

## **Theravance Biopharma Presents Positive Phase 2 Study Data on Velusetrag (TD-5108) for Treatment of Gastroparesis in "Poster of Distinction" at Digestive Disease Week (DDW) 2015**

### **Velusetrag Improved Gastric Emptying Time Across All Doses vs. Placebo; Velusetrag Produced a Clinically Meaningful Improvement in Gastric Emptying Time in Both Diabetic and Idiopathic Gastroparetic Patients**

GEORGE TOWN, GRAND CAYMAN -- (Marketwired) -- 05/18/15 -- Theravance Biopharma, Inc. (NASDAQ: TBPH) ("Theravance Biopharma" or the "Company") today announced the presentation of positive data from a Phase 2 study of velusetrag (TD-5108), an investigational drug for the treatment of patients with gastroparesis and other gastrointestinal motility disorders, in a "Poster of Distinction" at Digestive Disease Week (DDW) 2015 in Washington, D.C. Presented data showed that all three doses of velusetrag (5, 15 and 30 mg) reduced gastric emptying time (GE  $t_{1/2}$ ) compared to placebo in patients with either diabetic or idiopathic gastroparesis.

Findings from the study (study 0093) in 34 subjects with diabetic (n=18) or idiopathic (n=16) gastroparesis demonstrated reductions in GE  $t_{1/2}$ , in minutes and percentage of baseline GE  $t_{1/2}$ , of 35 (11%), 34 (8%) and 52 (21%) minutes at doses of 5, 15, and 30 mg, respectively, as compared to 13 (2%) minutes for placebo. The proportion of subjects demonstrating at least a 20% change from baseline in GE  $t_{1/2}$  was statistically significant for those subjects receiving velusetrag 30 mg (52%) compared to placebo (5%) (p=0.002). The proportion of subjects demonstrating at least a 20% change from baseline in GE  $t_{1/2}$  in the 5 mg and 15 mg velusetrag treatment groups was 26% and 20%, respectively. Importantly, similar reductions in GE  $t_{1/2}$  were observed in both diabetic and idiopathic gastroparetic subjects treated with velusetrag. All doses of velusetrag were generally well tolerated with diarrhea (n=16) and headache (n=6) as the most common adverse events. No on-treatment serious adverse events were observed.

Gastroparesis is a significant medical condition characterized by delayed gastric emptying of food and associated with nausea, vomiting, early satiety, postprandial fullness and upper abdominal pain. In the U.S., it is estimated to affect approximately six million individuals and includes two major sub classifications: diabetic gastroparesis (29% of the overall gastroparesis population) and idiopathic (36%). There is no approved treatment option for patients with idiopathic gastroparesis, and only one FDA-approved product (metoclopramide) for diabetic gastroparesis.

This study is the first study to evaluate gastric emptying, a diagnostic criterion for gastroparesis, in a patient population including both diabetic and idiopathic gastroparesis patients. Comparable studies of other investigational medicines have focused only on the diabetic population.

"Theravance Biopharma is the first company to evaluate a drug candidate for gastroparesis in a broad population that includes both diabetic and idiopathic gastroparetic patients. We are encouraged by the positive results of this study and delighted that our work was recognized by DDW with a 'Poster of Distinction,'" said Brett Haumann, MD, Senior Vice President, Clinical Development at Theravance Biopharma. "The ability of velusetrag to decrease gastric emptying time across all three doses in both diabetic and idiopathic gastroparesis patients, while demonstrating a favorable safety profile, underscores the shared confidence that we and our partner, Alfa Wassermann, have in the compound's potential therapeutic importance and scientific rationale for conducting a Phase 2b study. There is a clear need for a safe and effective treatment option for patients with gastroparesis, and we are pleased to be advancing the first agent that may be suitable for a broad range of patients with gastroparesis."

Based on the positive results from the Phase 2 trial, Theravance Biopharma initiated a Phase 2b study of velusetrag for the treatment of gastroparesis in March 2015. The ongoing Phase 2b study (study 0099) is a multicenter, double-blind, randomized, placebo-controlled, parallel-group trial that explores the efficacy and safety of velusetrag in patients with diabetic (n=100) or idiopathic (n=100) gastroparesis. Three doses of velusetrag (5, 15, and 30 mg once daily for 12 weeks) are being evaluated. The primary endpoint is the effect of velusetrag on symptoms in subjects with gastroparesis. The study also evaluates the effect of velusetrag on gastric emptying, and patient-reported outcome (PRO) measures. The study is being conducted in the U.S and Europe .

Velusetrag is being developed by Theravance Biopharma in collaboration with Alfa Wassermann (S.p.A.) ("Alfa Wassermann"). Under the terms of the agreement, Alfa Wassermann pays for the majority of the Phase 2 clinical costs and has an exclusive

option to develop and commercialize velusetrag in the European Union, Russia, China, Mexico and certain other countries, while Theravance Biopharma will retain full rights to velusetrag in the U.S., Canada, Japan and certain other countries.

"Our ongoing approach to advancing velusetrag is consistent with our stated product development strategy of leveraging our established commercial infrastructure within the U.S., while expanding our reach in key ex-U.S. markets through strategic collaborations with regional partners," stated Dr. Haumann. "We look forward to continuing the clinical advancement of velusetrag together with our partner Alfa Wassermann."

### **About Gastroparesis**

Gastroparesis is a disorder characterized by delayed gastric emptying and symptoms of gastric retention in the absence of mechanical obstruction. Approximately 36% and 29% of patients with gastroparesis have no known cause (i.e., idiopathic) or are diabetic, respectively. Post-prandial fullness, early satiety, bloating, abdominal discomfort (due to slow small bowel transit), nausea and vomiting are present in 46% to 97% of both diabetic and idiopathic gastroparesis patients with varying degrees of severity. Additional symptoms include weight loss and subsequent nutritional deficits.

The prevalence of gastroparesis in the US is estimated at approximately six million, or 1.8% of the population. Among patients with diabetes, 14% of Type I and 9% of Type II diabetics (approximately 2 million individuals) seek care for gastroparesis. It is estimated that there are 188,000 US hospital discharges annually with a diagnosis of gastroparesis.

### **About Velusetrag**

Velusetrag is an oral, once-daily investigational medicine discovered internally and developed for gastrointestinal motility disorders. It is a highly selective agonist with high intrinsic activity at the human 5-HT<sub>4</sub> receptor.

5-hydroxytryptamine receptor 4 (5-HT<sub>4</sub>) agonists are established as gastrointestinal (GI) prokinetic agents for the treatment of GI tract dysfunction, such as chronic constipation. Velusetrag (or TD-5108) is a 5-HT<sub>4</sub> receptor agonist that demonstrates high *in vitro* intrinsic activity and selectivity for the 5-HT<sub>4</sub> receptor and has no significant affinity for all other receptor types, ion channels, or enzymes tested. Velusetrag is being evaluated for the treatment of GI motility disorders.

### **About Theravance Biopharma**

The mission of Theravance Biopharma (NASDAQ: TBPH) is to create value from a unique and diverse set of assets: an approved product; a development pipeline of late-stage assets; and a productive research platform designed for long-term growth.

Our pipeline of internally discovered product candidates includes potential best-in-class opportunities in underserved markets in the acute care setting, representing multiple opportunities for value creation. VIBATIV<sup>®</sup> (telavancin), our first commercial product, is a once-daily dual-mechanism antibiotic approved in the U.S. and Europe for difficult-to-treat infections. TD-4208 is an investigational long-acting muscarinic antagonist (LAMA) being developed as a potential once-daily, nebulized treatment for COPD. Axelopran (TD-1211) is an investigational potential once-daily, oral treatment for opioid-induced constipation (OIC). Our earlier-stage clinical assets represent novel approaches for potentially treating diseases of the lung and gastrointestinal tract and infectious disease. In addition, we have an economic interest in future payments that may be made by GSK pursuant to its agreements with Theravance, Inc. relating to certain drug development programs, including the combination of fluticasone furoate, umeclidinium and vilanterol and (or the "Closed Triple").

With our successful drug discovery and development track record, commercial infrastructure, experienced management team and efficient corporate structure, we believe that we are well positioned to create value for our shareholders and make a difference in the lives of patients.

For more information, please visit [www.theravance.com](http://www.theravance.com).

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### **About Alfa Wassermann**

Alfa Wassermann is a private pharmaceutical group with Head Quarters in Bologna, Italy with its own Research, Development and Manufacturing facilities. It has a growing number of affiliate companies in both Europe as well as in emerging markets such as Russia, China and Mexico. Its main product is rifaximin, a gut-selective antibiotic, which has been prescribed for 28 years

under the Trade Name Normix<sup>®</sup>, Xifaxan<sup>®</sup> and others (approved in more than 40 countries, including the US). The company has also developed other important products: Sulodexide (Vessel<sup>®</sup>), a heparinoid for thromboembolic diseases, and Parnaparin (Fluxum<sup>®</sup>), a low molecular weight heparin for the treatment and prophylaxis of deep-vein thrombosis.

For more information, please visit Alfa Wassermann's web site at [www.alfawassermann.com](http://www.alfawassermann.com).

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*This press release contains certain "forward-looking" statements as that term is defined in the Private Securities Litigation Reform Act of 1995 regarding, among other things, statements relating to goals, plans, objectives and future events. Theravance Biopharma intends such forward-looking statements to be covered by the safe harbor provisions for forward-looking statements contained in Section 21E of the Securities Exchange Act of 1934 and the Private Securities Litigation Reform Act of 1995. Examples of such statements include statements relating to: the Company's strategies, plans and objectives, the Company's regulatory strategies and timing and results of clinical studies, the potential benefits and mechanisms of action of the Company's product and product candidates and the Company's expectations for product candidates through development and commercialization. These statements are based on the current estimates and assumptions of the management of Theravance Biopharma as of the date of the press release and are subject to risks, uncertainties, changes in circumstances, assumptions and other factors that may cause the actual results of Theravance Biopharma to be materially different from those reflected in the forward-looking statements. Important factors that could cause actual results to differ materially from those indicated by such forward-looking statements include, among others, risks related to: delays or difficulties in commencing or completing clinical studies, the potential that results from clinical or non-clinical studies indicate the Company's product candidates are unsafe or ineffective, the feasibility of undertaking future clinical trials for our product candidates based on FDA policies and feedback, dependence on third parties to conduct clinical studies, delays or failure to achieve and maintain regulatory approvals for product candidates, risks of collaborating with third parties to discover, develop and commercialize product and product candidates and risks associated with establishing and maintaining sales, marketing and distribution capabilities with appropriate expertise and supporting infrastructure. Other risks affecting Theravance Biopharma are described under the heading "Risk Factors" contained in Theravance Biopharma's Quarterly Report on Form 10-Q filed with the Securities and Exchange Commission (SEC) on May 13, 2015. In addition to the risks described above and in Theravance Biopharma's other filings with the SEC, other unknown or unpredictable factors also could affect Theravance Biopharma's results. No forward-looking statements can be guaranteed and actual results may differ materially from such statements. Given these uncertainties, you should not place undue reliance on these forward-looking statements. Theravance Biopharma assumes no obligation to update its forward-looking statements on account of new information, future events or otherwise, except as required by law.*

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