Mail Stop 4720

December 17, 2009

Peter M. Hecht
Chief Executive Officer
Ironwood Pharmaceuticals, Inc.
320 Bent Street
Cambridge, MA 02141

Re: Ironwood Pharmaceuticals, Inc.
Registration Statement on Form S-1
Filed November 20, 2009
File No. 333-163275

Dear Mr. Hecht:

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. We note that you intend to submit a number of confidential treatment requests in relation to certain agreements you intend to file by amendment to the registration agreement. Please note that you will be receiving comments to the confidential treatment requests under separate cover and that all confidential treatment issues must be resolved before we will consider a request for acceleration of the

registration statement. Please file these agreements, your confidential treatment requests and all other exhibits as soon as possible.

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 bone fide. We interpret this to mean that your range may not exceed $2 if you price below $20 and 10% if you price above $20.

4. Please note that where we provide examples to illustrate what we mean by our comments, they are examples and not exhaustive lists. If our comments are applicable to portions of the filing that we have not cited as examples, make the appropriate changes in accordance with our comments.

5. 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 that we may have comments regarding this material.

6. Throughout the registration statement, you cite various estimates, statistics and other figures. For example:

    - Page 77: “We estimate that in 2007, approximately 40 million people in the U.S. suffered from GERD.”
    - Page 78: the estimated number of people who suffered from IBC-S and CC in 2007, including the number of sufferers who sought medical care.
    - Page 78: “Due to patient’s lack of satisfaction with existing treatment options, about 70% of patients stop prescription therapy within one month.”
    - Page 79: “Patients with IBS-C and CC reportedly suffer from their symptoms on average 166 and 97 days per year, respectively, and over one-third have experienced their symptoms for more than ten years.”
    - Page 80: “We believe that there are over 10 million IBS-C and CC patients in the U.S. who suffer from multiple symptoms, are actively seeking therapy and are dissatisfied with current treatment options.”

    In the prospectus, please attribute these statements and other similar statements to the source from which you obtained the information. In addition, where you cite your own estimates, please explain how you arrived at those estimates and disclose any third-party sources you relied upon.

Prospectus Summary, page 1

7. Please revise your summary to present a balanced presentation by stating that you have a history of losses, quantifying your losses and stating that you expect to continue to incur losses for the foreseeable future.

8. Please balance the discussion of your strategy with a discussion of risks and obstacles. Please note that the cross reference to a discussion of the risks is not sufficient to balance the discussion of your strategy.

The Offering, page 4

9. Please clarify how many shares of class B shares will be issued to the holders of convertible preferred stock that was issued on November 13, 2009.

Risk Factors, page 8

Risks Related to Our Business and Industry, page 8

"Linaclotide may cause undesirable side effects…" page 9

10. Please describe the undesirable side effects that participants in the clinical trials experienced.

"We face potential product liability exposure…" page 15

11. Please disclose your level of product liability insurance coverage and briefly describe what potential liabilities are and are not covered. Please also disclose the cost to you of such coverage, if material.

"We may not be able to manage our business effectively if we lose any of our current management team or if we are unable to attract and motivate key personnel." page 18

12. If any of your key personnel intend to retire or resign in the near future, please revise to address such departure and the potential impact on your organization.

13. To the extent that you have experienced problems attracting and retaining key employees and management personnel in the recent past, please revise to describe these problems.

"We have not yet registered our trademarks in all of our potential markets…" page 22

14. To the extent that you have not obtained trademark protection in any jurisdictions you consider to be material, please identify these jurisdictions.

Risks Related to Our Finances and Capital Requirements, page 22

"We have incurred significant operating losses since our inception and anticipate that we will incur losses for the foreseeable future," page 22

15. Please quantify your losses in each of the last three years and quantify your accumulated deficit.

Risks Relating to Securities Markets and Investment in Our Stock, page 22

"We have operated as a private company and have no experience attempting to comply…," page 24

16. To the extent that you have identified any material weaknesses in your internal controls, please describe them.

"Our ability to use net operating loss and tax credit carryforwards and certain built-in losses …," page 25

17. Please quantify the net operating loss and tax credit carryforwards and built in losses that may be subject to limitation or loss.

"The concentration of our capital stock ownership with our founders, directors, executives…," page 25

18. Please disclose the percentage of your outstanding shares that will be held by the Class A shareholders and the percentage of your shares that will be held by Class B shareholders immediately following the offering. Additionally, compare the total votes that the Class A shareholders will have to the number of votes the Class B shareholders will have when voting on the identified issues.

Use of Proceeds, page 31

19. Please identify the other product candidates that you expect to advance using proceeds from this offering. Additionally, disclose the stage of development you expect to achieve for each of these product candidates.

Dilution, page 35

20. Please revise your dilution presentation to start with historical net tangible book value. Separately show the effect of your identified pro forma adjustments to arrive at your pro forma net tangible book value before the impact of your offering.

Management's Discussion And Analysis Of Financial Condition And Results Of Operations, page 40

Financial Overview, page 41

Research and development expenses, page 41

21. We believe that your disclosures about historical research and development expenses and estimated future expenses related to your major research and development projects could be enhanced for investors. While we recognize "linaclotide" is your lead product candidate, it appear to represent less than 50% of your total R&D costs for all periods presented. 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 expand your MD&A to disclose the following information for each of your major research and development projects.

    a. The costs incurred during each period presented and to date on each project;
    b. The nature, timing and estimated costs of the efforts necessary to complete each project;
    c. The anticipated completion dates of each project;
    d. The risks and uncertainties associated with completing development on schedule, and the consequences to operations, financial position and liquidity if each project is not completed timely; and finally
    e. The period in which material net cash inflows from significant projects are expected to commence for each project.

    Regarding a., if you do not maintain any research and development costs by project, disclose that fact and explain why management does not maintain and evaluate research and development costs by project. Provide other quantitative or qualitative disclosure that indicates the amount of the company's resources being used on the project.

    Regarding b. and c., disclose the amount or range of estimated costs and timing to complete the phase in process and each future phase. To the extent that information is not estimable, disclose those facts and circumstances indicating the uncertainties that preclude you from making a reasonable estimate.

Critical Accounting Policies and Estimates, page 42

Stock-based Compensation Expense, page 45

22. Since you have not disclosed an estimated offering price we are deferring a final evaluation of stock compensation and other costs recognized until the estimated offering price is specified. We may have further comment in this regard when the amendment containing that information is filed. In that amendment, please progressively bridge management's fair market value determinations to the current estimated IPO price range. Please reconcile and explain the differences between the mid-point of your estimated offering price range and the fair values included in your analysis.

23. Please expand your discussion of the method used to determine Volatility to disclose the factors considered in determining which public companies were the most similar. Tell us on a supplemental basis the names of the public companies used and why you consider them to be the most similar. Please provide us with the historical volatilities of these companies and their expected volatilities, if know.

Business, page 73

Our Company, page 73

24. Please revise your disclosure regarding each of the agreements with Forest Laboratories, Inc., Almirall, S.A. and Astellas Pharma Inc. For each agreement, please disclose the term and termination provisions and the potential range of royalty payments (for example, "low-teens" or "high-teens"). Additionally, please revise the discussion quantifying the amounts received to date to disclose the amount of equity investments separately.

25. Please identify your other candidates in clinical development, the indications that these products are intended to treat and the stage or development. Additionally, disclose how many products candidates are in preclinical development.

Long-Term Safety Studies, page 96

26. Please specify the jurisdictions whose regulatory requirements you reference in this section.

Executive Compensation, page 114

Compensation Discussion and Analysis, page 114

27. We note that you indicate that this section discusses "the most important factors" relevant to any analysis of your compensation policies and decisions. Please confirm that you have described all material factors and revise your disclosure accordingly.

Basis for Historical and Future Compensation Policies and Decisions, page 115

28. We note that Pearl Meyer compared your compensation data to "two confidential survey sources." Please note that to the extent you relied on comparable companies or surveys to determine compensation or to adjust compensation, the comparable companies and/or surveys should be identified. Please revise accordingly.

29. We note your statement that Pearl Meyer conducted a competitive assessment. What were the results of the assessment?

Process for Determining Individual Compensation and Role of Executive Officers, page 118

30. Please revise to discuss how the compensation committee uses the board's assessment of corporate performance to determine the appropriate size of pools for salary increases and stock options awards.

Compensation Actions in 2009, page 119

2009 Goals, page 119

31. Please revise your description of the weighted performance objectives to describe each goal with more specificity. To the extent any goals were quantified, the description of the goals should also be quantified. Please also indicate the relative weighting of each separate performance objective. You indicate that the company met 80% of its corporate objectives in 2008. Please specify which objectives were met and how the achievement of 80% of the corporate objectives translated into the level of compensation paid to each named executive officer.

32. Your discussion on page 118 indicates that your committee uses both corporate goals and individual goals. Please note your discussion should clarify which goals are corporate goals and which are individual goals. The discussion of the individual goals should indicate which officer(s) each goal applies to.

33. Please provide further analysis about how you determine the amount and, where applicable, the formula for each element of compensation you pay. See Item 402(b)(1)(v) of Regulation S-K.

34. Please identify the threshold in global pharmaceutical product sales that will result in vesting of 50% of the options issued to Dr. Currie. Similarly revise footnote 8 to the Outstanding Equity Awards at Fiscal Year – End (2009) table on pages 123 and 124.

35. Please explain the reason for setting a vesting schedule for some of your executive officers and using a milestone for Dr. Currie.

Underwriting, page 147

36. Please disclose which underwriters and their affiliates have provided services to the company and its affiliates in the past.

Consolidated Financial Statements, page F-1

Consolidated Statements of Operations, page F-4

37. Please revise your presentation of net loss throughout your filing to ensure that it includes the net loss attributed to the noncontrolling interest as required by FASB ASC 810-10-65-1b2. In this regard, it appears that your line item captioned "Net loss prior to amounts attributable to noncontrolling interest" is your consolidated net loss, while your line item captioned "Net loss" is your consolidated net loss attributable to common stockholders of Ironwood Pharmaceuticals, Inc.

Notes to Consolidated Financial Statements, page F-8

4. Collaboration and License Agreements, page F-21

38. Please provide us your authoritative support, citing specific GAAP guidance, for the accounting for the "contingent equity investment" and "forward purchase contract" recorded for Forest Laboratories and Almirall, S.A. Include guidance used in accounting for the initial valuation, remeasurement of fair value at each reporting period and Forest Lab's ultimate purchase of the convertible shares.

20. Microbia, Inc.

Sale of Securities in Microbia, Inc., page F-46

39. Please revise your disclosure to indicate the percentage ownership interest you retain in Microbia after your sale of common and preferred stock to T&L.

40. You disclose that T&L's investment in Microbia's convertible preferred stock is an investment in in-substance common stock. Please revise your disclosure to clarify the impact on your consolidation of Microbia. In this regard it would appear that you allocate the losses of Microbia to T&L and yourself assuming the outstanding preferred stock is converted into common stock. If so, please separately reference for us the authoritative literature you relied upon to support your accounting. In your response, please specifically indicate whether the convertible preferred stock is legally obligated to participate in the losses of Microbia.

* * *

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 James Peklenk at (202) 551-3661 or Mark Brunhofer at (202) 551-3638 if you have questions regarding comments on the financial statements and related matters. Please contact Nandini Acharya at (202) 551-3495, Suzanne Hayes at (202) 551-3675 or me at (202) 551-3715 with any other questions.

Sincerely,

Jeffrey Riedler
Assistant Director

cc: Paul M. Kinsella
Ropes & Gray LLP
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