**SYNOPSIS**

<table>
<thead>
<tr>
<th>Name of Sponsor/Company: LEO Pharma A/S</th>
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<tbody>
<tr>
<td>Name of Finished Product: Taclonex® Scalp Topical Suspension and Daivobet®/Dovobet®/Xamiol® gel</td>
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<tr>
<td>Name of Active Ingredient: calcipotriol 50 mcg/g plus betamethasone 0.5 mg/g (as dipropionate)</td>
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<tr>
<td>Title of Trial: Effect of Calcipotriol plus Betamethasone Dipropionate Topical Suspension on the HPA Axis and Calcium Metabolism in Adolescent Subjects (Aged 12 to 17 Years) with Scalp Psoriasis</td>
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<td>Investigator: United States of America was the international coordinating investigator.</td>
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<td>Trial Centre(s): 5 centres in the US.</td>
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<td>Publication: None at the time of this clinical study report.</td>
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<td>Trial Period: date of first enrolment (informed consent signed and CRF started): 12-Apr-2010</td>
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<td>date of last completed: 8-Aug-2012</td>
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<td>Phase of development: 2</td>
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<td>Objectives: Primary objective</td>
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<td>The primary objective was to evaluate the safety of once daily use of calcipotriol (50 mcg/g) + betamethasone (0.5 mg/g) (as dipropionate) gel in adolescent subjects (aged 12 to 17 years) with scalp psoriasis.</td>
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<tr>
<td>Secondary objective</td>
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<td>The secondary objective was to evaluate the efficacy of once daily use of calcipotriol (50 mcg/g) plus betamethasone (0.5 mg/g) (as dipropionate) gel in adolescent subjects (aged 12 to 17 years) with scalp psoriasis.</td>
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<td>Methodology: This was a national, multi-centre, prospective, non-controlled, open-label, single-group, 8-week trial in adolescent subjects (aged 12 to 17 years) with scalp psoriasis. The subjects were treated with calcipotriol 50 mcg/g plus betamethasone 0.5 mg/g (as dipropionate) gel once daily for up to 8 weeks.</td>
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<td>Number of Subjects (Planned and Analysed): A sufficient number of subjects were enrolled to ensure 30 subjects were evaluable for HPA (hypothalamic-pituitary-adrenal) axis suppression and calcium metabolism. In total, 31 subjects were treated with at least 1 application of investigational product and 29 subjects completed the trial.</td>
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**Name of Sponsor/Company:** LEO Pharma A/S

**Name of Finished Product:** Taclonex® Scalp Topical Suspension and Daivobet®/Dovobet®/Xamiol® gel

**Name of Active Ingredient:** calcipotriol 50 mcg/g plus betamethasone 0.5 mg/g (as dipropionate)

**Diagnosis and Main Criteria for Inclusion:**
- Psoriasis on the scalp
  - Signed informed consent given by parent(s) or legal guardian, or by the subject (according to national law) following their receipt of verbal and written information about the trial.
  - Subjects will receive verbal and written information and will provide written assent to the trial.
  - Subjects 12 to 17 years of age.
  - Either sex.
  - Any race or ethnicity.
  - Clinical signs of psoriasis vulgaris on trunk and/or limbs, or earlier diagnosed with psoriasis vulgaris on trunk and/or limbs.
  - At SV2 and Visit 1 a clinical diagnosis of scalp psoriasis which is:
    - amenable to topical treatment with a maximum of 60 g of study medication per week, and
    - of an extent of more than or equal to 20% of the scalp area
    - of at least moderate severity according to the investigator’s global assessment
  - Subjects with a normal HPA axis function at SV2 including serum cortisol concentration above 5 mcg/dl before adrenocorticotropic hormone (ACTH) challenge and serum cortisol concentration above 18 mcg/dl 30 minutes after ACTH challenge.
  - A serum albumin-corrected calcium below the upper reference limit at SV2.
  - Females of child-bearing potential must have a negative urine pregnancy test result and must agree to use a highly effective method of contraception during the trial.

**Investigational Product, Dose and Mode of Administration, Batch Numbers:**
LEO 80185 gel, calcipotriol 50 mcg/g plus betamethasone 0.5 mg/g (as dipropionate), once daily, cutaneous
Batch numbers used: [Redacted] and [Redacted]

**Duration of Treatment:**
8 weeks.

**Reference Therapy, Dose and Mode of Administration, Batch Number:**
No reference therapy was used.

**Criteria for Evaluation:**
**Primary Response Criteria – Safety**
The primary endpoints/response criteria were:
- Adverse drug reactions (ADRs).
- Subjects with serum cortisol concentration of ≤18 mcg/dl at 30 minutes after ACTH-challenge at Week 4, and Week 8.
- Subjects with serum cortisol concentration of ≤18 mcg/dl at 30 and 60 minutes after ACTH-challenge at Week 4, and Week 8.
- Change in albumin-corrected serum calcium from Baseline (SV2) to Week 4, Week 8, and end of treatment.
- Change in 24-hour urinary calcium excretion from Baseline (SV2) to Week 4, Week 8, and end of treatment.
- Change in urinary calcium:creatinine ratio from Baseline (SV2) to Week 4, Week 8 and, end of treatment.
Criteria for Evaluation (continued):

Secondary Response Criteria – Safety

The secondary safety endpoints/response criteria were:
- Adverse events (AEs)
- Change in serum phosphate from Baseline (SV2) to Week 4 and Week 8
- Change in 24-hour urinary phosphate excretion from Baseline (SV2) to Week 4 and Week 8
- Change in urinary phosphate:creatinine ratio from Baseline (SV2) to Week 4 and Week 8
- Change in 24-hour urinary hydroxyproline excretion from Baseline (SV2) to Week 4 and Week 8
- Change in urinary hydroxyproline:creatinine ratio from Baseline (SV2) to Week 4 and Week 8
- Change in plasma PTH from Baseline (SV2) to Week 4 and Week 8
- Change in other laboratory parameters from Baseline (SV2) to Week 4 and Week 8
- Reasons for withdrawal
- Change in blood pressure and heart rate from Baseline (SV2) to Week 4 and Week 8

Secondary Response Criteria – Efficacy

The secondary endpoints/response criteria were:
- Subjects with controlled disease (i.e., clear or almost clear) according to the investigator’s global assessment of disease severity at Weeks 2, 4, 8, and end of treatment.
- Percentage change in Total Sign Score (TSS; sum of severity scores for each individual clinical sign, redness, thickness, and scaliness) from Baseline to Weeks 2, 4, 8, and end of treatment.
- Subjects with success (Total Sign Score ≤ 1) at Weeks 2, 4, 8, and end of treatment.
- Subjects with controlled disease (defined as clear or very mild) according to the patient’s global assessment of disease severity at Weeks 2, 4, 8, and end of treatment.

Statistical Methods:

There was no formal statistical hypothesis to be evaluated. The trial results were summarised using descriptive statistics.
### Study Population:
A total of 31 subjects (mean age 14.8 years) were treated (in 5 centres) with at least one application of investigational product and 29 subjects completed the trial; one subject left the trial at Visit 3 (Week 4) as due to signs of adrenal suppression (serum cortisol concentration ≤ 18 mcg/dl) at 30 minutes after the ACTH-challenge and one subject was withdrawn at Visit 2 (Week 2) when it was discovered that the inclusion criterion regarding the HPA axis function was not fulfilled. Three subjects had cleared scalp psoriasis after 4-weeks treatment and left the trial at Visit 3 (Week 4) according to the study protocol.

### Efficacy Summary:
**Investigator’s Global Assessment (IGA) of Disease Severity**
Overall, the majority of subjects had improved during the trial. At end of treatment 54.8% (17 subjects) had controlled disease. There were no clinical relevant differences between males and females or between the age groups.

**Investigator’s Assessment of Clinical Signs – Total Sign Score (TSS) of Redness, Thickness, and Scaliness**
The mean TSS decreased (improved) over time, from 6.9 at Baseline to 2.9 at end of treatment; a 59.2% improvement. The percentage of subjects with TSS success (TSS ≤ 1) improved over time and was 38.7% at the end of treatment.

**Patient’s Global Assessment of Disease Severity and Patient Assessment of Itching**
Overall, the majority of subjects experienced an improvement during the trial as assessed by the Patient’s Global Assessment of disease severity. The percentage of subjects with controlled disease improved over time and 58.1% of the subjects had controlled disease the end of the treatment. Overall, there was an improvement in itching over time as assessed by the patients; at the end of treatment 90.3% (28 subjects) reported to have mild or none itching.

### Overall Efficacy Conclusion
In this small, non-controlled trial, LEO 80185 gel was effective in treating adolescents with scalp psoriasis.

### Safety Summary:
LEO 80185 gel was well tolerated in this adolescent population; there were no SAEs, few adverse events (none of them lesional/perilesional), and one adverse drug reaction that also lead to withdrawal.

One subject (3.3%) showed signs of possible adrenal suppression (serum cortisol concentration ≤ 18 mcg/dl) at 30 minutes after ACTH challenge at Week 4 (> 18 mcg/dl at 60 minutes after ACTH challenge). The suppression was reversible as evidenced by a normal challenge test at follow-up 4 weeks after end of treatment.

No cases of hypercalcaemia were reported and there were no clinically relevant increases in urinary calcium or other parameters of calcium metabolism.

There were no clinically relevant changes in the clinical laboratory assessment or in vital signs.

### Conclusion:
In conclusion, in this small, non-controlled trial, LEO 80185 gel was safe and effective in the treatment of psoriasis vulgaris on the scalp in adolescents.