Source: *4D Molecular Therapeutics, Inc.*

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4DMT Presents Additional Positive Interim Data from Intravitreal 4D-150 Phase 1/2 PRISM Clinical Trial in Patients with Wet AMD at ASRS 2023

- *Dose response demonstrated in favor of highest tested dose of 3E10 vg/eye, including 100% reduction in supplemental anti-VEGF injections (4 of 4 evaluable patients injection-free) and a clinically meaningful reduction in mean central subfield thickness (CST) at 36 weeks in patient population with high anti-VEGF need*
- *Assessment of outcomes beyond 36 weeks in the 3E10 vg/eye dose cohort showed a durable reduction in supplemental anti-VEGF injections, with 3 of 4 evaluable participants remaining injection-free beyond one year and one patient remaining injection-free during a maximum follow-up of 80 weeks; no change in safety profile observed*
- *Lower doses (1E10, 6E9 vg/eye) also highly active, with 5 of 10 patients requiring zero or one supplemental anti-VEGF injections and a 71% reduction in mean annualized supplemental anti-VEGF injection rate through 36 weeks*
- *Intravitreal 4D-150 remained well tolerated at all doses in all patients, with no Grade ≥1 inflammatory cells, hypotony, dose-limiting toxicities, or treatment-related serious adverse events (SAE) during follow-up through 36 weeks*
- *Phase 2 Dose Expansion (N=50) initial interim efficacy and safety data presentation expected at medical conference in H1 2024*

EMERYVILLE, Calif., July 29, 2023 (GLOBE NEWSWIRE) -- 4D Molecular Therapeutics (Nasdaq: FDMT, 4DMT or the Company), a clinical-stage biotherapeutics company harnessing the power of directed evolution for targeted genetic medicines, today announced additional positive interim clinical data from the Phase 1 Dose Exploration stage (N=15) of the 4D-150 Phase 1/2 PRISM clinical trial for patients with wet age-related macular degeneration (wet AMD). The data were presented at the 2023 American Society of Retinal Specialists (ASRS) Annual Meeting in Seattle, Washington on Saturday, July 29 by Christine N. Kay, M.D., a vitreoretinal surgeon and the Director of Electrophysiology, Retinal Genetics, and Clinical Trials at Vitreoretinal Associates in Gainesville, Florida. 4D-150 is a potentially transformative genetic medicine that utilizes 4DMT's evolved and customized retinotropic R100 vector, while targeting four VEGF family members. 4D-150 is being developed as a single dose, routine outpatient intravitreal therapy with the goal of reducing treatment burden and maintaining efficacy in patients with wet AMD and diabetic macular edema (DME).

"We are pleased to see continued evidence of a favorable safety profile and clinical activity, including clinically meaningful reductions in anti-VEGF treatment burden at all dose levels of intravitreal 4D-150 in these high anti-VEGF need patients," said Robert Kim, M.D., Chief Medical Officer of 4DMT. "In addition, 3 of 4 evaluable patients in the 3E10 vg/eye cohort are now anti-VEGF injection-free at one year and beyond, with up to 80 weeks of follow-up, demonstrating encouraging initial evidence of long-term durability. We look forward to continuing to follow these patients and presenting initial interim Phase 2 Dose Expansion data in H1 2024."

"The results announced today continue to support 4D-150's favorable overall clinical profile as a potentially transformative durable intravitreal therapeutic in VEGF-driven large market ophthalmologic diseases," said David Kirn, M.D., Co-founder and Chief Executive Officer of 4DMT. "We look forward to continuing to build upon 4D-150's strong profile to date in the randomized Phase 2 stage of the PRISM trial in patients with wet AMD and the Phase 2 SPECTRA trial in patients with DME. In addition, we intend to continue to rapidly advance our preclinical large market ophthalmology pipeline, including 4D-175 for geographic atrophy, leveraging the same clinically validated retinotropic R100 vector."

4D-150 Phase 1 Dose Exploration Interim Data Summary:

- 15 patients received a single intravitreal dose of 4D-150 across three dose cohorts (3E10, 1E10, and 6E9 vg/eye; n=5 each)
- Enrolled participants had a high need for anti-VEGF therapy, with mean annualized injection rates ranging from 8 to 11 across cohorts prior to 4D-150 treatment
- As of the data cutoff date of July 3, 2023, all patients had completed follow-up through at least 36 weeks
    - 4D-150 was well tolerated, with no reported Grade ≥1 inflammatory cells and no hypotony, dose-limiting toxicities, or treatment-related serious adverse events
    - All three doses demonstrated clinical activity in the study, with evidence of a dose response favoring the 3E10 vg/eye dose:

4D-150 clinical efficacy endpoints for evaluable patients in all three cohorts (n=14) at 36 weeks							
Dose Cohort	**Mean Prior Annualized Anti-VEGF Injection Rate**	**Post 4D-150 Treatment**	**Anti-VEGF Injection-Free**	**≤1 Anti-VEGF Injection**	**Mean Change in Annualized Anti-VEGF Injection Rate**	**Mean ±SE CST (µm)**	**Mean ±SE BCVA (Letters)**
3E10 vg/eye[a]	**11**		**4 of 4 (100%)**	**4 of 4 (100%)**	**(-)100%**	**Improved -74 ±59 (n=4)**	**Stable +2.0 ±1.5 (n=3)[b]**
6E9 & 1E10 vg/eye (combined)	**9**		**3 of 10 (30%)**	**5 of 10 (50%)**	**(-)71%**	**Stable +6 ±24 (n=10)**	**Stable +0.7 ±1.9[c] (n=9)**
1E10 vg/eye	8		2 of 5 (40%)	2 of 5 (40%)	(-)64%	Stable +35 ±32 (n=5)	Stable +3.6 ±1.6 (n=5)
6E9 vg/eye	9		1 of 5 (20%)	3 of 5 (60%)	(-)77%	Stable -23 ±34 (n=5)	Stable -3.0 ±3.1[d] (n=4)

Data cutoff as of July 3, 2023
Excludes patients with progressive cataract at time of BCVA measurement:

[a]Excludes Patient 5 (not Phase 2 BCVA-eligible and not evaluable)
[b]Mean ±SE of -0.3 ±2.2 when including all patients (n=4). Patient's BCVA has since improved post-cataract surgery.
[c]Mean ±SE of -0.5 ±2.1 when including all patients (n=10). Patient's BCVA has since improved post-cataract surgery.
[d]Mean ±SE of -4.6 ±2.9 when including all patients (n=5). Patient's BCVA has since improved post-cataract surgery.

- Initial durability demonstrated in 3E10 vg/eye dose cohort, with 3 of 4 evaluable patients injection-free beyond 1 year
    - First patient in 3E10 vg/kg cohort remains supplemental anti-VEGF injection-free at 80 weeks follow-up (longest on study) (data cutoff July 3, 2023)
    - A single patient (1 of 4 evaluable patients in the 3E10 vg/eye cohort) met supplemental injection criterion beyond 36 weeks at a single timepoint. Patient was well controlled on the basis of both BCVA and CST prior to developing a retinal hemorrhage, which has resolved with no significant change from baseline in BCVA (reported as "not related" to the test article)

Future Milestones for 4D-150 & Large Market Ophthalmology Portfolio with the Proprietary R100 Intravitreal Vector

- Initial interim efficacy data from Phase 2 Dose Expansion expected to be presented at a medical conference in H1 2024
- Expect to provide update regarding Phase 3 pivotal trial plans in Q1 2024 after initial discussion with FDA, which is anticipated in Q4 2023
- Expect to enroll first patient in Phase 2 SPECTRA clinical trial for DME in Q3 2023
- Program update for 4D-175 in geographic atrophy expected in Q4 2023

Data presented from 2023 ASRS Annual Meeting is available on the 4D Molecular Therapeutics website under Scientific Presentations: https://4dmoleculartherapeutics.com/technology/scientific-presentations.

About 4D-150 for Wet AMD

4D-150 is comprised of our customized and evolved intravitreal vector, R100, and a transgene payload that expresses both aflibercept and a VEGF-C inhibitory RNAi. This dual transgene payload inhibits 4 angiogenic 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 created this platform utilizing principles of directed evolution, a Nobel Prize-winning technology. 4D-150 is designed for single, low-dose intravitreal delivery.

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. 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.

About 4DMT

4DMT is a clinical-stage biotherapeutics company harnessing the power of directed evolution for genetic medicines targeting large market diseases. 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 customized 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. The 4DMT customized 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 AATLD.

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.

4D Molecular Therapeutics™, 4DMT™, Therapeutic Vector Evolution™, and the 4DMT logo are trademarks of 4DMT.

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-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.

Contacts:

Media:

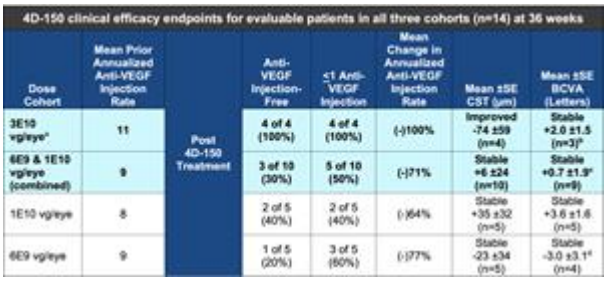
Katherine Smith
Evoke Canale
Katherine.Smith@evokegroup.com

Investors:

Julian Pei
Head of Investor Relations and Corporate Communications
Investor.Relations@4DMT.com
267-644-5097

A photo accompanying this announcement is available at https://www.globenewswire.com/NewsRoom/AttachmentNg/3a6dc3c8-0fb9-4cbb-9dc0-f8627fa4f9d0

Attachments:

- 

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