2 SYNOPSIS

NAME OF COMPANY: **Allergopharma Joachim Ganzer KG, Reinbek** **NAME OF FINISHED PRODUCT:** Phleum Cocktail **NAME OF ACTIVE INGREDIENT(S):** Cocktail of recombinant major allergens of Phleum	**INDIVIDUAL STUDY TABLE REFERRING TO PART IV OF DOSSIER** **Volume:** **Page:**	**(FOR NATIONAL AUTHORITY USE ONLY)**

Title:

A double-blind placebo-controlled dose-response study for evaluation of safety and efficacy of immunotherapy with a cocktail of recombinant major allergens of Timothy Grass Pollen (Phleum pratense) adsorbed to aluminium hydroxide in patients with IgE-mediated allergic rhinitis/rhinoconjunctivitis with or without bronchial asthma

Trial No. Follow-up Al0701rP**;** Trial Protocol Amendment 3 dated January 22, 2008

Investigator:

[redacted]

Study centre:

[redacted]

Publications:

Not applicable

Study period (Follow-up): IC-Testing from January 12, to February 20, 2009 Diaries evaluated in the six weeks between May 27, to July 7, 2008 Patients were offered three years of therapy after study end.	**Clinical phase:** II

Objectives:

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The aim of this study is to measure the tolerance and efficacy of 4 concentrations of a cocktail of recombinant major allergens of timothy grass (Phleum pratense) for specific immunotherapy (SIT) in grass pollen allergic patients suffering from allergic rhinitis / rhinoconjunctivitis with or without asthma (GINA I and II).

Methodology:

This study is an open label single arm study in which the patients who had formally been in a verum treatment arm were asked to repeat the IC-Test. The different concentrations of the IC-Test solutions were applied under blinding. Additionally, all patients were asked to keep a diary during the height of the 2008 pollen season for the purpose of calculating the symptom- and medication score (SMS).

Number of subjects:

Of the 40 patients in the former verum treatment group, 35 repeated the IC-Test during the follow-up. Additionally 9 of the 10 patients in the former placebo treatment group filled out a SMS diary. The follow-up thus included 47 patients.

Diagnosis and criteria for inclusion:

No additions were made.

Test product, dose and mode of administration, batch no.:

Allergenlyophylisat
for the Provocation test 6-grass pollen: [redacted]
Solution for lyoph. Test allergen:

Duration of treatment:

The follow-up treatment took place at one visit during which the IC-Test was performed.
All patients are being offered an active treatment of 3 years (acc. to WHO-recommendation)

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Reference therapy, dose and mode of administration, batch no.:

Not applicable

Criteria for evaluation:

Efficacy:

Repetition of the Secondary Endpoint:
Changes of the Early and Late Phase Reaction in specific IC test with natural allergen before and at the end of the double-blind, placebo-controlled phase after grass pollen season

Safety:

AEs and vital signs were documented.

Statistical methods:

Early and Late Phase Reactions in specific IC test will be determined 15 min. and 6 hours after application of the five concentrations of the natural allergen.
Diary evaluation will be done on the basis of documented symptoms and medication intake.
All evaluation is based on descriptive statistics and graphical output-

Summary and Conclusions:

Efficacy:

At screening as well as in the follow-up phase of this study for the patients who had received verum before the follow-up, it can clearly be seen that both the mean wheal and mean erythema sizes increase with increasing concentrations of allergens. This holds for the early and late phase reactions. Further, the mean wheal and mean erythema sizes were larger during the follow-up than at screening.

The evaluation of the SMS diaries was inconclusive.

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Safety: There were a total of 4 AEs during the follow-up visit distributed fairly evenly over the former verum treatment arms with one AE in the former treatment arm I, zero in former treatment arm 2, two in former treatment arm 3 and one in former treatment arm 4. Thus all doses of the IC-Test were well tolerated.

Vital signs were also taken as a safety measure. No laboratory tests were done in the follow-up.

Conclusions: Treatment with even very high doses of a cocktail of recombinant major allergens of timothy grass has been shown to be safe. The early phase reaction of the IC-Test seems to favour the former treatment arm 2 in terms of the smallest reactions. In the late phase reactions at higher concentrations of the IC-Test, the smaller reactions appear to occur in the former treatment arm 3.