Press Release:

TNFα-supplemented DL-4 culture system supports first-in-clinic Smart Immune ProTcell™ technology for immuno-deficient patients fighting cancers and infections

Rapid reset of immune system can provide marked benefits in clinical settings where patients are significantly immunocompromised

PARIS, France, September 29th, 2021 - Smart Immune SAS's unique ex-vivo biomimetic ProTcell™ 'thymus in a dish' platform technology, designed to generate specific human T-cell progenitor cells at scale with high purity, homogeneity, and yield, has been reinforced by data published in the peer-reviewed journal *Cellular & Molecular Immunology*[1].

These data show for the first time that adding tumor necrosis factor alpha (TNFα) to a DL-4-based culture system leads to the generation of a large number of nonmodified or genetically modified human T-lymphoid progenitors (HTLPs). These resulting HTLPs, possessing highly efficient T-cell potential through accelerated T-cell maturation, differentiation, and rearrangement as well as enhanced HTLP cell cycling and survival[1].

The study also highlighted the ability of the HTLPs to expeditiously propagate and differentiate into a fully polyclonal T-cell compartment including CD4+ and CD8+ T-cells with the appropriate TCR rearrangements as well as be compatible with gene modification, as illustrated by the efficient production of transduced genetically modified HTLPs from TNFα-supplemented HTLP cultures[1]. The possibility of genetically modifying ProTcells™ opens the door for a new generation of CAR-T cells, allowing terminal differentiation into the thymus, providing the opportunity for production of CAR-T cells with immense proliferative capacities and a long-life span, solving the existing hurdles of autologous and allogeneic CAR-T cell products which lose clinical efficacy due to exhaustion.

T-cells are key to providing immunity to foreign pathogens and are indispensable in fighting life-threatening blood cancers, infections, and primary immunodeficiency diseases. ProTcell™, developed by Smart Immune SAS, is a new generation of allogenic cell and gene therapy designed to reset the patient's immune system following allogeneic hematopoietic stem cell transplantation (HSCT) while reducing serious adverse events, morbidity, and mortality, thereby improving quality of life.

"The addition of TNFα to our ProTcell™ culture system could lead to a revolutionary CAR T-cell approach and establish a new opportunity for developing personalized hemopoietic stem cell transplants for patients based on ProTcell™ allogenic clinical grade T-cell progenitors," said Dr Isabelle André, Director of the Inserm Human Lymphohematopoiesis Laboratory at Institut *Imagine*, Paris, France, co-founder of Smart Immune and study author. "We are currently focusing on validating the platform *in vivo*, with the short-term goal of demonstrating that ProTcell™ can improve overall survival at 12 months and reduce serious adverse events* for patients having received an allogenic HSCT."

ProTcell™ is currently being evaluated in patients receiving an allogeneic HSCT for acute leukemia in an FDA-approved clinical trial.

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* Including graft versus host disease (GvHD), infections, and relapse.

About Smart Immune

Smart Immune believes that T-cell therapy should be accessible and affordable to all patients and, through its groundbreaking ProTcell™ platform, has developed clinical stage T-cell progenitors designed to improve prognosis for patients affected by malignant blood diseases or rare primary immunodeficiencies. The company is utilizing its unique ex-vivo biomimetic 'thymus in a dish' technology to culture specific T-cell progenitor subpopulations at scale and use them as cell or gene therapy. The company was founded in 2017 by Dr Isabelle André, Dr Karine Rossignol, and Pr Marina Cavazzana from Hôpital Necker-Enfants Malades AP-HP, a consultant pediatric hematologist and a pioneer in vector-based therapies and hematopoietic stem cell treatments.

About ProTcell™

The Smart Immune ProTcell™ platform generates allogenic T-cell progenitors that provide fully functional polyclonal T-cells within 3 months following an allogeneic HSCT while also reducing graft versus host disease (GvHD), infections and relapses thereby improving morbidity and mortality and shifting the benefice risk ratio for allogeneic medicine. When infused, ProTcell™ migrate to the patient's thymus where they expand, are selected, and then differentiate, resulting in fully functional T-cells, tolerant to the patient's own immune system and reactive to viral, fungal, and malignant antigens.

ProTcell™ has been accepted by the FDA as an Investigational New Drug (IND) for Acute Lymphocytic Leukemia (ALL) and Acute Myelocytic Leukemia (AML) and has also been granted fast-track designation under its expedited program for serious conditions. In 2021, the FDA granted orphan drug designation for ProTcell™ as a treatment to enhance cell engraftment in patients receiving hematopoietic stem cell transplant (HSCT) including hematologic malignancies and all forms of primary immunodeficiencies. ProTcell™ is currently being studies in two clinical trials in Europe, with two in the U.S. expected to start in Q4 2021. To learn more, please visit www.smart-immune.com

Reference:

1. Moirangthem RD, Ma K et al. Cellular & Molecular Immunology (2021) 18:1662–1676; https://doi.org/10.1038/s41423-021-00706-8

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