# Clinical trial results:
# A Phase Ib, Multicenter, Open-Label, 6-Week Study With a 48-Week Extension to Investigate the Pharmacokinetics, Safety, and Tolerability of Balovaptan in Children Ages 2-4 Years With Autism Spectrum Disorder

## Summary

| | |
|---|---|
| EudraCT number | 2019-000989-38 |
| Trial protocol | ES |
| Global end of trial date | 06 May 2020 |

**Results information**

| | |
|---|---|
| Result version number | v1 (current) |
| This version publication date | 07 October 2020 |
| First version publication date | 07 October 2020 |

## Trial information

**Trial identification**

| | |
|---|---|
| Sponsor protocol code | WP40877 |

**Additional study identifiers**

| | |
|---|---|
| ISRCTN number | - |
| ClinicalTrials.gov id (NCT number) | NCT04049578 |
| WHO universal trial number (UTN) | - |

Notes:

**Sponsors**

| | |
|---|---|
| Sponsor organisation name | Hoffmann-La Roche |
| Sponsor organisation address | Grenzacherstrasse 124, Basel, Switzerland, CH-4070 |
| Public contact | F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.com |
| Scientific contact | F. Hoffmann-La Roche AG, F. Hoffmann-La Roche AG, 41 616878333, global.trial_information@roche.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? | Yes |

Notes:

## Results analysis stage

| | |
|---|---|
| Analysis stage | Final |
| Date of interim/final analysis | 06 May 2020 |
| Is this the analysis of the primary completion data? | No |

| | |
|---|---|
| Global end of trial reached? | Yes |
| Global end of trial date | 06 May 2020 |
| Was the trial ended prematurely? | Yes |

Notes:

## General information about the trial

Main objective of the trial:

The main objective of this trial was to evaluate the pharmacokinetics, safety, andtolerability of 4 mg balovaptan once a day administered for 6 weeks to children 2-4 years old with Autism Spectrum Disorder.

Protection of trial subjects:

All study subjects were required to read and sign an Informed Consent Form.

Background therapy: -

Evidence for comparator: -

| | |
|---|---|
| Actual start date of recruitment | 19 December 2019 |
| Long term follow-up planned | No |
| Independent data monitoring committee (IDMC) involvement? | No |

Notes:

## Population of trial subjects

### Subjects enrolled per country

| | |
|---|---|
| Country: Number of subjects enrolled | United States: 2 |
| Worldwide total number of subjects | 2 |
| EEA total number of subjects | 0 |

Notes:

### 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) | 2 |
| Adolescents (12-17 years) | 0 |
| Adults (18-64 years) | 0 |
| From 65 to 84 years | 0 |
| 85 years and over | 0 |

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

Participants in this study included children 2-4 years old with autism spectrum disorder (ASD).

### Period 1

| | |
|---|---|
| Period 1 title | Overall Study (overall period) |
| Is this the baseline period? | Yes |
| Allocation method | Non-randomised - controlled |
| Blinding used | Not blinded |

### Arms

| | |
|---|---|
| **Arm title** | Balovaptan |

Arm description:

Participants were to receive an oral dose of balovaptan once a day (QD) for a 6-week treatment period, followed by an optional extension period of 48 weeks.

| | |
|---|---|
| Arm type | Experimental |
| Investigational medicinal product name | Balovaptan |
| Investigational medicinal product code | |
| Other name | |
| Pharmaceutical forms | Dispersible tablet |
| Routes of administration | Oral use |

Dosage and administration details:

Balovaptan dispersible tablet was administered once a day (QD) orally.

| **Number of subjects in period 1** | Balovaptan |
|---|---|
| Started | 2 |
| Completed | 1 |
| Not completed | 1 |
| Physician decision | 1 |

## Baseline characteristics

| Reporting groups | |
|---|---|
| Reporting group title | Balovaptan |
| Reporting group description: | |
| Participants were to receive an oral dose of balovaptan once a day (QD) for a 6-week treatment period, followed by an optional extension period of 48 weeks. | |

| Reporting group values | Balovaptan | Total | |
|---|---|---|---|
| Number of subjects | 2 | 2 | |
| Age categorical<br>Units: Subjects | | | |
| In utero | 0 | 0 | |
| Preterm newborn infants (gestational age < 37 wks) | 0 | 0 | |
| Newborns (0-27 days) | 0 | 0 | |
| Infants and toddlers (28 days-23 months) | 0 | 0 | |
| Children (2-11 years) | 2 | 2 | |
| Adolescents (12-17 years) | 0 | 0 | |
| Adults (18-64 years) | 0 | 0 | |
| From 65-84 years | 0 | 0 | |
| 85 years and over | 0 | 0 | |
| Age Continuous<br>Units: years | | | |
| arithmetic mean | 3.45 | | |
| standard deviation | ± 0.78 | - | |
| Sex: Female, Male<br>Units: Participants | | | |
| Female | 0 | 0 | |
| Male | 2 | 2 | |
| Race (NIH/OMB)<br>Units: Subjects | | | |
| American Indian or Alaska Native | 0 | 0 | |
| Asian | 0 | 0 | |
| Native Hawaiian or Other Pacific Islander | 0 | 0 | |
| Black or African American | 0 | 0 | |
| White | 2 | 2 | |
| More than one race | 0 | 0 | |
| Unknown or Not Reported | 0 | 0 | |
| Ethnicity (NIH/OMB)<br>Units: Subjects | | | |
| Hispanic or Latino | 1 | 1 | |
| Not Hispanic or Latino | 1 | 1 | |
| Unknown or Not Reported | 0 | 0 | |

## End points

### End points reporting groups

| Reporting group title | Balovaptan |
|---|---|

Reporting group description:

Participants were to receive an oral dose of balovaptan once a day (QD) for a 6-week treatment period, followed by an optional extension period of 48 weeks.

### Primary: Area Under the Curve at Steady State (AUCss) of Balovaptan

| End point title | Area Under the Curve at Steady State (AUCss) of Balovaptan[1] |
|---|---|

End point description:

| End point type | Primary |
|---|---|

End point timeframe:

Predose, 2, 4, 6 hours postdose at Week 2; predose at Week 6; predose at Week 12; predose at Week 24, predose at Week 54

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 for this end point.

| End point values | Balovaptan | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0[2] | | | |
| Units: day*ug/mL | | | | |
| arithmetic mean (standard deviation) | () | | | |

Notes:

[2] - Due to low enrollment number, analysis are not provided to protect participant confidentiality.

### Statistical analyses

No statistical analyses for this end point

### Primary: Plasma Concentration of Balovaptan

| End point title | Plasma Concentration of Balovaptan[3] |
|---|---|

End point description:

| End point type | Primary |
|---|---|

End point timeframe:

Predose, 2, 4, 6 hours postdose at Week 2; predose at Week 6; predose at Week 12; predose at Week 24, predose at Week 54

Notes:

[3] - 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 for this end point.

| End point values | Balovaptan | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0[4] | | | |
| Units: ng/mL | | | | |
| geometric mean (geometric coefficient of variation) | () | | | |

Notes:

[4] - Due to low enrollment, number analysis are not provided to protect participant confidentiality.

### Statistical analyses

No statistical analyses for this end point

## Primary: Plasma Concentration of M2 Metabolite, as Applicable

| End point title | Plasma Concentration of M2 Metabolite, as Applicable[5] |
|---|---|

End point description:

| End point type | Primary |
|---|---|

End point timeframe:

Predose, 2, 4, 6 hours postdose at Week 2; predose at Week 6; predose at Week 12; predose at Week 24, predose at Week 54

Notes:

[5] - 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 for this end point.

| End point values | Balovaptan | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0[6] | | | |
| Units: ng/mL | | | | |
| geometric mean (geometric coefficient of variation) | () | | | |

Notes:

[6] - Due to low enrollment number, analysis are not provided to protect participant confidentiality.

### Statistical analyses

No statistical analyses for this end point

## Primary: Plasma Concentation of M3 Metabolite

| End point title | Plasma Concentation of M3 Metabolite[7] |
|---|---|

End point description:

| End point type | Primary |
|---|---|

End point timeframe:

Predose, 2, 4, 6 hours postdose at Week 2; predose at Week 6; predose at Week 12; predose at Week 24, predose at Week 54

Notes:

[7] - 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 for this end point.

| End point values | Balovaptan | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0[8] | | | |
| Units: ng/mL | | | | |
| geometric mean (geometric coefficient of variation) | () | | | |

Notes:

[8] - Due to low enrollment number, analysis are not provided to protect participant confidentiality.

### Statistical analyses

No statistical analyses for this end point

## Primary: Plasma Concentration Ratio of M2 to Balovaptan, as Applicable

| End point title | Plasma Concentration Ratio of M2 to Balovaptan, as |
|---|---|

End point description:

| End point type | Primary |
|---|---|

End point timeframe:

Predose, 2, 4, 6 hours postdose at Week 2; predose at Week 6; predose at Week 12; predose at Week 24, predose at Week 54

Notes:

[9] - 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 for this end point.

| End point values | Balovaptan | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0[10] | | | |
| Units: ng/mL | | | | |
| geometric mean (geometric coefficient of variation) | () | | | |

Notes:

[10] - Due to low enrollment number, analysis are not provided to protect participant confidentiality.

### Statistical analyses

No statistical analyses for this end point

## Primary: Plasma Concentration Ratio of M3 to Balovaptan

| End point title | Plasma Concentration Ratio of M3 to Balovaptan[11] |
|---|---|

End point description:

| End point type | Primary |
|---|---|

End point timeframe:

Predose, 2, 4, 6 hours postdose at Week 2; predose at Week 6; predose at Week 12; predose at Week 24, predose at Week 54

Notes:

[11] - 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 for this end point.

| End point values | Balovaptan | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 0[12] | | | |
| Units: ng/mL | | | | |
| geometric mean (geometric coefficient of variation) | () | | | |

Notes:

[12] - Due to low enrollment number, analysis are not provided to protect participant confidentiality.

### Statistical analyses

No statistical analyses for this end point

## Secondary: Number of Participants With Adverse Events

| End point title | Number of Participants With Adverse Events |
|---|---|

End point description:

| End point type | Secondary |
|---|---|

End point timeframe:

Up to approximately week 20

| End point values | Balovaptan | | | |
|---|---|---|---|---|
| Subject group type | Reporting group | | | |
| Number of subjects analysed | 2 | | | |
| Units: Participants | | | | |
| number (not applicable) | 2 | | | |

### Statistical analyses

No statistical analyses for this end point

## Adverse events

| Adverse events information | |
|---|---|
| Timeframe for reporting adverse events: | |
| From the first study drug to the data cutoff date: 6 May 2020 (up to approximately 20 weeks) | |
| Adverse event reporting additional description: | |
| The safety population is defined as patients who received any amount of study treatment. | |
| Assessment type | Systematic |

| Dictionary used | |
|---|---|
| Dictionary name | MedDRA |
| Dictionary version | 23.0 |

| Reporting groups | |
|---|---|
| Reporting group title | Balovaptan |
| Reporting group description: | |
| Participants were to receive an oral dose of balovaptan once a day (QD) for a 6-week treatment period, followed by an optional extension period of 48 weeks. | |

| Serious adverse events | Balovaptan | | |
|---|---|---|---|
| Total subjects affected by serious adverse events | | | |
| subjects affected / exposed | 0 / 2 (0.00%) | | |
| number of deaths (all causes) | 0 | | |
| number of deaths resulting from adverse events | | | |

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

| Non-serious adverse events | Balovaptan | | |
|---|---|---|---|
| Total subjects affected by non-serious adverse events | | | |
| subjects affected / exposed | 2 / 2 (100.00%) | | |
| Investigations | | | |
| Blood thyroid stimulating hormone increased | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | | |
| occurrences (all) | 1 | | |
| Vascular disorders | | | |
| Haematoma | | | |
| subjects affected / exposed | 1 / 2 (50.00%) | | |
| occurrences (all) | 1 | | |
| Nervous system disorders | | | |

| | | | |
|---|---|---|---|
| Psychomotor hyperactivity<br>subjects affected / exposed<br>occurrences (all) | 1 / 2 (50.00%)<br>1 | | |
| Respiratory, thoracic and mediastinal disorders<br>Cough<br>subjects affected / exposed<br>occurrences (all) | 1 / 2 (50.00%)<br>1 | | |
| Metabolism and nutrition disorders<br>Abnormal weight gain<br>subjects affected / exposed<br>occurrences (all) | 1 / 2 (50.00%)<br>1 | | |

## More information

## Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? No

## Interruptions (globally)

Were there any global interruptions to the trial? No

## Limitations and caveats

Limitations of the trial such as small numbers of subjects analysed or technical problems leading to unreliable data.

Study was terminated. Recent analysis of Phase II balovaptan data in paediatric ASD did not support the continuation of this study. No new safety concerns were identified.

Notes: