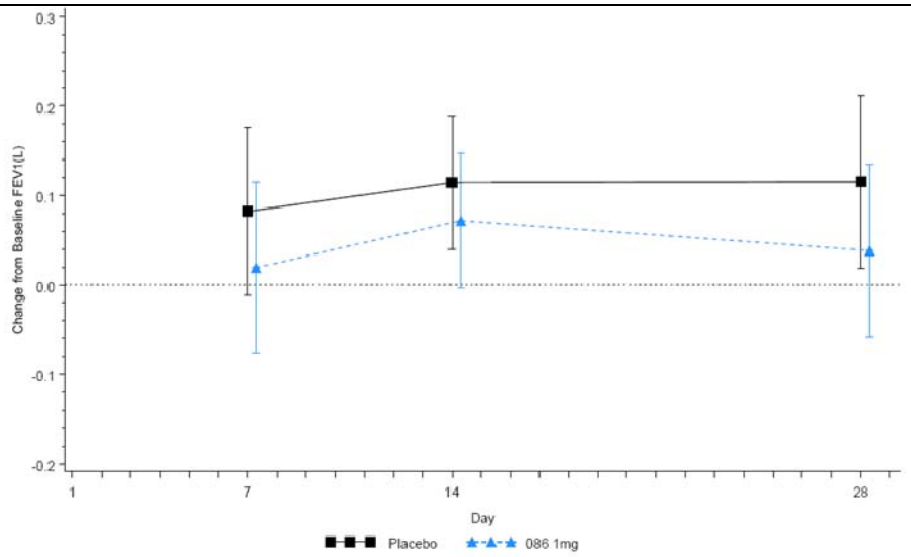
The study listed may include approved and non-approved uses, formulations or treatment regimens. The results reported in any single study may not reflect the overall results obtained on studies of a product. Before prescribing any product mentioned in this Register, healthcare professionals should consult prescribing information for the product approved in their country.

Study No: SIG112851	
Title: A randomised, placebo-controlled, two-way crossover study to determine the efficacy of repeat inhaled doses of GW870086 on FEV_1 in mild to moderate asthmatics.	
Rationale: This study evaluated the efficacy and safety of the novel inhaled corticosteroid GW870086 in mild-to-moderate asthmatics after 4 weeks of treatment using a dose that was deemed safe and was predicted to have a significant effect on forced expiratory volume in 1 second (FEV_1).	
Phase: IIa.	
Study Period: 09 JUL 2009 – 18 DEC 2009.	
Study Design: A randomised, placebo-controlled, two-way crossover repeat dose study.	
Centres: Eight study centres in Germany.	
Indication: None.	
Treatment: Following a 2-week run-in period, each subject was randomised to take part in two treatment sessions of 27 –2 days each, receiving inhaled GW870086 1 mg or placebo once daily.	
Objectives: To determine the efficacy of repeat inhaled doses of GW870086 once daily for 27 days on FEV_1 in mild to moderate asthmatics, compared with placebo.	
Statistical Methods: Based on estimates of within-subject standard deviation from previous studies (0.213), a sample size of 30 subjects would have 94% power to detect a difference of 0.2 L in change from baseline FEV_1 on Day 28 between GW870086 and placebo at the 5% two-sided significance level. To ensure approximately 30 subjects completed the study, 36 subjects were recruited. All FEV_1 data were analysed together using a repeated measures mixed effects analysis of variance (ANOVA). An estimate of the treatment difference between GW870086 and placebo on each day was calculated along with the associated 95% confidence interval (CI). The change from baseline daily pre-dose morning (AM) peak expiratory flow rate (PEFR) averaged for each subject for each week of the treatment period was analysed using mixed effects ANOVA. Baseline was defined as the average of the AM PEFR assessments on the 7 days prior to randomisation. Evening PEFR was analysed similarly. Total daily rescue was the number of puffs of salbutamol in a 24-h period. The total number of puffs of salbutamol per subject was calculated for each week (run-in and Weeks 1–4). A descriptive summary of these data was presented. Safety and other data were summarised and listed by treatment group.	
Study Population: Steroid-naïve non-smoking male and female (of non-childbearing potential) subjects aged 18–65 years, inclusive, with mild to moderate asthma. Subjects had FEV_1 of 40–85% predicted and had normal liver function test results. Subjects also had to show run-in daily asthma symptom scores of ‡1, regular salbutamol use and PEFR variability of ‡20%. Subjects whose asthma medication had changed during the run-in were to be excluded.	
Number of Subjects:	Total
Planned N	36
Dosed N	36
Completed n (%)	34 (94)
Total Number Subjects Withdrawn N (%)	2 (6)
Withdrawn due to Adverse Events n (%)	1(3)
Withdrawn at investigator's discretion n (%)	1(3)
Demographics	Total
N (All Subjects)	36
Females: Males	16: 20
Mean Age in years (standard deviation)	49.2 (11.12)
Mean Weight in kg (standard deviation)	78.66 (13.828)
White n (%)	36 (100)
Efficacy: Statistical analysis of change from baseline FEV_1 by day is summarised in the figure below. GW870086 1 mg once daily appeared to have little effect on FEV_1 while there was a moderate positive placebo effect at Day 14 and Day 28.	



A *post-hoc* exploratory analysis indicated that the placebo effect was more notable in Period 1, and in general there was a period effect with subject responses positive in Period 1 alone. Nevertheless, the placebo response was larger than the response to GW870086 1 mg at the 28 day time point, irrespective of period.

Peak expiratory flow rate: there was a paradoxical decrease from baseline after treatment with GW870086 1 mg compared with placebo for both AM and evening (PM) measures. The data showed no consistent pattern.

Rescue medication usage: The two treatment regimens resulted in similar salbutamol use over the 4 week treatment periods: the median number of puffs with both treatments was approximately 11–12 per week. Exploratory analysis found that salbutamol usage was similar between active and placebo groups in Period 1; however, in Period 2 subjects randomised to GW870086 used more rescue medication than the placebo group.

Safety results: Adverse event and serious adverse event (SAE) data were recorded from the start of investigational product and until the follow-up contact. Any SAEs related to study participation or related to a GSK concomitant medication were to be recorded from the time a subject consented to participate in the study up to and including the follow-up contact. The most frequently reported AEs are summarised below.

Adverse Events:	Placebo	GW870086 1 mg	Total
N (All Subjects)	36	35	36
No. subjects with AEs n (%)	13 (36)	10 (29)	19 (53)
Most Frequent AEs (more than one subject in the study)			
Headache	6 (17)	3 (9)	8 (22)
Nasopharyngitis	4 (11)	2 (6)	6 (17)
Depression	1 (3)	1 (3)	2 (6)
Oropharyngeal pain	1 (3)	1 (3)	2 (6)

Serious Adverse Events, n (%) [n considered by the investigator to be related, possibly related, or probably related to study medication]:

Serious Adverse Events:	Placebo	GW870086 1 mg	Total
N (All Subjects)	36	35	36
No. subjects with SAEs n (%)	1 (3) [0]	0	0
Peripheral vascular disorder	1 (3) [0]	0	0