FibroGenesis Identifies Mechanism Responsible for Blocking COVID19-Like Lung Inflammation

Regenerative Medicine Company Advances Development of Fibroblast-Based Product as an "Off the Shelf" Cell-Treatment for Coronavirus Acute Respiratory Distress Syndrome (ARDS)

HOUSTON, July 1, 2020 /PRNewswire/ -- FibroGenesis announced today identification of molecular mechanisms associated with the potent reduction of lung inflammation previously reported by the Company in an animal model of COVID-19 lung failure.

The Company disclosed data demonstrating that administration of PneumoBlast™ resulted in dramatic alterations of immunological signaling molecules called "cytokines". The studies showed that PneumoBlast™ reduced concentrations of the inflammatory cytokines interleukin-1 beta, interleukin-6, interleukin-8, interleukin-17, interleukin-18, and Tumor Necrosis Factor alpha, TNF*a*. Supporting the inflammation-inhibiting properties of PneumoBlast™, Company scientists observed an increase in anti-inflammatory cytokines interleukin-4, interleukin-10, interleukin-13 and interleukin-35, as well as regeneration-associated cytokines FGF-2 and HGF-1. The cytokines found to be manipulated by PneumoBlast™ are known to be associated with survival and recuperation from COVID-19.

Interleukin-1 beta (IL-1β): Mortality from acute respiratory distress syndrome (ARDS), is associated with increased IL-1β. Studies have shown that administration of Anakinra, a drug specifically designed to block IL-1β, reduces mortality in patients with a COVID-19 associated cytokine storm, one of the other causes of death.

Interleukin-6 (IL-6): In a review of 1,426 COVID-19 patients in nine separated studies, interleukin-6 levels were more than three times higher in patients with complicated COVID-19 compared with those with a non-complicated disease. Furthermore, it was shown that higher levels of interleukin-6 correlated with death. Supporting a causative role of interleukin-6 in pathology of COVID-19, studies have shown that administration of blocking antibodies to interleukin-6 reduces pathology of this disease.

Interleukin-8 (IL-8): Patients with ARDS show that elevated levels of IL-8 are associated with higher mortality. IL-8 is known to recruit and activate neutrophils in the lung. Under normal circumstances, neutrophils serve to fight infections. In the case of COVID-19, excessive neutrophils in the lung are believed to be associated with lethality.

Interleukin-17 (IL-17): Most of diseases associated with the immune system (Autoimmune diseases) have upregulated levels of both IL-17 and the cells which produce it, the Th17 cells. Patients with COVID-19 have dysfunctional blood vessels which predispose to excessive coagulation, believed to be caused by IL-17. Additionally, IL-17 stimulates neutrophil infiltration into lungs.

Previously reported by the Company:

In one set of experiments, control-untreated-mice possessed a lung wet weight to body weight ratio (LWW/BW) of 3.7 mg/g. Mice treated with lipopolysaccharide; an agent that induces COVID-19-like lung inflammation caused an increase of the LWW/BW ratio of 12.5 mg/g. Administration of bone marrow mesenchymal stem cells (BMSCs) to lipopolysaccharide-treated-mice only reduced the LWW/BW ratio to

9.9 mg/g. In strong contrast, PneumoBlast™ administration significantly reduced the LWW/BW ratio to 5.2 mg/g in lipopolysaccharide-treated-mice ($p < .001$). PneumoBlast™ showed a 37% improvement in outcome compared to BMSCs, which was statistically significant ($p < .005$). More importantly, after the introduction of PneumoBlast™ fibroblast cell therapy, average LWW/BW ratios returned to baseline control numbers of healthy lungs, which resulted in no statistical difference between recovered lungs and normal/healthy lungs using PneumoBlast™.

When the lung inflammation marker interleukin-6 was assessed, control mice possessed 532.3 pg/ml of the cytokine, whereas lipopolysaccharide administration caused an increase to 4400.1 pg/ml. Treatment with BMSCs resulted in a slight 26% decrease of IL-6 in the lipopolysaccharide-treated-mice to 3317.7 pg/ml, whereas PneumoBlast™ significantly reduced IL-6 by 80% to 896.2 pg/ml, which was highly significant ($p < .001$). The use of PneumoBlast™ resulted in a 54% improvement over BMSCs ($p < .001$). The introduction of PneumoBlast™ cell therapy resulted in a reduction of inflammation back to normal/healthy lung levels in just 24 hours.

“Expanding our research continues to build a compelling scientific justification for use of fibroblasts in treatment of COVID-19 ARDS,” said Tom Ichim, Ph.D., Chief Scientific Officer of FibroGenesis. PneumoBlast™ appears to offer new hope to patients suffering from COVID-19 associated lung disease.”

“We continue to be impressed with the potency of fibroblasts and their ability to effectively halt fluid accumulation in the lungs and repair the damage,” said Pete O’Heeron, President and CEO of FibroGenesis. “Compared to stem cells, fibroblasts appear to be a more robust and potent cell source.”

About FibroGenesis

Based in Houston, Texas, FibroGenesis, is a regenerative medicine company developing an innovative solution for chronic disease treatment using human dermal fibroblasts. Currently, FibroGenesis holds 220+ U.S. and international issued patents/patents pending across a variety of clinical pathways, including Disc Degeneration, Multiple Sclerosis, Parkinson's, Chronic Traumatic Encephalopathy, Cancer, Diabetes, Liver Failure and Heart Failure. Funded entirely by angel investors, FibroGenesis represents the next generation of medical advancement in cell therapy.

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