29 September 2015

# Positive headline data from RPL554 clinical study in COPD patients

New suspension formulation is well tolerated; results signal marked improvement in lung function

RPL554 remains on track for entry into Phase IIb clinical trials in 2H 2016

29 September 2015, Cardiff – Verona Pharma plc (AIM: VRP.L), the drug development company focused on first-in-class medicines to treat respiratory diseases, today announces encouraging positive headline data of the third and final part (part C) of a randomised, double blind, placebo controlled Single Ascending Dose (SAD) / Multiple Ascending Dose (MAD) clinical study in stable chronic obstructive pulmonary disease (COPD) patients. This study uses a new proprietary and commercially scalable nebulised suspension formulation of the Company's lead pipeline drug, RPL554.1,2 The primary objective of this part of the study was to show the safety and tolerability of the new drug formulation in stable COPD patients with moderate severity of disease.3 Measurement of lung function using FEV14 was included. Evaluation of the full data set is ongoing and will be presented in an appropriate scientific, peer-reviewed forum at a later date.

Highlights: Part C of study in 32 stable COPD patients with moderate disease severity

• Primary objective of study met: Drug formulation well tolerated at all dose levels; No serious adverse events reported

• Adverse event profile similar to that seen with placebo

• Absence of gastro-intestinal or cardiovascular adverse events

• RPL554 caused pronounced improvement in lung function

• Mean peak FEV1 increase ranged from 199ml to 257ml versus placebo

• Extent of bronchodilation exceeds that seen in earlier studies with original proof of concept formulation

• Data continue to support twice daily dosing regimen with RPL554

• Data consistent with that from earlier part A and B of study in healthy volunteers

• Evaluation of the full data set from this trial is ongoing

In the third part of the trial, nebulised RPL554, a novel dual PDE3/PDE4 inhibitor, was administered twice daily using a new proprietary, commercially scalable, suspension formulation to stable COPD patients with moderate disease severity for up to five-and-a-half consecutive days at doses significantly in excess of the previously used active dose.

Patients withheld their regular bronchodilator therapy for the duration of the treatment phase of the study.

The study met its primary objective and all doses of RPL554 were found to be well tolerated. As with earlier parts of the trial, which were conducted in healthy volunteers, there were no reports of serious adverse events and the adverse event profile was similar to that seen with placebo. In particular, there was an absence of gastro-intestinal or cardiovascular adverse events.

Lung function, as measured by peak FEV1, was increased in all dose groups and ranged between 199-257ml over placebo suggesting a clinically meaningful bronchodilator effect which will be confirmed in Phase IIb studies. In the highest dose there was a small increase in heart rate as might be expected from the pharmacology of the product.

The new commercially scalable formulation of RPL554 results in a uniform suspension of RPL554 and was designed to provide improved tolerability, allowing higher doses of RPL554 to be inhaled, yielding an optimised bronchodilator effect than with the previous prototype, solution formulation. Additionally the new formulation offers potential for improvements in convenience and compliance. Data to date supports this profile, suggesting a twice daily dosing regimen and is consistent with a longer residence time of the drug in lung tissue and slower release into the blood than with the original formulation. In addition, the commercial viability of the new formulation is underlined by significantly improved stability compared to the previous formulation.

Professor Dave Singh of the Medicines Evaluation Unit, University of Manchester, lead investigator on this study, commented: “I am very encouraged by the headline results of this study using the new suspension formulation of RPL554. The marked improvement in lung function seen in this initial small study shows that this product has potential to be a meaningful addition to existing treatment options for COPD.”

Dr. Jan-Anders Karlsson, Chief Executive of Verona Pharma, said: “We are excited by the robust and consistent results arising from our SAD/MAD study of RPL554 in both healthy volunteers and now, stable COPD patients with moderate disease severity. The data demonstrates that, as designed, the new commercially scalable, suspension formulation is well tolerated and has allowed us to extend the dose range and the duration of bronchodilation effect that can be produced in COPD patients. We will now fully analyse the data from this trial. While we need to discuss these results and confirm our further development plans for the drug with the appropriate regulatory authorities, we currently expect to begin Phase IIb studies in the second half of 2016.”

RPL554 is currently in development as a nebulised treatment for acute exacerbations in COPD patients in a hospital or home-care setting. The nebuliser bronchodilator market was worth about $1 billion in 2014 in the US.5 RPL554 also has potential as a novel drug for the maintenance therapy of COPD, for patients with asthma and cystic fibrosis.

Phase I and Phase II studies with RPL554 in the previous nebulised solution formulation were successfully conducted in over 100 subjects.6 Results collectively showed that the drug

5 IMS Consulting Group market research 20146 Franciosi, L.G., et al., Efficacy and safety of RPL554, a dual PDE3 and PDE4 inhibitor, in healthy volunteers and in patients with asthma or chronic obstructive pulmonary disease: findings from four clinical trials. Lancet Respir Med, 2013. 1(9): p. 714- 27 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 the development of a new formulation suitable for commercial scale-up.

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For further information please contact: Verona Pharma plc

**Verona Pharma plc**
Jan-Anders Karlsson, CEO
Tel: +44 (0)20 3283 4200
info@veronapharma.com

**N+1 Singer (Nominated Adviser and UK Broker)**
Aubrey Powell / James White
Tel: +44 (0)20 7496 3000

**FTI Consulting**
Simon Conway / Stephanie Cuthbert / Natalie Garland-

Collins
Tel: +44 (0)20 3727 1000
veronapharma@fticonsulting.com

**ICR, Inc. (US Media and Investor enquiries)**
James Heins
Tel: +1 203-682-8251
James.Heins@icrinc.com

Stephanie Carrington
Tel. +1 646-277-1282
Stephanie.Carrington@icrinc.com

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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.

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