December 11, 2022

Graphite Bio Presents Preclinical Data for Novel Sequencing Method Used to Determine Gene Editing Outcomes at 64th ASH Annual Meeting

Single-cell RNA sequencing of reticulocytes will be used to measure gene correction outcomes in sickle cell patients treated with nulabeglogene autogedtemcel (nula-cel)

SOUTH SAN FRANCISCO, Calif.--(BUSINESS WIRE)-- Graphite Bio, Inc. (Nasdaq: GRPH), a clinical-stage, next-generation gene editing company harnessing the power of high-efficiency precision gene repair to develop therapies with the potential to treat or cure serious diseases, today presented preclinical results supporting the use of a single-cell RNA sequencing method to assess gene correction outcomes in patients treated with nulabeglogene autogedtemcel (nula-cel), an investigational gene-edited therapy for sickle cell disease (SCD). The findings are being presented in a poster session at the 64th American Society of Hematology (ASH) Annual Meeting & Exposition taking place virtually and at the Ernest N. Morial Convention Center in New Orleans.

“Our goal is to cure sickle cell disease by directly correcting the underlying disease-causing genetic mutation in order to simultaneously reduce sickle hemoglobin production and restore healthy adult hemoglobin expression, thereby potentially alleviating all complications associated with the disease,” said Josh Lehrer, M.D., M. Phil., chief executive officer of Graphite Bio. “The novel single-cell RNA sequencing method that we developed will help us determine initial gene editing outcomes in patients treated with nula-cel, providing important preliminary information about the potential efficacy of the investigational therapy.”

Graphite Bio’s gene correction approach for SCD involves editing hematopoietic stem cells found in the bone marrow that develop into various types of blood cells such as red blood cells. Since red blood cells lose their nucleus and genomic DNA during maturation, tracking gene editing outcomes in mature red blood cells via nucleic acid sequencing is not possible. However, immature red blood cells called reticulocytes retain RNA that can be sequenced in order to assess gene correction levels.

Based on this knowledge, Graphite Bio scientists sought to develop a single-cell RNA sequencing method that could measure gene editing outcomes in reticulocytes. To establish proof-of-concept and evaluate the accuracy of the method, researchers measured the genetic makeup of reticulocytes from healthy donors (AA), people with sickle cell trait (AS) and those with sickle cell disease (SS), first in a mixture of AA:SS reticulocytes and then in a more complex mixture of AA:AS:SS reticulocytes. Results from both experiments demonstrated the single-cell RNA sequencing method’s ability to precisely and reproducibly measure and differentiate the AA, AS and SS reticulocytes. These data support the use of this method to determine initial gene editing outcomes in patients treated with nula-cel in order to support the clinical development of this investigational therapy.

The poster is now available on the Graphite Bio website here. Details of the poster presentation are as follows:

Poster Session II: 801. Gene Therapies
Poster #3468: Single-Cell RNA Sequencing of Sickle Cell Reticulocytes to Identify Beta-Globin Genotypes and Associated Gene Expression Differences
Presenting Author: Sebastian Treusch, Ph.D., director, genomics, Graphite Bio
Date and Time: Sunday, December 11, 6-8 p.m. CT
Location: Hall D

About nulabeglogene autogedtemcel (nula-cel)

Nula-cel, formerly GPH101, is an investigational gene-edited autologous hematopoietic stem cell (HSC) therapy designed to directly correct the genetic mutation that causes sickle cell disease (SCD). A serious, life-threatening inherited blood disorder, SCD affects approximately 100,000 people in the United States and millions of people around the world, making it one of the most prevalent monogenic blood diseases worldwide. Nula-cel is the first investigational therapy to use a highly differentiated gene correction approach that aims to efficiently and precisely correct the mutation in the beta-globin gene to decrease sickle hemoglobin (HbS) production and restore adult hemoglobin (HbA) expression, thereby potentially curing SCD. The U.S. Food and Drug Administration (FDA) granted Fast Track and Orphan Drug designations to nula-cel for the treatment of SCD.

Graphite Bio is evaluating nula-cel in the CEDAR trial, an open-label, multi-center Phase 1/2 clinical trial designed to assess safety, engraftment success, gene correction rates, total hemoglobin, as well as other clinical and exploratory endpoints and pharmacodynamics in patients with severe SCD.

About Graphite Bio

Graphite Bio is a clinical-stage, next-generation gene editing company driven to discover and develop cures for a wide range of serious and life-threatening diseases. The company is pioneering a precision gene editing approach that has the potential to transform human health by achieving one of medicine's most elusive goals: to precisely "find & replace" any gene in the genome. Graphite Bio's UltraHDR™ gene editing platform takes CRISPR beyond cutting and harnesses the power of high-efficiency precision DNA repair, also known as homology directed repair (HDR), to precisely correct genetic mutations, replace entire disease-causing genes with functional genes or insert new genes into predetermined, safe locations. The company was co-founded by academic pioneers in the fields of gene editing and gene therapy, including Maria Grazia Roncarolo, M.D., and Matthew Porteus, M.D., Ph.D.

Learn more about Graphite Bio by visiting www.graphitebio.com and following the company on LinkedIn and Twitter.

Forward-Looking Statements

Statements we make in this press release may include statements that are not historical facts and are considered forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (the "Securities Act"), and Section 21E of the

Securities Exchange Act of 1934, as amended (the "Exchange Act"). These statements may be identified by words such as "aims," "anticipates," "believes," "could," "estimates," "expects," "forecasts," "goal," "intends," "may," "plans," "possible," "potential," "seeks," "will" and variations of these words or similar expressions that are intended to identify forward-looking statements. Any such statements in this press release that are not statements of historical fact, including statements regarding the clinical and therapeutic potential of our gene editing platform and our product candidates, including nula-cel, and the value of our novel single-cell RNA sequencing method, may be deemed to be forward-looking statements. We intend these forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 27A of the Securities Act and Section 21E of the Exchange Act and are making this statement for purposes of complying with those safe harbor provisions.

Any forward-looking statements in this press release are based on Graphite Bio's current views about our plans, intentions, expectations, strategies and prospects only as of the date of this release and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements, which include, without limitation, the risks concerning Graphite Bio's programs and operations described in our periodic filings with the SEC, including our most recently filed periodic report, and subsequent filings thereafter. Graphite Bio explicitly disclaims any obligation to update any forward-looking statements except to the extent required by law.

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