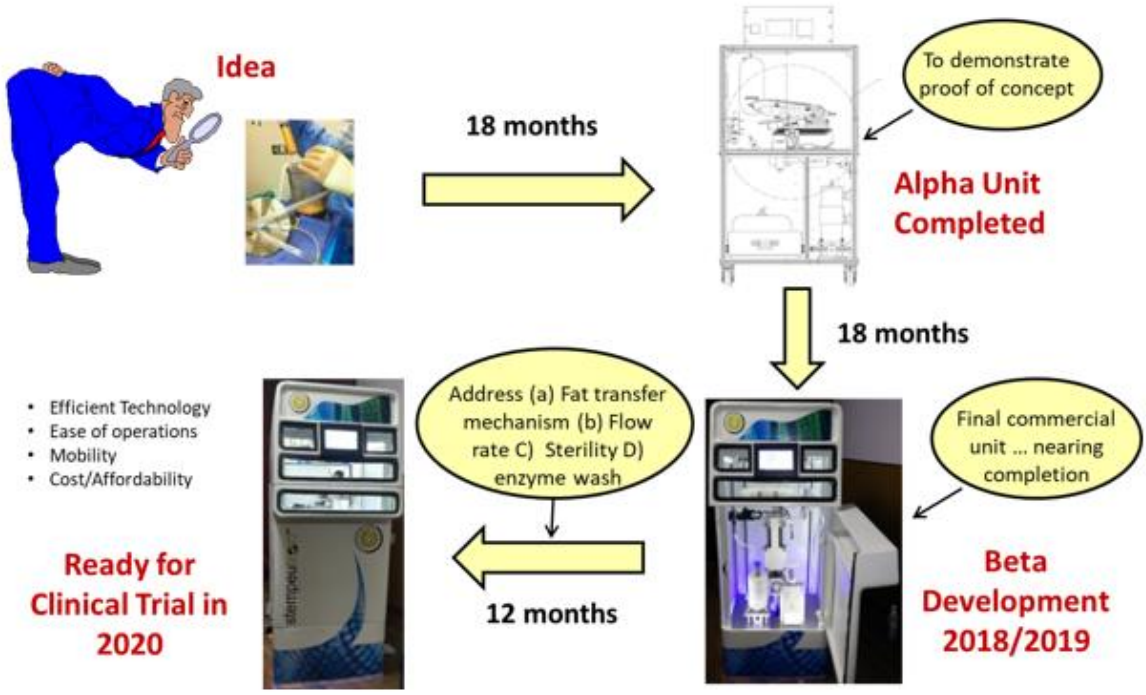
Stempeutron® development: Current Status:

The main operational modules required for digestion and filtration have been assembled into a fully automated alpha phase prototype device to generate proof-of-concept and confirm that development of such a device is technically feasible. In this alpha prototype, we have tested the ability of the washing and digestion chamber to process fat tissue upto a volume of 500 ml. The phase separation to distinguish between the fatty and the aqueous fractions has also been accomplished by vertical positioning of the digestion chamber. The aqueous fraction obtained post digestion was loaded on to the filtration unit and the SVF cells were successfully recovered from the collection chamber. The SVF cells isolated from the device have been compared with the cells isolated by the manual process from the same fat tissue samples. Results obtained from the device have been found to be equivalent to the manual process in terms of SVF cell yield, viability and composition. The relative percentage of adipose tissue derived stromal cells, endothelial and endothelial progenitor cells that are critical for tissue engraftment have also been found to be present in comparable numbers in the SVF obtained by the device and by the manual process. The biological function of these cells with respect to *in vitro* and *in vivo* angiogenesis is currently being determined. Taken together the data suggest that it is technically feasible to isolate SVF through this novel technology based device and proceed to the beta phase of building a completely automated and aseptic version of Stempeutron®.

Stempeutron® is currently in the beta stage of development and is proposed to enter the market in 2021. Availability of Stempeutron™ will have a significant beneficial impact on healthcare as it will greatly facilitate the penetration of affordable SVF-based therapy in hospitals and clinics in all parts of India and other markets. **Stempeutron™ is the FIRST indigenous device for stem cell isolation from INDIA and is poised to place Stempeutics as the market leader in applying fat-derived cell therapy in India and abroad.**

<u>Funding requirements:</u>

Approx. Rs 8Cr to make Beta unit ready for clinical studies and commercialize for one clinical application:



Fund will be utilized for the following activities:

a) Fat transfer mechanism
b) Increasing the flow rate in the filtration system
c) To address sterility of the device
d) Effective elimination of enzyme in the final SVF
e) Preclinical studies
f) Clinical studies
g) Marketing approval in India for one application