Mail Stop 6010

April 27, 2006

Michael D. Kishbauch
President and Chief Executive Officer
Achillion Pharmaceuticals, Inc.
300 George Street
New Haven, Connecticut 06511

Re: Achillion Pharmaceuticals, Inc.
Registration Statement on Form S-1
Filed March 31, 2006
File No. 333-132921

Dear Mr. Kishbauch:

We have reviewed your filing and have the following comments. Where indicated, we think you should revise your document in response to these comments. If you disagree, we will consider your explanation as to why our comment is inapplicable or a revision is unnecessary. Please be as detailed as necessary in your explanation. In some of our comments, we may ask you to provide us with information so we may better understand your disclosure. After reviewing this information, we may raise additional comments.

Please understand that the purpose of our review process is to assist you in your compliance with the applicable disclosure requirements and to enhance the overall disclosure in your filing. We look forward to working with you in these respects. We welcome any questions you may have about our comments or any other aspect of our review. Feel free to call us at the telephone numbers listed at the end of this letter.

FORM S-1

General

1. Please provide us proofs of all graphic, visual, or photographic information you will provide in the printed prospectus prior to its use, for example in a preliminary prospectus. Please note we may have comments regarding these materials.

2. Please note that when you file a pre-effective amendment containing pricing-related information, we may have additional comments. As you are likely aware, you must file this amendment prior to circulating the prospectus.

3. Please note that when you file a pre-effective amendment that includes your price range, it must be bona fide. We interpret this to mean your range may not exceed $2 if you price below $20 and 10% if you price above $20.

4. Comments related to your request for confidential treatment will be delivered under separate cover. Please be advised that we will not be in a position to consider a request for acceleration of effectiveness of the registration statement until we resolve all issues concerning the confidential treatment request.

Prospectus Summary

Overview, page 1

5. We note from the "Risks Associated with Our Business" section on page 3 and from "All of our drug candidates are still in the early stages of development . . ." on pages 9-10 that you do not currently have any approved products on the market and you do not expect to have any such products for at least several years. Please disclose this information in the "Overview" section of your Prospectus Summary.

6. Throughout your filing you have included statements relating to the market in which you expect your products to compete. Please revise to indicate the sources of information you have relied on in making these statements and provide us with copies of these reports. These copies should be marked to indicate the information supporting your statements.

Our Drug Candidates, page 1

7. Since your products will not initially be approved throughout the world, please revise the market size estimates so that they reflect only the markets in which the products will be approved initially, which we presume will be only the United States since the filing discusses only U.S. clinical trials. Cite a specific source for these market-size figures. Similarly revise the market size discussions on pages 43, 48, 53, and 56 in the Business section, citing a specific source for each dollar figure cited.

Risk Factors

We will need substantial additional capital to fund our operations . . . , page 6

8. The second half of the first paragraph of this risk factor discusses the drawbacks of raising additional capital, such as dilution, debt covenants, and the relinquishment of rights. Please move your discussion of these drawbacks to a new, separate risk factor.

If we are not able to attract and retain key management . . . , page 9

9. Please identify the "key members of [your] senior management," which you reference in the third sentence of this risk factor.

Our business has a substantial risk of product liability claims . . . , page 9

10. Please disclose the coverage limitation for your clinical trial insurance.

If clinical trials for our drug candidates are prolonged . . . , page 11

11. We note you discuss delays in patient enrollment in the second paragraph of this risk factor. If any other of the items listed in the bullet points has materially delayed the development of any of your products, please discuss the situation.

Litigation regarding patents, patent applications . . . , page 18

12. To the extent you are aware that you have any intellectual property that is being infringed upon or that you have been notified of a third party's belief that you are infringing on their intellectual property, please revise to disclose the situation and potential consequences.

13. Please disclose who has the obligations to take necessary actions to protect patents under your license and collaboration agreements. If you do not have the obligation to take action, do you have the right to take necessary actions if the other party does not?

Our costs will increase significantly as a result of operating . . . , page 23

14. As currently worded, this risk factor could apply to any public company. If you keep it in your document, please revise it so it is specific to your situation.

Use of Proceeds, page 25

15. Please state approximately how much funds you plan to use for each of the purposes listed. Please also state your reasonable estimate as to which stage of development you expect these proceeds will take you as to elvucitabine and ACH-806.

16. Please describe which "general corporate purposes" you plan to use the proceeds from this offering for. State an approximate dollar amount for each.

Management's Discussion and Analysis of Financial Condition and Results of Operations

Research and Development, page 32

1. Please refer to the Division of Corporation Finance "Current Issues and Rulemaking Projects Quarterly Update" under section VIII – Industry Specific Issues – Accounting and Disclosure by Companies Engaged in Research and Development Activities. You can find it at the following website address: http://www.sec.gov/divisions/corpfin/cfcrq032001.htm.

   Please disclose the following information for each of your major research and development projects:

   - The costs incurred during to date for the project;
   - The anticipated completion dates;
   - The risks and uncertainties associated with completing development on schedule, and the consequences to operations, financial position and liquidity if the project is not completed timely; and finally
   - The period in which material net cash inflows from significant projects are expected to commence.

   To the extent that information requested above is not known or estimable, disclose that fact and the reason why it is not known.

Critical Accounting Policies

Stock-Based Compensation, page 34

2. We note throughout your filing you reference an unrelated third-party valuation firm. The reference to an independent valuation firm equates to the use of a valuation expert. Please name the independent appraiser and provide the consent of the appraiser in the registration statement.

Liquidity and Capital Resources, page 38

17. We note you have received approximately $10.5 million under debt facilities. Please identify the lender, interest rate, maturity date, and any other material terms for each facility, and file each agreement as an exhibit to your registration statement.

Business

Our Drug Candidates, page 47

18. We note you plan to do a proof-of-concept trial for ACH-806. Please explain what a proof-concept trial is and how it fits into the typical three-phase clinical trial process.

Collaborations and Licenses

Gilead Sciences, page 60

19. We note you "have a one-time option to participate on a limited basis in the marketing effort in the United States."

    - Please discuss this option in more detail, including when the option becomes exercisable and the extent to which you will have the right to market ACH-806 if you exercise the option.
    - Please state the extent to which you will share in the revenues from sales of ACH-806 in the United States if you exercise the option and if you do not exercise the option.
    - Quantify the cap on costs related to the research program through proof-of-concept.
    - Finally, please revise your summary to clarify that Gilead has exclusive marketing and commercialization rights.

Vion Pharmaceuticals/Yale University, page 61

20. Please state the aggregate milestone payments you may be obligated to make. Also, if the agreement requires any minimum royalty payments, disclose the amount.

21. If any amounts have been paid to date, including an initial licensing fee, please quantify these amounts.

Emory University, page 61

22. Please quantify all amounts paid to date and quantify the milestone payments you may be obligated to make. Also, disclose the dollar amount of license maintenance payments and the amount of any minimum royalty payments. Finally, disclose the agreement's duration.

University of Maryland Baltimore County, page 61

23. Please clarify what you mean by "screening methodology and additional drug targets within the HIV capsid protein."

24. Please quantify all amounts paid to date and the aggregate milestone payments you may be obligated to make. Also, if the agreement requires any minimum royalty payments, disclose the amount. Finally, disclose the duration and termination provisions.

UMBC and Howard Hughes Medical Institute, page 61

25. Please state this agreement's duration, termination provisions, and any other material rights or obligations.

26. Please explain who has ownership rights of any novel inhibitors identified during the course of this collaboration.

Note 9. Preferred Stock, page F-17

3. You disclose that the preferred share convert into common stock at the initial conversion price, subject to adjustment. Please clarify the terms that allow for adjustments to the conversion price and whether you believe these adjustments lead to an obligation to issue a variable number of shares which would require liability classification under paragraph 12 of SFAS 150.

Note 10. Common Stock, Stock Options and Warrants, page F-19

4. Please provide an analysis of how you determined the fair value of the underlying common stock and any related stock-based compensation for each equity issuance. Please include an itemized chronological schedule covering all equity instruments issued since the beginning of 2005 through the date of your response. In addition, please disclose the following in the financial statements for each issuance:

    - The date of each issuance;
    - The number of options granted or shares issued;
    - The exercise price or per share amount paid;
    - Management's fair market value per share and significant factors, assumptions and methodologies used in determining fair value;
    - The intrinsic value, if any, per option;
    - The amount of any compensation expense recognized;

- The method used in valuing the issuance;
- Whether the valuation was contemporaneous or retrospective

If the valuation was not performed contemporaneously, please disclose in the Management's Discussion and Analysis the following information relating to your issuances of equity instruments:

- A discussion of significant factors, assumptions, and methodologies used in determining fair value
- A discussion of each significant factor contributing to the difference between the fair value as of the date of each grant and the estimated IPO price or if a contemporaneous valuation by an unrelated valuation specialist was obtained subsequent to the grants but prior to the IPO, the fair value as determined by that valuation
- The valuation alternative selected and the reason management chose not to obtain a contemporaneous valuation by an unrelated valuation specialist

Item 16. Exhibits and Financial Statement Schedules, page II-4

27. We note that some of your exhibits are not yet filed. Please note that once you have filed the remaining agreements as exhibits, we will need time to review the documents, and we may have comments on them.

28. Agreements filed pursuant to Item 601(b)(10) of Regulation S-K are typically material enough that their principal terms should also be discussed in the body of the filing. In your response letter, please tell us the page numbers on which exhibits 10.12, 10.13, 10.27, and 10.28 are discussed.

* * *

As appropriate, please amend your registration statement in response to these comments. You may wish to provide us with marked copies of the amendment to expedite our review. Please furnish a cover letter with your amendment that keys your responses to our comments and provides any requested information. Detailed cover letters greatly facilitate our review. Please understand that we may have additional comments after reviewing your amendment and responses to our comments.

We urge all persons who are responsible for the accuracy and adequacy of the disclosure in the filing to be certain that the filing includes all information required under the Securities Act of 1933 and that they have provided all information investors require for an informed investment decision. Since the company and its management are in possession of all facts relating to a company's disclosure, they are responsible for the accuracy and adequacy of the disclosures they have made.

Notwithstanding our comments, in the event the company requests acceleration of the effective date of the pending registration statement, it should furnish a letter, at the time of such request, acknowledging that:

- should the Commission or the staff, acting pursuant to delegated authority, declare the filing effective, it does not foreclose the Commission from taking any action with respect to the filing;

- the action of the Commission or the staff, acting pursuant to delegated authority, in declaring the filing effective, does not relieve the company from its full responsibility for the adequacy and accuracy of the disclosure in the filing; and

- the company may not assert staff comments and the declaration of effectiveness as a defense in any proceeding initiated by the Commission or any person under the federal securities laws of the United States.

In addition, please be advised that the Division of Enforcement has access to all information you provide to the staff of the Division of Corporation Finance in connection with our review of your filing or in response to our comments on your filing.

We will consider a written request for acceleration of the effective date of the registration statement as confirmation of the fact that those requesting acceleration are aware of their respective responsibilities under the Securities Act of 1933 and the Securities Exchange Act of 1934 as they relate to the proposed public offering of the securities specified in the above registration statement. We will act on the request and, pursuant to delegated authority, grant acceleration of the effective date.

We direct your attention to Rules 460 and 461 regarding requesting acceleration of a registration statement. Please allow adequate time after the filing of any amendment for further review before submitting a request for acceleration. Please provide this request at least two business days in advance of the requested effective date.

You may contact Dana Hartz at (202) 551-3648 or Mary Mast at (202) 551-3613 if you have questions regarding comments on the financial statements and related matters. Please contact Greg Belliston at (202) 551-3861 or me at (202) 551-3715 with any other questions.

Sincerely,

Jeffrey Riedler
Assistant Director

cc: Steven D. Singer, Esq.
Wilmer Cutler Pickering Hale and Dorr LLP
60 State Street
Boston, MA 02109