European Respiratory Society
Annual Congress 2012

Abstract Number: 1438

Publication Number: P2155

Abstract Group: 5.1. Airway Pharmacology and Treatment

Keyword 1: Experimental approaches **Keyword 2:** Biomarkers **Keyword 3:** COPD - exacerbations

Title: Design and implementation of a multi-part, flexible protocol to assess the tolerability and pharmacodynamic effects of PUR118 in healthy subjects and COPD patients

Ms. Lorna 4921 Patrick lorna.patrick@quotientbioresearch.com [2], Dr. Alyson 4920 Connor alyson.connor@quotientbioresearch.com [2], Dr. Stuart 4922 Mair stuart.mair@quotientbioresearchh.com MD [2], Dr. Joanne 4923 Collier joanne.collier@quotientbioresearch.com MD [2], Ms. Molly 4924 Rosano MRosano@pulmatrix.com [1] and Dr. John 4925 Hanrahan jhanrahan@pulmatrix.com MD [1]. [1] Dept of Clinical Research, Pulmatrix Inc., Lexington, MA, United States, MA 02421 and [2] Exploratory Clinical Pharmacology, Quotient Clinical, Nottingham, Nottinghamshire, United Kingdom, NG11 6JS .

Body: Background PUR118, an inhaled cationic airway lining modulator (iCALM), is a simple host-targeted therapy to prevent and control respiratory exacerbations. An innovative protocol was developed to establish single and multi-dose tolerability and early pharmacodynamic/efficacy data for this therapy. Objective To develop and conduct a flexible clinical protocol to obtain maximum data to support the further investigation of PUR118. Methods Data required to progress PUR118 development were identified and structured into a 4 part dose-ranging protocol in healthy subjects (HS) and COPD patients (COPD): 1. Crossover safety and tolerability of 3 single dose levels vs. placebo (12 HS) 2. 3 ascending dose 14-day safety and tolerability vs placebo (24 HS) 3. Parallel 3 dose level multi-dose safety and tolerability plus exploratory assessment of inflammatory biomarkers (sputum, serum, exhalation) in COPD 4. Impact of ascending of single dose vs. no treatment on mucociliary clearance velocity by gamma scintigraphy The design was flexible to allow dose escalation or de-escalation. Selection of exploratory biomarkers was adaptive and not pre-determined in the protocol. Results A highly-flexible 4 part protocol was designed, submitted to and approved by the MHRA and EC in 27 days. Parts 1 and 2 in HS are complete, Parts 3 and 4 are ongoing. Preliminary results show PUR118 is well tolerated in HS and subjects with COPD. Conclusions This multi-part dose- ranging protocol, developed and implemented in the UK, demonstrates its regulatory framework embraces innovative, highly flexible, multi-part trials in early clinical development strategies.