Clinical Evidence for Immune Reprogramming with Extracorporeal Mesenchymal Stromal Cell Therapy

Barcia, Rita N., PhD[1], Nguyen, Sunny, BS1, Brian O' Rourke , PhD1, Igo, Peter, BS[1], Tilles, Arno W., MD, MSBE[1], Elizabeth Lapointe[1], Chris Gemmiti, PhD [1], Brian LK Miller, MS, MBA[1], Parekkadan, Biju, PhD[1,2,3]

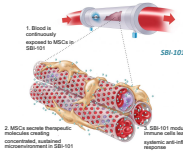
[1]Sentien Biotechnologies, Inc. 99 Hayden Ave, Suite 140, Lexington, MA 02421 [2] Department of Biomedical Engineering, Rutgers University, Piscataway, New Jersey 08854 [3]Center for Surgery, Innovation, and Bioengineering, Massachusetts General Hospital, Boston, MA 02114 [4]Harvard Stem Cell Institute, Cambridge, MA 02138

The Sentien Approach: Bringing blood to the MSCs

Bioactive molecules secreted by MSCs are the primary source of activity of these therapeutically promising cells. We have engineered a system to maximize delivery of therapy from MSCs to circumvent the half-life issues that have hindered MSC transplantation. This system overcomes the dosing constraints of IV infusion and potentiates a broad range of biological responses unparalleled in single molecule therapeutics.

Product Concept: Sentien is developing a combination product (SBI-101) that integrates allogeneic MSCs within an extracorporeal, blood contacting device to fundamentally change the administration route. **Instead of bringing MSCs to the blood, our product brings blood to the MSCs.**

SBI-101 therapy allows for extended delivery of MSC secreted factors, harnessing the potential of MSC therapy for systemic inflammatory diseases such as COVID-19.



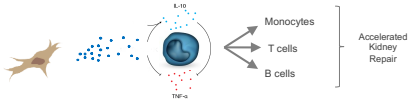
SBI-101 Acute Kidney Injury (AKI) trial

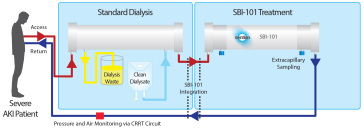
Phase I/II: Double blind, randomized, controlled, study at 2 doses to establish safety and pharmacologic POC (NCT03015623)

Miller et al., Kidney Int Rep. 2018

MSC Secreted Factors → Systemic Immunomodulation → Immune Cell Reprogramming

Therapeutic Hypothesis of MSC-Mediated Blood Reprogramming





All patients were on Continuous Renal Replacement Therapy (CRRT)

8-10 US based clinical sites

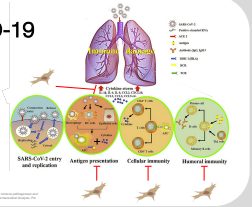
CRRT only (control)
CRRT + 250M cells (low dose)
CRRT + 750M cells (high dose)

Endpoints:
1: Safety
2: Renal specific efficacy
Exploratory: PK/PD biomarkers

An interim analysis was performed on the low dose cohort (n=4 in each group).

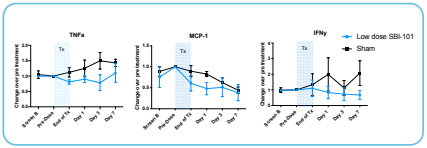
MSCs Therapy Ideally Suited for Severe COVID-19

Known MSC biology is very well suited to address the hyper-inflammation associated with severe COVID-19. By addressing a broad array of immune-mediated inflammatory pathways, MSCs can simultaneously address multiple aspects of the inflammatory cascade.



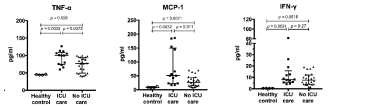
Immunomodulation observed in SBI-101 AKI Clinical Data Supports Therapeutic Hypothesis in COVID-19

SBI-101 AKI Patient data



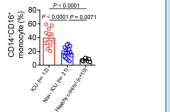
COVID-19 Patient data

TNF-α, MCP-1, and IFN-γ are all highly increased in COVID-19 ICU patients*



*Huang C. et al. Clinical features of patients infected with 2019 novel coronavirus in Wuhan, China. Lancet 2020; published online Jan 24.

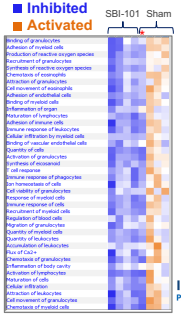
Inflammatory monocytes have positive correlations with severe pulmonary syndrome in patients infected 2019-nCoV**



**ZHOU, et al., Aberrant pathogenic GM-CSF+ T cells and inflammatory CD14+CD16+monocytes in severe pulmonary syndrome patients of a new coronavirus pre print

SBI-101 AKI Results are Consistent with Immune Reprogramming

SBI-101 Clinical Data in AKI Reflects Broad Immunomodulation



INGENUITY PATHWAY ANALYSIS

* Septic subject that got better has pathway profile similar to SBI-101 treatment

Phase 1b data suggests that SBI-101 broadly **inhibits immune-mediated inflammatory pathways**, including:

- **T cell response**
- **Maturation of lymphocytes**
- **Activation of lymphocytes**
- **Immune response of leukocytes**
- **Quantity of leukocytes**
- **Inflammation of Organ**

Ex-vivo MSC therapy using SBI-101 technology shows promise for severe COVID-19

Rita.barcia@sentienbiotech.com

Grant Funding Agencies:
NIDDK 5R44DK085766
NHLBI 4R44HL128659