Smart Immune Announces Research Collaboration with Memorial Sloan Kettering Cancer Center (MSKCC) to Expedite Development of a Next Generation CAR-T Through its Long Lasting, Exhaustion-Free CAR ProTcell™ Platform

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PARIS, France, Dec 9, 2021 – Smart Immune SAS, a clinical stage T-cell medicine company utilizing its proprietary ex-vivo biomimetic "thymus-in-a-dish" technology to develop T-cell progenitors (ProTcell™) to reset a rapid, safe and full immune reconstitution, announced today a research collaboration with Memorial Sloan Kettering Cancer Center (MSKCC). The intent of this collaboration is to expand its ProTcell™ pipeline with next generation CAR-ProTcell™ platform designed to address exhaustion of T cell therapy and fulfill unmet medical needs in the treatment of hematological and solid cancers.

This collaboration has been setup to rapidly develop the next generation of CAR-T cell therapies. Through its groundbreaking *ex vivo* thymus technology, Smart Immune aims to disrupt conventional approaches to CAR-T cell therapies by using its T-cell progenitors ie. ProTcell™ instead of mature T-cell and generate a naïve long lasting, exhaustion-free CAR-T cell population. As part of this collaboration, MSKCC will contribute to the development of the CAR-ProTcell™ platform with a first proof-of-concept (PoC) in a mouse-to-mouse model. Smart Immune will lead the humanized model PoC. This work has the potential to expedite the clinical development of next generation CAR-T cells combining long-term persistence, natural protection against infections, and low risk of graft-versus-host disease (GvHD) in allogeneic setting.

Refining upon the initial work of the Company's scientists (*Moirangthem et al., 2021*) demonstrating that ProTcell™ progenitors can be efficiently transduced with a lentiviral vector, MSKCC and Smart Immune scientists expect to further optimize transduction and culturing conditions to perform *in vitro* and *in vivo* prelinical studies on ProTcell™ transduced with a CD19 CAR lentiviral vector.

"The presence or absence of the $CD19^+$ cells in NSG mice after HSC transplantation would indicate the extent to which this new generation of CAR-T cells are efficient and will be the first example of a naïve CD19-CAR-T generated from early progenitor T-cells (ProTcell™) obtained in culture. It would be a huge advancement for the gene-therapy space," remarked Dr. Marina Cavazzana, co-founder and Chief Medical Officer of Smart Immune. In this way the direct tumor targeting capability of CAR-CD19-Pro-T-cells can be rapidly assessed in a murine model.

"MSKCC and Smart Immune will work together to foster the development of Smart Immune's next generation CAR-ProTcell™ platform," commented Dr. Marcel van den Brink, Head of the Division of Hematologic Malignancies at MSK, and collaborating scientist. "We look forward to continuing our research into a new therapeutic category of CAR-T cells using lymphoid progenitors T-cells, which due to their decade long lifespan, would remain free from exhaustion and have prolonged viability, over today's CAR-T therapies using mature T-cells."

Dr. van den Brink provides advisory services for Smart Immune.

About Smart Immune

Smart Immune's mission is to make T-cell therapy 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 cancers and infections. The company is utilizing its unique *ex-vivo* biomimetic 'thymus in a dish' technology to culture specific T-cell progenitor subpopulations at clinical scale and use them for cell or gene therapy. The company was founded in 2017 by Dr Isabelle André, Karine Rossignol, and Dr Marina Cavazzana from Hôpital Necker-Enfants Malades AP-HP, a 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 hematopoietic stem cell transplant (HSCT) while also reducing GvHD, infections and relapses thereby reducing morbidity and mortality and improving the benefice risk ratio for allogeneic medicine. When infused, ProTcell™ progenitors 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 Food and Drug Administration (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 like SCID. In 2021, the FDA granted orphan drug designation for ProTcell™ as a treatment to enhance cell engraftment in patients receiving HSCT including hematologic malignancies and all forms of primary immunodeficiencies. ProTcell™ is currently being studied in two clinical trials in Europe. One trial in the U.S. is opened and expected to start recruiting in early 2022. To learn more, please visit www.smart-immune.com

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