PRESS RELEASE

Two Issued U.S. Patents Granted to Cellectis for CRISPR Use in T-Cells

February 13, 2018 – New York (N.Y.) – Cellectis (Euronext Growth: ALCLS - Nasdaq: CLLS), a clinical-stage biopharmaceutical company focused on developing immunotherapies based on gene-edited allogeneic CAR T-cells (UCART), announced today the issuance of two U.S. patents - US 9,855,297 and US 9,890,393 - for the invention of certain uses of RNA-guided endonucleases, such as Cas9 or Cpf1, for the genetic engineering of T-cells. The patents came into force on January 2nd, 2018 and February 13th, 2018, respectively.

Both patents claim methods by which T-cells are gene edited using transient expression of CRISPR/Cas9 components. These inventions are based on the early work initiated by inventors at Cellectis when the CRISPR technology first came to light.

These therapeutic-focused patents follow the grant by the European Patent Office of patent No. EP3004337 for similar inventions and previous intellectual property that Cellectis has obtained over the last two decades for major gene editing technologies including meganucleases, TALEN®, MegaTAL and CRISPR.

“Cellectis is a pioneering gene editing company that has always been keen to be at the forefront of all gene editing technologies,” said Dr. André Choulika, Cellectis Chairman & CEO. “We have been the first to explore the potential of CRISPR in its early days in various applications, including therapeutics and plants. These early findings ultimately led to the grant of this set of new patents. As such, these patents only reinforce Cellectis’ leadership position in the gene editing industry.”

Convinced of their strong value for the future development of engineered CAR T-cells, Cellectis will make these patents available for licensing to companies that are willing to use CRISPR technologies in T-cells. The technical knowledge in these patents could, for example, help users engineer allogeneic CAR T-cells while suppressing genes involved in checkpoint inhibitions, such as PD-1, engineer drug resistance, or remove MHC (Major Histocompatibility Complex) related genes. The technology could also be used to insert a DNA CAR construct by gene targeting a specific locus in the genome of T-cells.

The inventors of these patents are Dr. André Choulika, Chairman & CEO of Cellectis and one of the pioneers in the development of nuclease-based genome editing technologies; Dr. Philippe Duchateau, Cellectis Chief Scientific Officer and seasoned gene editing expert; and Dr. Laurent Poirot, Cellectis Head of Early Discovery and expert of gene functions in immune cells.

Claims 1 and 2 of US 9,855,297:

1. A method of preparing genetically modified primary T-cells for immunotherapy comprising the steps of: (a) transfecting mRNA encoding an RNA-guided endonuclease into the primary T-cells, wherein the RNA-guided endonuclease is expressed from the transfected m RNA; (b) introducing a DNA vector that encodes a specific guide RNA, wherein the specific guide RNA directs the RNA-guided endonuclease to at least one targeted locus in the T-cell genome into the primary T-cells; (c) cleaving at least one targeted locus in the T-cell genome with the RNA-guided endonuclease; (d) generating a genetic modification at the site of the cleavage; and (e) expanding the resulting genetically modified T-cells.

2. The method of claim 1, wherein the RNA-guided endonuclease is Cas9.

Claim 1 of US 9,890,393:

1. A method of preparing T-cells for immunotherapy comprising the step of:

(a) genetically modifying primary T-cells by introduction and/or expression into the cells of at least:

- a RNA-guided endonuclease; and

- a specific guide RNA that directs said endonuclease to at least one targeted locus in the T-cell genome,

wherein said RNA-guided endonuclease is expressed from transfected mRNA;

wherein said RNA-guided endonuclease comprises the amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:2; and

(b) expanding the resulting cells.

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 18 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 Euronext Growth (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.

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