UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of the Securities Exchange Act of 1934

Date of Report (Date of earliest event reported): January 9, 2023

4D Molecular Therapeutics, Inc.
(Exact name of registrant as specified in its charter)

Delaware	**001-39782**	**47-3506994**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(IRS Employer Identification No.)**

5858 Horton Street #455
Emeryville, CA 94608
(Address of principal executive offices)(Zip Code)

Registrant's telephone number, including area code: (510) 505-2680

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of each class	Trading Symbol(s)	Name of each exchange on which registered
Common Stock, $0.0001 par value per share	FDMT	NASDAQ Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 8.01 Other Events.

On January 9, 2023, 4D Molecular Therapeutics, Inc. ("4DMT") reported product pipeline portfolio updates and preclinical product candidate additions for its large market ophthalmology and pulmonology programs, as well as clinical data and program updates for its 4D-310 Fabry disease program.

Ophthalmology Product Candidate Portfolio

4D-150 for the Intravitreal Treatment of Patients with Wet Age-Related Macular Degeneration ("wet AMD") and Patients with Diabetic Macular Edema ("DME")

Filed IND Application for Phase 2 SPECTRA Clinical Trial with Intravitreal 4D-150 in Patients with DME:

4DMT filed an Investigational New Drug ("IND") Application for 4D-150 in patients with DME in December 2022, following pre-IND correspondence and alignment with the U.S. Food and Drug Administration ("FDA"). The Phase 2 SPECTRA clinical trial design consists of a Dose Confirmation stage followed by a masked Dose Expansion stage in which patients will be randomized to receive a single intravitreal injection at one of two dose levels of 4D-150 or aflibercept in a 1:1:1 ratio (n=54 patients). The doses to be evaluated in DME are expected to be similar to those used in the 4D-150 wet AMD clinical trial. 4DMT expects to initiate enrollment in the third quarter of 2023.

Initiated Randomized Phase 2 of PRISM Clinical Trial of Intravitreal 4D-150 in Patients with Wet AMD:

4DMT also initiated in January 2023 the randomized Phase 2 stage of the Phase 1/2 PRISM clinical trial of 4D-150 in patients with wet AMD. Patients will be randomized in masked fashion to receive a single intravitreal injection at one of two dose levels of 4D-150 (3E10 and 1E10 vg/eye) or aflibercept in a 2:2:1 ratio (n=50 patients).

Expanded Portfolio with Preclinical Product Candidate 4D-175 for Geographic Atrophy ("GA"):

Preclinical development was initiated for a new product candidate designed for single dose intravitreal treatment of patients with GA. The GA product candidate will utilize 4DMT's proprietary R100 intravitreal vector currently used in the wet AMD and DME programs, and a transgene payload that addresses a complement pathway target.

GA is a highly prevalent disease with significant unmet medical need. It is estimated that there are over one million individuals with GA in the United States according to published data. There are no disease modifying therapies approved for GA to date.

4DMT anticipates that development and manufacturing activities will benefit from prior clinical experience and GMP manufacturing of three other R100-based ophthalmology product candidates that have been dosed in ophthalmology patients with wet AMD, X-Linked Retinitis Pigmentosa ("XLRP") and choroideremia.

Program Updates on Rare Disease Product Candidates 4D-125 for XLRP and 4D-110 for Choroideremia:

Enrollment of the Phase 1/2 clinical trials for 4D-125 and 4D-110 was completed in the fourth quarter of 2022 with 14 patients having been treated with 4D-125, and 13 with 4D-110. The safety and tolerability profiles for both product candidates remain unchanged from prior data releases. 4DMT will continue to follow these patients for 24 months to assess the magnitude and durability of key imaging endpoint changes in evaluable patients. 4DMT anticipates providing program and clinical data updates on 4D-125 for XLRP and 4D-110 for Choroideremia in 2024.

Pulmonology Product Portfolio

4D-710 for the Aerosol Treatment of Patients with Cystic Fibrosis ("CF") Lung Disease

Treated First Patient in High Dose Cohort on Phase 1/2 Clinical Trial with Aerosol Delivered 4D-710 in Patients with Cystic Fibrosis Lung Disease that is Not Amenable to Treatment with Cystic Fibrosis Transmembrane Conductance Regulator ("CFTR") Modulator Therapy:

Following three patients dosed in cohort 1 (1E15 vg), the first patient in the high dose cohort (2E15 vg) was treated in December 2022 and no 4D-710 related adverse events were reported through Day 28.

Expanded Portfolio with Initiation of Preclinical Research and Development of 4D-710 in Combination with CFTR Modulators:

Preclinical research was initiated with the combination of 4D-710 with CFTR modulator therapy to support development of 4D-710 in the approximately 85% of CF patients amenable to CFTR modulator therapy.

Expanded Portfolio with Addition of Preclinical Product Candidate 4D-725 for Alpha-1 Antitrypsin Deficiency:

Alpha-1 Antitrypsin Deficiency is a prevalent disease, affecting approximately 200,000 individuals in the United States and Europe according to the NIH. Despite there being approved therapies, there remains a significant unmet medical need.

Preclinical development was initiated for a new product candidate designed for single dose aerosol treatment of patients with alpha-1 antitrypsin lung disease; this product candidate utilizes 4DMT's proprietary A101 aerosol vector currently used in the CF program and expresses a genetically-validated transgene. 4DMT anticipates that development and manufacturing activities will benefit from prior clinical experience and GMP manufacturing of the A101-based 4D-710 product candidate that has been dosed in CF patients.

4D-310 for Fabry Disease Cardiomyopathy

Interim 4D-310 INGLAXA Phase 1/2 Clinical Trials Data in Patients with Fabry Disease:

Two clinical trials, one being conducted in the United States and one being conducted in Taiwan and Australia (Asia-Pacific) are evaluating a single intravenous administration of 4D-310 in patients with classic or late-onset Fabry disease. Six patients have been treated at a dose of 1E13 vg/kg with a corticosteroid immunomodulation regimen. There were 3 instances of atypical hemolytic uremic syndrome ("aHUS") across the 2 studies; these were the only treatment-related serious or greater than or equal to Grade 3 adverse events reported. The aHUS process resolved within approximately 2 to 4 weeks in all 3 patients. One episode of aHUS qualified as a grade 4 dose-limiting toxicity and required temporary hemodialysis in a 69-year-old man with underlying kidney dysfunction; the other two patients did not receive dialysis. No other clinically significant toxicities were reported, including no infusion-related reactions, and no clinically significant cardiac or liver toxicities (three patients had transient asymptomatic Grade 1 transaminase increases).

Cardiac Functional, Imaging, and Biopsy Data Promising in Patients Based on Evaluable Data to Date:

Cardiac clinical endpoint assessments (functional and imaging) were performed over time, and the Asia-Pacific trial also included a single early post-treatment cardiac biopsy evaluation. Cardiac clinical endpoint data (MRI, echocardiography, cardiopulmonary exercise testing ("CPET") and QOL assessment) from evaluations at baseline and 12 months after treatment were assessed. In addition, where available, patient results were compared with historical data from patients who received enzyme replacement therapy over 12 months. Three patients are evaluable for 12 month cardiac data (all on U.S. trial) as of the data cut-off date of December 5, 2022 (see Table below). All three patients demonstrated improvement in multiple cardiac endpoints.

One patient underwent cardiac biopsy at week 6 (n=1 in Asia-Pacific trial). All sample sections were positive for 4D-310 delivery by qPCR and widespread transgene expression was demonstrated at both the RNA level by RT-qPCR and ISH and protein levels by IHC.

Cardiac Clinical Endpoint Methods and Results

- Cardiopulmonary Exercise Testing to assess exercise function by peak VO2 (FDA-recommended primary endpoint): Improvement in two of three patients
- KCCQ QOL to assess cardiomyopathy-associated quality-of-life (FDA-recommended primary endpoint): Improvement in two of two patients abnormal at baseline; third patient remained stable at 100% through 12 months
- Echocardiography to assess left ventricular function by global longitudinal strain: Improvement in three of three patients (FDA-recommended supportive clinical trial endpoint)
- Cardiac MRI to assess substrate in heart: Improvement in two of two patients (one pending)

4D-310 Cardiac clinical endpoints results summary (data cut-off date of December 5, 2022):

Pts (U.S. Trial)	Native T1 (CMR) (ms)		GLS (Echo)		Peak VO2 (CPET) (mL/kg/min)		Cardiac QoL (KCCQ-23)		
	Baseline	Week 52	Baseline	Week 52	Baseline	Week 52	Baseline	Week 52 (Overall Summary Score)	Week 52 (Clinical Summary Score)
1	Abnormal	**Improved (+30.6)**	Borderline	**Improved (-2.5%)**	Abnormal	**Improved (+2.0)**	Normal	**Stable 100%**	**Stable 100%**
2	Abnormal	**Improved (+9.1)**	Normal	**Improved (-1.1%)**	Abnormal	**Improved (+7.0)**	Abnormal	**Improved (+11.7)**	**Improved (+5.7)**
3	Abnormal	*Pending*	Borderline	**Improved (-3.3%)**	Abnormal	-2.2	Abnormal	**Improved (+7.3)**	**Improved (+10.4)**
ERT natural history		Worsened (-4.0)[1]		Worsened (+1.1%)[1]		Worsened (-1.8)[2]		n.a.	n.a.

- *Minimal detectable difference (MDD): native T1 (29 ms); GLS (1.5%); Borderline: GLS range of -16 to -18%*
- *Minimal clinically important difference (MCID): peak VO2 (1.5 mL/kg/min); KCCQ (summary scores 5 points)*
- *References: 1. Nordin et al. Circ Cardiovasc Imaging 2019:e009430; 2. Lobo, Internal Medicine Journal 2008;38:407*

Alignment with FDA on Pivotal Clinical Trial Primary Endpoints for 4D-310 for Fabry Disease Cardiomyopathy:

4DMT proposed, and FDA communicated alignment with, the use of the following endpoints in a potential pivotal trial:

- Primary endpoint: Change from baseline at 12 and 24 months in cardiopulmonary exercise testing (peak VO2).
- Primary endpoint: Kansas City Cardiomyopathy Questionnaire (“KCCQ”; quality of life).
- Supportive endpoint: Left ventricular function as assessed by global longitudinal strain on echocardiography.

Next Steps for 4D-310 Clinical Development:

As of January 2023, 4DMT does not plan to enroll additional patients in the current Fabry disease clinical trials. The 4D-310 program will be evaluated in the second half of 2023 after 12-month clinical data are obtained on all six of the currently enrolled patients, including on-going safety and cardiac endpoints for a potential pivotal trial as recommended by the FDA: peak VO2 (CPET), Quality-of-life (KCCQ) and left ventricular function by global longitudinal strain (echocardiography). 4DMT does not plan to utilize the current corticosteroid regimen with 4D-310 in any future studies it decides to initiate. In parallel with patient followup, 4DMT intends to evaluate its preferred approach of utilizing the rituximab-sirolimus immune inhibition regimen with 4D-310; the rituximab and sirolimus combination is an established clinical regimen to prevent AAV-associated aHUS. 4DMT anticipates that any future clinical development of 4D-310 would be with the rituximab-sirolimus combination under new clinical trial protocol(s) and an amended, or new, IND(s).

Forward Looking Statement

This Current Report on Form 8-K 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, as well as the plans and related timing for the clinical development of and potential data readouts for 4D-150, 4D-310, 4D-710, 4D-125 and 4D-110. 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 Current Report on Form 8-K 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 Current Report on Form 8-K, 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.

SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned thereunto duly authorized.

4D MOLECULAR THERAPEUTICS, INC.

Date: January 26, 2023

By: /s/ August J. Moretti
August J. Moretti
Chief Financial Officer