4D Molecular Therapeutics Announces FDA Clearance of IND Application for 4D-710, an A101 Vector-based, Aerosol-delivered Gene Therapy for the Treatment of Cystic Fibrosis Lung Disease

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Initiation of 4D-710 Phase 1/2 clinical trial sites expected before year-end

EMERYVILLE, Calif., Oct. 06, 2021 (GLOBE NEWSWIRE) -- 4D Molecular Therapeutics (Nasdaq: FDMT), a clinical-stage gene therapy company harnessing the power of directed evolution for targeted gene therapies, announced that the U.S. Food and Drug Administration (FDA) has cleared the Investigational New Drug Application (IND) for 4D-710 for the treatment of patients with cystic fibrosis. The active IND enables the initiation of 4D-710 Phase 1/2 clinical study sites, which is expected before year-end.

“4D-710 is an aerosol-delivered gene therapy that has promise as a mutation agnostic treatment for patients with cystic fibrosis lung disease,” said David Kirn, M.D., Co-Founder and Chief Executive Officer of 4DMT. “4D-710 is designed to express high levels of the cystic fibrosis transmembrane conductance regulator (CFTR) protein directly within target cells lining the airway, enabling CFTR mutation-independent activity, and was also invented for resistance to pre-existing antibodies in humans. We plan to focus initially on the approximately 10-15% of all patients whose disease is not amenable to existing modulator medicines that target the CFTR protein. Ultimately, we believe 4D-710 has the potential to treat a broad cystic fibrosis patient population, including those patients treated with current CFTR modulators, all of which require daily dosing over the patient’s lifetime and generally result in only partial correction of lung function.”

“4D-710 is comprised of our targeted and evolved vector, A101, and a *micro*CFTR transgene,” said Robert Fishman, M.D., Chief Medical Officer of 4DMT. “A101 was invented not only for aerosol delivery diffusely throughout the lung airways and alveoli, but also for penetration through the mucus barrier and for resistance to pre-existing antibodies, both of which are potentially key attributes for successful treatment of these patients. 4D-710 has the potential to be a differentiated therapy for the treatment of cystic fibrosis lung disease due to its potentially corrective mechanism, expected ability to treat patients independent of CFTR mutation and resistance to AAV antibodies.”

The Phase 1/2 clinical trial is a multicenter, open-label, dose-escalation and dose-expansion trial of 4D-710 in patients (n=~18) with cystic fibrosis who are ineligible for CFTR modulator therapy or who have discontinued therapy due to adverse effects. The primary endpoint of the study is safety and tolerability. Secondary endpoints include assessments of clinical activity including lung function, plus transgene transfer and *micro*CFTR expression as measured within bronchoscopic biopsies and brushings.

As a result of the IND clearance for 4D-710 and in accordance with the terms of our collaboration with the CF Foundation, CF Foundation will purchase 125,715 shares of our common stock, for aggregate proceeds of approximately $4 million. The proceeds of the CF Foundation equity investment will be used to further support development of 4D-710.

About 4D-710 and Cystic Fibrosis

4D-710 is comprised of our targeted and evolved vector, A101, and a codon-optimized *micro*CFTR transgene. 4D-710 has the potential to treat a broad range of patients with cystic fibrosis lung disease, independent of the specific CFTR mutation, and is designed for efficient aerosol delivery to achieve CFTR expression within lung airway epithelial cells. 4D-710 is being initially developed in the approximately 10-15% of patients whose disease is not amenable to existing medicines targeting the CFTR protein. In patients with CFTR mutations whose disease is amenable to modulator medicines, these modulators do not fully restore normal lung function in most patients. Further, these chronic therapies require daily dosing for the patient’s lifetime. We therefore expect to eventually develop 4D-710 in this broader patient population, as a single agent and/or in combination with these CFTR modulator small molecule medicines.

Cystic fibrosis is the most common life-shortening inherited disease in the United States and results from mutations in the CFTR gene. Cystic fibrosis causes impaired lung function, inflammation and bronchiectasis and is commonly associated with persistent lung infections and repeated exacerbations due to the inability to clear thickened mucus from the lungs. These complications result in progressive loss of lung function and hospitalizations, and ultimately lead to end-stage respiratory failure. According to the CF Foundation, more than 30,000 people in the United States and more than 70,000 people worldwide are living with cystic fibrosis, with approximately 1,000 new cases of cystic fibrosis diagnosed in the United States each year. Patients with cystic fibrosis require lifelong treatment with multiple daily medications. Those with end-stage lung disease may undergo lung transplantation.

About 4DMT

4DMT is a clinical-stage company harnessing the power of directed evolution for targeted gene therapies. 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 advancing five product candidates in clinical development: 4D-310 for Fabry disease, 4D-125 for XLRP, 4D-150 for wet AMD, 4D-710 for cystic fibrosis and 4D-110 for choroideremia.

4D-310, 4D-125, 4D-150, 4D-710 and 4D-110 are our product candidates in clinical development and have not yet been approved for marketing by the U.S. FDA or any other regulatory authority. No representation is made as to the safety or effectiveness of 4D-310, 4D-125, 4D-150, 4D-710 or 4D-110 for the therapeutic use for which they are being studied.

Forward Looking Statements

This press release contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended (Securities Act), and Section 21E of the Securities Exchange Act of 1934, as amended. In some cases, you can identify forward-looking statements by terminology

such as “aim,” “anticipate,” “assume,” “believe,” “contemplate,” “continue,” “could,” “design,” “due,” “estimate,” “expect,” “goal,” “intend,” “may,” “objective,” “plan,” “positioned,” “potential,” “predict,” “seek,” “should,” “target,” “will,” “would” and other similar expressions that are predictions of or indicate future events and future trends, or the negative of these terms or other comparable terminology. All statements other than statements of historical facts contained in this press release are forward-looking statements. These forward-looking statements include, but are not limited to, statements about: 4D-710’s potential as a therapeutic product and the number of patients to enroll in 4D-710’s Phase 1/2 multicenter, open-label, dose-escalation and dose-expansion trial. Forward-looking statements are not guarantees of future performance and are subject to risks and uncertainties that could cause actual results and events to differ materially from those anticipated, including, but not limited to, risks and uncertainties related to: the company’s history of net operating losses and limited operating history; the company’s ability to obtain necessary capital to fund its clinical programs; the risk and uncertainties inherent in the clinical drug development process; the early stages of clinical development of the company’s product candidates and the limited regulatory and clinical experience to date for novel AAV gene therapy product candidates; the effects of COVID-19 or other public health crises on the company’s clinical programs and business operations; the company’s ability to obtain regulatory approval of and successfully commercialize its product candidates; any undesirable side effects or other properties of the company’s product candidates; the company’s reliance on third-party suppliers and other service providers; the outcomes of any current or future collaboration and license agreements; and the company’s ability to adequately maintain intellectual property rights for its product candidates. These and other risks are described in greater detail under the section titled “Risk Factors” contained in the company’s most recent Quarterly Report on Form 10-Q filed as of August 12, 2021, as well as any subsequent filings with the Securities and Exchange Commission. Any forward-looking statements that the company makes in this press release are made pursuant to the Private Securities Litigation Reform Act of 1995, as amended, and speak only as of the date of this press release. Except as required by law, the company undertakes no obligation to publicly update any forward-looking statements, whether as a result of new information, future events or otherwise.

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