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

DIVISION OF
CORPORATION FINANCE

January 19, 2018

Arthur Tzianabos
President and Chief Executive Officer
Homology Medicines, Inc.
45 Wiggins Avenue
Bedford, MA 01730

Re: Homology Medicines, Inc.
Draft Registration Statement on Form S-1
Submitted December 22, 2017
CIK No. 0001661998

Dear Dr. Tzianabos:

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.

Form DRS Submitted December 22, 2017

Prospectus Summary, page 1

1. We note your statement that you are "rapidly" advancing HMI-102 for the treatment of phenylketonuria into a Phase 1/2 clinical trial. Please balance your disclosure by stating here that you are a preclinical company, you have not submitted an IND for HMI-102 or any other product candidate, and that you will require additional capital to move beyond Phase 1/2. Please also remove the term "rapidly advancing" or tell us why you believe it is appropriate to use this term. Please supplementally tell us why you believe you will be to initiate a Phase 1/2 clinical trial in 2019. Please make similar disclosure in your

Business section.

2. We note your statement that you believe that your compelling preclinical data, scientific expertise, product development strategy, manufacturing capabilities and robust intellectual property position you as a leader in the development of genetic medicines. Given the early stage of your development and the competition in this space, please supplementally tell us the basis of your belief that you are a leader in the development of genetic medicines.

Pipeline Table, page 5

3. Please include a column for each of Phase 1, Phase 2, and Phase 3 in your product pipeline table here and on page 92.

Stock-Based Compensation
Critical Accounting Policies and Use of Estimates
Determination of Fair Value of Common Stock, page 81

4. Once you have an estimated offering price or range, please provide us an analysis explaining the reasons for the differences between the recent valuations of your common stock leading up to the IPO and the estimated offering price. This information will help facilitate our review of your accounting for equity issuances including stock compensation and beneficial conversion features.

Contractual Obligations and Commitments, page 86

5. Please include your obligations under the license agreements.

Business
Our Proprietary AAVHSCs, page 98

6. We note that the preclinical trials discussed in this section provide results without providing proper context for such results. For each of the pre-clinical trials discussed in this section, please disclose the date(s) of the trials, the sponsor and the location; scope and size; dosage and duration; and actual results observed. Please include this disclosure for trials you conducted as well as any third-party trials you use for comparison, such as the AAV trials mentioned in Figure 6 or the third party studies you cite in Figure 9. Please also state whether you have published the data for any of your preclinical studies.

Figure 5. In vivo Gene Editing, page 99

7. We note your statement that "while not illustrated, in subsequent studies at higher doses we have observed gene correction editing efficiencies of up to 20%." Please either provide a complete description of the study that resulted in such efficiencies, or delete

this statement. Please make similar revisions elsewhere that you mention this statistic, including your prospectus summary. Please only use this statistic to the extent that it is a balanced representation of the efficiencies you have observed in pre-clinical trials.

Competition, page 109

8. Please revise your discussion of competitive conditions by describing in greater detail the current landscape for patent protections in your industry. In this regard, we note that across several risk factors on pages 46 to 56 you address specific risks related to your intellectual property.

Intellectual Property, page 110

9. For each of your material licensed patents, please disclose (1) which patents or patent applications are material to HMI-102; (2) expected expiration dates for patent applications; and (3) the jurisdictions where patents are issued and patent applications are pending. Please also explain what you mean that certain patents are "generally" expected to expire in 2031 and 2034.

Collaboration and License Agreement with Novartis Institutes for BioMedical Research, Inc., page 112

10. We note that you are eligible to earn tiered royalties on net sales of licensed products by Novartis ranging from mid single-digit to low double-digit percentages. This disclosure is too broad and could imply that your royalty rate is up to 49%. Please revise your disclosure here and throughout the prospectus to give investors a reasonable idea of the amount of the royalty rate that does not exceed 10 percentage points

Consolidated Statements of Convertible Preferred Stock and Stockholders' Deficit for the Year Ended December 31, 2016, page F-5

11. Please explain the negative balance carried under Additional Paid-in Capital.

Notes to Consolidated Financial Statements
2. Summary of Significant Accounting Policies, page F-7

12. Please disclose your revenue recognition policy.

7. License Agreements
City of Hope, page F-13

13. Please disclose your obligations under the sponsored research agreement with COH.

General

14. 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.

15. 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 Keira Nakada at 202-551-3659 or Angela Connell at 202-551-3426 if you have questions regarding comments on the financial statements and related matters. Please contact Jeffrey Gabor at 202-551-2544 or Erin Jaskot at 202-551-3442 with any other questions.

Division of Corporation Finance
Office of Healthcare & Insurance

cc: Wesley Holmes