PRESS RELEASE

Cellectis Publishes Novel Methods to Improve the Safety of CAR T-Cell Therapy and Prevent CRS in the Journal of Biological Chemistry

Granulocyte-macrophage colony-stimulating factor inactivation in CAR T-Cells prevents monocyte-dependent release of key cytokine release syndrome mediators

February 25, 2019 – New York (N.Y.) – Cellectis (Euronext Growth: ALCLS; Nasdaq: CLLS), a biopharmaceutical company focused on developing immunotherapies based on allogeneic gene edited CAR T-cells (UCART), today announced the publication of a study in *The Journal of Biological Chemistry*, identifying Granulocyte Macrophage Colony Stimulating Factor (GMCSF) secreted by Chimeric Antigen Receptor (CAR) T-cells as a key factor promoting cytokine release syndrome (CRS). The accelerated report leverages these findings to elaborate an innovative engineering strategy that paves the way for developing safer UCART products.

Utilizing these results, Cellectis developed engineered GMCSF Knock-Out CAR T-cells through TALEN®-mediated gene inactivation. The inactivation of GMCSF in CAR T-cells was found to prevent secretion of pro-inflammatory cytokines by monocytes, without compromising CAR T-cell anti-tumor activity.

“CAR T-cells have achieved high rates of complete remission in hematological malignancies, however, this 'living drug' can show life-threatening inflammatory side effects including CRS and neurotoxicity that need to be addressed,” said Mohit Sachdeva, Ph.D., Innovation Project Leader at Cellectis. “Our engineering strategy circumvents such toxic side effects and propose safer, equally potent UCART-cells, to improve patients’ quality of life during treatment.”

“Today, tocilizumab or glucocorticoid treatments are considered the standard of care for CRS management,” added Julien Valton, Ph.D., Innovation Team Leader at Cellectis. “However, these treatments increase patient medication burden, add substantial costs and lengthen treatment time in intense care settings. To overcome these clinical challenges, we investigated the biogenesis of CRS and based on our findings, developed a CAR T-cell product candidate that could potentially prevent rather than treat CRS symptoms. We hope this approach can bypass CRS symptomatic treatments and improve the overall safety of CAR T-cell therapies for cancer patients.”

Julien Valton, Ph.D., Innovation Team Leader, Cellular Engineering & Adoptive CAR T-Cell Immunotherapy

Dr. Julien Valton obtained his Ph.D. at the University Joseph Fourier in Grenoble, France, where he was trained as an enzymologist. He then joined the Yale School of Medicine to apply his knowledge to therapeutic research by investigating the mechanism of inhibition of receptor tyrosine kinases that are involved in the development of gastrointestinal cancer. In 2009, he moved a step further into the field of applied science by joining the Innovation Department of Cellectis, where he actively participated in using and improving

TALEN® gene editing technology for targeted gene therapy and genome engineering. He is now using TALEN® along with protein engineering techniques to develop the next-generation CAR T-cells to treat different malignancies.

Mohit Sachdeva, Ph.D., Innovation Team Senior Scientist
Dr. Sachdeva is an experienced cancer biologist with expertise in immuno-oncology, having authored/co-authored approximately 20 manuscripts in peer-reviewed journals throughout his career. During his time at Cellectis, he has been studying pathways that could be exploited to engineer potent, yet safer, CAR T-cells using gene editing and targeted integration technologies. After receiving his Ph.D. at Southern Illinois University, he completed a successful post-doc at Duke University.

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About Cellectis
Cellectis is a clinical-stage biopharmaceutical company focused on developing a new generation of cancer immunotherapies based on gene-edited T-cells (UCART). By capitalizing on its 19 years of expertise in gene editing – built on its flagship TALEN® technology and pioneering electroporation system PulseAgile – Cellectis uses the power of the immune system to target and eradicate cancer cells.

Using its life-science-focused, pioneering genome engineering technologies, Cellectis' goal is to create innovative products in multiple fields and with various target markets. Cellectis is listed on the Nasdaq (ticker: CLLS) and on Euronext Growth (ticker: ALCLS). To find out more about us, visit our website: www.cellectis.com

Talking about gene editing? We do it. TALEN® is a registered trademark owned by Cellectis.

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on the risk factors that may affect company business and financial performance is included in Cellectis' Annual Report on Form 20-F and the financial report (including the management report) for the year ended December 31, 2017 and subsequent filings Cellectis makes with the Securities Exchange Commission from time to time. Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons why actual results could differ materially from those anticipated in the forward-looking statements, even if new information becomes available in the future.