4D Molecular Therapeutics Announces FDA Clearance of IND Application for 4D-150 Genetic Medicine for the Treatment of Diabetic Macular Edema

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- *4D-150 Phase 2 SPECTRA clinical trial for diabetic macular edema enrollment is expected to initiate in Q3 2023*
- *Initial Phase 1 PRISM clinical trial with 4D-150 for wet age-related macular degeneration further validates R100 intravitreal vector potential for other large market eye diseases including geographic atrophy*
- *Interim PRISM data for dose Cohorts 1, 2, & 3 (n=15) to be presented at the 2023 Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting*
- *Randomized Phase 2 portion of the Phase 1/2 PRISM clinical trial with 4D-150 for wet AMD is currently enrolling*

EMERYVILLE, Calif., Feb. 02, 2023 (GLOBE NEWSWIRE) -- 4D Molecular Therapeutics (Nasdaq: FDMT, "4DMT"), a clinical-stage biotherapeutics company harnessing the power of directed evolution for targeted genetic medicines, announced FDA clearance of the Investigational New Drug Application (IND) for 4D-150, an R100 vector-based intravitreal genetic medicine, for the treatment of patients with Diabetic Macular Edema (DME).

The Phase 2 SPECTRA clinical trial will assess 4D-150 in patients with DME. The study design consists of a Dose Confirmation stage followed by a masked Dose Expansion stage, in which patients will be randomized to receive a single intravitreal injection at one of two dose levels of 4D-150 or aflibercept in a 1:1:1 ratio (n=54 patients). The doses to be evaluated in DME are anticipated to be between 6E9 to 3E10 vg/eye. The IND clearance enables the initiation of SPECTRA clinical study sites, and 4DMT expects to begin enrollment in the third quarter of 2023.

Initial Cohort 1 data (n=5) from the Phase 1 portion of the Phase 1/2 PRISM clinical trial with 4D-150 for wet age-related macular degeneration (wet AMD) demonstrated a reduction in annualized anti-VEGF injection rate by over 95%, further validating the potential of our intravitreal R100 vector for other large market eye diseases such as geographic atrophy.

On January 9, 2023, 4DMT disclosed that the Company had initiated the randomized Phase 2 portion of the Phase 1/2 PRISM clinical trial for 4D-150 in patients with wet AMD. This portion of the trial is now enrolling patients. In addition, the Company intends to present interim data for dose Cohorts 1, 2, & 3 (n=15) at the 2023 ARVO Annual Meeting taking place April 23-27, 2023; at the time of the ARVO data presentation, all patients are predicted to have at least six months of follow-up following 4D-150 treatment.

"This is the sixth US IND submitted by 4DMT, and all six have been cleared by the FDA. The robustness and efficiency of our product design and development engine are based on sustained excellence by our manufacturing, preclinical, clinical, and regulatory teams," said David Kirn, M.D., Co-founder and Chief Executive Officer of 4DMT. "We are excited to have started enrolling the Phase 2 portion of our PRISM trial in wet AMD, and to evaluate the potential of 4D-150 in patients with DME who also require frequent anti-VEGF injections and have a high treatment burden."

About 4D-150 and Wet AMD and DME

4D-150 is comprised of our targeted and evolved intravitreal vector, R100, and a payload that expresses both aflibercept and a VEGF-C RNAi. R100 was invented at 4DMT through our proprietary Therapeutic Vector Evolution platform; we created this platform utilizing principles of directed evolution, a Nobel Prize-winning technology. This dual transgene payload inhibits 4 angiogenic factors: VEGF A, B, C and PlGF. 4D-150 is designed for a single low dose intravitreal delivery.

Wet AMD is a highly prevalent disease with an estimated incidence rate of 200,000 new patients per year in the United States, according to published data. Wet AMD is a type of macular degeneration where abnormal blood vessels (choroidal neovascularization or CNV) grow into the macula, the central area of the retina. As a consequence, CNV causes swelling and edema of the retina, bleeding and scarring, and causes visual distortion and reduced 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.

DME is a highly prevalent disease with significant unmet medical need. It is estimated that there are approximately one million individuals with DME in the United States according to published data. DME is characterized by swelling in the macula due to leakage from blood vessels. This can lead to blurred vision. DME is typically treated with intravitreal anti-VEGF agents administered approximately every 4-12 weeks.

About 4DMT

4DMT is a clinical-stage biotherapeutics company harnessing the power of directed evolution for targeted genetic medicines. 4DMT seeks to unlock the full potential of genetic medicines using its proprietary invention platform, Therapeutic Vector Evolution, which combines the power of the Nobel Prize-winning technology, directed evolution, with approximately one billion synthetic AAV capsid-derived sequences to invent targeted and evolved vectors for use in our product candidates. All of our vectors are proprietary to 4DMT and were invented at 4DMT, including the vectors utilized in our clinical-stage and preclinical pipeline product candidates: R100, A101, and C102. The Company is initially focused on five clinical-stage product candidates in three therapeutic areas for both rare and large market diseases: ophthalmology, pulmonology, and cardiology (Fabry disease cardiomyopathy). The 4DMT targeted and evolved vectors were invented with the goal of being delivered at relatively low doses through clinically routine, well-tolerated, and minimally invasive routes of administration, transducing diseased cells in target tissues efficiently, having reduced immunogenicity and, where relevant, having resistance to pre-existing antibodies. 4DMT is currently advancing five product candidates in clinical development: 4D-150 for wet AMD and DME, 4D-710 for cystic fibrosis lung disease, 4D-310 for Fabry disease cardiomyopathy, 4D-125 for XLRP, and 4D-110 for choroideremia. The 4D preclinical product candidates in development are: 4D-175 for geographic atrophy and 4D-725 for alpha-1 antitrypsin deficiency.

4D-150, 4D-710, 4D-310, 4D-125, and 4D-110 are our product candidates in clinical development and have not yet been approved for marketing by the US FDA or any other regulatory authority. No representation is made as to the safety or effectiveness of 4D-150, 4D-710, 4D-310, 4D-125, or 4D-110 for the therapeutic uses for which they are being studied.

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 4D-150, including plans for the clinical development and timing of the Phase 2 SPECTRA clinical trial. 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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