2. SYNOPSIS

Name of Sponsor/Company: Protalix Biotherapeutics 2 Snunit Street Science Park POB 455 Carmiel 20100, Israel Tel: 972-4-988-9488 Fax: 972-4-988-9489	Individual Study Table Referring to Part of the Dossier Volume: Page:	*(For National Authority Use only)*
Name of Finished Product: Taliglucerase alfa [plant cell expressed recombinant human glucocerebrosidase (prGCD)]		
Name of Active Ingredient: Taliglucerase alfa		

Title of Study: A Multicenter Extension Study of Taliglucerase alfa in Adult Subjects with Gaucher Disease

Investigators:

Site #	Principal Investigators	Affiliations
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*Deceased

Study Center(s): 9 study centers from 7 countries

Publication (reference): Not applicable

Studied Period (years): Date of first enrolment: 30Nov2011 Date of last completed: 08Jul2014	**Phase of Development:** Phase 3B

Objectives: The objective of study PB-06-007 was to further extend the assessment of the efficacy and safety of taliglucerase alfa in adult patients ≥18 years old with Gaucher disease who completed treatment in Protocol PB-06-001 and Protocol PB-06-003.

Methodology: This multi-center, extension trial was designed to extend the assessment of the efficacy and safety of taliglucerase alfa in adult patients (≥18 years old) with Gaucher disease, who completed 9 months of treatment in Study PB-06-001, and 30 months of treatment in Study PB-06-003 and further treatment for a maximum of 21 months or until taliglucerase alfa is commercially available at the discretion of the Sponsor. Patients received taliglucerase alfa every two weeks by IV infusion. Home therapy was implemented or continued, when feasible, for patients who were able to tolerate the infusions well based on approval of the investigator and the Medical Director.

Number of Patients (Planned and Analyzed): After completing Studies PB-06-001 and PB-06-003, 19 patients were enrolled into this extension study. Two (2) patients discontinued from the study, one (30 units/kg, [redacted]) due to a personal reason (difficulty taking sick leave from work for the infusions) after having received 5 infusions and one (60 units/kg, [redacted]) lost to follow up after having received 4 infusions. Seventeen (17) patients completed the study.

Diagnosis and Main Criteria for Inclusion:

- Successful completion of Studies PB-06-001 and PB-06-003
- Provided signed informed consent

Test Product, Dose and Mode of Administration: Taliglucerase alfa was administered at the same volume and infusion rate administered at the last treatment in protocol PB-06-003, every 2 weeks (+/- 4 days). The tolerability of the infusion was determined by signs and symptoms during the infusion and for one hour after the infusion in the clinic. The infusion rate could be adjusted according to individual subject symptoms and signs. Study drug was administered in the clinic or infusion center unless the Medical Director and Investigator approved home care based on the clinical condition of the subject and local practices and regulations.

Duration of Treatment: 21 months

Reference Therapy, dose and mode of administration, batch number: Not applicable

Criteria for Evaluation:
Efficacy Endpoint:

1. Spleen volume
2. Liver volume
3. Platelet count
4. Hemoglobin
5. Biomarkers: chitotriosidase and/or pulmonary and activation-regulated chemokine (PARC/CCL18)
6. Quantitative Chemical Shift Imaging (QCSI) in the subset of patients who had this test performed in Study PB-06-001
7. Bone mineral density by DEXA (dual-energy x-ray absorptiometry) in the subset of patients who had this test performed in Study PB-06-001

Safety Endpoint:

1. Adverse events
2. Vital signs
3. Physical examination
4. Concomitant medications
5. Laboratory test results
   - Hematology
   - Biochemistry
   - HbA1c (valid for subjects coming from PB-06-002 Study)
   - Protein Electrophoresis (valid for subjects coming from PB-06-002 Study)
   - Urinalysis
   - Anti-taliglucerase alfa antibodies
6. Echocardiogram
7. Hypersensitivity reactions: Patients experiencing severe or recurrent hypersensitivity reactions are analyzed for IgE antibody formation, Tryptase and complement.
8. Bone events

Statistical Methods: Descriptive statistics for continuous variables, sample size (n), mean and its standard error, standard deviation, median and range are presented; for categorical variables, count and percentages are presented.

The time points in the summary tables were counted continuously from studies PB-06-001 (9 months), PB-06-003 (30 months) and PB-06-007 (21 months), and denoted by months relative to baseline, 12 months (1 year), 24 months (2 years), 30 months (2.5 years), 36 months (3 years), 42 months (3.5 years), 48 months (4 years), 54 months (4.5 years) and 60 months (5 years).

No inferential statistics was performed for testing the change from baseline and/or for comparing between or among treatment groups.

Summary – Conclusions

Efficacy Results: The efficacy results of this extension study provide evidence that taliglucerase alfa maintains effectiveness for the treatment of adult patients with Gaucher disease for as long as 60 months. After 60 months of treatment, all 5 patients who developed IgG antibody to taliglucerase alfa during Study PB-06-007 had reductions in MN spleen volume (40% to 76%) and in MN liver volume (8% and 42%), as well as a mean increase in hemoglobin level which ranged between 5% - 27%. Additionally, 4 of the 5 patients had platelet count increases from baseline between 46% and 141% after 60 months of treatment, while one patient 30-008 with a low baseline (86,000/mm^3) platelet count showed a 25% decrease (22000/mm^3) after 60 months of treatment, however, this patient's hemoglobin level increased 5.6% from baseline at Month 60. The investigator did not initiate any change in treatment and all five patients completed the study.

The sensitivity analyses demonstrated that patients who discontinued from the study had no significant impact on the long-term primary efficacy findings.

Safety Results: Taliglucerase alfa was well tolerated through 5 years of administration in Gaucher disease patients naïve to enzyme replacement therapy.

Conclusion: Study PB-06-007 is an extension of two consecutive Phase 3 studies (PB-06-001 and PB-06-003) evaluating the efficacy and safety of taliglucerase alfa in adult patients with Gaucher disease naïve to enzyme replacement therapy. Nineteen (19) patients initially received 9 months of treatment from Study PB-06-001, a double-blind, randomized study comparing two dose levels of taliglucerase alfa, 30 and 60 units/kg, and continued in a 30 months extension Study PB-06-003 and an additional 21 months extension Study PB-06-007.

Data from treatment naïve adult patients treated with 30 units/kg and 60 units/kg of taliglucerase alfa demonstrate tolerability and efficacy as determined by clinically relevant parameters (e.g., organ volume size, hematological parameters, biomarker measurements).

Overall, these data indicate that taliglucerase alfa was well tolerated and effective during administration of up to 60 months.