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Pivotal Phase 3 Data Results for TRULANCE™ (plecanatide) in the Treatment of Chronic Idiopathic Constipation (CIC) Published in American Journal of Gastroenterology

NEW YORK--(BUSINESS WIRE)-- Synergy Pharmaceuticals Inc. (NASDAQ:SGYP) today announced that the *American Journal of Gastroenterology* has published detailed results from a pivotal Phase 3 trial that demonstrated the efficacy and safety of TRULANCE™ (plecanatide) for the treatment of adults with chronic idiopathic constipation (CIC).

On Jan. 19, TRULANCE was approved by the U.S. Food and Drug Administration (FDA) for the treatment of adult patients with CIC. TRULANCE is the first drug designed to replicate the function of uroguanylin, a naturally occurring and endogenous human gastrointestinal (GI) peptide that is thought to stimulate fluid secretion within the changing pH environment of the intestine.

"We are very pleased that our pivotal Phase 3 results are appearing in the *American Journal of Gastroenterology*, as these robust data demonstrate the efficacy and safety profile of TRULANCE, and add momentum to the FDA's recent approval of TRULANCE," said Gary S. Jacob, Ph.D., Chairman and CEO of Synergy Pharmaceuticals Inc. "The publication of these data are a testament to the dedication of our researchers and the hard work of our entire Synergy team, all of whom are excited to be bringing TRULANCE to healthcare providers and their patients with the upcoming launch of this drug."

TRULANCE will be available in the U.S. this quarter.

"There are millions of CIC patients in the U.S., many of whom suffer with symptoms that remain untreated or fail to respond to current treatments," said Satish S.C. Rao, M.D., Ph.D., Professor of Medicine and Director, Neurogastroenterology/Motility, Digestive Health Center at Augusta University. "TRULANCE has demonstrated efficacy with a low rate of adverse events, such as diarrhea, providing healthcare providers and their patients with an additional, much needed, new treatment option."

In this study, diarrhea was the most common adverse event (TRULANCE 3 mg, 5.9%; placebo, 1.3%).

The approved dosing regimen for TRULANCE is 3 mg taken orally, once daily, with or without food at any time of the day. TRULANCE can be swallowed whole or crushed in

applesauce for those who are unable to swallow medication.

Synergy has also completed two Phase 3 clinical trials for TRULANCE in irritable bowel syndrome with constipation (IBS-C), with positive top-line results of these trials announced in December 2016. Synergy plans to file a New Drug Application Supplement with Clinical Data (sNDA) this quarter with an expected 10-month review period from submission.

Indications and Usage

TRULANCE is a guanylate cyclase-C (GC-C) agonist indicated in adults for the treatment of chronic idiopathic constipation (CIC).

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 two placebo-controlled

clinical trials. Severe diarrhea was reported in 0.6% of 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).

Please click [here](#) for Full Prescribing Information.

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 and is being evaluated for IBS-C. With the exception of a single amino acid, TRULANCE is structurally related to uroguanylin, a naturally occurring and endogenous human GI peptide. Uroguanylin is thought to act in a pH-sensitive manner, targeting GC-C receptors primarily in the small intestine coinciding with areas of fluid secretion.

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 on analogs of uroguanylin, a naturally occurring human GI peptide, for the treatment of GI diseases and disorders. Synergy's proprietary uroguanylin analog platform includes one commercial product TRULANCE (plecanatide) and a second lead product candidate – dolcanatide. For more information, please visit www.synergypharma.com.

Forward-Looking Statement

This press release and any statements made for and during any presentation or meeting contain forward-looking statements related to Synergy Pharmaceuticals Inc. under the safe harbor provisions of Section 21E of the Private Securities Litigation Reform Act of 1995 and are subject to risks and uncertainties that could cause actual results to differ materially from those projected. These statements may be identified by the use of forward-looking words such as "anticipate," "planned," "believe," "forecast," "estimated," "expected," and "intend," among others. 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, the development, launch, introduction and commercial potential of TRULANCE; growth and opportunity, including peak sales and the potential demand for TRULANCE, as well as its potential impact on applicable markets; market size; 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; dependence upon third parties; our financial performance and results, including the risk that we are unable to manage our operating expenses or cash use for operations, or are unable to commercialize our products, within the guided ranges or otherwise as expected; 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 most recent periodic reports filed with the Securities and Exchange Commission, including Synergy's Form 10-K for the year ended December 31, 2015. 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 except as required by law.

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