4D Molecular Therapeutics Presents Non-Human Primate Preclinical Data at ASGCT on the 4D-150 Product Candidate for wet AMD and DME

May 12, 2021

- *4D-150 designed as an intravitreal gene therapy with dual transgenes expressing aflibercept and VEGF-C RNAi for the treatment of wet AMD and DME*
- *Preclinical NHP studies of 4D-150 demonstrated significant efficacy in the laser-induced choroidal neovascularization (CNV) model, including complete suppression of CNV lesions at the lowest dose of 1E11 vg /eye*
- *Preclinical acute biodistribution study demonstrated high anti-VEGF levels within the NHP eye with no evidence of uveitis or retinal abnormalities*

EMERYVILLE, Calif., May 12, 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 new preclinical data from non-human primate (NHP) studies of 4D-150, a dual transgene, intravitreal gene therapy inhibiting four distinct VEGF family members for the treatment of wet age-related macular degeneration (wet AMD) and diabetic macular edema (DME).

The data are being presented today in an oral presentation by Peter Francis, M.D., Ph.D., Chief Scientific Officer of 4DMT, at the American Society of Gene and Cell Therapy (ASGCT) 24th Annual Meeting.

Highlights from the oral presentation include:

- For the first time, 4DMT described the design of 4D-150: a dual transgene, intravitreal gene therapy inhibiting four distinct VEGF family members for the treatment of wet AMD and DME. The combination of transgenes independently encoding for VEGF-C RNAi and for aflibercept provides a multi-mechanistic approach to inhibiting angiogenesis.
- In the NHP laser-induced CNV model, a single intravitreal injection of 4D-150 resulted in 100% suppression of CNV lesions 4-weeks after laser administration, the primary endpoint of the study, including at the lowest dose tested of 1E11 vg/eye; no uveitis or retinal abnormalities were reported at this 1E11 vg/eye dose level.
- In an acute biodistribution study of 4D-150 in NHP, a single intravitreal injection resulted in both high levels of ocular aflibercept expression and VEGF-C miRNA expression within the retina at 4 weeks, with no evidence of uveitis or retinal abnormalities observed.
- A single intravitreal injection of a 4D-150 prototype at two dose-levels (1E11 & 1E12 vg/eye) resulted in sustained, durable ocular anti-VEGF expression through 12 months in the NHP laser-induced CNV model.

4D-150 Oral Presentation at the ASGCT 24th Annual Meeting

Title: A Multi-Mechanistic Anti-Angiogenic AAV Gene Therapy Product Candidate, 4D-150, for the Treatment of Wet Age-Related Macular Degeneration (wAMD) and Diabetic Macular Edema (DME): Intravitreal Biodistribution, Transgene Expression, Safety and Efficacy in Non-Human Primates

Session Date/Time: Wednesday May 12, 2021 5:30 PM - 7:15 PM EDT

Session Title: AAV Biology, Engineering, Immunology and Animal Modeling

Abstract number: 64

About wet AMD, DME and 4D-150

Wet AMD is a type of macular degeneration where abnormal blood vessels (CNV) grow into the macula and cause visual distortion and reduced acuity. The proliferation of abnormal blood vessels in the retina is stimulated by VEGF. There are on average 200,000 new incidences of wet AMD per year in the United States alone. High expression levels of VEGF appear to play a causal role in the symptoms of wet AMD.

Diabetic eye disease is a leading cause of vision loss and blindness in working-age adults and often occurs due to the development of DME. The prevalence of DME is high, affecting approximately 1.1 million adults in the United States.

4D-150 is designed as a dual transgene, intravitreal gene therapy inhibiting four distinct VEGF family members to prevent angiogenesis for the treatment of wet AMD and DME. We believe that targeting four distinct angiogenic factors with dual transgenes in patients with these retinal diseases has the potential for greater efficacy and/or lower required doses versus a single anti-VEGF therapy, including in patients with resistance to currently approved anti-VEGF therapies. Intravitreal delivery of biologics to the eye is routine, and therefore would be an advantage for a single dose therapy that could provide long-term efficacy in patients for whom compliance, or treatment resistance, is a problem.

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 conducting three clinical trials: 4D-125 is in a Phase 1/2 clinical trial for XLRP patients, 4D-110 is in a Phase 1 clinical trial for choroideremia patients and 4D-310 is in a Phase 1/2 clinical trial for Fabry disease patients.

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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, 4D-125, 4D-110, 4D-150 and 4D-710, including the therapeutic potential and clinical benefits thereof; whether 4DMT's approach with 4D-150 has the potential for greater efficacy versus a single anti-VEGF therapy, including for patients with resistance to currently approved anti-VEGF therapies; whether intravitreal delivery of biologics to the eye would be an advantage and whether it could provide long-term efficacy in patients for whom compliance, or treatment resistance, is a problem;and 4DMT's 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 4DMT has operations or does business, as well as on the timing and anticipated results of its clinical trials, strategy and future operations; the delay of any current or planned clinical trials for the development of 4DMT's drug candidates, the risk that the results of its clinical trials may not be predictive of future results in connection with future clinical trials; 4DMT's 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 4DMT's most recent Annual Report on Form 10-K that was filed on March 25, 2021, as well as any subsequent filings with the Securities and Exchange Commission. In addition, any forward-looking statements represent 4DMT's' views only as of today and should not be relied upon as representing its views as of any subsequent date. 4DMT 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.

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