PRESS RELEASE

Cellectis' Innovation Days event highlighted New Product Development, New Genome Surgery Platform .HEAL, and Manufacturing Capabilities

- *Four new product candidates under pre-clinical development announced; UCART20x22; the first allogeneic bi-specific CAR-T cell targeting B-cell malignancies, and three additional product candidates for solid tumors UCARTMESO (targeting Mesothelin), UCARTMUC1 (targeting Mucin 1)_, UCARTFAP (targeting Cancer Associated Fibroblasts)*

- *.HEAL, Cellectis' proprietary genome surgery HSC platform announced; initiating the Company's venture into new disease targets; Sickle Cell Anemia, Lysosomal storage disease (LSD) and Primary Immunodeficiencies*

- *Cellectis' GMP manufacturing facilities showcase new capabilities including; building more independence from contract manufacturing organizations and gain an increased control over gene and cell therapy process and development*

- *Proprietary integrated gene editing suite with Cellectis' electroporation device PulseAgile and GeneEngine™; expanding its electroporation capabilities*

June 14, 2021 – New York – Cellectis S.A. (NASDAQ: CLLS – EURONEXT GROWTH: ALCLS) (the "Company"), a clinical-stage biotechnological company employing its core proprietary technologies to develop products based on gene-editing with a portfolio of allogeneic chimeric antigen receptor (CAR) T-cells in the field of immuno-oncology and gene-edited hematopoietic stem cells ("HSC") in other therapeutic indications, featured the *Cellectis Innovation Days*, a company event held on May 24-28, virtually. Each episode, ranging from 16 to 48 minutes, provides an inside look into the Company's current and new product candidate pipeline, and manufacturing and technologies.

To watch a replay of all *Cellectis Innovation Days* episodes, click here.

"For the past four years, in addition to the clinical development of UCART22, UCARTCS1 and UCART123, we have been pushing forward the development our new pre-clinical UCART product candidates, venturing for the first time into the solid tumor space. Additionally, we are thrilled to announce Cellectis' .HEAL genome surgery HSC platform, a new arm of Cellectis which focuses on monogenic diseases, like Sickle Cell Anemia. Lastly, we revealed our new in-house GMP manufacturing facilities in France and the United States, and unveiled our ability to move our product candidates from the bench, to bedside, with best-in-class proprietary technologies and techniques. We look forward to disclosing the potential of our newly announced capabilities over the coming years, and presenting upcoming clinical & translational data at future conferences." said Dr. André Choulika, CEO, Cellectis.

Cellectis shared overview of the Company's proprietary and partnered product pipelines

To date, more than 120 patients have been administered allogeneic CAR T cells utilizing technology developed by Cellectis, both in Cellectis-sponsored clinical trials and those of our licensing partners Allogene and Servier.

UCARTCS1 in patients with relapsed/ refractory multiple myeloma (r/r MM)

- MELANI-01 is a phase 1 trial evaluating UCARTCS1 at escalating dose levels in patients with r/r MM.
- Cellectis presented the preliminary translational data from the first group of patients enrolled on the MELANI-01 study at American Society of Gene and Cell Therapy's 24th annual meeting.
- Early preliminary data validates CS1/SLAMF7 as a target for allogeneic CAR-T cells in multiple myeloma. UCARTCS1 expansion and persistence was observed and correlated with anti-myeloma activity, and changes in serum cytokines. The MELANI-01 trial is currently enrolling patients with protocol modifications including restarting at dose level (DL) -1, lower doses of lymphodepletion chemotherapy, which could address lymphopenia as well as result in added expansion; additional requirements for monitoring and management/prophylaxis for opportunistic infections, and cytokine release syndrome (CRS)/ hemophagocytic lymphohistiocytosis (HLH).
- The MELANI-01 clinical study protocol allows for up to 18 patients to enroll in the dose escalation period and 12-30 patients in the dose expansion period of the Phase 1. The MELANI-01 trial is currently enrolling patients at DL -1, the first of 3 planned dose levels .

UCART22 in patients with relapsed or refractory B cell acute lymphoblastic leukemia (r/r B-ALL)

- BALLI-01 is a phase 1 trial evaluating UCART22 at escalating dose levels in patients with r/r B-ALL.
- At the 62nd American Society of Hematology Annual Meeting, in December 2020, gave a first look at the BALLI-Study:
- Early preliminary data on a small number of patients who received UCART22 after fludarabine and cyclophosphamide pre-conditioning support proof of concept for the use of allogeneic CAR-T products targeting UCART22 in this setting.
- UCART22 demonstrated preliminary anti-leukemic activity with no unexpected toxicities in heavily pre-treated patients with ALL, establishingiproof of concept for this product candidate. Importantly, patient T cell recovery happened early in the treatment period, suggesting that the addition of alemtuzumab to the fludarabine and cyclophosphamide lymphodepletion regimen in order to prolong host T-cell suppression should allow for expansion and persistence of UCART22. These cohorts are currently enrolling.
- The BALLI clinical study protocol allows for up to 30patients to enroll in the dose escalation period and 53patients in the dose expansion period of the Phase 1/2a. The BALLI-01 trial is currently enrolling

patients at DL2i in the dose escalation of the FCA lymphodepletion cohort, with at least one additional dose level planned.

UCART123 in patients with relapsed or refractory acute myeloid leukemia (r/r AML)

- AMELI-01 is a phase 1 trial evaluating UCART123 at escalating dose levels in patients with r/r AML.

- Similar to the BALLI-01 trial, AMELI-01 employs a modified toxicity probability interval (mTPI) dose escalation design to evaluate progressive dose levels of UCART123 in concert with fludarabine and cylophosphamide or fludarabine, cyclophosphamide, and alemtuzumab lymphodepletion regimens in patients with r/r AML.

- The AMELI-01 clinical study protocol allows for up to 22 patients to enroll in the dose escalation period and 18-37 patients in the dose expansion period of the Phase 1. The AMELI-01 study is active at DL2i of the FCA lymphodepletion cohort.

Cellectis outlines four new UCART preclinical programs, targeting solid tumors

UCART20x22 ; the first allogeneic dual CAR T-cell candidate product for B-cell malignancies

- A derivative of UCART22, that newly includes an additional CAR targeting CD20.
- An allogeneic dual CART targeting both CD20 and CD22, both of which are highly expressed in B-cell malignancies.
- UCART20x22 adds CD20 CAR to UCART22 to increase breadth of antigen targeting; targeting two antigens simultaneously could lead to increased efficacy.
- Targeting both CD20 and CD22 is more likely to prevent tumor escape and is an alternative to approved autologous CART products targeting CD19.
- UCART20x22 uses TALEN® to disrupt the CD52 and TRAC genes, similar to UCART22 and UCART123 – thus bearing three genetic edits in total.
- Preclinical data show that UCART20x22 is able to kill tumor cells bearing CD20 even in the absence of CD22 antigen.

UCARTMESO for mesothelin-expressing solid tumors

- UCARTMESO is an allogeneic CAR T-cell product candidate targeting mesothelin.
- Mesothelin is a tumor-associated antigen that is highly and consistently expressed in mesothelioma and pancreatic cancer, and is also over-expresed in subsets of other solid tumors (ovarian cancer, non-small cell lung cancer, gastric cancer, triple-negative breast cancer).
- Four gene edits are made: TGFβ receptor (TGFBR2) knockout for resistance to immunosupressive microenvironment; TCR knockout to prevent graft versus host disease; CD52 knockout to confer resistance to a lymphodepleting CD52 monoclonal antibody; and mesothelin CAR lentiviral transduction.
- Preclinical data shows that TGFBR2-edited MESO CAR T-cells, exhibit high anti-tumor activity in vitro and in vivo.
- Targeting TGFβ signaling could be beneficial for multiple solid tumors.

UCARTMUC1 for Mucin 1-expressing epithelial cancers

- UCARTMUC1 is an allogeneic CAR T-cell targeting Mucin 1 for triple negative breast cancer and a variety of epithelial cancers. As other solid tumor targets can be plagued by safety concerns due to off-tumor expression, MUC1 is of high interest as its expression in normal epithelium is restricted to apical membranes. Additionally, its heavy glycosylation in normal tissue renders MUC1 undetectable by Cellectis' MUC1 CAR that only recognizes hypoglycosylated MUC1 present in cancer cells.
- UCARTMUC1 incorporates three TALEN® knockouts (TCR, B2M, and PD-1) with two knockins (IL-12 and HLA-E). In lieu of the deleted beta-2 microglobulin gene (part of MHC-1 complex), Cellectis has inserted the HLA-E gene to cloak the cells from immune detection by NK cells, thus increasing CART persistence.
- In lieu of the PD-1 gene, Cellectis has inserted the IL-12 gene to enhance tumor cell killing and attract other pro-inflammatory cells when induced by the MUC1 CAR binding tumor cells.
- Preclinical data indicates that UCARTMUC1 shows strong intratumoral expansion translating into promising preclinical anti-tumor activity in vivo.

UCARTFAPtargeting Cancer Associated Fibroblasts (CAFs) in the tumor microenvironment

- CAFs secrete a number of factors amounting to physical and chemical barriers preventing T-cell activity; reducing the amount of CAFs, will, in turn reduce the immunosuppressive signals emitted from the tumor and hopefully convert "cold" tumors into "hot" tumors that can then be targeted with checkpoint inhibitor therapy.
- By targeting the cancer-associated fibroblasts, Cellectis aims to erode the physical barrier encasing the tumor microenvironment that prevents T-cell (and CAR T-cell) infiltration into the tumor.
- TCR knocked out to prevent GVHD and beta-2 microglobulin knocked out to provide resistance to the patient's own T-cells.

Investment in GMP manufacturing facilities provides Cellectis with more independence and control over gene and cell therapy process and development and production

- Cellectis' manufacturing facility in Paris is 55,000 square feet and is planned to produce starting materials for manufacturing operations, to make cell banks, plasmids (for both mRNAs and vectors), as well as mRNAs and vectors. Production of key materials started in November 2020.
- Cellectis' GMP manufacturing facility in Raleigh, North Carolina is 82,000 square feet and is planned to include Cellectis' clinical and commercial UCART manufacturing operations.
- Cellectis believes it has the capacity to run 40 lots per year per manufacturing suite, with each lot generating between several dozen to 100+ doses depending on the cells required per patient body weight. Additionally, Cellectis believes it has the capacity to process two separate products simultaneously upon the planned completion of the second suite isolator train installation and qualification by the end of this year. Lastly, the clean core also contains shell space in which two additional suites (and a second supporting fill room) can be constructed, ultimately supporting up to four separate products simultaneously.
- The first UCART training run (from starting cells to vialed drug product) was completed in May 2021, and the facility is expected to be GMP-live by mid-year.

- After engineering runs for two different products, the first GMP clinical material is planned to be manufactured by the end of this year.

Cellectis' proprietary integrated gene editing suite; expanding electroporation capabilities

- Cellectis has its own proprietary gene editing capabilities, as well as an important patent portfolio which has been developed over a 21-year timeframe.
- Cellectis developed its proprietary electroporation device *PulseAgile,* associated reagents, buffers, and the process and electrical wave forms delivered during electroporation. ~96% of double KO was achieved in ~1B T cells in a single electroporation with PulseAgile, with robust yield and batch-to-batch consistency.
- Cellectis' electroporation platform is designed for rapid gene editing delivery optimization for any cell and payload type, especially for gene editing.
- Cellectis expanded its electroporation capabilities with its GeneEngine™, a proprietary versatile and robust closed system device allowing high scalability through repeat electroporations in a single chamber and capable of electroporating ~100 B T cells within 90 minutes.
- Additionally, Cellectis capitalized on its expertise with TALEN® technology (precision, activity and specificity) to develop a C-to-T TALE base editor (i.e. mediating *targeted* C•G to T•A base pair conversion in genomic DNA) showing promise in term of activity as well as specificity within the editing window.

Cellectis reveals .*HEAL*, a genome surgery platform for genetic diseases

.HEAL is a new gene editing platform developed by Cellectis that leverages the power of TALEN® technology, to allow highly efficient gene inactivation, insertion and correction in hematopoietic stem and progenitor cells (HSPCs). Cellectis highlighted programs in sickle cell disease (SCD), lysosomal storage disease (LSD) and primary immunodeficiencies.

.HEAL highlights lead product candidate TALGlobin01, an autologous ex vivo TALEN®-edited CD34+ HSC therapy for the treatment of SCD.

- TalGlobin-01 is developed with TALEN® technology to induce a double DNA strand break at the SCD-causing *HBB* gene and AAV particles containing a DNA repair template designed to correct the faulty HBB gene via endogenous homology directed repair (HDR). Under its current setting, this approach promotes about 60% HDR-mediated *HBB* gene correction and less than 20% of *HBB* gene inactivation in SCD patient HSPCs *in vitro*. This genetic correction has led to a sharp decrease of Sickle Hemoglobin (HbS) frequency from 90% to 20% and an increase of up to 80% of functional hemoglobin frequency after erythroid differentiation of corrected HSPCs *in vitro*.
- *In vivo* preclinical study showed that corrected HSPCs engrafted in the bone marrow of NSG mice and maintained up to 35% of *HBB* gene correction, 16 weeks post transplantation.

Lysosomal storage disorders (LSD)

- Cellectis has developed an artificial exon (ArtEx) strategy to introduce a corrected gene copy coding for the LSD enzyme into the intronic region of a gene expressed in myeloid cells. This approach would

avoid the potential collateral effect of knocking out the endogenous gene without a correct replacement.
- This editing strategy opens new avenues for the treatment of LSDs, as it would allow to address the systemic lack of lysosomal enzyme activity, including in the brain, and could be used to produce virtually any defective LSD enzyme. It represents a new platform, in which a single safe and well characterized TALEN® could be used to treat different LSDs.

RAG1 SCID

- RAG1 is an essential enzyme temporarily expressed in the early development of T and B cells, making traditional gene therapy approaches challenging in terms of spatio-temporal control.
- Cellectis collaborator Pr. Toni Cathomen (University of Freiburg, Germany) has used TALEN® , designed by Cellectis, in HSCs to insert a corrected copy of the gene into the intron 1 of the endogenous RAG1 making the transgene expression under the regulation of the RAG1endogenous promoter. Successful insertion was observed in ~30% of short-term progenitor cells and more importantly in ~20% of long-term progenitor cells. Corrected cells highly expressed RAG1 and the lineage differentiation of the CD34+ cells was not affected.

Hyper IgE syndrome

Still in collaboration with Pr. Toni Cathomen (University of Freiburg, Germany), Cellectis has developed a strategy applicable in HSCs and T-cells, in which a wild type cDNA sequence containing exon 9 to 24 is inserted into an intronic sequence of the STAT3 gene to restore its functionality. STAT3 is a signal transduction molecule that governs the cytokine response to extracellular signals. Mutation of STAT3 leads to Hyper IgE *Syndrome*. The expression level of STAT3 needs to be tightly regulated as two isoforms, STAT3α and STAT3β, that play oncogenic and tumor-suppressing roles, respectively, need to be expressed in certain ratio. This makes traditional gene therapy approaches very challenging. By using TALEN® designed by Cellectis, 70% of gene insertion could be achieved in poc experiments. Importantly, the STAT3α : STAT3β isoform expression ratio was maintained, which is a key step to restore function of STAT3 in patients.

About Cellectis

Cellectis is a gene editing company, developing first of its kind therapeutic products. Cellecties 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 hematopeitic stem cells for various diseases. As a clinical-stage biopharmaceutical company with over 21 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 life-saving 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 hematopeitic stem cells to treat blood disorders, immunodeficiencies and lysosomial 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.
Follow Cellectis on social media: @cellectis, LinkedIn and YouTube.

TALEN® is a registered trademark owned by Cellectis.

For further information, please contact:

Media contacts:
Margaret Gandolfo, Communications Manager, 646-628-0300, Margaret.gandolfo@cellectis.com
Conor McGoldrick, Zeno Group, 914-355-0927, Conor.Mcgoldrick@zenogroup.com

IR contact:
Eric Dutang, Chief Financial Officer, 646-630-1748, eric.dutang@cellectis.com

Disclaimer

This presentation 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 “ “believe,” “expect,” “plan,” “designed to,” “suggest”, “look forward,” “will,” “should,” “would” 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 our research and development projects and priorities, our pre-clinical project development efforts, the timing and progress of clinical trials (including with respect to patient enrollment and follow-up), the timing of our presentation of clinical data, the adequacy of our supply of clinical vials, the timing of completion of construction of our Raleigh, North Carolina manufacturing facility, and operational capabilities at our manufacturing facilities. 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 as well as the duration and severity of the COVID-19 pandemic and governmental and regulatory measures implemented in response to the evolving situation. 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, 2020 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.

###