4DMT Advances 4D-150 into Phase 3 for Second Large Market Retina Indication with Initiation of 4SIGHT in DME

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- *4D-150 is advancing into Phase 3 development for DME, a second multi-billion-dollar retinal disease market with significant unmet need*
- *First patients have been enrolled in 4SIGHT global Phase 3 trial (N=514) evaluating 4D-150 in a treatment-naïve DME population*
- *Updated 2-year data from SPECTRA Part 1 clinical trial in DME continue to demonstrate a favorable safety profile, durable vision and anatomic improvements and clinically meaningful treatment burden reduction*

EMERYVILLE, Calif., Sept. 28, 2026 (GLOBE NEWSWIRE) -- 4D Molecular Therapeutics (Nasdaq: FDMT; 4DMT or the Company), a leading late-stage biotechnology company advancing durable and disease-targeted therapeutics with potential to transform treatment paradigms and provide unprecedented benefits to patients, today announced that the first patients have been enrolled across multiple sites in the 4SIGHT Phase 3 clinical trial evaluating 4D-150 for the treatment of diabetic macular edema (DME). The Company also reported 2-year data from the SPECTRA clinical trial.

“The initiation of 4SIGHT marks an important step in advancing 4D-150 toward becoming a continuous backbone therapy for sustained control of major VEGF-driven retinal diseases,” said David Kirn, M.D., Co-founder, President and Chief Executive Officer of 4DMT. “The favorable safety profile, durable vision and anatomic improvements and clinically meaningful treatment burden reduction observed through two years in the SPECTRA Part 1 clinical trial in DME strengthen our confidence as we expand 4D-150 into the 4SIGHT Phase 3 trial in DME. Following enrollment completion of our two 4FRONT Phase 3 trials in wet AMD, 4SIGHT for DME represents our second Phase 3 program.”

4SIGHT: Phase 3 Trial Design and Regulatory Pathway

4SIGHT is a global Phase 3 multicenter, randomized, double-masked, aflibercept 2 mg (Q8W) comparator-controlled trial of intravitreal 4D-150 in treatment-naïve patients with DME (N=514). All patients will receive five aflibercept loading doses. The primary endpoint is non-inferiority in the mean change from baseline in best corrected visual acuity (BCVA) at Week 52. The key secondary endpoints are treatment burden reduction, comparing the number of aflibercept injections received in the 4D-150 arm versus the aflibercept comparator arm through Week 52, and the proportion of participants with a ≥2-step improvement from baseline in Early Treatment Diabetic Retinopathy Study Diabetic Retinopathy Severity Scale (ETDRS-DRSS) at Week 52. Patients in both arms will be eligible for supplemental aflibercept injections.

Similarly to the 4FRONT Phase 3 wet AMD trials, randomization requires on-trial demonstration of aflibercept responsiveness following the first three of five loading doses during the run-in period (central subfield thickness (CST) ≥10% reduction and ≤400 µm or CST <315 µm).

4D-150 for DME has U.S. Food and Drug Administration (FDA) Regenerative Medicine Advanced Therapy designation, and the Company has alignment with the FDA and the European Medicines Agency on potential Biologics License Application and marketing authorization application filings with the single 4SIGHT Phase 3 DME trial, based on data generated to date for 4D-150 in both the SPECTRA and PRISM clinical trials combined with data from the two Phase 3 clinical trials in the 4FRONT wet AMD program.

“Having treated patients across multiple retinal gene therapy programs over the past decade, including treating the first human patient with 4D-150 nearly five years ago and now enrolling the first patient in 4SIGHT, I believe the initiation of 4SIGHT represents an important milestone for our field,” said Arshad M. Khanani, M.D., M.A., FASRS, Director of Clinical Research at Sierra Eye Associates, Clinical Professor at the University of Nevada, Reno School of Medicine, and Chair of the 4DMT Retina Advisory Board. “In real-world practice, many patients with DME struggle to adhere to the frequent anti-VEGF injection schedule because of the substantial treatment burden and the need for numerous other physician visits, which may contribute to suboptimal visual outcomes. Based on the 2-year data from the SPECTRA trial, I believe a single in-office injection of 4D-150 has the potential to transform the treatment paradigm for DME by providing sustained disease control while reducing treatment burden.”

2-Year Results from SPECTRA Clinical Trial (Data Cutoff of March 12, 2026):

- Safety Results (N=22):
  - 4D-150 was well tolerated, with no intraocular inflammation at any timepoint
  - No ocular serious adverse events
  - No hypotony, endophthalmitis, vasculitis, choroidal effusions or retinal artery occlusions
  - No progression to proliferative diabetic retinopathy or vitreous hemorrhage
- Clinical Activity Results for Phase 3 Dose (3E10 vg/eye, n=9):
  - Mean gain in BCVA of +10.8 letters
  - Mean reduction in CST of -176 µm, as measured by optical coherence tomography
  - Supplemental Injections:
    - Utilized stringent supplemental criteria to maximize patient safety while assessing initial clinical activity
    - Post-aflibercept loading doses (3), patients required substantially fewer injections compared to on-label aflibercept 2mg Q8W:
      - 61% overall treatment burden reduction (5.2 mean supplemental injections per patient vs. 13.0 injections projected with on-label aflibercept 2 mg Q8W)
      - 75% estimated overall treatment burden reduction utilizing 4SIGHT Phase 3 supplemental injection criteria, which

are more in line with contemporary Phase 3 trials (3.2 estimated mean supplemental injections per patient vs. 13.0 injections projected with on-label aflibercept 2 mg Q8W; retrospective estimate, actual results in 4SIGHT may differ)

- 2 of 9 (22%) remained injection-free

Additional details on the SPECTRA data and 4SIGHT clinical trial design can be found in our corporate deck on our Investor Relations website.

About 4D-150

4D-150 is a potential continuous backbone therapy designed to provide multi-year, and potentially lifelong, sustained delivery of anti-VEGF biologics (aflibercept and anti-VEGF-C) within the retina following a single intravitreal injection. 4D-150 utilizes our customized and primate-evolved intravitreal AAV vector (R100), which was invented at 4DMT through our proprietary Therapeutic Vector Evolution platform, as well as a proprietary transgene payload designed for robust aflibercept expression plus an anti-VEGF-C inhibitory RNA. 4D-150 is being developed for wet age-related macular degeneration (wet AMD) and diabetic macular edema (DME), which each affect millions of patients globally, with the goal of freeing patients from burdensome injections while preserving vision.

About DME

DME, or diabetic macular edema, is a complication of diabetic retinopathy and is a highly prevalent disease with significant unmet medical need and poor treatment adherence. It is estimated that there are approximately one million individuals with DME in the U.S., according to published data. DME is characterized by inflammation and swelling in the macula due to leakage from blood vessels, which can lead to vision loss. DME is typically treated with intravitreal anti-VEGF agents administered approximately every 4-12 weeks, although patient compliance with therapy is poor and results in high unmet medical need.

About 4DMT

4DMT is a leading late-stage biotechnology company advancing durable and disease-targeted therapeutics with potential to transform treatment paradigms and provide unprecedented benefits to patients. The Company's lead product candidate, 4D-150, is designed to be a backbone therapy forming the foundation of treatment of blinding retinal vascular diseases by providing multi-year sustained delivery of anti-VEGF biologics (aflibercept and anti-VEGF-C) with a single intravitreal injection, which substantially reduces the treatment burden associated with current bolus injections. The Company's lead indication for 4D-150 is wet age-related macular degeneration and the second indication is diabetic macular edema, which are both in Phase 3 development. The Company's second product candidate is 4D-710, which is the first known genetic medicine to demonstrate successful delivery and expression of the CFTR transgene in the lungs of people with cystic fibrosis after aerosol delivery. 4D Molecular Therapeutics™, 4DMT™ Therapeutic Vector Evolution™, Backbone 4 Retina™ 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 U.S. Food and Drug Administration 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, treatment-burden reduction, durability and clinical benefits of, the potential market for, as well as the plans, announcements and related timing for the clinical development, regulatory interactions, and potential commercialization of our product candidates, including 4D-150. The words "may," "might," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "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:
Jenn Gordon
dna Communications
Media@4DMT.com

Investors:
Julian Pei
Head of Investor Relations and Strategic Finance
Investor.Relations@4DMT.com