2 SYNOPSIS

Name of Sponsor/Company Cephalon Australia Pty Ltd	Individual Study Table Referring to Part of the Dossier Volume Page:	(For National Authority Use only)
Name of Finished Product CEP-37247		
Name of Active Ingredient: CEP-37247		

Title of study: A multi-centre randomised, double-blind, placebo-controlled, dose ranging study to evaluate the safety, tolerability, efficacy, pharmacokinetics and immunogenicity of ART621 following multiple dose administration for 3 months in patients with rheumatoid arthritis concomitantly taking methotrexate.

Principal Investigator: [redacted] Australia.

Study centres: Four centres.

Publication: None

Studied period: 16 March 2009 (first subject first visit) to 28 October 2009 (last subject last visit)	**Phase of development:** IIa

Objectives: This is an abbreviated report so not applicable.

Methodology:

Subjects were randomly assigned to receive weekly doses of either ART621 (0.75 mg/kg, 1.5 mg/kg or 3.0 mg/kg) or matching placebo for 12 weeks. The first dose of ART621 or placebo was administered intravenously and the remaining 11 doses were to be administered subcutaneously.

While the study was ongoing, the sponsor Arana Therapeutics Limited was acquired by Cephalon Inc. of Frazer, Pennsylvania, United States of America. Subsequent to this transaction, Arana Therapeutics Limited changed its name to Cephalon Australia Pty Ltd and the study drug ART621 is also now referred to as CEP-37247.

The study commenced in March 2009 as planned but after 13 subjects had been randomised, study recruitment was put on hold in order to revise the doses of the study medication being used. Whilst on hold, the study was prematurely terminated on 11 November 2009 in favour of using the study medication in a different therapeutic area. The revised protocol was never released.

Number of subjects: Planned – 200 randomised subjects; **Actual** – 13 randomised subjects.

Diagnosis and main criteria for inclusion:

Male and female subjects (18 years or older) with active rheumatoid arthritis who were receiving stable doses of methotrexate.

Test product, dose and mode of administration:

On Day 1, subjects randomised to receive ART621 were administered an intravenous loading dose of ART621 (at a dose of 1.0 mg/kg, 1.5 mg/kg or 2.0 mg/kg) infused over an hour via an indwelling forearm cannula. The formulation was prepared by a pharmacist to a total volume of 70 mL and 50 mL of this was infused. From the end of Week 1 onwards ART621 (at a dose of 0.75 mg/kg, 1.5 mg/kg or 3.0 mg/kg) was administered via subcutaneous injection(s) to the lower abdomen every week for 11 weeks.

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Duration of treatment:

The total study duration was to be approximately 18 to 20 weeks consisting of a 2- to 4-week screening period, 12 weeks of treatment and 4 weeks of follow-up.

Reference therapy, dose and mode of administration, batch number:

On Day 1, subjects randomised to receive placebo were administered an intravenous loading dose of matching placebo infused over an hour via an indwelling forearm cannula. The formulation was prepared by a pharmacist to a total volume of 70 mL and 50 mL of this was infused. From the end of Week 1 onwards matching placebo was administered via subcutaneous injection(s) to the lower abdomen every week for 11 weeks.

Criteria for evaluation: Safety data only.

Summary and conclusions:

A total of 18 subjects signed an informed consent form and of these, 13 subjects were eligible for randomisation into the study.

No efficacy analyses were performed because of the premature termination of the study. The Safety Population was defined as all randomised subjects who had received at least one dose (or part of one dose) of study medication. All 13 randomised subjects (ART621 group: 10 subjects; placebo group: 3 subjects) were included in the Safety Population and the safety analysis was based on data collected during the study period of 16 March to 28 October 2009.

There were no deaths, serious adverse events or treatment-emergent adverse events (TEAEs) that led to discontinuation of study medication reported during the study. Seven subjects reported 43 TEAEs. All TEAEs were either mild or moderate in intensity. There appeared to be no relationship between an increase in dose and the occurrence of TEAEs. Four subjects reported 15 TEAEs that were considered by the investigator to be possibly, probably or definitely related to study medication: 3 subjects from the ART621 dose groups and 1 subject from the placebo group. One subject reported 8 TEAEs of injection site erythema.

Overall, the most frequently reported TEAEs were headache (3 subjects reported 9 events) and nausea (3 subjects reported 3 events). Of these, 1 subject with headache (0.75 mg/kg group) and 1 subject with nausea (placebo group) were considered by the investigator to be related to study medication.

Subject numbers were too small to draw any meaningful conclusions on any data; however, within the studied subjects, there appeared to be no new safety concerns.

Date of the report: 20 October 2010