PRESS RELEASE

An Expert Review on Allogeneic CAR-T for Cancer Published in *Nature Reviews Drug Discovery*

Cellectis and World Experts Review New Avenue of Allogeneic CAR T-cells, Optimization and Promises in Oncology

January 6, 2020 – New York (N.Y.) – Cellectis (Euronext Growth: ALCLS; Nasdaq: CLLS), a biopharmaceutical company focused on developing immunotherapies based on gene-edited allogeneic CAR T-cells (UCART), announced today the publication of a review in *Nature Reviews Drug Discovery* by Prof. Stéphane Depil[1*], Dr. Philippe Duchateau[2], Prof. Stephan Grupp[3], Prof. Ghulam Mufti[4] and Dr. Laurent Poirot[2]. The authors review the opportunities and challenges presented by universal allogeneic CAR T-cell therapies.

One of the most promising approaches in cancer treatment is chimeric antigen receptor (CAR) T-cell therapy, in which part of the body's own immunological defendors, T-cells, are redirected against cancerous cells after being engineered to express CARs. Since their initial development in the early 90s, CAR T-cells have evolved through several generations. The use of autologous (patient-derived) CAR T-cells has proven to be successful in treating people with certain blood cancers such as B-cell malignancies. However, autologous CAR T-cell therapy is not suitable for all patients, and it often requires a long and expensive manufacturing process since each treatment must be made individually for each patient.

Cellectis was the first company to develop and test an allogeneic CAR T-cell therapy in patients, where T-cells are derived from healthy donors. This gives rise to off-the-shelf product candidates which aim to be suitable for many patients as opposed to only a single person.

"We realized early on that refined gene-editing techniques were what was needed to take an allogeneic approach to CAR T-cell therapy," said Dr. Laurent Poirot, VP, Immunology Division, Cellectis. "Despite the complexity of this approach, we decided to follow this route because we are confident that it can provide the most impact for a maximum number of people living with severe cancers. This comprehensive review underlines just how much this technology has evolved in very little time. It also gives us exciting areas to explore as we continue to improve our product candidates."

One of the major challenges in the allogeneic approach involves mitigating the risk of graft-versus-host-disease (GvHD) — a medical complication that can present itself in people that have received tissues or cells from another person. The review examines aspects of this challenge and helps weigh the pros and cons associated with the different methods used to create allogeneic CAR T-cells. It also outlines some of the gene-editing work that Cellectis has done in this area along with complementary

approaches being taken by others in the field, such as using cells other than conventional T-cells, also known as alpha beta T-cells.

“Our immune system, including our T-cells, is incredibly sophisticated. We know that T-cells can now be retasked to successfully fight cancer. There are amazing approaches to gene editing that are driving progress towards the most safe and efficacious versions of allogeneic products. It is exciting to see these approaches applied to ‘off the shelf’ CAR T-cell products,” said Prof. Stephan Grupp, Chief of Cell Therapy and Transplant Section at the Children’s Hospital of Philadelphia, Professor of Pediatrics at the Perelman School of Medicine, and a member of Cellectis’ Clinical Advisory Board. “I’m looking forward to seeing emerging clinical data as well as even newer approaches, as Cellectis’ expertise in gene-editing technology continues to transform CAR-T”.

Off-the-shelf’ allogeneic CAR T cells: new development and current challenges

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About Cellectis
Cellectis is developing the first of its kind allogeneic approach for CAR-T therapies, pioneering the concept of off-the-shelf and ready-to-use gene-edited CAR-T cells to treat patients. As a clinical-stage biopharmaceutical company with over 20 years of expertise in gene editing, we are developing game-changer product candidates in immune-oncology. Utilizing TALEN®, our gene editing technology, and PulseAgile, our pioneering electroporation system, we are harnessing the power of the immune system to target and eradicate cancer cells.

As part of our commitment to a cure, Cellectis remains dedicated to its goal of providing life-saving UCART product candidates to address unmet need for multiple cancers including B-cell acute lymphoblastic leukemia (B-ALL), non-Hodgkin lymphoma (NHL) and multiple myeloma (MM). Cellectis is listed on the Nasdaq (ticker: CLLS) and on Euronext Growth (ticker: ALCLS).

Cellectis headquarters are in Paris, France, with additional locations in New York, New York and Raleigh, North Carolina. For more information, visit www.cellectis.com.

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