4DMT Presents Positive 60-Week Results from 4D-150 SPECTRA Clinical Trial in DME and Regulatory Update

July 31, 2025

- *4D-150 continues to be well tolerated with no intraocular inflammation observed at any timepoint or dose level*
- *4D-150 demonstrated durable and dose-dependent clinical activity with sustained gains in visual acuity and anatomic control*
- *Phase 3 dose (3E10 vg/eye) achieved clinically meaningful 78% reduction in treatment burden vs. projected on-label aflibercept 2mg Q8W*
- *EMA aligned with proposed single Phase 3 clinical trial being acceptable for regulatory submission for 4D-150 in DME, consistent with previously announced alignment with FDA*

EMERYVILLE, Calif., July 31, 2025 (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 positive results from the SPECTRA clinical trial evaluating 4D-150 in patients with diabetic macular edema (DME), and alignment with the European Medicines Agency (EMA) on a registrational pathway for 4D-150 in DME. The data, which included both the 52-week primary endpoint and 60-week analyses, were presented by David Almeida, M.D., MBA, Ph.D., Erie Retina Research in an oral presentation titled “Interim Results from the SPECTRA Phase 2a Clinical Trial Evaluating Intravitreal 4D-150 in Adults with Diabetic Macular Edema” at the 43rd Annual American Society of Retina Specialists (ASRS) Scientific Meeting.

“The positive results from the SPECTRA trial demonstrate the tolerability and consistent, durable clinical activity of 4D-150 in DME, highlighting the potential for the product candidate to become a backbone therapy that can dramatically reduce treatment burden compared to the labeled regimen of standard-of-care aflibercept 2mg every eight weeks,” said David Almeida, M.D., MBA, Ph.D. “4D-150 has the potential to fundamentally transform the treatment of DME by reducing treatment burden with a product that has adherence by design, while providing meaningful, lasting vision improvement. This is especially important in DME, which frequently occurs in a working-age population.”

Clinical Trial Design & Interim Data from 4D-150 SPECTRA Clinical Trial (Data Cutoff of May 2, 2025):

- Objectives: Evaluate safety and tolerability, and identify dose level for further evaluation
- Study Population:
  - Enrolled patients with high disease activity as measured by central subfield thickness (CST)
  - 22 patients enrolled across 3 dose levels:
    - 3E10 vg/eye (n=9) (Phase 3 dose)
    - Lower doses (1E10 vg/eye, n=12; 5E9 vg/eye, n=1)
      - 2 patients dosed with 1E10 vg/eye missed >50% of study visits and were considered not evaluable for injection burden or other efficacy parameters
- Safety Results Through 60 Weeks (n=22):
  - 4D-150 was well tolerated with no intraocular inflammation at any timepoint
    - No subjects required modification to the topical corticosteroid regimen, and all patients are currently off corticosteroids
  - No hypotony, endophthalmitis, vasculitis, choroidal effusions or retinal artery occlusions were reported
  - Mean intraocular pressure was within normal limits
- Efficacy Results Through 60 Weeks:
  - Utilized stringent supplemental aflibercept criteria to maximize patient safety while assessing initial clinical activity
  - Phase 3 Dose:
    - Sustained gain of best corrected visual acuity (BCVA) of +9.7 letters
    - Sustained improvement in anatomic control, with reduction of CST, as measured by optical coherence tomography (OCT), of -174 µm
  - Supplemental Injections: Post-aflibercept loading doses (3), patients treated with Phase 3 dose required substantially fewer supplemental injections compared to patients receiving lower doses or projected on-label aflibercept 2mg Q8W (expected Phase 3 comparator):
    - Mean supplemental injections per patient:
      - Phase 3 dose: 1.6
      - Lower doses: 3.7
      - Projected on-label aflibercept 2mg Q8W: 7.0
      - Dose response observed for Phase 3 dose vs. lower doses (58% fewer injections)
      - Phase 3 dose demonstrated a reduction of 78% vs. projected on-label aflibercept 2mg Q8W
    - 0-1 injections:
      - 5 of 9 overall (Phase 3 dose) vs. 2 of 11 (lower doses)
    - Injection-free:
      - 4 of 9 overall (Phase 3 dose) vs. 1 of 11 overall (lower doses)

4D-150 DME Phase 3 Regulatory Update

- Following U.S. Food and Drug Administration (FDA) alignment, as communicated in January 2025, EMA is also aligned that a single Phase 3 clinical trial, based on data generated to date for 4D-150 in both the SPECTRA and PRISM clinical trials combined with data from the two planned Phase 3 clinical trials in the 4FRONT wet age-related macular degeneration (wet AMD) program, would be acceptable as the basis for a marketing authorization application (MAA) submission for 4D-150 in DME

"The consistency of dose response, safety and efficacy data we've seen with 4D-150 across all patients evaluated in both DME and wet AMD reinforces our belief that 4D-150 has the potential to become a true backbone therapy, and may significantly improve the lives of millions of patients living with retinal vascular disease," said David Kirn, M.D., Co-founder and Chief Executive Officer of 4DMT. "With alignment from both FDA and EMA for a single Phase 3 DME trial to complement the 4FRONT wet AMD program, we believe we have a clear streamlined path to bring 4D-150 to patients with high unmet need in two of the most prevalent blinding retinal vascular diseases."

About 4D-150

4D-150 is an investigational agent with the potential to become a 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 the Company's customized and evolved intravitreal vector, R100, which was invented at 4DMT through the Company's 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 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 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 (aflibercept and anti-VEGF-C) with a single, safe, 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, which is currently in Phase 3 development, and second indication is diabetic macular edema. 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™, and the 4DMT logo are trademarks of 4DMT.

All of the Company's 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 the Company's 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 development plans for 4D-150 and interactions with FDA and EMA. 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 May 8, 2025 as well as any subsequent filings with the Securities and Exchange Commission. In addition, any forward-looking statements represent 4D Molecular Therapeutics' current views and should not be relied upon as representing its views as of any subsequent time. 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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