4DMT Completes Enrollment of Phase 2 PRISM Clinical Trial for Intravitreal 4D-150 in Patients with Wet AMD and Reports Interim Safety and Tolerability Data

July 17, 2023

- *Completed target enrollment of 50 patients in the randomized Phase 2 Dose Expansion stage of the PRISM clinical trial over approximately two quarters, nearly two quarters ahead of initial projections*
- *No reported treatment-emergent Grade ≥1 inflammatory cells or required deviations from protocol-specified topical corticosteroid taper, and no hypotony or treatment-related serious adverse events with maximum follow-up through 20 weeks (best available data as of July 3, 2023)*
- *Initial interim Phase 2 efficacy data expected to be presented at a medical conference in H1 2024*
- *Expect to provide update regarding Phase 3 pivotal trial plans in Q1 2024 after discussion with FDA in Q4 2023*

EMERYVILLE, Calif., July 17, 2023 (GLOBE NEWSWIRE) -- 4D Molecular Therapeutics (Nasdaq: FDMT, 4DMT, or the Company), a clinical-stage biotherapeutics company harnessing the power of directed evolution for targeted genetic medicines, today announced that it has completed enrollment of the Phase 2 Dose Expansion stage of the PRISM clinical trial for patients with wet age-related macular degeneration (wet AMD) over approximately two quarters, and that no significant 4D-150 safety events or inflammation have been reported to date.

“The rapid enrollment of the Phase 2 Dose Expansion stage of the PRISM trial is indicative of the high demand by wet AMD patients and physicians for a new safe and effective therapy delivered by routine outpatient intravitreal injection with the potential to significantly reduce the need for frequent anti-VEGF injections,” said Robert Kim, M.D., Chief Medical Officer of 4DMT. “We thank the PRISM investigators and patients for their enthusiasm for this important study as we rapidly advance 4D-150 towards the next stage of development.”

The Dose Expansion stage of the PRISM trial is a multicenter, randomized study designed to evaluate the safety and efficacy of 4D-150 at two different dose levels in wet AMD patients with high anti-VEGF need (annualized mean anti-VEGF injection frequency in preceding 12 months was approximately 10). The targeted enrollment of the trial was 50 wet AMD patients randomized 2:2:1 to 3E10 vg/eye or 1E10 vg/eye of 4D-150 or aflibercept. The Best-Corrected Visual Acuity (BCVA) inclusion criteria at baseline for this stage was 34-83 Early Treatment Diabetic Retinopathy Study (ETDRS) letters compared to 25-78 for the Phase 1 Dose Exploration stage.

As of July 3, 2023, for patients enrolled in Dose Expansion with maximum follow-up through 20 weeks, no treatment-emergent Grade ≥1 inflammatory cells or required deviations from the 20-week protocol-specified corticosteroid eyedrop taper were reported. In addition, no hypotony, no vasculitis and no treatment-related serious adverse events were reported.

Initial interim Phase 2 clinical activity data, and further safety data updates, are expected to be reported in H1 2024. We expect to have initial discussions with the FDA on Phase 3 pivotal trial design for 4D-150 for patients with wet AMD in Q4 2023, and we expect to provide an update on pivotal trial plans in Q1 2024.

“We are excited by the rapid pace and completion of enrollment of our Phase 2 PRISM trial driven by strong patient and physician interest,” said David Kirn, M.D., Co-founder and Chief Executive Officer of 4DMT. “We believe it speaks to 4D-150’s clinical differentiation, including its potential as a safe, single-dose, routine, intravitreal injection-based durable therapeutic, its multitargeted mechanism-of-action with inhibition of four VEGF family members, and our strong Phase 1 clinical activity signals reported to date. We believe that 4D-150’s differentiated profile has the potential to also drive rapid enrollment in our DME program, and we expect to enroll our first patient in the Phase 2 SPECTRA trial in Q3 2023. We remain committed to the advancement of our large market ophthalmology product candidates, including 4D-150 for wet AMD and DME as well as 4D-175 for geographic atrophy.”

Data from the Phase 2 PRISM clinical trial are preliminary and will require confirmation from longer follow-up. Preliminary data from 4DMT’s clinical trials that it announces or publishes may change as more patient data becomes available and are subject to audit and verification procedures that could result in material changes in the final data.

About 4D-150 for Wet AMD

4D-150 is comprised of our customized and evolved intravitreal vector, R100, and a transgene payload that expresses both aflibercept and a VEGF-C inhibitory RNAi. This dual transgene payload inhibits 4 angiogenic factors that drive wet AMD and DME: VEGF A, B, C and PIGF. R100 was invented at 4DMT through our proprietary Therapeutic Vector Evolution platform; we created this platform utilizing principles of directed evolution, a Nobel Prize-winning technology. 4D-150 is designed for single, low-dose intravitreal delivery.

About Wet AMD

Wet AMD is a highly prevalent disease with estimated incidence rate of 200,000 new patients per year in the United States. Wet AMD is a type of macular degeneration where abnormal blood vessels (choroidal neovascularization or CNV) grow into the macula, the central area of the retina. As a consequence, CNV causes swelling and edema of the retina, bleeding and scarring, and causes visual distortion and reduced acuity. The proliferation and leakage of abnormal blood vessels is stimulated by VEGF. This process distorts and can potentially destroy central vision and may progress to blindness without treatment.

About 4DMT

4DMT is a clinical-stage biotherapeutics company harnessing the power of directed evolution for genetic medicines targeting large market diseases. 4DMT seeks to unlock the full potential of genetic medicines using its proprietary invention platform, Therapeutic Vector Evolution, which combines the power of the Nobel Prize-winning technology, directed evolution, with approximately one billion synthetic AAV capsid-derived sequences to invent customized and evolved vectors for use in our product candidates. All of our vectors are proprietary to 4DMT and were invented at 4DMT, including the vectors utilized in our clinical-stage and preclinical pipeline product candidates: R100, A101, and C102. The Company is initially focused on five clinical-stage product candidates in three therapeutic areas for both rare and large market diseases: ophthalmology, pulmonology, and cardiology. The 4DMT customized and evolved vectors were 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. 4DMT is currently advancing five product candidates in clinical development: 4D-150 for wet AMD and DME, 4D-710 for cystic fibrosis lung disease, 4D-310 for Fabry disease cardiomyopathy, 4D-125 for XLRP, and 4D-110 for choroideremia. The 4D preclinical product candidates in development are: 4D-175 for geographic atrophy and 4D-725 for AATLD.

4D-150, 4D-710, 4D-310, 4D-125, and 4D-110 are our product candidates in clinical development 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-710, 4D-310, 4D-125, or 4D-110 for the therapeutic uses for which they are being studied.

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 the therapeutic potential, and clinical benefits of 4DMT's product candidates, as well as the plans, announcements and related timing for the clinical development of 4D-150. 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 risks and uncertainties that are described in greater detail in the section entitled "Risk Factors" in 4D Molecular Therapeutics' most recent Quarterly Report on Form 10-Q as well as any subsequent filings with the Securities and Exchange Commission. In addition, any forward-looking statements represent 4D Molecular Therapeutics' views only as of today and should not be relied upon as representing its views as of any subsequent date. 4D Molecular Therapeutics 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.

Contacts:

Media:

Katherine Smith
Evoke Canale
Katherine.Smith@evokegroup.com

Investors:

Julian Pei
Head of Investor Relations and Corporate Communications
Investor.Relations@4DMT.com
267-644-5097