4D Molecular Therapeutics Announces First Patient Dosed in Phase 1/2 Clinical Trial of 4D-310 for the Treatment of Fabry Disease

March 9, 2021

EMERYVILLE, Calif., March 09, 2021 (GLOBE NEWSWIRE) -- 4D Molecular Therapeutics (Nasdaq: 4DMT), a clinical-stage gene therapy company harnessing the power of directed evolution for targeted gene therapies, announced that the first patient has been dosed in the Phase 1/2 clinical trial of 4D-310 for the treatment of Fabry disease. Fabry disease is an inherited lysosomal storage disease with high unmet medical need that results from loss of function mutations in the alpha-galactosidase (AGA) enzyme.

“Through our Therapeutic Vector Evolution platform we apply the principles of directed evolution to invent targeted and evolved AAV vectors for the delivery of genes to specific tissue types. Dosing the first patient in the Phase 1/2 clinical trial of 4D-310 marks the third product candidate to be administered to patients, all of which utilize proprietary vectors derived from our Therapeutic Vector Evolution platform,” said David Kirn, MD, chief executive officer, co-founder and president of 4DMT. “4D-310 is designed with the goal of achieving a novel dual mechanism-of-action for these patients. 4D-310 is designed for both stable therapeutic AGA enzyme activity in the blood, as well as for intracellular production within affected tissues, including in cardiac muscle cells.”

“The unmet need for patients with Fabry disease is significant. Current standard of care enzyme replacement therapies are associated with a high-treatment burden, and due to the short half-life in the blood, patients lack therapeutic concentrations of AGA between infusions. Cardiovascular disease is still the leading cause of death in patients despite standard therapy. Gene therapy represents a promising therapeutic modality for patients with Fabry disease because of its potential as a one-time therapy that can deliver stable and sustained levels of AGA activity,” said Dr. Raphael Schiffmann, MD, Senior Vice President & Therapeutic Area Head, Cardiology at 4DMT. “The targeted organ distribution of 4D-310 in Fabry disease makes it likely that this therapy can also potentially treat the cardiomyopathy associated with Fabry disease, a critical disease manifestation that other therapies have been unable to address.”

The Phase 1/2 open-label, dose-exploration and dose-expansion study is expected to enroll up to 18 Fabry disease patients. The study is designed to assess the preliminary safety, tolerability, and maximum-tolerated or maximum-feasible dose of 4D-310. Key secondary endpoints include the assessment of biological activity including AGA enzyme activity and substrate concentrations in the blood over time. The first patient was dosed at University of Pittsburgh Medical Center (UPMC), Children’s Hospital of Pittsburgh under the direction of principal investigator Dr. Jerry Vockley MD, PhD, chief of genomic and genetic medicine.

About Fabry Disease and 4D-310

Affecting more than 50,000 people in the United States and European Union, Fabry disease is a genetic disorder of the *GLA* gene that results in the body’s inability to produce an enzyme called alpha-galactosidase or AGA, causing the accumulation of the substrate globotriaosylceramide-3 (Gb3) in critical organs, including the heart, kidney and blood vessels. Such substrate accumulation can lead to life-threatening hypertrophic cardiomyopathy, heart failure, arrhythmias, various degrees of kidney dysfunction and cerebrovascular stroke. Progression of the disease causes significant reduction in the quality of life and significant economic burden associated with greater patient needs for supportive care.

By using a targeted and evolved vector to deliver a functional copy of the *GLA* gene, we believe 4D-310 has the potential to be a promising treatment of Fabry disease. 4D-310 is administered via IV delivery and is designed to produce both high, stable AGA activity in the bloodstream and to generate AGA activity intracellularly within critical affected organs, including the heart.

About 4DMT

4DMT is a clinical-stage gene therapy company pioneering the development of product candidates using targeted and evolved AAV vectors. 4DMT seeks to unlock the full potential of gene therapy using its platform, Therapeutic Vector Evolution, which combines the power of directed evolution with approximately one billion synthetic capsid sequences to invent evolved vectors for use in targeted gene therapy products. The company is initially focused in three therapeutic areas: ophthalmology, cardiology, and pulmonology. The 4DMT targeted and evolved vectors are invented with the goal of being delivered through clinically routine, well-tolerated and minimally invasive routes of administration, transducing diseased cells in target tissues efficiently, having reduced immunogenicity and, where relevant, having resistance to pre-existing antibodies. 4DMT is currently conducting three clinical trials: 4D-125 is in a Phase 1/2 clinical trial for XLRP, 4D-110 is in a Phase 1 clinical trial for choroideremia and 4D-310 is in a Phase 1/2 clinical trial for Fabry disease.

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Cautionary Note Regarding Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, implied and express statements regarding plans and timelines for the clinical development of 4D-310, including the therapeutic potential and clinical benefits thereof; expectations regarding current and future interactions with the U.S. Food and Drug Administration (FDA); and 4D Molecular Therapeutics' strategy, business plans and focus. The words "may," “might,” "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," “expect,” "estimate," “seek,” "predict," “future,” "project," "potential," "continue," "target" and similar words or expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements in this press release are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this press release, including, without limitation, risks associated with: the impact of COVID-19 on countries or regions in which we have operations or do business, as well as on the timing and anticipated results of our clinical trials, strategy and future operations; the delay of any

current or planned clinical trials or the development of 4D Molecular Therapeutics' drug candidates, the risk that the results of our clinical trials may not be predictive of future results in connection with future clinical trials; 4D Molecular Therapeutics' ability to successfully demonstrate the safety and efficacy of its drug candidates; the timing and outcome of our planned interactions with regulatory authorities; and obtaining, maintaining and protecting our intellectual property. These and other risks and uncertainties are described in greater detail in the section entitled "Risk Factors" in 4D Molecular Therapeutics' Registration Statement on Form S-1 dated December 10, 2020, as well as any subsequent filings with the Securities and Exchange Commission. In addition, any forward-looking statements represent 4D Molecular Therapeutics' views only as of today and should not be relied upon as representing its views as of any subsequent date. 4D Molecular Therapeutics explicitly disclaims any obligation to update any forward-looking statements. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements.

4D-310 is our product candidate in clinical trials and has not yet been approved for marketing by the U.S. Food and Drug Administration. No representation is made as to the safety or effectiveness of 4D-310 for the therapeutic use for which it is being studied.

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