4DMT Presents Positive 52-Week Results from Phase 2b Cohort of PRISM Wet AMD Study and Long-term Durability Data Supporting 4D-150 4FRONT Global Registration Program

February 8, 2025

- *3E10 vg/eye achieved an 83% reduction in injection burden vs. projected on-label aflibercept 2 mg Q8W, 70% required 0-1 supplemental injection, and 57% were injection-free through 52 weeks*
- *In the recently diagnosed subgroup, which most resembles the Phase 3 4FRONT-1 and 4FRONT-2 patient populations, 87% required 0-1 supplemental injection and 80% were injection-free through 52 weeks*
- *Durable and stable aflibercept expression demonstrated across all 3E10 vg/eye PRISM cohorts, with up to two years of follow-up*
- *4D-150 continues to be well tolerated, with up to three years of follow-up*
- *4FRONT-1 and 4FRONT-2 are on target to initiate in Q1 and Q3 2025, respectively*
- *Company to host webcast on Monday, February 10, 2025 at 8:00 a.m. ET*

EMERYVILLE, Calif., Feb. 08, 2025 (GLOBE NEWSWIRE) -- 4D Molecular Therapeutics (Nasdaq: FDMT; 4DMT or the Company), a leading clinical-stage company focused on unlocking the full potential of genetic medicines to treat large market diseases, today announced positive initial interim 52-week data from the Phase 2b Population Extension cohort of the PRISM clinical trial evaluating 4D-150 in a broad wet age-related macular degeneration (wet AMD) patient population. Additional data were provided on the durability of aflibercept expression for up to two years. The data were presented by Dante Pieramici, M.D., in an oral presentation titled “Phase 2b Population Extension Cohort Evaluating 4D-150 in Neovascular Age-Related Macular Degeneration: 52-Week Results” at Angiogenesis, Exudation, and Degeneration 2025.

“We believe 4D-150 has paradigm-shifting potential. 4D-150 is designed to achieve favorable tolerability and robust and durable multi-year efficacy following routine intravitreal administration that enables seamless integration into retina clinics,” said David Kirn, M.D., Co-founder and Chief Executive Officer of 4DMT. “The data from the PRISM clinical trial, which evaluated wet AMD patients with a broad range of disease severity and duration, and the initial data from SPECTRA in diabetic macular edema (DME), demonstrate 4D-150’s potential to become the first backbone therapy forming the foundation for the treatment of vascular retinal diseases. The ability to deliver disease control with long-lasting freedom from frequent bolus injections addresses the primary unmet need for patients and physicians.”

Topline 52-Week Efficacy Results for 4D-150 3E10 vg/eye (Planned Phase 3 Dose) from Phase 2b Population Extension Cohort of PRISM (Data Cut-Off January 15, 2025):

- **Phase 2b (n=30): Broad Wet AMD Disease Activity**
  - Supplemental aflibercept injections:
    - 83% reduction, representing 0.97 mean supplemental injections per patient over 52-weeks vs. 6.0 injections projected with on-label aflibercept 2 mg Q8W
    - 70% 0-1 injection
    - 57% injection-free
  - Improved and maintained best corrected visual acuity (BCVA) of +2.2 letters
  - Durable central subfield thickness (CST) improvement with fewer fluctuations, as measured by optical coherence tomography (OCT), of -11 µm; -13 µm in supplemental injection-free patients
- **Phase 2b (n=15): Recently Diagnosed Subgroup**
  - Supplemental aflibercept injections:
    - 94% reduction, representing 0.33 mean supplemental injections per patient over 52-weeks vs. 6.0 injections projected with on-label aflibercept 2 mg Q8W
    - 87% 0-1 injection
    - 80% injection-free
  - Improved and maintained BCVA of +3.1 letters
  - Durable CST improvement with fewer fluctuations, as measured by OCT, of -10 µm; -20 µm in supplemental injection-free patients

4D-150 Safety Update from PRISM (Data Cut-Off January 15, 2025):

- 4D-150 continues to be well tolerated during up to three years of follow up in all patients treated with 3E10 vg/eye
  - 2.8% (2 of 71) had 4D-150–related 1+ intraocular inflammation (IOI) (SUN/NEI scales), which were transient 1+ vitreous cells noted at a single timepoint, as previously reported
  - 99% (70 of 71) completed steroid prophylaxis taper on schedule
  - 99% (70 of 71) remained completely off steroids
- No 4D-150–related hypotony, endophthalmitis, vasculitis, occlusive/non-occlusive retinal vasculitis, or choroidal effusions observed to date

"The promise of 4D-150 for both patients and clinicians lies in its potential to tackle one of the most pressing unmet needs in vascular retinal diseases —providing a long-lasting, effective treatment option that reduces the frequent burden of bolus anti-VEGF injections," said Dante Pieramici, M.D., a principal investigator of the PRISM study and member of the 4DMT Ophthalmology Advisory Board. "4D-150 offers a profound shift in how we manage our patients' care, potentially freeing them from the ongoing challenges of injection frequency while ensuring they maintain the vision improvement characteristic of current standard of care. The data from the PRISM study gives me great hope that 4D-150 can become the backbone of future retinal treatments for wet AMD, offering both clinical benefit and better quality of life for our patients."

PRISM Durability Update from All 3E10 vg/eye Cohorts

- Aqueous humor concentrations were studied serially every three months
- Durable and stable aflibercept expression demonstrated, with up to two years of follow-up, with aqueous humor concentrations consistently within projected therapeutic range

4D-150 Program Milestones

- 4FRONT-1 and 4FRONT-2 expected to initiate in Q1 and Q3 2025, respectively
- Two-year Phase 1/2a and 18-month Phase 2b PRISM data expected in Q4 2025
- Primary endpoint 52-week topline data from both 4FRONT-1 and 4FRONT-2 expected in H2 2027

Corporate Webcast Details

Title: 4D-150 in Broad Wet AMD Population: Interim 52-week Data from Phase 2b & Program Durability Update for 3E10 vg/eye (Phase 3 Dose)
Date/Time: Monday, February 10, 2025, at 8:00 a.m. ET
Registration: Link

An archived copy of the webcast will be available for up to one year by visiting the "Investors & Media" section of the 4DMT website: https://ir.4dmoleculartherapeutics.com/events.

The presentation from Angiogenesis, Exudation, and Degeneration 2025 will also be available on the 4DMT website: https://4dmoleculartherapeutics.com/pipeline/#posters-and-publications

About 4D-150
4D-150 is a potential backbone therapy that is designed to provide multi-year sustained delivery of anti-VEGF (aflibercept and anti-VEGF-C) from the retina with a single, safe, intravitreal injection. 4D-150 utilizes our customized and evolved intravitreal vector, R100, which was invented at 4DMT through our proprietary Therapeutic Vector Evolution platform. 4D-150 is being developed for wet AMD and DME, which both affect millions of patients globally, with the goal of freeing patients from burdensome injections while preserving vision.

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. It is estimated that the total prevalence of wet AMD in certain major markets, including the United States and the European Union, and Japan, will be greater than 4 million individuals in the next five years. Wet AMD is a type of macular degeneration in which abnormal blood vessels (macular neovascularization or MNV) grow into the macula, the central area of the retina. As a consequence, MNV causes swelling and edema of the retina, bleeding, and scarring, and causes visual distortion and reduced visual 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 late-stage biotechnology company focused on unlocking the full potential of genetic medicines to treat large market diseases in ophthalmology and pulmonology. 4DMT's proprietary invention platform, Therapeutic Vector Evolution, combines the power of directed evolution with approximately one billion synthetic AAV capsid-derived sequences to invent customized and evolved vectors for use in our wholly owned and partnered product candidates. Our lead program, 4D-150, is a potential backbone therapy that is designed to provide multi-year sustained delivery of anti-VEGF (aflibercept and anti-VEGF-C) targeted to the retina with a single, safe, intravitreal injection. Our second core program is 4D-710, which is the first known genetic medicine to demonstrate, in the lungs of people with cystic fibrosis (CF), successful delivery and expression of the CFTR transgene and initial clinical activity signals after aerosol delivery of a gene therapy. 4D Molecular Therapeutics™, 4DMT™, Therapeutic Vector Evolution™, and the 4DMT logo are trademarks of 4DMT.

All of our product candidates are in clinical or preclinical development and have not yet been approved for marketing by the FDA or any other regulatory authority. No representation is made as to the safety or effectiveness of our product candidates for the therapeutic uses for which they are being studied.

Learn more at www.4DMT.com and follow us on LinkedIn.

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 and market potential of 4DMT's product candidates, including 4D-150, as well as the plans, announcements, and related timing for the clinical development of and regulatory interactions regarding 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 filed on November 13, 2024 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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