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Verona Pharma Reports Encouraging Top-Line Data from Three-Day Phase 2 Trial Evaluating Nebulized Ensifentrine (RPL554) on Top of Dual Bronchodilator Therapy for COPD Maintenance Treatment

Results from this short clinical pharmacology trial inform and support further clinical development of ensifentrine as an add-on to dual and triple COPD therapy

Investment community conference call scheduled for 8 am EST on Monday, January 14, 2019

LONDON, Jan. 14, 2019 (GLOBE NEWSWIRE) -- Verona Pharma plc (AIM:VRP) (Nasdaq:VRNA) ("Verona Pharma"), a clinical-stage biopharmaceutical company focused on developing and commercializing innovative therapies for respiratory diseases, announces top-line data from its three-day Phase 2 clinical pharmacology trial evaluating the effect of two different doses (1.5 mg and 6.0 mg; twice daily) of nebulized ensifentrine (RPL554) when used on top of an inhaled long-acting muscarinic antagonist/long-acting beta2 agonist ("LAMA/LABA"), tiotropium/olodaterol (Stiolto® Respimat®). LAMA/LABA therapies are commonly used in the maintenance treatment of patients with moderate to severe chronic obstructive pulmonary disease ("COPD"). Patients already receiving inhaled corticosteroid ("ICS") therapy were allowed to continue to receive a stable dose of ICS throughout the study, thus providing additional data on "triple therapy" use.

Ensifentrine is an investigational first-in-class, inhaled, dual inhibitor of the enzymes phosphodiesterase 3 and 4 designed to have bronchodilator and anti-inflammatory properties, which is currently in development for the maintenance treatment of COPD, cystic fibrosis and asthma.

Highlights

- Primary endpoint of peak forced expiratory volume in one second ("FEV_1") after morning dose on day 3 of treatment was not met with statistical significance, although the ensifentrine 1.5 mg morning dose improved peak FEV_1 by 46 mL, compared to placebo.
  - Improvement in FEV_1, compared to placebo, with the 1.5 mg dose was maintained throughout the 24-hour period as measured on day 3.
- Importantly, peak FEV_1 after evening dose on day 3 showed statistically significant improvement, compared to placebo, with both doses, with ensifentrine 1.5 mg showing a 130 mL improvement ($p<0.001$) and ensifentrine 6.0 mg showing an 81 mL improvement ($p=0.002$).
- Ensifentrine at a 1.5 mg dose produced consistent improvements, compared to placebo, in average FEV_1 over 12 hours following the morning dose on days 1 to 3, with an improvement of approximately 50 mL on day 3. These improvements were not shown to be statistically significant when adjusted for multiple doses.
- Reductions in residual volume, compared to placebo, as measured by plethysmography were observed at all time points on day 3 with the 1.5 mg dose.
  - Statistically significant reductions in mean residual volume were observed 15 minutes following the evening dose on day 3, with ensifentrine 1.5 mg showing a reduction of 259 mL ($p<0.002$) and ensifentrine 6.0 mg showing a reduction of 142 mL ($p<0.036$).
- Ensifentrine 6.0 mg did not result in greater improvement in lung function as compared with the ensifentrine 1.5 mg dose.
- Ensifentrine was well tolerated at both doses with an adverse event profile consistent with that observed in prior studies.

"Achieving additional bronchodilator response of this magnitude in COPD patients that have previously been considered to be maximally bronchodilated on background dual or triple therapy in a short, three-day study is clinically meaningful and unprecedented," commented Dave Singh, M.D., Professor of Clinical Pharmacology and Respiratory Medicine, Medicines Evaluation Unit, University of Manchester. "The statistically significant reduction observed in residual volume for the ensifentrine 1.5 mg dose at certain time points, which is closely related to dyspnea or breathlessness, highlights the potential for ensifentrine to provide symptomatic improvement for patients with this progressive and debilitating disease. I look forward to seeing data from longer-term studies evaluating the bronchodilator and anti-inflammatory activity of this unique mechanism of action."

"Having demonstrated in previous studies the potential of ensifentrine to deliver benefits to patients on no or single bronchodilator therapy, we believe that this short study continues to support our view that ensifentrine may also be of benefit to more severe COPD patients on dual and triple therapy, for whom there are few other treatment options," said Jan-Anders Karlsson, PhD, CEO of Verona Pharma. "While we are disappointed that this exploratory Phase 2 study did not achieve statistical significance for its primary endpoint, these data give us clarity on the design, including dose and background therapy, for future long-term studies. We now have the opportunity to also include patients on dual and triple therapy, with the goal of further evaluating ensifentrine's potential to produce sustained bronchodilation and anti-inflammatory effect in this large number of symptomatic COPD patients."

In Phase 2 clinical trials completed to date, ensifentrine has been observed to result in bronchodilator effects when used alone or as an add-on treatment to other COPD bronchodilators, and has also shown anti-inflammatory effects in a standard challenge study with COPD-like inflammation in human subjects. Verona Pharma is currently conducting a Phase 2 trial to evaluate a dry powder inhaler formulation of ensifentrine for the maintenance treatment of COPD. The company also plans to evaluate ensifentrine in a metered-dose inhaler formulation as part of a comprehensive clinical program intended to fully demonstrate the clinical utility of ensifentrine in improving the standard of care for COPD.

Study Design

This study was a randomized, double-blind, three-way crossover trial (ClinicalTrials.gov Identifier: NCT0367367), conducted at sites in the U.S. and in the U.K., which enrolled 79 patients with COPD to investigate the efficacy and safety of nebulized ensifentrine (RPL554) on top of an inhaled LAMA/LABA, tiotropium/olodaterol (Stiolto® Respimat®), compared to placebo. Approximately 40% of patients were already receiving ICS anti-inflammatory therapy before the study and were allowed to continue to receive a stable dose of ICS throughout the study, thus providing additional data on "triple therapy" use. Following a 7- to 14-day washout period in advance of dosing and between study arms, patients received

three days of treatment with each of two dose strengths (1.5 mg or 6.0 mg) of nebulized ensifentrine or placebo twice daily. The primary endpoint of this trial was improvement in lung function with ensifentrine (as an add-on to tiotropium/olodaterol), compared to placebo, as measured by FEV_1, a standard measure of exhaled breath volume to evaluate respiratory function, four hours post-dose after the morning dose on day three. Secondary endpoints included lung function as measured by FEV_1 over time, reductions in residual volume, and safety and tolerability.

Conference Call
Verona Pharma will host an investment community conference call today at 8:00 a.m. Eastern Standard Time (1:00 p.m. Greenwich Mean Time) on Monday, January 14, 2019 to discuss the top-line data from the study disclosed in this press release.

Analysts and investors may participate in the conference call by utilizing the conference ID: 13686524 and dialing the following numbers:

- 1-877-423-9813 or + 1-201-689-8573 for callers in the United States
- 0 800 756 3429 for callers in the United Kingdom
- 0 800 182 0040 for callers in Germany

Those interested in listening to the conference call live via the internet may do so by visiting the "Events and Presentations" page on the "Investors" section of Verona Pharma's website at http://investors.veronapharma.com/events-and-presentations/events and clicking on the webcast link. Slides highlighting the top-line data will also be posted to the "Events and Presentations" page.

THIS ANNOUNCEMENT CONTAINS INSIDE INFORMATION FOR THE PURPOSES OF ARTICLE 7 OF REGULATION (EU) NO 596/2014.

About Chronic Obstructive Pulmonary Disease

Chronic obstructive pulmonary disease ("COPD") is a progressive and life-threatening respiratory disease for which there is no cure. Although COPD is thought to be underdiagnosed, globally, around 384 million people suffer from the disease. This number, according to the World Health Organization, is likely to increase in coming years, with estimates that COPD will become the third leading cause of death worldwide by 2030. The condition damages the airways and the lungs, leading to persistent symptoms of breathlessness, impacting a person's daily life and their ability to perform simple activities such as walking a short flight of stairs or carrying a suitcase. Many experience acute periods of worsening symptoms called 'exacerbations', often leading to emergency department visits or hospital admissions and are also associated with high mortality. In the United States alone, the 2010 total annual medical costs related to COPD were estimated to be $32 billion and are projected to rise to $49 billion in 2020. About 30-40% of moderate to severe COPD patients on triple inhaled therapy (ICS/LAMA/LABA) remain uncontrolled and continue to experience airway obstruction (breathing difficulties), COPD symptoms and exacerbations. There is an urgent need for drugs with novel mechanisms of action that can be used by these patients in addition to current therapies.

About Verona Pharma plc

Verona Pharma is a clinical-stage biopharmaceutical company focused on developing and commercializing innovative therapies for the treatment of respiratory diseases with significant unmet medical needs. Verona Pharma's product candidate, ensifentrine, is an investigational first-in-class, inhaled, dual inhibitor of the enzymes phosphodiesterase 3 and 4 that is designed to act as both a bronchodilator and an anti-inflammatory agent in a single compound. In previous clinical trials, the nebulized formulation of ensifentrine has been observed to result in bronchodilator effects when used alone or as an add-on treatment to other COPD bronchodilators. It has shown clinically meaningful and statistically significant improvements in lung function when administered in addition to frequently used short- and long-acting bronchodilators, such as tiotropium (Spiriva®), compared with such bronchodilators administered as a single agent. Ensifentrine improved FEV_1 over four weeks in patients with moderate-to-severe COPD when compared to placebo and improved COPD symptoms and quality of life in a Phase 2b multicenter European study performed in 403 patients. In addition, ensifentrine has shown anti-inflammatory effects in a standard challenge study with COPD-like inflammation in human subjects. Ensifentrine has been well tolerated in these studies, having been administered to more than 800 subjects in 13 clinical trials. Verona Pharma is developing ensifentrine for the treatment of COPD, CF, and asthma.

Forward-Looking Statements

This press release contains forward-looking statements. All statements contained in this press release that do not relate to matters of historical fact should be considered forward-looking statements, including, but not limited to, statements that there is an opportunity for additional bronchodilator and symptomatic improvement via the novel mechanism of action of ensifentrine and Verona Pharma's plans to carry out further long-term clinical studies of ensifentrine as an add-on to both single and dual bronchodilator therapy and the expectation that even more profound anti-inflammatory effects, leading to improvements in lung function, as well as improvements in symptoms will result.

These forward-looking statements are based on management's current expectations. These statements are neither promises nor guarantees, but involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from our expectations expressed or implied by the forward-looking statements, including, but not limited to, the following: our limited operating history; our need for additional funding to complete development and commercialization of RPL554, which may not be available and which may force us to delay, reduce or eliminate our development or commercialization efforts; the reliance of our business on the success of RPL554, our only product candidate under development; economic, political, regulatory and other risks involved with international operations; the lengthy and expensive process of clinical drug development, which has an uncertain outcome; serious adverse, undesirable or unacceptable side effects associated with RPL554, which could adversely affect our ability to develop or commercialize RPL554; potential delays in enrolling patients, which could adversely affect our research and development efforts; we may not be successful in developing RPL554 for multiple indications; our ability to obtain approval for and commercialize RPL554 in multiple major pharmaceutical markets; misconduct or other improper activities by our employees, consultants, principal investigators, and third-party service providers; material differences between our "top-line" data and final data; our reliance on third parties, including clinical investigators, manufacturers and suppliers, and the risks related to these parties' ability to successfully develop and commercialize RPL554; and lawsuits related to patents covering RPL554 and the potential for our patents to be found invalid or unenforceable. These and other important factors under the caption "Risk Factors" in our Annual Report on Form 20-F filed with the Securities and Exchange Commission ("SEC") on February 27, 2018, and our other reports filed with the SEC, could cause actual results to differ materially from those indicated by the forward-looking statements made in this press release. Any such forward-looking statements represent management's estimates as of the date of this press release. While we may elect to update such forward-looking statements at some point in the future, we disclaim any obligation to do so, even if subsequent events cause our views to change. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date of this press release.

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About Verona Pharma plc
Verona Pharma is a clinical-stage biopharmaceutical company focused on developing and commercializing innovative therapeutics for the treatment of respiratory diseases with significant unmet medical needs. Verona Pharma's product candidate, RPL554, is a first-in-class, inhaled, dual inhibitor of the enzymes phosphodiesterase 3 and 4 that acts as both a bronchodilator and an anti-inflammatory agent in a single compound. In clinical trials, treatment with RPL554 has been observed to result in statistically significant improvements in lung function as compared to placebo and has shown clinically meaningful and statistically significant improvements in lung function when added to two commonly used bronchodilators as compared to either bronchodilator administered as a single agent. RPL554 has also shown anti-inflammatory effects and been well tolerated in clinical trials. Verona Pharma is developing RPL554 for the treatment of chronic obstructive pulmonary disease (COPD), cystic fibrosis, and potentially asthma.

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These and other important factors could cause actual results to differ materially from those indicated by the forward-looking statements made in this press release. Any such forward-looking statements represent management's estimates as of the date of this press release. While we may elect to update such forward-looking statements at some point in the future, we disclaim any obligation to do so, even if subsequent events cause our views to change. These forward-looking statements should not be relied upon as representing our views as of any date subsequent to the date of this press release.

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