4DMT Announces First Patient Enrolled in 4D-150 Phase 2 SPECTRA Clinical Trial in DME, and Expansion of 4D-150 Phase 2 Stage in PRISM Clinical Trial in Wet AMD

September 7, 2023

- *First patient has been enrolled in the Dose Confirmation stage (n=18) of the Phase 2 SPECTRA clinical trial for intravitreal 4D-150 in patients with diabetic macular edema*
- *First patient enrolled in Population Extension cohort of Phase 2 stage of PRISM clinical trial in wet AMD (n=up to 45) to evaluate intravitreal 4D-150 in patients with lower anti-VEGF need compared with initial cohorts*
- *All PRISM patient cohorts to inform pivotal clinical trial design for 4D-150; FDA feedback on Phase 3 design expected in Q4 2023 with update expected in Q1 2024*
- *Initial interim data for SPECTRA Dose Confirmation and PRISM Population Extension cohort expected in 2024; guidance for randomized Phase 2 stage (n=50) in highest anti-VEGF need patients on-track for H1 2024*

EMERYVILLE, Calif., Sept. 07, 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 the first patient has been enrolled in the Dose Confirmation stage of the Phase 2 SPECTRA clinical trial evaluating intravitreal 4D-150 in patients with diabetic macular edema (DME), and that a Population Extension cohort has been added to the 4D-150 Phase 2 stage of the PRISM Clinical Trial in wet age-related macular degeneration (wet AMD).

“We are delighted to be advancing 4D-150 in our Phase 2 SPECTRA clinical trial in patients with DME, and to further study intravitreal 4D-150 in a broader patient population in wet AMD,” said Robert Kim, M.D., Chief Medical Officer of 4DMT. “DME is a major cause of vision loss among people with diabetes and may lead to blindness. Anti-VEGF agents are considered the mainstay of therapy for DME, yet the treatment burden with the current standard of care remains high. Based on its unique, multitargeted inhibition of four VEGF family members and the favorable clinical profile observed to date in the Phase 1/2 trial in wet AMD, 4D-150 has the potential to provide durable suppression of key pathogenic mediators in DME following a single intravitreal injection that can be administered in-office. In wet AMD, we believe that by expanding the patient population treated with 4D-150, we will further characterize 4D-150 in advance of our planned Phase 3 clinical trials, while taking advantage of strong enrollment momentum at clinical sites to date.”

“The continued rapid advancement of 4D-150 in DME and wet AMD demonstrates our commitment to large-market ophthalmology genetic medicines for patients in need, and shows physicians’ and patients’ interest in the transformative potential of single dose intravitreal 4D-150,” said David Kirn, M.D., Co-founder and Chief Executive Officer of 4DMT. “DME is an important opportunity for 4DMT, and we believe 4D-150’s differentiated profile in wet AMD will drive interest and strong enrollment in the SPECTRA trial. In wet AMD, 4D-150’s promising clinical profile to date in patients with the highest anti-VEGF need has enabled us to expand the PRISM trial to include a broader patient population in the Population Extension cohort. Importantly, we intend to include a broad wet AMD patient population in pivotal Phase 3 clinical trials with 4D-150. We look forward to sharing multiple clinical and regulatory milestones for 4D-150 in 2024.”

Phase 2 SPECTRA Clinical Trial (NCT05930561) for Patients with DME: Trial Design

- Multicenter, randomized, active-controlled, double-masked dose-ranging trial to evaluate the safety and efficacy of intravitreal 4D-150 in adults with DME
- Consists of two stages:
  - Dose Confirmation stage (n=18-24), eligible participants randomized 1:1:1 to receive a single intravitreal injection of 5E9 or 1E10 vg/eye of 4D-150 (initial dose levels) or aflibercept control (n=6 per cohort)
  - Dose Expansion stage (n=54), eligible participants randomized 1:1:1 to receive a single intravitreal injection of 4D-150 at one of two dose levels based on results from Dose Confirmation, or aflibercept control (n=18 per cohort)
- Key enrollment criteria:
  - Adult patients with diabetes mellitus with macular thickening secondary to DME involving the center of the fovea and decreased visual acuity attributable primarily to DME
  - Study enrolls both treatment-naïve and treatment-experienced DME patients
- Key endpoints:
  - Primary endpoint: annualized number of aflibercept injections in study eye
  - Additional endpoints include:
    - Incidence and severity of adverse events
    - Changes from baseline in best-corrected visual acuity (BCVA) and central subfield thickness (CST)
    - Percentage of subjects with a ≥2 and ≥3-Step Diabetic Retinopathy Severity (DRS) improvement from baseline on the Early Treatment Diabetic Retinopathy Study Diabetic Retinopathy Severity Scale (ETDRS-DRSS)

Population Extension Cohort of Phase 2 Stage of PRISM Clinical Trial (NCT05197270) for Patients with Wet AMD

- Open-label evaluating intravitreal 4D-150 3E10 and 1E10 vg/eye dose levels in patients with wet AMD
- Key enrollment criteria:
  - Currently receiving anti-VEGF treatment in the study eye and have demonstrated a clinical response
    - 1-6 anti-VEGF injections in last 12 months, in contrast to initial Phase 1/2 cohorts in which patients required ≥6 anti-VEGF injections in last 12 months
- First patient has been enrolled in this cohort

Expected Upcoming Milestones for 4D-150 for Wet AMD and DME

- PRISM Phase 2 Dose Expansion (n=50) initial interim data expected in H1 2024
- Update regarding Phase 3 pivotal trial plans for wet AMD expected in Q1 2024 following initial discussion with FDA in Q4 2023
- Initial interim data from 4D-150 DME Phase 2 Dose Confirmation stage expected in 2024
- Initial interim data from 4D-150 wet AMD Population Extension cohort expected in 2024

About 4D-150 for Wet AMD and DME

4D-150 comprises our customized and evolved intravitreal vector, R100, and a transgene cassette 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 PlGF. 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 DME

DME is a highly prevalent disease with significant unmet medical need. It is estimated that there are approximately one million individuals with DME in the United States according to published data. DME is characterized by swelling in the macula due to leakage from blood vessels. This can lead to blurred vision. DME is typically treated with intravitreal anti-VEGF agents administered approximately every 4-12 weeks.

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.

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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.

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