# SYNOPSIS

| NAME OF SPONSOR/COMPANY:<br>Ortho Biotech Clinical Affairs, LLC.<br><br>NAME OF FINISHED PRODUCT:<br>Procrit®<br>NAME OF ACTIVE INGREDIENT(S):<br>Epoetin Alfa | INDIVIDUAL STUDY TABLE REFERRING TO PART OF THE DOSSIER<br><br>Volume:<br><br>Page: | (FOR NATIONAL AUTHORITY USE ONLY) |
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| **Protocol No.: Protocol CR004597**<br>**Title of Study: A Randomized, Double-Blind, Placebo-Controlled Study Evaluating Weekly PROCRIT® (Epoetin alfa) Administration on Hemoglobin Response and Safety in Diabetic Subjects with the Anemia of Chronic Kidney Disease (CKD)** | | |
| **Study Initiation Date:** 11 March 2005<br>**Study Completion Date**: 16 September 2005<br>The study was terminated early because of low recruitment of subjects. | | **Phase of development**: 2 |
| **Objectives**: The primary objective was to compare the proportion of subjects receiving either PROCRIT® or placebo who were able to achieve a hemoglobin (Hb) response defined by at least a 1 g/dL increase from baseline (Week 1) by Week 17. The secondary objectives included evaluation of health related quality of life (HRQL), Hb change over time, time to Hb response, time to achieve at least a 1 g/dL rise in Hb from baseline, and transfusion utilization. The tertiary objectives included evaluation of work productivity, physical function, renal function, and predictors of Hb response. | | |
| **Methodology**: At the screening visit (up to 7 days prior to randomization at Week 1) before any protocol-specific procedure was performed, subjects read, understood, and signed an informed consent form. Subjects who met the inclusion/ exclusion criteria were randomized to receive 1 of 2 treatments, PROCRIT® or placebo. The randomization was balanced by using randomly permuted blocks and balanced by the GFR before study entry. The GFR categories for entry were 15 to < 30, 30 to < 60, and 60 to ≤ 90 mL/minute/1.73m$^2$.<br>The starting dose of study drug (PROCRIT® or placebo) administered at the Week 1 visit was 10,000 U (1.0 mL) given subcutaneously (SC) every week (QW). Weekly dose titrations for each subject were based on the Hb measurements obtained 48 hours prior to the dosing visit. The target range for Hb in the study was 12.0 – 12.5 g/L. Dose increases were allowed at the Week 5 visit or thereafter. An interactive voice-response system (IVRS) was used to ensure accurate dose titrations. The IVRS provided the investigators and study staff with dosing information according to the protocol specifications for increasing the dose or holding the dose of study drug, depending on the level of Hb and the rate of change in Hb. The maximal dose of study drug allowed was 20,000 U (2 x 1.0 mL) given SC QW with a maximum of 1.0 mL per injection site.<br>Investigators followed a schedule of procedures when conducting the following evaluations or measurements for safety and efficacy: medical history; physical examination including height, weight, and vital signs; concomitant medication, clinical laboratory parameters (hematology, clinical chemistry, urinalysis), serum iron, serum ferritin, and total iron binding capacity; hemoglobin A1c, parathyroid hormone, thyroid stimulating hormone, C-reactive protein, erythrocyte sedimentation rate, and glomerular filtration rate (GFR). To assess HRQL the following validated instruments were administered at the visits as detailed in the time and events schedule in Appendix 1.1 of this report: Linear Analog Scale Assessment (LASA), Short Form-36 Health Survey (SF-36), Work Productivity and Activity Impairment Questionnaire: General Health (WPAI-GH) and 6 Minute Walk Test (6MWT). Adverse events were collected and monitored throughout the study.<br>The study duration consisted of a 16-week treatment period followed by additional post-treatment visits at Week 17 and Week 20. | | |
| **Criteria for Evaluation**: To be randomized, subjects had to be males or females ≥ 18 years of age, have a clinical diagnosis of diabetes mellitus (DM), a history of proteinuria or microalbuminuria, and a GFR between 15 and 90 mL/minute/1.73m$^2$. Other criteria included, but were not limited to: a Hb value ≥ 9 g/dL and ≤ 11 g/dL. | | |
| **Number of Subjects**: Eleven subjects were randomized in the study: 5 males and 6 females. | | |

# SYNOPSIS (CONTINUED)

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EFFICACY RESULTS: No efficacy analyses were performed because the study was terminated early.

SAFETY RESULTS: Overall, 5 subjects reported 22 AEs. Three subjects randomized to placebo reported 16 AEs and 2 subjects randomized to PROCRIT® reported 6 AEs. Of the 22 AEs, the investigator assessed 15 to be mild, 6 to be moderate, and 1 to be severe in intensity. The majority of AEs (n=10) were assessed to be doubtfully related to study drug, 8 as possibly related, and 4 as not related. All subjects recovered from the AEs, except 1 subject who had arthralgia that didn't resolve at the time of the last visit. No patterns were seen in the type and number of AEs by treatment group, demographic, or baseline characteristics. Owing to the small numbers of subjects in the study, single occurrences of AEs were distributed across system organ classes and preferred terms.

No deaths occurred during this study. Two subjects experienced SAEs: one subject (placebo Subject 11001) experienced hypoglycemia and a second subject (PROCRIT® Subject 03001) experienced syncope with fall, and spinal compression. The investigator assessed the hypoglycemia as severe in intensity and not related to study drug, and the 2 AEs, syncope with fall and spinal compression, as moderate in intensity and doubtfully related to study drug.

No abnormalities in vital signs or laboratory parameters were reported as AEs.

CONCLUSION: No meaningful conclusions were drawn due to the small sample of subjects. An efficacy analysis could not be conducted. No significant safety findings were noted.

Date of the report: 19 December 2005

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