PRESS RELEASE

Cellectis Presents Clinical Data on AMELI-01 and Preclinical Data on Multiplex Engineering for Superior Generation of CAR T-cells at ASGCT 2023

May 17, 2023 – New York (NY) – 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, today presents clinical data on its Phase 1 AMELI-01 clinical trial (evaluating UCART123) that were unveiled in an oral presentation at the 64th American Society of Hematology (ASH) annual meeting, as well as preclinical data on multiplex engineering for superior generation of CAR T-cells, at the American Society of Gene and Cell Therapy (ASGCT) 2023 Annual Meeting.

Oral presentation:

AMELI-01, a study evaluating UCART123, an allogeneic CAR T-cell product candidate, in relapsed/refractory acute myeloid leukemia (r/r AML)

The oral presentation highlights the following clinical data:

Preliminary Clinical Data from the AMELI-01 Study Presented at ASH 2022

AMELI-01 is a Phase 1 open-label dose-escalation trial evaluating the safety, tolerability, expansion and preliminary activity of UCART123 given at escalating dose levels after lymphodepletion (LD) with either fludarabine and cyclophosphamide (FC) or FC with alemtuzumab (FCA) in patients with relapsed or refractory acute myeloid leukemia (r/r AML).

The oral presentation reviewed preliminary data from patients who received UCART123 at one of the following dose levels: dose level 1 (DL1) $2.5x10^5$ cells/kg; dose level 2 (DL2) $6.25x10^5$ cells/kg; intermediate dose level 2 (DL2i) $1.5x10^6$ cells/kg; or dose level 3 (DL3) $3.30x10^6$ cells/kg after lymphodepletion with FC ([n=8], DL1 – DL3) or FCA ([n=9], DL2 & DL2i).

Preliminary Safety Data

The FCA LD regimen resulted in robust lymphodepletion for greater than 28 days in all patients. Seven out of nine patients demonstrated UCART123 expansion, with maximum concentration (C_{max}) ranging from 13,177 to 330,530 copies/µg DNA, an almost nine-fold increase compared with FC LD, and a significant increase in area under the curve (AUC) (0-28 days) (p=0.04; FC 10.2 vs. FCA 34.9).

Cytokine release syndrome (CRS) occurred in eight patients in the FC arm and nine patients in the FCA arm. In the FC arm, one patient experienced Grade 3 immune effector cell-

associated neurotoxicity syndrome (ICANS) and two patients experienced Grade 4 protocol-defined dose limiting toxicities (DLTs) secondary to CRS. In the FCA arm, two patients experienced Grade 5 DLTs secondary to CRS.

Preliminary Efficacy Data

Evidence of UCART123 anti-tumor activity was observed in four patients out of fifteen at DL2 or above with best overall responses in the FCA arm. Two out of eight patients (25%) at DL2 in the FCA arm achieved meaningful response:

- A patient who failed five prior lines of therapy experienced a durable minimal residual disease (MRD) negative complete response (CR) with full count recovery at Day 56 that continues beyond one year.
- A patient with stable disease achieved greater than 90% bone marrow blast reduction (60% to 5%) at Day 28.

The preliminary data show that adding alemtuzumab to the FC LD regimen was associated with sustained lymphodepletion and significantly higher UCART123 cell expansion, which correlated with improved anti-tumor activity.

Patient Enrollment in a 2-Dose Regimen Arm

Overall, these preliminary data support the continued administration of UCART123 after FCA lymphodepletion in patients with r/r AML. Based on observed UCART123 expansion patterns and cytokine profiles, pursuant to an amended protocol, a second dose of UCART123 is given after 10-14 days to allow for additional UCART123 expansion and clinical activity without the use of additional lymphodepletion. The UCART123 cell expansion from the second dose of UCART123, in the setting of reduced disease burden, is expected to be safe and allow for clearance of residual disease.

“These clinically meaningful preliminary data from the AMELI-01 study are very encouraging for patients and for the future of allogeneic CART-cell therapy. AML is a disease with an urgent need for alternative treatment options for patients, and we are excited to be moving the study forward,” said Dr. Mark Frattini, M.D., Ph.D., Chief Medical Officer at Cellectis. “We have now implemented a two-dose regimen arm for our AMELI-01 trial and we look forward to sharing future updates as they become available.”

Title: AMELI-01: A Phase I Trial of UCART123v1.2, an Anti-CD123 Allogeneic CAR-T Cell Product, in Adult Patients with Relapsed or Refractory (R/R) CD123+ Acute Myeloid Leukemia (AML)

Presenter: Daniel Lee, M.D., Director, Clinical Sciences at Cellectis

Session Date/Time: 5/17/2023 - 3:45 PM – 5:30PM PDT**Session Title:** CAR Engineering and Production Advances for Targeting Hematologic and Solid Tumor Malignancies**Session Room:** 502 AB**Final Abstract Number:** 94

A copy of the ASGCT oral presentation will be available on Cellectis’ website after the presentation: https://www.cellectis.com/en/investors/scientific-presentations/

Poster Presentation:

Expanding the scope of multiplex engineering for superior generation of efficient CAR T-cells

In recent years, advances in genomic-based cellular engineering are bringing us a step closer to conquering solid tumors. This glimpse of success also demonstrated that we need to be able to creatively customize and equip CAR T-cells to target these tumors.

In this presentation, Cellectis shows that we can use the state-of-the-art TALEN® technology to precisely edit up to four loci simultaneously while delivering several additional payloads to increase the efficacy and persistence of CAR T-cells.

The preclinical data demonstrate that multiplexed engineering does not compromise CAR T-cell function, which can even be enhanced and display improved anti-tumor activity. Thus, multiplexed engineering at superior efficiency rates while preserving genomic integrity has the potential to generate highly functional CAR T-cells to advance in the fight against solid tumors.

Cellectis takes it a step further and uses a curated combination of genome engineering technologies including TALE base editors (TALE-BE) to increase the efficiency of multiplexed gene editing while protecting genomic integrity.

“The immunosuppressive barriers of the tumor microenvironment antagonize CAR T-cells and have limited our ability to target solid tumors. These preclinical data show that we can precisely select and combine an array of gene and cell engineering approaches to produce armored CAR T-cells with high efficiency rates. With this strategy, we can focus on unmeet clinical needs and equip CAR T-cells with enhanced activity to help us in our quest to defeat solid tumors” said Beatriz Aranda Orgilles, Ph.D., Team Leader at Cellectis.

<u>The poster presentation at ASGCT highlights the following preclinical data:</u>

- Optimization of delivery timings and selection of compatible TALEN® pairs provides high editing efficiency while attenuating potential TALEN® crosstalk.
- TALEN® and TALE-BE technologies can be integrated in the generation of CAR T-cells to provide high gene editing rates while preserving genomic safety.
- CAR T-cells can be engineered to carry multiple edits and simultaneously exhibit several key features to combat solid tumors: immuno-evasive properties, secretion of the pro-inflammatory cytokine IL-12, resistance to the immunosuppressive pathways PD-1 and TGFB1.
- Multi-equipped CAR T-cells can efficiently target *in vivo* and *in vitro* models of triple negative breast cancer, an aggressive tumor that to date has limited therapeutic possibilities.

Title: Expanding the Scope of Multiplex Engineering for Superior Generation of Efficient CAR T-cells

Presenter: Beatriz Aranda Orgilles, Ph.D., Team Leader at Cellectis

Session Date/Time: 5/17/2023 12:00 PM PDT
Session Title: Wednesday Poster Session
Poster Board Number: 604

Final Abstract Number: 604

Poster of the presentation will be available on Cellectis' website after the presentation: https://www.cellectis.com/en/investors/scientific-presentations/

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 23 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 "anticipate," "believe," "intend", "expect," "plan," "scheduled," "could" 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 advancements, timing and progress of clinical trials, the adequacy and continuity of supply of clinical supply and alemtuzumab, the ability of an anti-CD52 as alemtuzumab to improve any efficacy and the potential benefit of UCART product candidates, the potential of our innovation and 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, 2022 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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