4DMT Highlights Robust and Durable Clinical Activity for 4D-150 and Design of 4FRONT Phase 3 Program at 4D-150 Wet AMD Development Day

September 18, 2024

- *4D-150 demonstrated robust and durable clinical activity across all wet age-related macular degeneration (wet AMD) patient populations based on longest available follow-up data*
  - *In broad population (Phase 2b), 70% injection-free through 52 weeks*
  - *In severe population (Phase 1/2a), 83% overall reduction in annualized injections through 52 weeks*
- *4D-150 continues to be safe and well tolerated with intraocular inflammation (IOI) profile numerically similar (2.8% transient 1+ vitreous cells) to approved anti-VEGF agents*
- *4FRONT Phase 3 program designed to maximize 4D-150's potential, including probabilities of clinical, regulatory and commercial success across global markets*
- *Corporate webcast to be held on September 18, 2024 at 4:15 p.m. ET*

EMERYVILLE, Calif., Sept. 18, 2024 (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 data showing continued robust and durable clinical activity, based on longest interim follow-up data from the Phase 1/2 PRISM clinical trial, and 4FRONT Phase 3 study design, which will be presented at its 4D-150 Wet AMD Development Day.

"We continue to build support for 4D-150 with positive interim data from PRISM showcasing clear reduction in overall treatment burden and potential multiyear clinical benefit in previously treated patients, with an emerging safety profile comparable to approved anti-VEGF agents. In addition, we have assembled an exceptional senior leadership team with deep late-stage drug development, regulatory and commercial experience in large market ophthalmology to design and execute our upcoming pivotal studies," said David Kirn, M.D., Co-founder and Chief Executive Officer of 4DMT. "We expect to initiate 4FRONT-1, our first 4D-150 Phase 3 study in wet AMD, in Q1 2025. We look forward to continuing the rapid advancement of this potentially paradigm shifting product candidate that addresses the limits of current treatment options for patients with wet AMD."

"As prudent medicine developers, we began our clinical development program for 4D-150 in the most severe wet AMD patients in the Phase 1/2a portion of PRISM. After observing favorable tolerability and clinical activity results, we and our investigators felt confident in 4D-150's potential across a broad range of wet AMD patients and designed the Phase 2b cohort," said Robert Kim, M.D., Chief Medical Officer of 4DMT. "We believe the interim data from Phase 2b demonstrates strong clinical activity, especially in more recently diagnosed patients."

4D-150 Wet AMD Development Day Key Highlights:

Positive Interim Data from 4D-150 Phase 1/2 PRISM Study

- Clinical Activity (based on data cutoff of September 3, 2024):
  - Robust and durable treatment burden reduction observed in all PRISM populations studied with the planned Phase 3 dose of 3E10 vg/eye of 4D-150 (**Based on Kaplan-Meier method for calculating endpoint with follow-up through 52 weeks (Phase 1/2a) and variable follow-up through 32–52 weeks (Phase 2b); **Defined as diagnosed ≤6 months*)
    - **Phase 1/2a Severe (n=24, through 52 weeks):**
      - 83% overall reduction in annualized injections
      - 52% received 0 or 1 injection*
      - 44% injection-free*
    - **Phase 2b Broad (n=30, through 52 weeks):**
      - 89% overall reduction in annualized injections
      - 80% received 0 or 1 injection*
      - 70% injection-free*
    - **Phase 2b Recently Diagnosed** (n=15, through 52 weeks):**
      - 98% overall reduction in annualized injections
      - 100% received 0 or 1 injection*
      - 87% injection-free*
  - Central Subfield Thickness (CST): sustained anatomic control with fewer fluctuations
  - Mean best corrected visual acuity (BCVA): stable (Phase 1/2a) or sustained improved (Phase 2b)
- Safety (based on data cutoff of August 23, 2024):
  - 4D-150 continues to be well tolerated with favorable safety profile
  - Rate of 4D-150 IOI numerically similar to that reported for approved anti-VEGF agents
    - Wet AMD:
      - 2.8% (2 of 71) had 4D-150–related IOI at any timepoint
        - 2 patients had transient 1+ vitreous cells

        - 99% (70 of 71) completed steroid prophylaxis taper on schedule
        - 97% (69 of 71) remained off steroids completely
    - Diabetic Macular Edema (DME; SPECTRA trial):
        - No patients treated at any dose (n=22) have experienced IOI events at any timepoint
  - No 4D-150–related hypotony, endophthalmitis, vasculitis, choroidal effusions or retinal artery occlusions observed to date across both the wet AMD and the DME programs

4FRONT Wet AMD Planned Phase 3 Program Key Design Elements

- Company planning for global 4FRONT Phase 3 development program comparing a single dose of 4D-150 3E10 vg/eye to on-label aflibercept 2mg Q8 weeks:
  - Initiation of 4FRONT-1 clinical trial (N=500) expected in Q1 2025
  - Eligibility criteria: 1) Patients must be both recently diagnosed and treatment naïve wet AMD patients, and 2) Randomization requires on study demonstration of aflibercept responsiveness
- Program expected to include two double-masked, randomized, controlled noninferiority trials:
  - Primary endpoint: noninferiority in BCVA
  - Sham controlled to support masking
  - All patients randomized to receive 3 total loading doses per aflibercept label
- Supplemental aflibercept injection criteria for 4D-150 arm optimized to protect primary BCVA endpoint and to maximize reduction of supplemental treatment burden; no supplemental injections allowed in control arm
- Study design has been aligned with feedback from U.S. Food and Drug Administration (FDA) under RMAT designation
- Alignment ongoing with European Medicines Agency (EMA) under PRIME designation

Carlos Quezada-Ruiz, M.D., FASRS, SVP, Therapeutic Area Head, Ophthalmology of 4DMT added, “Given the consistent emerging safety profile and strong signs of promising clinical activity across a broad range of wet AMD patients, including three patients from our Phase 1a who have gone 2-3 years without the need for supplemental aflibercept injections, we are excited to rapidly advance 4D-150 into Phase 3. We have worked closely with global regulatory agencies and our Ophthalmology Advisory Board to maximize the probabilities of clinical, regulatory and commercial success of the 4FRONT Phase 3 program. In partnership with the retina community, we are eager to begin enrollment in 4FRONT-1 and potentially bring a paradigm shifting treatment option to patients.”

“Our patients with wet AMD require frequent life-long treatment with intravitreal injections, leading to a high treatment burden and suboptimal outcomes in the real world compared to clinical trials,” said Arshad M. Khanani, M.D., M.A., FASRS, Director of Clinical Research at Sierra Eye Associates and Clinical Professor at University of Nevada, Reno. “Based on the data to date, 4D-150 has the potential to decrease treatment burden and control wet AMD with a safe, single routine intravitreal injection while maintaining vision and anatomy. I am looking forward to working with the 4DMT team, the Ophthalmology Advisory Board, and investigators on the 4FRONT Phase 3 global development program to advance this potential treatment option for all our patients with wet AMD.”

4D-150 Wet AMD Development Day Webcast Details

Title:	4D-150 Wet AMD Development Day
Date/Time:	Wednesday, September 18, 2024 from 4:15 p.m. to 6:15 p.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.

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 (major markets), and Japan, will be greater than 4 million individuals in the next five years. Wet AMD is a type of macular degeneration where 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 4D-150 for Wet AMD

4D-150 combines 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 four members of the VEGF angiogenic family of 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 developed this platform utilizing principles of directed evolution, a Nobel Prize-winning technology. 4D-150 is designed for single, low-dose intravitreal delivery for transgene expression from the retina without significant inflammation.

About 4DMT

4DMT is a leading clinical-stage genetic medicines 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 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 wholly owned and partnered product candidates. Our product design, development, and manufacturing engine helps us efficiently create and advance our diverse product pipeline with the goal of revolutionizing medicine with potential curative therapies for millions of patients. Currently, 4DMT is advancing six clinical-stage and one preclinical product candidate, each tailored to address rare and large market diseases in ophthalmology, pulmonology and cardiology. In addition, 4DMT is also advancing programs in CNS through a gene editing partnership. 4D Molecular Therapeutics™, 4DMT™, Therapeutic Vector Evolution™, and the 4DMT logo are trademarks of 4DM

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 (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, clinical benefits of 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, 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