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Synergy Pharmaceuticals to Present New Analysis of Therapeutic Risk and Benefit of TRULANCE® (plecanatide) and Linaclotide in Chronic Idiopathic Constipation (CIC) Patients at Digestive Disease Week (DDW)

NEW YORK--(BUSINESS WIRE)-- Synergy Pharmaceuticals Inc. (NASDAQ: SGYP), a biopharmaceutical company focused on the development and commercialization of novel gastrointestinal (GI) therapies, today announced that the company will present a new risk/benefit analysis from pooled Phase 3 study data evaluating TRULANCE® (plecanatide) and linaclotide for the treatment of adults with chronic idiopathic constipation (CIC). These findings will be presented as a poster today at DDW 2018 in Washington D.C.

To provide further clinical perspective on the two medications, a retrospective analysis of pooled data from five Phase 3 clinical trials of similar patient populations and identical treatment durations calculated the number needed to harm (NNH) and number needed to treat (NNT) values. The analysis also assessed the relative therapeutic risk/benefit profile, or the likelihood of one treatment to be helpful or harmful (LHH), calculated as the NNH/NNT ratio.

Lower NNT values indicate that fewer patients need to be treated before seeing a clinical benefit, and higher NNH values indicate a larger number of patients need to be treated before seeing a detrimental effect. In the analysis, TRULANCE 3 mg and linaclotide 72 and 45 mcg doses demonstrated similar NNT values. The NNH value for TRULANCE was approximately three-fold higher than the NNT value, indicating that TRULANCE patients are three times more likely to experience a beneficial effect before experiencing a harmful effect. The NNH values for linaclotide 72 mcg and 145 mcg were each lower than the respective NNT values, indicating that, for both doses of linaclotide, patients are more likely to experience a harmful effect before experiencing a beneficial effect. LHH values greater than 1 indicate relative therapeutic benefit, while LHH values less than 1 indicate relative risk. The LHH values for TRULANCE, linaclotide 72 mcg and linaclotide 145 mcg were 2.7, 0.6 and 0.7, respectively. Findings from this LHH assessment indicated a favorable risk/benefit profile for TRULANCE.

“The TRULANCE LHH value, based on the plecanatide CIC trials, indicates a favorable risk/benefit profile for this product,” said Darren M. Brenner, M.D., Associate Professor

of Medicine (Gastroenterology and Hepatology) and Surgery at Northwestern Feinberg School of Medicine. “We don’t have data from head-to-head clinical trials, so analyses like these may be useful in clinical assessments when considering prescription options for the treatment of CIC”.

TRULANCE is the only prescription medication for adults with CIC and IBS-C that can be taken once-daily, with or without food, at any time of the day.

Indications and Usage

TRULANCE (plecanatide) 3 mg tablets is indicated in adults for the treatment of Chronic Idiopathic Constipation (CIC) and Irritable Bowel Syndrome with Constipation (IBS-C).

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 four placebo-controlled clinical trials for CIC and IBS-C. Severe diarrhea was reported in 0.6% of TRULANCE-treated CIC patients, and in 1% of TRULANCE-treated IBS-C 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).
- In the two combined IBS-C clinical trials, the most common adverse reaction in TRULANCE-treated patients (incidence ≥2% and greater than in the placebo group) was diarrhea (4.3% vs 1% placebo).

Please also see the full Prescribing Information, including Box Warning, for additional risk information.

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 two 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.

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 TRULANCE®

TRULANCE® (plecanatide) is a once-daily tablet approved for adults with CIC or IBS-C. With the exception of a single amino acid substitution for greater binding affinity, TRULANCE is structurally identical to uroguanylin, a naturally occurring and endogenous human GI peptide. Uroguanylin activates GC-C receptors in a pH-sensitive manner primarily in the small intestine, stimulating fluid secretion and maintaining stool consistency necessary for regular bowel function.

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 GI platform includes one commercial product TRULANCE® (plecanatide) and a second product candidate, 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 Annual Report on Form 10-K for the year ended December 31, 2017 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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