Synergy Pharmaceuticals Presents Positive Phase 2b Study Results for Plecanatide in Patients with Irritable Bowel Syndrome with Constipation

Data Presented at the American College of Gastroenterology Annual Scientific Meeting

NEW YORK-- Synergy Pharmaceuticals Inc. (NASDAQ:SGYP) today announced the presentation of results from a phase 2b dose-ranging study assessing plecanatide’s safety and efficacy in 424 adult patients (mITT population= 423) with irritable bowel syndrome with constipation (IBS-C). Data presented at ACG demonstrate that plecanatide, once-daily oral tablet, significantly improved complete spontaneous bowel movement (CSBM) frequency, bowel habits, treatment satisfaction and significantly reduced abdominal pain in patients with IBS-C throughout the 12 week treatment period. Notably, patients taking 3.0 and 9.0 mg plecanatide showed statistically significant improvement in the Overall Responder rate, a secondary analysis in this study and the endpoint required for FDA approval in IBS-C (41.9% and 40%, respectively, compared to 24.7% for placebo).

The data were presented by lead author, Philip B. Miner Jr., M.D., President and Medical Director of the Oklahoma Foundation for Digestive Research.

“Plecanatide demonstrated a clear improvement in efficacy at the higher dose range (3.0 and 9.0 mg) but measures of incidence and severity of diarrhea and withdrawals due to diarrhea did not show evidence of a consistent dose-response,” said Dr. Miner. “These data are consistent with the clinical profile observed in patients with chronic idiopathic constipation (CIC) and are likely a benefit of plecanatide’s unique pharmacology as an analog of the natural GC-C agonist, uroguanylin.”

“These data further support our decision to assess two doses (3.0 and 6.0 mg) in our pivotal phase 3 IBS-C program and the ongoing pivotal phase 3 CIC trials,” said Gary S. Jacob, Ph.D., Chairman and CEO of Synergy Pharmaceuticals Inc. “We are especially encouraged by the robust efficacy demonstrated at both 3.0 and 9.0 mg in the Overall Responder rate, which is the primary endpoint required for FDA approval in IBS-C. We believe plecanatide has the ideal profile for treating patients in a chronic setting, offering important dosing flexibility and a predictable treatment response with excellent efficacy and superior tolerability.”

Synergy plans to initiate the pivotal phase 3 IBS-C clinical development program in the fourth quarter of this year.
To access the data as presented by Dr. Miner at ACG, please visit the Presentations section of Synergy’s website at www.synergypharma.com.

**IBS-C Phase 2b Study Design**

This was a randomized, 12-week, double-blind, placebo-controlled, dose-ranging study to assess the safety and efficacy of plecanatide in 423 adult patients with IBS-C. The study evaluated the effects of 0.3, 1.0, 3.0 or 9.0 mg plecanatide or placebo administered orally, once-daily to adults meeting Rome III criteria for IBS-C. In addition, patients were required to meet the criteria for the IBS-C subtype, which is further characterized by stool pattern, such that ≥ 25% of defecations are hard or lumpy stools and ≤ 25% of defecations are loose or watery stools. During pre-treatment at baseline, patients were required to have at least 3 days in each week with pain scores ≥ 3 on a 0 to 10 scale.

The primary efficacy endpoint was the change from baseline in the mean number of complete spontaneous bowel movements (CSBMs) per week over the 12-week treatment period. Secondary endpoints included: (1) Abdominal Pain Intensity, (2) Stool Consistency, (3) Overall Responder (%) and (4) Abdominal Pain Responder (%). Stool Consistency was measured using the Bristol Stool Form Scale (BSFS) and Abdominal Pain Intensity was measured on an 11-point severity scale (0 to 10). An Overall Responder fulfilled both ≥ 30% reduction in worst abdominal pain and an increase of ≥ 1 CSBMs from baseline in the same week for at least 50% of the weeks (i.e. 6/12 weeks).

**About Plecanatide**

Plecanatide is Synergy’s lead uroguanylin analog in late-stage clinical development to treat patients with IBS-C and CIC. Uroguanylin is a natural gastrointestinal (GI) hormone produced by humans in the small intestine and plays a key role in regulating the normal functioning of the digestive tract through its activity on the guanylate cyclase-C (GC-C) receptor. The GC-C receptor is known to be a primary source for stimulating a variety of beneficial physiological responses. Orally administered plecanatide mimics uroguanylin's natural functions by binding to and activating the GC-C receptor to stimulate fluid and ion transit required for normal bowel function. Synergy has successfully completed a large, multi-center clinical trial of plecanatide in 951 patients with CIC and is currently enrolling patients in two pivotal phase 3 CIC trials. Synergy recently announced that it had successfully completed an end-of-phase 2 meeting with the FDA on its phase 2b IBS-C study with plecanatide and plans to initiate the phase 3 IBS-C registration program in 4Q 2014.

**About Synergy Pharmaceuticals**

Synergy Pharmaceuticals (NASDAQ:SGYP) is a biopharmaceutical company focused on the development of novel therapies based on the naturally occurring human GI hormone, uroguanylin, to treat GI diseases and disorders. Synergy’s next-generation uroguanylin analog, SP-333, is currently in phase 2 development for opioid-induced constipation and is also 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 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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