4DMT Announces FDA Clearance of IND Application for 4D-175 Genetic Medicine for the Treatment of Geographic Atrophy

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- *4D-175 comprises the proprietary low-dose intravitreal R100 AAV vector and a codon-optimized transgene encoding a highly functional shortened form of human complement factor H (sCFH)*
- *Complement factor H (CFH) variants with reduced function are a well-validated genetic risk factor for geographic atrophy (GA), with approximately 75% of age-related macular degeneration (AMD) patients carrying a high-risk variant of CFH*
- *Over 150 patients have been treated with the R100 vector, including those with wet AMD and diabetic macular edema, further validating the modularity of our Therapeutic Vector Evolution platform*
- *Enrollment for Phase 1 GAZE clinical trial is expected to begin in H2 2024*

EMERYVILLE, Calif., June 24, 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 U.S. Food and Drug Administration (FDA) clearance of the Investigational New Drug Application (IND) for 4D-175, an R100 vector-based intravitreal genetic medicine, for the treatment of patients with GA.

The Phase 1 GAZE clinical trial will assess 4D-175 in patients with GA secondary to AMD. The study design consists of an open-label, sequential cohort Dose Exploration stage, in which patients will receive a single intravitreal injection of 4D-175 at one of three dose levels. Clinical trial objectives include safety and tolerability, definition of the Phase 2 trial dose level(s), transgene expression and biological activity. The IND clearance enables the initiation of GAZE clinical study sites, and 4DMT expects to begin enrollment in H2 2024.

“GA is a leading cause of irreversible vision loss for over 5 million people globally and while current bolus complement inhibitor treatments reduce the rate of growth in GA lesions, they require burdensome monthly or bimonthly intravitreal injections and do not demonstrate functional vision benefit,” said David Kirn, M.D., Co-founder and Chief Executive Officer of 4DMT. “4D-175 has the potential for durable clinical benefit with a single intravitreal injection, greatly reducing the current treatment burden for patients, which may lead to better long-term vision outcomes. In Phase 1, we aim to explore safety and transgene expression levels to select doses for Phase 2. We look forward to beginning enrollment in the Phase 1 GAZE clinical trial in the second half of 2024.”

sCFH is an engineered and optimized version of *CFH* that can fit into adeno associated virus (AAV) vectors with robust expression and full functionality confirmed in human cells *in vitro*, as well as in multiple preclinical animal models and species *in vivo*. The construct was co-invented by Wenchao Song, Ph.D., Professor of Pharmacology at the Perelman School of Medicine at the University of Pennsylvania. Dr. Song has extensive experience researching complement-mediated inflammatory, autoimmune and thrombotic vasculopathy disorders. Restoring *CFH* function through targeted delivery of a therapeutic *sCFH* transgene could restore normal complement regulation and reduce retinal injury that manifests as progressive GA. Preclinical proof-of-concept for this approach using 1) human *sCFH* delivered systemically using an AAV vector in a mouse model of atypical hemolytic uremic syndrome (aHUS) and 2) a mouse version of *sCFH* delivered using an AAV vector in mouse models of C3 glomerulopathy and aHUS each demonstrated recovery from complement dysregulation, reduced organ damage and improved survival.

Preclinical data from 4D-175 *in vitro* and *in vivo* characterization studies were presented at the 2024 ARVO Annual Scientific Meeting in May; the presentation can be found on the 4DMT website here.

About Geographic Atrophy

Geographic atrophy (GA) is a highly prevalent disease with a significant unmet medical need. It is estimated that there are approximately 2.5 million individuals with GA in the United States and major European markets, and an estimated 5 million individuals globally. GA is an advanced and severe form of age-related macular degeneration (AMD) that leads to irreversible vision loss. GA is characterized by atrophic lesions in the outer retina that affect central vision and lead to irreversible vision loss. Progressive loss of central vision leads to difficulties driving, reading, and completing basic daily tasks. As a result, GA has a major impact on quality of life. Complement-mediated inflammation is recognized as a main contributor to the development and worsening of GA. The only FDA approved treatments for GA are complement inhibitors administered by intravitreal (IVT) injection once every 4-9 weeks.

About 4D-175 for Geographic Atrophy

4D-175 combines the customized and evolved intravitreal vector, R100, and a codon-optimized transgene encoding a highly functional shortened form of human complement factor H (*sCFH*). The genetic medicine candidate is designed to provide durable transgene expression in the retina without significant inflammation following a single, low-dose intravitreal injection. The *sCFH* payload is designed to restore normal complement regulation, which has the potential to slow progression of disease.

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, and clinical benefits of 4DMT's product candidates, as well as the plans, announcements and related timing for the clinical development of 4D-175. 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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