4D Molecular Therapeutics Announces First Patient Dosed in Phase 1/2 Clinical Trial of 4D-710, an A101 AAV Vector-based, Aerosol-delivered Genetic Medicine for the Treatment of Cystic Fibrosis

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EMERYVILLE, Calif., April 04, 2022 (GLOBE NEWSWIRE) -- 4D Molecular Therapeutics, Inc. (4DMT) (Nasdaq: FDMT), a clinical-stage biotherapeutics company harnessing the power of directed evolution for targeted genetic medicines, announced that the first patient has been dosed in its Phase 1/2 clinical trial of 4D-710 in patients with cystic fibrosis.

“The dosing of the first patient in the 4D-710 Phase 1/2 clinical trial in cystic fibrosis marks an important milestone for our company and for the patients we aim to benefit,” said Robert Fishman, M.D., Chief Medical Officer and Pulmonology Therapeutic Area Head of 4DMT. “4D-710 utilizes the aerosol-delivered A101 vector developed at 4DMT through our proprietary Therapeutic Vector Evolution platform. To date, our platform has produced five clinical-stage product candidates that incorporate three different proprietary and novel capsids. We are seeking to unlock the full potential of genetic medicines through our platform and to fulfill the promise of transformative biotherapeutics to benefit patients.”

“4D-710 is designed for aerosol delivery to achieve CFTR expression within lung airway epithelial cells,” said Jennifer L. Taylor-Cousar, M.D., M.S.C.S, Professor of Medicine and Pediatrics at National Jewish Health and lead principal investigator for the Phase 1/2 clinical trial. “This therapy has the potential to treat a broad range of people with cystic fibrosis independent of their specific CFTR mutations. It could benefit both people with cystic fibrosis who aren’t able to take CFTR modulators as well as those who have a substantial residual deficit in lung function in spite of modulator therapy.”

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. In the dose-escalation phase, two dose levels of 4D-710 will be examined in a 3+3 design. The primary endpoint of the study is safety and tolerability. Secondary endpoints include assessments of clinical activity including lung function, plus exploratory endpoints on the feasibility of detecting transgene transfer and *micro*CFTR expression as measured in bronchoscopic biopsies and brushings.

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, independent of the specific CFTR mutation, and is designed for 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, the improvement in lung function is variable. We therefore expect to potentially 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 a major inherited disease caused by mutations in the CFTR gene. 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. Cystic fibrosis is a multisystem disorder affecting the lungs, digestive system and reproductive tract. Lung disease is the leading cause of morbidity and mortality. 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. Patients with cystic fibrosis require lifelong treatment with multiple daily medications. These complications result in progressive loss of lung function and hospitalizations, and ultimately lead to end-stage respiratory failure.

About 4DMT

4DMT is a clinical-stage company harnessing the power of directed evolution for targeted genetic medicines. 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 genetic medicine products. The company is initially focused on five clinical-stage products in three therapeutic areas: ophthalmology, cardiology (including Fabry disease) 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. The five 4DMT product candidates in clinical development are: 4D-310 for Fabry disease, 4D-150 for wet AMD, 4D-125 for XLRP, 4D-110 for choroideremia and 4D-710 for cystic fibrosis.

4D-310, 4D-150, 4D-125, 4D-110 and 4D-710 are in clinical trials and have not yet been approved for marketing by the US FDA or any other regulatory authority. No representation is made as to the safety or effectiveness of 4D-310, 4D-150, 4D-125, 4D-110 or 4D-710 for the therapeutic use for which they are being studied. 4D Molecular Therapeutics™, 4DMT™, Therapeutic Vector Evolution™, and the 4DMT logo are trademarks of 4DM.

Cautionary Note Regarding 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, including its potential to effectively treat a broad range of patients with cystic fibrosis

independent of their specific CFTR mutations and the company's plans for developing 4D-710. 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 Annual Report on Form 10-K filed as of March 28, 2022, 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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