



## Clinical trial results:

### Efficacy of twice daily application of LEO 124249 ointment 30 mg/g for 12 weeks on eyebrow alopecia areata. Exploratory Phase 2a

#### Summary

|                          |                |
|--------------------------|----------------|
| EudraCT number           | 2017-002720-24 |
| Trial protocol           | DK             |
| Global end of trial date | 16 May 2018    |

#### Results information

|                                |               |
|--------------------------------|---------------|
| Result version number          | v1 (current)  |
| This version publication date  | 03 April 2019 |
| First version publication date | 03 April 2019 |

#### Trial information

##### Trial identification

|                       |          |
|-----------------------|----------|
| Sponsor protocol code | EXP-1377 |
|-----------------------|----------|

##### Additional study identifiers

|                                    |             |
|------------------------------------|-------------|
| ISRCTN number                      | -           |
| ClinicalTrials.gov id (NCT number) | NCT03325296 |
| WHO universal trial number (UTN)   | -           |

Notes:

#### Sponsors

|                              |   |
|------------------------------|---|
| Sponsor organisation name    | LEO Pharma A/S  |
| Sponsor organisation address | Industriparken 55, Ballerup, Denmark, 2750  |
| Public contact               | Clinical Disclosure Specialist, LEO Pharma A/S, +45 44945888, disclosure@leo-pharma.com |
| Scientific contact           | Clinical Disclosure Specialist, LEO Pharma A/S, +45 44945888, disclosure@leo-pharma.com |

Notes:

#### Paediatric regulatory details

|  |    |
|--|----|
| Is trial part of an agreed paediatric investigation plan (PIP)       | No |
| Does article 45 of REGULATION (EC) No 1901/2006 apply to this trial? | No |
| Does article 46 of REGULATION (EC) No 1901/2006 apply to this trial? | No |

Notes:

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**Results analysis stage**

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|  |                 |
|--|-----------------|
| Analysis stage                                       | Final           |
| Date of interim/final analysis                       | 26 October 2018 |
| Is this the analysis of the primary completion data? | Yes             |
| Primary completion date                              | 16 May 2018     |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 16 May 2018     |
| Was the trial ended prematurely?                     | Yes             |

Notes:

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**General information about the trial**

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Main objective of the trial:

To evaluate the efficacy of twice daily topical LEO 124249 ointment 30 mg/g compared with LEO 124249 ointment vehicle on hair growth in subjects with alopecia areata on eyebrows.

Protection of trial subjects:

This clinical trial was conducted to conform to the principles of the Declaration of Helsinki as adopted by the 18th World Medical Association General Assembly, 1964, and the amendment from Somerset West, South Africa, October 1996. All subjects received written and verbal information concerning the clinical trial. Subjects were asked to consent that their personal data were recorded, collected, processed and could be transferred to other countries in accordance with any national legislation regulating privacy and data protection.

Background therapy: -

Evidence for comparator: -

|   |                  |
|---|------------------|
| Actual start date of recruitment                          | 07 November 2017 |
| Long term follow-up planned                               | No               |
| Independent data monitoring committee (IDMC) involvement? | No               |

Notes:

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**Population of trial subjects**

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**Subjects enrolled per country**

|                                      |             |
|--------------------------------------|-------------|
| Country: Number of subjects enrolled | Denmark: 13 |
| Worldwide total number of subjects   | 13          |
| EEA total number of subjects         | 13          |

Notes:

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**Subjects enrolled per age group**

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|   |    |
|---|----|
| In utero                                  | 0  |
| Preterm newborn - gestational age < 37 wk | 0  |
| Newborns (0-27 days)                      | 0  |
| Infants and toddlers (28 days-23 months)  | 0  |
| Children (2-11 years)                     | 0  |
| Adolescents (12-17 years)                 | 0  |
| Adults (18-64 years)                      | 13 |
| From 65 to 84 years                       | 0  |

|                   |   |
|-------------------|---|
| 85 years and over | 0 |
|-------------------|---|

## Subject disposition

### Recruitment

Recruitment details:

The subjects were recruited in Denmark, at 2 sites, between 7-Nov-2017 and 22-Mar-2018.

### Pre-assignment

Screening details:

Main inclusion criteria: clinical unequivocal diagnosis of alopecia areata (AA), maximal duration of current disease episode of 3 years and no ongoing eyebrow hair growth at study start

Main exclusion criteria: diffuse type AA, subjects with skin condition(s) or use of treatments which could put subject at risk or interfere with trial assessments

### Period 1

|                              |                                   |
|------------------------------|-----------------------------------|
| Period 1 title               | Treatment period (overall period) |
| Is this the baseline period? | Yes                               |
| Allocation method            | Randomised - controlled           |
| Blinding used                | Double blind                      |
| Roles blinded                | Investigator, Subject             |

Blinding implementation details:

The packaging and labelling of the 2 investigational medical products contained no evidence of their identity. There is a slight colour difference between the products. However, the difference is only discernible on close inspection with both products compared side by side. Neither the subject nor the investigator were allowed to see the 2 products at the same time. Subjects from the same household were not allowed to participate.

### Arms

|  |                             |
|--|-----------------------------|
| Are arms mutually exclusive?           | Yes                         |
| <b>Arm title</b>                       | LEO 124249 ointment 30 mg/g |
| Arm description: -                     |                             |
| Arm type                               | Experimental                |
| Investigational medicinal product name | LEO 124249 ointment 30 mg/g |
| Investigational medicinal product code |                             |
| Other name                             |                             |
| Pharmaceutical forms                   | Ointment                    |
| Routes of administration               | Topical use                 |

Dosage and administration details:

Twice daily topical application on both eyebrows for 12 weeks

|  |                             |
|--|-----------------------------|
| <b>Arm title</b>                       | LEO 124249 ointment vehicle |
| Arm description: -                     |                             |
| Arm type                               | Placebo                     |
| Investigational medicinal product name | LEO 124249 ointment vehicle |
| Investigational medicinal product code |                             |
| Other name                             |                             |
| Pharmaceutical forms                   | Ointment                    |
| Routes of administration               | Topical use                 |

Dosage and administration details:

Twice daily topical application on both eyebrows for 12 weeks

| <b>Number of subjects in period 1</b> | LEO 124249<br>ointment 30 mg/g | LEO 124249<br>ointment vehicle |
|---------------------------------------|--------------------------------|--------------------------------|
| Started                               | 9                              | 4                              |
| Completed                             | 8                              | 3                              |
| Not completed                         | 1                              | 1                              |
| Trial ended prematurely               | 1                              | 1                              |

## Baseline characteristics

### Reporting groups

|                                |                             |
|--------------------------------|-----------------------------|
| Reporting group title          | LEO 124249 ointment 30 mg/g |
| Reporting group description: - |                             |
| Reporting group title          | LEO 124249 ointment vehicle |
| Reporting group description: - |                             |

| Reporting group values                             | LEO 124249 ointment 30 mg/g | LEO 124249 ointment vehicle | Total |
|--|-----------------------------|-----------------------------|-------|
| Number of subjects                                 | 9                           | 4                           | 13    |
| Age categorical<br>Units: Subjects                 |                             |                             |       |
| In utero   | 0                           | 0                           | 0     |
| Preterm newborn infants (gestational age < 37 wks) | 0                           | 0                           | 0     |
| Newborns (0-27 days)                               | 0                           | 0                           | 0     |
| Infants and toddlers (28 days-23 months)           | 0                           | 0                           | 0     |
| Children (2-11 years)                              | 0                           | 0                           | 0     |
| Adolescents (12-17 years)                          | 0                           | 0                           | 0     |
| Adults (18-64 years)                               | 9                           | 4                           | 13    |
| From 65-84 years                                   | 0                           | 0                           | 0     |
| 85 years and over                                  | 0                           | 0                           | 0     |
| Age continuous<br>Units: years                     |                             |                             |       |
| arithmetic mean                                    | 42.8                        | 45.0                        |       |
| standard deviation                                 | ± 12.2                      | ± 11.5                      | -     |
| Gender categorical<br>Units: Subjects              |                             |                             |       |
| Female   | 4                           | 3                           | 7     |
| Male   | 5                           | 1                           | 6     |

### Subject analysis sets

|                            |                   |
|----------------------------|-------------------|
| Subject analysis set title | Full analysis set |
| Subject analysis set type  | Full analysis     |

Subject analysis set description:

The full analysis set includes all randomised subjects. The safety analysis set includes the randomised subjects who received at least 1 application of the investigational medicinal product. This set is identical to the full analysis set.

| Reporting group values                             | Full analysis set |  |  |
|--|-------------------|--|--|
| Number of subjects                                 | 13                |  |  |
| Age categorical<br>Units: Subjects                 |                   |  |  |
| In utero   | 0                 |  |  |
| Preterm newborn infants (gestational age < 37 wks) | 0                 |  |  |
| Newborns (0-27 days)                               | 0                 |  |  |

|  |        |  |  |
|--|--------|--|--|
| Infants and toddlers (28 days-23 months) | 0      |  |  |
| Children (2-11 years)                    | 0      |  |  |
| Adolescents (12-17 years)                | 0      |  |  |
| Adults (18-64 years)                     | 13     |  |  |
| From 65-84 years                         | 0      |  |  |
| 85 years and over                        | 0      |  |  |
| Age continuous                           |        |  |  |
| Units: years                             |        |  |  |
| arithmetic mean                          | 43.5   |  |  |
| standard deviation                       | ± 11.6 |  |  |
| Gender categorical                       |        |  |  |
| Units: Subjects                          |        |  |  |
| Female                                   | 7      |  |  |
| Male                                     | 6      |  |  |

## End points

### End points reporting groups

|                                |                             |
|--------------------------------|-----------------------------|
| Reporting group title          | LEO 124249 ointment 30 mg/g |
| Reporting group description: - |                             |
| Reporting group title          | LEO 124249 ointment vehicle |
| Reporting group description: - |                             |
| Subject analysis set title     | Full analysis set           |
| Subject analysis set type      | Full analysis               |

Subject analysis set description:

The full analysis set includes all randomised subjects. The safety analysis set includes the randomised subjects who received at least 1 application of the investigational medicinal product. This set is identical to the full analysis set.

### Primary: Change from baseline to Week 12 of investigator evaluated overall area score of eyebrow hair growth

|                 |  |
|-----------------|--|
| End point title | Change from baseline to Week 12 of investigator evaluated overall area score of eyebrow hair growth <sup>[1]</sup> |
|-----------------|--|

End point description:

|                      |         |
|----------------------|---------|
| End point type       | Primary |
| End point timeframe: |         |
| Day 1 to Week 12     |         |

Notes:

[1] - No statistical analyses have been specified for this primary end point. It is expected there is at least one statistical analysis for each primary end point.

Justification: No statistical analysis is provided due to lack of efficacy, as demonstrated by an unplanned blinded futility analysis.

| End point values                     | LEO 124249 ointment 30 mg/g | LEO 124249 ointment vehicle |  |  |
|--------------------------------------|-----------------------------|-----------------------------|--|--|
| Subject group type                   | Reporting group             | Reporting group             |  |  |
| Number of subjects analysed          | 9                           | 4                           |  |  |
| Units: area score                    |                             |                             |  |  |
| arithmetic mean (standard deviation) | 0.0 (± 0.5)                 | 0.0 (± 0.0)                 |  |  |

### Statistical analyses

No statistical analyses for this end point

### Secondary: Treatment-emergent adverse events

|  |                                   |
|--|-----------------------------------|
| End point title  | Treatment-emergent adverse events |
| End point description:   |                                   |
| The treatment-emergent adverse events include adverse events relating to local tolerability. |                                   |
| End point type   | Secondary                         |
| End point timeframe:   |                                   |
| Day 1 to Week 16   |                                   |



| <b>End point values</b>     | LEO 124249<br>ointment 30<br>mg/g | LEO 124249<br>ointment<br>vehicle |  |  |
|-----------------------------|-----------------------------------|-----------------------------------|--|--|
| Subject group type          | Reporting group                   | Reporting group                   |  |  |
| Number of subjects analysed | 9                                 | 4                                 |  |  |
| Units: number of events     | 7                                 | 4                                 |  |  |

### Statistical analyses

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No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From subject signing informed consent form to Week 16

|                 |                |
|-----------------|----------------|
| Assessment type | Non-systematic |
|-----------------|----------------|

### Dictionary used

|                 |        |
|-----------------|--------|
| Dictionary name | MedDRA |
|-----------------|--------|

|                    |      |
|--------------------|------|
| Dictionary version | 20.1 |
|--------------------|------|

### Reporting groups

|                       |                             |
|-----------------------|-----------------------------|
| Reporting group title | LEO 124249 ointment 30 mg/g |
|-----------------------|-----------------------------|

Reporting group description: -

|                       |                             |
|-----------------------|-----------------------------|
| Reporting group title | LEO 124249 ointment vehicle |
|-----------------------|-----------------------------|

Reporting group description: -

| Serious adverse events                            | LEO 124249<br>ointment 30 mg/g | LEO 124249<br>ointment vehicle |  |
|---|--------------------------------|--------------------------------|--|
| Total subjects affected by serious adverse events |                                |                                |  |
| subjects affected / exposed                       | 1 / 9 (11.11%)                 | 0 / 4 (0.00%)                  |  |
| number of deaths (all causes)                     | 0                              | 0                              |  |
| number of deaths resulting from adverse events    | 0                              | 0                              |  |
| Infections and infestations                       |                                |                                |  |
| Pilonidal cyst                                    |                                |                                |  |
| subjects affected / exposed                       | 1 / 9 (11.11%)                 | 0 / 4 (0.00%)                  |  |
| occurrences causally related to treatment / all   | 0 / 1                          | 0 / 0                          |  |
| deaths causally related to treatment / all        | 0 / 0                          | 0 / 0                          |  |

Frequency threshold for reporting non-serious adverse events: 0 %

| Non-serious adverse events                            | LEO 124249<br>ointment 30 mg/g | LEO 124249<br>ointment vehicle |  |
|---|--------------------------------|--------------------------------|--|
| Total subjects affected by non-serious adverse events |                                |                                |  |
| subjects affected / exposed                           | 4 / 9 (44.44%)                 | 2 / 4 (50.00%)                 |  |
| Injury, poisoning and procedural complications        |                                |                                |  |
| Face injury   |                                |                                |  |
| subjects affected / exposed                           | 1 / 9 (11.11%)                 | 0 / 4 (0.00%)                  |  |
| occurrences (all)                                     | 1                              | 0                              |  |
| General disorders and administration site conditions  |                                |                                |  |

|   |   |   |  |
|---|---|---|--|
| Application site pruritus<br>subjects affected / exposed<br>occurrences (all)   | 1 / 9 (11.11%)<br>1                           | 1 / 4 (25.00%)<br>1                           |  |
| Gastrointestinal disorders<br>Vomiting<br>subjects affected / exposed<br>occurrences (all)  | 0 / 9 (0.00%)<br>0                            | 1 / 4 (25.00%)<br>1                           |  |
| Respiratory, thoracic and mediastinal disorders<br>Oropharyngeal pain<br>subjects affected / exposed<br>occurrences (all)   | 1 / 9 (11.11%)<br>1                           | 0 / 4 (0.00%)<br>0                            |  |
| Skin and subcutaneous tissue disorders<br>Pruritus<br>subjects affected / exposed<br>occurrences (all)  | 0 / 9 (0.00%)<br>0                            | 1 / 4 (25.00%)<br>1                           |  |
| Psychiatric disorders<br>Depression<br>subjects affected / exposed<br>occurrences (all)   | 1 / 9 (11.11%)<br>1                           | 0 / 4 (0.00%)<br>0                            |  |
| Infections and infestations<br>Influenza<br>subjects affected / exposed<br>occurrences (all)<br><br>Gastroenteritis<br>subjects affected / exposed<br>occurrences (all) | 2 / 9 (22.22%)<br>2<br><br>0 / 9 (0.00%)<br>0 | 0 / 4 (0.00%)<br>0<br><br>1 / 4 (25.00%)<br>1 |  |

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

| Date             | Amendment  |
|------------------|--|
| 07 February 2018 | The main reason for this amendment was to revise 2 of the inclusion criteria to reduce the number of screening failures and to aid recruitment into the trial.   |
| 28 March 2018    | The main reason for this amendment was to revise 1 of the exclusion criteria to align with the first amendment. The factor 'site' was added to the statistical analysis model. In addition, informed consent date and demographics were added to the data that must be collected for screening failures. |

Notes:

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### Interruptions (globally)

Were there any global interruptions to the trial? Yes

| Date        | Interruption  | Restart date |
|-------------|---|--------------|
| 16 May 2018 | An unplanned futility analysis was conducted and on the basis of this analysis the trial was terminated prior to completion. For this reason, the trial was reported as an abbreviated report in accordance with ICH E3. Results for 2 secondary efficacy endpoints were therefore neither analysed nor reported. | -            |

Notes:

### Limitations and caveats

None reported