10 May 2016

Verona Pharma announces positive results from “add-on” Phase II trial with RPL554

RPL554 produced over 60% additional bronchodilation on top of standard of care bronchodilators in COPD patients

Data implies RPL554, alone or in combination with other bronchodilators, may reduce dyspnea, a major debilitating symptom of COPD

10 May 2016, Cardiff – Verona Pharma plc (AIM: VRP.L), the drug development company focused on first-in-class medicines to treat respiratory diseases, today announces highly positive headline data from a Phase IIa study that assessed the bronchodilator effect of nebulised RPL554 administered on top of salbutamol and ipratropium bromide in patients with COPD. RPL554 is a novel inhaled dual PDE3/PDE4 inhibitor with both bronchodilator and anti-inflammatory properties in the same molecule, which is currently in development as a nebulised treatment for acute exacerbations in chronic obstructive pulmonary disorder (COPD) patients in a hospital or for maintenance treatment in a home-care setting. Such patients typically require additional bronchodilation, despite being on approved COPD bronchodilator medications such as salbutamol, a beta2-agonist, and ipratropium bromide, an anti-muscarinic.

Highlights

- Primary objective of study met
- RPL554 produced a highly significant (p≤0.001) and a clinically meaningful additional (>60%) bronchodilation on top of the administered standard of care bronchodilators, salbutamol and ipratropium bromide
- The bronchodilator effects seen with the combinations were significantly (p≤0.001) larger than those of either salbutamol or ipratropium bromide alone, which were in turn all significantly greater than placebo Secondary objectives also met including
- The combination of RPL554 with salbutamol or ipratropium bromide caused a significant reduction (p=0.0002 and p=0.004 respectively) in trapped air in the lung (residual volume) as compared to salbutamol or ipratropium bromide alone
- Suggesting that RPL554 treatment may reduce dyspnea, a major debilitating symptom of COPD1
- Consistent with previous studies, RPL554 was well tolerated both alone and in combination • No effect on vital signs or ECG parameters
- No gastro-intestinal adverse events recorded

Professor Dave Singh of the Medicines Evaluation Unit, University of Manchester and Principal Investigator in this trial, commented:
“Achieving more than an additional 60% improvement in lung function on administration of RPL554 in moderate to severe COPD patients, already pre-treated with standard of care bronchodilators, is clinically highly significant, especially as the addition of RPL554 appears to be well tolerated.”

[1] Dyspnea (shortness of breath) in COPD patients is often associated with hyperinflation of the lungs resulting from a higher residual volume of air

Dr Jan-Anders Karlsson, the CEO of Verona Pharma, said:

“The robustly positive results from this well-controlled Phase IIa trial vindicate the rationale for developing a novel bronchodilator for treatment of patients with moderate to severe disease and acute exacerbations of COPD, who will typically already be on other bronchodilators, but require additional relief.”

“With the successful conclusion of this trial, we now believe we have the required data in hand from our Phase IIa studies to progress RPL554 confidently into a Phase IIb clinical trial programme. This will explore further its potential as a novel nebulised treatment for moderate to severe COPD patients in a hospital or home-care setting, a multi-billion dollar market.”

The nebuliser bronchodilator market was worth about $1 billion in 2014 in the US.2 RPL554 also has potential as a novel drug for the maintenance therapy of COPD, and for patients with asthma and cystic fibrosis.

Details of the clinical study
In this Phase II randomised, double blind, placebo controlled, six-way crossover study patients with moderate to severe COPD were randomised to receive a single dose from a blinded pressured metered dose inhaler (pMDI), containing either salbutamol (200 micrograms) or placebo followed by a single dose from a second blinded pMDI which contained ipratropium bromide (40 micrograms) or placebo. This was followed immediately by a single double blind dose of nebulised RPL554 (6mg) or placebo. Lung function was measured pre-dose and up to 12h post dose. The administered salbutamol and ipratropium bromide doses used in this study are standard approved doses of these medications for COPD patients. 30 subjects completed the study.

The study met its primary objective of a statistically significant increase in peak forced expiratory volume in one second, FEV1, ($p<0.001$) and a statistically significant increase in average FEV1 response over 8 hours ($p<0.001$). All treatments including RPL554 when given as single agents were significantly ($p<0.001$) better than placebo. RPL554 added over 60% additional bronchodilation on top of either salbutamol or ipratropium bromide.

Secondary outcome measures were change in lung volumes and airway conductance as well as safety. There was a marked, statistically significant reduction in trapped air in the lung (residual volume) indicating an improvement in lung hyperinflation. As with FEV1, the combination of RPL554 and either salbutamol or ipratropium was more effective than either agent alone. This should translate into an improvement in dyspnea (shortness of breath), a major debilitating symptom of COPD, and suggests that RPL554 is having an effect both in central and peripheral airways. RPL554 was well tolerated both alone and in combination with the other bronchodilators used in the study. There was no effect of RPL554 alone or in combination on vital signs or ECG parameters

The study was conducted at The Medicines Evaluation Unit (“MEU”), one of the UK's leading contract research organisations under principal investigator Professor Dave Singh.

The data from the study reported today will help inform the trial design for the forthcoming Phase IIb study, which it is currently expected to commence in early 2017.

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.
