



## Clinical trial results:

**Interventional, randomized, double-blind, cross-over, placebo-controlled study to investigate the effects of nalmefene after single dose on the blood oxygen level dependent (BOLD) fMRI signal in the ventral striatum to reward responding in the monetary incentive delay task (MIDT), in non-treatment seeking subjects with alcohol dependence following alcohol challenge**

### Summary

|                          |                 |
|--------------------------|-----------------|
| EudraCT number           | 2013-001154-98  |
| Trial protocol           | GB              |
| Global end of trial date | 30 October 2014 |

### Results information

|                                |              |
|--------------------------------|--------------|
| Result version number          | v1 (current) |
| This version publication date  | 25 June 2016 |
| First version publication date | 25 June 2016 |

### Trial information

#### Trial identification

|                       |        |
|-----------------------|--------|
| Sponsor protocol code | 15660A |
|-----------------------|--------|

#### Additional study identifiers

|                                    |                  |
|------------------------------------|------------------|
| ISRCTN number                      | -                |
| ClinicalTrials.gov id (NCT number) | NCT01969617      |
| WHO universal trial number (UTN)   | -                |
| Other trial identifiers            | HMR code: 13-506 |

Notes:

### Sponsors

|                              |  |
|------------------------------|--|
| Sponsor organisation name    | H. Lundbeck A/S  |
| Sponsor organisation address | Ottiliavej 9, Valby, Denmark,  |
| Public contact               | Lundbeck Clinical Trials, H Lundbeck A/S,<br>LundbeckClinicalTrials@lundbeck.com |
| Scientific contact           | Lundbeck Clinical Trials, H Lundbeck A/S,<br>LundbeckClinicalTrials@lundbeck.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**

|  |                 |
|--|-----------------|
| Analysis stage                                       | Final           |
| Date of interim/final analysis                       | 30 October 2014 |
| Is this the analysis of the primary completion data? | Yes             |
| Primary completion date                              | 30 October 2014 |
| Global end of trial reached?                         | Yes             |
| Global end of trial date                             | 30 October 2014 |
| Was the trial ended prematurely?                     | No              |

Notes:

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**General information about the trial**

Main objective of the trial:

To investigate the effects of nalmefene after single dose on the blood oxygen level dependent (BOLD) functional magnetic resonance imaging (fMRI) signal in the ventral striatum to reward responding using the monetary incentive delay task (MIDT) task following alcohol clamp challenge.

Protection of trial subjects:

The trial was conducted in accordance with the Declaration of Helsinki (2008) and ICH Good Clinical Practice (1996)

Background therapy: -

Evidence for comparator: -

|   |                 |
|---|-----------------|
| Actual start date of recruitment                          | 14 January 2014 |
| Long term follow-up planned                               | No              |
| Independent data monitoring committee (IDMC) involvement? | No              |

Notes:

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**Population of trial subjects****Subjects enrolled per country**

|                                      |                    |
|--------------------------------------|--------------------|
| Country: Number of subjects enrolled | United Kingdom: 22 |
| Worldwide total number of subjects   | 22                 |
| EEA total number of subjects         | 22                 |

Notes:

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**Subjects enrolled per age group**

|   |    |
|---|----|
| 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)                      | 22 |
| From 65 to 84 years                       | 0  |
| 85 years and over                         | 0  |

## Subject disposition

### Recruitment

Recruitment details:

The trial was conducted at one site in UK (single centre study)

### Pre-assignment

Screening details:

Subjects who met each of the inclusion and none of the exclusion criteria were eligible to participate in the study

### Period 1

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

### Arms

|                              |                  |
|------------------------------|------------------|
| Are arms mutually exclusive? | Yes              |
| <b>Arm title</b>             | Selincro/Placebo |

Arm description:

Subjects were randomised to receive 18 mg Selincro (nalmefene) on Day 1 and matching placebo on Day 8. There was a washout period of at least 1 week between dosing/scanning days.

|  |                    |
|--|--------------------|
| Arm type                               | Experimental       |
| Investigational medicinal product name | Selincro           |
| Investigational medicinal product code |                    |
| Other name                             | Nalmefene          |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

Dosage and administration details:

Single dose of Selincro 18 mg, orally

|  |          |
|--|----------|
| Investigational medicinal product name | Placebo  |
| Investigational medicinal product code |          |
| Other name                             |          |
| Pharmaceutical forms                   | Tablet   |
| Routes of administration               | Oral use |

Dosage and administration details:

Single dose, tablet, orally

|                  |                  |
|------------------|------------------|
| <b>Arm title</b> | Placebo/Selincro |
|------------------|------------------|

Arm description:

Subjects were randomised to receive placebo on Day 1 and 18 mg Selincro (nalmefene) on Day 8. There was a washout period of at least 1 week between dosing/scanning days.

|  |          |
|--|----------|
| Arm type                               | Placebo  |
| Investigational medicinal product name | Placebo  |
| Investigational medicinal product code |          |
| Other name                             |          |
| Pharmaceutical forms                   | Tablet   |
| Routes of administration               | Oral use |

Dosage and administration details:

Single dose, tablet, orally

|  |                    |
|--|--------------------|
| Investigational medicinal product name | Selincro           |
| Investigational medicinal product code |                    |
| Other name                             | Nalmefene          |
| Pharmaceutical forms                   | Film-coated tablet |
| Routes of administration               | Oral use           |

Dosage and administration details:

Single dose of Selincro 18 mg, orally

| <b>Number of subjects in period 1</b> | Selincro/Placebo | Placebo/Selincro |
|---------------------------------------|------------------|------------------|
| Started                               | 11               | 11               |
| Completed                             | 11               | 10               |
| Not completed                         | 0                | 1                |
| Adverse event, non-fatal              | -                | 1                |

## Baseline characteristics

### Reporting groups

|                       |               |
|-----------------------|---------------|
| Reporting group title | overall trial |
|-----------------------|---------------|

Reporting group description: -

| Reporting group values                                | overall trial | Total |  |
|---|---------------|-------|--|
| Number of subjects                                    | 22            | 22    |  |
| Age categorical                                       |               |       |  |
| Units: Subjects                                       |               |       |  |
| In utero  | 0             | 0     |  |
| Preterm newborn infants<br>(gestational age < 37 wks) | 0             | 0     |  |
| Newborns (0-27 days)                                  | 0             | 0     |  |
| Infants and toddlers (28 days-23<br>months)           | 0             | 0     |  |
| Children (2-11 years)                                 | 0             | 0     |  |
| Adolescents (12-17 years)                             | 0             | 0     |  |
| Adults (18-64 years)                                  | 22            | 22    |  |
| From 65-84 years                                      | 0             | 0     |  |
| 85 years and over                                     | 0             | 0     |  |
| Gender categorical                                    |               |       |  |
| Units: Subjects                                       |               |       |  |
| Female  | 0             | 0     |  |
| Male  | 22            | 22    |  |
| Race  |               |       |  |
| Units: Subjects                                       |               |       |  |
| Asian   | 1             | 1     |  |
| Black or African American                             | 2             | 2     |  |
| White   | 18            | 18    |  |
| Other   | 1             | 1     |  |

## End points

### End points reporting groups

|  |                  |
|--|------------------|
| Reporting group title  | Selincro/Placebo |
| Reporting group description:<br>Subjects were randomised to receive 18 mg Selincro (nalmefene) on Day 1 and matching placebo on Day 8. There was a washout period of at least 1 week between dosing/scanning days. |                  |
| Reporting group title  | Placebo/Selincro |
| Reporting group description:<br>Subjects were randomised to receive placebo on Day 1 and 18 mg Selincro (nalmefene) on Day 8. There was a washout period of at least 1 week between dosing/scanning days.          |                  |
| Subject analysis set title   | Selincro         |
| Subject analysis set type  | Full analysis    |
| Subject analysis set description:<br>18 mg Nalmefene   |                  |
| Subject analysis set title   | Placebo          |
| Subject analysis set type  | Full analysis    |
| Subject analysis set description:<br>Placebo   |                  |

### Primary: Blood oxygen level dependent (BOLD) fMRI signal in the ventral striatum to reward responding using the monetary incentive delay task (MIDT) task

|  |  |
|--|--|
| End point title                                | Blood oxygen level dependent (BOLD) fMRI signal in the ventral striatum to reward responding using the monetary incentive delay task (MIDT) task |
| End point description:                         |  |
| End point type                                 | Primary  |
| End point timeframe:<br>4-6 hours after dosing |  |

| End point values            | Selincro             | Placebo              |  |  |
|-----------------------------|----------------------|----------------------|--|--|
| Subject group type          | Subject analysis set | Subject analysis set |  |  |
| Number of subjects analysed | 18                   | 18                   |  |  |
| Units: Percent change       | 16                   | 25                   |  |  |

### Statistical analyses

|  |                                  |
|--|----------------------------------|
| Statistical analysis title   | Reward respond signal (activity) |
| Statistical analysis description:<br>The analysis was a paired t-test (a linear mixed-effects model, with subject as the random effect and drug condition as the fixed effect).<br><br>Data were excluded in the MIDT for three sessions (head movement), so 18 subjects were included in the analysis |                                  |
| Comparison groups  | Selincro v Placebo               |

|   |                       |
|---|-----------------------|
| Number of subjects included in analysis | 36                    |
| Analysis specification                  | Pre-specified         |
| Analysis type                           | other <sup>[1]</sup>  |
| P-value                                 | = 0.013               |
| Method                                  | Mixed models analysis |

Notes:

[1] - Mixed effect Model Repeat Measurement

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

From dosing to end of study

|                 |            |
|-----------------|------------|
| Assessment type | Systematic |
|-----------------|------------|

### Dictionary used

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

|                    |      |
|--------------------|------|
| Dictionary version | 16.1 |
|--------------------|------|

### Reporting groups

|                       |          |
|-----------------------|----------|
| Reporting group title | Selincro |
|-----------------------|----------|

Reporting group description: -

|                       |         |
|-----------------------|---------|
| Reporting group title | Placebo |
|-----------------------|---------|

Reporting group description: -

| Serious adverse events                            | Selincro       | Placebo        |  |
|---|----------------|----------------|--|
| Total subjects affected by serious adverse events |                |                |  |
| subjects affected / exposed                       | 0 / 21 (0.00%) | 0 / 22 (0.00%) |  |
| number of deaths (all causes)                     | 0              | 0              |  |
| number of deaths resulting from adverse events    | 0              | 0              |  |

Frequency threshold for reporting non-serious adverse events: 5 %

| Non-serious adverse events                            | Selincro         | Placebo         |  |
|---|------------------|-----------------|--|
| Total subjects affected by non-serious adverse events |                  |                 |  |
| subjects affected / exposed                           | 10 / 21 (47.62%) | 4 / 22 (18.18%) |  |
| Vascular disorders                                    |                  |                 |  |
| Hot flush   |                  |                 |  |
| subjects affected / exposed                           | 2 / 21 (9.52%)   | 0 / 22 (0.00%)  |  |
| occurrences (all)                                     | 2                | 0               |  |
| Nervous system disorders                              |                  |                 |  |
| Headache  |                  |                 |  |
| subjects affected / exposed                           | 6 / 21 (28.57%)  | 0 / 22 (0.00%)  |  |
| occurrences (all)                                     | 6                | 0               |  |
| Sinus Headache  |                  |                 |  |
| subjects affected / exposed                           | 1 / 21 (4.76%)   | 0 / 22 (0.00%)  |  |
| occurrences (all)                                     | 1                | 0               |  |
| Somnolence  |                  |                 |  |



|   |                     |                     |  |
|---|---------------------|---------------------|--|
| subjects affected / exposed<br>occurrences (all)        | 1 / 21 (4.76%)<br>1 | 0 / 22 (0.00%)<br>0 |  |
| General disorders and administration<br>site conditions |                     |                     |  |
| Chills  |                     |                     |  |
| subjects affected / exposed                             | 1 / 21 (4.76%)      | 0 / 22 (0.00%)      |  |
| occurrences (all)                                       | 1                   | 0                   |  |
| Vessel Puncture Site Haematoma                          |                     |                     |  |
| subjects affected / exposed                             | 1 / 21 (4.76%)      | 0 / 22 (0.00%)      |  |
| occurrences (all)                                       | 1                   | 0                   |  |
| Catheter Site Pain                                      |                     |                     |  |
| subjects affected / exposed                             | 0 / 21 (0.00%)      | 1 / 22 (4.55%)      |  |
| occurrences (all)                                       | 0                   | 1                   |  |
| Gastrointestinal disorders                              |                     |                     |  |
| Nausea  |                     |                     |  |
| subjects affected / exposed                             | 4 / 21 (19.05%)     | 0 / 22 (0.00%)      |  |
| occurrences (all)                                       | 4                   | 0                   |  |
| Vomiting  |                     |                     |  |
| subjects affected / exposed                             | 2 / 21 (9.52%)      | 0 / 22 (0.00%)      |  |
| occurrences (all)                                       | 2                   | 0                   |  |
| Dyspepsia   |                     |                     |  |
| subjects affected / exposed                             | 0 / 21 (0.00%)      | 1 / 22 (4.55%)      |  |
| occurrences (all)                                       | 0                   | 1                   |  |
| Skin and subcutaneous tissue disorders                  |                     |                     |  |
| Dermatitis Allergic                                     |                     |                     |  |
| subjects affected / exposed                             | 0 / 21 (0.00%)      | 1 / 22 (4.55%)      |  |
| occurrences (all)                                       | 0                   | 1                   |  |
| Psychiatric disorders                                   |                     |                     |  |
| Anxiety   |                     |                     |  |
| subjects affected / exposed                             | 0 / 21 (0.00%)      | 1 / 22 (4.55%)      |  |
| occurrences (all)                                       | 0                   | 1                   |  |

## **More information**

### **Substantial protocol amendments (globally)**

Were there any global substantial amendments to the protocol? No

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### **Interruptions (globally)**

Were there any global interruptions to the trial? No

### **Limitations and caveats**

None reported