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): October 25, 2021

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 Number)**

5858 Horton Street #455
Emeryville, California 94608
(Address of principal executive offices, including 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**	**The 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 October 25, 2021, 4D Molecular Therapeutics, Inc. ("4DMT") announced interim clinical data from its Phase 1/2 clinical trial of intravenous 4D-310 in patients with Fabry disease and provided a clinical data update from its on-going Phase 1/2 clinical trial of 4D-110 in patients with choroideremia.

4D-310 for Fabry Disease Interim Clinical Data Summary

The data described below are from 4DMT's ongoing Phase 1/2 dose-escalation and dose-expansion clinical trial assessing intravenous 4D-310, 4DMT's targeted and evolved C102 vector-based product candidate designed for a broad Fabry disease patient population. The primary endpoint of the trial is safety and tolerability. Key secondary endpoints include change from baseline in serum AGA activity and serum lyso-Gb3. The data cutoff date was October 12, 2021.

As of the data cut-off date, three patients with Fabry disease were enrolled, with post-treatment follow-up ranging from six weeks to six months. These patients were enrolled in the 1E13 vg/kg cohort, the lower of two planned dose escalation cohorts: 1E13 vg/kg and 3E13 vg/kg. Prior to dose-escalation, the trial is designed to allow enrollment of an additional 6 patients in the 1E13 vg/kg dose cohort. An oral corticosteroid prophylaxis taper was administered over 10 weeks post-dosing.

Key Baseline Characteristics

All three patients currently enrolled are patients with classic Fabry disease, defined as having AGA activity less than 5% of mean normal in peripheral blood white cells and having one or more clinical characteristics such as acroparesthesia, hypohidrosis, angiokeratoma or cornea verticillata.

Consistent with the classic Fabry disease phenotype, all three patients had serum AGA activity below mean normal at baseline, ranging from 0 to 0.42 nmol/hr/mL (population normal range: 4.44 to 27.42 nmol/hr/mL; population mean normal 9.9 nmol/hr/mL).

All three patients had prior experience on enzyme replacement therapy (ERT). Patients 1 and 3 were enrolled while receiving ERT (ON-ERT). Patient 2 had prior experience with ERT but was not receiving ERT (OFF-ERT) for approximately 13 months prior to dosing. Consistent with prior ERT use, each patient had positive baseline anti-AGA antibody titers:

- Patient 1: Baseline anti-AGA antibody titer 1:947
- Patient 2: Baseline anti-AGA antibody titer 1:99,900
- Patient 3: Baseline anti-AGA antibody titer 1:13,900

4D-310 Preliminary Clinical Activity Summary

Following 4D-310 infusion, mean serum AGA enzyme activity was within, or significantly above, the normal range in all three patients, despite pre-treatment anti-AGA antibody titer positivity in all patients.

Lyso-Gb3 substrate concentrations in serum decreased significantly in Patient 2, who enrolled in the trial OFF-ERT and therefore with an elevated lyso-Gb3 level.

Lyso-Gb3 substrate concentrations in serum remained low and stable in Patients 1 and 3 following discontinuation of ERT.

- Patients 1 & 3:
    - Baseline: Both patients were receiving ERT and at baseline had low-lyso-Gb3 and positive pre-treatment anti-AGA antibody titers (1:947 to 13,900, respectively).
    - AGA Enzyme Activity: Both patients demonstrated an increase in serum AGA enzyme activity significantly above the normal range at all timepoints through last follow-up. Mean post-treatment serum AGA enzyme activity in patients 1 & 3 were well above the normal range at 2,506% (25-fold) and 2,114% (21-fold) mean normal (248.1 and 209.3 nmol/hr/mL, respectively).

- Lyso-Gb3: Patient 1 serum lyso-Gb3 remained low and stable through week 26 and after ERT discontinuation at week 14. Patient 3 serum lyso-Gb3 remained low and stable through week 6 and following ERT discontinuation at week 2.

- Patient 2:
  - Baseline: Patient 2 entered the trial OFF-ERT but had prior ERT treatment that was stopped approximately 13 months prior to dosing. As a result, Patient 2 had a high baseline lyso-Gb3 level (101 ng/mL). Patient 2 also had the highest pre-treatment anti-AGA antibody titer of all three patients treated and of all patients screened (1:99,900).
  - AGA Enzyme Activity: Patient 2 demonstrated a significant increase in serum AGA enzyme activity into the normal range. Mean serum AGA enzyme activity increased to 58% of mean normal (5.7 nmol/hr/mL).
  - Lyso-Gb3: Lyso-Gb3 decreased significantly (>50%) within the first four weeks and remained stable through week 12.

4D-310 Interim Safety Data Summary

4D-310 demonstrated a manageable safety profile in all three patients and no dose-limiting toxicities were observed.

No serious adverse events were reported with Patient 1 and 3, and these patients did not have either atypical hemolytic uremic syndrome (aHUS) or liver toxicity, which are the 2 primary class-related toxicities associated with systemically administered AAV.

Patient 2 developed transient, self-limited aHUS within approximately one week following treatment and was admitted to the hospital for observation and hydration and was discharged after four days. As a result of hospitalization, this event was classified as a serious adverse event (SAE). The patient received no complement inhibitors; kidney function recovered without further intervention. Laboratory parameters for this patient improved daily throughout this observation period, and no lasting clinical sequelae resulted. Transient and asymptomatic grade 1 (mild) transaminitis (AST/ALT) was also observed in this patient at a separate and single protocol-defined time point. Beyond what was observed in Patient 2, no other SAEs were reported.

4DMT expects to continue enrolling patients at the 1E13 vg/kg dose-level. In addition, 4DMT plans to exclude patients with anti-AGA antibody titers >1:25,000.

4D-110 for Choroideremia Clinical Data Update Summary

4D-110 is currently being studied in an ongoing Phase 1/2 dose escalation clinical trial in patients with choroideremia. To date, six patients with clinically advanced choroideremia have been enrolled. A standard 3+3 dose escalation design was used. Patients were enrolled in one of two dose cohorts: 3E11 vg/eye (cohort 1; n=3) and 1E12 vg/eye (cohort 2; n=3).

To date, at the 3E11 vg/eye dose (Cohort 1), 4D-110 was well-tolerated with no dose-limiting toxicities or SAEs. Initial signals of clinical activity were observed at this dose, through anatomical measurements of the retinal pigment epithelium (RPE) by fundus autofluorescence area and photoreceptors by ellipsoid zone area.

Based on the totality of the initial clinical data, we expect to continue enrolling at the 3E11 vg/eye dose level.

At the 1E12 vg/eye dose, pigment dispersion (iris transillumination) was observed in three patients in the 1E12 vg/eye cohort approximately seven to nine months following treatment. Two cases were asymptomatic and one patient reported mild glare. In each case the investigator described this as an SAE but no hospitalization or medical intervention was initiated. We believe this pigment dispersion finding is consistent with REP1 transgene overexpression in iris pigment epithelial cells (IPE); no association with inflammation was evident.

Forward-Looking Statements

This Current Report on Form 8-K contains forward-looking statements for purposes of the safe harbor provisions of the Private Securities Litigation Reform Act of 1995. Forward-looking statements include statements regarding statements about: 4D-310's potential as a therapeutic product, 4D-110's potential as a therapeutic product, the dose level for future patients to enroll in 4D-110's Phase 1/2 dose-expansion trial and the future enrollment plans

for 4D-310. In some cases you can identify these statements by forward-looking words such as "may," "will," "continue," "anticipate," "intend," "could," "project," "expect" or the negative or plural of these words or similar expressions. Forward-looking statements are not guarantees of future performance and are subject to risks and uncertainties that could cause actual results and events to differ materially from those anticipated, including, but not limited to: the impact of COVID-19 on countries or regions in which 4DMT has operations or does business, as well as on the timing and anticipated results of 4DMT's clinical trials, strategy and future operations; the delay of any current or planned clinical trials for the development of 4DMT's drug candidates, the risk that the results of its clinical trials, including any initial data therefrom, may not be predictive of future clinical trial results, including those from current and future clinical trials; 4DMT's ability to successfully demonstrate the safety and efficacy of its drug candidates; the timing and outcome of 4DMT's planned interactions with regulatory authorities; and obtaining, maintaining and protecting its intellectual property. 4DMT discusses many of these risks in greater detail under the heading "Risk Factors" contained in its quarterly report on Form 10-Q for the quarter ended June 30, 2021, which is on file with the Securities and Exchange Commission. 4DMT expressly disclaims any intent or obligation to update these forward-looking statements, except as required by law.

SIGNATURES

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

4D MOLECULAR THERAPEUTICS, INC.

Date: October 26, 2021

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