November 9, 2016

Synergy Pharmaceuticals Reports Third Quarter 2016 Financial Results and Business Update

NEW YORK--(BUSINESS WIRE)-- Synergy Pharmaceuticals Inc. (NASDAQ:SGYP), a biopharmaceutical company focused on the development and commercialization of novel gastrointestinal (GI) therapies, today reported its financial results and business update for the three months ended September 30, 2016.

“This was another exciting quarter for Synergy,” said Gary S. Jacob, Ph.D., Chairman and Chief Executive Officer of Synergy Pharmaceuticals Inc. “I am encouraged by our continued positive interactions with FDA and the steady progress being made by our highly experienced and talented leadership team in preparing our organization, as well as the market, for the anticipated launch of plecanatide early next year.”

“We are expecting several transformative events in the coming months, including top-line results from our two plecanatide phase 3 IBS-C trials by year-end and a January 29, 2017 PDUFA date for plecanatide in CIC,” added Dr. Jacob. “As we move forward, we will continue to make appropriate, well-timed investments to ensure that plecanatide is positioned for a successful launch upon approval and will soon be available to patients, healthcare providers and payers.”

Third Quarter 2016 and Recent Highlights

Research & Development

Plecanatide CIC Development Update

- The plecanatide new drug application (NDA) in chronic idiopathic constipation (CIC) is currently under review by the Food and Drug Administration (FDA) and the Prescription Drug User Fee Act (PDUFA) target action date is January 29, 2017. Plecanatide is the first investigational therapy designed to replicate the activity of uroguanylin, a naturally occurring human GI peptide, by working locally primarily in the proximal small intestine to stimulate digestive fluid movement and support regular bowel function.
- The late-cycle review meeting with the FDA was completed and no significant issues were identified. The FDA previously informed us that there are no plans at this time for an advisory committee meeting in connection with the review of the plecanatide NDA in CIC. The plecanatide NDA in CIC is supported by two double-blind, placebo-controlled phase 3 trials and one long-term open-label safety study. Over 3,500 patients have been exposed to plecanatide in the CIC clinical development program.

- Two posters were presented on the plecanatide CIC clinical data at the American College of Gastroenterology (ACG) annual scientific meeting in October 2016.

    - ***Safety and Tolerability of Plecanatide in Patients with Chronic Idiopathic Constipation: Long-term Evidence from an Open-Label Study***
        - Data presented from the long-term open-label safety study showed plecanatide was associated with low adverse events and low discontinuation rates in patients with CIC who received plecanatide (3 mg or 6 mg) once-daily for up to 72 weeks. The most common adverse events were diarrhea (7.1%) and urinary tract infection (2.2%). The remainder of adverse events occurred in less than 2% of patients treated with plecanatide. Adverse events leading to discontinuation occurred in 5.3% of patients treated with plecanatide, with discontinuation due to diarrhea occurring in 3.1% of patients. In addition, this study asked patients about level of treatment satisfaction and desire to continue treatment. The median score for treatment satisfaction was 4.0 (4=quite satisfied) and for continuation of treatment was 4.0 (4=quite likely).
    - ***Efficacy and Safety of Plecanatide in the Treatment of Chronic Idiopathic Constipation (CIC): Pooled Results from Two Phase 3 Studies***
        - Pooled results from two previously reported double-blind placebo-controlled phase 3 CIC trials confirmed patients treated with plecanatide showed a significantly greater response rate of durable overall complete spontaneous bowel movements compared to placebo (20.5% in 3 mg and 19.8% in 6mg dose groups compared to 11.5% in placebo; $p<0.001$ for both doses). This is the primary endpoint defined by the FDA for regulatory approval in CIC. This integrated analysis also showed consistent safety data with adverse event rates similar across plecanatide-treatment groups and placebo (30.6% in 3 mg and 31.1% in 6 mg dose groups compared to 28.7% in placebo). Diarrhea was the most common adverse event (4.6% in 3 mg and 5.1% in 6 mg compared to 1.3% in placebo). Discontinuation rates were low across all treatment groups (4.1% in 3.0 mg and 4.5% in 6.0 mg dose groups compared to 2.2% in placebo).

<u>Plecanatide IBS-C Development Update</u>

- Patient enrollment has been completed in the two double-blind, placebo-controlled phase 3 clinical trials with plecanatide in IBS-C patients. Top-line data in both trials are expected by the end of this year. The primary endpoint in both trials is the percentage of patients who are Overall Responders during the 12-week treatment period. An Overall Responder, as defined by the FDA, is a patient who is a weekly responder (i.e. meets both a 30% abdominal pain intensity reduction and stool frequency increase criteria in the same week) for at least 6 of the 12 treatment weeks. Plecanatide previously met this endpoint in a phase 2b trial with 424 IBS-C patients that was completed in 2014.
- The IBS-C pre-NDA meeting with the FDA was completed in September 2016. Pending approval of plecanatide in the CIC indication, we plan to file a New Drug Application Supplement with Clinical Data (sNDA) for plecanatide in IBS-C in the first

quarter of 2017 and expect a 10-month review period from submission.

Commercial Planning & Launch Preparation

“We are laser-focused on our key strategic imperatives of product readiness, market and brand readiness and organizational readiness,” said Troy Hamilton, Executive Vice President and Chief Commercial Officer of Synergy Pharmaceuticals Inc. “Based on our extensive market research, advisory board meetings and interactions with payers, healthcare providers and patients to-date, we are very encouraged about the positive impact that plecanatide will have in the market place as a differentiated therapeutic option for patients with CIC. We are also pleased with the progress our technical operations team has made this year to ensure plecanatide product supply will be ready and available to physicians and patients by our anticipated launch early next year. We strongly believe that we have the right strategy and right team to successfully launch plecanatide and address the unmet needs of a growing GI market.”

Product Readiness

Key Highlights

- Met all technical operations timelines to-date and remain on-track to complete all activities by the anticipated launch of plecanatide in early 2017.
- Established a robust supply chain and actively producing commercial product.
- Continuing to build trade and sample stock for launch in early 2017.
- Implemented 3PL distribution network.
- Established strong Quality Management Systems.

Market/Brand Readiness

Key Highlights

- Generated substantial customer insights through qualitative and quantitative market research that will include more than 2,700 HCPs and more than 5,000 patients/consumers by the end of 2016.
- Conducted multiple productive advisory boards with national and regional GI Key Opinion Leaders and payers.
- Finalized plecanatide brand vision, brand positioning, value proposition, core marketing strategies and launch tactics; our message platform and a creative campaign will be completed and ready by year-end.
- Initiated pre-launch multimedia and digital campaigns to drive company awareness and disease education, focusing on current unmet medical needs of patients with CIC.
- Developed a compliant, value maximizing, and cost-effective promotional mix to reach the broadest universe of prescribers.

- Market Access team has conducted meetings with all key commercial and public payers, representing approximately 230 million covered lives in the U.S.

Organizational Readiness

Key Highlights

- National and regional market access teams have been active and in the field introducing Synergy Pharmaceuticals to payers since January 2016.
- Medical education efforts initiated in March 2016 and included strong corporate presence and key data presentations at Digestive Disease Week and ACG.
- Hired regional sales leaders averaging more than 10 years of GI experience who are driving important pre-launch initiatives and who will support an effective hybrid sales infrastructure that will be deployed at launch.
- Initiated a partnership with Publicis Touchpoint Solutions, Inc. to implement a cost-effective, flexible hybrid sales force, leveraging highly experienced sales representatives who will be fully dedicated to supporting the launch and adoption of plecanatide.
- Established a focused and efficient sales force strategy, combined with a comprehensive multi-channel approach, to reach the key prescribers and influencers at launch.
- Implemented all critical IT and compliance systems.

Financial Results

- As of September 30, 2016, we had approximately $109.1 million of cash and cash equivalents on hand as compared to approximately $111.8 million cash and cash equivalents and available for sale securities as of December 31, 2015.
- Net cash used in operating activities was $92.0 million in the nine months ended September 30, 2016, as compared to $70.7 million in the nine months ended September 30, 2015.
- Research and development expenses in the third quarter of 2016 were approximately $24.6 million, as compared to $20.4 million in the third quarter of 2015. These increased expenses were primarily a result of higher spending on IBS-C studies, additional technical operations and medical affairs operating expenses as well as drug product related costs for our commercial launch in the first quarter of 2017.
- Selling, general and administrative expenses were approximately $13.9 million in the third quarter of 2016, as compared to approximately $2.7 million in the third quarter of 2015. These increased expenses primarily reflect commercial preparedness and planning expenses to support an anticipated launch of plecanatide during the first quarter of 2017.
- On May 6, 2016, we closed on a registered direct offering of approximately 30 million shares of our common stock with gross proceeds of approximately $89.8

million.

- As of September 30, 2016, the principal balance on our 7.50% Convertible Senior Notes (“Notes”) due 2019 was $79.2 million as compared to $159.0 million at December 31, 2015.
- We had 179.8 million and 113.7 million common shares issued and outstanding at September 30, 2016 and December 31, 2015, respectively, which reflects primarily an increase in the issuance of shares from the first quarter conversions of the Notes and the common stock offering noted above.
- Net loss in the third quarter of 2016 was $40.2 million, as compared to a net loss of $26.0 million incurred in the third quarter of 2015.

About Synergy Pharmaceuticals Inc.

Synergy is a biopharmaceutical company focused on the development and commercialization of novel gastrointestinal (GI) therapies. The Company has pioneered discovery, research and development efforts around analogs of uroguanylin, a naturally occurring human GI peptide, for the treatment of GI diseases and disorders. Synergy discovered, is developing and controls 100% worldwide rights to its proprietary uroguanylin analog platform that includes two lead product candidates - plecanatide and dolcanatide. Plecanatide is Synergy's first uroguanylin analog currently being evaluated for use as a once-daily tablet for chronic idiopathic constipation (CIC) and irritable bowel syndrome with constipation (IBS-C). Dolcanatide is Synergy's second uroguanylin analog currently being explored for ulcerative colitis. For more information, please visit www.synergypharma.com.

Forward-Looking Statements

Certain statements in this press release are forward-looking within the meaning of the Private Securities Litigation Reform Act of 1995. These statements may be identified by the use of forward- looking words such as "anticipate," "planned," "believe," "forecast," "estimated," "expected," and "intend," among others. These forward-looking statements are based on Synergy's current expectations and actual results could differ materially. There are a number of factors that could cause actual events to differ materially from those indicated by such forward-looking statements. These factors include, but are not limited to, substantial competition; our ability to continue as a going concern; our need for additional financing; uncertainties of patent protection and litigation; uncertainties of government or third party payer reimbursement; limited sales and marketing efforts and dependence upon third parties; and risks related to failure to obtain FDA clearances or approvals and noncompliance with FDA regulations. As with any pharmaceutical under development, there are significant risks in the development, regulatory approval and commercialization of new products. There are no guarantees that future clinical trials discussed in this press release will be completed or successful or that any product will receive regulatory approval for any indication or prove to be commercially successful. Investors should read the risk factors set forth in Synergy's Annual Report on Form 10-K for the year ended December 31, 2015 and other periodic reports filed with the Securities and Exchange Commission. While the list of factors presented here is considered representative, no such list should be considered to be a complete statement of all

potential risks and uncertainties. Unlisted factors may present significant additional obstacles to the realization of forward-looking statements. Forward-looking statements included herein are made as of the date hereof, and Synergy does not undertake any obligation to update publicly such statements to reflect subsequent events or circumstances.

Synergy Pharmaceutical Inc.
Condensed Consolidated Balance Sheets

($ in thousands)	**September 30, 2016 (unaudited)**	**December 31, 2015**
Assets		
Cash, cash equivalents and available for sale securities	$ 109,090	$ 111,750
Prepaid expenses and other current assets	1,744	3,305
Total Current assets	110,834	115,055
Other assets	978	874
Total assets	$ 111,812	$ 115,929
Liabilities and Stockholders' Equity/(Deficit)		
Total Current Liabilities	$ 23,517	$ 19,579
Senior Convertible Notes, net	76,070	151,241
Derivative financial instruments – warrants	171	322
Total Liabilities	99,758	171,142
Total Stockholders’ Equity/(Deficit)	12,054	(55,213)
Total Liabilities and Stockholders' Equity/(Deficit)	$ 111,812	$ 115,929

Condensed Consolidated Statement of Operations
($ in thousands except share and per share data)
(unaudited)

	Three Months Ended September 30, 2016	Three Months Ended September 30, 2015	Nine Months Ended September 30, 2016	Nine Months Ended September 30, 2015
Revenues	$ —	$ —	$ —	$ —
Costs and Expenses:				
Research and development	24,610	20,424	72,396	58,147
Selling, general and administrative	13,872	2,728	30,497	14,727
Loss from Operations	(38,482)	(23,152)	(102,893)	(72,874)
Other Loss:				
Interest and investment expense, net	(1,674)	(4,291)	(10,383)	(13,815)
Debt conversion expense	—	—	(25,615)	—
Change in fair value of financial instruments	(87)	1,446	151	(364)
Total Other Loss	(1,761)	(2,845)	(35,847)	(14,179)
Net Loss	$ (40,243)	$ (25,997)	$ (138,740)	$ (87,053)
Net Loss per Common Share, Basic and Diluted	$ (0.22)	$ (0.23)	$ (0.89)	$ (0.85)
Weighted Average Common Shares Outstanding	179,786,580	111,328,339	155,410,353	102,838,814

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