4D Molecular Therapeutics Announces Interim Clinical Data from Phase 1/2 Clinical Trial of 4D-710 for Cystic Fibrosis Lung Disease at NACFC 2022

November 3, 2022

- Cohort 1 lung bronchoscopy sample results demonstrate widespread delivery and expression of the 4D-710 CFTRΔR transgene in 100% of samples from all three patients
- Cohort 1 safety and tolerability of 4D-710 demonstrated to date, with no drug-related adverse events following aerosol delivery
- Cohort 1 enrollment completed; Cohort 2 enrollment on-going
- Conference call & webcast to be held today at 1:30 p.m. PT

EMERYVILLE, Calif., Nov. 03, 2022 (GLOBE NEWSWIRE) -- 4D Molecular Therapeutics, Inc. (Nasdaq: FDMT), a clinical-stage biotherapeutics company harnessing the power of directed evolution for targeted genetic medicines, announced that interim clinical data from the Phase 1/2 clinical trial of 4D-710 for cystic fibrosis lung disease were presented at the North American Cystic Fibrosis Conference (NACFC). The presentation focused on safety, tolerability, and delivery and expression of the 4D-710 CFTRΔR transgene in lung tissue samples from patients enrolled in cohort 1 (n=3; 1E15 vg). 4D Molecular Therapeutics will host a conference call today, November 3, 2022, at 1:30 p.m. PT to discuss the interim clinical data.

“We are honored by the selection of our late-breaking clinical data for presentation both in the NACFC symposium today and in the clinical plenary session tomorrow,” said David Kirn, M.D., Co-founder and Chief Executive Officer of 4DMT. “These landmark CFTR expression data were achieved in the CF population with the highest unmet medical need, those who are not eligible for CFTR modulators. These interim results underscore the encouraging potential of 4D-710 for patients with cystic fibrosis lung disease, and the potential of our proprietary A101 vector for other lung diseases. Finally, these results further validate our Therapeutic Vector Evolution platform.”

Dr. Jennifer L. Taylor-Cousar, Professor, Departments of Medicine and Pediatrics, and Co-Director, Adult Cystic Fibrosis Program; Director, Cystic Fibrosis Foundation Therapeutics Development Center, National Jewish Health; and the lead principal investigator on the 4D-710 phase 1/2 clinical trial, presented the clinical data at the NACFC 2022 conference.

Dr. Taylor-Cousar added, “In our Phase 1/2 clinical trial, I’m very encouraged by the robust and widespread transgene expression demonstrated in all three participants’ lungs at this first dose level. The clinical data are the first to date to demonstrate, in the lungs of people with cystic fibrosis, successful delivery and expression of the CFTR transgene after aerosol delivery of a gene therapy. Notably, expression was seen in 100% of lung tissue samples analyzed. Delivery and expression of CFTR represents a critical and successful first step toward achieving our goal of benefiting people with CF who are not eligible for modulator therapy. We look forward to continuing to enroll the study at the next dose level, as well as to additional follow-up with these study participants to assess clinical activity.”

Background

- The 4D-710 product candidate comprises the CFTRΔR transgene and the proprietary targeted and evolved synthetic capsid vector A101 for aerosol delivery.
- A101 was invented at 4DMT through directed evolution (using our Therapeutic Vector Evolution platform) for aerosol delivery throughout the lungs, penetration of the mucus barrier, resistance to pre-existing antibodies in humans, and efficient transduction and transgene expression in lung airway cells.
- The Cohort 1 clinical trial data summarized below are as of the data cutoff date of October 7, 2022.

Cohort 1 Clinical Safety Results

- 4D-710 was well tolerated, with no 4D-710-related adverse events following aerosol delivery.
- The aerosol delivery procedure for 4D-710 was well tolerated. One patient experienced grade 1 dry throat and fatigue during aerosol delivery.

Cohort 1 Clinical Lung Biomarker Results: Assessing Transgene Delivery and Expression

- 4D-710-mediated CFTRΔR transgene delivery and expression were assessed by both endobronchial biopsies and brushings (six locations in total) at week 4 post-treatment.
- Successful widespread delivery and expression of the 4D-710 CFTRΔR transgene was demonstrated.
- All three patients’ lungs demonstrated evidence of CFTRΔR transgene expression.
- *Evidence of 4D-710-mediated CFTRΔR Transgene DNA Delivery:*
  - 100% of endobronchial biopsies from the three patients (5 of 5) were positive.
- *Evidence of 4D-710-mediated CFTRΔR Transgene RNA Expression:*
  - 100% (11 of 11) of endobronchial lung samples from the three patients were positive; these include both positive biopsies (5 of 5) and brushings (6 of 6).
  - All 3 major cell types demonstrated transgene expression: ciliated columnar cells, goblet cells and basal cells.
  - Machine learning driven image analyses estimated that ~40% of bronchial epithelial cells were positive for CFTRΔR RNA by ISH (range 36-47%).

Planned Future Directions for 4D-710 & the A101 Vector

- Cohort 2 enrollment is underway (n=3-6 patients) in this Phase 1/2 trial.
- Patients on trial are being assessed over 12 months after dosing for changes from baseline in spirometry results, including percent predicted FEV1, and quality of life (CFQ-R instrument).
- 4DMT expects to share additional data from this 4D-710 clinical trial in 2023.
- 4DMT is developing preclinical research candidates comprising the A101 vector in the pulmonology therapeutic area.

Conference Call Information

4D Molecular Therapeutics will host a conference call and live webcast on November 3, 2022 at 1:30 .p.m PT. Registration and dial-in for the conference call can be accessed through the 4D Molecular Therapeutics website under Events & Presentations in the Investors section through the following link: https://ir.4dmoleculartherapeutics.com/events. An archived replay of the webcast will be available following the event.

The presentations from NACFC will also be available on the 4D Molecular Therapeutics website under Scientific Presentations: https://4dmoleculartherapeutics.com/technology/scientific-presentations.

About 4D-710 and Cystic Fibrosis

4D-710 is comprised of our targeted and evolved vector, A101, and a codon-optimized CFTRΔR 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 15% of patients whose disease is not amenable to existing CFTR modulator medicines targeting the CFTR protein. In patients with CFTR mutations whose disease is amenable to modulator medicines, the improvement in lung function is incomplete and 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, approximately 40,000 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. The complications of the disease result in progressive loss of lung function and hospitalizations, and ultimately lead to end-stage respiratory failure.

About 4DMT

4DMT is a clinical-stage biotherapeutics company harnessing the power of directed evolution for targeted genetic medicines. 4DMT seeks to unlock the full potential of genetic medicines using its platform, Therapeutic Vector Evolution, which combines the power of directed evolution with approximately one billion synthetic AAV capsid-derived sequences to invent targeted and evolved vectors for use in our products. The company is initially focused on five clinical-stage products in three therapeutic areas for both rare and large market diseases: ophthalmology, cardiology (including Fabry disease) and pulmonology. The 4DMT targeted and evolved vectors are invented with the goal of being delivered at relatively low doses 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-150 for wet AMD and DME, 4D-310 for Fabry disease, 4D-710 for cystic fibrosis, 4D-125 for XLRP and 4D-110 for choroideremia.

4D-150, 4D-310, 4D-710, 4D-125 and 4D-110 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-150, 4D-310, 4D-710, 4D-125, and 4D-110 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; the safety and tolerability of 4D-710; the potential of our proprietary A101 vector for other lung diseases or in the pulmonology therapeutic area generally; expectations regarding the expression of CFTRΔR transgene in patients dosed with 4D-710; expectations related to transgene expression of 4D-710 in the major cell types; the company’s plans for developing 4D-710; anticipated enrolled in cohort 2 of the phase 1/2 trial for 4D-710; and expectations regarding the release of data for the 4D-710 clinical 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 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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