United States securities and exchange commission logo

November 10, 2020

David Kirn
Chief Executive Officer
4D Molecular Therapeutics Inc.
5858 Horton Street #455
Emeryville, CA 94608

Re: 4D Molecular Therapeutics Inc.
Draft Registration Statement on Form S-1
Submitted October 14, 2020
CIK No. 0001650648

Dear Dr. Kirn:

We have reviewed your draft registration statement and have the following comments. In some of our comments, we may ask you to provide us with information so we may better understand your disclosure.

Please respond to this letter by providing the requested information and either submitting an amended draft registration statement or publicly filing your registration statement on EDGAR. If you do not believe our comments apply to your facts and circumstances or do not believe an amendment is appropriate, please tell us why in your response.

After reviewing the information you provide in response to these comments and your amended draft registration statement or filed registration statement, we may have additional comments.

Draft Registration Statement on Form S-1

Prospectus Summary
Overview, page 1

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 candidatescan 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.
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.

Our Therapeutic Vector Evolution Platform, page 2

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

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.

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.

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.

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.

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.

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."

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 PlGF. Please revise these statements to eliminate any

implication that 4D-150 is effective and to provide the data that support these claims.

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.

You may contact Jenn Do at 202-551-3743 or Jeanne Baker at 202-551-3691 if you have
questions regarding comments on the financial statements and related matters. Please contact
Ada Sarmento at 202-551-3798 or Suzanne Hayes at 202-551-3675 with any other questions.

Sincerely,

Division of