4DMT Presents Interim Data from 4D-310 INGLAXA Phase 1/2 Clinical Trials for Fabry Disease Cardiomyopathy at WORLDSymposium™ 2024

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- *4D-310 demonstrated clinically meaningful cardiac endpoint improvements through 12-24 months in contractility (echocardiography), peak VO_2 (cardiopulmonary exercise testing) and/or cardiac quality of life (KCCQ) in all five evaluable patients*
- *Cardiac biopsies were obtained from a patient at week 6 and 24 and showed robust and durable delivery, transgene expression and clearance of Gb3 substrate in cardiomyocytes*
- *No new treatment-related adverse events > Grade 1 since last interim update and through 12-33 months; previously reported cases of atypical hemolytic uremic syndrome (aHUS) (n=3) fully resolved*
- *FDA submission of data from non-human primate (NHP) study evaluating 4D-310 with rituximab/sirolimus (R/S) immunosuppressive regimen in Q2 2024*
- *Efficient delivery, transgene expression and clinical activity now demonstrated in the clinic with three proprietary vectors generated from 4DMT's Therapeutic Vector Evolution platform*

EMERYVILLE, Calif., Feb. 12, 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 updated interim safety and efficacy data on six adults with Fabry disease cardiomyopathy treated with a single intravenous (IV) infusion of 4D-310 (1E13 vg/kg) with follow-up of 12-33 months overall, including 12-24 month follow-up data on cardiac contractility, exercise capacity, quality of life and cardiac biopsy data. The data was presented in a late-breaking session at WORLD*Symposium* ™ 2024 in San Diego, California on Friday, February 9, 2024.

"We are pleased to see 4D-310 continue to consistently demonstrate clinical activity across multiple important cardiac endpoints including cardiac function, exercise capacity and quality of life," said Robert Kim, M.D., Chief Medical Officer of 4DMT. "Current therapies do not adequately address Fabry-related cardiovascular manifestations, and cardiovascular disease is the most common cause of death in these patients. 4D-310 continues to be well tolerated, with the previously reported cases of aHUS having fully resolved and no new drug-related adverse events over Grade 1 reported."

"These promising clinical results continue to validate our Therapeutic Vector Evolution platform, as well as the potential of the C102 vector for targeted IV delivery to cardiomyocytes. Cardiac biopsies also showed robust and durable delivery and transgene expression from 4D-310, and remarkably, a reduction in Gb3 substrate in cardiomyocytes," said David Kirn, M.D., Co-founder and Chief Executive Officer of 4DMT. "No approved therapy has been shown to definitively clear accumulated Gb3 from cardiomyocytes in patients with Fabry disease, which speaks to 4D-310's highly differentiated profile. We remain on-track to submit results from the non-clinical study to evaluate 4D-310 in NHPs with the R/S immunosuppressive regimen to the FDA in Q2 2024 to address the clinical hold."

INGLAXA Phase 1/2 Clinical Trial Design & Enrollment

- Dose escalation and dose expansion trial assessing a single IV infusion of 4D-310 in a broad and diverse Fabry disease patient population
- Enrolled six patients, each treated with 1E13 vg/kg of 4D-310 and a prophylactic corticosteroid immunosuppressive regimen
  - Protocol amended to change immunosuppressive regimen to rituximab and sirolimus (enrollment on this amendment pending)
- Cardiac biopsies allowed at week 6 and 26 in the INGLAXA-2 trial (to date, one patient had biopsies performed)

INGLAXA Phase 1/2 Interim Data Summary (Data Cutoff: December 5, 2023)

- **Safety and Tolerability**
  - Previously reported cases of aHUS (n=3) have fully resolved
  - No clinically significant cardiac or liver toxicities
  - No new 4D-310–related adverse events > Grade 1 since the last interim update in February 2023
- **Echocardiography Contractility Assessments (Global Longitudinal Strain, GLS)**
  - Improved GLS in all five evaluable patients by month 12
  - Two patients who reached 24 months of follow-up both showed clinically meaningful improvement with change from baseline exceeding the minimal detectable difference of -1.5% (-2.8 and -2.9%, respectively)
- **Cardiopulmonary Exercise Testing (CPET) Peak VO_2 Assessments**
  - 3 of 4 evaluable patients demonstrated clinically meaningful improvement by CPET peak VO_2 with change from baseline exceeding the minimal clinically important difference (MCID) of +1.5 at month 12 (+1.8, +2.0 & +7.0)
  - One patient who reached 24 months of follow up continued to show meaningful improvement with change from baseline exceeding the MCID of +1.5 (+7.8)

- **Cardiac Quality of Life Assessments (Kansas City Cardiomyopathy Questionnaire)**
  - Two patients had low baseline scores <90 (scale 0-100); both patients had clinically meaningful improvements in QOL (exceeding the MCID of +5)
    - One patient had 12 months follow-up: Clinical & Overall Summary Scores improved by +5.7 and +11.7, respectively
    - One patient had 24 months follow-up: Clinical & Overall Summary Scores improved by +12.5 and +8.3, respectively
  - Three patients had baseline values >90 (92.7, 100 & 100); all remained stable through 12-24 months (+1.1 to -1.6).
- **Cardiac Biopsy Assessments of Transgene Expression and Substrate Clearance**
  - Cardiac biopsies at week 6 and 26 from one patient showed robust & durable 4D-310–mediated transgene expression in cardiomyocytes
    - All samples positive for transgene RNA (ISH) & AGA protein (IHC)
    - At week 26, mean Gb3 inclusion body volume per cardiomyocyte was reduced 15% from week 6 and 61% vs. historical sample collected approximately 7 years prior to enrollment and analyzed independently by investigator

Detailed results can be found in the Scientific Posters and Publications section of our website here.

Next Steps for Development of 4D-310

- FDA submission of data from the NHP study evaluating the safety and biodistribution of IV 4D-310 with the R/S immunosuppressive regimen compared to the prior prednisone regimen expected in Q2 2024

About 4D-310 and Fabry Disease Cardiomyopathy

4D-310 utilizes the cardiac targeted and evolved C102 vector to efficiently deliver a functional copy of the *GLA* gene (encodes for AGA enzyme) to the heart after a single low dose IV administration. The product candidate is designed to generate high local levels of AGA directly within heart tissue, as well as other affected organs, with the goal of reversing the cardiomyopathy in Fabry patients. Cardiomyopathy is the leading cause of death in the Fabry disease population.

Affecting more than 50,000 people in the United States and European Union, Fabry disease is a genetic disorder of the *GLA* gene that results in the body's inability to produce AGA, causing accumulation of the substrate globotriaosylceramide (Gb3) in critical organs, including the heart, kidney, and blood vessels. Cardiomyopathy is the leading cause of death in the Fabry disease patient population. Such substrate accumulation can lead to life-threatening hypertrophic cardiomyopathy, heart failure, arrhythmias, various degrees of kidney dysfunction and cerebrovascular stroke. Significant unmet medical needs remain for these patients despite enzyme replacement therapy (ERT), the current standard of care. ERT requires biweekly intravenous dosing which markedly decreases patients' quality of life. In addition, while benefit has been demonstrated in the kidney, ERT has not been shown to clearly benefit the heart.

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 five clinical-stage and two preclinical product candidates, 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 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 of 4DMT's product candidates, as well as the plans, announcements and related timing for the clinical development of our clinical and preclinical product candidates, and related timing for the clinical development of 4D-310. 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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