Synergy Pharmaceuticals Presents Plecanatide Results From a Large Multicenter Clinical Study at Late-Breaking Abstract Session During Digestive Disease Week 2013

NEW YORK, May 21, 2013 (GLOBE NEWSWIRE) -- Synergy Pharmaceuticals Inc. (Nasdaq:SGYP), a developer of new drugs to treat patients with gastrointestinal disorders and diseases, today presented positive safety and efficacy results from its large multicenter trial of plecanatide in patients with chronic idiopathic constipation (CIC) at Digestive Disease Week (DDW) in Orlando, FL.

The data were presented at the Late-Breaking Abstract Session of the American Gastroenterological Association (AGA) by lead author Dr. Philip B. Miner, President and Medical Director of the Oklahoma Foundation for Digestive Research.

Plecanatide, Synergy's investigational drug for the treatment of CIC and irritable bowel syndrome with constipation (IBS-C), is a guanylate cyclase-C (GC-C) agonist. This novel drug mimics the function of the natural human peptide hormone, uroguanylin.

The clinical trial was designed to evaluate whether plecanatide could increase the number of complete spontaneous bowel movements (CSBMs), as well as benefit other bowel measures associated with the constipated state such as stool consistency and straining, along with general quality of life, in people with CIC. In the study, 951 patients with CIC were randomized to four study arms to determine the efficacy and safety of three oral doses of plecanatide (0.3, 1.0, or 3.0 mg, daily), compared to placebo, over the course of a 12-week dosing regimen.

"All three doses of plecanatide demonstrated statistically significant improvement in the number of complete, spontaneous bowel movements experienced by study participants who responded to treatment," said Dr. Miner. "In addition to increased frequency of CSBMs, participants reported improvements in other symptoms of chronic constipation, including decreased stool hardness and straining. All doses of plecanatide appeared to be safe and well tolerated, and safety data were consistent with Synergy's previous Phase I and IIa trials of plecanatide."
"We are very pleased to share these compelling new data at DDW supporting the efficacy and safety of plecanatide as a potential new treatment for patients suffering with CIC," said Dr. Gary S. Jacob, President and CEO of Synergy. "We are moving full-speed ahead with development of plecanatide to treat CIC, and plan to initiate pivotal trials in the second half of 2013. In addition, we presently have a Phase 2b trial of plecanatide in IBS-C patients underway and expect to release top-line data in 1Q2014."

Key clinical findings presented at DDW:

**Efficacy**

Increasing efficacy was observed at increasing dose levels of plecanatide. The greatest improvement in CSBM was observed at the 3 mg plecanatide dose. Other efficacy results include:

- Over the course of the 12-week study, 19% of participants treated daily with 3 mg plecanatide were durable* responders (vs. 10.7% for placebo; p<0.01).
- More than half of patients dosed at 3 mg plecanatide treatment experienced an increase of at least one CSBM per week relative to baseline (52.3% vs. 36.8% for placebo; p<0.001).
- Participants achieved their first spontaneous bowel movement after ingestion of 3 mg plecanatide in less than half the time of those taking placebo (median time of 12.5 hours plecanatide vs. 27.3 for placebo; p<0.001).
- Statistically significant improvements in other key secondary endpoints were also observed, including stool consistency and straining (3 mg plecanatide vs. placebo; p<0.001).
- Responders to treatment reported statistically significant improvements in constipation-associated symptoms and quality of life relative to baseline (3 mg plecanatide vs. placebo; p<0.001).

**Safety**

In this large multicenter trial, all doses of plecanatide studied appeared to be safe and well tolerated. There were no serious adverse events attributed to study treatment. The most common adverse event reported was diarrhea (9.7% at 3 mg plecanatide vs. 1.3% placebo). Notably, study withdrawal due to diarrhea was infrequent (3% at 3 mg plecanatide vs. 0.4% for placebo). All but one case of diarrhea was mild or moderate in severity.

**Late-Breaking Abstract Session Citation**

Abstract # 925g: Plecanatide, a Novel Guanylate-Cyclase C (GC-C) Receptor Agonist, is Efficacious and Safe in Patients with Chronic Idiopathic Constipation (CIC): Results from a 951 Patient, 12 Week, Multi-Center Trial. Miner, Philip B.¹; Surowitz, Ron²; Fogel, Ron³; Koltun, William⁴; Drossman, Douglas A.⁵; Camilleri, Michael⁶; Mangel, Allen⁷; Barrow,
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(ClinicalTrials.gov Identifier: NCT01429987)

*Durable responder is defined as: a responder in at least 9 of 12 weeks of study, and a responder in at least 3 of the last 4 weeks of treatment.

**About Digestive Disease Week**

Digestive Disease Week\(^®\) (DDW\(^®\)) is the largest international gathering of physicians, researchers and academics in the fields of gastroenterology, hepatology, endoscopy and gastrointestinal surgery. Jointly sponsored by the American Association for the Study of Liver Diseases (AASLD), the American Gastroenterological Association (AGA) Institute, the American Society for Gastrointestinal Endoscopy (ASGE) and the Society for Surgery of the Alimentary Tract (SSAT), DDW takes place May 18 – 21, 2013, at the Orange County Convention Center, FL. The meeting showcases more than 5,000 abstracts and hundreds of lectures on the latest advances in GI research, medicine and technology. More information can be found at [www.ddw.org](http://www.ddw.org).

**About Synergy Pharmaceuticals Inc.**

Synergy is a biopharmaceutical company focused on the development of new drugs to treat patients with gastrointestinal disorders and diseases. Synergy's lead proprietary drug candidate, plecanatide, is a synthetic analog of the natural human peptide hormone, uroguanylin, and functions by activating the guanylate cyclase-C (GC-C) receptor on epithelial cells of the GI tract. Synergy completed positive Phase I and Phase II clinical trials in patients with chronic idiopathic constipation (CIC). Detailed positive findings from its large multicenter trial of plecanatide in patients with CIC are being presented at Digestive Disease Week (DDW) in Orlando, FL and will be published this year. Synergy is also developing plecanatide for the treatment of irritable bowel syndrome with constipation (IBS-C), having initiated the first trial in IBS-C patients in late 2012. Synergy's second GC-C agonist, SP-333, is in clinical development for the treatment of ulcerative colitis (UC). The first Phase I trial in healthy volunteers was recently completed. More information is available at [http://www.synergypharma.com](http://www.synergypharma.com)

**About Chronic Constipation**

Chronic constipation is the most common digestive complaint in the United States and the world. About 15%, or 45 million people, suffer from chronic constipation in the U.S., with a
similar prevalence in other developed countries. Although chronic constipation affects both men and women of every age, it disproportionately impacts women as well as the elderly, a large and growing population.

Current treatments provide temporary relief, but because they fail to address the underlying causes of chronic constipation, they do not normalize patients' bowel function. Such treatments are also associated with unpleasant side effects, the most common of which is diarrhea, causing patients to see-saw between extremes. As a result, most doctors and their patients are dissatisfied with current treatments for chronic constipation.

Chronic constipation is also a significant driver of healthcare costs. Healthcare systems are spending millions of dollars annually to diagnose and treat this disorder, including $820 million annually on over-the-counter laxatives in the U.S. alone.

About Plecanatide

Plecanatide is a promising investigational drug being developed by Synergy Pharmaceuticals for the treatment of chronic idiopathic constipation (CIC) and irritable bowel syndrome with constipation (IBS-C). Plecanatide is a member of a new class of essentially non-systemic oral drugs, known as guanylate cyclase-C (GC-C) agonists. GC-C agonists act by targeting GC-C receptors in the gut. By acting locally in the proximal intestine, plecanatide promotes intestinal fluid secretion needed for normal bowel function and reduces the abdominal symptoms that are often associated with GI disorders. Plecanatide is a synthetic analog of uroguanylin, a natural human peptide hormone that regulates ion and fluid transport in the GI tract. Uroguanylin binds to and activates GC-C receptors on mucosal epithelial cells lining the GI tract. Activation of these receptors triggers an increase in a key intracellular mediator called cyclic guanosine monophosphate (cGMP) which induces fluid secretion into the intestinal lumen necessary for normal bowel movements. Increased cGMP has also been demonstrated to produce other physiologic benefits related to abdominal discomfort, pain, and bloating. Preclinical studies suggest that orally-administered plecanatide mimics the function of uroguanylin, acting locally in the proximal intestine to stimulate secretion of fluid, thereby facilitating bowel movements and ameliorating GI inflammation.

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, 2012 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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