Asthma is associated with mast cell activation and prostaglandin D₂ (PGD₂) generation. PGD₂ exerts pro-inflammatory activity via chemokine/cytokine receptor-homologous molecule expressed on Th2 cells (CRTh2). The activity of CRTh2 antagonist ARRY-502 was studied in mild to moderate asthmatic adults in a double-blind, placebo-controlled 4-week Phase 2a study. Enrolled patients were free of internal corticosteroids with an FEV₁ predicted of 60-85% and elevated T2-associated biomarkers. The primary endpoint was change from baseline FEV₁ compared to placebo. Secondary endpoints included additional spirometry evaluations, measures of asthma control and two quality of life (QOL) assessments. Safety was evaluated by incidence and severity of adverse events, vital signs, laboratory and EKG parameters. Potential participants were screened and randomized to receive 200 mg ARRY-502 (n = 93) or matching placebo (n = 91). FEV₁ improved 3.9% compared to placebo (p < 0.001, p = 0.001 and p = 0.007, respectively). Asthma and Rhinitis QOL improved compared to placebo (p = 0.012, p = 0.007, p = 0.007, respectively). Activity outcomes between ARRY-502 and placebo were numerically and statistically greater in T2 high (baseline) patients (FEV₁ = 6.7% vs. 0.008). These results support the activity of ARRY-502 in mild asthma patients and warrant further development.

**Main Inclusion and Exclusion Criteria**

**Inclusion Criteria**

- ≥16 years of age
- Asthma diagnosed ≥40 years of age
- Aerosol treatment ≤4 weeks
- Asthma Control Questionnaire (ACQ) ≤0.75
- No use of ICS or LABA within 4 weeks
- FEV₁ ≥50% predicted
- Compliance ≥80% of study medication

**Exclusion Criteria**

- Active or recent (within 1 year) malignancy
- Treatment with other CRTh2 antagonists
- History of anaphylaxis
- History of severe adverse events

**Patient Demographics**

- Gender (male): 58%
- Race (white): 61%
- Mean age range: 37 (19, 67) vs 35 (18, 48)
- Mean BMI range: 25.6 (18.3, 32) vs 24.8 (17.5, 34)
- Allergic Rhinoconjunctivitis (AR): 36%
- Mean MCAI range: 2.3 (1.1, 3.4) vs 2.4 (1.3, 4.0)
- Mean FEV₁ (% predicted): 73.2 (60.4) vs 71.6 (64.4)
- Mean FEV₁ reversibility: 25% (16.0) vs 25% (15.77)
- Median Exhaled Nitric Oxide (eNO) level: 5.6 (1.3, 9.8)
- Median FENO level: 49.4 (28.23) vs 47.1 (26.34)

**Patient Disposition**

- 99% completed (N=91)
- 96% completed (N=93)
- 96% completed (N=92)
- 96% completed (N=93)
- 96% completed (N=92)
- 96% completed (N=93)

**Study Design**

Randomized Placebo Controlled Study: 4 weeks oral dosing at 200 mg BD of ARRY-502 in mild to moderate persistent asthma with ICS washout

**Safety**

- Adverse Events: ARRY-502 group: 38% vs. placebo group: 49%
- Asthma exacerbations: 9 patients on placebo 4 patients on ARRY-502
- Treatment related AEs were reported in 5% of patients
- All were mild in severity
- No treatment-emergent SAEs in patients receiving ARRY-502
- ARRY-502 treatment was not associated with significant changes in safety signals

**ARY 502 is:**

- Activity in poorly controlled mild-to-moderate asthma with improvements in sputum, symptoms, and short-acting beta agonist use
- Well tolerated with the capacity to suppress clinically meaningful improvement in asthma exacerbations
- No notice in the presence of active Type 2 cytokine associated inflammation consistent with its mechanism of action

These results support the activity of ARRY-502 in mild asthma patients and warrant further development.