



DIVISION OF
CORPORATION FINANCE

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

June 21, 2019

Maria Maccicchini, Ph.D.
President and Chief Executive Officer
Annovis Bio, Inc.
1055 Westlakes Drive, Suite 300
Berwyn, PA 19312

**Re: Annovis Bio, Inc.
Amendment No. 1 Draft Registration Statement on Form S-1
Submitted May 24, 2019
CIK No. 0001477845**

Dear Dr. Maccicchini:

We have reviewed your amended 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.

Amendment No. 1 to Draft Registration Statement on Form S-1

Prospectus Summary, page 1

1. We note your disclosure on page 1 that you have a "ready program" to conduct a second Phase 2a study in PD patients. Please explain what you mean.
2. We note your disclosure that you expect your lead compound to be efficacious and that you showed in studies that ANVS-401 was safe on page 1, that you expect to obtain FDA approval in 2024 on page 2 and that clinical studies and preclinical data have established and/or proven the safety or efficacy of ANVS-401 on page 3. As your product candidate has not received FDA approval, it is premature to suggest or imply that it is safe or effective. Also, there can be no certainty as to when or if you will receive FDA approval. Please revise your disclosure here and all similar statements throughout the

prospectus accordingly. We will not object to statements that your product candidate was well-tolerated or to presentation in the Business section of the trial endpoints, the extent to which the end points were met or were not met, or the aggregate or summary data collected from your trials.

3. We note your disclosure on page 2 that successful termination of the Alzheimer's disease and Parkinson's disease study will "de-risk" ANVS-401 for use in neurodegenerative diseases and will validate the target and pathway. Please remove this statement and any other statements that imply that you will be successful in mitigating risk associated with drug development. Please also tell us what you mean by stating that termination of the study will validate the target and pathway.
4. We note statements throughout that imply efficacy, such as "lowering their high levels of APP will restore axonal transport and homeostasis...and normalize their memory loss and dementia," and "ANVS-401 treatment restores normal axonal transport and prevents or restores all those events all the way to preserving nerve cell health." In addition, we note that your description of ANVS-401 under "Pathway Engagement" includes numerous statements claiming efficacy, such as "full recovery of memory, learning and brain function," "normalizes all the functions that are negatively affected by disturbances of the transport," and "normalizes the affected function in all diseases that we tested it in." These are just examples. Please substantially revise your disclosure throughout your prospectus to remove these statements as determinations of efficacy are solely within the authority of the FDA.
5. We note your statement here and in the Business section that you have an ongoing Phase 2a proof-of-concept study in AD patients. Please tell us the status of the study, including the number of patients enrolled and whether you have started the study. Please add similar disclosure in the Business section.
6. You state that you have conducted clinical trials with 125 humans and these trials have shown promising clinical signals, including normalized levels of neurotoxic proteins. However, it appears that these results were only observed in your proof of concept study in five patients with mild cognitive impairment. Please revise to remove the implication that the clinical signals you list were observed in 125 humans and clarify that the AD patients had only mild cognitive impairment.
7. Please provide us with support for your statement that AD and PD are the two largest medical needs for the aging U.S. population and two potentially largest markets.
8. Please revise your statement that focusing on AD in the DS population "perfectly represents AD" as this statement suggests that your studies in this population will translate to approval in the AD population generally.
9. Please explain your references to Parexel and Posiphen, as there is no explanation in the prospectus as to the relevance of these terms.

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10. We note your disclosure on page 5 that you have a Scientific Advisory Board. Please describe the role or function of the Scientific Advisory Board and whether there are any rules or procedures governing such board. Please also provide us with support for your statement that the board is composed of "world-renowned scientists."
11. We note that you intend to conduct chronic toxicology studies in rats and dogs with the funds from the offering. Given that you are already testing ANVS-401 in humans, please explain the relevance of the animal toxicology study and whether it is necessary for you to continue studies in humans.

Implications of Being an Emerging Growth Company, page 7

12. 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

We have concentrated our research and development efforts on the treatment of AD and PD..., page 18

13. Please revise this risk factor to provide detail regarding the particular challenges in obtaining FDA approval for AD and PD. For example, we note your statement on page 80 that since 2003, there have been over 500 clinical studies and no compound has shown efficacy.

If we fail to comply with our obligations under our existing intellectual property license, page 37

14. Please expand this risk factor to disclose the term of the license agreement and under what circumstances Horizon would be able to terminate your license.

Industry and Other Data, page 55

15. Please revise to clarify your liability for statements included in the prospectus, regardless of the fact that you did not verify them and cannot guarantee their accuracy.

Use of Proceeds, page 57

16. We note your disclosure on page 6 that you intend to complete both Phase 2a studies with the funds raised in this offering. Please revise this section to make it clear that you expect the proceeds to be sufficient to fund both Phase 2a studies through completion, if accurate. In addition, we note your statement that the Phase 2a trial in AD patients is presently run and paid for by the Alzheimer's Disease Cooperative Study. Please tell us what obligations you have, if any, to fund this trial and whether you will have to reimburse ADCS. Please also tell us whether you have any agreement with ADCS relating to this study. If so, please provide materially complete disclosure of the

agreement and file it as an exhibit to the registration statement, or tell us why you believe you are not required to do so.

17. Please revise to clarify what you mean by the remaining proceeds will be used to "provide runway" while raising money for the Phase 3 studies in AD-DS and PD.

Founders' Vision, page 78

18. Please revise this section to provide a balanced discussion of your business. Please also remove your statements that you have engineered medicines that normalize brain homeostasis and that you have been able to "stop every step leading to destruction up to the last step that is nerve cell death." We note that your company is a clinical stage company and you have not yet established, and may never establish, the safety or efficacy of your product candidate. Please also remove the suggestion that investing in your company will help "patients [who] are desperately waiting for a solution to their problems" and will "solve neurodegeneration and protect nerve cells from dying." Your disclosure in this section should be appropriately balanced to account for the risks of drug development. Please also provide the basis for your statement that "neurodegenerative diseases represent the biggest challenge facing us today."

Business

Target Engagement, page 82

19. Please revise the two tables on this page to make them more legible. Please make similar revisions to the tables on page 89.

Reproducible Results Across Species, page 92

20. Please remove your statement that it is rare to see "perfect reproducibility" across species or tell us why you believe this is an appropriate statements. Categorizing the observation of similar effects in various species as "perfect reproducibility" suggests that success in animal models guarantees success in humans. In addition, given your limited observations in humans, it is not appropriate to make this conclusion.

Intellectual Property, page 100

21. We note your disclosure that your patent portfolio includes patents licensed from the NIH. Please clarify whether this is referencing the patents that are licensed from Horizon. If not, please file the license agreement with the NIH as an exhibit and provide a summary of the material terms in the Material Agreements section on page 102.
22. We note that certain of your patents in 2021 or 2022. Please revise your disclosure to explain the material impact, if any, of the patent expirations on your business and on the success of ANVS-401. Please add risk factor disclosure to the extent appropriate.

Material Agreements, page 102

23. Please revise this section to disclose the duration of the license agreement and the termination provisions. We note your disclosure on page 37 that you will have to pay royalties on sales pursuant to this agreement. Please disclose the amounts and the royalty term. Please also tell us whether the current or contemplated Phase 2a trials trigger the \$230,000 payment and whether you plan to use any of the offering proceeds to pay amounts due under this agreement.

Management, page 113

24. Please revise to briefly discuss, for each director, the specific experience, qualifications, attributes or skills that led to the conclusion that the person should serve as a director for your company, in light of your business and structure. Refer to Item 401(e) of Regulation S-K.

Key Collaborators, page 114

25. Please disclose the specific role of the "Key Collaborators" and whether they are compensated or are party to any agreement with the company.

Board Composition

Election of Directors, page 116

26. We note your disclosure that your directors may only be removed for cause by the affirmative vote of the holders of at least two-thirds of your outstanding voting stock. It appears that Delaware law does not allow corporations to require a supermajority vote for the removal of directors or to restrict the removal of directors by shareholders to cases of cause unless the board is classified or the directors are elected via cumulative voting. Refer to *Frechter v. Zier*, C.A. No. 12038-VCG (Del. Ch. Jan. 24, 2017), *In re VAALCO Energy, Inc. Consolidated Stockholder Litigation*, C.A. No. 11775VCL (Del. Ch. Dec. 21, 2015) and Section 141(k) of the Delaware General Corporation Law. Please advise.

Principal Stockholders, page 126

27. Please revise your disclosure to identify the natural person or persons who have voting and investment control of the shares held by Ben Franklin Technology Partners.

Description of Capital Stock, page 128

28. We note that you refer shareholders to, in part, the relevant provisions of the Delaware General Corporation Law. It is not appropriate to qualify your disclosure by reference to information that is not included in the filing or filed as an exhibit. Please revise accordingly.

Choice of Forum, page 130

29. We note your disclosure that the Court of Chancery of the State of Delaware is the exclusive forum in which you and your directors may be sued by your stockholders. Please disclose whether that includes actions arising under the Securities Act or Exchange Act. In that regard, we note that Section 27 of the Exchange Act creates exclusive federal jurisdiction over all suits brought to enforce any duty or liability created by the Exchange Act or the rules and regulations thereunder, and Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all suits brought to enforce any duty or liability created by the Securities Act or the rules and regulations thereunder. If your exclusive forum provision applies to Securities Act claims, please also revise your disclosure to state that there is uncertainty as to whether a court would enforce such provision and that investors cannot waive compliance with the federal securities laws and the rules and regulations thereunder. If it does not apply to actions arising under the Securities Act or Exchange Act, please also ensure that the exclusive forum provision in your governing documents states this clearly.

Notes to Financial Statements

Note 2: Summary of Significant Accounting Policies

(f) Research and Development, page F-8

30. In Management's Discussion and Analysis of Financial Condition and Results of Operations at the top of page 72 you indicate that a \$128,000 increase in intellectual property legal costs is included in research and development (R&D) expenses in 2018. The inclusion of these legal costs appears to conflict with your statement in the General and Administrative (G&A) Expenses disclosure on page 69 that professional fees for legal services, including patent-related expenses are included in G&A expenses. Please tell us the nature of these intellectual property legal costs and how their inclusion in R&D expenses is consistent with the guidance in ASC 730-10-55-2i.

Note 7: Redeemable Convertible Preferred Stock and Stockholders' Equity

c) Redeemable Convertible Preferred Stock, page F-15

31. You disclose that upon an initial public offering of your common stock with gross proceeds of at least \$20 million your preferred stock will convert at the applicable per share conversion rate; \$0.50 per share for Series A and \$0.90 per share for Series A-1. Based on the over \$6.5 million carrying value of your Series A preferred stock it appears that more than 13 million share of common should be issued, yet your disclosure on page 9 and throughout your filing implies a one-for-one conversion rate between your preferred and common stock. Please tell us why the carrying value of your Series A preferred stock is greater than the implied \$0.50 per share issuance price and why a one-for-one conversion ratio into common stock is appropriate.

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General

32. Please provide us proofs of all graphics, visual, or photographic information you will provide in the printed prospectus prior to its use, for example in a preliminary prospectus. Please note that we may have comments regarding this material.

You may contact Mark Brunhofer at 202-551-3638 or Lisa Vanjoske at 202-551-3614 if you have questions regarding comments on the financial statements and related matters. Please contact Ada Sarmento at 202-551-3798 or Erin Jaskot at 202-551-3442 with any other questions.

Sincerely,

Division of Corporation Finance
Office of Healthcare & Insurance

cc: John W. Kauffman