November 17, 2020

VIA EDGAR

United States Securities and Exchange Commission Division of Corporation Finance 100 F Street, N.E. Washington, D.C. 20549-6010

- Attention: Ada Sarmento Suzanne Hayes Jenn Do Jeanne Baker
  - Re: 4D Molecular Therapeutics, Inc. Draft Registration Statement on Form S-1 Submitted October 14, 2020 CIK No. 0001650648

#### Ladies and Gentlemen:

4D Molecular Therapeutics, Inc. (the "*Company*") has submitted to the U.S. Securities and Exchange Commission (the "*Commission*") on the date hereof a revised Registration Statement on Form S-1 (the "*Registration Statement*"). The Company previously submitted to the Commission on October 14, 2020 a draft Registration Statement on Form S-1 (the "*Draft Submission*") on a confidential basis pursuant to Title I, Section 106 under the Jumpstart Our Business Startups Act. The Registration Statement has been revised to reflect the Company's responses to the comment letter to the Draft Submission received on November 10, 2020 from the staff of the Commission (the "*Staff*"), and we are hereby providing the Company's responses to the Staff's letter.

For ease of review, we have set forth below each of the numbered comments of the Staff's letter in bold type followed by the Company's responses thereto.

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<u>Prospectus Summary</u> <u>Overview, page 1</u>

1. Please balance the disclosure in the summary with disclosure that your product candidates are based on a novel AAV gene therapy technology with which there is limited regulatory and clinical experience and that few gene therapy products have been approved by the FDA or comparable foreign regulatory agencies. Therefore, it is difficult to predict how long it will take to development your product candidates and obtaining regulatory approval. Also disclose in the summary that the regulatory approval process for novel product candidates can be more expensive and take longer than for other, better known or extensively studied therapeutic modalities. Finally, revise your disclosure on page 5 and page 117 that you will "apply [y]our modular product design and engineering approach to accelerate the pace of product development" to remove any implication that you will be able to accelerate the development of your product candidates as such statements are speculative.

*Response*: The Company respectfully acknowledges the Staff's comment and has revised the disclosure on pages 1, 2 and 6 of the Registration Statement and throughout the Registration Statement where applicable.

2. Please delete the statements that an evolved vector increases the likelihood of success and could accelerate the pace of product development and that your competitive advantages and experience uniquely position you to successfully create, develop and manufacture targeted gene therapies. Given the number of product candidates that never receive FDA approval, the time required to obtain approval and the number of companies currently developing product candidates, your statements that you are in a unique position, have an increased likelihood of success and can develop products more quickly is not appropriate.

*Response*: The Company respectfully acknowledges the Staff's comment and has revised the disclosure on pages 1, 6, 149, 158 and 166 of the Registration Statement and throughout the Registration Statement where applicable.

#### Our Therapeutic Vector Evolution Platform, page 2

3. Please substantiate your statement that you have developed an "industry-leading" collection of synthetic capsid sequences.

*Response*: The Company respectfully acknowledges the Staff's comment and has revised the disclosure on pages 2 and 117 of the Registration Statement to remove this disclosure.

4. Please revise your disclosure here and in the Business section to provide appropriate context for various conclusions and predictions as to the performance of your product candidates and revise and/or remove any statements that imply safety or efficacy as

safety and efficacy are determinations that are solely within the authority of the FDA or similar foreign regulators. For example, we note statements that your vectors "achieved enhanced delivery, increased transgene expression, reduced immunogenicity and/or improved antibody resistance when compared to conventional AAV vectors," that you expect to demonstrate improved safety and efficacy of your product candidates versus conventional AAV vectors and various other claims regarding the superiority of your product candidates to those using conventional AAV vectors, including certain statements in the sections regarding competition and differentiation of your various product candidates. Please revise your disclosure to remove any suggestion that there is an expectation that your product candidates will be safe and effective or will have improved safety and efficacy over conventional AAV vectors and instead refer to the relevant objective data from your preclinical trials or studies that relate to your product candidate's performance.

*Response*: The Company respectfully acknowledges the Staff's comment and has revised the disclosure on pages 1, 2, 124, 126, 127, 138, 140 and 146 of the Registration Statement and throughout the Registration Statement where applicable.

5. We note your disclosure here and in the Business section regarding preclinical head-to- head comparisons between your targeted and evolved vectors with relevant conventional AAV vectors. If you have not conducted actual head-to-head trials, please revise your disclosure to clearly state this fact and disclose why you believe these comparisons are appropriate. If you provide disclosure regarding results from other trials, expand your disclosure to provide the other information regarding these trials that would help an investor make a meaningful comparison (e.g., number of subjects, dosage, how the baseline was measured in each study, etc.).

*Response*: The Company respectfully acknowledges the Staff's comment and has revised the disclosure on pages 138, 139, 140 and 143 of the Registration Statement and throughout the Registration Statement where applicable.

#### Our Product Candidate Pipeline, page 3

6. We note your disclosure on page 166 that planning is underway for an IND-enabling GLP toxicology and biodistribution study of 4D-710 in NHP. Please revise the pipeline table to shorten the line for 4D-710 and revise the anticipated milestone accordingly. We also note that you have included in your pipeline table 4D-710, 4D-135, 4D-3XX and 4D-7XX, all of which appear to be in the discovery phase. Given the early-stage development of these programs, please explain why each program is sufficiently material to your business to warrant inclusion in your pipeline table.

*Response*: The Company respectfully advises the Staff that it has updated the disclosure on pages 166 and 171 of the Registration Statement to reflect that 4D-710's IND-enabling GLP toxicology and biodistribution studies are currently underway.

Accordingly, the Company respectfully informs the Staff that it does not believe the presentation of 4D-710 in its pipeline table (the "*Pipeline Table*") needs to be modified.

In response to the Staff's comment regarding the inclusion of 4D-710 in the Pipeline Table, the Company believes that the inclusion of this product candidate is appropriate as the Company has engaged IND-enabling studies for it and anticipates initiating a Phase 1/2 clinical trial within the second half of 2021. Further, the Company believes it is material disclosure for an investor as part of the use of proceeds, as set forth on page 87 of the Registration Statement, is designated to be used to fund 4D-710's ongoing IND-enabling study activities.

In response to the Staff's comment regarding the inclusion of 4D-135, 4D-3XX and 4D-7XX in the Pipeline Table, the Company respectfully informs the Staff that it has revised its disclosure on page 3 of the Registration Statement and throughout the Registration Statement where applicable to remove these programs (the "*Discovery Programs*") from the Pipeline Table and, similar to several other recently public clinical-stage biopharmaceutical companies, has included in the Registration Statement a separate table summarizing the Company's most advanced research and discovery programs (the "*Discovery Program Table*"). The Company believes that it is appropriate to include the Discovery Program Table separate from the Pipeline Table as part of the use of proceeds, as set forth on page 87 of the Registration Statement, is designated to be used to fund other research and development activities which includes the Discovery Programs, and the Discovery Programs are relevant to an investor's understanding of the Company's longer term strategy and approach, including the potential for, and types of, additional development programs that may result from the Company's discovery efforts utilizing its Therapeutic Vector Evolution platform. Further, the inclusion of these Discovery Programs further illustrates for an investor how the Company intends to utilize the Therapeutic Vector Evolution platform's modularity to develop other product candidates utilizing its current vectors.

# 7. Please explain what is involved in "lead-optimization" and why you believe this is a separate and distinct development phase, as opposed to part of vector discovery and/or IND-Enabling studies.

*Response*: The Company respectfully acknowledges the Staff's comment and has revised the disclosure on page 3 of the Registration Statement and throughout the Registration Statement where applicable.

Further, the Company respectfully informs the Staff that it views lead optimization as a distinct development phase, as compared to the Target Vector Profile ("*TVP*") selection process and IND-enabling studies, because different research and development tasks are conducted during this phase. For example, as compared to TVP selection, where the Company utilizes its Therapeutic Vector Evolution platform to initially identify vectors from its libraries with the strongest match to the TVP that it will then advance through preclinical studies, in the lead optimization phase of clinical development the Company is engaging in *in vivo* and *ex vivo* studies to determine which of the identified vectors to advance through

the more extensive studies needed for a potential IND submission. Similarly, the IND-enabling studies phase of clinical development is different as the Company generally conducts studies in addition to the *in vivo* and *in vitro* studies done in the lead optimization phase, such as GLP toxicology studies, to prepare for a potential IND submission.

#### Implications of Being an Emerging Growth Company, page 7

8. Please supplementally provide us with copies of all written communications, as defined in Rule 405 under the Securities Act, that you, or anyone authorized to do so on your behalf, present to potential investors in reliance on Section 5(d) of the Securities Act, whether or not they retain copies of the communications.

*Response*: The Company respectfully acknowledges the Staff's comment and undertakes that it will provide the Staff with any written materials that it or anyone authorized to do so on its behalf presents to potential investors in reliance on Section 5(d) of the Securities Act.

#### **Risk Factors**

#### Our success depends on our ability to protect our intellectual property and our proprietary technologies, page 51

#### 9. Please revise this risk factor to disclose the patent rights or technologies subject to march-in rights.

*Response*: The Company respectfully acknowledges the Staff's comment and has revised the disclosure on page 52 of the Registration Statement accordingly.

#### Use of Proceeds, page 86

10. Please revise to clarify whether you expect that you will able to complete the IND- enabling studies for 4D-150 and 4D-710 and the Phase 1/2 clinical trial for 4D-125 using the proceeds from this offering.

*Response*: The Company respectfully acknowledges the Staff's comment and has revised the disclosure on page 87 of the Registration Statement accordingly.

#### **Business**

#### **Our Proprietary Therapeutic Vector Evolution Platform, page 140**

11. Please substantiate your statement that you have the "largest and most diverse portfolio of targeted and evolved vectors in the field of gene therapy."

*Response*: The Company respectfully acknowledges the Staff's comment and has revised the disclosure on page 145 of the Registration Statement to remove this disclosure.

Competition and Differentiation: AAV Gene Therapy for wet AMD and Diabetic Retinopathy, page 150

12. We note your disclosure that, to your knowledge, 4D-150 would be the only AAV gene therapy asset in wet AMD and DR that has shown superior transduction on human retinal cells ex vivo versus conventional AAV vectors such as AAV2 and is the first gene therapy product candidate for the eye to directly inhibit three different angiogenic growth factor targets, including VEGF and PIGF. Please revise these statements to eliminate any implication that 4D-150 is effective and to provide the data that support these claims.

*Response*: The Company respectfully acknowledges the Staff's comment and has revised the disclosure on pages 138 and 155 of the Registration Statement accordingly.

## Strategic Collaborations, page 172

13. Please provide the current expiration date for the last-to-expire licensed patent right under the Roche Agreement, the uniQure agreements and the UC Agreements.

*Response*: The Company respectfully acknowledges the Staff's comment and has revised the disclosure on pages 176, 177 and 179 of the Registration Statement accordingly.

\* \* \*

We hope the foregoing answers are responsive to your comments. Please do not hesitate to contact me by telephone at (650) 463- 4693 or by fax at (650) 463-2600 with any questions or comments regarding this correspondence.

Very truly yours,

/s/ Phillip S. Stoup Phillip S. Stoup, Esq. of LATHAM & WATKINS LLP

cc: David Kirn, M.D., 4D Molecular Therapeutics, Inc. August J. Moretti, 4D Molecular Therapeutics, Inc. Benjamin A. Potter, Esq., Latham & Watkins LLP David Peinsipp, Esq., Cooley LLP Charles S. Kim, Esq., Cooley LLP Kristin VanderPas, Esq., Cooley LLP