4D Molecular Therapeutics Announces FDA Clearance of IND Application for 4D-150, a Dual-Transgene Intravitreal Gene Therapy for Patients with wet AMD

October 6, 2021

Initiation of 4D-150 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-150 for wet age-related macular degeneration (wet AMD). The active IND enables the initiation of 4D-150 Phase 1/2 clinical trial sites, which is expected before year-end.

“4D-150 is a dual-transgene intravitreal gene therapy encompassing the R100 capsid which was invented through Therapeutic Vector Evolution with the goal of robust and safe delivery to all regions and major cell types within the retina at relatively low doses,” said David Kirn, M.D., Co-Founder and Chief Executive Officer of 4DMT. “We believe that 4D-150’s design, which targets four distinct angiogenic factors with dual transgenes, has the potential for broad, robust and durable efficacy after a single low dose intravitreal administration in patients with wet AMD. 4D-150 has the potential to be administered at significantly lower doses compared to other intravitreal AAV gene therapy approaches, and 4D-150 clinical development builds on the favorable tolerability profile to date with the same R100 capsid utilized in our 4D-125 X-linked retinitis pigmentosa (XLRP) program at significantly higher doses. While 4D-125 has been well-tolerated at 1E12 vg/eye, we believe 4D-150 has the potential for clinical activity at substantially lower doses.”

“4D-150 represents numerous firsts in the AAV gene therapy space and underscores 4DMT’s commitment to innovation,” said Peter Francis, M.D., Ph.D., Chief Scientific Officer. “4D-150 is the first R100-based product candidate to enter clinical development in a large market disease. In addition, it is not only the first clinical-stage dual-transgene AAV gene therapy utilizing an evolved vector, but also the first vectorized RNAi AAV gene therapy product candidate utilizing an evolved vector to enter clinical development.”

The Phase 1/2 clinical trial is a dose-escalation and randomized, controlled, masked expansion trial of intravitreal 4D-150 and is expected to enroll approximately 60 adults with wet AMD. In the dose-escalation phase, multiple dose levels of 4D-150 will be examined in an open-label, 3+3 design with an initial dose of 3E10 vg/eye. In dose expansion, patients (n=50) will be randomized 2:2:1 to receive one of 2 dose levels of 4D-150 (n=20 for each dose level) or aflibercept (n=10). The primary endpoints of the study are safety and tolerability. Secondary endpoints include the number of supplemental aflibercept injections received, and change from baseline in best corrected visual acuity (BCVA) over time.

About 4D-150 and wet AMD

4D-150 is a dual-transgene, intravitreal gene therapy designed to inhibit four distinct VEGF factors and prevent angiogenesis and vascular permeability for the treatment of wet AMD. 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 therapies that target a single VEGF factor, including in patients refractory to currently approved anti-VEGF therapies. Intravitreal delivery of biologics to the eye is routine, and a single dose intravitreal gene therapy that could provide long-term efficacy in patients would be an advantage for patients who struggle with treatment burden and/or treatment resistance. 4D-150 builds on the excellent tolerability to date of the R100 capsid in the 4D-125 XLRP clinical program at doses up to 1E12 vg/eye. In the non-human primate retinal laser-induced CNV model data presented in May 2021 at the annual conference of the American Society of Gene and Cell Therapy, at doses ranging from 1E11 to 1E12 vg/eye, 4D-150 intravitreal injection resulted in 100% suppression of grade 4 angiogenic lesions.

Wet AMD is a type of macular degeneration in which abnormal blood vessels grow into the macula and cause visual distortion, reduced acuity and, in some cases, blindness. The proliferation of abnormal blood vessels in the retina is stimulated by VEGF family members. There are approximately 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.

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-150’s potential as a therapeutic product and the number of patients to enroll in 4D-150’s Phase 1/2 dose-escalation and randomized, controlled, masked 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.

Contacts:

Media:

Carolyne Zimmermann
Chief Business Officer
czimmermann@4dmt.com

Investors:

Mike Zanoni
VP, Investor Relations
mzanoni@4dmt.com