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.: FFR30008
Title: A Randomized, Double-Blind, Placebo-Controlled, Parallel-Group, Multicenter Study to Evaluate the Safety and Efficacy of Once-Daily, Intranasal Administration of GW685698X Aqueous Nasal Spray 50mg* and 100mcg* for 12 Weeks in Pediatric Subjects Ages 2 to <12 Years with Perennial Allergic Rhinitis (PAR)
Rationale: GW685698X (fluticasone furoate) is a novel corticosteroid with potent glucocorticoid activity. Because of the well-established efficacy and tolerability of corticosteroids in the treatment of allergic rhinitis, fluticasone furoate is being developed as a nasal spray for perennial allergic rhinitis (PAR).
Phase: III
Study Period: 23 February 2005 to 23 November 2005
Study Design: Multicenter, 12-week, double-blind, randomized, parallel-group, placebo-controlled trial. There was a 7- to 14-day screening period during which baseline symptoms were collected. A follow-up phone call was made 3 to 5 days after the last visit.
Centres: A total of 61 centers enrolled subjects: 39 in the United States, 5 in Argentina, 5 in Italy, 4 in Slovakia, 3 in Mexico, 3 in Finland, and 2 in Chile. Two additional sites (one in the US and one in Finland) screened subjects but no subjects were randomized.
Indication: Perennial allergic rhinitis
Treatment: *GW685698X aqueous nasal spray 110mcg (actual), 55mcg (actual); Drug content of Fluticasone Furoate Nasal Spray was approximated at 25mcg/spray in all Phase 3 clinical trial documentation pending confirmation from final batch and stability testing. Final testing and analyses determined one spray to contain 27.5mcg of fluticasone furoate, equating to 55mcg for the recommended pediatric starting dose of one spray administered to each nostril and if needed increasing to 110mcg given two sprays administered to each nostril. Subjects were randomized to a 12-week treatment with once-daily (QD) fluticasone furoate nasal spray 55mcg, fluticasone furoate nasal spray 110mcg, or vehicle placebo nasal spray.
Objectives: To compare the safety and efficacy of fluticasone furoate nasal spray 55mcg and 110mcg QD versus vehicle placebo nasal spray over a period of 12 weeks and to determine the optimal dose in pediatric subjects ages 2 to <12 years with PAR. To characterize the systemic exposure to fluticasone furoate within the doses under study in pediatric subjects ages 2 to <12 years with PAR over a period of 12 weeks.
Primary Outcome/Efficacy Variable: Mean change from baseline over the first 4 weeks of treatment in daily reflective total nasal symptom scores (rTNSS) in subjects ages 6 to <12 years. The total nasal symptom score (TNSS) is the sum of the four individual symptom scores for rhinorrhea, nasal congestion, nasal itching, and sneezing where each symptom is scored on a scale of 0 to 3. The rTNSS is a rating of the severity of symptoms over the previous 12 hours and was performed in the morning (AM rTNSS) and evening (PM rTNSS). The daily rTNSS is the average of the AM rTNSS and PM rTNSS assessments.
Secondary Outcome/Efficacy Variables: Key Secondary: • Mean change from baseline over the first 4 weeks of treatment in AM, pre-dose instantaneous total nasal symptom scores (iTNSS) in subjects ages 6 to <12 years; • Overall evaluation of response to therapy for the first 4 weeks of the treatment period in subjects ages 6 to <12 years. The Overall Evaluation of Response to Therapy was based on a 7-point categorical scale where the subjects (and/or subject's parent/guardian) rated their perception of the change or lack of change in their allergic symptoms after 4 weeks of treatment. The seven categories were: significantly improved, moderately improved, mildly improved, no change, mildly worse, moderately worse, and significantly worse.
Statistical Methods: The primary and secondary efficacy analysis method was the pairwise comparison of treatment groups (each dose of fluticasone furoate vs. placebo) using the analysis of covariance (ANCOVA) with adjustments for baseline value, country, age, and gender. Efficacy data were analyzed for a subset of subjects 6 to <12 years of age in the Reduced Intent-to-Treat (RITT) Population. The ITT Population was defined as all randomized subjects who received at least one dose of study drug. The RITT Population excluded all subjects at one U.S. site (because of study conduct irregularities based on the standard GSK monitoring and auditing practices). The treatment comparison for the key secondary efficacy endpoint of overall evaluation of response to therapy data was analyzed using a logistic regression analysis model adjusting for age, gender, country, and treatment. To support the efficacy findings, similar analyses were performed for the primary and key secondary endpoints on the RITT Population (subjects 2 to <12

years of age).
The multiple comparisons between each of the two active doses and placebo for the primary efficacy endpoint were performed in sequence (fluticasone furoate 110mcg vs. placebo, and then fluticasone furoate 55mcg vs. placebo) to control the overall significance level of 0.05 on the primary efficacy endpoint.
No multiplicity adjustments were made on key or other secondary efficacy endpoints. For all secondary efficacy endpoints, any p-value $\leq$0.05 for the comparison of fluticasone furoate 110mcg vs. placebo and fluticasone furoate 55mcg vs. placebo was identified as (nominally) significant without regard to any issues of multiplicity.
A total of 432 subjects (144 subjects per treatment arm) ages 6 to <12 years were required for this study. The standard deviation for the mean change from baseline in daily rTNSS over the first 4 weeks of the treatment period was assumed to be 2.6, based on a previous GlaxoSmithKline (GSK) allergy rhinitis study. Using a two-sample t-test with a two-sided significance level of 0.05, the chosen sample size provided 90% power to detect a difference of 1.0 between active treatment and placebo.
The study planned an enrollment of approximately 144 subjects ages 2 to <6 years (48 per treatment group), approximately 25% of the total randomized subjects, so as to provide sufficient safety data and supportive efficacy data in this younger age group.
The study randomization was stratified by country and age group (approximately 25% in children ages 2 to <6 years and 75% in children ages 6 to <12 years).
Safety data were summarized based on the ITT Population. Study population and safety data were also summarized by age group (2 to <6 years and 6 to <12 years), whenever appropriate. Urinary cortisol (UC) data (subjects 6 to <12 years of age) were also analyzed for the UC Population, which excluded subjects whose urine samples were considered to have confounding factors that could affect the interpretation of the results. The Pharmacokinetic (PK) Population included all subjects who provided plasma samples for measurement of fluticasone furoate concentration.

Study Population: Male and female subjects 2 to <12 years of age with a diagnosis of PAR.

Number of Subjects (ITT):	Placebo	Fluticasone Furoate (FF) 55mcg	Fluticasone Furoate (FF) 110mcg
Planned, N	192	192	192
Ages 6 to <12 years	144	144	144
Ages 2 to <6 years	48	48	48
Randomized, N	188	185	185
Ages 6 to <12 years	147	145	142
Ages 2 to <6 years	38	40	42
Ages ≥12	3 (2)	0	1 (<1)
Completed, n (%)	161 (86)	163 (88)	168 (91)
Total Number Subjects Withdrawn, N (%)	27 (14)	22 (12)	17 (9)
Withdrawn due to Adverse Events, n (%)	8 (4)	6 (3)	2 (1)
Withdrawn due to Lack of Efficacy, n (%)	0	0	1 (<1)
Withdrawn for other reasons, n (%)	19 (10)	16 (9)	14 (8)
Demographics:	Placebo	FF 55mcg	FF 110mcg
N (ITT)	188	185	185
Females: Males, n	81:107	84:101	83:102
Mean Age, years (SD)	7.9 (2.47)	7.7 (2.59)	7.4 (2.50)
White, n (%)	141 (75)	136 (74)	131 (71)
Primary Efficacy Results: Daily rTNSS: RITT: 6 to <12 years			
	Placebo N=147	FF 55mcg N=144	FF 110mcg N=140
Weeks 1-4, n	145	144	140
LS mean change (SE)	-3.41 (0.24)	-4.16 (0.24)	-3.86 (0.24)
LS mean difference vs. placebo	---	-0.754	-0.452
95% CI for the mean difference vs. placebo	---	-1.24, -0.27	-0.95, 0.04
p-value vs. placebo	---	0.003	0.073

Key Secondary Outcome Variables: RITT: 6 to <12 years			
AM Pre-dose iTNSS			
Weeks 1-4, n	145	144	140
LS mean chg (SE)	-2.87 (0.24)	-3.62 (0.24)	-3.52 (0.23)
LS mean difference vs. placebo	---	-0.751	-0.651
95% CI for the mean difference vs. placebo	---	-1.24, -0.27	-1.14, -0.16
Overall Evaluation of Response to Therapy			
Response, n (%)	138	128	127
Significantly improved	27 (20)	40 (31)	33 (26)
Moderately improved	55 (40)	46 (36)	41 (32)
Mildly improved	31 (22)	29 (23)	36 (28)
No change	18 (13)	12 (9)	15 (12)
Mildly worse	3 (2)	0	1 (<1)
Moderately worse	3 (2)	0	1 (<1)
Significantly worse	1 (<1)	1 (<1)	0
Safety Results (ITT Population): All AEs occurring between Visit 1 (Screening) and Visit 9/Early Withdrawal were collected. On-therapy AEs were defined as events with an onset date the same as or after treatment start date but prior to or the same as the treatment stop date + 1. In addition, a follow-up contact was made to all subjects 3 to 5 days after study completion (Visit 9/Early Withdrawal) to assess post-treatment AEs.			
Most Frequent Adverse Events – On-Therapy	Placebo N=188	FF 55mcg N=185	FF 110mcg N=185
Subjects with any AE(s), n (%)	111 (59)	103 (56)	109 (59)
Headache	23 (12)	20 (11)	21 (11)
Nasopharyngitis	20 (11)	17 (9)	16 (9)
Cough	10 (5)	8 (4)	13 (7)
Pyrexia	7 (4)	13 (7)	12 (6)
Epistaxis	11 (6)	11 (6)	12 (6)
Pharyngolaryngeal pain	13 (7)	13 (7)	10 (5)
Bronchitis	11 (6)	11 (6)	8 (4)
Pharyngitis	4 (2)	4 (2)	7 (4)
Vomiting	3 (2)	3 (2)	7 (4)
Upper respiratory tract infection	4 (2)	3 (2)	6 (3)
Sinusitis	5 (3)	6 (3)	4 (2)
Influenza	3 (2)	5 (3)	4 (2)
Asthma	8 (4)	5 (3)	1 (<1)
Pain in extremity	3 (2)	5 (3)	0
Tonsillitis	3 (2)	5 (3)	4 (2)
Scab	0	2 (<1)	5 (3)
Diarrhea	5 (3)	4 (2)	4 (2)
Serious Adverse Events - On-Therapy n (%) [n considered by the investigator to be related to study medication]			
Subjects with any SAEs, n (%) - Includes both fatal and non-fatal events	0	1 (<1) [0]	1 (<1) [0]
Peritonitis	0	1 (<1) [0]	0
Appendicitis	0	0	1 (<1) [0]
Subjects with fatal SAEs, n	0	0	0

Conclusion:
See publications below

Publications:

Máspero JF, Rosenblut A, Finn A, Lim J, Wu W, Philpot E. Safety and efficacy of fluticasone furoate in pediatric patients with perennial allergic rhinitis. Otolaryngol Head Neck Surg. 2008;138(1): 30 - 37.

Máspero JF, Rosenblut A, Finn A, Lim J, Wu W, Faris M, Philpot E. Once-daily fluticasone furoate nasal spray (FF) is safe and effective in the long-term treatment of perennial allergic rhinitis (PAR) in children ages 2 to 11 years. J Allergy Clin Immunol. 2007;119(1): S304 (abstract).

Máspero J, Rosenblut A, Finn A, J Lim J, Wu W, Philpot E. Safety of fluticasone furoate* nasal spray in children with perennial allergic rhinitis (*USAN approved name). Allergy 2007;62(Suppl. 83): 381 (abstract).

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