

Via Facsimile and U.S. Mail  
Mail Stop 6010

August 11, 2006

Mr. Vicente Anido, Jr., Ph.D.  
President and CEO  
ISTA Pharmaceuticals, Inc.  
15295 Alton Parkway  
Irvine, CA 92618

**Re: Form 10-K for Fiscal Year Ended December 31, 2005**  
**Filed March 6, 2006**  
**File No. 0-31255**

Dear Mr. Anido, Jr.:

We have limited our review of your filing to the issues we have addressed in our comments. In our comments, we ask you to provide us with information so we may better understand your disclosure.

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.

**Form 10-K for the year ended December 31, 2005**

Management's Discussion and Analysis  
Research and development expenses, page 28

1. Please expand your disclosure by referring 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#secviii>. Please provide us the following information, in disclosure-type information for each of your major research and development projects:

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

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.

Selling, General and Administrative expenses, page 29

2. Please tell us why it is appropriate to expense the entire \$10 million payment to Allergan for the rights to market and sell Vitrase for all uses in the United States and other specified markets.

Contractual Obligations, page 31

3. Refer to your table of contractual obligations. Please provide us, in disclosure-type format, a revised table of contractual obligations and related disclosures [to the table](#) to reflect the following:
  - Provide your product purchase commitment and license fee payable with Biozyme in your contractual obligations table. If the long-term liability obligation included in the table of contractual obligation is the purchase commitment and license fee payable with Biozyme then please disclose that fact.
  - Include in the table the aggregate milestones that could be paid under collaboration agreements or disclose as a note to the table the reason that the amounts are not included.
  - Include in the table the royalty payments to be made to Allergan or disclose as a note to the table the reason that the payments are not included.

Critical Accounting Policies and Estimates

Revenue Recognition, page 32

4. With regards to your revenue recognition policy documented here as a critical accounting policy and within your notes to the consolidated financial statements, we believe that your disclosure related to estimates of items that reduce gross revenue such as product returns, chargebacks, customer rebates and other discounts and allowances could be improved. Please provide us, in disclosure-type format, the following:
- a) The nature and amount of each accrual at the balance sheet date and the effect that could result from using other reasonably likely assumptions than what you used to arrive at each accrual such as a range of reasonably likely amounts or other type of sensitivity analysis.
  - b) The factors that you consider in estimating each accrual such as historical return of products, levels of inventory in the distribution channel, estimated remaining shelf life, price changes from competitors and introductions of generics and/or new products.
  - c) To the extent that information you consider in b) is quantifiable, disclose both quantitative and qualitative information and discuss to what extent information is from external sources (e.g., end-customer prescription demand, third-party market research data comparing wholesaler inventory levels to end-customer demand). For example, in discussing your estimate of product that may be returned, consider disclosing and discussing, preferably by product and in tabular format, the total amount of product (in sales dollars) that could potentially be returned as of the balance sheet date and disaggregated by expiration period.
  - d) If applicable, discuss any shipments made as a result of incentives and/or in excess of your customer's ordinary course of business inventory level. Discuss your revenue recognition policy for such shipments.
  - e) A roll forward of the accrual for each estimate for each period presented showing the following:
    - Beginning balance,
    - Current provision related to sales made in current period,
    - Current provision related to sales made in prior periods,
    - Actual returns or credits in current period related to sales made in current period,
    - Actual returns or credits in current period related to sales made in prior periods, and
    - Ending balance.

- f) A results of operations discussion of the amount of and reason for the period to period fluctuations for each type of reduction of gross revenue, such as product returns, chargebacks, customer rebates and other discounts and allowances) including the effect that changes in your estimates of these items had on your revenues and operations.

Report of Independent Accountants, page F-2

5. Since the report filed does not contain a typed signature of Ernst & Young LLP, please confirm that they provided a manually signed report that is the same as the one included in your filing and that you have retained it for your records.

Note 1. Organization and Summary of Significant Accounting Policies  
Revenue Recognition, page F-11

6. Please provide us an accounting analysis supporting your classification of royalties paid "creditable" by milestone payments as a reduction of revenue.

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Please provide us the information requested within 10 business days of the date of this letter or tell us when you will provide a response prior to the expiration of the 10-day period. Please furnish a letter with your response that keys your response to our comments. Detailed letters greatly facilitate our review. You should file the letter on EDGAR under the form type label CORRESP. Please understand that we may have additional comments after reviewing your response 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 Exchange Act of 1934 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.

In connection with responding to our comments, please provide, in your letter, a statement from the company acknowledging that:

- the company is responsible for the adequacy and accuracy of the disclosure in the filing;
- staff comments or changes to disclosure in response to staff comments do not foreclose the Commission from taking any action with respect to the filing;
- and

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- the company may not assert staff comments 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 our review of your filing or in response to our comments on your filing.

You may contact Sasha Parikh, Staff Accountant, at (202) 551-3627 or Joseph Roesler, Accounting Branch Chief, at (202) 551-3628 if you have questions regarding the comments. In this regard, do not hesitate to contact me, at (202) 551-3679.

Sincerely,

Jim B. Rosenberg  
Senior Assistant Chief Accountant