Poseida Therapeutics to Present New Preclinical Data Supporting Non-Viral Gene Editing with P-KLKB1-101 for the Treatment of Hereditary Angioedema

Data to be highlighted in a Distinguished Industry Oral Abstract presentation at the American College of Allergy, Asthma & Immunology (ACAAI) 2024 Scientific Meeting

SAN DIEGO, Oct. 24, 2024 /PRNewswire/ -- Poseida Therapeutics, Inc. (Nasdaq: PSTX), a clinical-stage allogeneic cell therapy and genetic medicines company advancing differentiated non-viral treatments for patients with cancer, autoimmune, and rare diseases, today announced the upcoming presentation of new preclinical data supporting the potential of P-KLKB1-101, a liver-directed genetic medicine that uses the Company's Cas-CLOVER™ Site-Specific Gene Editing System, for the treatment of patients with hereditary angioedema (HAE). The data showed high-fidelity KLKB1 gene editing for the targeted correction of HAE, the ability for controlled dose response, favorable tolerability and liver editing within the predicted therapeutic range.

"The newest preclinical data for P-KLKB1-101 support our goal to develop a gene editing treatment option for HAE with encouraging early tolerability, safety and efficacy results," said Blair Madison, Ph.D., Chief Scientific Officer, Gene Therapy at Poseida Therapeutics. "We achieved a highly effective, therapeutically relevant reduction of kallikrein in our new humanized pre-clinical mouse model at a low 0.125 mg/kg dose, marking an improvement in our lipid nanoparticle delivery efficiency. These tools could potentially enable therapeutic gene editing in other liver-relevant targets, considering the high fidelity editing of Cas-CLOVER and the promising delivery efficiency we are seeing with our proprietary lipid and LNP in pre-clinical studies."

HAE is a rare inherited disorder characterized by recurrent episodes of fluid accumulation outside of blood vessels, causing rapid swelling of tissues. The swelling is caused by unchecked activation of the kallikrein-bradykinin cascade due to deficiency of the C1 esterase inhibitor, a protein that is involved in regulating vascular permeability and the contact system. Patients with HAE are in need of a durable, effective, and convenient treatment option that eliminates recurrent attacks.

P-KLKB1-101 is a fully non-viral investigational gene editing therapy designed to enable high fidelity editing at the pre-kallikrein gene, or *KLKB1*, for correction of HAE. It utilizes the Cas-CLOVER nuclease, which is engineered for high specificity, to achieve site-specific gene editing.

Key Highlights from P-KLKB1-101 Data to be Presented at ACAAI

- P-KLKB1-101 enabled highly efficient KLKB1 editing and reduction of kallikrein in cultured primary human hepatocytes, with all off-target edits consistently at or below 0.1%, including at high dose levels.
- P-KLKB1-101 yielded controlled, dose-dependent reductions in kallikrein protein levels and activity in a new humanized mouse model. The reduction in plasma kallikrein levels was stable and persisted for at least 180 days (latest time point assessed). In this model, the targeted therapeutic level of KLKB1 editing was achieved with a single dose, and a 58% reduction of kallikrein levels at the minimally effective dose of 0.125 mg/kg.
- Interim non-human primate (NHP) data demonstrate that P-KLKB1-101 had favorable tolerability and achieved liver editing approaching the desired therapeutic range. Ongoing lead optimization of P-KLKB1-101 yielded a 29% increase in potency (as measured by on-target KLKB1 editing) relative to a historical dose-matched benchmark.
- Poseida's novel ionizable lipid and lipid nanoparticle (LNP) enables potent in vivo delivery of P-KLKB1-101 and a controlled dose response.

Presentation Details
The data will be presented on Saturday, October 26 by Dr. Madison at the American College of Allergy, Asthma & Immunology (ACAAI) 2024 Scientific Meeting in Boston:

Title: Highly Specific Non-Viral Gene Editing with P-KLKB1-101 for Hereditary Angioedema
Abstract #: 8063
Session: Distinguished Industry & Late-breaking Oral Abstracts – Session 1
Session Date/Time: Saturday, October 26, 4:30-6:00 p.m. ET (presentation at 5:03 p.m. ET)

About P-KLKB1-101
P-KLKB1-101 is an investigational liver-directed non-viral gene editing approach designed using the Cas-CLOVER™ Site-Specific Gene Editing System, Poseida's proprietary high-fidelity nuclease. P-KLKB1-101 is designed for site-specific gene editing of the KLKB1 gene for the treatment of hereditary angioedema (HAE). This rare inherited disorder results in the swelling of the skin, intestinal tract, and airways, which can be both debilitating and life-threatening. Preclinical data demonstrates therapeutically relevant reduction of pre-kallikrein levels in both mouse and non-human primate models.

About Cas-CLOVER
The Cas-CLOVER™ Site-Specific Gene Editing System employs dual RNA-guided DNA targeting for high fidelity editing. The dual guide RNA targeting provides spatial restrictions on each of two Cas-CLOVER molecules after interacting with specific DNA sequences. This interaction then allows Clo051 cutting at the target site. The result is a highly specific edit by the Cas-CLOVER nuclease, and a low incidence of unwanted off-target edits, with 25-fold greater fidelity than CRISPR/Cas9.

About Poseida Therapeutics, Inc.
Poseida Therapeutics is a clinical-stage biopharmaceutical company advancing differentiated allogeneic cell therapies and genetic medicines with the capacity to cure. The Company's pipeline includes investigational allogeneic CAR-T cell therapies for hematologic cancers, autoimmune diseases, and solid tumors, as well as investigational in vivo genetic medicines that address patient populations with high unmet medical need. The Company's approach is based on its proprietary genetic editing platforms, including its non-viral transposon-based DNA delivery system,

Cas-CLOVER™ Site-Specific Gene Editing System, Booster Molecule and nanoparticle gene delivery technologies, as well as in-house GMP cell therapy manufacturing. The Company has formed strategic collaborations with Roche and Astellas to unlock the promise of cell therapies for cancer patients. Learn more at www.poseida.com and connect with Poseida on X and LinkedIn.

Forward-Looking Statements
Statements contained in this press release regarding matters that are not historical facts are "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Such forward-looking statements include statements regarding, among other things, the potential capabilities and benefits of the Company's technology platforms and product candidates, including P-KLKB1-101; the quote from Dr. Madison; and the Company's plans and strategy with respect to developing its technologies and product candidates. Because such statements are subject to risks and uncertainties, actual results may differ materially from those expressed or implied by such forward-looking statements. These forward-looking statements are based upon the Company's current expectations and involve assumptions that may never materialize or may prove to be incorrect. Actual results could differ materially from those anticipated in such forward-looking statements as a result of various risks and uncertainties, which include, without limitation, the fact that interim data from the Company's preclinical trials may change as more data become available; the Company's reliance on third parties for various aspects of its business; risks and uncertainties associated with development and regulatory approval of novel product candidates in the biopharmaceutical industry; the Company's ability to retain key scientific or management personnel; whether any of the Company's product candidates will be shown to be effective, safe and reliable; and the other risks and uncertainties described in the Risk Factors section of Poseida's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on August 5, 2024, and in other filings Poseida makes with the SEC from time to time. All forward-looking statements contained in this press release speak only as of the date on which they were made. The Company undertakes no obligation to update such statements to reflect events that occur or circumstances that exist after the date on which they were made, except as required by law.

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