4DMT Announces Positive Phase 2 PRISM Interim Results for Intravitreal 4D-150 in a Broad Wet AMD Population Affirming Favorable Safety Profile and Robust Clinical Activity

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- *Robust reduction in anti-VEGF injection treatment burden through Week 24 achieved in 30 patients at planned Phase 3 dose (3E10 vg/eye) with 89% reduction in annualized injection rate; 93% of patients received 0 or 1 injection and 77% were injection-free*
- *Improvement in mean best corrected visual acuity (BCVA) from baseline through Week 24 achieved at 3E10 vg/eye dose (+4.2 letters); dose response in favor of 3E10 vg/eye dose demonstrated (+5.7 letters vs low dose)*
- *3E10 vg/eye dose demonstrated sustained and greater anatomic control without fluctuations*
- *Favorable safety profile confirmed in 139 patients treated to date with 4D-150 across wet age-related macular degeneration (wet AMD; PRISM trial) and diabetic macular edema (DME; SPECTRA trial)*
- *No significant inflammation reported in 51 patients treated to date with 3E10 vg/eye dose and topical corticosteroid regimen*
- *Company to host live webcast today at 6:30 a.m. ET with Arshad M. Khanani, M.D., M.A., FASRS, lead Principal Investigator in the PRISM clinical trial*

EMERYVILLE, Calif., July 17, 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 positive initial interim 24-week landmark data from the Population Extension cohort of the PRISM Phase 2 Clinical Trial, which evaluated intravitreal 4D-150 in a broad wet AMD patient population. The data were presented by Raj K. Maturi, M.D., in an oral presentation titled, “Phase 2 Population Extension Cohort in the PRISM Trial Evaluating 4D-150 in Adults with Neovascular Age-related Macular Degeneration,” at the American Society of Retina Specialists (ASRS) Annual Scientific Meeting held in Stockholm, Sweden.

“The positive interim data presented today, coupled with previously reported data from the Dose Expansion cohort of high treatment burden patients, further reinforce our planned regulatory pathway demonstrates 4D-150’s broad potential to treat and preserve vision for the long term for all patient populations with wet AMD,” said David Kirn, M.D., Co-founder and Chief Executive Officer of 4DMT. “In addition, the growing safety and efficacy database for 4D-150 continues to validate the product candidate’s potential as a pipeline-in-a-product, with multiple potential multi-billion ophthalmology market opportunities including wet AMD, DME and diabetic retinopathy (DR). We anticipate data readouts from the SPECTRA study in DME in Q4 this year, which we believe will have potential readthrough to DR.”

“The initial benefits of the current treatment paradigm of repeated bolus anti-VEGF injections are not maintained long-term in wet AMD patients due to undertreatment and fluctuations in retinal thickness, leading to vision loss over time,” said Robert Kim, M.D., Chief Medical Officer. “The data presented on 4D-150 continue to show its promise as a potentially safe, routine and one-time intravitreal treatment with the long-term objective to preserve vision for millions of wet AMD patients, regardless of their treatment burden or disease severity. We continue to work closely with the FDA and EMA, under our RMAT and PRIME designations, to finalize our Phase 3 clinical trial design that we expect to share in September 2024.”

“Patients suffering from wet AMD face a substantial treatment burden, requiring frequent intravitreal injections throughout their lives, which significantly impacts quality of life not only for the patients themselves but also for their families and caregivers,” 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. “The PRISM Phase 2 data at 24 weeks across multiple populations, and long-term data collected over two and a half years, confirms 4D-150’s potential to significantly reduce the treatment burden and maintain vision through a safe, single intravitreal injection. I look forward to contributing to the Phase 3 trial, and to further advancing this treatment option for individuals with wet AMD.”

4D-150 Phase 2 PRISM Population Extension Cohort Background & Baseline Characteristics: Broad Range of Disease Activity and Prior Anti-VEGF Treatment

The cohort evaluated 4D-150 in wet AMD patients with broad disease activity (no minimum or maximum central subfield thickness (CST)) and prior anti-VEGF treatment (1-6 anti-VEGF injections in the prior 12 months).

The trial enrolled 45 patients at two dose level arms of 4D-150:

- 30 at 3E10 vg/eye (planned Phase 3 dose)
- 15 at 1E10 vg/eye (low dose control)

The dose arms enrolled in the cohort were generally well-balanced. Mean CST was 329 µm and mean number of actual injections in the prior 12 months was 4.4.

Phase 2 PRISM Population Extension Cohort Topline Interim 24-Week Landmark Results (Data cutoff: June 24, 2024)

- 4D-150 was safe and well tolerated:
    - Intraocular inflammation analysis:
        - Planned Phase 3 dose (3E10 vg/eye)
            - No anterior chamber inflammation (30 of 30 patients)
            - No significant vitreous inflammation (30 of 30 patients; trace vitreal cells noted in one patient)
            - All 30 patients completed local steroid prophylaxis on schedule and did not resume

        - Low dose (1E10 vg/eye)
            - No significant anterior chamber inflammation (15 of 15 patients; trace anterior chamber cells noted in one patient)
            - No vitreous inflammation in 14 of 15 patients, one patient with mild to moderate inflammation (1 of 45 total, ~2% overall); vitreous cells also observed in untreated fellow eye
    - No 4D-150–related serious adverse events (SAEs) or study eye SAEs
    - No hypotony, retinal vasculitis, choroidal effusions, retinal artery occlusions
- 24-week landmark analysis for key efficacy endpoints:
    - Planned Phase 3 dose (3E10 vg/eye) – robust anti-VEGF treatment reduction:
        - 89% reduction in mean annualized injection rate
        - 93% received 0 or 1 injection
        - 77% injection-free; dose response evident (60% on low dose arm)
    - Visual acuity and retina anatomic outcomes:
        - Improved BCVA in 3E10 vg/eye arm patients: +4.2 Early Treatment Diabetic Retinopathy Study (ETDRS) letter improvement from baseline overall, and +4.7 letter improvement observed for injection-free patients (improvement independent of number of prior anti-VEGF doses)
        - BCVA dose response demonstrated in favor of 3E10 vg/eye dose: +5.7 letter improvement in BCVA for patients in planned Phase 3 dose arm vs low dose arm
        - CST: sustained and greater anatomic control without fluctuations for the 3E10 vg/eye dose arm; improvement (decrease) in CST from baseline greater in supplemental injection-free patients than in overall population (-32 vs -9 µm)

PRISM Phase 1 Long-Term Follow-Up Update (Data cutoff: June 24, 2024)

- All three Phase 1 patients treated with 3E10 vg/eye previously reported as injection-free beyond 52 weeks remain injection-free through ~2 to 2.5 years of follow-up
- Mean BCVA remains unchanged from baseline through ~2 years (+1 letter from baseline)
- Mean CST remains stable, without fluctuations, and decreased from baseline through ~2 years (-110 microns from baseline)
- Safety results maintained in all 15 patients treated to the cutoff date (up to 2.5 years of follow-up) with no new inflammation and no change in steroid status

4D-150 Overall Safety Update Across Wet AMD and DME Patients

- 4D-150 continues to be safe and well tolerated across all patients dosed to date (n=139) in both PRISM (wet AMD, n=117) and SPECTRA (DME, n=22) clinical trials
- 51 patients treated in the PRISM and SPECTRA studies at 3E10 vg/eye dose and topical corticosteroid prophylactic regimen had no significant inflammation, hypotony, retinal vasculitis, choroidal effusions or retinal artery occlusions with up to 2.5 years of follow-up; no recurrent inflammation post steroid taper
- 22 DME patients treated in the SPECTRA study had no inflammation, hypotony, retinal vasculitis, choroidal effusions or retinal artery occlusions with up to 36-weeks of follow-up; completed topical corticosteroid prophylactic regimen on schedule and did not resume

Planned Next Steps and Upcoming Milestones for 4D-150

- Phase 3 planning:
    - Phase 3 clinical trial alignment ongoing with FDA and EMA under RMAT and PRIME designations
    - Update on final Phase 3 clinical trial design expected in September 2024
    - First Phase 3 clinical trial initiation expected in Q1 2025
- PRISM wet AMD Phase 2 additional landmark analyses:
    - 52-week landmark analyses for both 1) severe disease activity/high treatment burden (Dose Expansion) & 2) broad wet AMD disease activity (Population Extension) cohorts expected in February 2025
- SPECTRA DME Phase 2 initial landmark analyses:
    - Interim 24-week landmark analysis from Part 1 Dose Confirmation cohort (n=22) expected in Q4 2024

Corporate Webcast Details

Title:	4D-150 Initial Interim 24-week Landmark Analysis from PRISM Phase 2 Population Extension Cohort in Broad Wet AMD
Date/Time:	Wednesday, July 17, 2024 at 6:30 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: https://ir.4dmoleculartherapeutics.com/events.

The presentation from the ASRS Annual Scientific Meeting will also be available on the 4DMT website: https://4dmoleculartherapeutics.com/pipeline/#posters-and-publications

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 (macular neovascularization or MNV) grow into the macula, the central area of the retina. As a consequence, MNV 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 4D-150 for Wet AMD

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 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 and market potential of 4DMT's product candidates, as well as the plans, announcements, and related timing for the clinical development of and regulatory interactions regarding 4D-150 and 4D-150's potential to be a pipeline-in-a-product. 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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