



Verona Pharma

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RPL554 MAD study in healthy volunteers confirms excellent tolerability; dosing of COPD patients commences

Multiple ascending dose study of RPL554 in healthy volunteers completed successfully; excellent tolerability at all dose levels tested

Results continue to support twice daily dosing regimen with new RPL554 formulation

Up to 30 COPD patients to be treated in multiple ascending dose study; results expected Q3 2015

8 June 2015, Cardiff – Verona Pharma plc (AIM: VRP.L), the drug development company focused on first-in-class medicines to treat respiratory diseases, today announces the successful completion of the second phase of a Multiple Ascending Dose (MAD) study in which nebulised RPL554, a novel dual PDE3/PDE4 inhibitor, was administered to healthy subjects for up to five consecutive days at doses up to 16x larger than the previously used active dose. RPL554 is currently in development as a nebulised treatment for acute exacerbations in COPD patients in a hospital or home-care setting. The nebulised bronchodilator market was worth about \$1 billion in 2014 in the US1.

The completed MAD study showed that the drug was well tolerated across all dose levels and no maximum tolerated dose was reached. As found in the interim results from the single ascending dose (SAD) part of this trial, repeat dosing with the new formulation resulted in a longer residence time for RPL554 in the lung and slower release into the blood stream, suggesting that twice daily dosing may be appropriate.

The Company also announces the commencement of a multiple ascending dose study in up to 30 moderate chronic obstructive pulmonary disease (COPD) patients, where each dose will be given for five consecutive days. The primary objective here is to further confirm the safety and tolerability seen in earlier parts of the trial, as well as to investigate bronchodilation in these COPD patients. This study is the final part of a Phase I/II clinical trial with RPL554, using a new proprietary nebulised formulation.

The dose range, for both MAD studies, is based on the successfully completed SAD part of this trial in which nebulised RPL554 was delivered at doses up to 16x that previously shown to produce bronchodilation. As noted in Verona Pharma's press release on 23 March 2015, RPL554, in this study in 50 healthy volunteers, was well-tolerated and was without effect on cardiovascular parameters and without nausea or vomiting at any dose.

The trial is being performed at the Medicines Evaluation Unit in Manchester by lead investigator Professor Dave Singh.

Dr Jan-Anders Karlsson, Chief Executive Officer of Verona Pharma, said:

"This proof of concept trial with our new proprietary formulation for nebulised RPL554 continues to generate very encouraging results. The drug appears to be very well tolerated on both single and multiple dosing even at significantly elevated levels compared to previous doses tested. The final phase of this trial will be conducted in COPD patients and will examine both the safety and bronchodilator response at higher doses. We have already demonstrated in previous trials at lower doses using an earlier formulation that RPL554 is a potent bronchodilator with broad anti-inflammatory activity in a single molecule. Accordingly we eagerly await the results from the final part of this study, expected in Q3 2015.

"We are initially developing nebulised RPL554 as a treatment for acute exacerbations in COPD, where we believe it has significant market potential. We continue to believe that the emerging profile of RPL554 suggests that it could potentially become an important addition to available treatment options both as a

monotherapy and, as a result of its unique mechanism of action, as a combination partner for existing drugs for COPD.”

Phase I and Phase II studies with RPL554 in its previous nebulised formulation were successfully conducted in over 100 subjects.² Results collectively showed that the drug is a very potent bronchodilator with the ability to elicit a unique anti-inflammatory response. In these initial studies, patients treated with RPL554 had an adverse event profile which was similar to that in patients treated with placebo. The original nebulised formulation of the drug used in these studies was devised to provide proof-of-concept data, before developing the new formulation suitable for commercial scale- up.

It is expected that the new formulation of RPL554 will result in a significantly improved therapeutic index in COPD patients, implying that they should be able to inhale higher doses with prolonged effect, than the previous prototype formulation, offering potential for improvements in convenience and compliance, as well as health economic benefit. In addition, the commercial viability of the new formulation is underlined by significantly improved stability compared to the previous formulation. RPL554 also has potential as a novel therapy in patients with asthma and cystic fibrosis.

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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.

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.

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 development of DPI and MDI formulations of RPL554 and the potential for these formulations to increase the market opportunity for the product, if approved.

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.