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Pearl Therapeutics Advances its Long-Acting Bronchodilator Combination Product Candidate into Four Additional Phase 2 Studies

REDWOOD CITY, CALIF., June 16, 2011 – Pearl Therapeutics Inc. today announced the advancement of its dual combination product candidate, PT003 and its individual components, PT001 and PT005 into a series of planned Phase 2 studies in patients with moderate-to-severe COPD. PT003 (GFF MDI) is an investigational inhaled combination bronchodilator product comprising glycopyrrolate (GP), a long-acting muscarinic antagonist (LAMA), and formoterol (FF), a well-known, established, long-acting beta-2 agonist (LABA), delivered together for the first time via a hydrofluoroalkane metered dose inhaler (HFA MDI), using a proprietary cosuspension formulation approach. These Phase 2 studies are designed to expand findings from the Company’s recently concluded Phase 2b study of PT003 and strengthen the safety and efficacy foundation of the Company’s Phase 3 program, which is expected to start in late 2012. Specifically they will provide further insight into the individual component doses, compare clinical activity to that of a short-acting anticholinergic agent and assess any cardiovascular effects.

The Phase 2 studies in this series include:

1. A randomized, double-blind study of four doses of PT001 (GP MDI) compared to placebo and Atrovent® HFA inhalation aerosol, a short-acting muscarinic antagonist;
2. A randomized, double-blind study of three doses of PT005 (FF MDI) compared to placebo and Foradil® Aerolizer®;
3. A randomized, double-blind cardiovascular safety study of PT003, PT005, PT001 and Foradil® Aerolizer®; and
4. A randomized, double-blind study of four doses of PT003 compared with its components, PT001 and PT005.

“With the success of our first Phase 2b study behind us, we are advancing PT003 and its components without delay into this planned series of four Phase 2 studies,” said [Chuck Bramlage](#), Pearl’s chief executive officer. “Pearl has instituted an iterative and integrated clinical and product development process that allows us to conduct clinical studies rapidly while maintaining a high level of rigor. Combining our novel scientific platform with our unique operational construct, we were able to complete an eight-arm, randomized, active- and placebo-controlled Phase 2b study of PT003 in fewer than nine months. We anticipate completing the four new Phase 2 studies in about 12 months, making top-line results available by mid 2012. Following the conclusion of these studies, we will meet with the U.S. Food and Drug Administration to review plans for a registrational Phase 3 program of PT003.”

With the exception of the cardiovascular safety study, the primary endpoints of the Phase 2 studies will be improvement in bronchodilation as assessed by change in FEV₁* AUC₀₋₁₂ relative to baseline. The cardiovascular safety study will measure the change in mean heart rate averaged over 24 hours following chronic administration of PT003,

PT005, PT001 or Foradil compared to baseline obtained during the screening period. Heart rate will be evaluated using Holter monitoring. More than 500 patients with moderate-to-severe COPD will be enrolled in these four studies.

“The insights we gained from our first Phase 2b study, and those from the forthcoming Phase 2 studies will provide a strong foundation for selecting the most effective and safe doses of GP and FF in PT003 for Phase 3 trials,” added [Colin Reisner](#), chief medical officer and executive vice president of clinical development and medical affairs at Pearl Therapeutics. “We are building additional confidence in our dose selection by comparing GP efficacy with that of a short-acting muscarinic antagonist, Atrovent, in our Phase 2 study of PT001 before progressing into Phase 3. This will strengthen our GP clinical experience beyond our already completed assessment of GP against a long-acting muscarinic antagonist, Spiriva.”

Pearl’s new Phase 2 studies follow the successful conclusion of the Company’s first Phase 2b study, in which patients administered PT003 experienced superior bronchodilation compared to those administered the individual components, PT001 and PT005, in a head-to-head comparison following the expectations set under FDA’s combination rule. Further, PT003 also showed superior bronchodilation compared to active comparators, Spiriva[®] HandiHaler[®] and Foradil[®] Aerolizer[®]. This assessment was based on the primary endpoint of FEV₁ AUC₀₋₁₂ after one week, as well as secondary endpoints, peak FEV₁ after one and seven days, and trough FEV₁. Primary and secondary endpoints from this Phase 2b study were presented in May 2011 at the American Thoracic Society annual meeting. This poster may be downloaded from the [Publications](#) page of the Pearl website. The five studies in Pearl’s Phase 2 program are fully funded by proceeds of the Company’s 2010 Series C financing.

Since its inception in 2007, Pearl has completed four early stage clinical trials on PT003, PT001 and PT005, along with a suite of non-clinical toxicology studies, and generated comprehensive data on product design and robustness, to boost its confidence in the scientific and clinical merit of the four new Phase 2b studies.

About COPD

Chronic obstructive pulmonary disease (COPD) is a preventable and treatable lung disease that is the fourth leading cause of death in the United States. Each year 12 million Americans are diagnosed with COPD and an additional 12 million Americans may have COPD but remain undiagnosed. Research shows that many do not get optimal treatment.

Bronchodilator medications are central to symptom management and are prescribed on an as-needed or regular basis to prevent or reduce symptoms. Long-acting inhaled bronchodilators have been shown to be most effective and convenient. Combining bronchodilators of different pharmacological classes, as recommended by [The Global Initiative for Chronic Obstructive Lung Diseases \(GOLD\)](#), has been shown to improve efficacy and may decrease the risk of side effects compared to increasing the dose of a single bronchodilator. As the course of COPD progresses, regular treatment with inhaled glucocorticosteroids may be added to bronchodilator treatment. Pearl is developing inhaled combination products designed to optimize the treatment of COPD.

About Pearl Therapeutics

Pearl Therapeutics is a privately held company developing combination therapies for the treatment of highly prevalent respiratory diseases, including chronic obstructive pulmonary disease and asthma. Pearl is rapidly advancing a pipeline of products including PT003, an inhaled, fixed-dose combination bronchodilator product

comprised of a long-acting muscarinic antagonist (LAMA) and a long-acting beta-2 agonist (LABA) delivered via a metered dose inhaler (HFA MDI); and PT010, a triple-combination product that combines the LAMA and LABA components of PT003 with an inhaled corticosteroid (ICS) for twice-daily administration from an HFA MDI for the treatment of severe COPD. Both PT003 and PT010 are developed with Pearl's proprietary porous particle cosuspension technology, which allows the formulation of multiple products in the MDI format, with highly stable, robust and aerodynamically efficient drug delivery. Founded in 2006, Pearl Therapeutics is privately held and backed by 5AM Ventures, Clarus Ventures, New Leaf Ventures and Vatera Healthcare. For more information, please visit www.pearltherapeutics.com.

** FEV₁ (forced expiratory volumes in one second) is a common measurement of lung function in patients with asthma, cystic fibrosis, and COPD and is typically used to predict the severity of pulmonary disease. AUC (area under the curve) is a measure of therapeutic benefit over a period of time.*

Editor's note: Atrovent® (Ipratropium Bromide) and Spiriva® HandiHaler® (tiotropium bromide inhalation powder) are registered trademarks of Boehringer Ingelheim Pharmaceuticals; Foradil® is a registered trademark of Astellas Pharma; and Aerolizer® is a registered trademark of Novartis AG.

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