4DMT Announces Positive Long-Term Data from Phase 1/2 PRISM Clinical Trial in Wet AMD Supporting 4D-150's Potential as a Backbone Therapy with Consistent and Durable Benefit over Multiple Years

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- *4D-150 demonstrated consistent and durable benefit across all three patient cohorts as evidenced by maintenance of visual acuity, control of retinal anatomy and reduction of treatment burden at all time points with up to 2 years of follow-up*
- *Strong dose response in favor of Phase 3 dose (3E10 vg/eye) continues to be demonstrated*
- *4D-150 continues to be well tolerated with no new safety or intraocular inflammation findings, consistent with previous updates, with up to 3.5 years of follow-up*
- *4FRONT-1 Phase 3 enrollment continues to exceed initial expectations, with over 200 patients randomized to date; the global 4FRONT-2 Phase 3 clinical trial enrollment remains on track for expected completion in H2 2026*

EMERYVILLE, Calif., Nov. 06, 2025 (GLOBE NEWSWIRE) -- 4D Molecular Therapeutics (Nasdaq: FDMT, 4DMT or the Company), a leading late-stage biotechnology company advancing durable and disease-targeted therapeutics with potential to transform treatment paradigms and provide unprecedented benefits to patients, today announced positive interim 1.5- to 3.5-year data from the Phase 1/2 PRISM clinical trial evaluating 4D-150 in patients with wet age-related macular degeneration (wet AMD). The data will be presented in detail at an upcoming scientific conference.

Interim Data from PRISM (Best Available as of Data Cutoff August 22, 2025):

Patient Cohort Overview

- Phase 2b (n=30, all patients reached year 1.5):
  - Broad disease activity
- Phase 2b subgroup: Recently diagnosed (n=15):
  - Broad disease activity diagnosed within 6 months of trial entry
  - This subgroup is most comparable to the cohort in the Phase 3 4FRONT clinical trials
- Phase 1/2a (n=24, all patients have reached year 2):
  - Severe, recalcitrant disease activity

Maintained Visual Acuity and Sustained Control of Retinal Anatomy in All Cohorts

- Consistent maintenance of visual acuity as measured by best corrected visual acuity through up to 2 years
- Consistent control of retinal anatomy (central subfield thickness as measured on optical coherence tomography), with fewer fluctuations through up to 2 years

Treatment Burden Reduction: Sustained, Durable Disease Control with Fewer Anti-VEGF Injections Through Up to 2 Years

Patients maintained a consistent and clinically meaningful reduction in supplemental injections following 4D-150 both in year 1 and in follow-up through year 1.5 (Phase 2b cohort) and Year 2 (Phase 1/2a cohort).

Treatment Burden Reduction Following 4D-150 (Mean Supplemental Injections vs. Comparator)		
Cohorts:	**Through Year 1**	**Through Year 1.5 (Phase 2b) & Year 2 (Phase 1/2a)**
Phase 2b[1] Subgroup: Recently Diagnosed (Phase 3 comparable)	**94%**	**92%**
Phase 2b[1]: Broad	**83%**	**82%**
Phase 1/2a[2]: Severe, Recalcitrant	**83%**	**79%**

[1]Compared to projected aflibercept 2mg Q8 weeks (Phase 3 comparator)
[2]Compared to mean injections in prior 12 months

Durability Maintained Consistently Across 6-Month Intervals Through Up to 2 Years

Patients maintained a consistent and clinically meaningful reduction in supplemental injections in 6-month intervals following dosing with 4D-150,

supporting durable disease control across all measured intervals through up to 2 years of follow-up.

	Mean Supplemental Anti-VEGF Injections per Patient by 6-month Segments Post-4D-150			
Cohorts:	*0 to 6 Months Includes impact of 4D-150 & aflibercept loading dose(s)**	**6 - 12 Months**	**12 - 18 Months**	**18 - 24 Months**
Phase 2b Subgroup: Recently Diagnosed (Phase 3 comparable)	*0.1*	**0.2**	**0.4**	*pending*
Phase 2b: Broad	*0.4*	**0.6**	**0.6**	*pending*
Phase 1/2a: Severe, Recalcitrant	*0.5*	**1.3**	**1.2**	**1.2**

*Week –1 in Phase 1/2a, Week –1 & 4 in Phase 2b

Consistent Dose Response on Treatment Burden Reduction Across All Cohorts Favors Phase 3 Dose (3E10 vg/eye) Compared to Lower Dose (1E10 vg/eye)

- Phase 2b subgroup recently diagnosed (at 1.5 years): 92% vs. 77%
- Phase 2b (at 1.5 years): 82% vs. 73%
- Phase 1/2a (at 2 years): 79% vs. 69%

Safety Data for Phase 3 Dose (3E10 vg/eye, n=71)

- 4D-150 continues to be well tolerated:
  - Safety Endpoint – intraocular inflammation:
    - As previously reported, within approximately the first 6 months (28 weeks) post-4D-150 dosing, 2.8% (2 of 71) of patients had 4D-150-related 1+ (mild) intraocular inflammation (IOI) (SUN/NEI scales), which were transient 1+ vitreous cells noted at a single timepoint
    - Following the first 28 weeks post-4D-150 dosing, no new cases of inflammation with approximately 1.5 to more than 3.5 years of follow-up on all patients as of the data cutoff
    - 99% (70 of 71) completed steroid prophylaxis taper on schedule
    - 99% (70 of 71) remained completely off steroids
  - No 4D-150-related hypotony, endophthalmitis, vasculitis, occlusive/non-occlusive retinal vasculitis or choroidal effusions observed to date

“The interim data from PRISM demonstrate the meaningful treatment burden reduction, vision maintenance and excellent tolerability we’ve observed from 4D-150, highlighting its remarkable consistency, durability, and potential to redefine clinical practice as a backbone therapy for wet AMD and other retinal vascular diseases,” said David Kirn, M.D., Co-founder and Chief Executive Officer of 4DMT. “With the robust PRISM dataset and our APAC region strategic partnership with Otsuka announced last week, we are well positioned for global success in our Phase 3 4FRONT clinical trials, which continue to enroll ahead of initial projections.”

“The ongoing burden of frequent anti-VEGF injections for patients with wet AMD remains a significant global unmet need, often leading to suboptimal visual outcomes due to under-treatment and fluctuating disease activity. 4D-150 has the potential to address this challenge by offering a durable and effective treatment that eliminates or substantially reduces the need for repeated injections while maintaining disease control and preserving vision,” said Arshad M. Khanani, M.D., M.A., FASRS, Director of Clinical Research at Sierra Eye Associates and Clinical Professor at University of Nevada, Reno. “Recent results from the PRISM study further support this potential, demonstrating the durable efficacy and consistent safety of a single intravitreal injection of 4D-150 in a broad wet AMD population. These long-term findings are clinically meaningful and provide new hope for improving real-world outcomes for patients with wet AMD.”

Further details can be found on the “Investors” section of the 4DMT website at https://ir.4dmoleculartherapeutics.com/events.

About 4D-150

4D-150 is a potential backbone therapy designed to provide multi-year, and potentially lifelong, sustained delivery of anti-VEGF (aflibercept and anti-VEGF-C) from the retina with a single, safe, intravitreal injection. 4D-150 utilizes our customized and evolved intravitreal AAV vector, R100, which was invented at 4DMT through our proprietary Therapeutic Vector Evolution platform. 4D-150 is being developed for wet AMD and DME which both affect millions of patients globally, with the goal of freeing patients from burdensome injections while preserving vision.

About Wet AMD

Wet AMD, or wet age-related macular degeneration, is a highly prevalent disease, with more than 4 million individuals expected to be affected in the next five years in certain major markets, including the U.S., the EU and Japan. The disease also has a high incidence, with 200,000 individuals estimated to be newly diagnosed every year in the U.S. alone. Wet AMD is a type of macular degeneration in which abnormal blood vessels grow into the macula (macular neovascularization or MNV), the central area of the retina. MNV causes swelling and edema of the retina, bleeding and scarring, leading to visual distortion and reduced visual acuity. The proliferation and leakage of abnormal blood vessels is stimulated by VEGF. This process distorts and, without treatment, can potentially destroy central vision and may progress to blindness.

About 4DMT

4DMT is a leading late-stage biotechnology company advancing durable and disease-targeted therapeutics with potential to transform treatment paradigms and provide unprecedented benefits to patients. The Company's lead product candidate 4D-150 is designed to be a backbone therapy forming the foundation of treatment of blinding retinal vascular diseases by providing multi-year sustained delivery of anti-VEGF (aflibercept and anti-VEGF-C) with a single, safe, intravitreal injection, which substantially reduces the treatment burden associated with current bolus injections. The Company's lead indication for 4D-150 is wet age-related macular degeneration, which is currently in Phase 3 development, and second indication is diabetic macular edema. The Company's second product candidate is 4D-710, which is the first known genetic medicine to demonstrate successful delivery and expression of the CFTR transgene in the lungs of people with cystic fibrosis after aerosol delivery. 4D Molecular Therapeutics™, 4DMT™ Therapeutic Vector Evolution™, and the 4DMT logo are trademarks of 4DMT.

All of the Company's product candidates are in clinical or preclinical development and have not yet been approved for marketing by the U.S. Food and Drug Administration or any other regulatory authority. No representation is made as to the safety or effectiveness of the Company's 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, clinical development plans, and success of clinical trials for 4D-150, including the planned timeline for clinical trial enrollments. 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 filed on August 11, 2025, as well as any subsequent filings with the Securities and Exchange Commission. In addition, any forward-looking statements represent 4D Molecular Therapeutics' current views and should not be relied upon as representing its views as of any subsequent time. 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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