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# **Synergy Pharmaceuticals' TRULANCE™ (Plecanatide) Receives U.S. FDA Approval for the Treatment of Adults with Chronic Idiopathic Constipation**

NEW YORK--(BUSINESS WIRE)-- Synergy Pharmaceuticals Inc. (NASDAQ:SGYP) announced today that the U.S. Food and Drug Administration (FDA) has approved TRULANCE™ (plecanatide) for the treatment of adults with chronic idiopathic constipation (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 which results in a stool consistency associated with more regular bowel function.

This Smart News Release features multimedia. View the full release here:

<http://www.businesswire.com/news/home/20170119006330/en/>

“We are thrilled with the approval of TRULANCE because it provides an additional, much-needed, new treatment option to help adults with chronic idiopathic constipation and their healthcare providers manage this condition,” said Gary S. Jacob, Ph.D., Chairman and CEO of Synergy Pharmaceuticals Inc. “I am confident that we truly have the right team with the right strategic vision and the right launch plan to successfully bring TRULANCE into this large but underserved market.”

CIC is a complex, functional GI disorder defined by symptoms including fewer than three bowel movements a week and hard-to-pass or incomplete bowel movements, for which there is no identifiable cause.<sup>1,2</sup> CIC affects approximately 33 million Americans and an estimated 14 percent of the global population.<sup>2</sup>

The efficacy and safety of TRULANCE was evaluated in the largest Phase 3 CIC clinical trials to date, which included more than 2,600 patients in two randomized, 12-week, double-blind, placebo-controlled studies of TRULANCE.

Over 12 weeks, patients treated with TRULANCE achieved a significantly greater efficacy responder rate — the primary endpoint defined by the FDA for regulatory approval in CIC — in both studies compared to placebo (Study 1: 21% vs. 10%; Study 2: 21% vs. 13%,  $p < 0.005$  for both studies). Efficacy responders were defined as patients who had at least three complete spontaneous bowel movements (CSBMs) in a given week and an increase of at least one CSBM over baseline in the same week for at least nine weeks out of the 12-week period, including at least three of the last four weeks.

Over 12 weeks, patients who received TRULANCE in both studies also had improvements as compared to placebo in stool frequency (as measured by the number of spontaneous bowel movements per week), stool consistency (as measured by the Bristol Stool Form Scale) and straining with bowel movements.

"The impact of chronic constipation on the lives of affected patients is often underestimated," said William D. Chey, M.D., Professor of Medicine, Director of the GI Physiology Laboratory, and Co-Director of the Michigan Bowel Control Program at the University of Michigan. "TRULANCE presents an exciting new treatment option for patients with chronic constipation. Its efficacy and safety profile, plus its negligible systemic absorption, are attractive attributes that make it a welcome addition to our treatment options."

In an integrated analysis of both studies, diarrhea was the most common adverse reaction, reported in 5% of patients treated with TRULANCE compared to 1% of patients treated with placebo. Overall discontinuation rates were low among patients treated with TRULANCE and placebo (4% vs. 2%, respectively) and the most common adverse reaction leading to discontinuation was diarrhea (2% for TRULANCE compared to 0.5% in placebo).

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.

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

Synergy has also completed two Phase 3 clinical trials for TRULANCE in irritable bowel syndrome with constipation (IBS-C) and plans to file a New Drug Application Supplement with Clinical Data (sNDA) later 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  $\geq 2\%$  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.<sup>2</sup> People with CIC have persistent symptoms of difficult and infrequent bowel movements.<sup>1</sup> 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.<sup>1</sup>

## **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 uroguanylin analogs for the treatment of functional GI disorders and inflammatory bowel disease. Synergy's proprietary uroguanylin analog platform includes two lead product candidates – plecanatide and dolcanatide. For more information, please visit [www.synergypharma.com](http://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.

<sup>1</sup> Thomas R, Luthin D. Current and emerging treatments for irritable bowel syndrome with constipation and chronic idiopathic constipation: focus on prosecretory agents.

*Pharmacotherapy Pub.* 2015; 613-630.

<sup>2</sup> Soares NC, Ford AC. Prevalence of, and risk factors for chronic idiopathic constipation in the community: systematic review and meta-analysis. *Am J Gastroenterol.* 2011;106(9):1582-1591.

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