Synergy Pharmaceuticals Announces Positive Results in First Phase 3 Trial of Plecanatide in Patients with Irritable Bowel Syndrome with Constipation (IBS-C)

NEW YORK--(BUSINESS WIRE)-- Synergy Pharmaceuticals Inc. (NASDAQ:SGYP) today announced positive top-line results from the first of two pivotal phase 3 clinical trials evaluating the efficacy and safety of plecanatide, an investigational once-daily orally-administered compound, in 1,135 adult patients with irritable bowel syndrome with constipation (IBS-C).

Preliminary analysis of the data indicates that both plecanatide 3 mg and 6 mg doses met the study’s primary endpoint and showed statistical significance in the percentage of patients who were Overall Responders compared to placebo during the 12-week treatment period (21.5% in 3 mg and 24.0% in 6 mg dose groups compared to 14.2% in placebo; p=0.009 for 3 mg and p<0.001 for 6 mg). 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.

The most common adverse event was diarrhea which occurred in 3.2% of patients in 3 mg and 3.7% of patients in 6 mg dose groups compared to 1.3% of placebo-treated patients.

“We are very pleased with these results,” said Gary S. Jacob, Ph.D., Chairman and CEO of Synergy Pharmaceuticals Inc. “These data reinforce our strong belief that plecanatide may represent an important new treatment option for the millions of patients currently suffering from IBS-C. We look forward to the results of our second phase 3 IBS-C trial with plecanatide later this month.”

Four patients in the trial (0.4%) experienced serious adverse events but there was no imbalance across treatment groups in either incidences or individual serious adverse events. Overall, the rates of withdrawal from treatment because of an adverse event were low (1.9% in 3 mg and 1.8% in 6 mg dose groups compared to 0 in placebo) and discontinuations due to diarrhea were infrequent (0.8% in 3 mg and 1.6% in 6 mg dose groups compared to 0 in placebo).

Additionally, plecanatide is under review by the Food and Drug Administration (FDA) for the treatment of chronic idiopathic constipation (CIC) and the Prescription Drug User Fee
Act (PDUFA) target action date is January 29, 2017. Pending approval in the CIC indication, the company plans to file a New Drug Application Supplement with Clinical Data (sNDA) for plecanatide in IBS-C in Q1 2017.

The Plecanatide Phase 3 IBS-C Program

Design

The plecanatide phase 3 IBS-C program includes two randomized, 12-week, double-blind, placebo-controlled trials evaluating the efficacy and safety of plecanatide treatment (3 mg and 6 mg doses), taken as a tablet once-a-day in patients with IBS-C. Both trials included a two-week pre-treatment baseline period, a 12-week treatment period, and a two-week post-treatment follow-up period. The phase 3 IBS-C program was designed to support regulatory submission in the U.S.

The first phase 3 IBS-C trial was conducted in North America and assessed 1,135 patients (28.2% males and 71.8% females) that were randomly assigned to take 3 mg or 6 mg plecanatide or placebo once-a-day during the 12-week treatment period (377 patients in the 3 mg dose group, 379 patients in the 6 mg dose group and 379 patients in the placebo group).

Primary Endpoint

The primary endpoint for 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 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. The Overall Responder endpoint is the current regulatory endpoint required for U.S. approval in IBS-C.

Patient Population

Patients were selected using Rome 3 criteria for IBS-C. Patients with IBS-C are defined by Rome III Criteria as having a history of constipation and abdominal pain for at least 6 months, including hard or lumpy stools for 25% or more of defecations, loose or watery stools for 25% or less of defecations, and abdominal pain or discomfort for 3 days or more per month for the last 3 months.

About Irritable Bowel Syndrome with Constipation (IBS-C)

Irritable bowel syndrome (IBS) is a chronic, complex condition subtyped by the predominant stool form: constipation (IBS-C), diarrhea (IBS-D), or mixed (IBS-M). It is estimated that the prevalence of IBS-C in the U.S. adult population is approximately 4 to 5 percent, though this number may vary as patients often fluctuate between the three subtypes of IBS. IBS is characterized by abdominal pain or discomfort associated with two or more of the following: improvement with defecation, onset associated with a change in frequency of stool, or onset associated with a change in form (appearance) of stool.

About Plecanatide
Plecanatide is a peptide made up of 16 amino acids and, with the exception of a single amino acid substitution, it is identical to uroguanylin. Plecanatide is the first investigational drug designed to replicate the function of uroguanylin, a naturally occurring and endogenous human GI peptide which acts in a pH-sensitive manner targeting GC-C receptors primarily in the proximal small intestine. Plecanatide stimulates fluid secretion and promotes stool consistency necessary to support normal bowel function.

About Synergy Pharmaceuticals

Synergy is a biopharmaceutical company focused on the development and commercialization of novel GI therapies. The company has pioneered discovery, research and development efforts around uroguanylin analogs for the treatment of functional GI disorders and inflammatory bowel disease. Synergy’s proprietary uroguanylin analog technology platform includes two lead product candidates – plecanatide and dolcanatide. For more information, please visit www.synergypharma.com.

Forward-Looking Statement

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, 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.

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