



4DMT Announces Landmark Publication of 4D-150 Preclinical Data for the Treatment of Neovascular Retinopathies in IOVS

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- Landmark publication in leading ophthalmology research journal demonstrates the power of 4DMT's Therapeutic Vector Evolution platform to invent potentially best-in-class customized vectors and transformative genetic medicines
- Proprietary intravitreal vector R100 demonstrated superior transduction and transgene expression compared to AAV2, the standard AAV serotypes used in retinal gene therapies, in all three human retinal cell types evaluated in vitro (up to ~10-fold improvement), and in all primate retinal cell layers after intravitreal injection in vivo
- Intravitreal administration of the R100 vector-based 4D-150 genetic medicine in nonhuman primate wet AMD model was well tolerated, led to robust retinal expression of dual transgenes (aflibercept and anti-VEGF C) and complete suppression of severe CNV choroidal neovascularization lesions
- 4D-150 wet AMD (PRISM) and DME (SPECTRA) Phase 1/2 clinical trials are currently underway; 4FRONT Phase 3 program in wet AMD on target to initiate in Q1 2025

EMERYVILLE, Calif., Dec. 16, 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 the publication of landmark preclinical data demonstrating the potential of the Company's proprietary Therapeutic Vector Evolution (TVE) platform, intravitreal R100 vector and the R100-based genetic medicine 4D-150. Pioneering efficacy and safety results in a difficult-to-treat nonhuman primate (NHP) model of wet age-related macular degeneration (wet AMD) demonstrated the potential of 4D-150 to substantially reduce the treatment burden and improve long-term vision outcomes for patients with wet AMD, diabetic macular edema (DME) and diabetic retinopathy (DR). The data were published in *Investigative Ophthalmology & Visual Science (IOVS)*; December 2024 issue. *IOVS* is the journal of the Association for Research in Vision and Ophthalmology (ARVO), a leading basic and translational research association in ophthalmology.

The publication entitled, "Design and Characterization of a Novel Intravitreal Dual-Transgene Genetic Medicine for Neovascular Retinopathies," reports the results of preclinical discovery, engineering and characterization studies evaluating the safety, retinal cell transduction, transgene expression and clinical activity of proprietary evolved intravitreal vector R100 and 4D-150, an R100-based genetic medicine carrying 2 therapeutic transgenes: 1) a codon-optimized sequence encoding aflibercept, a recombinant protein that inhibits VEGF-A, VEGF-B and PlGF, and 2) a microRNA sequence that inhibits expression of VEGF-C. The data showed that R100 demonstrated significantly superior human retinal cell transduction compared to AAV2, and intravitreal administration of 4D-150 to nonhuman primates was well tolerated and led to robust panretinal expression of both transgenes, especially within the macula region; AAV2 was unable to transduce deep retinal cell layers in the same model. In a difficult-to-treat primate laser-induced choroidal neovascularization model of wet AMD, 4D-150 completely prevented grade IV angiogenic lesions at all tested doses.

"We founded 4DMT with the belief that the Nobel Prize-winning technology of directed evolution could be applied to invent highly optimized and customized AAV vectors for any tissue in the body. This proprietary Therapeutic Vector Evolution approach has been validated through clinical results with three different proprietary vectors for transgene payload delivery to the retina (R100, intravitreal), lung airways (A101, aerosol) and heart (C102, intravenous). R100 was invented to be a potentially best-in-class intravitreal vector to address and overcome the limitations of conventional vectors for the retina, and we are now leveraging R100 in our 4D-150 product candidate to potentially bring to market the first large market genetic medicine to transform vision outcomes for millions of patients with wet AMD and diabetic eye diseases," said David Kim, M.D., senior author of the paper and Co-founder and Chief Executive Officer of 4DMT. "This innovative disease-modifying genetic medicine is designed to continuously suppress all four major molecular drivers of these diseases for years, directly at the site of the disease within the macula, following a single routine clinic-based intravitreal injection. Standard of care bolus anti-VEGF therapies, which generate billions in annual sales, cannot achieve this transformative mechanism of action. The robust results in our primate models reinforce our confidence in 4D-150's efficacy in patients."

The publication is available online at the [IOVS](#) website and on the [Scientific Publications](#) page of the 4DMT website.

About 4D-150

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 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 (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 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 DME

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, which 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 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 4DMT

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 and market potential of 4DMT's product candidates, and its R100, A101 and C102 vectors, as well as the plans, announcements, and related timing for the clinical development of, regulatory interactions regarding, and potential commercialization of 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.

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