Mail Stop 6010 January 13, 2006

Mr. Thomas B. King
President And Chief Executive Officer
Alexza Pharmaceuticals, Inc.
1020 East Meadow Circle
Palo Alto, California 94303

Re: Alexza Pharmaceuticals, Inc.
Registration Statement on Form S-1, file no. 333-130644
Filed December 22, 2005

Dear Mr. King:

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 supplemental information so we may better understand your disclosure. After reviewing this information, we may or may not 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 on any other aspect of our review. Feel free to call us at the telephone numbers listed at the end of this letter.

General

1. 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.

2. 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.

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

4. 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.

Prospectus Summary, pages 1-6

5. Throughout the registration statement, you refer to your product candidates as "novel." As you have stated that you are currently focusing on small molecule drugs that have been in use for many years and are well characterized, it appears that it is your drug delivery system that is novel. Please revise to clarify.

6. You have stated here and throughout your filing that you are developing products to treat patients suffering from acute migraine headaches, panic attacks, acute agitation in patients with schizophrenia and acute pain. You have also stated that you have focused on small molecule drugs that have been in use for many years. It is unclear whether you are developing new formulations of these drugs that are already in use, if you are developing new drugs using the same active ingredients or if your development activities are solely related to the drug delivery system. Please clarify.

7. We note your statement that there are currently no drugs approved for the acute treatment of associated panic attacks. Is alprazolam currently used for the treatment of other diseases or conditions?

8. Please explain what you mean by "IMS MIDAS data."

9. We note your statement on page 2 that you "estimate that over 25 million postoperative patients experience inadequate pain relief, . . . and approximately 65% of patients diagnosed with cancer experience breakthrough cancer pain." Please disclose how you arrived at these estimates.

10. Please explain the meaning of a "substrate."

11. As you have chosen to include a summary of your strategy, please balance this discussion by including a discussion of the risks and obstacles you must address in implementing this strategy. This discussion should be at least as prominent as the discussion of your strategy. Additionally, include a discussion of your history of losses, accumulated deficit, that you have no commercially viable products or FDA approved products, potential adverse effects of your product candidates including the effects discussed on page 9 and that you expect to continue incurring substantial losses for the foreseeable future and may never achieve profitability to further balance the discussion in the summary.

Risk Factors, pages 7-27

General

12. Please revise each subheading to ensure it reflects the risk that you discuss in the text. Many of your subheadings currently either merely state a fact about your business or describe an event that may occur in the future. Succinctly state in your subheadings the risks that result from the facts or uncertainties. For example, see the following:

    - "We rely on third parties to supply the components of our devices." (Page 14)

    - "If we do not establish strategic partnerships, we will have to undertake development and commercialization efforts on our own." (Pages 14-15)

    - "The Staccato system cannot be used to deliver many types of drugs." (Page 16)

"We will need substantial additional capital in the future. . . ." Pages 8-9

13. Please incorporate into this discussion the rate at which you are currently burning cash on a monthly basis.

"We may not be able to produce our devices cost effectively." Page 12

14. We note that because your products candidates "contain electronic and other components in addition to the active pharmaceutical ingredients" they may be cost prohibitive. Please explain why.

"We rely on third parties to conduct our preclinical studies and our clinical trials. . . ." Page 13

"We rely on third parties to supply the active pharmaceutical ingredient in our product candidates." Pages 13-14

"We rely on third parties to supply the components of our devices. . . ." Page 14

15. To the extent you have not already done so, please identify the third parties that you substantially rely on for conducting your preclinical studies and clinical trials, for supplying the APIs used in your product candidates and for supplying the components of your devices. Also, to the extent you have any agreements with such parties, please so indicate and describe in your Business section the material terms of the agreements. You should also file the agreements as exhibits to the registration statement. If you have determined that you are not substantially dependent on these parties, please provide us with an analysis supporting this determination.

"If we do not establish strategic partnerships, we will have to undertake development and commercialization efforts on our own." Pages 14-15

16. Please explain in your discussion in this risk factor that establishing strategic partnerships is a key element of your business strategy.

"Litigation or other proceedings or third party claims …" Page 18

17. If you are aware of any infringement claims, please disclose this information here.

"Competition in the pharmaceutical industry is intense. . . ." Pages 19-20

18. Are you aware of any other pharmaceutical companies developing a deep lung inhalation drug delivery system? If you are, this information should be discussed in this risk factor and in the competition discussion in the Business section.

"If we are unable to establish sales and marketing capabilities . . . ." Page 20

19. To the extent practicable, please quantify the expected costs to establish sales and marketing capabilities. We note that this is a key element of your business strategy.

"If we lose our key personnel . . . ." Pages 20-21

20. To the extent known, please disclose the projected time frame and cost of your hiring the additional executive management personnel needed to execute your business plan.

21. Please name all your key executive officers and personnel and their positions with the company.

22. To the extent that you have experienced problems attracting and retaining key personnel in the recent past, please revise to describe these problems. Additionally, if any key employee has plans to retire or leave your company in the near future, please revise the discussion to disclose this information.

23. Please state whether you maintain employment contracts with key executive officers and personnel and disclose any termination payments you may be required to make under such agreements.

24. Please disclose whether you have key life insurance policies on any employees.

"We use hazardous chemicals and highly combustible materials in our business. . . ." Page 23

25. Please disclose whether you maintain insurance for the use of hazardous materials and, if so, the level of coverage. Please also disclose the cost to you of such coverage, if material.

26. Please discuss if you have been the subject of any investigations in the past.

Use of Proceeds, page 30

27. As to each of your four product candidates, please clarify what stage of development you expect to achieve using the proceeds from the offering.

28. Please revise to state the amount in reference to "existing capital resources."

Management's Discussion and Analysis of Financial Condition and Results of Operations, pages 37-47

Overview, pages 37-39

29. In a recent release called "Commission Statement about Management's Discussion and Analysis of Financial Condition and Results of Operations," the staff stated that "the development of MD&A disclosure should begin with management's identification and evaluation of what information, including the potential effects of known trends, commitments, events, and uncertainties, is important to providing investors and others an accurate understanding of the company's current and prospective financial position and operating results." Release Nos. 33-8056; 34-45321; FR-61. Accordingly, your MD&A overview should be a more focused discussion that highlights the key points that are covered in greater detail in the MD&A section, with emphasis on the key trend and analytical points. For example, on page 42 you state that you expect grant revenue to decline in the future. If this is a key trend, please address this in the overview. Please revise. We may have further comments.

Research and Development Expenses, page 38

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

a. The nature, timing and estimated costs of the efforts necessary to complete the project;
b. The anticipated completion dates;
c. 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
d. The period in which material net cash inflows from significant projects are expected to commence.

Regarding a. and b., 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.

Preclinical Study and Clinical Trial Accruals, page 39

31. Please revise to provide greater insight into the quality and variability of how the estimate for preclinical study and clinical trial accruals is determined. Please address the following factors in your discussion:

- How the company arrived at the estimate
- How accurate the estimate/assumption has been in the past
- How much the estimate/assumption is reasonably likely to change in the future

Stock-based compensation, page 40

32. Please disclose in the financial statements the following information for equity instruments granted during the 12 months prior to the date of the most recent balance sheet included in the filing as well as issuances since that date:

- For each grant date, the number of options or shares granted, the exercise price, the fair value of the common stock, and the intrinsic value, if any, per option
- Whether or not the valuation used to determine the fair value of the equity instruments was contemporaneous or restrospective
- Whether or not the valuation specialist was a related party

33. Please disclose in the Management's Discussion and Analysis the following information relating to your issuances of equity instruments:

- A more in-depth discussion of significant factors, assumptions, and specific 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

Results of Operations, pages 42-44

34. Please revise your MD&A so that there is more focus on analysis as required by our recent MD&A Release No. 33-8350; 34-48960; FR-72 (December 19, 2003). In that release, we explained that, "MD&A requires . . . an 'analysis' of known material trends, events, demands, commitments and uncertainties. MD&A should not be merely a restatement of financial statement information in a narrative form . . . . A thorough analysis often will involve discussing both the intermediate effects of those matters and the reasons underlying those intermediate effects." For example, please explain why you expect grant revenue to decline in the future as stated on page 42, and what led to the addition of new government grants from 2003 to 2004 as discussed on page 43. Please review your entire MD&A and revise accordingly. We may have further comments.

Liquidity and Capital Resources, pages 44-45

35. Please describe the key assumptions you refer to on page 45 as they relate to your working capital and capital expenditure needs for the next 18 months. For example, what clinical trials or preclinical trials does this assumption assume you will have performed.

Business, pages 48-66

General

36. Please explain the meaning of technical terms the first time they appear. Set forth below are a few examples of terms that should be explained.
    - "titration"
    - "PK properties"
    - "transdermal and transmucosal forms"

Overview, pages 48-49

37. We note your statement on page 48 that you believe your Staccato technology will enable you "to move a compound from initial screening through filing of an IND in 12 to 18 months." Please disclose if you were able to accomplish this for your current product candidates. If not, please explain why you believe you will be able to accomplish this for product candidates in the future.

Market Opportunity, page 52

38. Please provide the basis for your belief that approximately seven million patients are unable to take triptan medications safely or have insufficient therapeutic response.

AZ-001 (Staccato prochlorperazine), pages 54-56

39. Please revise your disclosure here to explain the significance and meaning of "$p<0.05$".

40. Please provide further explanation of the intent to treat population and the treatment received population. This discussion is unclear. Were these two separate trials?

41. If they were not two separate trials, the following statements appear inconsistent:

    "Although analysis of all patients randomized in the trial, known as an intent to treat, or ITT, population, demonstrated positive trends for headache pain relief, the improvement compared to placebo was not statistically significant for AZ-001 at specific time point for the pain-free score." [From the second full paragraph on page 53];

"The TR population pain-free score were statistically significant compared to placebo for the 10mg dose group at 30, 45, 60 and 120 minute time points." [From the fifth full paragraph on page 53]

Please explain.

42. Please provide a textual discussion of the graph provided on page 54.

AZ-002 (Staccato alprazolam), pages 54-56

43. Please briefly describe the side effects referred to on page 55.

Manufacturing, page 58

44. Please revise the discussion of your agreement with Autoliv ASP to disclose any amounts paid/received to date and the range of amounts you would be required to pay Autoliv if you terminate the agreement.

Employees, page 66

45. Please disclose the number of part-time employees you have, if any.

Patents and Proprietary Rights, page 64

46. You state that you hold over 20 U.S patents and your describe four of them. Please revise to describe the nature of the remaining patents.

Facilities, page 66

47. Please revise to disclose the amount of your annual lease payments for the two properties listed.

Executive Compensation, page 73

48. Please provide compensation information for the year ended December 2005 in addition to the information for the year ended 2004.

Financial Statements

Balance Sheet, page F-3

49. Please revise to present receivables from affiliates as a deduction from stockholders' equity. Refer to Staff Accounting Bulletin 4:G.

Note 11. Convertible Preferred Stock, page F-30

50. Please tell us what consideration was given to recording a beneficial conversion feature for the 40,435,438 shares of convertible preferred stock issued in November and December 2004. Refer to EITFs 00-27 and 98-5.

Note 12. Warrants page F-33

51. Please discuss the registration rights agreement in the footnotes and clearly outline its requirements and any related damages that may be incurred. Discuss the potential amount of damages possible under the contract, whether any cap exists to limit such damages, and the details of any options to have such damages settled in shares.

52. Please tell us why you do not believe your warrants meet the criteria of a derivative in SFAS 133. Specifically address each criteria and tell us if the warrants have a cashless exercise feature.

53. It appears that the registration rights agreement requires you to deliver registered shares upon exercise of your warrants. Refer to paragraphs 14 – 18 of EITF 00-19, which discuss the accounting treatment when a contract is not permitted to be settled in unregistered shares. It appears the warrants may be required to be classified as a liability under EITF 00-19 at fair value, with changes in fair value recorded in earnings (similar to a derivative under SFAS 133).

Note 17. Subsequent Events, page F-37
Officer Notes Receivable, page F-37

54. Please clarify the accounting treatment for the extinguishment of debt in December 2005 and additional amounts paid for taxes and clarify the methodology used to value the change in exercise price. You state that you will settle the transaction based on the intended offering price in your initial public offering. Clarify the intended accounting treatment when you settle the transaction, since it appears the settlement is in a different period than the extinguishment of debt. Tell us the basis for your accounting treatment including any GAAP literature that supports your accounting.

Item 16. Exhibits and Financial Statement Schedules, page II-3

55. Please file your remaining exhibits, including the legal opinion with your next amendment or as soon as it becomes available as we will need time to review it prior to granting effectiveness of the registration statement.

* * * * *

As appropriate, please amend your filing 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 supplemental 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 filings reviewed by the staff to be certain that they have provided all information investors require for an informed 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 this action 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 a 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 Sasha Parikh at (202) 551-3627 or Mary Mast at (202) 551-3613 if you have questions regarding comments on the financial statements and related matters. Please contact Sonia Barros at (202) 551-3655 or Suzanne Hayes at (202) 551-3675 with any other questions.

Sincerely,

Jeffrey P. Riedler
Assistant Director

cc: James C. T. Linfield, Esq.
Brent D. Fassett, Esq.
Cooley Godward LLP
380 Interlocken Crescent, #900
Broomfield, Colorado 80021