Smart Immune Announces Acceptance of Two Abstracts Covering Preclinical Research and Clinical Data at the American Society of Hematology

Data Presented at ASH Underscores the Potential of the Smart-Immune Platform That Can Generate *ex-vivo* T- cell progenitors and NK- Cells for the Treatment of Primary Immunodeficiencies, and Cancers

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PARIS, France, Nov 5, 2021 – Smart Immune SAS, a T-cell medicine company utilizing its proprietary ex-vivo biomimetic "thymus in a dish" technology to develop allogeneic T-cell progenitors Smart-101 (ProTcell™) for rapid immune reconstitution, announced today the presentation of clinical data and preclinical research at the 63rd annual meeting of the American Society of Hematology (ASH), taking place December 11-14 in Atlanta, Georgia. Preliminary data in these abstracts became available on the ASH conference website 9:00 AM ET yesterday. Recently, Smart-Immune has also announced the commencement of its first US clinical trial using its T-cell progenitor product (Smart-101) for the treatment of patients with AML and ALL who receive allogeneic hematopoietic stem cell transplant (allo-HSCT).

"For a young company like ours, the selection of abstracts at a prestigious hematology conference like ASH is a recognition of the potential of our platform technology to uniquely and selectively generate large numbers of T- and/or NK-progenitors with the purity and reproducibility necessary for clinical use," commented Karine Rossignol, the Chief Executive Officer and co-founder of Smart-Immune. "These abstracts selected represent a decade of research by my co-founders Drs. Marina Cavazzana and Isabelle Andre to create a short and elegantly simple 7-day culture system to generate lymphoid progenitors allowing a fast (within 100 days instead of 1-2 years) a polyclonal reconstitution of a fully functional immune system able to fight cancers and infections, changing drastically the prognosis of patients. With widespread applicability across primary immunodeficiencies, and hematological cancers, and three clinical trials launched, Smart-Immune is the first company to bring allogenic human progenitor cells into clinical development."

Abstracts accepted at ASH include:

1) Rapid and Safe T Cell Immune Reconstitution By T Cell Progenitor Injection Following Haploidentical Transplantation for Severe Combined Immunodeficiency (SCID).

   Presenter: Despina Moshous, Hospital Necker Enfants Malades
   Session Name: 704. Cellular Immunotherapies: Clinical: Poster I
   Session Date: Dec 11th, 2021
   Session Time: 5:30 PM - 7:30 PM
   Room: Georgia World Congress Center, Hall B5

   Abstract Synopsis: Severe Combined Immunodeficiency (SCID), is a severe form of primary immunodeficiency, responsible for the death, within the first few months of life, if not treated with HSCT. In the absence of an HLA-identical HSC donor, an urgent haploidentical HSCT is proposed to newborns with Severe Combined Immunodeficiency (SCID). The authors describe how the Delta-4 ligand based, culture system, that is at the core of the Company's invention, can

be used to generate the earliest CD7+ T-cell progenitors (Smart-101) from such a haploidentical donor. Patient outcomes for two SCID babies being treated in the ongoing Smart-Immune phase 1/2 trial in SCID, who receive Smart-101 after allogeneic HSCT is discussed. Available data indicate that when Smart-101 is used at the optimal window of time in the early weeks after birth, rapid immune reconstitution with CD3+, CD4+, CD8+ and CD19+ T-cells may result in freedom from infections and GvHD and can be lifesaving for such SCID babies. These preliminary results deserve further investigation, which will be performed as part of our ongoing clinical study.

2) Ex Vivo Production Of Large Numbers Of Genetically Modified NK Cells From Cord Blood Or Mobilized Peripheral Blood $CD34^+$ Cells Using Notch Ligand Delta-Like 4 Culture System

Presenter: Ranjita Devi Moirangthem, Smart-Immune SAS
Session Name: 703. Cellular Immunotherapies: Basic and Translational: Poster II
Session Date: Dec 12th, 2021
Session Time: 6:00 PM - 8:00 PM
Room: Georgia World Congress Center, Hall B5

Abstract Synopsis: In this research the authors extend the utility of the Company's proprietary Delta-4 ligand based, feeder free, culture platform from generating not just pure allogeneic T-cell CD7+ progenitors (Smart-101), but also being able to generate T-cell free, CD56+ NK-cells (Smart-103) when culture conditions are modified to be NK-conducive. Expansion of these NK-progenitors result in NK populations with normal surface markers, gene expression patterns and cytotoxicity seen in NK cells immunoselected from human beings. Allogeneic NK-therapy is at its infancy but provides many advantages over T-cell therapy in it being free from graft-versus-host disease and downstream cytokine storm in the recipient. Moreover, the Company's NK-cells are also easily gene modifiable such that the transgene is robustly expressed in the NK population, paving the way for possible future CAR- NK development expanding our technology to both lymphoid populations, i.e., T and Nk cells.

"At Smart-Immune, we are first and foremost focused on validating that our first cell-therapy product, which is our early progenitor T-cells (Smart-101) devoid of any form of genetic engineering, is of easy access and safe to patients in both the short-term and long-term," said Dr. Marina Cavazzana, co-founder and Chief Medical Officer of Smart-Immune. "Smart-101 has to be safe and effective in what it is intended to do i.e., shorten the lymphoid immunodeficient period from 18 months to 3-6 months, benefiting infection, graft versus host (GvHD) and relapse rates, and possibly augmenting survival. Proving this in 2022-2023 will pave the way for our next phase of clinical programs starting early 2024 using CAR-ProTcell™ where our progenitor T-cells could bear efficient transgenes to fight cancers."

A description of all three US and European clinical trials using Smart-Immune's progenitor populations can be found on the Company's website: Smart-Immune.com

To learn more about the US clinical trial for Smart-101 in pediatric and adult leukemia, please refer to: ClinicalTrials.gov (Trial Identifier: NCT04959903)

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 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 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 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 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 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

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