



## 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
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##### 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:

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**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:

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**General information about the trial**

Main objective of the trial:

The main objective of this trial was to evaluate the pharmacokinetics, safety, and tolerability 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:

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**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:

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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)	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

<b>Arm title</b>	Balovaptan
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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
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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			
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			
Units: years			
arithmetic mean	3.45		
standard deviation	± 0.78	-	
Sex: Female, Male			
Units: Participants			
Female	0	0	
Male	2	2	
Race (NIH/OMB)			
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)			
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 <sup>[1]</sup>
End point description:	

End point type	Primary
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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 <sup>[2]</sup>			
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 <sup>[3]</sup>
End point description:	

End point type	Primary
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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.

<b>End point values</b>	Balovaptan			
Subject group type	Reporting group			
Number of subjects analysed	0 <sup>[4]</sup>			
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 <sup>[5]</sup>
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End point description:

End point type	Primary
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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.

<b>End point values</b>	Balovaptan			
Subject group type	Reporting group			
Number of subjects analysed	0 <sup>[6]</sup>			
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 Concentration of M3 Metabolite

End point title	Plasma Concentration of M3 Metabolite <sup>[7]</sup>
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End point description:

End point type	Primary
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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.

<b>End point values</b>	Balovaptan			
Subject group type	Reporting group			
Number of subjects analysed	0 <sup>[8]</sup>			
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
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End point description:

End point type	Primary
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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.

<b>End point values</b>	Balovaptan			
Subject group type	Reporting group			
Number of subjects analysed	0 <sup>[10]</sup>			
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 <sup>[11]</sup>
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End point description:

End point type	Primary
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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.

<b>End point values</b>	Balovaptan			
Subject group type	Reporting group			
Number of subjects analysed	0 <sup>[12]</sup>			
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
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End point description:

End point type	Secondary
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End point timeframe:

Up to approximately week 20

<b>End point values</b>	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
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	23.0
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### Reporting groups

Reporting group title	Balovaptan
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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 subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1		
Respiratory, thoracic and mediastinal disorders Cough subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 1		
Metabolism and nutrition disorders Abnormal weight gain subjects affected / exposed occurrences (all)	1 / 2 (50.00%) 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

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.
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Notes: