January 29, 2015

Synergy Pharmaceuticals Completes Patient Enrollment for the Second Pivotal Phase 3 Trial of Plecanatide in Patients with Chronic Idiopathic Constipation

Top-line data from the second phase 3 CIC trial expected in 3Q 2015

NEW YORK-- Synergy Pharmaceuticals Inc. (NASDAQ:SGYP) today announced that it has successfully completed patient enrollment in the second of two pivotal phase 3 trials evaluating the safety and efficacy of two plecanatide doses (3.0 and 6.0 mg) in patients with chronic idiopathic constipation (CIC). Synergy announced that it had completed patient enrollment in the first phase 3 CIC trial on January 8, 2015.

Each of the two randomized, 12-week, double-blind, placebo-controlled phase 3 trials are evaluating plecanatide, once-daily oral tablets, in approximately 1350 adult patients with CIC. The primary endpoint is the proportion of patients who are *Overall Responders* during the 12-week treatment period. An *Overall Responder* is a patient who fulfills both ≥ 3 complete spontaneous bowel movements (CSBMs) per week plus an increase of ≥ 1 CSBM from baseline in the same week, for 9 out of the 12 weeks, including ≥ 3 of the last 4 weeks. Plecanatide has met this endpoint and demonstrated statistical significance at the 3.0 mg dose in a phase 2b CIC trial evaluating 951 patients with CIC.

Synergy expects top-line data results from the first phase 3 CIC trial in 2Q 2015 and top-line data results from the second phase 3 CIC trial in 3Q 2015. The company plans to file its first NDA with plecanatide in the CIC indication in the fourth quarter of this year. Plecanatide 3.0 and 6.0 mg doses are also being evaluated in the ongoing phase 3 registration program for irritable bowel syndrome with constipation (IBS-C).

About Plecanatide

Plecanatide is Synergy's lead uroguanylin analog in late-stage clinical development to treat patients with CIC and IBS-C. Uroguanylin is a naturally occurring gastrointestinal (GI) hormone produced by humans in the small intestine and plays a key role in regulating the normal functioning of the digestive tract through its activity on the guanylate cyclase-C (GC-C) receptor. The GC-C receptor is known to be a primary source for stimulating a variety of beneficial physiological responses. Orally administered plecanatide mimics uroguanylin's functions by binding to and activating the GC-C receptor to stimulate fluid

and ion transit required for normal bowel function. Synergy has successfully completed a phase 2b trial of plecanatide in 951 patients with CIC and this announcement concerns the second of two ongoing phase 3 CIC trials. Synergy initiated the plecanatide pivotal phase 3 program for irritable bowel syndrome with constipation in 4Q 2014.

About Synergy Pharmaceuticals Inc.

Synergy Pharmaceuticals (NASDAQ:SGYP) is a biopharmaceutical company focused on the development of novel therapies to treat GI diseases and disorders. The company's proprietary platform technology is based on the naturally occurring human GI hormone – uroguanylin - a key regulator of normal GI physiology. Synergy has created two unique analogs of uroguanylin - plecanatide and SP-333 – both designed to mimic the hormone's natural activity and target a variety of GI conditions. SP-333 has successfully completed a phase 2 study in patients with opioid-induced constipation and is presently being evaluated for the treatment of ulcerative colitis. For more information, please visit www.synergypharma.com.

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, 2013 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.

Synergy Pharmaceuticals:

Gem Gokmen, 212-584-7610
Senior Director, Corporate Communications
ggokmen@synergypharma.com

Source: Synergy Pharmaceuticals Inc.