

Cellectis Publishes Article in Nature Communications Unveiling Novel Immune-Evasive Universal Allogeneic CAR T-cells with Potential for Improved Persistence

New York, NY – June 30, 2022 – Cellectis (the "Company") (Euronext Growth: ALCLS – NASDAQ: CLLS), a clinical-stage biotechnology company using its pioneering geneediting platform to develop life-saving cell and gene therapies, today publishes research data on its novel immune-evasive universal CAR T-cells in *Nature Communications*, following an oral presentation at the American Society of Cell and Gene Therapy (ASGCT) on May 16.

Cellectis' next generation of universal CAR T-cells have the potential to improve the persistence and to allow large-scale deployment of T-cell product candidates in allogeneic settings against multiple malignancies.

Universal CAR T-cell therapies are poised to revolutionize the treatment of selected hematologic malignancies. However, realizing the full potential of CAR T in an allogeneic setting requires universal CAR T-cells that can kill target tumor cells, avoid depletion by the host immune system via the host versus graft reaction (HvG), and proliferate without attacking host tissues via the graft versus host reaction (GvH).

While the prevention of GvH can be readily addressed by the inactivation of T cell receptor T $\alpha\beta$ (TCR $\alpha\beta$) expression in a CAR T-cell, prevention of HvG remains a major challenge.

To address this challenge, the Cellectis investigators engineered CAR T-cells to be deficient in Class 1 major histocompatibility complex (MHC-1) and to express the Natural Killer (NK) inhibitor HLA-E, in order to endow them with immune-evasive properties toward alloreactive Tc ells and NK cells.

"This engineering approach is very promising and could enable the universal CAR Tcells to become transiently invisible to NK and alloreactive T-cells, allowing them to eradicate tumor cells before being rejected by the patient's immune system. This could enable the broad use of universal CAR T-cells in allogeneic settings, for the benefit of a wider population of patients." said Julien Valton, Ph.D., Vice President Gene Therapy at Cellectis.

"One potential advantage of this approach is to spare endogenous immune effectors and allow them to work in concert with CAR T-cells in the fight against hard-to-treat *cancers, including solid tumors*" said Laurent Poirot, Ph.D. Senior Vice President Immuno-Oncology at Cellectis.

The research data show that:

- Endowing universal CAR T-cells with immune-evasive properties via TALEN®mediated gene editing and adeno-associated virus (AAV)-dependent gene insertion, is highly efficient and specific, transferable to different CAR constructs and adaptable to conventional CAR T-cell manufacturing processes.
- Immune-evasive universal CAR T-cells overcame alloresponsive T-cell and NK cells attacks and exhibit prolonged antitumor activity, even in the presence of highly active NK cells.
- Immune-evasive properties against NK cells from most healthy donors and acute myeloid leukemia (AML) patients were similar, demonstrating the robustness and transportability of this hypoimmunogenic approach to persistence and warranting further evaluation in preclinical and clinical settings

This article is available on Nature Communications' website by clicking on this link: <u>https://www.nature.com/articles/s41467-022-30896-2</u>

About Cellectis

Cellectis is a clinical-stage biotechnology company using its pioneering gene-editing platform to develop life-saving cell and gene therapies. Cellectis utilizes an allogeneic approach for CAR-T immunotherapies in oncology, pioneering the concept of off-the-shelf and ready-to-use gene-edited CAR T-cells to treat cancer patients, and a platform to make therapeutic gene editing in hemopoietic stem cells for various diseases. As a clinical-stage biopharmaceutical company with over 22 years of expertise in gene editing, Cellectis is developing life-changing product candidates utilizing TALEN®, its gene editing technology, and PulseAgile, its pioneering electroporation system to harness the power of the immune system in order to treat diseases with unmet medical needs. As part of its commitment to a cure, Cellectis remains dedicated to its goal of providing lifesaving UCART product candidates for multiple cancers including acute myeloid leukemia (AML), B-cell acute lymphoblastic leukemia (B-ALL) and multiple myeloma (MM). .HEAL is a new platform focusing on hemopoietic stem cells to treat blood disorders, immunodeficiencies and lysosomal storage diseases.

Cellectis' headquarters are in Paris, France, with locations in New York, New York and Raleigh, North Carolina.

Cellectis is listed on the Nasdaq Global Market (ticker: CLLS) and on Euronext Growth (ticker: ALCLS).

For more information, visit www.cellectis.com

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Forward-looking Statements

This press release contains "forward-looking" statements within the meaning of applicable securities laws, including the Private Securities Litigation Reform Act of 1995. Forward-looking statements may be identified by words such as "anticipate," "believe," "intend", "expect," "plan," "scheduled," "could," "would" and "will," or the negative of these and similar expressions. These forward-looking statements, which are based on our management's current expectations and assumptions and on information currently available to management. Forward-looking statements include statements about the potential of our research or preclinical programs. These forward-looking statements are made in light of information currently available to us and are subject to numerous risks and uncertainties, including with respect to the numerous risks associated with biopharmaceutical product candidate development. With respect to our cash runway, our operating plans, including product development plans, may change as a result of various factors, including factors currently unknown to us. Furthermore, many other important factors, including those described in our Annual Report on Form 20-F and the financial report (including the management report) for the year ended December 31, 2021 and subsequent filings Cellectis makes with the Securities Exchange Commission from time to time, as well as other known and unknown risks and uncertainties may adversely affect such forwardlooking statements and cause our actual results, performance or achievements to be materially different from those expressed or implied by the forward-looking statements. 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.