

October 18, 2018



## **Corbus Pharmaceuticals Presents Data on Impact of Lenabasum on Inflammation of Airway Macrophages from Cystic Fibrosis Lungs at the 2018 North American Cystic Fibrosis Conference**

- *Study demonstrates that lenabasum decreases inflammatory biomarkers and increases pro-resolving mediators in airway macrophages from cystic fibrosis patients*
- *Cystic fibrosis is a life-threatening rare genetic disease that affects ~30,000 patients in the U.S. and ~70,000 patients worldwide*
- *Chronic inflammation and subsequent fibrosis damages multiple organs in cystic fibrosis including the lungs, impairs organ function, and reduces health-related quality of life*

Norwood, MA, Oct. 18, 2018 (GLOBE NEWSWIRE) -- Corbus Pharmaceuticals Holdings, Inc. (NASDAQ: CRBP) ("Corbus" or the "Company"), a clinical stage drug development company with the industry's leading pipeline focused on treating inflammatory and fibrotic diseases by targeting the endocannabinoid system, announced today that it presented new data demonstrating lenabasum's effect on airway macrophages harvested from human cystic fibrosis lungs at the [2018 North American Cystic Fibrosis Conference](#) being held October 18-20, 2018 in Denver, CO.

Lenabasum is the Company's novel, synthetic oral endocannabinoid-mimetic drug, designed to resolve chronic inflammation and halt fibrosis. Lenabasum is currently being evaluated in four clinical programs in diffuse cutaneous systemic sclerosis ("SSc"), cystic fibrosis ("CF"), dermatomyositis ("DM") and systemic lupus erythematosus ("SLE").

Mark Tepper, Ph.D., President and Chief Scientific Officer of Corbus, presented abstract #250 titled, "*Lenabasum Reduces LPS-Induced Inflammation in Airway Macrophages from Human Cystic Fibrosis Lungs,*" during Poster Session I, today, Thursday, October 18, 2018 from 11:15 am – 1:45 pm MT.

Dr. Tepper commented, "We are excited by the positive data from this study and believe that these findings fit with the observed effects of lenabasum in CF airway inflammatory responses. The positive clinical data from the Phase 2 study of lenabasum in CF inspired us to explore whether lenabasum could directly reduce inflammation in airway macrophages,

which are one of the key inflammatory cells that cause significant damage in the lungs of people with CF. We believe the results from this study are significant as they demonstrate for the first time a dramatic reduction in sphingosine kinase 1 (SPHK1), a key regulator of inflammation.”

The study evaluated airway macrophages (“AMs”) that were recovered from surgically removed lungs from CF patients undergoing lung transplants to determine the effect of lenabasum on the production and secretion of inflammatory cytokines and other biomarkers of inflammation and resolution. Adherent AMs were treated with endotoxin from *Pseudomonas aeruginosa* (LPS). A treatment of 6 hours was selected based on maximal mRNA transcript expression and detection of protein secretion in 3-day-old cultured AMs. Treatment with vehicle did not affect the expression of inflammatory biomarkers, whereas lenabasum did. Lenabasum was used at the concentration of 1, 3 and 10 µM. A summary of the results being presented is below:

### **Summary of Study Results**

Utilizing a translational model consisting of exposure of primary cultures of CF human AMs to LPS, the study indicates that lenabasum:

- Decreases inflammatory cytokines induced by LPS in CF patients’ AMs.
- Decreases the levels of spliced XBP-1, a key transcription factor implicated in excessive inflammatory responses of CF human AMs.
- Triggers the biosynthesis of LXA4, a key pro-resolution mediator, in LPS stimulated CF human AMs.
- Decreases the expression of sphingosine kinase 1, the rate limiting enzyme for generation of sphingosine 1-phosphate, a key mediator of inflammation.
- Triggers the biosynthesis of the pro-resolution eicosanoid 15-deoxy-Δ<sup>12,14</sup>-PGJ<sub>2</sub>, a natural PPAR-gamma agonist which acts to resolve inflammation.

The poster is now available on Corbus’ website and can be accessed [here](#).

Corbus is currently evaluating lenabasum for the treatment of cystic fibrosis in a Phase 2b multicenter, double-blinded, randomized, placebo-controlled study. The study will enroll approximately 415 subjects with CF who are at least 12 years of age and at increased risk for pulmonary exacerbations. The primary efficacy outcome is the event rate of pulmonary exacerbations, which is the average number of pulmonary exacerbations per subject per time period. Secondary efficacy outcomes include other measures of pulmonary exacerbations, change in Cystic Fibrosis Questionnaire-Revised Respiratory domain score and change in forced expiratory volume in 1 second (FEV<sub>1</sub>), % predicted. The study will be conducted in approximately 100 sites across North America, Europe and Australia. Subjects are centrally randomized to one of three cohorts to receive lenabasum 20 mg twice per day, lenabasum 5 mg twice per day, or placebo twice per day for 28 weeks in a 2:1:2 ratio.

This Phase 2b CF study was designed with input from the Cystic Fibrosis Therapeutics Development Network and the European Cystic Fibrosis Society Clinical Trials Network and is funded in part by a Development Award for up to \$25 million from the Cystic Fibrosis Foundation.

Corbus expects to report topline results for the Phase 2b CF study in 2020. For more

information on the Phase 2 study, please visit [ClinicalTrials.gov](https://ClinicalTrials.gov) and reference Identifier NCT03451045.

## **About Cystic Fibrosis**

Cystic fibrosis (CF) is a chronic, rare, genetic disease caused by mutations of the cystic fibrosis transmembrane conductance regulator (CFTR) gene. CF affects approximately 70,000 people in the U.S. and Europe. In people with CF, thick secretions build up in the lungs, pancreas and other organs. In the lungs, the mucus blocks airways, making it easy for bacteria to grow and infections to occur. These infections can severely damage the lungs over time and lead to respiratory failure. People affected by CF may have trouble digesting their food and may develop diabetes as a complication due to the disease's effect on the pancreas. A person with CF may also experience pulmonary exacerbations (PEX), which are an acute worsening of inflammation in the lungs with an increase in respiratory symptoms (for example, cough, shortness of breath) accompanied by an acute decrease in lung function. PEX are responsible for about half of long-term decline in lung function experienced by people with CF. More exacerbations are associated with greater lung function decline. Nearly 1 in 3 people with CF require treatment for PEX in any given year, and treatment success of PEX is currently described as "suboptimal." PEX can cost up to \$120K per year in people with severe lung disease and are associated with higher one-year risk of death. Despite the major advances in treatment of CF over the last several decades, there has been a minimal reduction in the proportion of individuals who have PEX treated with IV antibiotics. Several classes of drugs have been considered to treat the underlying inflammation, though Ibuprofen is the only anti-inflammatory drug currently recommended for the long-term treatment of CF airway inflammation. Despite this recommendation, very few eligible patients are prescribed ibuprofen because of side effects and monitoring requirements.

## **About Lenabasum**

Lenabasum is a rationally-designed, oral, small-molecule that selectively binds as an agonist to the cannabinoid receptor type 2 (CB2). CB2 is preferentially expressed on activated immune cells, fibroblasts, muscle cells, and endothelial cells. In both animal and human studies conducted to-date, lenabasum induces the production of Specialized Pro-resolving lipid Mediators ("SPMs") that activate endogenous pathways which resolve inflammation and speed bacterial clearance without immunosuppression. Lenabasum also has a direct effect on fibroblasts to limit production of fibrogenic growth factors and extracellular connective tissue that lead to tissue fibrosis (scarring). Data from animal models and human clinical studies show lenabasum reduces expression of genes and proteins involved in inflammation and fibrosis. Lenabasum demonstrates promising activity in animal models of skin and lung inflammation and fibrosis in systemic sclerosis (SSc). Lenabasum is also active in animal models of lung infection and inflammation in cystic fibrosis and joint inflammation and scarring in rheumatoid arthritis.

Lenabasum has demonstrated favorable safety and tolerability profiles in clinical studies to date. Lenabasum improved multiple physician-assessed and patient-reported efficacy outcomes in Phase 2 studies in patients with diffuse cutaneous SSc and skin-predominant dermatomyositis. Lenabasum also reduced pulmonary exacerbations in a Phase 2 cystic fibrosis study. Additional clinical studies are being conducted and/or planned to confirm these results and support applications for regulatory approval.

## **About Corbus**

Corbus Pharmaceuticals Holdings, Inc. is a Phase 3 clinical-stage pharmaceutical company focused on the development and commercialization of novel therapeutics to treat inflammatory and fibrotic diseases by leveraging its industry leading pipeline of endocannabinoid system-targeting drug candidates. The Company's lead product candidate, lenabasum, is a novel, synthetic, oral, selective cannabinoid receptor type 2 (CB2) agonist designed to resolve chronic inflammation and fibrotic processes. Lenabasum is currently being evaluated in systemic sclerosis, cystic fibrosis, dermatomyositis, and systemic lupus erythematosus.

Corbus licensed the exclusive worldwide rights to develop, manufacture and market drug candidates from more than 600 novel compounds targeting the endocannabinoid system from Jenrin Discovery LLC. The pipeline includes CRB-4001, a 2<sup>nd</sup> generation, peripherally-restricted, selective cannabinoid receptor type 1 (CB1) inverse agonist specifically designed to eliminate blood-brain barrier penetration and brain CB1 receptor occupancy that mediate the neuropsychiatric issues associated with first-generation CB1 inverse agonists. Potential indications for CRB-4001 include NASH, primary biliary cholangitis, idiopathic pulmonary fibrosis, radiation-induced pulmonary fibrosis, myocardial fibrosis after myocardial infarction and acute interstitial nephritis, among others. CRB-4001 is scheduled to enter a Phase 1 study in 2019 followed a National Institutes of Health (NIH)-funded first-in-patient Phase 2 study.

For more information, please visit [www.CorbusPharma.com](http://www.CorbusPharma.com) and connect with the Company on [Twitter](#), [LinkedIn](#), and [Facebook](#).

## **Forward-Looking Statements**

This press release contains certain forward-looking statements within the meaning of Section 27A of the Securities Act of 1933 and Section 21E of the Securities Exchange Act of 1934 and Private Securities Litigation Reform Act, as amended, including those relating to the Company's product development, clinical and regulatory timelines, market opportunity, competitive position, possible or assumed future results of operations, business strategies, potential growth opportunities and other statement that are predictive in nature. These forward-looking statements are based on current expectations, estimates, forecasts and projections about the industry and markets in which we operate and management's current beliefs and assumptions.

These statements may be identified by the use of forward-looking expressions, including, but not limited to, "expect," "anticipate," "intend," "plan," "believe," "estimate," "potential," "predict," "project," "should," "would" and similar expressions and the negatives of those terms. These statements relate to future events or our financial performance and involve known and unknown risks, uncertainties, and other factors which may cause actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Such factors include those set forth in the Company's filings with the Securities and Exchange Commission. Prospective investors are cautioned not to place undue reliance on such forward-looking statements, which speak only as of the date of this press release. The Company undertakes no obligation to publicly update any forward-looking statement, whether as a result of new information, future events or otherwise.

Source: Corbus Pharmaceuticals Holdings, Inc.

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