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<b>Study No.:</b> FFA112202
<b>Title:</b> A Multi-Centre, Randomized, Double Blind Cross-Over Study to Assess the Non-Inferiority of GW685698X 200mcg Once Daily and 100mcg Twice Daily in Adult and Adolescent Patients with Asthma
<b>Rationale:</b> This trial was designed to assess for non-inferiority of trough FEV <sub>1</sub> (forced expiratory volume in one second) of once daily GW685698X compared to twice daily GW685698X. Fluticasone propionate was included for assay sensitivity and as an active control for comparison against placebo.
<b>Phase:</b> IIb
<b>Study Period:</b> 09 October 2008 – 17 March 2009
<b>Study Design:</b> This was a multi-center, randomized, double blind, cross-over study
<b>Centres:</b> 16 centers in the United States
<b>Indication:</b> Asthma
<b>Treatment:</b> Subjects meeting eligibility criteria were randomized to one of 12 treatment sequences: <ul style="list-style-type: none"> <li>• 6 sequences contained GW685698X 200 mcg once daily, GW685698X 100 mcg twice daily and placebo</li> <li>• 6 sequences contained fluticasone propionate 200 mcg once daily, fluticasone propionate 100 mcg twice daily and placebo, each delivered by a DISKUS.</li> </ul>
<b>Objectives:</b> The purpose of this study was to assess for non-inferiority of GW685698X 200 mcg of trough FEV <sub>1</sub> (forced expiratory volume in one second) of once daily GW685698X compared to twice daily GW685698X 100mcg in adolescent and adult subjects 12 years of age and older with asthma.
<b>Primary Outcome/Efficacy Variable:</b> The primary efficacy endpoint was the trough (pre- rescue bronchodilator) FEV <sub>1</sub> at the end of each treatment period.
<b>Secondary Outcome/Efficacy Variable(s):</b> There were no other efficacy endpoints assessed in this study.
<b>Statistical Methods:</b> The primary efficacy endpoint of trough FEV <sub>1</sub> at day 28 of each treatment period was analyzed using mixed effects analysis of covariance (ANCOVA) with fixed effects of treatment, period, sex and age. Subject was fitted as a random effect and the period baseline measurement was included as part of a bivariate response.
<b>Study Population:</b> A total of 327 male and female subjects were screened, of which 190 were randomized. All 190 randomized subjects received at least one dose of study medication and comprised the Intent-to-Treat Population. Male or female subjects were eligible for entry if they were 12 years of age or older. Eligible female subjects must have been non-pregnant and non-lactating, and females of childbearing potential committed to consistent and correct use of an acceptable method of birth control. Eligible subjects had persistent asthma as defined by the National Institutes of Health, with a $\geq 12\%$ and $\geq 200\text{mL}$ reversibility of FEV <sub>1</sub> and an FEV <sub>1</sub> of 40%-85% of the predicted normal value. Subjects must have been using short-acting beta2-agonist bronchodilator

	Novel DPI	FP DISKUS	Total
Number of Subjects:	147	43	190
Planned, N	84	24	108
Randomised, N	147	43	190
Completed, n (%)	134 (91)	41 (95)	175 (92)
Total Number Subjects Withdrawn, N (%)	13 (9)	2 (5)	15 (8)
Withdrawn due to Adverse Events n (%)	0	0	0
Withdrawn due to Lack of Efficacy n (%)	5 (3)	1 (2)	6 (3)
Withdrawn for other reasons n (%)	8 (5)	1 (2)	9 (5)
<b>Demographics</b>			
N (ITT)	147	43	190
Females: Males	87:60	21:22	108:82
Mean Age, years (SD)	31.4 (15.30)	35.2 (16.03)	32.3 (15.51)
White, n (%)	90 (61)	22 (51)	112 (59)
Asian, n (%)	2 (1)	1 (3)	3 (2)
American Indian or Alaska Native, n (%)	1 (<1)	0	1 (<1)
African American/African Heritage & American Indian or Alaska Native and White, n (%)	1 (<1)	0	1 (<1)
African American/African Heritage, n (%)	50 (34)	20 (47)	70 (37)
Native Hawaiian or other Pacific Islander	1 (<1)	0	1 (<1)
African American/African Heritage & White	2 (1)	0	2 (1)
<b>Primary Efficacy Results:</b>			
	Placebo	FP 200mcg OD	FP 100mcg BD
N	187	42	43
Day 28 FEV <sub>1</sub> (L)			
LS Mean	2.605	2.693	2.737
SE	0.0434	0.0535	0.0533
LS Mean Change from period baseline	0.112	0.199	0.244
SE	0.0186	0.0365	0.0361
Difference from Placebo			
LS Mean Difference		0.087	0.132
95% CI		(0.014, 0.161)	(0.059, 0.205)
p-value		0.020	<0.001
<b>Secondary Outcome Variable(s):</b>			
There were no other efficacy endpoints assessed in this study.			
An on therapy adverse event (AE) was defined as an AE with onset on or after the start date of study medication but not later than one day after the last date of study medication.			
<b>Most Frequent Adverse Events – On-Therapy</b>			
	Placebo	FP 200mcg OD	FP 100mcg BD

N	187	42	43
Subjects with any AE(s), n(%)	26 (14)	2 (5)	3 (7)
Upper respiratory tract infection	2 (1)	0	0
Nasopharyngitis	1 (<1)	0	1 (2)
Sinusitis	1 (<1)	0	0
Headache	2 (1)	0	0
Pharyngitis	2 (1)	0	0
Nausea	1 (<1)	0	1 (2)
Cellulitis	2 (1)	0	0
Dysphonia	0	1 (2)	0
Heart rate increased	0	1 (2)	0
Arthralgia	0	0	1 (2)
<b>Serious Adverse Events - On-Therapy</b>			
No subject had a serious adverse event during this study.			

**Conclusion:**

The data presented includes a partial summary of the placebo and fluticasone propionate treatment arms. A conclusion will be included with the trial results in the full study summary.

**Publications:** None