4DMT Announces Positive Interim Data from 4D-150 SPECTRA Clinical Trial in DME and Alignment with FDA on Registrational Path

January 10, 2025

- *Across all DME patients dosed to date, 4D-150 continues to be well tolerated with no intraocular inflammation observed at any timepoint or dose level*
- *3E10 vg/eye demonstrated strong signals of clinical activity with sustained gain of BCVA of +8.4 letters and reduction of CST of -194 µm from baseline through Week 32*
- *3E10 vg/eye achieved an 86% reduction in injection burden vs. projected on-label aflibercept 2mg Q8W and dose response with 61% reduction vs. 1E10 vg/eye, with 0.6 mean supplemental injections per patient through Week 32*
- *FDA aligned with proposed single Phase 3 clinical trial being acceptable for the basis of a BLA submission for 4D-150 in DME, based on review of data from SPECTRA and PRISM (wet AMD) clinical trials to date and planned global Phase 3 clinical development program for wet AMD*

EMERYVILLE, Calif., Jan. 10, 2025 (GLOBE NEWSWIRE) -- 4D Molecular Therapeutics (Nasdaq: FDMT, 4DMT or the Company), a leading clinical-stage genetic medicines company focused on unlocking the full potential of genetic medicines to treat large market diseases, today announced positive topline interim data from Part 1 of the SPECTRA clinical trial evaluating 4D-150 in diabetic macular edema (DME) and alignment with the U.S. Food and Drug Administration (FDA) on registrational pathway for 4D-150 in DME.

“The promising initial safety and clinical activity data of 4D-150 in DME patients, together with the promising results in wet age-related macular degeneration (wet AMD), reinforces the potential applicability of 4D-150 across multiple VEGF-driven retinal diseases,” said Carlos Quezada-Ruiz, M.D., FASRS, SVP, Therapeutic Area Head, Ophthalmology. “4D-150 represents a potentially transformative new therapeutic option for the approximately one million DME patients in the U.S. alone. 4D-150 has the potential to set a new backbone therapy providing multi-year sustained VEGF inhibition in the retina with a single, safe, intravitreal injection. If approved, 4D-150 could significantly reduce the need for frequent bolus injections and address the current real-world challenge of patient adherence to therapy, thereby leading to better disease management and vision outcomes.”

Clinical Trial Design & Interim Data from 4D-150 SPECTRA Part 1 Clinical Trial (Data Cutoff of December 13, 2024):

- Objectives: Evaluate safety and tolerability and identify dose level for further evaluation
  - Utilized stringent supplemental aflibercept criteria and enrolled patients with high central subfield thickness (CST) to maximize patient safety and assess initial clinical activity
- Study Population:
  - 22 patients enrolled across 3 dose levels: 3E10 vg/eye (n=9), 1E10 vg/eye (n=12), 5E9 vg/eye (n=1); 1 patient in 1E10 vg/eye arm terminated the study due to death unrelated to 4D-150, prior to completion of a post-baseline assessment
- Safety (n=21):
  - 4D-150 was well tolerated with no intraocular inflammation at any timepoint
    - All patients completed the 16-week topical corticosteroid taper on schedule and remained completely off steroids
  - No hypotony, endophthalmitis, vasculitis, choroidal effusions or retinal artery occlusions
- Efficacy Results Through 32 Weeks:
  - 3E10 vg/eye arm:
    - Sustained gain of best corrected visual acuity (BCVA) of +8.4 letters
    - Sustained reduction of CST, as measured by optical coherence tomography (OCT), of -194 µm
  - Supplemental injections: Post-aflibercept loading doses (3), 3E10 vg/eye achieved substantially fewer supplemental injections compared to 1E10 vg/eye and projected on-label aflibercept 2mg Q8W:
    - Mean injections per patient:
      - 3E10 vg/eye: 0.6, 1E10 vg/eye: 1.4, projected on-label aflibercept 2mg Q8W: 4.0
      - 3E10 vg/eye demonstrated a reduction of 61% vs. 1E10 vg/eye
      - 3E10 vg/eye demonstrated a reduction of 86% vs. projected on-label aflibercept 2mg Q8W
    - 0-1 injections:
      - 8 of 9 overall (3E10 vg/eye) vs. 5 of 10 (1E10 vg/eye, 1 patient missed Week 24-32 visits)
    - Injection-free:
      - 5 of 9 overall (3E10 vg/eye) vs. 2 of 10 overall (1E10 vg/eye)
      - 5 of 8 in patients treated per protocol (3E10 vg/eye)
- Results to be presented in a corporate webcast on February 10, 2025
- 52-week interim data update expected at a scientific conference in mid-2025
- Data slides can be found on the “Investors” section of the 4DMT website at https://ir.4dmoleculartherapeutics.com/

4D-150 DME Phase 3 Regulatory Update & Next Steps

- 3E10 vg/eye has been selected as the Phase 3 dose
- Based on data generated to date for 4D-150 in both the SPECTRA and PRISM clinical trials, FDA is aligned that a single Phase 3 clinical trial, combined with data from the two planned Phase 3 clinical trials in the 4FRONT wet AMD program, would be acceptable as the basis of a BLA submission for 4D-150 in DME
- Per FDA feedback, the Company may proceed to Phase 3 (SPECTRA Part 2 no longer needed) and is aligned with key design elements of a Phase 3 clinical trial with approximately 300-400 patients total with a primary endpoint of BCVA noninferiority vs. on-label aflibercept 2mg (5 loading doses and Q8W), and revised supplemental injection criteria (less stringent compared to Part 1 SPECTRA, in line with prior successful Phase 3 DME clinical trials)
- Next steps for DME development to be presented in a corporate webcast on February 10, 2025

“The highly differentiated tolerability and promising clinical activity profile to date for 4D-150, and supportive feedback we received from the FDA in both wet AMD and DME, is a testament to 4D-150’s differentiated product design based on our proprietary R100 vector and our strong team, including our global Ophthalmology Advisory Board,” said David Kirn, M.D., Co-founder and Chief Executive Officer of 4DMT. “The alignment with the FDA on the design and path forward for a single Phase 3 trial in DME is a positive step forward in our ability to realize 4D-150’s potential as a pipeline-in-a-product, which may unlock DME as a second large market indication shortly after wet AMD."

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 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 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, 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.

Contacts:

Media:
Katherine Smith
Inizio Evoke Comms
Media@4DMT.com

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