



DIVISION OF
CORPORATION FINANCE

UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

November 12, 2010

Gary S. Jacob
President and CEO
Synergy Pharmaceuticals, Inc.
420 Lexington Ave., Suite 1609
New York, NY 10170

**Re: Synergy Pharmaceuticals, Inc.
Form 10-K for the year ended December 31, 2009
File No. 333-131722**

Dear Mr. Jacob:

We have reviewed your October 18, 2010 response to our October 6, 2010 letter and have the following comments.

Please respond to this letter within ten business days by providing the requested information and draft disclosure, or by advising us when you will provide this information. Please furnish us a letter on EDGAR under the form type label CORRESP that keys your responses to our comments.

After reviewing the information you provide us in response to our comments, we may have additional comments.

Compensation Discussion and Analysis, page 52

1. We note your response to comment one and the fact the report was prepared on March 16, 2006. Please expand the disclosure to explain what you mean by the phrase that "cash compensation data contained in the report had a common effective date of July 1, 2006" which date is subsequent to the date of the report.

Notes to the Financial Statements

9. Related Parties, page F-20

2. In your response to prior comment three you stated that a significant difference in market value between Callisto and Synergy does not exist when you consider the 113.2 million shares issuable in addition to Callisto's 54.5 million shares of common stock outstanding. You also stated that after taking into account the shares potentially outstanding upon the exercise of warrants and conversion of convertible preferred stock, there could be 167.7 million shares that you assumed would result in a market value of \$85.5 million for Callisto. Please tell us how you factored in the potential dilution in Callisto's recent

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common stock price of \$.51 due to an increase in the number of common shares outstanding of over 300%. Please also assess the likelihood of Callisto's exercise of the warrants and conversion of preferred stock in light of your statement that Callisto's drug development programs have experienced a number of failures over the past few years.

You may contact Sasha Parikh, Staff Accountant, at (202) 551-3627 or Gus Rodriguez, Accounting Branch Chief, at (202) 551-3752 if you have questions regarding the processing of your response as well as any questions regarding comments on the financial statements and related matters. Please contact John Krug, Staff Attorney, at (202) 551-3862 with questions on any of the other comments. In this regard, do not hesitate to contact me at (202) 551-3679.

Sincerely,

Jim B. Rosenberg
Senior Assistant Chief Accountant