Mail Stop 6010

October 12, 2005

Mr. Michael Grey
President and Chief Executive Officer
SGX Pharmaceuticals, Inc.
10505 Roselle Street
San Diego, CA 92121

Re: SGX Pharmaceuticals, Inc.
Form S-1 Registration Statement
File No. 333-128059

Dear Mr. Grey:

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.

Comments applicable to the entire filing

1. We note that your filing contains numerous omissions throughout the prospectus which relate to the offering price range or the number of shares you will sell. These omissions include but are not limited to:

* Summary Financial Data
* Use Of Proceeds
* Capitalization
* Dilution
* The Option Grants Table
* Shares Eligible For Future Sale
* The Principal Stockholders Table
* Description of Capital Stock

Rule 430A requires you to include this information in your filing based upon an estimate of the offering price within a bona fide range you disclose on the cover page and based upon an estimate of the number of shares you will sell. We consider a bona fide range to be $2 if the price is under $20 and 10% if it is above $20. You should include the required information in an amendment prior to circulating a "red herring" prospectus.

2. Provide us with copies of all the graphic, photographic or artistic materials you intend to include in the prospectus prior to its printing and use. Please note that we may have comments. Please also note that all textual information in the graphic material should

be brief and comply with the plain English guidelines regarding jargon and technical language.

3. Comments on your application for confidential treatment will be provided in a separate letter when they are available. Please note that we will not be in a position to accelerate effectiveness until all issues relating to your confidential treatment request have been resolved.

4. In a number of places in your document you have used technical jargon that is not likely to be understood by your readers. Technical jargon should not appear in the forefront of the prospectus. Please refer to Rule 421 of Regulation C. In the remainder of the prospectus you should minimize the use of jargon. If you cannot convey information without using jargon, please explain what the jargon means at the first place the terms appear. Here are some examples of technical jargon that needs to be replaced:

* Third-line treatment
* Second-line treatment
* Myelodysplastic Syndromes
* Lead compounds
* Proprietary fragment-based drug discovery platform
* Well-validated but challenging targets
* Lead optimization stage
* Receptor tyrosine kinases
* Dose-escalation trial
* Refractory to prior treatment
* Single-arm, open-label clinical trial
* Primary clinical endpoint
* Control therapy
* Has been powered to detect a doubling of the historical CR rate...
* Fast track designation
* Well-validated and suited for lead discovery
* Surrogate endpoints
* Mucositis
* Aplasia and sepsis
* Generic class of dioxolanes
* Patent estate
* Surrogate endpoints

To the extent that these terms cannot be replaced by suitable alternatives, please revise to explain the meaning of these terms the first time each one is used.

5. Throughout your document you have used a large number of acronyms that are not likely to be familiar to your readers. The use of acronyms is a convenience for the writer, but it forces readers to learn a new vocabulary in order to understand the disclosure in your document. Please delete all of the acronyms except those which can be commonly found in general interest publications. Examples of acronyms that should be deleted include:

* AML
* CR
* CRp
* CI
* CML
* MDS
* ATU
* MAA

Table of Contents Page

6. Please refer to the next to last paragraph on this page (and the next to last bullet on page 5). In it you state that references to a number of specified documents are references to the documents that "will be in effect upon completion of this offering." Please delete this statement as it is likely to confuse readers. The documents filed as exhibits to this registration statement, and discussed in the filing, should be the documents that will be in effect upon completion of this offering.

7. Please refer to the last paragraph on this page in which you appear to disclaim liability for your disclosures. It is not appropriate to disclaim liability for information you include in your registration statement. Please delete the paragraph.

Prospectus Summary

8. Please delete the phrase "is qualified in its entirety by the information appearing elsewhere in this prospectus" from the introductory paragraph. The statement is legalistic and inappropriate.

9. Please refer to the table at the bottom of page 1, and a similar table that appears on page 48. In the column called "Program/Indication" you have included industry jargon and acronyms. In the column called "Status" you have included a parenthetical phrase at the end of each item, (e.g. data expected 2H06) which also appears to be industry jargon. Please revise the table to eliminate all of the jargon or to ensure that the meaning of the term is sufficiently explained.

10. In the table, you appear to state that you will submit an IND to the FDA in the fourth quarter of 2006 for a drug called BCR-ABL that is currently in preclinical development. It is unclear to us how you can make such a prediction at this stage of development. Please disclose the factual basis for this prediction, or in the alternative, delete it.

11. The disclosure currently included in your summary is unbalanced. While you have included a discussion of your positive opinions and beliefs regarding your proposed products and anticipated results of clinical studies, you have not included any discussion of the negative aspects of your business, and have not clearly indicated that positive results are not assured. Please limit the discussion of your disclosed products to the targeted indication and the stage of clinical trials. Move the remaining details, including any discussion of the results of clinical trials, to the Business section and balance this disclosure with a discussion explaining that later stage testing might not support the results of earlier testing. Additionally, revise the disclosure to discuss the negative aspects of your business. The negative aspects should include your history of losses, the fact that you do not have FDA approval for any for any of your products, that if you don't obtain fast track designation for Troxatyl your timeline for NDA submission and approval could be extended by several years and that your technology "platform" has not yet resulted in any actual new drugs. The discussion of the negative aspects should be disclosed as prominently as the positive aspects and should not be separated from the discussion of the positive aspects.

12. Please note that in order to use the terms "Phase I/II" and "Phase II/III" your clinical trials must meet all the requirements of both referenced phases of clinical trials. For each time the phrase is used, supplementally confirm that all of the requirements of each phase of testing have been met or revise to use an alternative term to describe the phase of clinical trials.

13. Explain your basis for believing that FAST is capable of producing at least one new IND per year beginning in 2006.

14. Please balance the discussion of your strategy with a discussion of the risks and obstacles you will encounter in implementing this strategy.

Risk Factors - page 8

We cannot be certain that our clinical trial design for our ongoing pivotal Phase II/III clinical trial of Troxatyl for the third-line treatment of AML will be sufficient to lead to regulatory approval. - page 8

15. The current subheading on this risk factor is very vague and indirect. Please revise it to more specifically identify the risk and its potential adverse consequences. As we understand it, the actual risk is that you have chosen a research design that is different from that recommended by the FDA, and you have foregone a Special Protocol Assessment which would have given you the FDA`s concurrence on the design and size of the clinical trial intended to form the primary basis of an effectiveness claim. As a consequence, you can`t be certain that the design, conduct and data analysis approach you plan on using for your trial will be sufficient to allow you to submit an NDA for the drug, or to receive approval for the drug. Please revise the subheading accordingly.

While we may seek to take advantage of various regulatory mechanisms intended to accelerate drug development and approval...there is no guarantee that the FDA will permit us to do so. - page 9

16. Please revise the subheading to more specifically identify the risk and include the potential adverse consequences. It appears from the body of the risk factor that one very significant adverse consequence is that you could not submit an NDA for Troxatyl until the third quarter of 2009 at the earliest instead of the "late 2006 or early 2007" indicated in the summary section of the prospectus.

Because we exclusively licensed our product candidate, Troxatyl, from Shire and our rights are subject to certain licenses to Shire from third parties, any dispute with Shire or between Shire and any of thes third parties may adversely affect our ability to develop and commericialize Troxatyl. - page 13

17. Are there any material limitations to Shire`s rights under its agreements with Yale University and University of Georgia Research Foundation? When do these agreements expire?

We are at an early stage of development, particularly in our internal development programs, and we may never attain product sales. - page 13

18. This risk factor subheading is also too vague and generic to be meaningful. Please revise it to more adequately summarize the risk identified in the body of the risk factor. You should also clarify it to make clear whether you are referring only to your FAST technology and its potential results, or to the development of Troxatyl as well. Although the risk factor appears to be discussing the drug development program, we note that Troxatyl is mentioned in the last sentence.

If we fail to establish new collaborations and other commercial agreements, we may have to reduce or limit our internal drug discovery and development efforts. - page 14

19. Please refer to the caveat included in the fifth sentence of this risk factor to the effect that although you refer to may of your

commercial arrangements with other pharmaceutical and biotechnology companies as "partnerships" or "collaborations," in many cases you are only providing specific services for fees and milestone payments without any interest in future product sales or profits. The use of these terms to describe agreements for which you are only providing services for a fee is inappropriate. Please revise the disclosure throughout the document accordingly and confirm to us that the only agreements and arrangements described in this document as "partnerships" or "collaborations" are those in which you have future interests at stake.

We are dependent on our collaborations, and events involving these collaborations or any future collaborations could prevent us from developing or commercializing product candidates. - page 14

20. The first full paragraph of this risk factor is repeated in the carryover paragraph at the top of page 15. Please delete the repetitive disclosure.

Our drug discovery efforts are dependent on continued access to and use of our beamline facility...page 16

21. Please revise the subheading to identify how you might be adversely affected.

22. Please disclose, in the risk factor, how many beamline facilities there are, whether other facilities are comparable to your current facility and how long it might take you to obtain equivalent access to a comparative alternate facility. You need to provide an adequate factual context for analyzing this risk and its potential adverse consequences.

If our competitors develop drug discovery technologies that are more advanced than ours...page 16

23. The subheading does not appear to adequately summarize all of the information in the body of the risk factor. Please separate the discussion of the competitive environment for Troxatyl from the discussion of the competitive environment for your fragment-based drug discovery activities and present each discussion under an appropriate subheading.

We may not be able to obtain patent term extension/restoration or other exclusivity for our products. - page 26

24. The information in this risk factor is too vague and generic to be meaningful. Please expand it to include a factual context that ties the risk to your specific products. In this regard, we have also noted the discussion in the last paragraph of page 49. We think the discussion on page 49 is also too generic to be meaningful. Please expand it as well.

Future sales of our common stock may cause our stock price to decline. - page 28

25. It will be difficult for a potential investor to sort out and remember all of the numbers included in this risk factor. Please present the numerical information in the tabular format included in the examples contained in Staff Legal Bulletin No. 7, as revised.

26. Please include more information regarding the "automatic annual increases" that will be included in the share reserves, and identify the potential adverse consequences resulting from these increases. We may have additional comments.

Use of Proceeds - page 31

27. Please expand the discussion in this section to quantify the

amount of proceeds you anticipate using for each stated purpose.

28. Please indicate, clearly, whether you anticipate that the proceeds from this offering will enable you to complete the development of Troxatyl. If not, discuss how far along in the process you anticipate the proceeds will enable you to go.

29. We note your statement that you may use a portion of the proceeds
to repay a portion of your debt. Please include the information specified in Instruction 4 to Item 504 of Regulation S-K.

Captialization - page 32

30. Please specifically state that the table sets forth your cash and
cash equivalents and your capitalization as of June 30, 2005.

Management`s Discussion and Analysis

Financial Operations Overview

Research and Development Expense, page 38

31. 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. For each of your major research and development projects please disclose the costs incurred during each period presented and to date on the project.

Critical Accounting Policies and Estimates

Stock-Based Compensation Expense, page 40

32. We note the supplemental information provided on September 22, 2005 regarding management`s pricing of stock option grants. Please
be aware that we may have additional comments upon finalization of price range.

Results of Operations

Six Months Ended June 30, 2004 Compared to 2005 - page 41

33. Please provide more detail regarding the personnel reductions referenced under "General and Administrative." Also, please refer to
the two risk factors on page 20 that relate to increasing the size of
your organization and attracting and keeping personnel. The reduction in personnel seems to be inconsistent with the risks described on page 20. Please explain how this reduction in personnel
relates to the risk factors describing your need for additional personnel and your ability to attract and keep employees.

Liquidity and Capital Resources - page 43

34. Please refer to the discussion of the proposed financing agreement located on page 44. When the agreement is signed it should
be filed as an exhibit to the registration statement.

35. Identify the lender on your line of credit and file the loan agreement as an exhibit.

36. Also, please expand the discussion here and in the "Use of Proceeds" section to explain, in reasonable detail, how you will use
the additional funds from the loan.

Cash Flows - page 44

37. Please revise your discussion to address the underlying reasons
for fluctuations in net cash used in operations. It is insufficient
to reiterate information currently presented within the Consolidated
Statement of Cash Flows.

Contractual Obligations - page 46

38. We note that you are required to make milestone payments based on successful development and approval of Troxatyl and will be required to make royalty payments based on net sales. Please include these amounts within the table or provide a discussion of your obligations and why you are unable to estimate the timing of payments within the notes to the table.

39. Please update this information through September 30, 2005. If you finalize the new debt agreement after that date, you should also include it in the table.

Business - page 48

40. Please note that we have not completed our review of your application for confidential treatment. We may have additional comments on your disclosure in conjunction with that review.

Troxatyl - page 48

41. On page 49, disclose the amounts paid to date to Shire and the aggregate amount of potential milestone payments to Shire. If the agreement with Shire calls for minimum royalty payments in any year, disclose the aggregate minimum royalty payments.

Acute Myelogenous Leukemia - page 50

42. Please refer to the second paragraph under this heading. You need to expand the discussion to explain the significance of your finding that the low-level toxicities you observed were not age-related.

43. If you only acquired the rights to Troxatyl in July of 2004, it is unclear how you could have patients that have experienced "durations of response" of over 12 months in the Phase I/II clinical trial. Does this mean Shire was conducting this trial at the time you acquired the rights to this drug?

44. Please refer to the discussion of your current Phase II/III clinical trial. If the M.D. Anderson Cancer Center article was not published until August of 2005, it is not clear how you could have begun a trial in July 2005 using the information contained in that article. Please revise the disclosure to explain this.

45. The discussion in this section contains a good deal of technical jargon that is not likely to be familiar to investors not involved in your industry. Please revise the disclosure throughout the section to replace the technical jargon with plain English, or where you cannot eliminate the technical language, explain what the terms mean at the first place they appear. For example, explain what you mean when you say that the "clinical trial has been powered to detect a doubling of the historical CR rate of 4.7% derived from the ...database."

Research Programs - page 54

46. When does your agreement with Pierre Fabre Medicament expire? Does the agreement provide for any payments to be made/received? If it does, please quantify the amount of any payments to date and any aggregate future payments and clarify who has the obligation to make these payments.

47. It appears that the agreement with Pierre Fabre Midicament has not been filed as an exhibit. Please file the agreement or provide us with a written analysis supporting your determination that it is

not required to be filed.

Collaborations, Commercial Agreements and Grants - page 56

48. For each agreement that provides for payments to be made/received, quantify all amounts paid to date and all potential future payments and clarify which party has the obligation to make these payments.

49. We note that you have filed agreements with UroGene as exhibits to the registration statement. Please revise to describe these agreements.

Related Party Transactions - page 88

50. Please refer to footnote 2 to the table on page 88. Dr. Papadopoulos may not disclaim ownership of securities that have not been included in the table. Please revise the table to include the 19,454 shares referenced in the footnote. A similar revision should be made to the tables on pages 89, 90 and 93.

Underwriting - page 102

51. Tell us whether any of the lead underwriters or any other broker dealers who may participate in the syndicate may offer and/or sell the shares electronically. If so, identify them in this section and disclose that they will be offering the shares electronically. Tell us the procedures they will use in their selling effort and how they intend to comply with the requirements of Section 5 of the Securities Act of 1933 particularly with regard to how offers and final confirmations will be made and how and when purchasers will fund their purchases.

52. Tell us whether you intend to do a "directed share offering". If so, please disclose in this section the number of shares you will offer and to whom you will make the offer. Provide us with any material you have sent or intend to send to these potential purchasers such as a "friends and family letter". Tell us when you first sent them or intend to send them to these potential purchasers. Tell us whether the sale will be handled by you directly or by the underwriting syndicate. Tell us the procedures you or the underwriter will employ in making the offering and how you will assure that this offer will meet the requirements of Section 5 of the Securities Act and Rule 134. We may have further comments.

53. Tell us whether you or the underwriters have any arrangements with a third party to host or access your preliminary prospectus on the internet. Also, tell us who the party is and the address of the website. Describe the material terms of the agreement and provide us with a copy of any written agreement. Provide us with copies of all information concerning your company or the offering that appears on the third party website. We may have further comments.

54. Confirm that you have described the nature and extent of any possible short sales by the underwriters. To the extent applicable, address the points enumerated in Section VIII.A.3. of the Division of Corporation Finance's "Current Issues Outline" regarding syndicate short sales. The June 16, 2000 version is available on the SEC's website, www.sec.gov.

Consolidated Financial Statements

Notes to Consolidated Financial Statements

Note 1. Organization and Summary of Significant Accounting

Policies

Stock-Based Compensation, page F-10

55. We note in your disclosure that $10.5 million of deferred stock compensation was recorded in the six months ended June 30, 2005. However the analysis that was provided to us supplementally indicates that $9.9 million was recorded. Please advise or revise.

Research and Development, page F-13

56. Please expand your research and development policy to include the types of costs included in R&D, including salaries, contractor fees, building costs, utilities, administrative expenses and allocations of corporate costs.

Note 2. Balance Sheet Details

Property and Equipment, page F-16

57. We note that you have entered into property and equipment leases that qualify as capital leases under SFAS 13. As such, please provide information required by paragraph 16a(ii).

Note 5. Redeemable Convertible Preferred Stock

58. Please provide a roll-forward of the balance of redeemable convertible preferred shares outstanding for each class of preferred shares for each period presented as required by paragraph 28(c) of Rule 5-02 of Regulation S-X.

Note 6. Stockholders' Deficit

Common Stock Issuable, page F-21

59. Please provide a description of the current accounting treatment for the variable number of common shares issuable as a result of the conversion of the note payable to Millennium Pharmaceuticals, Inc. during 2003 and 2004 into a right to receive common stock. Additionally, please provide a detail description of the basis for this accounting treatment, including specific references to the accounting literature relied upon and you consideration of the provision of SFAS 150.

Accountants Consent

60. Provide a currently dated and appropriately signed consent from your independent accountants in the amendment for which you will request effectiveness.

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

You may contact Vanessa Robertson at 202-551-3649 or Kevin Woody at 202-551-3629 if you have questions regarding comments on the financial statements and related matters. Please contact Mary K. Fraser at 202-551-3609 or me at 202-551-3610 with any other questions.

Regards,

Jeffrey P. Riedler
Assistant Director

Cc: Frederick T. Muto, Esq.
Cooley Godward LLP
4401 Eastgate Mall
San Diego, CA 92121
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