The FLAGSHIP Study: A 12-week Phase II Study to Evaluate the Efficacy and Safety of AQX-1125 Following Exacerbations in Patients with Chronic Obstructive Pulmonary Disease (COPD) by Targeting the SHIP1 Pathway

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Design: Randomised, double-blind, placebo-controlled, parallel group, study of unstable COPD. Approximately 400 subjects with a recent exacerbation in two subsets: (1) at least 100 presenting for outpatient treatment and (2) at least 100 hospitalised for not more than 7 days and discharged within the last 3 days.

Rationale: Based on human and animal studies, AQX-1125, by activating SHIP1 and reducing the activation of several PIP3-mediated kinases, alters the migration and activation of various inflammatory cells, including neutrophils, mast cells and lymphocytes.

Oral AQX-1125 daily has been well tolerated for up to 10 consecutive days in normal healthy volunteers (NHV) and 7 consecutive days in NHVs challenged with inhaled lipopolysaccharide. Generally mild AEs were observed, similar to placebo.

Objective: Effect of oral AQX-1125 over 12 weeks on recurrent exacerbations as measured by EXACT (EXAcerbation of Chronic pulmonary disease Tool) in subjects with COPD following a recent exacerbation.
Secondary objectives are to evaluate effects on: COPD Assessment Tool (CAT) score; Pulmonary function (including FEV_1); Safety by AEs, physical examination, vital signs, ophthalmic examination, laboratory tests, weight, ECG, and concomitant medications; Plasma PK; Biomarkers of inflammation in blood and serum (including RNA expression)

Selected Inclusion criteria: Male or female aged ≥40 years; COPD for at least 18 months; Chronic productive cough for at least 3 months in each of the 2 years prior to screening; At least 2 documented exacerbations in previous 18 months; Post-bronchodilator FEV_1/ FVC ratio of <0.70 and predicted FEV_1 30%-80% of normal; Former smoker or current smoker (at least 10 pack years); Contraception if sexually active.

Selected Exclusion criteria: Other lung disease; Treatment with roflumilast or theophylline within 1 month; Lobar pneumonia within last 3 months; Hospitalisation for >7 days for current acute exacerbation, or intubation; Previous exacerbations required >3 weeks to stabilise.

Timelines: Results 1H2015

Conclusion: A potentially disease-modifying drug for unstable COPD is urgently needed. This study examines one such novel candidate in a new paradigm of COPD study – the unstable, frequent exacerbator, using a recently developed patient reported outcome.