Cellectis Demonstrates Fine and Predictable Tuning of TALEN® Gene Editing Targeting to Improve T-cell Adoptive Immunotherapy

Optimized multiplex gene editing for "off-the-shelf" PD-1 inhibition resistant CAR T-cells

November 20, 2017 – New York (N.Y.) – Cellectis (Alternext: ALCLS - Nasdaq: CLLS), a clinical-stage biopharmaceutical company focused on developing immunotherapies based on gene-edited allogeneic CAR T-cells (UCART), announced today the publication of a study in *Molecular Therapy — Nucleic Acids* describing the educated engineering of highly specific and efficient TAL nucleases (TALEN®) targeting PD1, a key T-cell immune checkpoint.

In this report, Anne-Sophie Gautron, Ph.D., Alexandre Juillerat, Ph.D., and their collaborators used a strategy developed by Cellectis to control TALEN® targeting based on a proprietary technology leveraging the exclusion capacities of non-conventional RVDs. This approach allows combined disruptions of the desired *TRAC* and *PDCD1* loci by TALEN® while eliminating low frequency off-site processing. By adjusting a few RVDs, they provided a rapid and straightforward redesign of optimal TALEN® combinations for multiplex gene editing. This approach can greatly benefit gene editing for therapeutic applications where high editing efficiencies need to be associated with maximal specificity and safety.

Anne-Sophie Gautron, Ph.D. Project leader Immunotherapy
Dr. Anne-Sophie Gautron, Ph.D., graduated in immunology from the University Pierre et Marie Curie/Pasteur Institute, Paris 6, France. After receiving her Ph.D. in immunology in 2009 from the University René Descartes, Paris 5, France, she joined the Neurology and Immunobiology departments at Yale University, Connecticut, where she studied the role of regulatory T-cells in inhibiting pathogenic Th1 and Th17-cell responses. In 2014, she joined the Early Discovery team of Cellectis in Paris, France, working on the development of the next generation of CAR T-cells for adoptive immunotherapy. In 2017, she joined the CAR development group to lead projects associated with the development of new CAR-expressing engineered T-cells for administration as "off-the-shelf" immunopharmaceuticals for cancer treatment.

Alexandre Juillerat, Ph.D. Innovation Team leader
Dr. Alexandre Juillerat, Ph.D., graduated in Chemistry from the University of Lausanne, Switzerland. After receiving in 2006 his Ph.D. in protein engineering from the École Polytechnique Fédérale de Lausanne (EPFL, Switzerland), he moved to the laboratory of Structural Immunology at the Institut Pasteur in Paris, France, performing structure-function studies on a major adhesin of plasmodium falciparum. In 2010, he joined the R&D department of Cellectis in Paris, France, working on the development and implementation of sequence specific designer nucleases including the transcription activator-like effector nucleases TALEN®. He then joined the Cellectis facility based in

New York, NY, USA, leading projects associated with the development of the T-cell chimeric antigen receptor (CAR) technology.

Fine and predictable tuning of TALEN gene editing targeting for improved T-cell adoptive immunotherapy
Anne-Sophie Gautron[1,3], Alexandre Juillerat[2,3], Valérie Guyot[1], Jean-Marie Filhol[1], Emilie Dessez[1], Aymeric Duclert[1], Philippe Duchateau[1] and Laurent Poirot[1].
[1]Cellectis SA, 8 rue de la croix Jarry, 75013 Paris, FRANCE
[2]Cellectis Inc, 430E, 29th street, NYC, NY 10016, USA
[3]These authors contributed equally to this work.
http://www.sciencedirect.com/science/article/pii/S2162253117302664?via=ihub

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 17 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 market (ticker: CLLS) and on the NYSE Alternext market (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 the Cellectis Group.

For further information, please contact:

Media contacts:
Jennifer Moore, VP of Communications, 917-580-1088, media@cellectis.com
Caitlin Kasunich, KCSA Strategic Communications, 212-896-1241, ckasunich@kcsa.com

IR contact:
Simon Harnest, VP of Corporate Strategy and Finance, 646-385-9008, simon.harnest@cellectis.com

Disclaimer

This press release contains "forward-looking" statements that are based on our management's current expectations and assumptions and on information currently available to management. Forward-looking statements involve known and unknown risks, uncertainties and other factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Further information on the risks factors that may affect company business and financial performance, is included in filings Cellectis makes with the Security Exchange Commission from time to time and its financial reports. Except as required by law, we assume no obligation to update these forward-looking statements publicly, or to update the reasons actual results could differ materially from those anticipated in the forward-looking statements, even if new information becomes available in the future.

###