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Title: Efficacy and safety of BI 671800, an oral CRTH2 antagonist in controller naïve patients with poorly-controlled asthma

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Body: Background BI 671800 is an antagonist of the PGD2 receptor, CRTH2. PGD2 stimulates bronchoconstriction and allergic airway inflammation in animal models. Inhibition of CRTH2 may reduce airway inflammatory cells, IL -4, -5, -13 production, serum IgE and airway hyper reactivity. Objective To investigate the efficacy and safety of BI 671800 versus placebo and fluticasone proprionate (FP) in controller-naïve patients with poorly-controlled asthma. Methods Adults with asthma (FEV_1 60-85% and ACQ >= 1.5) were enrolled in a randomized, double-blind, parallel arm study comparing BI 671800 50, 200 or 400 mg bid with matching placebo bid or FP 110 µg bid for six weeks. The primary study outcome was change in trough FEV_1. Results 388 patients were randomised (mean age 37.4 years, FEV_1 72.7%, ACQ 2.29). Changes from baseline in adjusted mean (SE) trough morning FEV_1% predicted versus placebo were 3.08% (1.65), 3.59% (1.60) and 3.98% (1.64) for 50, 200 and 400 mg BI 671800 bid respectively, and 8.61% (1.68) for FP (one-sided $p < 0.025$ for 200 and 400 mg bid and FP), achieving the primary efficacy outcome for the study. Change in ACQ mean (SE) scores versus placebo were 0.07 (0.11), -0.08 (0.11) and -0.06 (0.11) for 50, 200 and 400 mg BI 671800 bid respectively, and -0.33 (0.12) for FP (one sided $p < 0.025$ for FP). No significant imbalance in adverse events, or differences in vital signs or laboratory

assessments were observed. Conclusion Treatment with BI 671800 was associated with a significant improvement in FEV_1 in controller-naïve patients with poorly-controlled asthma. BI 671800 was well tolerated at total daily doses up to 800 mg for 6 weeks.