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

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- *Intravitreal 4D-150 was well-tolerated with no inflammation in 14 of 15 patients and only trace mixed cells at a single timepoint in one patient; no dose-limiting toxicities, treatment-related serious adverse events (SAE) or hypotony reported across all three dose cohorts with follow-up of 24 – 64 weeks*
- *Dose response demonstrated in favor of high dose 3E10 vg/eye, including superior reduction in supplemental anti-VEGF injections and mean central subfield thickness (CST) reduction*
- *80% of patients in the 3E10 vg/eye high dose cohort did not require supplemental anti-VEGF injections through 36 weeks following a single intravitreal dose of 4D-150*
- *Clinically-meaningful improvement in mean CST of -92 µm at 36 weeks, and stable best corrected visual acuity (BCVA), following a single 3E10 vg/eye intravitreal dose of 4D-150*
- *Phase 2 Dose Expansion stage of PRISM trial (n=50 patients) more than 50% enrolled; enrollment completion expected Q3 this year*
- *Company to host live webcast today at 8:00 a.m. ET with retinal expert Arshad Khanani, M.D., M.A., FASRS*

EMERYVILLE, Calif., April 27, 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 positive interim clinical data from the Phase 1 Dose Exploration stage (three doses, n=15) of the 4D-150 Phase 1/2 PRISM clinical trial for wet age-related macular degeneration (wet AMD). 4D-150, a novel genetic medicine that utilizes 4DMT's evolved and customized R100 vector for intravitreal delivery to the retina, was well-tolerated at all doses. All doses demonstrated clinical activity, including a reduction in anti-VEGF injection burden, stable or improved retinal edema and thickness, and stable visual acuity. A dose response was demonstrated in favor of the high dose 3E10 vg/eye. Interim data from the study will be presented today in an oral presentation titled, "Interim results for the Phase 1/2 PRISM Trial evaluating 4D-150, a dual-transgene intravitreal genetic medicine in individuals with neovascular (wet) age-related macular degeneration," at the 2023 Association for Research in Vision and Ophthalmology (ARVO) Annual Meeting in New Orleans, LA at 11:30 a.m. ET.

"4D-150 is the first retinal genetic medicine that is designed to inhibit all four VEGF-related molecules that drive disease in wet AMD," said Robert Kim, M.D., Chief Medical Officer. "We are impressed by the clinical activity reported today, especially in the high dose cohort where 80% of patients did not require anti-VEGF injections through 36 weeks. We continue to execute relentlessly on enrolling the Phase 2 Dose Expansion stage of the PRISM trial in an effort to advance this potentially transformative therapy into late-stage development as soon as possible."

Arshad M. Khanani, M.D., M.A., FASRS, Managing Partner and Director of Clinical Research at Sierra Eye Associates, Clinical Associate Professor at University of Nevada, Reno, and a Principal Investigator in the 4D-150 PRISM clinical trial, added, "I continue to be encouraged by the tolerability and clinical activity of a single intravitreal injection of 4D-150 in high-need patients with wet AMD. Given the stabilization or improvements seen in retinal anatomy and maintenance of vision up to 9 months, I believe 4D-150 has the potential to be a transformative treatment for patients with wet AMD and to greatly reduce their treatment burden."

"These clinical data on 4D-150 represent another important milestone for patients with wet AMD and for 4DMT," said David Kirn, M.D., Co-founder and Chief Executive Officer of 4DMT. "We believe these results further validate the potential of our intravitreal R100 vector, for the safe delivery of effective transgene payloads at relatively low doses, and our Therapeutic Vector Evolution platform. These promising interim clinical data and excellent progress on Phase 2 enrollment further demonstrate the power of our product design and development engine."

Phase 1/2 PRISM Clinical Trial for Patients with Wet AMD: Design and Baseline Characteristics

- Phase 1 Dose Exploration stage (n=15; three dose cohorts of 5 patients each at 3E10, 1E10 and 6E9 vg/eye) followed by a randomized Phase 2 Dose Expansion stage (n=50, randomized 2:2:1 to 3E10 vg/eye or 1E10 vg/eye of 4D-150 or aflibercept)

- Patients enrolled in the Dose Exploration stage of the trial were patients with high need of anti-VEGF therapy with a mean annualized injection rate between 8 and 11 per cohort in the 12 months prior to 4D-150 treatment across all three dose cohorts
- Patients received a single intravitreal dose of 4D-150. Topical corticosteroids were administered at tapering doses over 20 weeks
- All data below are as of the data cutoff date of April 3, 2023

Phase 1 Dose Exploration Interim Safety Data

- A single intravitreal dose of 4D-150 was well-tolerated through 24 weeks in all 15 patients:
    - 14 of 15 patient had no inflammation reported; one patient had a single episode of asymptomatic trace mixed vitreous cells that resolved without intervention
    - 14 of 15 patients completed the protocol-mandated 20-week topical corticosteroid taper and did not receive further steroids; a single patient continued beyond 20 weeks by the treating physician for asymptomatic non-inflammatory trace pigmented cells
    - No dose-limiting toxicities, 4D-150-related serious adverse events (SAE) or hypotony reported
- Patients in the 3E10 vg/eye high dose cohort had extended follow-up beyond 24 weeks (n=5, with a range of 36-64 weeks); there was no inflammation, and no 4D-150-related SAEs or dose-limiting toxicities reported during this time period

Phase 1 Dose Exploration Interim Clinical Activity Data

- All three doses demonstrated clinical activity in the study, with the highest dose at 3E10 vg/eye demonstrating the greatest level of activity at 24 weeks:

4D-150 clinical efficacy endpoints for all cohorts (n=15) at 24 weeks (maximum follow-up for all patients)						
Dose Cohort	**Mean Prior Annualized Anti-VEGF Injection Rate**		**Anti-VEGF Injection-Free**	**Mean Change in Annualized Anti-VEGF Injection Rate**	**Mean ±SE CST (µm)**	**Mean ±SE BCVA (Letters)**
3E10 vg/eye	**11**	**Post 4D-150 Treatment**	**4 of 5 (80%)**	**(-)84%**	**Improved -78** ±49	**Stable** -4.0 ±4.5
1E10 vg/eye	8		2 of 5 (40%)	(-)68%	Stable +38 ±37	Stable +1.4 ±3.5
6E9 vg/eye	9		2 of 5 (40%)	(-)80%	Stable +3 ±25	Stable -1.2 ±4.2

- In the long-term follow up for the 3E10 vg/eye cohort at 36 weeks (n=5):
    - 4 of 5 patients (80%) remained supplemental aflibercept injection-free
    - Mean CST showed clinically-meaningful improvement (-92 µm)
    - Mean BCVA remained stable
- Of 3 patients with follow-up beyond 36 weeks, 2 of 3 patients remained injection-free at 56-64 weeks; in all 3 patients at last follow-up between 56-64 weeks, CST was improved

Phase 1 Dose Exploration Interim Aflibercept Biomarker Data

- 4D-150-mediated expression of the aflibercept transgene protein was demonstrated in the

aqueous humor (AH) of the eye at 12 weeks after 4D-150 injection in 91% (10 of 11) of patient samples evaluated to date[1]

- Mean AH aflibercept concentrations dose-related, and predicted to be in therapeutic range for all cohorts

1) Injection-free at 12 weeks, sample results available at time of data cutoff

Future Directions for 4D-150 & Large Market Ophthalmology Portfolio with the R100 Vector

- 4D-150 in wet AMD:
  - Randomized Phase 2 Dose Expansion (n=50, randomized 2:2:1 to 3E10 vg/eye or 1E10 vg/eye of 4D-150 or aflibercept) of the PRISM trial is more than 50% enrolled
  - Enrollment completion expected in Q3 2023 (previously Q4 2023)
  - Initial interim Phase 2 data expected in H1 2024
- 4D-150 in Diabetic Macular Edema (DME): Randomized Phase 2 SPECTRA clinical trial evaluating 4D-150 in DME
  - First patient enrollment in Phase 2 SPECTRA clinical trial expected in Q3 2023
  - Initial data expected in 2024
- 4D-175 for geographic atrophy (R100 + short-form human complement factor H): Program update in Q4 2023

Webcast Information:

4D Molecular Therapeutics will host a webcast today, Thursday, April 27, 2023 at 8:00 a.m. Eastern Time to discuss clinical data and development plans. Dr. Arshad Khanani will also join today's webcast.

Title:	4D-150 Phase 1/2 PRISM Interim Clinical Data Webcast and Q&A
Date/Time:	Thursday, April 27, 2023, 8:00 a.m. ET
Registration:	Link

An archived copy of the webcast will be available for up to one year by visiting the “Investors & Media” section of the 4DMT website at https://ir.4dmoleculartherapeutics.com/events.

About 4D-150 for Wet AMD and DME

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 PIGF. 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 and DME

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.

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. DME is characterized by swelling in the macula (central retina) 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 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

(Fabry disease cardiomyopathy). 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.

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; the timing and status of clinical trial enrollment and data being available for 4D-150, with respect to the PRISM and SPECTRA clinical trials; and the timing of program updates being available for 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 Annual Report on Form 10-K, 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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