15 March 2016

Verona Pharma reports positive results from RPL554 dose-finding study

Study demonstrates drug has substantial bronchodilator effect and excellent tolerability at broad range of doses

Data continues to suggest drug could be meaningful new addition, alone or in combination, for the treatment of COPD

15 March 2016, Cardiff – Verona Pharma plc (AIM: VRP.L), the drug development company focused on first-in-class medicines to treat respiratory diseases, today announces positive headline data from a Phase IIa dose-finding clinical study using the Company's new proprietary nebulised formulation of RPL554. RPL554 is a novel inhaled PDE3/PDE4 inhibitor with both bronchodilator and antiinflammatory properties in the same molecule, currently in development as a nebulised treatment for acute exacerbations in chronic obstructive pulmonary disorder (COPD) patients in a hospital or homecare setting. Such patients typically require additional bronchodilation as well as anti-inflammatory treatment despite being on maximum doses of approved COPD medications (which often contain salbutamol).

Highlights

• Primary objective of study met
o Nebulised RPL554 demonstrated a dose-dependent bronchodilator response in asthma patients; the response was highly statistically significant ($p<0.0001$) at all doses tested[1]

• The maximum bronchodilator effect of RPL554 in this study was comparable to the effect observed with the supramaximal dose (7.5mg) of nebulised salbutamol used in this study[2]

• RPL554 did not elicit any serious adverse events or adverse events of concern at any dose
o Large dose range (0.4 to 24mg) examined; suggests RPL554 potentially has a very large safety margin
o Fewer adverse events recorded with RPL554 than with nebulised salbutamol
o No gastro-intestinal adverse events or cardiovascular events of concern

• We continue to expect a Phase II clinical study examining nebulised RPL554 as an add-on treatment to standard bronchodilators to report top-line data in Q2 2016

Dr Jan-Anders Karlsson, the CEO of Verona Pharma, said:
"We are very excited by the results from our dose-finding study for RPL554. It is very pleasing that the maximum bronchodilator effect of RPL554 is comparable to that seen with the highest dose of salbutamol used in the study - a dose equivalent to the highest dose of salbutamol used to treat acute exacerbations of COPD in the emergency department - it is noteworthy that this was achieved with fewer adverse events. The data generated in this study emphasises its pronounced bronchodilator effect, and combined with its unique anti-inflammatory effects, we continue to believe that RPL554 could be an important, and much needed, new treatment option, either alone or as an add-on to existing drugs, for patients with COPD."

Professor Leif Bjermer of Skane University, Lund, Sweden, lead investigator on this study, commented:
"This well-designed and successfully executed dose-ranging study of nebulised RPL554 in moderate asthmatics demonstrated the drug has a linear and thus predictable pharmacokinetic profile, and produced similar bronchodilation but with less side effects compared to a very high dose of salbutamol, used as a comparator. The drug was well tolerated, and few adverse events were recorded. Together, this suggests that the drug could have a large therapeutic index. With further clinical testing, RPL554 could become an important, and much needed novel treatment option, for

patients with COPD and other airway's disease."

The intent of the study was to demonstrate a dose-dependent bronchodilator effect of RPL554 and compare to nebulised salbutamol. In the hospital setting, the usual starting nebulised dose of salbutamol is 2.5mg but occasionally up to 3 times this dose (7.5mg) is used to produce additional bronchodilation in severely ill patients. We compared RPL554 to both the standard dose and the very high dose of salbutamol to evaluate maximum bronchodilator effects and tolerability.

In this randomised, double-blind, placebo-controlled, seven way crossover Phase IIa study, 29 patients with mild to moderate persistent asthma each received four doses of nebulised RPL554 (0.4 to 24 mg), as well as two doses of nebulised salbutamol (2.5mg and 7.5mg), or placebo. In addition to the largest dose tested in previous studies (24mg), lower doses of the new proprietary nebulised formulation of RPL554 than had been used before, were explored to identify a minimally effective dose. The study was performed at Celerion (Belfast, Ireland) and Skane University Hospital (Lund, Sweden).

The study met its primary objective, with nebulised RPL554 demonstrating a dose-dependent bronchodilator response in asthma patients. RPL554 pharmacokinetics were linear across the whole dose range. At the highest doses of both compounds, RPL554 produced the same maximum bronchodilator effect as salbutamol. Even the lowest RPL554 dose of 0.4mg was significantly superior ($p<0.0001$) to placebo as a bronchodilator. All doses of RPL554 were found to be well tolerated and the data supports the use of RPL554 in a twice daily dosing regimen. There were no reports of serious adverse events and fewer adverse events were seen with RPL554 than with salbutamol. Salbutamol produced well-acknowledged adverse events for this drug including tremor, tachycardia, palpitations, and a reduction in blood potassium levels. The large dosing range (60 fold) of RPL554 suggests a potentially large therapeutic index.

RPL554 is currently in development as a nebulised treatment for acute exacerbations in COPD patients in a hospital or home-care setting. The data from the study reported today will help inform dose selection in the Phase IIb trial, which it is currently expected to commence in early 2017.

The nebuliser bronchodilator market was worth about $1 billion in 2014 in the US.[3] RPL554 has potential as a novel drug for the maintenance therapy of COPD, and for patients with asthma and cystic fibrosis.

-Ends-

[1] The study was carried out in asthmatics as typically a dose response relationship to bronchodilators can be more accurately
established in this group of patients, compared to COPD patients

[2] Salbutamol is probably the most effective and widely used bronchodilator in asthma and COPD patients. The typical nebulised
salbutamol dose range is 2.5mg and sometimes 5mg. A 7.5mg dose of nebulised salbutamol is sometimes used to treat acute
exacerbations of COPD or asthma in the emergency department = a supramaximal dose

[3] IMS Consulting Group market research 2014

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

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.
