November 19, 2014

Synergy Pharmaceuticals Announces Positive Results of SP-333 Phase 2 Trial in Patients with Opioid-Induced Constipation

NEW YORK-- Synergy Pharmaceuticals Inc. (NASDAQ:SGYP) today announced positive top-line results from a phase 2 trial assessing safety, efficacy and dose-response of three different once-daily oral SP-333 tablets (1.0, 3.0 and 6.0 mg) compared with placebo in 289 patients with opioid-induced constipation (OIC). Preliminary analysis of the data indicates SP-333 met the study's primary endpoint and demonstrated statistically significant improvement in mean change from baseline in the number of spontaneous bowel movements (SBMs) during Week 4 of the treatment period. SP-333 was safe and well tolerated at all doses.

"SP-333 is the first and only GC-C agonist to demonstrate efficacy in treating OIC patients," said Gary S. Jacob, Ph.D., Chairman and CEO of Synergy Pharmaceuticals Inc. "Synergy now has a clinically validated platform technology consisting of two very unique GC-C agonists – plecanatide and SP-333 – both analogs of the natural GC-C agonist, uroguanylin, with proven efficacy and excellent tolerability for treating a variety of gastrointestinal conditions. We look forward to evaluating the full dataset over the coming weeks and plan to present additional results at an appropriate scientific meeting."

Trial Results

SP-333 3.0 and 6.0 mg doses demonstrated statistically significant improvement in mean change from baseline in the number of SBMs during Week 4 of the treatment period (increase from baseline of 3.2, 3.4 and 1.8 for 3.0, 6.0 mg and placebo dose groups, respectively; p= 0.009 and 0.005 for the comparison of 3.0 and 6.0 mg SP-333 with placebo). SP-333 treatment effect was immediate and sustained throughout the four weeks. Additionally, SP-333 3.0 and 6.0 mg dose groups showed statistically significant improvement in a key secondary endpoint analysis of complete spontaneous bowel movement (CSBM) frequency (increase from baseline of 2.54, 2.39 and 1.36 for 3.0, 6.0 mg and placebo dose groups, respectively; p= 0.003 and 0.01 for the comparison of 3.0 and 6.0 mg SP-333 with placebo).

All doses were safe and well tolerated with only four serious adverse events reported (2 for placebo, 1 for the 3.0 mg and 1 for the 6.0 mg dose groups). Diarrhea incidence was low

and was the most commonly reported adverse event (4.0%, 5.4%, 9.7% and 0% for 1.0, 3.0, 6.0 mg and placebo dose groups, respectively). Only two patients withdrew from the study due to diarrhea (both in the 6.0 mg dose group).

Trial Design

The multi-center, randomized, double-blind clinical trial was designed to compare a four week dose-ranging regimen of SP-333, once-daily oral tablet, against placebo in patients with constipation taking opioid analgesics for chronic, non-cancer pain for at least three months. The study evaluated patients with OIC who had less than 3 spontaneous bowel movements (SBMs) per week and who experienced constipation related symptoms.

About SP-333

SP-333 is Synergy's next-generation uroguanylin analog in development for the treatment of OIC and mild-to-moderate ulcerative colitis. SP-333 is designed to be a highly potent and stable version of the naturally occurring gastrointestinal (GI) hormone, uroguanylin, and resistant to proteolysis in gastric intestinal fluids. SP-333 is currently being evaluated in a phase 1b study in patients with ulcerative colitis.

About Synergy Pharmaceuticals

Synergy Pharmaceuticals (NASDAQ: SGYP) is a biopharmaceutical company focused on the development of novel therapies based on the naturally occurring human hormone, uroguanylin, to treat GI diseases and disorders. Synergy has created two unique analogs of uroguanylin – plecanatide and SP-333 – designed to mimic the natural hormone's activity on the intestinal guanylate cyclase-C (GC-C) receptor and target a variety of GI conditions. Plecanatide is currently in two pivotal phase 3 trials for chronic idiopathic constipation (CIC) and recently reached the halfway mark for patient enrollment in the first CIC registration trial. Synergy plans to release topline data from the first CIC registration trial in the second quarter of 2015. In April 2014, the Company announced positive top-line data results with plecanatide in a phase 2b study for irritable bowel syndrome with constipation (IBS-C). Synergy plans to initiate its pivotal phase 3 IBS-C program with plecanatide in the fourth quarter of this year. 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 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 Form 10-K for the year ended December 31, 2013 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.

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