



## Clinical trial results:

### A 12-week, open-label, dose-escalating, phase 2 study to evaluate the effects of MBX-8025 in patients with Homozygous Familial Hypercholesterolemia (HoFH)

#### Summary

EudraCT number	2014-004856-68
Trial protocol	NO NL FR
Global end of trial date	15 February 2016

#### Results information

Result version number	v1 (current)
This version publication date	26 March 2017
First version publication date	26 March 2017
Summary attachment (see zip file)	Synopsis (2-synopsis.pdf)

#### Trial information

##### Trial identification

Sponsor protocol code	CB8025-21427
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02472535
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	CymaBay Therapeutics, Inc
Sponsor organisation address	7999 Gateway Blvd, suite 130, Newark, CA, United States, 94560
Public contact	Pol Boudes, CymaBay Therapeutics, Inc., 001 5102938815, pboudes@cymabay.com
Scientific contact	Pol Boudes, CymaBay Therapeutics, Inc., 001 5102938815, pboudes@cymabay.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:

## Results analysis stage

Analysis stage	Final
Date of interim/final analysis	15 February 2016
Is this the analysis of the primary completion data?	Yes
Primary completion date	15 February 2016
Global end of trial reached?	Yes
Global end of trial date	15 February 2016
Was the trial ended prematurely?	No

Notes:

## General information about the trial

Main objective of the trial:

Primary:

To evaluate the effect of MBX-8025 on Low Density Lipoprotein Cholesterol (LDL-C).

Protection of trial subjects:

If AEs were severe and drug related, the subject stopped treatment and entered the follow-up period.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	29 April 2015
Long term follow-up planned	No
Independent data monitoring committee (IDMC) involvement?	Yes

Notes:

## Population of trial subjects

### Subjects enrolled per country

Country: Number of subjects enrolled	Norway: 2
Country: Number of subjects enrolled	Canada: 5
Country: Number of subjects enrolled	Netherlands: 2
Country: Number of subjects enrolled	France: 4
Worldwide total number of subjects	13
EEA total number of subjects	8

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)	0
Adolescents (12-17 years)	0
Adults (18-64 years)	11
From 65 to 84 years	2
85 years and over	0

## Subject disposition

### Recruitment

Recruitment details: -

### Pre-assignment

Screening details:

The screening period was a maximum of 2 weeks. All subjects had to confirm eligibility on Visit 2 (Week 0) prior to entering the run-in period

### Period 1

Period 1 title	2 weeks screening period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

### Arms

Arm title	single-arm
Arm description: -	
Arm type	Cohort
No investigational medicinal product assigned in this arm	

<b>Number of subjects in period 1</b>	single-arm
Started	13
Completed	13

### Period 2

Period 2 title	Run-in period
Is this the baseline period?	Yes <sup>[1]</sup>
Allocation method	Not applicable
Blinding used	Not blinded

### Arms

Arm title	2 weeks treatment with placebo
Arm description: 2 weeks treatment with placebo	
Arm type	Cohort

Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

The placebo treatment was administered PO once daily and only during the run-in period. The placebo was a gelatin capsule, containing all ingredients in the investigational product, except for the active pharmaceutical ingredient, MBX-8025. Only 1 batch of placebo was used: batch number 14G058.

Notes:

[1] - Period 1 is not the baseline period. It is expected that period 1 will be the baseline period.

Justification: Period 2 is the Baseline period

<b>Number of subjects in period 2</b>	2 weeks treatment with placebo
Started	13
Completed	13

### Period 3

Period 3 title	Treatment Phase 1
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

### Arms

<b>Arm title</b>	4 weeks treatment with 50 mg daily
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Arm description:

4 weeks treatment with 50 mg daily

Arm type	Cohort
Investigational medicinal product name	MBX-8025
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

The test product was MBX-8025 capsules (50 mg). Dosing was oral (PO), once daily, in doses of 50 mg (first 4-week treatment period). The 50 mg MBX-8025 test product was batch number 14G059.

<b>Number of subjects in period 3</b>	4 weeks treatment with 50 mg daily
Started	13
Completed	13

#### Period 4

Period 4 title	Treatment Phase 2
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

#### Arms

<b>Arm title</b>	4 weeks treatment with 100 mg daily
Arm description: 4 weeks treatment with 100 mg daily	
Arm type	Cohort
Investigational medicinal product name	MBX-8025
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

#### Dosage and administration details:

The test product was MBX-8025 capsules (50 or 100 mg). Dosing was oral (PO), once daily, in doses of 100 or 50 mg (second 4-week treatment period). The 50 mg MBX-8025 test product was batch number 14G059, and the 100 mg MBX-8025 test product was batch number 14G060.

<b>Number of subjects in period 4</b>	4 weeks treatment with 100 mg daily
Started	13
Completed	13

#### Period 5

Period 5 title	Treatment Phase 3
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

## Arms

<b>Arm title</b>	4 weeks treatment with 200 mg daily
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Arm description:

4 weeks treatment with 200 mg daily

Arm type	Cohort
Investigational medicinal product name	MBX-8025
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Capsule
Routes of administration	Oral use

Dosage and administration details:

The test product was MBX-8025 capsules (50 or 100 mg). Dosing was oral (PO), once daily, in doses of 200, 100, or 50 (third 4-week treatment period). The 50 mg MBX-8025 test product was batch number 14G059, and the 100 mg MBX-8025 test product was batch number 14G060.

<b>Number of subjects in period 5</b>	4 weeks treatment with 200 mg daily
Started	13
Completed	13

## Period 6

Period 6 title	Follow-up period
Is this the baseline period?	No
Allocation method	Not applicable
Blinding used	Not blinded

## Arms

<b>Arm title</b>	2 weeks follow-up
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Arm description:

2 weeks follow-up

Arm type	Cohort
No investigational medicinal product assigned in this arm	

<b>Number of subjects in period 6</b>	2 weeks follow-up
Started	13
Completed	13

## Baseline characteristics

### Reporting groups

Reporting group title	Run-in period
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Reporting group description: -

Reporting group values	Run-in period	Total	
Number of subjects	13	13	
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)	0	0	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	11	11	
From 65-84 years	2	2	
85 years and over	0	0	
Age continuous			
Units: years			
arithmetic mean	41.2		
full range (min-max)	18 to 85	-	
Gender categorical			
Units: Subjects			
Female	5	5	
Male	8	8	



## End points

### End points reporting groups

Reporting group title	single-arm
Reporting group description: -	
Reporting group title	2 weeks treatment with placebo
Reporting group description: 2 weeks treatment with placebo	
Reporting group title	4 weeks treatment with 50 mg daily
Reporting group description: 4 weeks treatment with 50 mg daily	
Reporting group title	4 weeks treatment with 100 mg daily
Reporting group description: 4 weeks treatment with 100 mg daily	
Reporting group title	4 weeks treatment with 200 mg daily
Reporting group description: 4 weeks treatment with 200 mg daily	
Reporting group title	2 weeks follow-up
Reporting group description: 2 weeks follow-up	

### Primary: Safety

End point title	Safety <sup>[1]</sup>
End point description:	
End point type	Primary
End point timeframe: 4 weeks	

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: Please see attached synopsis

End point values	4 weeks treatment with 50 mg daily	4 weeks treatment with 100 mg daily	4 weeks treatment with 200 mg daily	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	13	13	
Units: Subjects with at least one TEAE	7	8	5	

### Statistical analyses

No statistical analyses for this end point

### Primary: Efficacy

End point title	Efficacy <sup>[2]</sup>
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End point description:

End point type	Primary
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End point timeframe:

4 weeks

Notes:

[2] - 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: Please see attached synopsis

End point values	4 weeks treatment with 50 mg daily	4 weeks treatment with 100 mg daily	4 weeks treatment with 200 mg daily	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	13	13	13	
Units: % Mean Maximum Change in LDL-C				
number (not applicable)	-13.2	-10.5	-10.7	

### Statistical analyses

No statistical analyses for this end point

## Adverse events

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### Adverse events information<sup>[1]</sup>

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Timeframe for reporting adverse events:

From baseline through week 16

Assessment type	Systematic
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### Dictionary used

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Dictionary name	MedDRA
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Dictionary version	18.0
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Frequency threshold for reporting non-serious adverse events: 5 %

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Notes:

[1] - There are no non-serious adverse events recorded for these results. It is expected that there will be at least one non-serious adverse event reported.

Justification: Please see attached synopsis

## **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