PRESS RELEASE

Cellectis Unveils a Non-Viral Gene Therapy Approach for Sickle Cell Disease in Nature Communications

New York, NY – **June 12, 2024** – Cellectis (the "Company") (Euronext Growth: ALCLS - NASDAQ: CLLS), a clinical-stage biotechnology company using its pioneering gene-editing platform to develop life-saving cell and gene therapies, announced today the publication of a scientific article in Nature Communications, unveiling a non-viral gene therapy approach for sickle cell disease.

Sickle cell disease (SCD) is one of the most common inherited diseases worldwide. SCD is caused by a single point mutation in the *HBB* gene, which encodes the β subunit of hemoglobin (Hb). Normally, red blood cells adopt a disc-like shape that allows them to move easily through the blood vessels and deliver oxygen throughout the body. In sickle cell disease, red blood cells become crescent or "sickle"-shaped, a dysfunctional state that impairs blood flow, oxygen delivery and triggers multiple debilitating symptoms including intense pain crisis.

Cellectis leverages TALEN® technology and a non-viral gene repair template delivery to develop a clinically relevant gene editing process in hematopoietic stem and progenitor cells (HSPCs). This process enables efficient *HBB* gene correction with high precision, specificity and minimal genomic adverse events.

Applying this *HBB* gene correction process to SCD patient-HSPCs results in over 50% expression of normal adult hemoglobin in mature red blood cells and in the correction of sickle phenotype, without inducing β-thalassemic phenotype. Edited HSPCs engraft efficiently in an immunodeficient murine model and maintain clinically relevant levels of *HBB* gene correction events. This comprehensive preclinical data package sets the stage for the therapeutic application of autologous gene corrected HSPCs to address SCD.

"The unique combination of TALEN® technology, non-viral DNA repair template design and Cellectis' PulseAgile proprietary electroporation system enabled us to set up a precise, efficient and clinically relevant *HBB* gene correction process in long term hematopoietic stem and progenitor cells from SCD patients" said Julien Valton, Ph.D., Vice President Gene Therapy at Cellectis. "SCD is a devastating blood disorder affecting millions of individuals worldwide. The TALEN® gene therapy approach could represent a new alternative treatment, especially for patients with limited therapeutic options. This gene editing process bears a strong therapeutic potential as it could be easily used to correct point mutations associated to many other genetic diseases."

Research data showed that:

- TALEN® technology, coupled to non-viral DNA correction template delivery, achieves high *HBB* gene correction efficiencies in healthy donor - and SCD patient - HSPCs *in vitro*.

- *HBB* gene correction translates into an efficient rescue of functional Adult Hemoglobin (HbA) and a significant decrease of dysfunctional Sickle Hemoglobin (HbS) and Sickle red blood cells.

- TALEN® nuclease activity is highly specific with only one off-target site detected at the *HBD* locus.

- Corrected HSPCs display long-term *in vivo* engraftment capacity in murine animal model, indicating their strong potential for therapeutic applications towards SCD.

The article is available on Nature Communications website by clicking on this link: https://doi.org/10.1038/s41467-024-49353-3

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 24 years of experience and 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. 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).

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 "could," and "potential," 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, include statements about the potential benefit and potential development of the Company's research and development 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. 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, 2023 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 forward-looking 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.

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