CALLISTO PHARMACEUTICALS INC
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December 07, 2012

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**UNITED STATES**
**SECURITIES AND EXCHANGE COMMISSION**
**Washington, D.C. 20549**

# SCHEDULE 14A

Proxy Statement Pursuant to Section 14(a) of
the Securities Exchange Act of 1934 (Amendment No. )

Filed by the Registrant ý

Filed by a Party other than the Registrant o

Check the appropriate box:

o Preliminary Proxy Statement

o **Confidential, for Use of the Commission Only (as permitted by Rule 14a-6(e)(2))**

ý Definitive Proxy Statement

o Definitive Additional Materials

o Soliciting Material under §240.14a-12

**CALLISTO PHARMACEUTICALS, INC.**

(Name of Registrant as Specified In Its Charter)

(Name of Person(s) Filing Proxy Statement, if other than the Registrant)

Payment of Filing Fee (Check the appropriate box):

ý No fee required.

o Fee computed on table below per Exchange Act Rules 14a-6(i)(1) and 0-11.
(1) Title of each class of securities to which transaction applies:

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(4) Proposed maximum aggregate value of transaction:

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o Fee paid previously with preliminary materials.

o Check box if any part of the fee is offset as provided by Exchange Act Rule 0-11(a)(2) and identify the filing for which the offsetting fee was paid previously. Identify the previous filing by registration statement number, or the Form or Schedule and the date of its filing.

(1) Amount Previously Paid:

(2) Form, Schedule or Registration Statement No.:

(3) Filing Party:

(4) Date Filed:

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**PROXY STATEMENT/PROSPECTUS**
**OF**
**SYNERGY PHARMAECUTICALS INC.**
**2012 ANNUAL MEETING OF STOCKHOLDERS**

**PROXY STATEMENT**
**OF**
**CALLISTO PHARMACEUTICALS, INC.**
**SPECIAL MEETING OF STOCKHOLDERS**

**YOUR VOTE IS VERY IMPORTANT**

Synergy Pharmaceuticals Inc., which we refer to as Synergy, and Callisto Pharmaceuticals, Inc., which we refer to as Callisto, have entered into a merger agreement, as amended, pursuant to which Callisto will merge with and into Synergy, which transaction is referred to as the merger. Synergy and Callisto believe that the merger will enhance stockholders value for both Synergy and Callisto stockholders by (i) providing a method by which the Callisto stockholders can more directly share in the growth of Synergy and (ii) improving the share price of Synergy's common stock as a result of intended cost savings synergies. Before we complete the merger, the stockholders of Synergy and Callisto must approve and adopt the merger agreement. Callisto stockholders will vote to approve and adopt the merger agreement, as amended, and the other transactions and matters described below at a special meeting of stockholders to be held on January 3, 2013. Synergy stockholders will vote to approve and adopt the merger agreement and the other transactions and matters described below at an annual meeting of stockholders to be held on January 3, 2013.

The holders of Callisto common stock will receive in the merger 0.1799 of a share of Synergy common stock in exchange for each share of Callisto common stock (the "Exchange Ratio") and the 22,295,000 shares of Synergy common stock held by Callisto will be canceled. In addition, each stock option exercisable for shares of Callisto common stock that is outstanding at the effective time of the merger will be assumed by Synergy and converted into a stock option to purchase the number of shares of Synergy's common stock that the holder would have received if such holder had exercised such stock option for shares of Callisto common stock prior to the merger and exchanged such shares for shares of Synergy's common stock in accordance with the Exchange Ratio. In addition, each Callisto stock option exercisable for shares of Synergy common stock that is outstanding at the effective time of the merger will be assumed by Synergy and each outstanding warrant or obligation to issue a warrant to purchase shares of Callisto common stock, whether or not vested, shall be cancelled.

Synergy common stock is currently listed on The NASDAQ Capital Market under the symbol "SGYP." On November 30, 2012, the most recent practicable trading day prior to the printing of this Joint Proxy Statement/Prospectus, the closing price of Synergy common stock was $5.53 per share. The market price of the Synergy common stock may fluctuate before the completion of the merger, therefore, you are urged to obtain current market quotations for Synergy common stock. Synergy expects to issue an aggregate of 28,597,905 shares of its common stock in the merger upon completion of the merger, not including assumed stock options. We anticipate that the closing of the merger will occur not later than three business days following the affirmative Synergy and Callisto stockholder votes.

We are asking stockholders of Synergy to adopt and approve the merger agreement at the annual meeting of stockholders to take place on January 3, 2013, at 10:00 am Eastern Time, at the offices of Sichenzia Ross Friedman Ference LLP, 61 Broadway, 32nd Floor, New York, New York 10006. As this will be the annual meeting of Synergy stockholders, Synergy stockholders will also be asked to vote on Synergy director nominees, vote to approve an amendment to Synergy's 2008 Equity Compensation Incentive Plan to increase the number of shares of Synergy common stock reserved for issuance from 7,500,000 to 15,000,000, vote to amend Synergy's Amended and Restated Certificate of Incorporation to increase the number of shares of common stock authorized for issuance from 100,000,000 to 200,000,000, to ratify the appointment of BDO USA, LLP as Synergy's independent registered public accounting firm, approve, on an advisory basis, the compensation of Synergy's named executive officers and recommend, on an advisory basis, the frequency with which Synergy should conduct future stockholder advisory votes on named executive officer compensation.

We are asking stockholders of Callisto to adopt and approve the merger agreement at a special meeting of Callisto stockholders to take place on January 3, 2013, at 1:00 pm Eastern Time, at the offices of Callisto Pharmaceuticals, Inc., 420 Lexington Avenue, Suite 1609, New York, New York 10170. We cannot complete the merger unless Callisto and Synergy stockholders adopt and approve the merger agreement.

After careful consideration, the Synergy and Callisto Boards of Directors have unanimously approved the merger agreement and the respective proposals referred to above, and each of the Synergy and Callisto Boards of Directors has determined that it is advisable to enter into the merger. Each of the Board of Directors of Synergy and the Board of Directors of Callisto recommends that its respective stockholders vote "FOR" the respective proposals described in the accompanying Joint Proxy Statement/Prospectus.

**PLEASE GIVE ALL OF THE DETAILED INFORMATION ON SYNERGY, CALLISTO AND THE MERGER CONTAINED IN THE JOINT PROXY STATEMENT/PROSPECTUS YOUR CAREFUL ATTENTION, ESPECIALLY THE DISCUSSION IN THE SECTION ENTITLED "RISK FACTORS" BEGINNING ON PAGE 31 OF THIS JOINT PROXY STATEMENT/PROSPECTUS.**

**Neither the Securities and Exchange Commission nor any state securities regulators has approved or disapproved the Synergy common stock to be issued under this Joint Proxy Statement/Prospectus or passed upon the adequacy or accuracy of this Joint Proxy**

**Statement/Prospectus. Any representation to the contrary is a criminal offense.**

**This Joint Proxy Statement/Prospectus is not an offer to sell the Synergy common stock and it is not soliciting an offer to buy the Synergy common stock in any state where the offer or sale is not permitted.**

Joint Proxy Statement/Prospectus dated December 3, 2012 and to be mailed on or around December 5, 2012.

Please also see "Where You Can Find More Information" on page 178.

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## ADDITIONAL INFORMATION

**This Joint Proxy Statement/Prospectus incorporates business and financial information about Synergy and Callisto that is not included in or delivered with this document. This information is available from Synergy or Callisto without charge by first class mail or equally prompt means within one business day of receipt of your request, excluding exhibits unless the exhibit has been specifically incorporated by reference into the information that this document incorporates. To obtain timely delivery, you must request the information no later than five business days before you must make your investment decision. In the case of Synergy stockholders, this means that you must make your request no later than December 27, 2012, and in the case of Callisto stockholders, this means that you must make your request no later than December 27, 2012. If you want to receive a copy of any document incorporated by reference, please request it in writing or by telephone from the appropriate company at the following address:**

**Synergy Pharmaceuticals Inc.**
**420 Lexington Avenue, Suite 1609**
**New York, New York 10170**
**Attention: Bernard F. Denoyer, Secretary**
**Telephone: (212) 297-0020**

**Callisto Pharmaceuticals, Inc.**
**420 Lexington Avenue, Suite 1609**
**New York, New York 10170**
**Attention: Bernard F. Denoyer, Secretary**
**Telephone: (212) 297-0010**

Stockholders may also consult Synergy's or Callisto's websites for more information concerning the merger described in this Joint Proxy Statement/Prospectus and each of the parties thereto. Synergy's website is www.synergypharma.com and Callisto's website is www.callistopharma.com. Information included on these websites is not incorporated by reference into this Joint Proxy Statement/Prospectus.

This Joint Proxy Statement/Prospectus is dated December 3, 2012 and is first being mailed to the stockholders of Callisto and the stockholders of Synergy on or about December 5, 2012.

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# Synergy Pharmaceuticals Inc.

**420 Lexington Avenue, Suite 1609**
**New York, New York 10170**
**(212) 297-0020**

**NOTICE OF ANNUAL MEETING OF STOCKHOLDERS OF**
**SYNERGY PHARMACEUTICALS INC.**
**TO BE HELD ON JANUARY 3, 2013**

To the Stockholders of Synergy Pharmaceuticals Inc.:

The annual meeting of Synergy Pharmaceuticals Inc., a Delaware corporation, will be held on January 3, 2013, at 10:00 a.m., Eastern Time, at the offices of Sichenzia Ross Friedman Ference LLP, 61 Broadway, 32nd Floor, New York, New York 10006 for the following purposes:

1. To consider and vote upon a proposal to adopt and approve the Agreement and Plan of Merger, dated as of July 20, 2012, as amended on October 15, 2012, by and between Synergy Pharmaceuticals Inc. and Callisto Pharmaceuticals, Inc, as described in the attached Joint Proxy Statement/Prospectus;

2. To consider and vote upon an adjournment of the meeting, if necessary, if a quorum is present, to solicit additional proxies if there are not sufficient votes in favor of Proposal No. 1;

3. To amend Synergy's 2008 Equity Compensation Incentive Plan to increase the number of shares of Synergy common stock reserved for issuance from 7,500,000 to 15,000,000, as described in the attached Joint Proxy Statement/Prospectus;

4. To amend Synergy's Amended and Restated Certificate of Incorporation to increase the number of shares of common stock authorized for issuance from 100,000,000 to 200,000,000, as described in the attached Joint Proxy Statement/Prospectus;

5. To re-elect seven (7) current Synergy directors whose terms will continue until the 2013 Annual Meeting of Stockholders;

6. To ratify the appointment by the Audit Committee of the Board of Directors of BDO USA, LLP as the independent registered public accounting firm of Synergy Pharmaceuticals Inc. for its fiscal year ending December 31, 2012;

7. To approve, on an advisory basis, the compensation of Synergy's named executive officers;

8. To recommend, on an advisory basis, a three-year frequency with which Synergy should conduct future stockholder advisory votes on named executive officer compensation; and

9. To transact such other business as may properly come before the meeting or any adjournment or postponement thereof.

The Board of Directors of Synergy has fixed November 29, 2012 as the record date for the determination of stockholders entitled to notice of, and to vote at, the Synergy annual meeting and any adjournment or postponement thereof. Only stockholders of record at the close of business on the record date are entitled to notice of, and to vote at, the Synergy annual meeting. Only stockholders or their proxy holders and Synergy guests may attend the meeting. A list of stockholders entitled to vote will be kept at the offices of Synergy Pharmaceuticals Inc., 420 Lexington Avenue, Suite 1609, New York, New York for ten days before the meeting. At the close of business on the record date, Synergy had * shares of common stock outstanding and entitled to vote.

/s/ GARY S. JACOB

Gary S. Jacob, *Chief Executive Officer*

December 3, 2012

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**Your vote is important.**

**The affirmative vote of the holders of a majority of the votes cast in person or by proxy at the Synergy annual meeting is required to approve Proposal No. 2 regarding an adjournment of the special meeting, if necessary, if a quorum is present, to solicit additional proxies if there are not sufficient votes in favor of Proposal No. 1, Proposal No. 3, Proposal No. 6, Proposal No. 7 and Proposal No. 8. In addition, the affirmative vote of the holders of a majority of the votes cast in person or by proxy at the Synergy annual meeting is required for approval of Proposal No. 3, Proposal No. 6, Proposal No. 7 and Proposal No. 8. The affirmative vote of the holders of a majority of the shares of Synergy common stock outstanding on the record date for the Synergy annual meeting is required for approval of Proposal No. 1 and 4. For the election of directors (Proposal No. 5), the seven nominees receiving the most "For" votes from the shares having voting power present in person or represented by proxy will be elected. You are urged to attend the annual meeting in person, but if you are unable to do so, the Board of Directors would appreciate the prompt return of the enclosed proxy card, dated and signed, or, if your proxy card or voting instruction form so indicates, your prompt vote electronically via the Internet or telephone. *We strongly encourage you to vote electronically if you have that option.***

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# Callisto Pharmaceuticals, Inc.

**420 Lexington Avenue, Suite 445**
**New York, NY 10170**
**(212) 297-0010**

**NOTICE OF SPECIAL MEETING OF STOCKHOLDERS OF**
**CALLISTO PHARMACEUTICALS, INC.**
**TO BE HELD ON JANUARY 3, 2013**

To the Stockholders of Callisto Pharmaceuticals, Inc:

A special meeting of stockholders of Callisto Pharmaceuticals, Inc., a Delaware corporation, will be held on January 3, 2013, at 1:00 p.m., Eastern Time, at the offices of Callisto Pharmaceuticals, Inc., 420 Lexington Avenue, Suite 1609, New York, New York 10170, for the following purposes:

1. To consider and vote upon a proposal to adopt and approve the Agreement and Plan of Merger, dated as of July 20, 2012, as amended on October 15, 2012, by and between Synergy Pharmaceuticals Inc. and Callisto Pharmaceuticals, Inc., as described in the attached Joint Proxy Statement/Prospectus;

2. To consider and vote upon an adjournment of the special meeting, if necessary, if a quorum is present, to solicit additional proxies if there are not sufficient votes in favor of Proposal No. 1; and

3. To transact such other business as may properly come before the meeting or any adjournment or postponement thereof.

Only stockholders of record at the close of business on November 29, 2012 may vote at the special meeting or any adjournment or postponement thereof. A list of stockholders entitled to vote will be kept at Callisto, 420 Lexington Avenue, Suite 1609, New York, NY 10170, for ten days before the special meeting.

**Please do not send any certificates for your stock at this time.**

/s/ GARY S. JACOB

Gary S. Jacob, *Chief Executive Officer*

December 3, 2012

**Your vote is important.**

**The affirmative vote of the holders of a majority of the outstanding shares of common stock in person or by proxy at the Callisto special meeting is required to approve Proposal No. 1, regarding adoption and approval of the merger agreement. The affirmative vote of the holders of a majority of the votes cast in person or by proxy at the Callisto special meeting is required to approve Proposal No. 2 regarding an adjournment of the special meeting, if necessary, if a quorum is present, to solicit additional proxies if there are not sufficient votes in favor of Proposal No. 1. You are urged to attend the special meeting in person, but if you are unable to do so, the Board of Directors would appreciate the prompt return of the enclosed proxy card, dated and signed, or, if your proxy card or voting instruction form so indicates, your prompt vote by telephone or internet. If you sign, date and mail your proxy card without indicating how you wish to vote, your proxy will be counted as a vote in favor of the adoption of the merger agreement and an adjournment of the Callisto special meeting, if necessary, if a quorum is present, to solicit additional proxies if there are not sufficient votes in favor of Proposal No. 1. If you fail to return your proxy card or vote by telephone or internet, the effect will be a vote against the adoption of the merger agreement and your shares will not be counted for purposes of determining whether a quorum is present at the Callisto special meeting. If you do attend the Callisto special meeting and wish to vote in person, you may withdraw your proxy and vote in person. If your shares are held in "street name" by your broker or other nominee, only that holder can vote your shares and the vote cannot be cast unless you provide instructions to your broker. You should follow the directions provided by your broker regarding how to instruct your broker to vote your shares.**

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## CHAPTER ONE THE MERGER

## QUESTIONS AND ANSWERS ABOUT THE MERGER

**Q:**

**What is the merger?**

A:

Synergy and Callisto have entered into an Agreement and Plan of Merger, dated as of July 20, 2012, as amended on October 15, 2012, which is referred to as the merger agreement. The merger agreement contains the terms and conditions of the proposed business combination of Synergy and Callisto. Under the merger agreement, Callisto will merge with Synergy, which transaction is referred to as the merger. At the effective time of the merger, each share of Callisto common stock outstanding immediately prior to the effective time of the merger will be converted into the right to receive 0.1799 of a share of Synergy common stock and the 22,295,000 shares of Synergy common stock held by Callisto will be canceled. In addition, each stock option exercisable for shares of Callisto common stock that is outstanding at the effective time of the Merger will be assumed by Synergy and converted into a stock option to purchase the number of shares of Synergy's common stock that the holder would have received if such holder had exercised such stock option for shares of Callisto common stock prior to the Merger and exchanged such shares for shares of Synergy common stock in accordance with the Exchange Ratio. In addition, each Callisto stock option exercisable for shares of Synergy common stock that is outstanding at the effective time of the Merger will be assumed by Synergy and each outstanding warrant or obligation to issue a warrant to purchase shares of Callisto common stock, whether or not vested, shall be cancelled.

**Q:**

**Why are the two companies proposing to merge?**

A:

Synergy and Callisto are proposing the merger because, among other things, it is believed that the merger will enhance stockholders value for both Synergy and Callisto stockholders by (i) providing a method by which the Callisto stockholders can more directly share in the growth of Synergy and (ii) resulting in improvement in the share price of Synergy's common stock as a result of anticipated cost savings synergies. Callisto has not been able to fund itself since early 2008 and has relied solely on advances from Synergy to continue its operating activities. From July 2008 through September 30, 2012, Callisto has accumulated $2,655,594 in indebtedness to Synergy, primarily to fund the cost of being a public company. Management estimates that the ongoing cost of a public audit, D&O insurance, printers, transfer agents and other administrative costs associated with being a publicly traded company have totaled between $250,000 and $300,000 per annum. For a discussion of Synergy's and Callisto's reasons for the merger, please see the sections entitled "Chapter One The Merger Transaction Recommendation of the Synergy Board of Directors and the Reasons for the Merger" and "Chapter One The Merger Transaction Recommendation of the Callisto Board of Directors and the Reasons for the Merger" in this Joint Proxy Statement/Prospectus.

**Q:**

**What will happen in the merger?**

A:

In the merger, Callisto will be merged into Synergy and will cease to exist. Based solely upon the outstanding shares of Synergy common stock on November 29, 2012 and Callisto's outstanding shares of common stock on November 29, 2012, immediately following the completion of the merger, Callisto stockholders will own approximately 39.5% of the combined company's outstanding common stock. Based upon the fully-diluted outstanding shares of Synergy and Callisto on November 29, 2012, immediately following the completion of the merger, Callisto security holders would own approximately 38.8% of the combined company's fully diluted outstanding common stock.

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**Q:** **Why am I receiving this Joint Proxy Statement/Prospectus?**

A: You are receiving this Joint Proxy Statement/Prospectus because you have been identified as a stockholder of either Synergy or Callisto as of the applicable record date, and you are entitled to vote at such company's stockholder meeting. This document serves as both a joint proxy statement of Synergy and Callisto used to solicit proxies for the stockholder meetings, and as a prospectus of Synergy used to offer shares of Synergy common stock in exchange for shares of Callisto common stock in the merger. This Joint Proxy Statement/Prospectus contains important information about the merger and the stockholder meetings of Synergy and Callisto, and you should read it carefully.

**Q:** **Is my vote necessary to complete the Merger?**

A: Yes. The companies have agreed to combine the two companies upon the terms and conditions of the merger agreement that is described in this Joint Proxy Statement/Prospectus. You are receiving these proxy materials to help you decide, among other matters, how to vote your shares with respect to the proposed merger.

The merger cannot be completed unless, among other things, the stockholders of both Synergy and Callisto approve the merger agreement and the transactions contemplated thereby. **Your vote is important. Synergy and Callisto encourage you to vote as soon as possible.**

**Q:** **On what matters are Synergy stockholders being asked to vote?**

A: Synergy stockholders are asked to vote on the following items:

- the adoption and approval of the merger agreement, described under "Chapter One The Merger Agreement" on page 91;
- the adjournment of the annual meeting, if necessary, if a quorum is present, to solicit additional proxies if there are not sufficient votes in favor of the adoption of the merger agreement;
- the approval of the increase in the number of shares authorized under Synergy's 2008 Equity Compensation Incentive Plan, as described under "Chapter Six Synergy Annual Meeting Proposals Synergy Proposal No. 3 Approval of an Increase in the number of authorized shares issuable under the Synergy's 2008 Equity Compensation Incentive Plan" beginning on page 151;
- the approval of the increase in the number of shares of common stock authorized for issuance from 100,000,000 to 200,000,000, as described under "Chapter Six Synergy Annual Meeting Proposals Synergy Proposal No. 4" beginning on page 153;
- the re-election of seven (7) current Synergy directors to hold office until the 2013 Synergy annual meeting as described under "Chapter Six Synergy Annual Meeting Proposals Synergy Proposal No. 5" beginning on page 155;
- the ratification of the appointment of BDO USA, LLP as the independent registered public accounting firm of Synergy for its fiscal year ending December 31, 2012 as described under "Chapter Six Synergy Annual Meeting Proposals Synergy Proposal No. 6" beginning on page 173;

the approval, on an advisory basis, of the compensation of Synergy's named executive officers as described in the compensation discussion and analysis, the compensation tables, and the related disclosures contained in this Joint Proxy Statement/Prospectus as described under "Chapter Six  Synergy Annual Meeting Proposals  Synergy Proposal No. 7" beginning on page 174;

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approval of a three-year frequency for holding an advisory vote on executive compensation as described under "Chapter Six Synergy Annual Meeting Proposals Synergy Proposal No. 8" beginning on page 175; and

such other matters as may properly come before the Synergy meeting.

**Q:** **What vote of Synergy stockholders is required to approve the proposals?**

A:

The vote required of Synergy stockholders for each of (i) the adoption and approval of the merger agreement with Callisto and (ii) the approval of an amendment to Synergy's Amended and Restated Certificate of Incorporation to increase the number of shares of common stock authorized for issuance from 100,000,000 to 200,000,000, is the approval of a majority of the outstanding common stock of the corporation entitled to vote.

The vote required of Synergy stockholders for each of (i) the approval of an increase to the number of authorized shares issuable under Synergy's 2008 Equity Incentive Compensation Plan, (ii) the ratification of BDO USA, LLP as the independent registered public accounting firm, (iii) the advisory vote on the approval of executive compensation, (iv) the advisory vote on the frequency of holding an advisory vote on executive compensation, and (v) an adjournment of the meeting, if necessary, if a quorum is present, to solicit additional proxies if there are not sufficient votes in favor of the issuance of the shares of Synergy common stock, is the approval of a majority of the votes present, in person or by proxy, and entitled to vote on the matter.

Please note, however, that the proposals regarding the approval of executive compensation and the frequency of holding such an advisory vote are advisory only and will not be binding. The results of the votes on those two advisory proposals will be taken into consideration by the Board of Directors of Synergy when making future decisions regarding these matters.

Director Elections: Each director nominee receiving a majority of the votes cast will be elected as a director. This means that the number of shares voted "FOR" a director nominee must exceed the number of votes cast "AGAINST" that director nominee in order for that nominee to be elected as a director. If, however, the number of nominees exceeds the number of directors to be elected (a situation Synergy does not anticipate), the directors shall be elected by a plurality of the shares present in person or by proxy at the meeting and entitled to vote on the election of directors. A plurality means that the seven (7) director nominees that receive the highest number of votes cast will be elected. In either event, shares not present at the meeting and shares voting "ABSTAIN" have no effect on the election of directors.

**Q:** **What constitutes a quorum for the Synergy Annual Meeting?**

A:

A majority of the outstanding shares of Synergy's common stock entitled to vote being present in person or represented by proxy constitutes a quorum for the annual meeting. If a quorum is not present, the stockholders present, in person or by proxy, may adjourn the meeting, without notice other than announced at the meeting, to another place, if any, date or time.

**Q:** **On what matters are Callisto stockholders being asked to vote?**

A:

Callisto stockholders will be asked to vote on the following items:

adoption and approval of the merger agreement as described under "Chapter One The Merger The Merger Agreement" on page 91;

adjournment of the special meeting, if necessary, if a quorum is present, to solicit additional proxies if there are not sufficient votes in favor of adoption of the merger agreement; and

such other matters as may be properly presented at the Callisto special meeting.

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**Q:**

**What vote of Callisto stockholders is required to approve the proposals?**

A:

The vote required of Callisto Stockholders for the adoption and the approval of the merger agreement is the approval of a majority of the outstanding common stock of the corporation entitled to vote and for an adjournment of the special meeting, if necessary, if a quorum is present, to solicit additional proxies if there are not sufficient votes in favor of the adoption and approval of the merger agreement, is the approval of a majority of the votes present, in person or by proxy, and entitled to vote on the matter.

**Q:**

**What constitutes a quorum for the Callisto Special Meeting?**

A:

A majority of the outstanding shares of Callisto's common stock entitled to vote being present in person or represented by proxy constitutes a quorum for the special meeting. If a quorum is not present, the stockholders present, in person or by proxy, may adjourn the meeting, without notice other than announced at the meeting, to another place, if any, date or time.

**Q:**

**When and where are the stockholder meetings?**

A:

The Synergy annual meeting will take place on January 3, 2013 at 10:00 a.m., Eastern Time, at the offices of Sichenzia Ross Friedman Ference LLP, 61 Broadway, 32nd Floor, New York, New York 10006.

The Callisto special meeting will take place on January 3, 2013 at 1:00 p.m., Eastern Time, at the offices of Callisto Pharmaceuticals, Inc., 420 Lexington Avenue, Suite 1609, New York, New York, 10170.

**Q:**

**Who is entitled to vote at Synergy's Annual Meeting?**

A:

Each outstanding share of Synergy's common stock entitles its holder to cast one vote on each matter to be voted upon at the annual meeting. Only stockholders of record at the close of business on the record date, November 29, 2012, are entitled to receive notice of the annual meeting and to vote the shares of common stock that they held on that date at the meeting, or any adjournment or postponement of the meeting. If your shares are held for you as a beneficial holder in "street name," please refer to the information forwarded to you by your bank, broker or other holder of record to see what you must do to vote your shares.

A complete list of stockholders entitled to vote at the annual meeting will be available for examination by any stockholder at Synergy's corporate headquarters, 420 Lexington Avenue, Suite 1609, New York, New York, 10170, during normal business hours for a period of ten days before the annual meeting and at the time and place of the annual meeting.

**Q:**

**Who is entitled to vote at Callisto's Special Meeting?**

A:

Each outstanding share of Callisto's common stock entitles its holder to cast one vote on each matter to be voted upon at the special meeting. Only stockholders of record at the close of business on the record date, November 29, 2012, are entitled to receive notice of the special meeting and to vote the shares of common stock that they held on that date at the meeting, or any adjournment or postponement of the meeting. If your shares are held for you as a beneficial holder in "street name," please refer to the information forwarded to you by your bank, broker or other holder of record to see what you must do to vote your shares.

**Q:**

**How do the boards of directors of Synergy and Callisto recommend I vote?**

A:

The Boards of Directors of both companies have recommended that stockholders vote Yes for the merger. After careful consideration, Synergy's Board of Directors has determined by unanimous

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vote the merger to be fair to Synergy stockholders and in their best interests, and declared the merger advisable. Synergy's Board of Directors approved the merger agreement and recommends that Synergy stockholders adopt and approve the merger agreement.

After careful consideration, Callisto's Board of Directors has determined, by unanimous vote, the merger to be fair to Callisto stockholders and in their best interests, and declared the merger advisable. Callisto's Board of Directors approved the merger agreement and recommends the adoption and approval of the merger agreement by Callisto stockholders. In considering the recommendation of the Callisto Board of Directors with respect to the merger agreement, Callisto stockholders should be aware that certain directors and officers of Callisto have certain interests in the merger that are different from, or are in addition to, the interests of Callisto stockholders generally. We encourage you to read the sections titled "Interests of Synergy Directors and Executive Officers in the Merger" and "Interests of Callisto Directors and Executive Officers" on pages 89 and 90 for a discussion of these interests.

**Q:**

**How do I vote?**

A:

You may vote by mail by completing, signing and dating your proxy card and returning it in the enclosed, postage-paid and addressed envelope. If you mark your voting instructions on the proxy card, your shares will be voted:

- as you instruct; and
- according to the best judgment of the proxy holders if a proposal comes up for a vote at the annual or special meeting that is not on the proxy card.

If you return a signed card, but do not provide voting instructions, your shares will be voted:

- if you are a Synergy stockholder, FOR the issuance of shares of Synergy common stock in the merger, FOR the approval of an increase to the number of authorized shares issuable under Synergy's 2008 Equity Incentive Compensation Plan, FOR the approval of an increase in the number of authorized shares of common stock, FOR the re-election of the current Synergy directors, FOR the ratification of BDO USA, LLP as the independent registered public accounting firm, FOR the advisory vote on the approval of executive compensation, FOR the recommendation, on an advisory basis, a three-year frequency with which Synergy should conduct future stockholder advisory votes on executive officer compensation and FOR an adjournment of the meeting, if necessary, if a quorum is present, to solicit additional proxies if there are not sufficient votes in favor of the issuance of the shares of Synergy common stock;
- if you are a Callisto stockholder, FOR the adoption and approval of the merger agreement and FOR adjournment of the special meeting, if necessary, if a quorum is present, to solicit additional proxies if there are not sufficient votes in favor of adoption of the merger agreement; and
- according to the best judgment of the proxy holders if a proposal properly comes up for a vote at the annual or special meeting that is not on the proxy card.

If you are a stockholder of record of Synergy, you may also vote on the Internet at www.pstvote.com/synergy2012. If you are a stockholder of record of Callisto, you may also vote on the internet at www.pstvote.com/callisto2012. See the instructions on your proxy card or voting instruction form. ***You are strongly encouraged to vote electronically.***

**Q:**

**What do I do if I want to change my vote?**

A:

You may send in a later-dated, signed proxy or proxy card to your company's Secretary before your meeting or you can attend your meeting in person and vote. You may also revoke your proxy by

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sending a notice of revocation to your company's Secretary at 420 Lexington Ave., Suite 1609, New York, NY 10170. If you voted by the Internet, you can submit a later vote using such method.

**Q:**

**If my shares are held in "street name" by my broker, bank or other nominee, will my broker, bank or other nominee vote my shares for me?**

A:

If you do not provide your broker, bank or nominee with instructions on how to vote your "street name" shares, your broker, bank or nominee will not be permitted to vote them on the matters that are to be considered by the Synergy stockholders and the Callisto stockholders at their respective meetings relating to the merger. You should therefore be sure to provide your broker with instructions on how to vote your shares.

If you wish to vote your shares in person, you must bring to the meeting a letter from the broker, bank or nominee confirming your beneficial ownership in the shares to be voted.

**Q:**

**What is the effect of abstentions and broker non-votes?**

A:

Abstentions with respect to Synergy Proposal No. 1 and Proposal No. 4 and Callisto Proposal No. 1 will have the same effect as an AGAINST vote. Abstentions with respect to all other proposals will have no effect on the outcome of the vote. Abstentions will be counted for the purpose of determining a quorum at the stockholder meetings.

Matters subject to stockholder vote are classified as "routine" or "non-routine." In the case of non-routine matters, brokers may not vote shares held in "street name" for which they have not received voting instructions from the beneficial owner ("Broker Non-Votes"), whereas they may vote those shares in their discretion in the case of any routine matter. Broker Non-Votes will be counted for purposes of calculating whether a quorum is present at the stockholder meetings, but will not be counted for purposes of determining the numbers of votes present in person or represented by proxy and entitled to vote with respect to a particular proposal. Broker Non-Votes for Synergy Proposals No. 1 and 4 and Callisto Proposal No. 1 will have the same effect as an AGAINST vote. Synergy Proposals No. 1, 2, 3, 4, 5, 7 and 8 as well as Callisto Proposals No. 1 and 2 are non-routine matters, but the Synergy Proposal No. 6 is a routine matter. Therefore, it is important that you complete and return your proxy early so that your vote may be recorded.

Votes cast by proxy or in person at the stockholder meetings will be tabulated by the inspectors of election appointed for the stockholder meetings, who also will determine whether a quorum is present.

**Q:**

**What appraisal rights do stockholders have in connection with the merger?**

A:

The holders of Synergy common stock do not have any right to an appraisal of the value of their shares in connection with the merger. The holders of Callisto common stock do have a right to an appraisal of the value of their shares in connection with the merger if they do not vote for the merger and if they follow certain procedures described in the section entitled "Chapter One The Merger The Merger Transaction Appraisal Rights" beginning on page 85.

**Q:**

**What happens if I do not return a proxy card or otherwise provide proxy instructions?**

A:

If you are a Synergy stockholder, the failure to return your proxy card or otherwise provide proxy instructions could be a factor in establishing a quorum for the annual meeting of Synergy stockholders for purposes of approving the issuance of shares pursuant to the merger agreement or other actions sought to be taken, which is required to transact business at the meeting. If you are a Callisto stockholder, the failure to return your proxy card or otherwise provide proxy instructions could be a factor in establishing a quorum for the special meeting of Callisto stockholders for purposes of approving the merger agreement, which is required to transact business at the meeting.

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**Q:**

**Should I send in my stock certificates now?**

A:

No. If the merger is completed, Synergy will send Callisto stockholders written instructions for exchanging their stock certificates. Synergy stockholders will keep their existing certificates.

**Q:**

**When do you expect the merger to be completed?**

A:

Both Synergy and Callisto are working towards completing the merger as quickly as possible. We hope to complete the merger by February 14, 2013. However, the exact timing of completion of the merger cannot be determined yet because completion of the merger is subject to a number of conditions.

**Q:**

**How many authorized but unissued shares of Synergy common stock will exist after the closing of the merger?**

A:

Following the closing of the merger, we anticipate that there will be approximately 127,591,006 shares of authorized but unissued Synergy common stock. In addition to the number of issued and outstanding shares of Synergy common stock after the closing of the merger, Synergy will be required to reserve approximately 16,446,756 shares for future issuance following the merger as follows: (i) approximately 8,461,930 shares for issuance of Synergy common stock as a result of outstanding Synergy stock options; (ii) approximately 5,647,203 shares for issuance of Synergy common stock as a result of outstanding Synergy warrants; (iii) 1,000,000 shares for issuance of outstanding Callisto warrant to purchase shares of Synergy Common Stock to be assumed in connection with the merger and (iv) 1,337,623 shares for issuance of outstanding stock options assumed in connection with the merger.

**Q:**

**What are the federal income tax consequences of the merger?**

A:

Neither Synergy nor Callisto has requested or received a ruling from the Internal Revenue Service that the merger will qualify as a reorganization. The merger is intended to qualify as a reorganization pursuant to Section 368(a) of the Internal Revenue Code of 1986, as amended, or the Code. Assuming that the merger qualifies as a reorganization, Callisto stockholders should not recognize any gain or loss for U.S. federal income tax purposes if they exchange their Callisto shares solely for shares of Synergy common stock.

Tax matters are very complicated, and the tax consequences of the merger to each Callisto stockholder will depend on the facts of that stockholder's particular situation. You are urged to consult your own tax advisors regarding the specific tax consequences of the merger, including tax return reporting requirements, the applicability of federal, state, local and foreign tax laws and the effect of any proposed changes in the tax laws. See "Chapter One The Merger The Merger Transaction Certain U.S. Federal Income Tax Consequences of the Merger" beginning on page 82.

**Q:**

**Whom do I call if I have questions about the meetings or the merger?**

A:

Synergy stockholders may call Synergy Investor Relations at 212-297-0020. Callisto stockholders may call Callisto Investor Relations at 212-297-0010.

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## SUMMARY

*This summary highlights selected information from this Joint Proxy Statement/Prospectus and may not contain all of the information that is important to you. This summary discusses all of the material aspects of the merger. However, to understand the merger fully and for a more complete description of the legal terms of the merger, you should read this Joint Proxy Statement/Prospectus and the documents we have referred you to carefully. You may obtain the information incorporated by reference into this proxy statement/prospectus without charge by following the instructions in the section entitled "Chapter Eight Additional Information for Stockholders Where You Can Find More Information" on page 178.*

### The Companies

***Synergy Pharmaceuticals Inc.***
**420 Lexington Avenue, Suite 1609**
**New York, New York 10170**
**(212) 297-0020**

Synergy Pharmaceuticals Inc. is a development stage biopharmaceutical company focused primarily on the development of drugs to treat gastrointestinal, or GI, disorders and diseases. Synergy's lead product candidate is plecanatide (formerly called SP-304), a guanylyl cyclase C, or GC-C, receptor agonist, to treat GI disorders, primarily chronic constipation, or CC, and constipation-predominant-irritable bowel syndrome, or IBS-C. CC and IBS-C are functional gastrointestinal disorders that afflict millions of sufferers worldwide. CC is primarily characterized by constipation symptoms but a majority of these patients report experiencing bloating and abdominal discomfort as among their most bothersome symptoms. IBS-C is characterized by frequent and recurring abdominal pain and/or discomfort associated with chronic constipation. Synergy is also developing SP-333, its second generation GC-C receptor agonist for the treatment of gastrointestinal inflammatory diseases, such as ulcerative colitis, or UC.

***Callisto Pharmaceuticals, Inc.***
**420 Lexington Avenue, Suite 1609**
**New York, New York 10170**
**(212) 297-0010**

Callisto Pharmaceuticals, Inc. is a development stage biopharmaceutical company that until May 9, 2012, focused primarily on the development of drugs to treat gastrointestinal disorders and diseases. Prior to May 9, 2012, Callisto operated as a holding company through two controlled subsidiaries: Synergy and Callisto Research Labs, LLC (100% owned). On May 9, 2012, Synergy closed an underwritten public offering of 10 million shares of common stock at an offering price of $4.50 per share, resulting in gross proceeds of $45 million before deducting underwriting discounts, commissions and other estimated offering expenses of approximately $3 million (the "Offering"). As a result Callisto's equity ownership in Synergy decreased to approximately 34% and Callisto's management determined that Callisto no longer had control over the operations and decision making of Synergy. Therefore, Callisto deconsolidated Synergy and derecognized the Synergy assets, liabilities, and non-controlling interest from its financial statements (the "Deconsolidation").

### The Merger Agreement (see page 91)

A copy of the merger agreement, as amended, is attached as Annex A and Annex B to this Joint Proxy Statement/Prospectus and is incorporated herein by reference. *Synergy and Callisto encourage you to read the entire merger agreement, as amended, carefully because it is the principal document governing the merger.* We currently expect that the merger will be completed during the first quarter of 2013. However, we cannot predict the actual timing of the completion of the merger.

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**Merger Consideration (see page 91)**

If the merger is completed, Callisto will merge with and into Synergy, and Synergy will survive the merger. Each Callisto stockholder will receive, in exchange for each share of Callisto common stock held or deemed to be held by such stockholder immediately prior to the closing of the merger, 0.1799 shares of Synergy Common Stock and the 22,295,000 shares of Synergy common stock held by Callisto will be canceled. As a result, immediately after the merger Callisto stockholders will own approximately 38.8% of the outstanding shares of the combined company on a fully diluted basis and Synergy stockholders will own approximately 61.2% of the outstanding shares of the combined company on a fully diluted basis.

In addition, each stock option exercisable for shares of Callisto common stock that is outstanding at the effective time of the Merger will be assumed by Synergy and converted into a stock option to purchase the number of shares of Synergy's common stock that the holder would have received if such holder had exercised such stock option for shares of Callisto common stock prior to the Merger and exchanged such shares for shares of Synergy's common stock in accordance with the Exchange Ratio, respectively. In addition, each Callisto stock option exercisable for shares of Synergy common stock that is outstanding at the effective time of the Merger will be assumed by Synergy and each outstanding warrant or obligation to issue a warrant to purchase shares of Callisto common stock, whether or not vested, shall be cancelled.

For a more complete description of the merger consideration to be issued by Synergy and the treatment of Callisto options , please see the section entitled "Chapter One  The Merger  The Merger Agreement" in this Joint Proxy Statement/Prospectus.

**Risks Relating to the Merger (see page 31)**

In evaluating the adoption of the merger agreement or the issuance of shares of Synergy common stock in the merger, you should carefully read this Joint Proxy Statement/Prospectus and especially consider the factors discussed in the section titled "Chapter One  The Merger  Risk Factors," starting on page 31, for a description of risks relating to the merger, the combined company's businesses, and Synergy's common stock.

**Reasons for the Merger**

**Recommendation of the Synergy Board of Directors and its Reasons for the Merger (see page 64)**

The Synergy Board of Directors approved the merger based on a number of factors, including, among other factors, the following:

- the potential opportunity for the two companies to integrate their operations and development processes and to combine their technological resources to increase functionality and bring drug therapies to market faster;

- the competitive and market environments in which Synergy and Callisto operate, and the potential for the merger to enhance the scale of Synergy's ability to compete effectively in those environments;

- historical and current information about each of the combining companies and their businesses, prospects, financial performance and condition, operations, technology, management and competitive position, before and after giving effect to the merger and the merger's potential effect on stockholder value, including public reports filed with the SEC, analyst estimates, market data and management's knowledge of the industry;

- the potential cost savings synergies derived from the Merger, thus enhancing stockholders value. Callisto has not been able to fund itself since early 2008 and has relied solely on advances from

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Synergy to continue its operating activities. From July 2008 through June 30, 2012, Callisto has accumulated $1,936,609 of indebtedness to Synergy, primarily to fund the cost of being a public company. Management estimates that the ongoing cost of a public audit, D&O insurance, printers, transfer agents and other administrative costs associated with being a publicly traded company have totaled between $250,000 and $300,000 per annum;

the results of the due diligence review of Callisto's business and operations by Synergy's management, legal advisors and financial advisors;

the terms and conditions of the merger agreement;

the likelihood that the merger will be consummated on a timely basis; and

the opinion of Synergy's financial advisor, dated October 15, 2012, to the Synergy board of directors that, as of such date and based on and subject to the assumptions, limitations, qualifications and other matters set forth in the opinion, the exchange ratio of 0.1799 shares of Synergy common stock to be issued in exchange for each share of Callisto common stock pursuant to the merger agreement was fair to Synergy from a financial point of view.

The Synergy Board of Directors considered the potential risks of the merger, including, but not limited to, the following:

the risks, challenges and costs inherent in combining the operations of two companies and the substantial expenses to be incurred in connection with the merger, including the possibility that delays or difficulties in completing the integration could adversely affect the combined company's operating results and preclude the achievement of some benefits anticipated from the merger;

the possible volatility, at least in the short term, of the trading price of Synergy's common stock resulting from the merger announcement;

the possible loss of key management, technical or other personnel of either of the combining companies as a result of the management and other changes that will be implemented in integrating the businesses;

the risk of diverting management's attention from other strategic priorities to implement merger integration efforts;

the possibility that the reactions of existing and potential competitors to the combination of the two businesses could adversely impact the competitive environment in which the companies operate;

the risk that the merger might not be consummated in a timely manner, or that the merger might not be consummated at all;

the risk to Synergy's business, operations and financial results in the event that the merger is not consummated;

the risk that the anticipated benefits of product integration and interoperability and cost savings will not be realized;

the potential incompatibility of business cultures; and

various other applicable risks associated with the combined company and the merger, including those described in the section of this Joint Proxy Statement/Prospectus entitled "Risk Factors" beginning on page 31.

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**Recommendation of the Callisto Board of Directors and its Reasons for the Merger (see page 72)**

The Callisto Board of Directors approved the merger based on a number of factors, including, among other factors, the following:

- the strategic rationale for the merger and the potential benefits of the contemplated transaction;
- the possible alternatives to the merger, including the possibility of continuing to operate as an independent entity and the perceived risks thereof, and the potential for an alternative combination transaction to the merger based upon the discussions held by Callisto and senior management, with the assistance of Callisto's financial advisor;
- current and historical information concerning Callisto's and Synergy's respective businesses, operations, management, financial performance and conditions, technology, operations, prospects and competitive position, before and after giving effect to the merger and the merger's potential effect on stockholder value;
- the potential business, operational and financial synergies that may be realized over time by the combined company following the merger. Callisto has not been able to fund itself since early 2008 and has relied solely on advances from Synergy to continue its operating activities. From July 2008 through September 30, 2012, Callisto has accumulated $2,655,594 of indebtedness to Synergy, primarily to fund the cost of being a public company. Management estimates that the ongoing cost of a public audit, D&O insurance, printers, transfer agents and other administrative costs associated with being a publicly traded company have totaled between $250,000 and $300,000 per annum;
- its knowledge of the business, operations, financial condition and earnings of Synergy, taking into account the results of the due diligence review of Synergy;
- the likelihood that the merger will be completed;
- current financial market conditions and historical market prices, volatility and trading information with respect to Callisto's and Synergy's common stock;
- the terms of the merger agreement, including the parties' representations, warranties and covenants, and the conditions to their respective obligations;
- the consideration to be received by Callisto stockholders in the merger, including the form of such consideration, which enables Callisto's stockholders to continue to have a substantial equity interest in the combined company following the merger, as well as the fact that the shares of Synergy common stock to be received by Callisto's stockholders will be received in a tax-free exchange; and
- the opinion of Callisto's financial advisor, dated October 11, 2012 to the Callisto special committee of the board of directors that as of July 20, 2012, based on and subject to the assumptions, limitations, qualifications and other matters set forth in the opinion, the exchange ratio of 0.1799 shares of Synergy common stock to be issued in exchange for each share of Callisto common stock pursuant to the merger agreement was fair to the Callisto stockholders from a financial point of view.

The Callisto Board of Directors considered the potential risks of the merger, including, but not limited to, the following:

the fact that because of the fixed exchange ratio of 0.1799 shares of Synergy common stock for each share of Callisto common stock, if Synergy's share price declines prior to the consummation of the merger, the consideration to be received by the stockholders of Callisto would also decline;

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the inability of Callisto's stockholders to realize the long-term value of the successful execution of Callisto's current strategy as an independent company;

the risks associated with remaining an independent company, including increased competition, industry consolidation trends, difficulties of achieving scale, the significant and increasing cost of complying with obligations as a publicly traded company, anticipated operating performance and a review of ongoing product development initiatives;

the possibility that the merger might not be completed and the potential effects of the public announcement and pendency of the merger on management attention;

the trading values of Callisto's common stock relative to trading values of Synergy's common stock;

the fact that certain of the directors and executive officers of Callisto may have conflicts of interest in connection with the merger, as they may receive certain benefits that are different from, and in addition to, those of the other stockholders of Callisto;

that, while the merger is expected to be completed, there can be no assurance that all conditions to the parties' obligations to complete the merger will be satisfied, and as a result, it is possible that the merger may not be completed, even if the merger agreement is adopted by the stockholders of Callisto;

the risk of not realizing all of the anticipated strategic benefits between Callisto and Synergy and the risk that other anticipated benefits might not be realized;

the risk that the merger may not be consummated in a timely manner or that the merger may not be consummated at all;

the substantial costs to be incurred in connection with the merger, including the costs of integrating the businesses of Callisto and Synergy and the transaction expenses arising from the merger; and

various other applicable risks associated with the combined company and the merger, including the risks described in the section titled "Risk Factors" beginning on page 42.

**Opinion of Synergy's Financial Advisor (see page 66)**

In connection with the merger, Canaccord Genuity Inc., or Canaccord Genuity, Synergy's financial advisor, delivered to the Special Project Committee of the Synergy Board of Directors an opinion, dated July 20, 2012, as to the fairness, from a financial point of view and as of the date of such opinion, to Synergy of the issuance of the shares of Synergy common stock to be issued in the merger pursuant to the terms of the merger agreement entered into on July 20, 2012 (prior to being amended). Subsequently, Canaccord Genuity delivered to the Special Project Committee of the Synergy Board of Directors an opinion, dated October 15, 2012, as to the fairness, from a financial point of view and as of the date of such opinion, to Synergy of the issuance of the shares of Synergy common stock to be issued in the merger pursuant to the merger agreement, as amended by amendment no. 1 entered into on October 15, 2012. The full text of Canaccord Genuity's opinion is attached to this Joint Proxy Statement/Prospectus as Annex C and is incorporated into this Joint Proxy Statement/Prospectus by reference. Holders of Synergy common stock are encouraged to read Canaccord Genuity's opinion carefully in its entirety for a description of the procedures followed, assumptions made, matters considered and qualifications and limitations on the review undertaken by Canaccord in connection with its opinion. **Canaccord Genuity's opinion was addressed to the Special Project Committee of the Synergy Board of Directors, was only one of many factors considered by the Special Project Committee and the Synergy Board of Directors in their evaluation of the merger and only addresses the fairness, from a financial point of view, to Synergy of the issuance of the shares of Synergy common stock to be**

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**issued in the merger. Canaccord Genuity's opinion does not address the merits of the underlying decision by Synergy to engage in the merger or related transactions or the relative merits of the merger or related transactions as compared to any other transaction or business strategy in which Synergy might engage and is not intended to, and does not, constitute a recommendation to any stockholder as to how such stockholder should vote or act with respect to the merger or related transactions or any other transaction or business strategy in which Synergy might engage.**

**Opinion of Callisto's Financial Advisor (see page 74)**

In connection with the merger, the Callisto Board of Directors originally received an opinion, dated July 20, 2012, from Brean Murray, Carret & Co., LLC, Callisto's financial advisor, as to the fairness, from a financial point of view and as of the date of such opinion, to Callisto of the Exchange Ratio provided for in the merger which at the time was .17 of a share of Synergy common stock for each share of Callisto common stock. Subsequently, Synergy and Callisto entered into an amendment to the merger agreement dated October 15, 2012, which among other things, increased the Exchange Ratio to .1799 of a share of Synergy common stock in exchange for each share of Callisto common stock, and extended the stockholder lock up period to 24 months. In connection with the amendment to the merger agreement, the Callisto Board of Directors received an opinion, dated October 11, 2012, from Brean Murray that as of the execution of the merger agreement on July 20, 2012, prior to the impact of the merger announcement on the market, the increased Exchange Ratio, from a financial point of view was fair to Callisto. See "Chapter One The Merger Risk Factors Risk Factors Related to the Merger" on page 31. The full text of Brean Murray's opinion is attached to this Joint Proxy Statement/Prospectus as Annex D and is incorporated into this Joint Proxy Statement/Prospectus by reference. Holders of Callisto common stock are encouraged to read Brean Murray's opinion carefully in its entirety for a description of the procedures followed, assumptions made, matters considered and qualifications and limitations on the review undertaken by Brean Murray in connection with its opinion. **Brean Murray's opinion was addressed to the Special Committee of the Callisto Board of Directors, was only one of many factors considered by the Callisto Board of Directors in its evaluation of the merger and only addresses the fairness of the exchange ratio from a financial point of view to Callisto. Brean Murray's opinion does not address the merits of the underlying decision by Callisto to engage in the merger or related transactions or the relative merits of the merger or related transactions as compared to any other transaction or business strategy in which Callisto might engage and is not intended to, and does not, constitute a recommendation to any stockholder as to how such stockholder should vote or act with respect to the merger or related transactions or any other transaction or business strategy in which Callisto might engage.**

**Interests of Certain Persons in the Merger**

In considering the recommendation of the Callisto board of directors with respect to approving the merger, Callisto stockholders should be aware that certain members of the board of directors and executive officers of Callisto have interests in the merger that may be different from, or in addition to, interests they have as Callisto stockholders. For example, following the consummation of the merger, certain directors and executive officers of Callisto will continue to serve on the board of directors and management, respectively, of the combined company. In addition, certain executive officers and directors of Callisto entered into voting agreements with Callisto in connection with the merger.

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The following table sets forth the beneficial ownership interest of the principal stockholders in Callisto, Synergy and the combined company:

| | Synergy | | Callisto | | Combined Company | |
|---|---|---|---|---|---|---|
| Name | Number of shares | Percentage** | Number of shares | Percentage*** | Number of shares | Percentage**** |
| Gabriele M. Cerrone | 1,389,378(1) | 2.1% | 3,417,292(2) | 2.1% | 2,004,149 | 2.7% |
| Gary S. Jacob | 813,670(3) | 1.2% | 1,851,745(4) | 1.2% | 1,146,799 | 1.6% |
| Bernard Denoyer | 79.445(5) | * | 300,000(6) | * | 133,415 | * |
| John P. Brancaccio | 135,688(7) | * | 283,759(8) | * | 186,736 | * |
| Randall K. Johnson | | | 260,636(9) | * | 46,888 | * |
| Kunwar Shailubhai | 538,331(10) | * | 325,000(11) | * | 596,799 | 1.0% |
| Chris McGuigan | 119,401(11) | * | | | 119,401 | * |
| Thomas Adams | 117,492(11) | * | | | 117,492 | * |
| Melvin K. Spigelman | 172,247(11) | * | | | 172,247 | * |
| Alan F. Joslyn | 55,000(11) | * | | | 55,000 | * |
| R. Merrill Hunter | 3,305,200 | 5.0% | 25,376,872 | 16.0% | 7,870,499 | 10.9% |

*
Less than one percent (1%)

**
Percentage of Synergy is based upon 66,130,746 shares of common stock outstanding as of November 29, 2012.

***
Percentage of Callisto is based upon 158,965,565 shares of common stock outstanding as of November 29, 2012.

****
Percentage of common stock of the combined company is based on 72,433,621 shares of common stock of the combined company outstanding upon the consummation of the merger and assumes that the exchange ratio to be used in connection with the merger is approximately 0.1799 shares of Synergy common stock for each share of Callisto common stock.

(1)
Consists of 187,470 shares of common stock held by Mr. Cerrone, 462,531 shares of common stock issuable upon exercise of stock options held by Mr. Cerrone, 443,760 shares of common stock held by Panetta Partners, Ltd and 295,617 shares of common stock issuable upon exercise of warrants held by Panetta Partners, Ltd. Mr. Cerrone is the sole director of Panetta Partners, Ltd. and in such capacity exercises voting and dispositive control over securities owned by Panetta Partners, Ltd. despite him having only a small pecuniary interest in such securities.

(2)
Includes 1,368,055 shares of common stock issuable upon exercise of stock options.

(3)
Consists of 288,296 shares of common stock, 50,413 shares of common stock issuable upon exercise of warrants and 474,961 shares of common stock issuable upon exercise of stock options.

(4)
Includes 1,597,500 shares of common stock issuable upon exercise of stock options.

(5)
Consists of 2,952 shares of common stock, 1,476 shares of common stock issuable upon exercise of warrants and 75,017 shares of common stock issuable upon exercise of stock options.

(6) Consists of shares of common stock issuable upon exercise of stock options.

(7) Consists of shares of common stock issuable upon exercise of stock options.

(8) Includes 170,123 shares of common stock issuable upon exercise of stock options.

(9) Includes 140,500 shares of common stock issuable upon exercise of stock options.

(10) Consists of 88,018 shares of Synergy common stock, 12,788 shares of Synergy common stock issuable upon exercise of warrants and 437,526 shares of Synergy common stock issuable upon exercise of stock options.

(11) Consists of shares of common stock issuable upon exercise of stock options.

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**Regulatory Approvals**

Synergy must comply with applicable federal and state securities laws in connection with the issuance of shares of Synergy common stock to Callisto's stockholders and the filing of this Joint Proxy Statement/Prospectus with the Securities and Exchange Commission, or the SEC. As of the date hereof, the registration statement of which this Joint Proxy Statement/Prospectus is a part has not become effective.

Please see the section entitled "Chapter One The Merger Transaction Regulatory Approvals" in this Joint Proxy Statement/Prospectus.

**Accounting Treatment of the Merger**

As Callisto does not meet the definition of a business under ASC 805, the merger will not be accounted for as a business combination. The merger is expected to be accounted for as a recapitalization of Synergy, effected through exchange of Callisto shares for Synergy shares, and the cancellation of Synergy shares held by Callisto. The excess of Synergy shares issued to Callisto shareholders over the Synergy shares held by Callisto is the result of a discount associated with the restricted nature of the Synergy shares to be received by Callisto shareholders. Therefore, considering this discount, the share exchange has been determined to be equal from a fair value stand point. Upon the effective date of the Merger, Synergy will account for the merger by assuming Callisto's net liabilities. Synergy's financial statements will reflect the operations of Callisto prospectively and will not be restated retroactively to reflect the historical financial position or results of operations of Callisto.

**Material U.S. Federal Income Tax Consequences**

It is expected that the merger will qualify as a reorganization within the meaning of Section 368(a) of the Code, and the completion of the merger is conditioned on the receipt by Callisto of an opinion from its outside counsel to the effect that the merger will qualify as such a reorganization. If the merger qualifies as a reorganization, Callisto stockholders generally will not recognize gain or loss upon the receipt of Synergy common stock in exchange for Callisto common stock in connection with the merger.

**Tax matters are very complicated, and the tax consequences of the merger to a particular stockholder will depend in part on such stockholder's circumstances. Accordingly, you are urged to consult your own tax advisor for a full understanding of the tax consequences of the merger to you, including the applicability and effect of federal, state, local and foreign income and other tax laws. For more information on the federal income tax effect of the merger, see the section entitled "Chapter One The Merger Transaction Certain U.S. Federal Income Tax Consequences of the Merger."**

**Comparison of Stockholder Rights**

If Synergy and Callisto successfully complete the merger, holders of Callisto common stock will become Synergy stockholders, and their rights as stockholders will be governed by Synergy's second amended and restated certificate of incorporation and bylaws. There are differences between the certificates of incorporation and bylaws of Synergy and Callisto. Since Callisto and Synergy are both Delaware corporations, the rights of Callisto stockholders will continue to be governed by Delaware law after the completion of the merger. See "Chapter Five Comparison of Rights of Holders of Synergy Common Stock and Callisto Common Stock" in this Joint Proxy Statement/Prospectus for more information.

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**Appraisal Rights in Connection with the Merger**

Under Delaware law, Callisto common stockholders are entitled to appraisal rights in connection with the merger. Holders of Synergy common stock are not entitled to appraisal rights in connection with the merger. For more information about appraisal rights, see the provisions of Section 262 of the DGCL, attached as Annex G to this Joint Proxy Statement/Prospectus, and the section entitled "Chapter One The Merger Transaction Appraisal Rights" in this Joint Proxy Statement/Prospectus.

**Conditions to Completion of the Merger**

Synergy and Callisto are required to complete the merger only if certain customary conditions are satisfied or waived, including, but not limited to:

- approval of the merger by stockholders holding a majority of the outstanding shares of Callisto common stock in person or by proxy at Callisto's special meeting;
- approval of the merger by stockholders holding a majority of the outstanding shares of Synergy common stock in person or by proxy at Synergy's annual meeting;
- the filing and effectiveness of a registration statement under the Securities Act of 1933, as amended, in connection with the issuance of Synergy common stock in the merger;
- the respective representations and warranties of Synergy and Callisto, shall be true and correct in all material respects as of the date of the merger agreement and the closing;
- each executive of Synergy or any of its subsidiaries and Callisto or any of its subsidiaries shall have delivered a waiver of rights to payments, bonuses, vesting, acceleration or other similar rights that are or may be triggered by the merger;
- the shares of Synergy common stock to be issued in the merger and such other shares of Synergy common stock to be reserved for issuance in connection with the merger shall have been approved for listing on The NASDAQ Capital Market;
- no material adverse effect with respect to Synergy or Callisto or their respective subsidiaries shall have occurred since the date of the merger agreement and the closing of the merger;
- performance or compliance in all material respects by Synergy and Callisto with their respective covenants and obligations in the merger agreement; and
- Callisto shall have obtained any consents or waivers of approvals required in connection with the merger.

**Termination of the Merger Agreement**

The merger agreement may be terminated at any time before the completion of the merger, whether before or after the required stockholder approval to complete the merger has been obtained, as set forth below:

by mutual written consent of Synergy and Callisto, duly authorized by their respective boards of directors;

by either Synergy or Callisto if the merger is not consummated by the date that is 6 months after the signing date of the merger agreement for any reason; *provided, however*, that this right to terminate is not available to any party whose action or failure to act has been a principal cause of the failure of the merger to occur on or before such date;

by either Synergy or Callisto if a court, administrative agency, commission, governmental or regulatory authority issues a final and nonappealable order, decree or ruling or taken, any other

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action having the effect of permanently restraining, enjoining or otherwise prohibiting the merger;

by either Synergy or Callisto if the requisite approval of the stockholders of Callisto is not obtained by reason of the failure to obtain the requisite vote at a meeting of the stockholders of Callisto, duly convened therefore or at any adjournment or postponement; *provided, however*, that this right to terminate is not available to Callisto if the failure to obtain the requisite approval of the stockholders of Callisto was caused by the action or failure to act of Callisto, and such action or failure to act constitutes a breach of the merger agreement;

by Synergy if a triggering event (as defined below) occurs;

by Callisto, upon a breach of any representation, warranty, covenant or agreement on the part of Synergy set forth in the merger agreement, or if any representation or warranty of Synergy becomes untrue, such that the conditions to the merger would not be satisfied as of the time of such breach or as of the time such representation or warranty becomes untrue; *provided, however*, that if such inaccuracy in Synergy's representations and warranties or breach by Synergy is curable by Synergy through the exercise of its commercially reasonable efforts, then Callisto may not terminate the merger agreement for thirty (30) calendar days following the delivery of written notice from Callisto to Synergy of such breach, provided Synergy continues to exercise commercially reasonable efforts to cure such breach (it being understood that Callisto may not terminate the agreement if such breach by Synergy is cured during such thirty (30) calendar day period); or

by Synergy, upon a breach of any representation, warranty, covenant or agreement on the part of Callisto set forth in the merger agreement, or if any representation or warranty of Callisto becomes untrue, such that the conditions to the merger would not be satisfied as of the time of such breach or as of the time such representation or warranty becomes untrue; *provided, however*, that if such inaccuracy in Callisto' representations and warranties or breach by Callisto is curable by Callisto through the exercise of its commercially reasonable efforts, then Synergy may not terminate the merger agree-ment for thirty (30) calendar days following the delivery of written notice from Synergy to Callisto of such breach, provided Callisto continues to exercise commercially reasonable efforts to cure such breach (it being understood that Synergy may not terminate the agreement if such breach by Callisto is cured during such thirty (30) calendar day period); or

by Synergy if a change that is materially adverse to the business, assets, capitalization, financial condition or results of operations with respect to Callisto or its subsidiaries occurs since the date of the merger agreement; *provided, however*, that if such change is curable by Callisto through commercially reasonable efforts, then Synergy may not terminate the merger agreement for thirty (30) calendar days following the occurrence of such change, provided Callisto continues to exercise commercially reasonable efforts to cure the effect that is materially adverse to the business, assets, capitalization, financial condition or results of operations with respect to Callisto (it being understood that Synergy may not terminate the agreement if such breach by Callisto is cured during such thirty (30) calendar day period).

a "*triggering event*" has occurred if (i) the board of directors of Callisto or any of its committees has withdrawn or has amended or modified in a manner adverse to Synergy its recommendation in favor of the adoption and approval of the merger agreement or the approval of the merger; (ii) Callisto failed to include in the proxy statement/prospectus the recommendation of the board of directors of Callisto in favor of the adoption and approval of the merger agreement and the approval of the merger; (iii) the board of directors of Callisto failed to reaffirm its recommendation in favor of the adoption and approval of the merger agreement and the approval of the merger within five (5) business days after Synergy requests in writing that such

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recommendation be reaffirmed at any time following the announcement of a superior offer; (iv) the board of directors of Callisto or any of its committees has approved or recommended any superior offer; (v) Callisto has entered into any letter of intent or similar document accepting any acquisition proposal; or (vi) a tender or exchange offer relating to securities of Callisto has been commenced by a person unaffiliated with Synergy or its stockholders and Callisto has not sent to its security holders pursuant to Rule 14e-2 promulgated under the Securities Act, within ten (10) business days after such tender or exchange offer is first published, a statement indicating that Callisto recommends rejection of such tender or exchange offer.

**Voting Agreements**

In connection with the execution of the merger agreement, certain stockholders of Callisto, indicated below, entered into voting agreements with Synergy and Callisto pursuant to which, among other things, each of these stockholders agreed, to vote all of their shares of Callisto capital stock in favor of the approval of the merger and against any matter that would result in a breach of the merger agreement by Callisto and any proposal made in opposition to, or in competition with, the consummation of the merger and the other transactions contemplated by the merger agreement. As of November 29, 2012, these stockholders owned an aggregate of 27,680,354 shares of the issued and outstanding Callisto capital stock, representing approximately 17.4% of the issued and outstanding shares of Callisto capital stock. The stockholders who have entered into Voting Agreements, include, Gabriele Cerrone, Gary Jacob, Bernard Denoyer, John Brancaccio, Randall Johnson and R. Merrill Hunter.

**Management of the Combined Company Following the Merger**

Effective as of the closing of the merger, the combined company will have a seven member board of directors, which is anticipated to be comprised of Thomas Adams, Chris McGuigan, Melvin Spigelman and Alan Joslyn, from Synergy's board of directors, and Gabriele Cerrone, Gary Jacob and John Brancaccio, current members of both Callisto's and Synergy's board of directors. In addition, effective as of the closing of the merger, the combined company's executive officers, is anticipated to be comprised of Kunwar Shailubhai, from Synergy and Gary Jacob and Bernard Denoyer, current officers of both Callisto and Synergy.

**Matters to Be Considered at the Meetings**

***Synergy***

Synergy stockholders will be asked to vote on proposals related to the following:

the approval of the merger agreement;

an adjournment of the meeting, if necessary, if a quorum is present, to solicit additional proxies if there are not sufficient votes in favor of the issuance of the shares of Synergy common stock;

the approval of an increase to the number of authorized shares issuable under Synergy's 2008 Equity Incentive Compensation Plan;

the approval of an increase in the number of shares of common stock authorized for issuance;

the re-election of seven current Synergy directors;

the ratification of BDO USA, LLP as the independent registered public accounting firm.

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the approval, on an advisory basis, of the compensation of Callisto's named executive officers as described in the compensation discussion and analysis, the compensation tables, and the related disclosures contained in this Joint Proxy Statement/Prospectus; and

approval of a three-year frequency for holding an advisory vote on executive compensation;

The Synergy board of directors recommends that Synergy stockholders vote "FOR" all of the proposals set forth above. For further discussion of the Synergy annual meeting, see "Chapter Six Synergy Annual Meeting Proposals," beginning on page 151.

***Callisto***

Callisto stockholders will be asked to consider and vote on the following proposals:

the adoption and approval of the merger agreement; and

adjournment of the special meeting, if necessary, if a quorum is present, to solicit additional proxies if there are not sufficient votes in favor of adoption of the merger agreement.

The Callisto board of directors recommends that Callisto stockholders vote "FOR" all of the proposals set forth above. For further discussion of the Callisto special meeting, see "Chapter Seven Callisto Special Meeting Proposals," beginning on page 177.

**Where You Can Find More Information**

If you would like more information about Synergy or Callisto, you should refer to the documents filed by each company with the SEC. The companies have identified these documents and have set out instructions as to how you can obtain copies of these documents beginning on page 178 under the section "Chapter Eight Additional Information for Stockholder Where You Can Find More Information."

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## CAUTIONARY STATEMENT REGARDING FORWARD-LOOKING INFORMATION

This document contains certain forward-looking information about Synergy, Callisto and the combined company that is intended to be covered by the safe harbor for "forward-looking statements" provided by the Private Securities Litigation Reform Act of 1995. These statements may include statements for the period after the completion of the merger. Representatives of Synergy and Callisto may also make forward-looking statements. Forward-looking statements are statements that are not historical facts. Words such as "expect," "believe," "will," "may," "anticipate," "plan," "estimate," "intend," "should," "can," "likely," "could" and similar expressions are intended to identify forward-looking statements. These statements include statements about the expected benefits of the merger, information about the combined company's objectives, plans and expectations, the likelihood of satisfaction of certain conditions to the completion of the merger and whether and when the merger will be completed. Forward-looking statements are not guarantees of performance. These statements are based upon the current beliefs and expectations of the management of each of Synergy and Callisto and are subject to risks and uncertainties, including the risks described in this Joint Proxy Statement/Prospectus under the section "Risk Factors," that could cause actual results to differ materially from those expressed in, or implied or projected by, the forward-looking information and statements.

In light of these risks, uncertainties, assumptions and factors, the results anticipated by the forward-looking statements discussed in this Joint Proxy Statement/Prospectus or made by representatives of Synergy or Callisto may not occur. Readers are cautioned not to place undue reliance on these forward-looking statements, which speak only as of the date hereof or, in the case of statements made by representatives of Synergy or Callisto, on the date those statements are made. All subsequent written and oral forward-looking statements concerning the merger or the combined company or other matters addressed in this Joint Proxy Statement/Prospectus and attributable to Synergy or Callisto or any person acting on behalf of either are expressly qualified in their entirety by the cautionary statements contained or referred to in this section. Except to the extent required by applicable law or regulation, neither Synergy nor Callisto undertakes any obligation to update or publish revised forward-looking statements to reflect events or circumstances after the date hereof or the date of the forward-looking statements or to reflect the occurrence of unanticipated events.

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## SELECTED HISTORICAL FINANCIAL DATA

### SELECTED HISTORICAL FINANCIAL DATA OF SYNERGY

The following table sets forth the selected consolidated financial data of Synergy and has been derived from Synergy's audited consolidated financial statements. Consolidated balance sheets as of December 31, 2011, 2010, 2009, 2008 and 2007, as well as consolidated statements of operations for the years ended December 31, 2011, 2010, 2009, 2008 and 2007 and the reports thereon incorporated by reference in this Joint Proxy Statement/Prospectus. You should read this information in conjunction with Synergy's consolidated financial statements and related notes included in Synergy's Annual Report on Form 10-K for the year ended December 31, 2011 which is incorporated herein by reference. The statement of operations data for the nine months ended September 30, 2012 and 2011 and the balance sheet data as of September 30, 2012 have been derived from unaudited financial statements contained in the Quarterly Report on Form 10-Q for the quarter ended September 30, 2012 which is incorporated herein by reference. Historical results are not necessarily indicative of the results to be expected in the future.

| | Year ended December 31, | | | | | Nine Months ended September 30, | |
|---|---|---|---|---|---|---|---|
| | 2011 | 2010 | 2009 | 2008 | 2007 | 2012 | 2011 |
| | (in thousands, except per share data) | | | | | | |
| **Consolidated Statement of Operations Data:** | | | | | | | |
| Revenues | $ | $ | $ | $ | $ | $ | $ |
| Costs and Expenses: | | | | | | | |
| Research and development | 13,419 | 9,559 | 3,733 | 1,773 | | 21,210 | 7,715 |
| Purchased in-process research and development | | | | 28,157 | | | |
| General and administrative | 6,746 | 6,562 | 4,467 | 1,799 | | 5,493 | 4,525 |
| Loss from Operations | (20,165) | (16,121) | (8,200) | (31,729) | | (26,703) | (12,240) |
| Other income | 363 | 494 | | | | 255 | |
| Interest and investment income | 90 | 108 | 75 | 5 | | 150 | 64 |
| Interest expense | (12) | | | | | | (12) |
| Change in Fair Value of Financial Instruments | 5,257 | 297 | | | | (1,169) | 3,346 |
| Loss from Continuing Operations | (14,467) | (15,222) | (8,125) | (31,724) | | (27,466) | (8,842) |
| Net Loss from Discontinued Operations | | | | (32) | (20) | | |
| Net Loss | $ (14,467) | $ (15,222) | $ (8,125) | $ (31,756) | $ (20) | $ (27,466) | $ (8,842) |
| Net Loss per common share, basic and diluted | $ (0.30) | $ (0.34) | $ (0.22) | $ (0.54) | $ | $ (0.46) | $ (0.19) |
| Weighted Average Common Shares Outstanding(a) | 47,598 | 44,875 | 36,641 | 59,300 | 82,541 | 60,194 | 46,708 |

(a) Restated for one for two (1:2) reverse stock split effective on November 30, 2011

| | December 31, | | | | | September 30, |
|---|---|---|---|---|---|---|
| | 2011 | 2010 | 2009 | 2008 | 2007 | 2012 |
| | (in thousands) | | | | | |
| **Consolidated Balance Sheet Data:** | | | | | | |

| | | | | | | |
|---|---|---|---|---|---|---|
| Cash and cash equivalents | $ 13,245 | $ 1,708 | $ 7,153 | $ 216 | $ 2 | $ 37,367 |
| Working capital | 11,561 | (2,307) | 6,487 | (1,172) | (14) | 33,677 |
| Total assets | 15,870 | 4,401 | 9,211 | 922 | 4 | 41,330 |
| Total stockholder's equity | $ 9,797 | $ (4,099) | $ 7,484 | $ (1,156) | $ (11) | $ 31,691 |

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**SELECTED HISTORICAL FINANCIAL DATA OF CALLISTO**

The statement of operations data for the years ended December 31, 2011, 2010 and 2009 and the balance sheet data as of December 31, 2011 and 2010 have been derived from Callisto's audited financial statements contained in the Annual Report on Form 10-K for the year ended December 31, 2011 included as Annex H to this Joint Proxy Statement/Prospectus. The statement of operations data for the nine months ended September 30, 2012 and 2011 and the balance sheet data as of September 30, 2012 have been derived from unaudited financial statements contained in the Quarterly Report on Form 10-Q for the quarter ended September 30, 2012 included as Annex I to this Joint Proxy Statement/Prospectus.

| | Year ended December 31, | | | Nine Months Ended September 30, | |
|---|---|---|---|---|---|
| | 2011 | 2010 | 2009 | 2012 | 2011 |
| | (in thousands except for per share data) | | | | |
| Revenues | $ | $ | $ | $ | $ |
| Costs and Expenses: | | | | | |
| Research and development | 13,319 | 9,589 | 3,424 | 7,880 | 7,611 |
| Government grants | | | | 3 | |
| General and administrative | 7,610 | 7,343 | 5,106 | 3,177 | 5,124 |
| Loss from Operations | (20,929) | (16,932) | (8,530) | (11,060) | (12,735) |
| Gain on deconsolidation of Synergy | | | | 120,393 | |
| Loss related to equity method investment | | | | (5,751) | |
| Interest and investment income | 2 | 26 | 25 | 21 | |
| Other income/(expense) | (12) | (323) | (437) | 45 | (10) |
| Tax credit (expense) | 368 | 1,026 | | (298) | |
| Loss on debt extinguishment | | (2,100) | | | |
| Change in fair value of derivative instruments | 5,257 | (15,345) | (9,414) | (431) | 3,346 |
| Net Income (Loss) | (15,314) | (33,648) | (18,355) | 102,919 | (9,399) |
| Net Loss (income) of subsidiary attributable to non-controlling interest | 8,521 | 7,854 | | 6,958 | 4,624 |
| Net income/(loss) available to Callisto common stockholders | (6,793) | (25,794) | (18,356) | 109,877 | (4,775) |
| Series A Preferred stock conversion rate change and beneficial conversion feature accreted as a dividend | | | (137) | | |
| Series B Preferred stock conversion rate change and beneficial conversion feature accreted as a dividend | | | (1,679) | | |
| Cumulative effect of adopting ASC Topic 815 January 1, 2009 | | | | | |
| Net Loss attributable to common stockholders | $ (6,793) | $ (25,794) | $ (20,172) | $ 109,877 | $ 4,775) |
| *Weighted Average Common Shares Outstanding* | | | | | |
| Basic | 158,299 | 69,033 | 51,395 | 158,634 | 158,225 |
| Diluted | 158,299 | 69,033 | 51,395 | 159,201 | 158,225 |
| *Net Loss per Common Share* | | | | | |
| Basic and Diluted | $ (0.10) | $ (0.37) | $ (0.39) | $ 0.69 | $ (0.03) |

| | As of December 31, | | September 30, |
|---|---|---|---|
| | 2011 | 2010 | 2012 |
| | (In thousands) | | |
| **Selected Consolidated Balance Sheet Data:** | | | |
| Cash and cash equivalents | $ 13,245 | $ 1,709 | $ |
| Working (deficit) capital | 9,755 | (3,807) | (1,739) |
| Total assets | 14,512 | 3,357 | 114,527 |

| | | | |
|---|---|---|---|
| Deficit accumulated during the development stage | (142,366) | (135,573) | (59,105) |
| Total stockholders' (deficiency) equity | 6,523 | (7,198) | 110,132 |

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**UNAUDITED PRO FORMA**
**COMBINED CONSOLIDATED FINANCIAL INFORMATION OF SYNERGY AND CALLISTO**

The following unaudited pro forma combined consolidated financial information assumes that each share of Callisto common stock will be exchanged for 0.1799 shares of Synergy common stock. Utilizing the exchange ratio of 0.1799, it is anticipated that Callisto common stockholders will own approximately 39.5% of the voting stock of the combined company after the merger.

The unaudited pro forma combined consolidated financial information is based upon the assumption that the total number of shares of Callisto common stock outstanding immediately prior to the completion of the merger will be 158,965,565 and utilizes the exchange ratio of 0.1799 which will result in 28,597,905 shares of Synergy common stock being issued in the transaction. Callisto options will convert into options to purchase Synergy common stock.

The following unaudited pro forma combined consolidated financial statements as of September 30, 2012 combine the historical consolidated financial statements of Synergy and Callisto. The unaudited pro forma combined consolidated financial statements give effect to the proposed merger as if the merger occurred on September 30, 2012 with respect to the consolidated statement of condition, and at the beginning of the periods for the nine months ended September 30, 2012 and the twelve months ended December 31, 2011, with respect to the consolidated statements of income.

The notes to the unaudited pro forma combined consolidated financial statements describe the pro forma amounts and adjustments presented below. **This pro forma data is not necessarily indicative of the operating results that Synergy would have achieved had it completed the merger as of the beginning of the period presented and should not be considered as representative of future operations.**

The unaudited pro forma combined consolidated financial information presented below is based on, and should be read together with, the historical financial information that Synergy and Callisto have included in this Joint Proxy Statement/Prospectus as of and for the indicated periods.

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**UNAUDITED PRO FORMA CONDENSED CONSOLIDATED BALANCE SHEETS**

**$000's**

| | Synergy Pharmaceuticals Inc. September 30, 2012 | Callisto Pharmaceuticals, Inc. September 30, 2012 | Eliminations and Merger Adjustments | Synergy Pharmaceuticals Inc. Pro Forma September 30, 2012 |
|---|---|---|---|---|
| ASSETS | | | | |
| Current assets: | | | | |
| Cash and cash equivalents | $ 17,244 | $ | $ | $ 17,244 |
| Available-for-sale securities | 20,124 | | | 20,124 |
| Prepaid expenses and other current assets | 1,285 | | | 1,285 |
| Total current assets | 38,653 | | | 38,653 |
| Property and equipment net | 2 | | | 2 |
| Security deposits | 19 | 74 | | 93 |
| Due from related parties | 2,656 | | (2,656)(2) | |
| Investment in Synergy | | 114,453 | (114,453)(1) | |
| Total assets | $ 41,330 | $ 114,527 | $ (117,109) | $ 38,748 |
| LIABILITIES AND STOCKHOLDERS' EQUITY | | | | |
| Current liabilities: | | | | |
| Accounts payable | 2,506 | 1,625 | | 4,131 |
| Accrued expenses and other | 2,470 | 114 | | 2,584 |
| Total current liabilities | 4,975 | 1,739 | | 6,715 |
| Derivative Liability | 4,663 | | | 4,663 |
| Due to related parties | | 2,656 | (2,656)(2) | |
| Total liabilities | 9,639 | 4,395 | (2,656) | 11,378 |
| Stockholder's equity: | | | | |
| Common Stock | 7 | 16 | (16)(1) | 7 |
| Additional paid-in-capital | 128,760 | 169,221 | (173,543)(1) | 124,438 |
| Deficit accumulated during development stage | (97,075) | (59,105) | 59,105(1) | (97,075) |
| Total stockholders' equity | 31,691 | 110,132 | (114,454) | 27,370 |
| Total Liabilities and Stockholders' equity | $ 41,330 | $ 114,527 | $ (117,109) | $ 38,748 |

(1) Represents adjustment for (i) elimination of Callisto's investment in Synergy $114,453, (ii) elimination of Callisto accumulated deficit $59,105 and (iii) elimination of Callisto capital stock $16.

(2) Represents elimination of Callisto note payable to Synergy.

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**UNAUDITED PROFORMA CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS**
**NINE MONTHS ENDED SEPTEMBER 30, 2012**

**$(000's) except earnings per share**

| | Synergy Pharmaceutical, Inc Nine Months Ended September 30, 2012 | Callisto Pharmaceutical, Inc. Nine Months Ended September 30, 2012 | Eliminations and Merger Adjustments | Synergy Pharmaceutical, Inc. Nine Months Ended September 30, 2012 Pro Forma |
|---|---|---|---|---|
| Revenues | $ | $ | $ | $ |
| Costs and Expenses | | | | |
| Research and development | 21,210 | 7,880 | (7,880)(1) | 21,210 |
| Government grants | | 4 | | 4 |
| General and administrative | 5,493 | 3,177 | (2,401)(1) | 6,268 |
| Loss from operations | (26,703) | (11,061) | 10,281 | (27,482) |
| Gain on deconsolidation of Synergy | | 120,393 | (120,393)(2) | |
| Loss related to equity method investment | | (5,751) | 5,751(2) | |
| Interest and investment income (expense) | 150 | 21 | (21)(3) | 150 |
| Other income and (expenses) | 256 | 45 | (45)(3) | 256 |
| Tax credit/(expense) | | (298) | | (298) |
| Change in FV of financial instruments | (1,169) | (431) | 431(4) | (1,169) |
| Net loss | (27,466) | 102,919 | (103,996) | (28,543) |
| less: Net loss attributable to non-controlling interest | | 6,958 | (6,958) | |
| Net Income/(loss) available to common stockholders | $ (27,466) | $ 109,877 | $ (110,954) | $ (28,543) |
| *Weighted average common shares outstanding* | | | | |
| basic | 60,194 | 158,624 | (152,331)(5) | 66,497 |
| diluted(6) | 60,194 | 159,201 | (152,898)(5) | 66,497 |
| *Net income (loss) per common share* | | | | |
| Basic | $ (0.46) | $ 0.69 | | $ (0.43) |
| diluted(6) | $ (0.46) | $ 0.69 | | $ (0.43) |

(1) Represents elimination of Synergy expenses that were consolidated with Callisto from January 1, 2012 through May 9, 2012 (date of deconsolidation).

(2) Represents adjustment for elimination of gain on deconsolidation of investment in Synergy, upon deconsolidation on May 9, 2012, and loss related to equity method investment accounting from May 9, 2012 through September 30, 2012.

(3) Represents adjustment for elimination of interest income and expense related to Callisto's note payable to Synergy.

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(4) Represents adjustment of Synergy's change in fair value of financial instruments that were consolidated with Callisto from January 1, 2012 through May, 9, 2012.

(5) Represents elimination of Callisto's weighted average shares outstanding, net of additional 6,302,905 Synergy shares issued as a result of the Merger, weighted as though these incremental shares had been issued on January 1, 2012.

(6) Basic and diluted net loss per share is presented in conformity with ASC Topic 260, Earnings per Share, ("ASC Topic 260"+A125). In accordance with this guide, basic and diluted net loss per common share was determined by dividing net loss applicable to common stockholders by the weighted-average common shares outstanding during the period. Diluted weighted-average shares for Synergy are the same as basic weighted-average shares because shares issuable pursuant to the exercise of stock options would have been antidilutive.

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**UNAUDITED PROFORMA CONDENSED CONSOLIDATED STATEMENTS OF OPERATIONS**
**YEAR ENDED DECEMBER 31, 2011**

**$(000's) except earnings per share**

| | Synergy Pharmaceuticals, Inc. Year Ended December 31, 2011 | Callisto Pharmaceuticals, Inc. Year Ended December 31, 2011 | Eliminations and Merger Adjustments | Synergy Pharmaceuticals, Inc. Year Ended December 31, 2011 Pro Forma |
|---|---|---|---|---|
| Revenues | $ | $ | $ | $ |
| Costs and Expenses | | | | |
| Research and development | 13,419 | 13,318 | (13419)(1) | 13,318 |
| General and administrative | 6,745 | 7,610 | (6,745)(1) | 7,610 |
| Loss from operations | (20,164) | (20,929) | (20,164) | (20,929) |
| Interest and investment income (expense) | 87 | 2 | (87)(2) | 2 |
| Interest expense | (12) | (12) | 12(1) | (12) |
| Tax credit | 362 | 368 | (362)(1) | 368 |
| Change in FV of financial instruments | 5,257 | 5,257 | (5,257)(3) | 5,257 |
| Total other income (expenses) | 5,697 | 5,615 | (5,697) | 5,615 |
| Net loss | (14,467) | (15,314) | (14,467) | (15,314) |
| less: Net loss attributable to non-controlling interest | | 8,521 | (8,521) | |
| Net Income/(loss)attributable to common stockholders | $ (14,467) | $ (6,793) | $ (5,946) | $ (15,314) |
| *Weighted average common shares outstanding* | | | | |
| Basic and Diluted(5) | 47,598 | 158,298 | (151,995)(4) | 53,901 |
| *Net income (loss) per common share* | | | | |
| Basic and Diluted(5) | $ (0.30) | $ (0.10) | | $ (0.28) |

(1) Represents elimination of Synergy income and expenses that were consolidated with Callisto for the year ended December 31, 2011.

(2) Represents adjustment for elimination of Synergy interest income related to Callisto's note payable to Synergy.

(3) Represents adjustment of Synergy's change in fair value of financial instruments that were consolidated with Callisto for the year ended December 31, 2011.

(4) Represents elimination of Callisto's weighted average shares outstanding, net of additional 6,302,905 Synergy shares issued as a result of the Merger, weighted as though these incremental shares had been issued on January 1, 2012.

(5) Basic and diluted net loss per share is presented in conformity with ASC Topic 260, Earnings per Share , ("ASC Topic 260"+A125). In accordance with this guide, basic and diluted net loss per common share was determined by dividing net loss applicable to common stockholders by the weighted-average common shares outstanding during the period. Diluted weighted-average shares for Synergy are

the same as basic weighted-average shares because shares issuable pursuant to the exercise of stock options would have been antidilutive.

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**COMPARATIVE HISTORICAL AND UNAUDITED PRO FORMA PER SHARE DATA**

The following tables set forth certain historical per share data of Synergy and Callisto combined per share data on an unaudited pro forma and pro forma equivalent basis after giving effect to the merger using the acquisition method of accounting, and assuming 0.1799 shares of Synergy common stock exchanged for each share of Callisto common stock outstanding as of the effective date of the merger. The following data should be read in conjunction with the separate historical consolidated financial statements of Synergy and Callisto included in this Joint Proxy Statement/Prospectus. The unaudited pro forma combined per share data do not necessarily indicate the operating results that would have been achieved had the merger been completed as of the beginning of the earliest period presented and should not be taken as representative of future operations. The results may have been different if the companies had always been combined. No cash dividends have ever been declared or paid on Synergy common stock or Callisto common stock.

| | Nine Months Ended September 30, 2012 | Year Ended December 31, 2011 |
|---|---|---|
| **Synergy Historical** | | |
| Loss per share basic and diluted | $ (0.46) | $ (0.30) |
| Weighted average common shares outstanding basic and diluted | 60,194,004 | 47,598,240 |
| Book value per share | $ 0.53 | $ 0.21 |
| **Callisto Historical** | | |
| Income (Loss) per share basic and diluted | $ 0.69 | $ (0.10) |
| Weighted average common shares outstanding basic | 158,633,596 | 158,298,920 |
| Weighted average common shares outstanding diluted | 159,201,398 | 158,298,920 |
| Book value per share | $ 0.69 | $ 0.04 |
| **Pro Forma Combined Consolidated** | | |
| Loss per share from continuing operations basic and diluted | $ (0.43) | $ (0.28) |
| Weighted average common shares outstanding basic and diluted | 66,496,909 | 53,901,145 |
| Book value per share | $ 0.41 | $ 0.12 |

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## MARKET PRICE AND DIVIDEND INFORMATION

***Recent Share Prices***

***Synergy***

From August 11, 2008 until February 18, 2011, Synergy's common stock was quoted on the Over the Counter Bulletin Board under the symbol "SGYP.OB." From February 22, 2011 until November 30, 2011 Synergy's common stock was traded on the OTC QB under the symbol "SGYP." Since December 1, 2011 Synergy's common stock has been traded on The NASDAQ Capital Market under the symbol "SGYP". As of November 29, 2012, Synergy had approximately 83 holders of record of Synergy common stock. The following table shows the reported high and low closing prices per share for Synergy's common stock as reported on the Over the Counter Bulletin Board, the OTC QB and The NASDAQ Capital Market during the periods indicated.

| | High* | Low* |
|---|---|---|
| **Year ended December 31, 2010** | | |
| First quarter | $ 16.90 | $ 11.20 |
| Second quarter | $ 22.00 | $ 14.60 |
| Third quarter | $ 15.00 | $ 5.00 |
| Fourth quarter | $ 10.10 | $ 6.00 |
| **Year ended December 31, 2011** | | |
| First quarter | $ 10.98 | $ 5.72 |
| Second quarter | $ 8.90 | $ 6.00 |
| Third quarter | $ 8.70 | $ 4.10 |
| Fourth quarter | $ 4.68 | $ 3.35 |
| **Year ended December 31, 2012** | | |
| First quarter | $ 4.48 | $ 3.35 |
| Second quarter | $ 5.93 | $ 3.90 |
| Third quarter | $ 5.00 | $ 3.74 |
| Fourth quarter (through November 29, 2012) | $ 5.53 | $ 3.03 |

* All per share amounts have been restated to reflect a one for two (1:2) reverse stock split effective November 30, 2011.

***Callisto***

Callisto's common stock currently trades on the OTC QB under the symbol "CLSP". As of November 29, 2012, Callisto had approximately 114 holders of record of Callisto common stock. The

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following table shows the reported high and low closing prices per share for Callisto's common stock as reported on the OTC QB.

| | High | Low |
|---|---|---|
| **Year ended December 31, 2010** | | |
| First quarter | $ 0.49 | $ 0.18 |
| Second quarter | $ 0.43 | $ 0.30 |
| Third quarter | $ 0.41 | $ 0.22 |
| Fourth quarter | $ 0.86 | $ 0.30 |
| **Year ended December 31, 2011** | | |
| First quarter | $ 0.70 | $ 0.54 |
| Second quarter | $ 0.70 | $ 0.49 |
| Third quarter | $ 0.63 | $ 0.41 |
| Fourth quarter | $ 0.48 | $ 0.25 |
| **Year ended December 31, 2012** | | |
| First quarter | $ 0.4698 | $ 0.23 |
| Second quarter | $ 0.72 | $ 0.415 |
| Third quarter | $ 0.72 | $ 0.40 |
| Fourth quarter (through November 30, 2012) | $ 0.64 | $ 0.44 |

***Market Value of Securities***

On July 19, 2012, the last trading day before the public announcement of the signing of the merger agreement, the last sale prices per share of Synergy common stock on The NASDAQ Capital Market and Callisto common stock on the OTC QB were $4.50 and $0.69, respectively. On November 30, 2012, the latest practicable date before the date of this Joint Proxy Statement/Prospectus, the closing prices per share of Synergy common stock on The NASDAQ Capital Market and Callisto common stock on the OTC QB were $5.53 and $0.53, respectively. Callisto stockholders are encouraged to obtain current market quotations for Synergy common stock and Callisto common stock and to review carefully the other information contained, or incorporated by reference, in this Joint Proxy Statement/Prospectus. See "*Chapter Eight Additional Information for Stockholders Where You Can Find More Information,*" at page 178 of this Joint Proxy Statement/Prospectus. Following the merger, Synergy' common stock will continue to be listed on The NASDAQ Capital Market, and there will be no further market for Callisto common stock.

***Penny Stock***

Callisto's common stock may be subject to the "penny stock" rules adopted under Section 15(g) of the Exchange Act. The penny stock rules generally apply to companies whose common stock is not listed on a national securities exchange and trades at less than $5.00 per share and have a tangible net worth of at least $5,000,000, subject to certain exceptions. These rules require, among other things, that brokers who trade penny stock to persons other than "established customers" complete certain documentation, make suitability inquiries of investors and provide investors with certain information concerning trading in the security, including a risk disclosure document and quote information under certain circumstances.

***Dividend Policy***

Synergy has never declared or paid any cash dividends on its common stock. Synergy currently intends to retain future earnings, if any, to finance the expansion of its business. As a result, Synergy does not anticipate paying any cash dividends in the foreseeable future.

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## RISK FACTORS

*In addition to the other information included in and incorporated by reference into this Joint Proxy Statement/Prospectus, Callisto's stockholders should consider carefully the matters described below in determining whether to approve the merger, and the transactions contemplated thereby, and Synergy's stockholders should consider carefully the matters described below in determining whether to approve the issuance of Synergy common stock to Callisto stockholders pursuant to the merger agreement. Please also refer to the information under the heading "Risk Factors" set forth in Item 1A in each of Synergy's Annual Report on Form 10-K for the fiscal year ended December 31, 2011 and Callisto's Annual Report on Form 10-K for the fiscal year ended December 31, 2011, each of which is incorporated by reference into this Joint Proxy Statement/Prospectus. See "Where You Can Find More Information" on page 178.*

### RISKS RELATED TO THE MERGER

***All of Callisto's executive officers and all but one of its directors have conflicts of interest that may influence them to support or approve the merger without regard to your interests.***

All of the Callisto officers will be employed by the combined company and certain directors will continue to serve on the board of directors of the combined company following the consummation of the merger. In addition, all of the Callisto officers and some of the directors have a direct or indirect financial interest in both Callisto and Synergy. These interests, among others, may influence such executive officers and directors of Callisto to support or approve the merger. For a more information concerning the interests of Callisto' executive officers and directors, see the sections entitled "The Merger  Interests of Callisto' Directors and Executive Officers in the Merger" in this Joint Proxy Statement/Prospectus.

***The exchange ratio is not adjustable based on the market price of Synergy common stock so the merger consideration at the closing may have a greater or lesser value than it had at the time the merger agreement was signed.***

The parties to the merger agreement have set the exchange ratio for the Callisto common stock and the exchange ratio is not adjustable. Any changes in the market price of Synergy common stock will not affect the number of shares holders of Callisto common stock will be entitled to receive upon consummation of the merger. Therefore, if the market price of Synergy common stock declines from the market price on the date of the merger agreement prior to the consummation of the merger, Callisto stockholders could receive merger consideration with considerably less value. Similarly, if the market price of Synergy common stock increases from the market price on the date of the merger agreement prior to the consummation of the merger, Callisto stockholders could receive merger consideration with considerably more value than their shares of Callisto common stock and the Synergy stockholders immediately prior to the merger will not be compensated for the increased market value of the Synergy common stock. The merger agreement does not include a price-based termination right. Because the exchange ratio does not adjust as a result of changes in the value of Synergy common stock, for each one percentage point that the market value of Synergy common stock rises or declines, there is a corresponding one percentage point rise or decline, respectively, in the value of the total merger consideration issued to the Callisto stockholders. For example, on July 20, 2012, the date of the execution of the merger agreement, the closing price of Synergy common stock, as reported on The NASDAQ Capital Market, was $4.34 per share. Assuming that a total of 28,597,905 shares of Synergy common stock are issued to Callisto stockholders upon the closing of the merger at a per share value of $4.34 per share (excluding the value of assumed stock options and warrants), the aggregate merger consideration to be issued to Callisto stockholders in the merger would be approximately $124.1 million. If, however, the closing price of Synergy common stock on the date of closing of the merger had declined from $4.34 per share to, for example, $3.46 per share, a decline of 20%, the

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aggregate merger consideration to be issued to Callisto stockholders in the merger would decrease approximately $24.8 million to approximately $99.3 million in total.

***The combined company's stock price is expected to be volatile, and the market price of its common stock may drop following the merger.***

The market price of the combined company's common stock could be subject to significant fluctuations following the merger. Moreover, the stock markets in general have experienced substantial volatility that has often been unrelated to the operating performance of individual companies. These broad market fluctuations may also adversely affect the trading price of the combined company's common stock.

In the past, following periods of volatility in the market price of a company's securities, stockholders have often instituted class action securities litigation against those companies. Such litigation, if instituted, could result in substantial costs and diversion of management attention and resources, which could significantly harm the combined company's profitability and reputation.

***The market price of the combined company's common stock may decline as a result of the merger.***

The market price of the combined company's common stock may decline as a result of the merger if the combined company does not achieve the perceived benefits of the merger as rapidly or to the extent anticipated by Synergy or Callisto or investors, financial or industry analysts.

***Synergy and Callisto stockholders may not realize a benefit from the merger commensurate with the ownership dilution they will experience in connection with the merger.***

If the combined company is unable to realize the strategic and financial benefits currently anticipated from the merger, Synergy stockholders will have experienced an approximately 9.6% dilution of their ownership interests in Synergy.

***The combined company may not experience the anticipated strategic benefits of the merger***

The respective management of Synergy and Callisto believes that the merger would provide certain strategic benefits that may not be realized by each of the companies operating as standalones. Specifically, Synergy believes the merger would provide certain strategic benefits which would enable Synergy to accelerate its business plan through an increased access to capital in the public equity markets. There can be no assurance that these anticipated benefits of the merger will materialize or that if they materialize will result in increased stockholder value or revenue stream to the combined company.

***During the pendency of the merger, Synergy and Callisto may not be able to enter into certain transactions with another party because of restrictions in the merger agreement, which could adversely affect their respective businesses.***

Covenants in the merger agreement impede the ability of Synergy and Callisto to complete certain transactions that are not in the ordinary course of business, pending completion of the merger. As a result, if the merger is not completed, the parties may be at a disadvantage to their competitors because the parties will have been prevented from entering into arrangements with possible financial and or other benefits to them. In addition, any such transactions could be favorable to such party's stockholders.

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***If the conditions to the merger are not met, the merger will not occur.***

Even if the merger is approved by the stockholders of Synergy and Callisto, specified conditions must be satisfied or waived in order to complete the merger, including, among others:

- the filing and effectiveness of a registration statement under the Securities Act of 1933, as amended, in connection with the issuance of Synergy common stock in the merger;
- the respective representations and warranties of Synergy and Callisto, shall be true and correct in all material respects as of the date of the merger agreement and the closing;
- each executive of Synergy or any of its subsidiaries and Callisto or any of its subsidiaries shall have delivered a waiver of rights to payments, bonuses, vesting, acceleration or other similar rights that are or may be triggered by the merger;
- no material adverse effect with respect to Synergy or Callisto or its subsidiaries shall have occurred since the date of the merger agreement and the closing of the merger;
- performance or compliance in all material respects by Synergy and Callisto with their respective covenants and obligations in the merger agreement;
- Callisto shall have obtained any consents and waivers of approvals required in connection with the merger; and
- no material adverse effect with respect to Synergy or Callisto or its subsidiaries shall have occurred since the date of the merger agreement.

These and other conditions are described in detail in the merger agreement, as amended, a copy of which is attached as *Annex A and Annex B* to this Joint Proxy Statement/Prospectus. Synergy and Callisto cannot assure you that all of the conditions to the merger will be satisfied. If the conditions to the merger are not satisfied or waived, the merger will not occur or will be delayed, and Synergy and Callisto each may lose some or all of the intended benefits of the merger.

***If there are Callisto stockholders that exercise their appraisal rights, the surviving corporation in the merger will be responsible for the resulting cash payment obligation.***

If the merger is completed, holders of Callisto common stock are entitled to appraisal rights under Section 262 of the DGCL, or Section 262, provided that they comply with the conditions established by Section 262. If there are Callisto stockholders who exercise such rights and complete the process required by the DGCL, Synergy, as the surviving company in the merger, will be obligated to pay such stockholders the pre-merger cash value of their Callisto stock as determined by the Delaware Court of Chancery.

***Should the merger not qualify as tax free reorganization, Callisto stockholders may recognize capital gain or loss with respect to the shares received in the merger.***

In connection with the merger, Callisto received a tax opinion of Wilk Auslaunder LLP that the merger will be treated as a "reorganization" within the meaning of Section 368 of the Internal Revenue Code of 1986, as amended. The failure of the merger to qualify as a reorganization within the meaning of Section 368(a) of the Code would result in a Callisto stockholder recognizing capital gain or loss with respect to the shares of Callisto stock surrendered by such stockholder equal to the difference between the stockholder's basis in the shares and the fair market value, as of the effective time of the merger, of the Synergy stock received in exchange for the Callisto stock on the closing date of the merger. In such event, a stockholder's aggregate basis in the Synergy common stock so received would equal its fair market value and such stockholder's holding period would begin the day after the merger.

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A dissenting stockholder who receives cash will be required to recognize gain or loss in the same manner as described above.

***Synergy and Callisto will incur substantial expenses whether or not the merger is completed.***

Synergy and Callisto will incur substantial expenses related to the merger whether or not the merger is completed. Synergy currently expects to incur approximately $325,000 in transactional expenses and Callisto currently expects to incur approximately $300,000 in transactional expenses. See the section entitled "Chapter One The Merger The Merger Agreement Termination" on page 97.

***The pro forma financial statements are presented for illustrative purposes only and may not be an indication of the combined company's financial condition or results of operations following the merger.***

The pro forma financial statements contained in this Joint Proxy Statement/Prospectus are presented for illustrative purposes only and may not be an indication of the combined company's financial condition or results of operations following the merger for several reasons. For example, the pro forma financial statements have been derived from the historical financial statements of Synergy and Callisto and certain adjustments and assumptions have been made regarding the combined company after giving effect to the merger. The information upon which these adjustments and assumptions have been made is preliminary, and such adjustments and assumptions are difficult to make with complete accuracy. Moreover, the pro forma financial statements do not reflect all costs that are expected to be incurred by the combined company in connection with the merger. For example, the impact of any incremental costs incurred in integrating the two companies is not reflected in the pro forma financial statements. As a result, the actual financial condition and results of operations of the combined company following the merger may not be consistent with, or evident from, these pro forma financial statements.

In addition, the assumptions used in preparing the pro forma financial information may not prove to be accurate, and other factors may affect the combined company's financial condition or results of operations following the merger. Any potential decline in the combined company's financial condition or results of operations may cause significant variations in the stock price of the combined company. See the section entitled "Chapter One The Merger Selected Historical Financial Data Unaudited Pro Forma Condensed Combined Consolidated Financial Information" beginning on page 23.

***The merger agreement limits Callisto's ability to pursue alternative business combinations.***

Certain "no shop" provisions included in the merger agreement make it difficult for Callisto to sell its business to a party other than Synergy. These provisions include the general prohibition on Callisto soliciting any acquisition transaction. See "Chapter One The Merger The Merger Agreement Certain Covenants No Solicitation" beginning on page 94 of this Joint Proxy Statement/Prospectus, and "Chapter One The Merger The Merger Agreement Termination" beginning on page 97. These provisions might discourage a third party with an interest in acquiring all of or a significant part of Callisto from considering or proposing an acquisition, including a proposal that might be more advantageous to the stockholders of Callisto when compared to the terms and conditions of the merger described in this Joint Proxy Statement/Prospectus.

***Although Brean Murray's opinion was given to Callisto's board of directors on July 20, 2012, the date of the execution of the merger agreement, and re-issued on October 11, 2012, it does not reflect any changes in market and economic circumstances after July 20, 2012.***

To the extent there may have been any changes in the operations and prospects of Synergy or Callisto and/or changes in general market and economic conditions subsequent to July 20, 2012, which could make Callisto's value now greater than its value as of July 20, 2012 (the date of the merger agreement and of the analysis conducted by Brean Murray), any such developments will have no effect

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whatsoever on Brean Murray's opinion or the Exchange Ratio, which was been fixed at $0.1799 under the merger agreement, as amended. Brean Murray's opinion, including the October 11, 2012 re-issued opinion, was based on financial, economic, monetary, market and other conditions and circumstances as in effect on, and the information made available to them on July 20, 2012, the date of the execution of the merger agreement. While neither the Callisto nor Synergy board of directors is aware of any changes in the operations and prospects of Synergy or Callisto and/or changes in general market and economic conditions subsequent to July 20, 2012, which could make Callisto's value greater than its value as of July 20, 2012 (the date of the merger agreement and the analysis conducted by Brean Murray), or lead to the conclusion that the consideration to be received in the merger by Callisto's shareholders is not fair, there can be no assurance given that changes in the operations and prospects of Synergy or Callisto and/or changes in general market and economic conditions subsequent to July 20, 2012, could make Callisto's value, on the effective date of the merger greater than its value as of July 20, 2012. Brean Murray has undertaken no obligation to update its opinion for changes subsequent to July 20, 2012 and similarly, Canaccord Genuity has undertaken no obligation to update its opinion, dated October 15, 2012, delivered to Synergy for changes subsequent to October 15, 2012. For a description of the opinion that the Callisto board of directors received from its financial advisor and a summary of the material financial analyses it provided to the Callisto board of directors in connection with rendering such opinion, please refer to the section entitled "Chapter One The Merger The Merger Transaction Opinion of Callisto's Financial Advisor" beginning on page 74. For a description of the opinion that the Synergy board of directors received from its financial advisor and a summary of the material financial analyses it provided to the Synergy board of directors in connection with rendering such opinion, please refer to the section entitled "Chapter One The Merger The Merger Transaction Opinion of Synergy's Financial Advisor" beginning on page 74.

***The merger and related transactions are subject to approval by the stockholders of both Synergy and Callisto.***

In order for the merger to be completed, both Synergy's and Callisto's stockholders must approve the merger agreement, which requires the affirmative vote of the holders of at least a majority of the outstanding shares of Callisto common stock entitled to vote. In addition, under applicable NASDAQ rules, Synergy's stockholders must approve the issuance of the shares of Synergy common stock to Callisto stockholders as part of the merger consideration. Approval of the issuance of shares of Synergy common stock to Callisto stockholders requires approval by a majority of the outstanding shares of Synergy common stock entitled to vote.

***Several lawsuits have been filed against Callisto and Synergy challenging the merger, and an adverse ruling in any such lawsuit may delay or prevent the merger from being completed.***

Callisto, members of Callisto's board of directors, or director defendants, and Synergy have been named as defendants in a number of putative class action lawsuits brought by certain Callisto stockholders challenging the merger and generally alleging, among other things, that the director defendants, aided and abetted by Synergy, breached their fiduciary duties to Callisto stockholders by entering into the merger agreement for merger consideration each plaintiff claims is inadequate and pursuant to a process the plaintiff claims to be flawed. The lawsuits seek, among other things, to enjoin the defendants from consummating the merger on the agreed-upon terms or to rescind the merger to the extent already implemented, as well as damages, expenses, and attorney's fees. The existence of these lawsuits could delay the completion of, or jeopardize Callisto's and Synergy's ability to complete, the merger. For more information about the lawsuits related to the merger, see "Chapter One The Merger The Merger Transaction Legal Proceedings Relating to the Merger" beginning on page 90.

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## RISKS RELATED TO SYNERGY AND CALLISTO AS A COMBINED ENTITY

### Risks Related to the Business of Synergy and the Combined Entity

***Synergy's business and stock price may be adversely affected if the acquisition of Callisto is not completed.***

Synergy's acquisition of Callisto is subject to several customary conditions, including the effectiveness of this registration statement and the approvals of the transaction by the stockholders of Callisto and Synergy.

If Synergy's acquisition of Callisto is not completed, Synergy could be subject to a number of risks that may adversely affect Synergy's business and stock price, including:

- the current market price of shares of Synergy's common stock reflects a market assumption that the acquisition will be completed;
- Synergy must pay costs related to the merger; and
- Synergy would not realize the benefits it expects from acquiring Callisto.

***Synergy is at an early stage of development as a company, currently has no source of revenue and may never become profitable.***

Synergy is a development stage biopharmaceutical company. Currently, it has no products approved for commercial sale and, to date, it has not generated any revenue. Its ability to generate revenue depends heavily on:

- demonstration in current and future clinical trials that its product candidate, plecanatide for the treatment of CC and IBS-C, is safe and effective;
- its ability to seek and obtain regulatory approvals, including with respect to the indications it is seeking;
- successful manufacture and commercialization of its product candidates; and
- market acceptance of its products.

All of Synergy's existing product candidates are in various stages of development and will require extensive additional preclinical and clinical evaluation, regulatory review and approval, significant marketing efforts and substantial investment before they could provide Synergy with any revenue. As a result, if Synergy does not successfully develop, achieve regulatory approval and commercialize plecanatide, it will be unable to generate any revenue for many years, if at all. Synergy does not anticipate that it will generate revenue for several years, at the earliest, or that it will achieve profitability for at least several years after generating material revenue, if at all. If Synergy is unable to generate revenue, it will not become profitable, and it may be unable to continue its operations.

***Synergy does not have any products that are approved for commercial sale and therefore does not expect to generate any revenues from product sales in the foreseeable future, if ever.***

Synergy currently does not have any products that are approved for commercial sale. To date, Synergy has funded its operations primarily from sales of its securities. Synergy has not received, and does not expect to receive for at least the next several years, if at all, any revenues from the commercialization of its product candidates. To obtain revenues from sales of its product candidates, Synergy must succeed, either alone or with third parties, in developing, obtaining regulatory approval for, manufacturing and marketing drugs with commercial potential. Synergy may never succeed in these activities, and may not generate sufficient revenues to continue its business operations or achieve

profitability.

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***Synergy has incurred significant losses since inception and anticipates that it will incur continued losses for the foreseeable future.***

As of September 30, 2012, Synergy had an accumulated deficit of $97,075,397. As of December 31, 2011, Synergy had an accumulated deficit of $69,609,018. Synergy expects to incur significant and increasing operating losses for the next several years as it expands its research and development, continues its clinical trials of plecanatide for the treatment of GI disorders, acquires or licenses technologies, advances other product candidates into clinical development, including SP-333, completes clinical trials, seeks regulatory approval and, if it receives FDA approval, commercializes its products. Because of the numerous risks and uncertainties associated with product development efforts, Synergy is unable to predict the extent of any future losses or when it will become profitable, if at all. If Synergy is unable to achieve and then maintain profitability, the market value of its common stock will likely decline.

***Synergy's independent registered public accounting firm has expressed substantial doubt about its ability to continue as a going concern, which may hinder its ability to obtain future financing.***

Synergy's consolidated financial statements as of December 31, 2011 were prepared under the assumption that it will continue as a going concern for the next twelve months. Synergy's independent registered public accounting firm has issued a report that included an explanatory paragraph referring to its recurring losses from operations and expressing substantial doubt in its ability to continue as a going concern without additional capital becoming available. Synergy's ability to continue as a going concern is dependent upon its ability to obtain additional equity or debt financing, attain further operating efficiencies, reduce expenditures, and, ultimately, to generate revenue. The financial statements do not include any adjustments that might result from the outcome of this uncertainty.

***Synergy will need to raise substantial additional capital to fund its operations, and its failure to obtain funding when needed may force Synergy to delay, reduce or eliminate its product development programs.***

During the nine months ended September 30, 2012, Synergy's operating activities used net cash of $23,070,861. During the twelve months ended December 31, 2011, Synergy's operating activities used net cash of $21,231,254. Synergy expects to continue to spend substantial amounts to:

- continue clinical development of plecanatide to treat GI disorders;
- continue development of other product candidates, including SP-333;
- finance its general and administrative expenses;
- prepare regulatory approval applications and seek approvals for plecanatide and other product candidates, including SP-333;
- license or acquire additional technologies;
- manufacture product for clinical trials;
- launch and commercialize its product candidates, if any such product candidates receive regulatory approval; and
- develop and implement sales, marketing and distribution capabilities.

Synergy will be required to raise additional capital to complete the development and commercialization of its current product candidates and to continue to fund operations at the current cash expenditure levels. Synergy future funding requirements will depend on many factors, including, but not limited to:

- the rate of progress and cost of its clinical trials and other development activities;

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any future decisions Synergy may make about the scope and prioritization of the programs it pursues;

the costs of filing, prosecuting, defending and enforcing any patent claims and other intellectual property rights;

the costs of manufacturing product;

the costs and timing of regulatory approval;

the costs of establishing sales, marketing and distribution capabilities;

the effect of competing technological and market developments;

the terms and timing of any collaborative, licensing and other arrangements that Synergy may establish; and

general market conditions for offerings from biopharmaceutical companies.

Worldwide economic conditions and the international equity and credit markets have recently significantly deteriorated and may remain depressed for the foreseeable future. These developments could make it more difficult for Synergy to obtain additional equity or credit financing, when needed.

Synergy cannot be certain that funding will be available on acceptable terms, or at all. To the extent that Synergy raises additional funds by issuing equity securities, its stockholders may experience significant dilution. Any debt financing, if available, may involve restrictive covenants that impacts Synergy's ability to conduct its business. If Synergy is unable to raise additional capital when required or on acceptable terms, it may have to significantly delay, scale back or discontinue the development and/or commercialization of one or more of its product candidates. Synergy also may be required to:

seek collaborators for its product candidates at an earlier stage than otherwise would be desirable and on terms that are less favorable than might otherwise be available; and/or

relinquish license or otherwise dispose of rights to technologies, product candidates or products that it would otherwise seek to develop or commercialize itself on unfavorable terms.

***Synergy is largely dependent on the success of its lead product candidate, plecanatide, and it cannot be certain that this product candidate will receive regulatory approval or be successfully commercialized.***

Synergy currently has no products for sale, and it cannot guarantee that it will ever have any drug products approved for sale. Synergy and its product candidates are subject to extensive regulation by the FDA and comparable regulatory authorities in other countries governing, among other things, research, testing, clinical trials, manufacturing, labeling, promotion, selling, adverse event reporting and recordkeeping. Synergy is not permitted to market any of its product candidates in or outside the United States until it receives approval of a new drug application, or NDA, for a product candidate from the FDA or the equivalent approval from a foreign regulatory authority. Obtaining FDA approval is a lengthy, expensive and uncertain process. Synergy currently has one lead product candidate, plecanatide for the treatment of GI disorders, and the success of its business currently depends on its successful development, approval and commercialization. This product candidate has not completed the clinical development process; therefore, Synergy has not yet submitted an NDA or foreign equivalent, or received marketing approval for this product candidate anywhere in the world.

The clinical development program for plecanatide may not lead to commercial products for a number of reasons, including if Synergy fails to obtain necessary approvals from the FDA or foreign regulatory authorities because its clinical trials fail to demonstrate to their satisfaction

that this product candidate is safe and effective. Synergy may also fail to obtain the necessary approvals if it has inadequate financial or other resources to advance its product candidates through the clinical trial process. Any failure or delay in completing clinical trials or obtaining regulatory approval for

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plecanatide in a timely manner would have a material adverse impact on Synergy's business and its stock price.

***Synergy will need to obtain FDA approval of any proposed product brand names, and any failure or delay associated with such approval may adversely impact its business.***

A pharmaceutical product cannot be marketed in the U.S. or other countries until it has completed rigorous and extensive regulatory review processes, including approval of a brand name. Any brand names Synergy intends to use for its product candidates will require approval from the FDA regardless of whether Synergy has secured a formal trademark registration from the U.S. Patent and Trademark Office, or the PTO. The FDA typically conducts a review of proposed product brand names, including an evaluation of potential for confusion with other product names. The FDA may also object to a product brand name if it believes the name inappropriately implies medical claims. If the FDA objects to any of Synergy's proposed product brand names, it may be required to adopt an alternative brand name for its product candidates. If Synergy adopts an alternative brand name, it would lose the benefit of its existing trademark applications for such product candidate and may be required to expend significant additional resources in an effort to identify a suitable product brand name that would qualify under applicable trademark laws, not infringe the existing rights of third parties and be acceptable to the FDA. Synergy may be unable to build a successful brand identity for a new trademark in a timely manner or at all, which would limit its ability to commercialize its product candidates.

***Clinical trials involve a lengthy and expensive process with an uncertain outcome, and results of earlier studies and trials may not be predictive of future trial results.***

Synergy's product candidates may not prove to be safe and efficacious in clinical trials and may not meet all the applicable regulatory requirements needed to receive regulatory approval. In order to receive regulatory approval for the commercialization of its product candidates, Synergy must conduct, at its own expense, extensive preclinical testing and clinical trials to demonstrate safety and efficacy of these product candidates for the intended indication of use. Clinical testing is expensive, can take many years to complete, if at all, and its outcome is uncertain. Failure can occur at any time during the clinical trial process.

The results of preclinical studies and early clinical trials of new drugs do not necessarily predict the results of later-stage clinical trials. The design of Synergy's clinical trials is based on many assumptions about the expected effects of its product candidates, and if those assumptions are incorrect may not produce statistically significant results. Preliminary results may not be confirmed on full analysis of the detailed results of an early clinical trial. Product candidates in later stages of clinical trials may fail to show safety and efficacy sufficient to support intended use claims despite having progressed through initial clinical testing. The data collected from clinical trials of Synergy's product candidates may not be sufficient to support the filing of an NDA or to obtain regulatory approval in the United States or elsewhere. Because of the uncertainties associated with drug development and regulatory approval, Synergy cannot determine if or when it will have an approved product for commercialization or achieve sales or profits.

***Delays in clinical testing could result in increased costs to Synergy and delay its ability to generate revenue.***

Synergy may experience delays in clinical testing of its product candidates. Synergy does not know whether planned clinical trials will begin on time, will need to be redesigned or will be completed on schedule, if at all. Clinical trials can be delayed for a variety of reasons, including delays in obtaining regulatory approval to commence a clinical trial, in securing clinical trial agreements with prospective sites with acceptable terms, in obtaining institutional review board approval to conduct a clinical trial at a prospective site, in recruiting patients to participate in a clinical trial or in obtaining sufficient supplies of clinical trial materials. Many factors affect patient enrollment, including the size of the patient population, the proximity of patients to clinical sites, the eligibility criteria for the clinical trial,

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competing clinical trials and new drugs approved for the conditions Synergy is investigating. Clinical investigators will need to decide whether to offer their patients enrollment in clinical trials of Synergy's product candidates versus treating these patients with commercially available drugs that have established safety and efficacy profiles. Any delays in completing its clinical trials will increase Synergy's costs, slow down its product development and timeliness and approval process and delay its ability to generate revenue.

***The FDA's expectations for clinical trials may change over time, complicating the process of obtaining evidence to support approval of Synergy's product candidates.***

In March 2010, the FDA's Center for Drugs Evaluation and Research, or CDER, released a draft guidance entitled: "Irritable Bowel Syndrome  Clinical Evaluation of Products for Treatment" to assist the product sponsors developing new drugs for the treatment of IBS. In pertinent part, this document provides recommendations for IBS clinical trial design and endpoints, and describes the need for the future development of patient-reported outcome, or PRO, instruments for use in IBS clinical trials. The clinical trials Synergy has planned for plecanatide are designed to follow the recommendations included in this draft guidance. Synergy cannot predict when the draft guidance will be finalized and, if it is finalized, whether the final version will include the same recommendations, or whether its currently planned clinical trials of plecanatide will meet the final recommendations.

When finalized, the guidance document will represent the FDA's thinking on the clinical evaluation of products for the treatment of IBS. FDA guidance documents, however, do not establish legally enforceable requirements, should be viewed only as recommendations, and may be changed at any time. Therefore, even insofar as Synergy intends to follow the recommendations provided in the draft guidance document and the final guidance document when revealed, Synergy cannot be sure that the FDA will accept the results of its clinical research even if such research follows the recommendations in the guidance document.

***Synergy may be required to suspend or discontinue clinical trials due to unexpected side effects or other safety risks that could preclude approval of its product candidates.***

Synergy's clinical trials may be suspended at any time for a number of reasons. For example, it may voluntarily suspend or terminate its clinical trials if at any time it believes that they present an unacceptable risk to the clinical trial patients. In addition, the FDA or other regulatory agencies may order the temporary or permanent discontinuation of Synergy's clinical trials at any time if they believe that the clinical trials are not being conducted in accordance with applicable regulatory requirements or that they present an unacceptable safety risk to the clinical trial patients.

Administering any product candidate to humans may produce undesirable side effects. These side effects could interrupt, delay or halt clinical trials of Synergy's product candidates and could result in the FDA or other regulatory authorities denying further development or approval of its product candidates for any or all targeted indications. Ultimately, some or all of Synergy's product candidates may prove to be unsafe for human use. Moreover, Synergy could be subject to significant liability if any volunteer or patient suffers, or appears to suffer, adverse health effects as a result of participating in Synergy's clinical trials.

***If Synergy fails to comply with healthcare regulations ,it could face substantial enforcement actions, including civil and criminal penalties and its business, operations and financial condition could be adversely affected.***

As a developer of pharmaceuticals, even though Synergy does not intend to make referrals of healthcare services or bill directly to Medicare, Medicaid or other third-party payors, certain federal and state healthcare laws and regulations pertaining to fraud and abuse, false claims and patients' privacy rights are and will be applicable to Synergy's business. Synergy could be subject to healthcare

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fraud and abuse laws and patient privacy laws of both the federal government and the states in which it conducts its business. The laws include:

- the federal healthcare program anti-kickback law, which prohibits, among other things, persons from soliciting, receiving or providing remuneration, directly or indirectly, to induce either the referral of an individual, for an item or service or the purchasing or ordering of a good or service, for which payment may be made under federal healthcare programs such as the Medicare and Medicaid programs;

- federal false claims laws which prohibit, among other things, individuals or entities from knowingly presenting, or causing to be presented, claims for payment from Medicare, Medicaid, or other third-party payors that are false or fraudulent, and which may apply to entities like us which provide coding and billing information to customers;

- the federal Health Insurance Portability and Accountability Act of 1996, which prohibits executing a scheme to defraud any healthcare benefit program or making false statements relating to healthcare matters and which also imposes certain requirements relating to the privacy, security and transmission of individually identifiable health information;

- the Federal Food, Drug, and Cosmetic Act, which among other things, strictly regulates drug manufacturing and product marketing, prohibits manufacturers from marketing drug products for off-label use and regulates the distribution of drug samples; and

- state law equivalents of each of the above federal laws, such as anti-kickback and false claims laws which may apply to items or services reimbursed by any third-party payor, including commercial insurers, and state laws governing the privacy and security of health information in certain circumstances, many of which differ from each other in significant ways and often are not preempted by federal laws, thus complicating compliance efforts.

If Synergy's operations are found to be in violation of any of the laws described above or any governmental regulations that apply to us, it may be subject to penalties, including civil and criminal penalties, damages, fines and the curtailment or restructuring of its operations. Any penalties, damages, fines, curtailment or restructuring of Synergy's operations could adversely affect its ability to operate its business and its financial results. Although compliance programs can mitigate the risk of investigation and prosecution for violations of these laws, the risks cannot be entirely eliminated. Any action against Synergy for violation of these laws, even if it successfully defends against it, could cause Synergy to incur significant legal expenses and divert management's attention from the operation of its business. Moreover, achieving and sustaining compliance with applicable federal and state privacy, security and fraud laws may prove costly.

***If Synergy is unable to satisfy regulatory requirements, it may not be able to commercialize its product candidates.***

Synergy needs FDA approval prior to marketing its product candidates in the United States. If it fails to obtain FDA approval to market its product candidates, it will be unable to sell its product candidates in the United States and Synergy will not generate any revenue.

The FDA's review and approval process, including among other things, evaluation of preclinical studies and clinical trials of a product candidate as well as the manufacturing process and facility, is lengthy, expensive and uncertain. To receive approval, we must, among other things, demonstrate with substantial evidence from well-designed and well-controlled pre-clinical testing and clinical trials that the product candidate is both safe and effective for each indication for which approval is sought. Satisfaction of these requirements typically takes several years and the time needed to satisfy them may vary substantially, based on the type, complexity and novelty of the pharmaceutical product. Synergy cannot predict if or when it will submit an NDA for approval for any of its product candidates currently under development. Any approvals Synergy may obtain may not cover all of the clinical

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indications for which it is seeking approval or may contain significant limitations on the conditions of use.

The FDA has substantial discretion in the NDA review process and may either refuse to file Synergy's NDA for substantive review or may decide that its data is insufficient to support approval of its product candidates for the claimed intended uses. Following any regulatory approval of its product candidates, Synergy will be subject to continuing regulatory obligations such as safety reporting, required and additional post marketing obligations, and regulatory oversight of promotion and marketing. Even if Synergy receives regulatory approvals, the FDA may subsequently seek to withdraw approval of Synergy's NDA if it determines that new data or a reevaluation of existing data show the product is unsafe for use under the conditions of use upon the basis of which the NDA was approved, or based on new evidence of adverse effects or adverse clinical experience, or upon other new information. If the FDA does not file or approve Synergy's NDA or withdraws approval of its NDA, the FDA may require that Synergy conducts additional clinical trials, preclinical or manufacturing studies and submit that data before it will reconsider Synergy's application. Depending on the extent of these or any other requested studies, approval of any applications that Synergy submits may be delayed by several years, may require Synergy to expend more resources than it has available, or may never be obtained at all.

Synergy will also be subject to a wide variety of foreign regulations governing the development, manufacture and marketing of its products. Whether or not FDA approval has been obtained, approval of a product by the comparable regulatory authorities of foreign countries must still be obtained prior to marketing the product in those countries. The approval process varies and the time needed to secure approval in any region such as the European Union or in a country with an independent review procedure may be longer or shorter than that required for FDA approval. Synergy cannot assure you that clinical trials conducted in one country will be accepted by other countries or that an approval in one country or region will result in approval elsewhere.

***If Synergy's product candidates are unable to compete effectively with marketed drugs targeting similar indications as its product candidates, Synergy's commercial opportunity will be reduced or eliminated.***

Synergy faces competition generally from established pharmaceutical and biotechnology companies, as well as from academic institutions, government agencies and private and public research institutions. Many of its competitors have significantly greater financial resources and expertise in research and development, manufacturing, preclinical testing, conducting clinical trials, obtaining regulatory approvals and marketing approved products than Synergy does. Small or early-stage companies may also prove to be significant competitors, particularly through collaborative arrangements with large, established companies. Synergy's commercial opportunity will be reduced or eliminated if its competitors develop and commercialize GI drugs that are safer, more effective, have fewer side effects or are less expensive than Synergy's product candidates. These potential competitors compete with Synergy in recruiting and retaining qualified scientific and management personnel, establishing clinical trial sites and patient enrollment for clinical trials, as well as in acquiring technologies and technology licenses complementary to Synergy's programs or advantageous to its business.

If approved and commercialized, plecanatide will compete with at least two currently approved prescription therapies for the treatment of CC and IBS-C, Amitiza and Linzess. In addition, over-the-counter products are also used to treat certain symptoms of CC and IBS-C. Synergy believes other companies are developing products that will compete with plecanatide should they be approved by the FDA. For example, velusetrag, is being developed by Theravance, Inc. and has completed Phase 2 clinical trials for CC. To Synergy's knowledge, other potential competitors are in earlier stages of development. If potential competitors are successful in completing drug development for their product candidates and obtain approval from the FDA, they could limit the demand for plecanatide.

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Synergy expects that its ability to compete effectively will depend upon its ability to:

- successfully and rapidly complete clinical trials and submit for and obtain all requisite regulatory approvals in a cost-effective manner;
- maintain a proprietary position for its products and manufacturing processes and other related product technology;
- attract and retain key personnel;
- develop relationships with physicians prescribing these products; and
- build an adequate sales and marketing infrastructure for its product candidates.

Because Synergy will be competing against significantly larger companies with established track records, it will have to demonstrate that, based on experience, clinical data, side-effect profiles and other factors, its products, if approved, are competitive to other products. If Synergy is unable to compete effectively in the GI drug market and differentiate its products from other marketed GI drugs, it may never generate meaningful revenue.

***Synergy currently has no sales and marketing organization. If it is unable to establish a direct sales force in the United States to promote its products, the commercial opportunity for its products may be diminished.***

Synergy currently has no sales and marketing organization. If any of its product candidates are approved by the FDA, it intends to market that product through its own sales force. Synergy will incur significant additional expenses and commit significant additional management resources to establish this sales force. Synergy may not be able to establish these capabilities despite these additional expenditures. It will also have to compete with other pharmaceutical and biotechnology companies to recruit, hire and train sales and marketing personnel. If Synergy elects to rely on third parties to sell its product candidates in the United States, it may receive less revenue than if it sold its products directly. In addition, although Synergy would intend to use due diligence in monitoring their activities, it may have little or no control over the sales efforts of those third parties. In the event Synergy is unable to develop its own sales force or collaborate with a third party to sell its product candidates, it may not be able to commercialize its product candidates which would negatively impact its ability to generate revenue.

***Synergy may need others to market and commercialize its product candidates in international markets.***

Currently, Synergy does not have any plans to enter international markets. In the future, if appropriate regulatory approvals are obtained, Synergy intends to commercialize its product candidates in international markets. However, Synergy has not decided how to commercialize its product candidates in those markets. Synergy may decide to build its own sales force or sell its products through third parties. If Synergy decides to sell its product candidates in international markets through a third party, it may not be able to enter into any marketing arrangements on favorable terms or at all. In addition, these arrangements could result in lower levels of income to Synergy than if it marketed its product candidates entirely on its own. If Synergy is unable to enter into a marketing arrangement for its product candidates in international markets, it may not be able to develop an effective international sales force to successfully commercialize those products in international markets. If Synergy fails to enter into marketing arrangements for its products and is unable to develop an effective international sales force, itsability to generate revenue would be limited.

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***If the manufacturers upon whom Synergy relies fail to produce plecanatide and its product candidates, including SP-333, in the volumes that it requires on a timely basis, or fails to comply with stringent regulations applicable to pharmaceutical drug manufacturers, Synergy may face delays in the development and commercialization of its product candidates.***

Synergy does not currently possess internal manufacturing capacity. It currently utilizes the services of contract manufacturers to manufacture its clinical supplies. With respect to the manufacturing of plecanatide, Synergy has executed supply agreements with two contract manufacturers sufficient to meet its foreseeable clinical trial requirements. Any curtailment in the availability of plecanatide, however, could result in production or other delays with consequent adverse effects on us. In addition, because regulatory authorities must generally approve raw material sources for pharmaceutical products, changes in raw material suppliers may result in production delays or higher raw material costs.

Synergy continues to pursue additional API and drug product supply agreements with other manufacturers. Synergy may be required to agree to minimum volume requirements, exclusivity arrangements or other restrictions with the contract manufacturers. Synergy may not be able to enter into long-term agreements on commercially reasonable terms, or at all. If Synergy changes or adds manufacturers, the FDA and comparable foreign regulators may require approval of the changes. Approval of these changes could require new testing by the manufacturer and compliance inspections to ensure the manufacturer is conforming to all applicable laws and regulations, including good manufacturing practices, or GMP. In addition, the new manufacturers would have to be educated in or independently develop the processes necessary for the production of Synergy's product candidates. Peptide manufacturing is a highly specialized manufacturing business. While Synergy believes it will have long term arrangements with a sufficient number of contract manufacturers, if it loses a manufacturer, it would take Synergy a substantial amount of time to identify and develop a relationship, and seek regulatory approval, where necessary, for an alternative manufacturer.

The manufacture of pharmaceutical products requires significant expertise and capital investment, including the development of advanced manufacturing techniques and process controls. Manufacturers of pharmaceutical products may encounter difficulties in production, particularly in scaling up production. These problems include difficulties with production costs and yields, quality control, including stability of the product and quality assurance testing, shortages of qualified personnel, as well as compliance with federal, state and foreign regulations. In addition, any delay or interruption in the supply of clinical trial supplies could delay the completion of Synergy's clinical trials, increase the costs associated with conducting its clinical trials and, depending upon the period of delay, require Synergy to commence new clinical trials at significant additional expense or to terminate a clinical trial.

Synergy is responsible for ensuring that each of its contract manufacturers comply with the GMP requirements of the FDA and other regulatory authorities from which it seeks to obtain product approval. These requirements include, among other things, quality control, quality assurance and the maintenance of records and documentation. The approval process for NDAs includes a review of the manufacturer's compliance with GMP requirements. Synergy is responsible for regularly assessing a contract manufacturer's compliance with GMP requirements through record reviews and periodic audits and for ensuring that the contract manufacturer takes responsibility and corrective action for any identified deviations. Manufacturers of plecanatide and other product candidates, including SP-333, may be unable to comply with these GMP requirements and with other FDA and foreign regulatory requirements, if any.

While Synergy will oversee compliance by its contract manufacturers, ultimately it will not have control over its manufacturers' compliance with these regulations and standards. A failure to comply with these requirements may result in fines and civil penalties, suspension of production, suspension or delay in product approval, product seizure or recall, or withdrawal of product approval. If the safety of

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plecanatide or other product candidates is compromised due to a manufacturers' failure to adhere to applicable laws or for other reasons, Synergy may not be able to obtain regulatory approval for or successfully commercialize plecanatide or other product candidates, and it may be held liable for any injuries sustained as a result. Any of these factors could cause a delay of clinical trials, regulatory submissions, approvals or commercialization of plecanatide or other product candidates, entail higher costs or result in Synergy being unable to effectively commercialize plecanatide or other product candidates. Furthermore, if Synergy's manufacturers fail to deliver the required commercial quantities on a timely basis and at commercially reasonable prices, it may be unable to meet demand for any approved products and would lose potential revenues.

***Synergy may not be able to manufacture its product candidates in commercial quantities, which would prevent it from commercializing its product candidates.***

To date, Synergy's product candidates have been manufactured in small quantities for preclinical studies and clinical trials. If any of Synergy's product candidates is approved by the FDA or comparable regulatory authorities in other countries for commercial sale, it will need to manufacture such product candidate in larger quantities. Synergy may not be able to increase successfully the manufacturing capacity for any of its product candidates in a timely or economic manner, or at all. Significant scale-up of manufacturing may require additional validation studies, which the FDA must review and approve. If Synergy is unable to increase successfully the manufacturing capacity for a product candidate, the clinical trials as well as the regulatory approval or commercial launch of that product candidate may be delayed or there may be a shortage in supply. Synergy's product candidates require precise, high quality manufacturing. Synergy's failure to achieve and maintain these high quality manufacturing standards in collaboration with its third-party manufacturers, including the incidence of manufacturing errors, could result in patient injury or death, product recalls or withdrawals, delays or failures in product testing or delivery, cost overruns or other problems that could harm its business, financial condition and results of operations.

***Materials necessary to manufacture Synergy's product candidates may not be available on commercially reasonable terms, or at all, which may delay the development and commercialization of its product candidates.***

Synergy relies on the third-party manufacturers of its product candidates to purchase from third-party suppliers the materials necessary to produce the bulk active pharmaceutical ingredients, or APIs, and product candidates for its clinical trials, and it will rely on such manufacturers to purchase such materials to produce the APIs and finished products for any commercial distribution of its products if it obtains marketing approval. Suppliers may not sell these materials to Synergy's manufacturers at the time they need them in order to meet Synergy's required delivery schedule or on commercially reasonable terms, if at all. Synergy does not have any control over the process or timing of the acquisition of these materials by its manufacturers. Moreover, it currently does not have any agreements for the production of these materials. If Synergy's manufacturers are unable to obtain these materials for its clinical trials, testing of the affected product candidate would be delayed, which may significantly impact its ability to develop the product candidate. If Synergy or its manufacturers are unable to purchase these materials after regulatory approval has been obtained for one of Synergy's products, the commercial launch of such product would be delayed or there would be a shortage in supply of such product, which would harm Synergy's ability to generate revenues from such product and achieve or sustain profitability.

***Synergy's product candidates, if approved for sale, may not gain acceptance among physicians, patients and the medical community, thereby limiting Synergy's potential to generate revenues.***

If one of Synergy's product candidates is approved for commercial sale by the FDA or other regulatory authorities, the degree of market acceptance of any approved product by physicians,

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healthcare professionals and third-party payors and its profitability and growth will depend on a number of factors, including:

- demonstration of safety and efficacy;
- changes in the practice guidelines and the standard of care for the targeted indication;
- relative convenience and ease of administration;
- the prevalence and severity of any adverse side effects;
- budget impact of adoption of Synergy's product on relevant drug formularies and the availability, cost and potential advantages of alternative treatments, including less expensive generic drugs;
- pricing and cost effectiveness, which may be subject to regulatory control;
- effectiveness of Synergy's or any of its partners' sales and marketing strategies;
- the product labeling or product insert required by the FDA or regulatory authority in other countries; and
- the availability of adequate third-party insurance coverage or reimbursement.

If any product candidate that Synergy develops does not provide a treatment regimen that is as beneficial as, or is perceived as being as beneficial as, the current standard of care or otherwise does not provide patient benefit, that product candidate, if approved for commercial sale by the FDA or other regulatory authorities, likely will not achieve market acceptance. Synergy's ability to effectively promote and sell any approved products will also depend on pricing and cost-effectiveness, including its ability to produce a product at a competitive price and its ability to obtain sufficient third-party coverage or reimbursement. If any product candidate is approved but does not achieve an adequate level of acceptance by physicians, patients and third-party payors, Synergy's ability to generate revenues from that product would be substantially reduced. In addition, its efforts to educate the medical community and third-party payors on the benefits of its product candidates may require significant resources, may be constrained by FDA rules and policies on product promotion, and may never be successful.

***Guidelines and recommendations published by various organizations can impact the use of Synergy's products.***

Government agencies promulgate regulations and guidelines directly applicable to Synergy and to its products. In addition, professional societies, practice management groups, private health and science foundations and organizations involved in various diseases from time to time may also publish guidelines or recommendations to the health care and patient communities. Recommendations of government agencies or these other groups or organizations may relate to such matters as usage, dosage, route of administration and use of concomitant therapies. Recommendations or guidelines suggesting the reduced use of Synergy's products or the use of competitive or alternative products that are followed by patients and health care providers could result in decreased use of Synergy's proposed products.

***If product liability lawsuits are successfully brought against Synergy, it may incur substantial liabilities and may be required to limit commercialization of its product candidates.***

Synergy faces an inherent risk of product liability lawsuits related to the testing of its product candidates, and will face an even greater risk if it sells its product candidates commercially. Currently, Synergy is not aware of any anticipated product liability claims with respect to its product candidates. In the future, an individual may bring a liability claim against Synergy if one of its product candidates causes, or merely appears to have caused, an injury. If Synergy cannot successfully defend itself against

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the product liability claim, it may incur substantial liabilities. Regardless of merit or eventual outcome, liability claims may result in:

- decreased demand for Synergy's product candidates;
- injury to its reputation;
- withdrawal of clinical trial participants;
- costs of related litigation;
- initiation of investigations by regulators;
- substantial monetary awards to patients or other claimants;
- distraction of management's attention from Synergy's primary business;
- product recalls;
- loss of revenue; and
- the inability to commercialize its product candidates.

Synergy has clinical trial liability insurance with a $5,000,000 aggregate limit. Synergy intends to expand its insurance coverage to include the sale of commercial products if marketing approval is obtained for its product candidates. Synergy's current insurance coverage may prove insufficient to cover any liability claims brought against it. In addition, because of the increasing costs of insurance coverage, Synergy may not be able to maintain insurance coverage at a reasonable cost or obtain insurance coverage that will be adequate to satisfy liabilities that may arise.

***Synergy's failure to successfully discover, acquire, develop and market additional product candidates or approved products would impair its ability to grow.***

As part of its growth strategy, Synergy intends to develop and market additional products and product candidates. It is pursuing various therapeutic opportunities through its pipeline. Synergy may spend several years completing its development of any particular current or future internal product candidate, and failure can occur at any stage. The product candidates to which Synergy allocates its resources may not end up being successful. In addition, because Synergy's internal research capabilities are limited, it may be dependent upon pharmaceutical and biotechnology companies, academic scientists and other researchers to sell or license products or technology to it. The success of this strategy depends partly upon its ability to identify, select, discover and acquire promising pharmaceutical product candidates and products. Failure of this strategy would impair Synergy's ability to grow.

The process of proposing, negotiating and implementing a license or acquisition of a product candidate or approved product is lengthy and complex. Other companies, including some with substantially greater financial, marketing and sales resources, may compete with Synergy for the license or acquisition of product candidates and approved products. Synergy has limited resources to identify and execute the acquisition or in-licensing of third-party products, businesses and technologies and integrate them into its current infrastructure. Moreover, Synergy may devote resources to potential acquisitions or in-licensing opportunities that are never completed, or it may fail to realize the anticipated benefits of such efforts. Synergy may not be able to acquire the rights to additional product candidates on terms that it finds acceptable, or at all.

In addition, future acquisitions may entail numerous operational and financial risks, including:

exposure to unknown liabilities;

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disruption of Synergy's business and diversion of its management's time and attention to develop acquired products or technologies;

incurrence of substantial debt, dilutive issuances of securities or depletion of cash to pay for acquisitions;

higher than expected acquisition and integration costs;

difficulty in combining the operations and personnel of any acquired businesses with its operations and personnel;

increased amortization expenses;

impairment of relationships with key suppliers or customers of any acquired businesses due to changes in management and ownership; and

inability to motivate key employees of any acquired businesses.

Further, any product candidate that Synergy acquires may require additional development efforts prior to commercial sale, including extensive clinical testing and approval by the FDA and applicable foreign regulatory authorities. All product candidates are prone to risks of failure typical of pharmaceutical product development, including the possibility that a product candidate will not be shown to be sufficiently safe and effective for approval by regulatory authorities.

***Even if Synergy's product candidates receive regulatory approval, they may still face future development and regulatory difficulties.***

Even if U.S. regulatory approval is obtained, the FDA may still impose significant restrictions on a product's indicated uses or impose ongoing requirements for potentially costly post-approval studies. Plecanatide and other product candidates, including SP-333, would also be subject to ongoing FDA requirements governing the labeling, packaging, storage, advertising, promotion, recordkeeping and submission of safety and other post-market information. In addition, manufacturers of drug products and their facilities are subject to continual review and periodic inspections by the FDA and other regulatory authorities for compliance with GMP, regulations. If Synergy or a regulatory agency discovers previously unknown problems with a product, such as adverse events of unanticipated severity or frequency, or problems with the facility where the product is manufactured, a regulatory agency may impose restrictions on that product or the manufacturer, including requiring withdrawal of the product from the market or suspension of manufacturing. If Synergy, its product candidates or the manufacturing facilities for its product candidates fail to comply with applicable regulatory requirements, a regulatory agency may:

issue warning letters;

impose civil or criminal penalties;

suspend regulatory approval;

suspend any ongoing clinical trials;

refuse to approve pending applications or supplements to applications filed by Synergy;

impose restrictions on operations, including costly new manufacturing requirements;

seize or detain products or request us to initiate a product recall; or

pursue and obtain an injunction.

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***Drugs approved to treat IBS have been subject to considerable post-market scrutiny, with consequences up to and including voluntary withdrawal of approved products from the market. This may heighten FDA scrutiny of Synergy's product candidates before or following market approval.***

Products approved for the treatment of IBS have been subject to considerable post-market scrutiny. For example, in 2007, Novartis voluntarily discontinued marketing Zelnorm (tegaserod), a product approved for the treatment of women with IBS-C, after the FDA found an increased risk of serious cardiovascular events associated with the use of the drug. Earlier, in 2000, Glaxo Wellcome withdrew Lotronex (alosetron), which was approved for women with severe diarrhea-prominent IBS, after the manufacturer received numerous reports of adverse events or AEs, including ischemic colitis, severely obstructed or ruptured bowel, or death. In 2002, the FDA approved the manufacturer's application to make Lotronex available again, on the condition that the drug only be made available through a restricted marketing program.

Although plecanatide is being investigated for IBS, plecanatide is from a different pharmacologic class than Zelnorm or Lotronex, and would not be expected to share the same clinical risk profile as those agents. Nevertheless, because these products are in the same or related therapeutic classes, it is possible that the FDA will have heightened scrutiny of plecanatide or any other agent under development for IBS. This could delay product approval, increase the cost of Synergy's clinical development program, or increase the cost of post-market study commitments for its IBS product candidates, including plecanatide.

***Even if Synergy's product candidates receive regulatory approval in the United States, it may never receive approval to commercialize them outside of the United States.***

In the future, Synergy may seek to commercialize plecanatide and/or other product candidates, including SP-333, in foreign countries outside of the United States. In order to market any products outside of the United States, Synergy must establish and comply with numerous and varying regulatory requirements of other jurisdictions regarding safety and efficacy. Approval procedures vary among jurisdictions and can involve product testing and administrative review periods different from, and greater than, those in the United States. The time required to obtain approval in other jurisdictions might differ from that required to obtain FDA approval. The regulatory approval process in other jurisdictions may include all of the risks detailed above regarding FDA approval in the United States as well as other risks. Regulatory approval in one jurisdiction does not ensure regulatory approval in another, but a failure or delay in obtaining regulatory approval in one jurisdiction may have a negative effect on the regulatory processes in others. Failure to obtain regulatory approvals in other jurisdictions or any delay or setback in obtaining such approvals could have the same adverse effects detailed above regarding FDA approval in the United States. As described above, such effects include the risks that plecanatide or other product candidates may not be approved for all indications for use included in proposed labeling or for any indications at all, which could limit the uses of plecanatide or other product candidates and have an adverse effect on Synergy's products' commercial potential or require costly post-marketing studies.

***Synergy relies on third parties to conduct its clinical trials. If these third parties do not successfully carry out their contractual duties or meet expected deadlines, Synergy may not be able to seek or obtain regulatory approval for or commercialize its product candidates.***

Synergy has agreements with third-party contract research organizations, or CROs, under which it has delegated to the CROs the responsibility to coordinate and monitor the conduct of its clinical trials and to manage data for its clinical programs. Synergy, its CROs and its clinical sites are required to comply with current Good Clinical Practices, or GCPs, regulations and guidelines issued by the FDA and by similar governmental authorities in other countries where it is conducting clinical trials. Synergy has an ongoing obligation to monitor the activities conducted by its CROs and at its clinical sites to

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confirm compliance with these requirements. In the future, if Synergy, its CROs or its clinical sites fail to comply with applicable GCPs, the clinical data generated in its clinical trials may be deemed unreliable and the FDA may require Synergy to perform additional clinical trials before approving oitsmarketing applications. In addition, Synergy's clinical trials must be conducted with product produced under cGMP regulations, and will require a large number of test subjects. Synergy's failure to comply with these regulations may require it to repeat clinical trials, which would delay the regulatory approval process.

If CROs do not successfully carry out their contractual duties or obligations or meet expected deadlines, if they need to be replaced, or if the quality or accuracy of the clinical data they obtain is compromised due to their failure to adhere to Synergy's clinical protocols, regulatory requirements or for other reasons, Synergy's clinical trials may be extended, delayed or terminated, and it may not be able to obtain regulatory approval for or successfully commercialize its product candidates. As a result, its financial results and the commercial prospects for its product candidates would be harmed, its costs could increase, and its ability to generate revenue could be delayed.

***If Synergy fails to attract and keep senior management and key scientific personnel, it may be unable to successfully develop its product candidates, conduct its clinical trials and commercialize its product candidates.***

Synergy's success depends in part on its continued ability to attract, retain and motivate highly qualified management, clinical and scientific personnel and on its ability to develop and maintain important relationships with leading academic institutions, clinicians and scientists. Synergy is highly dependent upon its senior management and scientific staff, particularly Gary S. Jacob, Ph.D., its President and Chief Executive Officer and Kunwar Shailubhai, Ph.D., its Chief Scientific Officer. The loss of services of Dr. Jacob or one or more of Synergy's other members of senior management could delay or prevent the successful completion of its planned clinical trials or the commercialization of its product candidates.

The competition for qualified personnel in the biotechnology and pharmaceuticals field is intense. Synergy will need to hire additional personnel as it expands its clinical development and commercial activities. It may not be able to attract and retain quality personnel on acceptable terms given the competition for such personnel among biotechnology, pharmaceutical and other companies.

***Synergy will need to increase the size of its organization, and it may experience difficulties in managing growth.***

Synergy is a small company with sixteen employees as of November 30, 2012. To continue its clinical trials and commercialize its product candidates, it will need to expand its employee base for managerial, operational, financial and other resources. Future growth will impose significant added responsibilities on members of management, including the need to identify, recruit, maintain and integrate additional employees. Over the next 12 months depending on the progress of its planned clinical trials, Synergy plans to add additional employees to assist it with its clinical programs. Synergy's future financial performance and its ability to commercialize its product candidates and to compete effectively will depend, in part, on its ability to manage any future growth effectively. To that end, Synergy must be able to:

manage development efforts effectively;

manage its clinical trials effectively;

integrate additional management, administrative, manufacturing and sales and marketing personnel;

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maintain sufficient administrative, accounting and management information systems and controls; and

hire and train additional qualified personnel.

Synergy may not be able to accomplish these tasks, and its failure to accomplish any of them could harm its financial results and impact its ability to achieve development milestones.

***Reimbursement may not be available for Synergy's product candidates, which would impede sales.***

Market acceptance and sales of Synergy's product candidates may depend on coverage and reimbursement policies and health care reform measures. Decisions about formulary coverage as well as levels at which government authorities and third-party payors, such as private health insurers and health maintenance organizations, reimburse patients for the price they pay for Synergy's products as well as levels at which these payers pay directly for its products, where applicable, could affect whether Synergy is able to commercialize these products. Synergy cannot be sure that reimbursement will be available for any of these products. Also, Synergy cannot be sure that coverage or reimbursement amounts will not reduce the demand for, or the price of, its products. Synergy has not commenced efforts to have its product candidates reimbursed by government or third party payors. If coverage and reimbursement are not available or are available only at limited levels, Synergy may not be able to commercialize its products.

In recent years, officials have made numerous proposals to change the health care system in the United States. These proposals include measures that would limit or prohibit payments for certain medical treatments or subject the pricing of drugs to government control. In addition, in many foreign countries, particularly the countries of the European Union, the pricing of prescription drugs is subject to government control. If Synergy's products are or become subject to government regulation that limits or prohibits payment for its products, or that subjects the price of its products to governmental control, it may not be able to generate revenue, attain profitability or commercialize its products.

As a result of legislative proposals and the trend towards managed health care in the United States, third-party payers are increasingly attempting to contain health care costs by limiting both coverage and the level of reimbursement of new drugs. They may also impose strict prior authorization requirements and/or refuse to provide any coverage of uses of approved products for medical indications other than those for which the FDA has granted market approvals. As a result, significant uncertainty exists as to whether and how much third-party payers will reimburse patients for their use of newly-approved drugs, which in turn will put pressure on the pricing of drugs.

***Healthcare reform measures could hinder or prevent Synergy's product candidates' commercial success.***

The U.S. government and other governments have shown significant interest in pursuing healthcare reform. Any government-adopted reform measures could adversely impact the pricing of healthcare products and services in the United States or internationally and the amount of reimbursement available from governmental agencies or other third party payors. The continuing efforts of the U.S. and foreign governments, insurance companies, managed care organizations and other payors of health care services to contain or reduce health care costs may adversely affect Synergy's ability to set prices for its products which it believes are fair, and its ability to generate revenues and achieve and maintain profitability.

New laws, regulations and judicial decisions, or new interpretations of existing laws, regulations and decisions, that relate to healthcare availability, methods of delivery or payment for products and services, or sales, marketing or pricing, may limit Synergy's potential revenue, and it may need to revise its research and development programs. The pricing and reimbursement environment may change in the future and become more challenging due to several reasons, including policies advanced by the