4DMT Focuses Pipeline to Prioritize 4D-150 in Wet AMD & DME and 4D-710 in CF and Extends Cash Runway

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- *Strategically focused pipeline optimizes resource allocation to progress two product candidates with strongest clinical proof of concept: 4D-150 for wet AMD and DME and 4D-710 for cystic fibrosis*
- *After alignment with FDA and EMA on trial designs for the 4D-150 Phase 3 4FRONT program in wet AMD, 4FRONT-1 and 4FRONT-2 trials on track to initiate in Q1 2025 and Q3 2025 respectively*
- *Primary endpoint 52-week topline data for both 4FRONT-1 and 4FRONT-2 expected in H2 2027*
- *Cash runway extended under updated operating plan; unaudited cash, cash equivalents and marketable securities of $506M as of December 31, 2024 expected to fund operations into 2028*

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 a strategically focused pipeline, updated Phase 3 4FRONT program plans, initial 4FRONT guidance and resulting updated cash runway guidance.

“4DMT was founded to address the challenges posed by traditional AAVs and to bring genetic medicines to market to transform outcomes for millions of patients. Over 10 years we created a diverse pipeline to bring this vision closer to reality with seven named product candidates across three therapeutic areas utilizing three novel, clinically-validated vectors,” said David Kirn, M.D., Co-founder and Chief Executive Officer of 4DMT. “We have prioritized two product candidates with the strongest clinical proof of concept and high potential to impact the most patients to fulfil our mission. In addition, our ongoing regulatory interactions support an efficient path to Biologics License Applications (BLA) for 4D-150 in both wet age-related macular degeneration (wet AMD) and diabetic macular edema (DME).”

Strategically Focused Pipeline

Core Programs: Updates & Upcoming Milestones

Large Market Ophthalmology Focus

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, well tolerated, intravitreal injection. 4D-150 is being developed for wet AMD and DME, each of which affects millions of patients globally, with the goal of preserving vision and relieving patients from burdensome repeated bolus injections, which can total up to 12 per year. 4DMT will focus the majority of its R&D resources and operations on global development and pre-commercial planning for 4D-150 in wet AMD.

- **4D-150 for Wet AMD:**
  - Ongoing Phase 1/2 PRISM clinical trial currently in long-term follow-up:
    - 52-week interim data from Phase 2b cohort of the PRISM clinical trial to be presented at Angiogenesis, Exudation, and Degeneration 2025 on Saturday, February 8, 2025
    - Corporate webcast to discuss data to be held on Monday, February 10, 2025
  - Phase 3 4FRONT program overview and updates:
    - Trial designs and CMC plans aligned with U.S. Food & Drug Administration (FDA) under RMAT designation and European Medicines Agency (EMA) under PRIME designation, based on multiple interactions through December 2024
    - 4FRONT-1 and 4FRONT-2 are on target to initiate in Q1 and Q3 2025, respectively
    - 4FRONT-1 and 4FRONT-2 clinical trial design:
      - Primary endpoint: best corrected visual acuity (BCVA) noninferiority of 4D-150 3E10 vg/eye to aflibercept 2mg Q8W
      - Enrichment criteria: Randomization requires on study demonstration of aflibercept responsiveness
      - Supplemental aflibercept injection criteria for 4D-150 arm optimized to protect primary BCVA endpoint and to maximize reduction of supplemental treatment burden; criteria to be disclosed prior to trial initiation. No supplemental injections allowed in control arm
      - Target enrollment of 400 patients per trial
        - Designed with ≥90% power for primary endpoint of BCVA noninferiority of 4D-150 versus aflibercept 2mg Q8 weeks (margin of 4.5 letters) and supports required program safety database for BLA submission
      - 4FRONT-1 to enroll treatment naïve population and 4FRONT-2 to enroll both treatment naïve and previously treated population, diagnosed within the last six months
    - Primary endpoint 52-week topline data from both 4FRONT-1 and 4FRONT-2 expected in H2 2027
- **4D-150 for DME:**
  - Ongoing SPECTRA Part 1 follow-up continues:
    - Announced positive 32-week interim data today in separate press release
      - Results and next steps to be presented in a corporate webcast on February 10, 2025
    - 52-week interim data update expected at a scientific conference in mid-2025
  - Announced regulatory update, in separate press release issued today, summarizing written FDA feedback. Based on review of

SPECTRA and PRISM data to date, combined with data from the two planned Phase 3 clinical trials in the 4FRONT wet AMD program, a single Phase 3 trial of 300-400 patients is acceptable for BLA submission and the Company may directly proceed into Phase 3 (SPECTRA Part 2 no longer needed)

Pulmonology Program

4DMT's proprietary A101 vector is the first known AAV vector to demonstrate successful delivery and expression of the CFTR transgene in the lungs of people with cystic fibrosis (CF) following aerosol delivery. Given A101-enabled product candidate 4D-710's proof of delivery, safety data and initial clinical activity signals, and ongoing support from the Cystic Fibrosis Foundation and collaboration with Therapeutics Development Network, the Company intends to complete Phase 1 enrollment in H1 2025, approach the FDA with a pivotal trial proposal mid-2025, and evaluate additional funding options to further advance 4D-710 into late-stage development.

- **4D-710 for CF Lung Disease:**
  - Phase 1 AEROW enrollment completed in November 2024 (Cohorts 3 & 4 fully enrolled with n=3 each), follow-up ongoing; trial allows up to an additional 3 people with CF at these dose levels
    - Interim data update expected to be presented in mid-2025 at a scientific conference, including available measurements of ppFEV$_1$, CFQ-R-R (quality-of-life instrument), lung clearance index and serial airway biopsies and brushings collected at 4-8 weeks and beyond 12 months post-dosing

Programs with Reduced Capital Allocation

While we believe the therapeutics below hold significant potential, at this time no further significant investment is expected on these programs, pending additional financing or partnerships.

- 4D-175 for geographic atrophy (preclinical with open IND)
- 4D-725 for alpha-1-antitrypsin deficiency lung disease (preclinical)
- 4D-310 for Fabry disease cardiomyopathy (ongoing Phase 1)

Following a comprehensive review of its portfolio, the Company has decided to terminate the development of the early-stage rare disease clinical programs evaluating 4D-110 for choroideremia and 4D-125 for X-linked retinitis pigmentosa.

Given the promising portfolio of product candidates and vectors owned and developed by 4DMT, 4DMT will not be investing additional capital into new preclinical product candidates at this time.

Updated Financial Guidance

As a result of its strategically focused pipeline, resource reallocation and discontinued future investment plans on non-core product candidates, the Company has extended its cash runway. Under the updated operating plan, based on unaudited cash, cash equivalents and marketable securities of $506M as of December 31, 2024, the Company now expects its current cash to fund operations into 2028. Cash runway includes full execution and topline 52-week data from 4FRONT-1 and 4FRONT-2 Phase 3 clinical trials in wet AMD, and ongoing early-stage development for DME and CF. Additionally, the Company will explore value-creating partnership opportunities and other strategic financing options.

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, regulatory interactions regarding, and potential commercialization of our product candidates, including 4D-150 and 4D-710, and statements regarding our anticipated resource allocation and cash runway. 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.

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