March 1, 2017

Synergy Pharmaceuticals Reports Fourth Quarter and Full Year 2016 Financial Results and Business Update

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 full year and the three months ended December 31, 2016.

“The approval of TRULANCE™ (plecanatide) in the United States for the treatment of adults with chronic idiopathic constipation was a tremendous event not just for Synergy, but also for the millions of patients with CIC who have been in need of a new therapeutic option,” said Gary S. Jacob, PhD, Chairman and Chief Executive Officer of Synergy Pharmaceuticals Inc. “I am pleased with the progress our team has made implementing a strong and compelling commercial plan, a robust high quality supply chain, and ensuring that the Synergy organization, healthcare providers and payers, are well prepared for the launch of TRULANCE this month. In addition, we are continuing our efforts to bring TRULANCE to patients with irritable bowel syndrome with constipation, as we remain on-track to file a supplemental new drug application (sNDA) this month.”

“Together with the approval of TRULANCE, the fourth quarter of 2016 and beginning of 2017 were marked by several key accomplishments, including positive top-line results in two Phase 3 trials of TRULANCE in IBS-C which will support the sNDA filing and the recent publication of our Phase 3 CIC data in the American Journal of Gastroenterology. We’ve also strengthened our balance sheet and enhanced our strategic options as we completed a $125 million financing, continued to reduce our convertible debt and successfully eliminated restrictive covenants associated with that debt. These achievements put Synergy in an excellent position for future growth as we begin to commercialize our first product, TRULANCE.”

Fourth Quarter 2016 and Recent Highlights

TRULANCE™ (plecanatide) CIC Update

- On January 19, 2017, the United States (U.S.) Food and Drug Administration (FDA) approved our first product, plecanatide, under the trademarked name TRULANCE, for the treatment of adults with chronic idiopathic constipation (CIC). The efficacy and safety of TRULANCE was evaluated in the largest Phase 3 CIC clinical trials to date, which included more than 2,600 patients in two randomized, 12-week, double-blind, placebo-controlled studies of TRULANCE. In an integrated analysis of both studies, diarrhea was the most common adverse reaction, reported in 5% of patients

treated with TRULANCE compared to 1% of patients treated with placebo. The recommended adult dosage of TRULANCE is 3 mg taken orally, once daily, with or without food. TRULANCE will be available in the U.S. this quarter.

TRULANCE IBS-C Development Update

- In December 2016, we announced positive top-line results in the two Phase 3 clinical trials of TRULANCE for the treatment of adults with IBS-C. In both trials, TRULANCE met the study's primary endpoint showing statistical significance in the percentage of patients who were overall responders compared to placebo during the 12-week treatment period. An Overall Responder, as defined by the FDA, is a patient who fulfills both ≥ 30% reduction in worst abdominal pain and an increase of ≥ 1 complete spontaneous bowel movement (CSBM) from baseline, in the same week, for at least 50% of the 12 treatment weeks. This is the current primary endpoint required for FDA approval in IBS-C. In both studies, the most common adverse event was diarrhea (Study 1 = 3.2% at 3 mg and 3.7% at 6 mg compared to 1.3% at placebo; Study 2 = 5.4% at 3 mg and 4.3% at 6 mg compared to 0.6% at placebo). We plan to file a new drug application supplement with clinical data (sNDA) in the first quarter of 2017 and expect a 10-month review period from submission. We plan to present additional Phase 3 data from the two IBS-C trials at an appropriate scientific meeting later this year.

TRULANCE Launch Update

We are focused on three key strategic imperatives to achieve our objective of ensuring that TRULANCE is ready for launch this quarter:

- Product Readiness
- Market and Brand Readiness
- Organizational Readiness

Product Readiness

- Established a robust supply chain process and quality management system.
- Implemented our third party logistics (3PL) distribution network.
- Trade and sample stock manufactured and on-track for launch this quarter.
- Launching TRULANCE 3 mg in an innovative 30-count blister pack.

Market and Brand Readiness

- We are very encouraged by the feedback we have received from our market research, advisory boards and field-based customer meetings.
    - Completed extensive market research with more than 2,700 healthcare providers and over 5,300 patients.
    - Conducted multiple advisory boards with national and regional GI key opinion leaders, other healthcare providers and payers.

    - Since January 2016, our market access team has been meeting with key payer customers that represent over 230 million covered lives in the U.S.

- Initiated pre-launch multimedia and digital campaigns to drive company awareness and disease education, focusing on current unmet needs of patients with CIC.
- Finalized TRULANCE core marketing strategies and launch tactics, including a compliant, value-optimizing, cost effective promotional mix to reach the broadest universe of prescribers.
- Co-pay card programs and other patient assistance programs in place which will help us achieve access in 2017.
- Finalized pricing strategy for TRULANCE and will launch with a wholesale acquisition cost (WAC) of $353.48.

Organizational Readiness

- Utilizing a hybrid sales model to reach key prescribers and influencers at launch.
    - Less than 20% of prescribers in the U.S. currently account for over 70% of the branded constipation prescription market. These prescribers, which include gastroenterologists and primary care physicians, will be the focus of our field force at launch.
- Hired Synergy Regional Business Directors averaging 11 years of management experience and over 10 years in relevant GI fields.
- Hired Synergy Regional GI Account Specialists averaging 13 years of pharmaceutical experience and 8.5 years of GI experience.
- Partnered with Publicis Touchpoint Solutions, Inc. who have hired highly experienced sales representatives that will be fully dedicated to TRULANCE at launch.
    - Our Publicis Touchpoint sales representatives have an average of 11.5 years of pharmaceutical experience, and nearly 6 years of GI experience, with over 90% coming from other peer GI and PCP companies.
- Medical education efforts have been ongoing since March 2016.

Financial Results

- As of December 31, 2016, we had approximately $82.4 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 $129.8 million in the year ended December 31, 2016, as compared to $101 million in the year ended December 31, 2015.
- Research and development expenses in the fourth quarter of 2016 were approximately $17.2 million, as compared to $19.9 million in the fourth quarter of 2015. These decreased expenses were primarily a result of completion of IBS-C studies.

- Selling, general and administrative expenses were approximately $25.2 million in the fourth quarter of 2016, as compared to approximately $7.1 million in the fourth quarter of 2015. These increased expenses primarily reflect commercial preparedness and planning expenses to support an anticipated launch of Trulance during the first quarter of 2017.
- On January 31, 2017, Synergy entered into an underwriting agreement to issue and sell 20,325,204 shares of common stock of the Company in an underwritten public offering. The Offering closed on February 6, 2017, yielding net proceeds of approximately $121.6 million, after deducting underwriting discounts and commissions and estimated offering expenses payable by the Company.
- As of December 31, 2016, the principal balance on our 7.50% Convertible Senior Notes ("Notes") due 2019 was $23.5 million as compared to $159 million at December 31, 2015.
- We had 202.7 million and 113.7 million common shares issued and outstanding at December 31, 2016 and December 31, 2015, respectively, which reflects primarily an increase in the issuance of shares from the conversions of Notes, equity offering in May 2016 and exercise of warrants.
- Net loss in the fourth quarter of 2016 was $59.9 million, as compared to a net loss of $30.4 million incurred in the fourth quarter of 2015.

Indications and Usage

TRULANCE is a guanylate cyclase-C (GC-C) agonist indicated in adults for the treatment of chronic idiopathic constipation (CIC).

IMPORTANT SAFETY INFORMATION

WARNING: RISK OF SERIOUS DEHYDRATION IN PEDIATRIC PATIENTS

Trulance™ is contraindicated in patients less than 6 years of age; in nonclinical studies in young juvenile mice administration of a single oral dose of plecanatide caused deaths due to dehydration. Use of Trulance should be avoided in patients 6 years to less than 18 years of age. The safety and efficacy of Trulance have not been established in pediatric patients less than 18 years of age.

Contraindications

- Trulance is contraindicated in patients less than 6 years of age due to the risk of serious dehydration.
- Trulance is contraindicated in patients with known or suspected mechanical gastrointestinal obstruction.

Warnings and Precautions

Risk of Serious Dehydration in Pediatric Patients

- Trulance is contraindicated in patients less than 6 years of age. The safety and effectiveness of Trulance in patients less than 18 years of age have not been established. In young juvenile mice (human age equivalent of approximately 1 month to less than 2 years), plecanatide increased fluid secretion as a consequence of stimulation of guanylate cyclase-C (GC-C), resulting in mortality in some mice within the first 24 hours, apparently due to dehydration. Due to increased intestinal expression of GC-C, patients less than 6 years of age may be more likely than older patients to develop severe diarrhea and its potentially serious consequences.
- Use of Trulance should be avoided in patients 6 years to less than 18 years of age. Although there were no deaths in older juvenile mice, given the deaths in young mice and the lack of clinical safety and efficacy data in pediatric patients, use of Trulance should be avoided in patients 6 years to less than 18 years of age.

Diarrhea

- Diarrhea was the most common adverse reaction in the two placebo-controlled clinical trials. Severe diarrhea was reported in 0.6% of patients.
- If severe diarrhea occurs, the health care provider should suspend dosing and rehydrate the patient.

Adverse Reactions

- In the two combined CIC clinical trials, the most common adverse reaction in Trulance-treated patients (incidence ≥2% and greater than in the placebo group) was diarrhea (5% vs 1% placebo).

Please click here for Full Prescribing Information.

About Chronic Idiopathic Constipation (CIC)

CIC affects approximately 14 percent of the global population, disproportionately affecting women and older adults. People with CIC have persistent symptoms of difficult-to-pass and infrequent bowel movements. In addition to physical symptoms including abdominal bloating and discomfort, CIC can adversely affect an individual's quality of life, including increasing stress levels and anxiety.

About Irritable Bowel Syndrome with Constipation (IBS-C)

Irritable bowel syndrome (IBS) is a chronic gastrointestinal disorder characterized by recurrent abdominal pain and associated with 2 or more of the following: related to defecation, associated with a change in the frequency of stool, or associated with a change in the form (appearance) of the stool. IBS can be subtyped by the predominant stool form: constipation (IBS-C), diarrhea (IBS-D), or mixed (IBS-M). Those within the IBS-C subtype experience hard or lumpy stools more than 25 percent of the time they defecate, and loose or watery stools less than 25 percent of the time. It is estimated that

the prevalence of IBS-C in the U.S. adult population is approximately 4 to 5 percent, although this number may vary as patients often fluctuate between the three subtypes of IBS.

About TRULANCE™

TRULANCE™ (plecanatide) is a once-daily tablet approved for adults with CIC and is being evaluated for IBS-C. With the exception of a single amino acid, TRULANCE is structurally identical to uroguanylin, a naturally occurring and endogenous human GI peptide. Uroguanylin is thought to act in a pH-sensitive manner, targeting GC-C receptors primarily in the small intestine coinciding with areas of fluid secretion.

About Synergy Pharmaceuticals Inc.

Synergy is a biopharmaceutical company focused on the development and commercialization of novel GI therapies. The company has pioneered discovery, research and development efforts on analogs of uroguanylin, a naturally occurring and endogenous human GI peptide, for the treatment of GI diseases and disorders. Synergy's proprietary uroguanylin analog platform includes one commercial product TRULANCE (plecanatide) and a second lead product candidate - dolcanatide. 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, 2016 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.
Consolidated Balance Sheets

($ in thousands)	December 31, 2016	December 31, 2015
Assets		
Cash, cash equivalents and available-for-sale securities	$ 82,387	$ 111,750
Inventories	5,640	—
Prepaid expenses and other current assets	889	3,305
Total Current assets	88,916	115,055
Other assets	936	874
Total assets	$ 89,852	$ 115,929
Liabilities and Stockholders' Equity/(Deficit)		
Total Current Liabilities	$ 29,430	$ 19,579
Senior convertible notes, net	22,665	151,241
Derivative financial instruments – warrants	216	322
Total Liabilities	52,311	171,142
Total Stockholders’ Equity/(Deficit)	37,541	(55,213)
Total Liabilities and Stockholders' Equity/(Deficit)	$ 89,852	$ 115,929

Synergy Pharmaceutical Inc.
Consolidated Statement of Operations

($ in thousands except share and per share data)	Three Months Ended December 31, 2016	Three Months Ended December 31, 2015	Year Ended December 31, 2016	Year Ended December 31, 2015
Revenues	$ —	$ —	$ —	$ —
Costs and Expenses:				
Research and development	17,166	19,881	89,562	78,028
Selling, general and administrative	25,232	7,066	55,724	21,794
Loss from Operations	(42,398)	(26,947)	(145,286)	(99,822)
Other Loss/Income:				
Interest and investment expense, net	(3,007)	(3,469)	(13,390)	(17,284)
Debt conversion expense	(14,543)	—	(40,158)	—
State R&D tax credits	126	—	121	—
Change in fair value of financial instruments	(45)	(30)	106	(394)
Total Other Loss	(17,469)	(3,499)	(53,321)	(17,678)
Net Loss	$ (59,867)	$ (30,446)	$ (198,607)	$ (117,500)
Net Loss per Common Share, Basic and Diluted	$ (0.31)	$ (0.27)	$ (1.21)	$ (1.11)
Weighted Average Common Shares Outstanding	190,093,786	113,678,306	164,437,548	105,570,960

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Synergy Pharmaceuticals Inc.
Gem Hopkins, 212-584-7610
VP, Investor Relations and Corporate Communications
ghopkins@synergypharma.com

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