



## Clinical trial results:

### A Phase I/II Open Label Study in Previously Studied, SBC-103 Treatment Naïve MPS IIIB Subjects to Investigate the Safety, Pharmacokinetics, and Pharmacodynamics/Efficacy of SBC-103 Administered Intravenously

#### Summary

EudraCT number	2015-001983-20
Trial protocol	GB
Global end of trial date	18 August 2017

#### Results information

Result version number	v1 (current)
This version publication date	02 March 2018
First version publication date	02 March 2018

#### Trial information

##### Trial identification

Sponsor protocol code	NGLU-CL01-T
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##### Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02618512
WHO universal trial number (UTN)	-

Notes:

#### Sponsors

Sponsor organisation name	Alexion Pharmaceuticals
Sponsor organisation address	100 College Street, New Haven, United States, 06510
Public contact	European Clinical Trial Information, Alexion Europe SAS, +33 1 47 10 06 06, ClinicalTrials.EU@alexion.com
Scientific contact	European Clinical Trial Information, Alexion Europe SAS, +33 1 47 10 06 06, ClinicalTrials.EU@alexion.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	31 October 2017
Is this the analysis of the primary completion data?	Yes
Primary completion date	18 August 2017
Global end of trial reached?	Yes
Global end of trial date	18 August 2017
Was the trial ended prematurely?	Yes

Notes:

## General information about the trial

Main objective of the trial:

To evaluate the safety and tolerability of intravenous administration of SBC-103 in previously studied, SBC-103 treatment naïve subjects with mucopolysaccharidosis III, type B (MPS IIIB, Sanfilippo B) who participated in the NGLU-CL01 study.

Protection of trial subjects:

NOT APPLICABLE

Background therapy:

NOT APPLICABLE

Evidence for comparator:

Comparator was not used.

Actual start date of recruitment	17 September 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	United Kingdom: 3
Worldwide total number of subjects	3
EEA total number of subjects	3

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)	3
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:

This study (NGLU-CL01-T) was conducted in MPS IIIB patients who participated in the NGLU-CL01 study, a non-interventional study that evaluated structural brain abnormalities and BBB integrity by MRI and CSF-AI. All subjects enrolled in the NGLU-CL01 study were  $\geq 5$  years of age and had a definitive diagnosis of MPS IIIB.

### Pre-assignment

Screening details:

Participants from NGU-CL01 Study were eligible for enrollment in NGLU-CL01-T.  
Subjects who met all of the inclusion criteria and none of the exclusion criteria were eligible to participate in this study

### Period 1

Period 1 title	Overall Trial (overall period)
Is this the baseline period?	Yes
Allocation method	Not applicable
Blinding used	Not blinded

Blinding implementation details:

NOT APPLICABLE.

### Arms

Arm title	SBC-103
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Arm description:

Subjects were treated with 1 mg/kg IV every other week for a minimum of 12 weeks. After evaluation of 12 weeks of safety and tolerability data, subjects were dose-escalated to 3 mg/kg every other week.

Arm type	Experimental
Investigational medicinal product name	SBC-103
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

Subjects were treated with 1 mg/kg IV for a minimum of 12 weeks. After evaluation of 12 weeks safety and tolerability data the individual subject dose were increased to 3 mg/kg every other week up to 3 years (156 weeks). The planned study duration was 156 weeks. Due to the early study termination, the actual study duration was 96 weeks.

<b>Number of subjects in period 1</b>	SBC-103
Started	3
Completed	3

## Baseline characteristics

### Reporting groups

Reporting group title	Overall Trial (overall period)
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Reporting group description: -

Reporting group values	Overall Trial (overall period)	Total	
Number of subjects	3	3	
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)	3	3	
Adolescents (12-17 years)	0	0	
Adults (18-64 years)	0	0	
From 65-84 years	0	0	
85 years and over	0	0	
Gender categorical Units: Subjects			
Female	1	1	
Male	2	2	

## End points

### End points reporting groups

Reporting group title	SBC-103
Reporting group description:	
Subjects were treated with 1 mg/kg IV every other week for a minimum of 12 weeks. After evaluation of 12 weeks of safety and tolerability data, subjects were dose-escalated to 3 mg/kg every other week.	

### Primary: The primary endpoint of this study is safety and tolerability of SBC-103 in subjects with MPS IIIB

End point title	The primary endpoint of this study is safety and tolerability of SBC-103 in subjects with MPS IIIB <sup>[1]</sup>
End point description:	
Measured by number of patients reporting adverse events.	
End point type	Primary
End point timeframe:	
Baseline to 96 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: No comparative analysis was done. 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.

<b>End point values</b>	SBC-103			
Subject group type	Reporting group			
Number of subjects analysed	3			
Units: patients	3			

### Statistical analyses

No statistical analyses for this end point

## Adverse events

### Adverse events information

Timeframe for reporting adverse events:

2 Years

Assessment type	Systematic
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### Dictionary used

Dictionary name	MedDRA
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Dictionary version	19
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### Reporting groups

Reporting group title	Overall Trial
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Reporting group description: -

Serious adverse events	Overall Trial		
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 3 (66.67%)		
number of deaths (all causes)	0		
number of deaths resulting from adverse events	0		
Injury, poisoning and procedural complications			
Wound dehiscence			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Surgical and medical procedures			
Catheter placement			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Skin and subcutaneous tissue disorders			
Erythema multiforme			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences causally related to treatment / all	0 / 1		
deaths causally related to treatment / all	0 / 0		
Infections and infestations			
Device related infection			

subjects affected / exposed	2 / 3 (66.67%)		
occurrences causally related to treatment / all	0 / 2		
deaths causally related to treatment / all	0 / 0		

Frequency threshold for reporting non-serious adverse events: 1 %

<b>Non-serious adverse events</b>	Overall Trial		
Total subjects affected by non-serious adverse events			
subjects affected / exposed	3 / 3 (100.00%)		
General disorders and administration site conditions			
Pyrexia			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	5		
Catheter site pain			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	2		
Gait disturbance			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	2		
Pain			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	2		
Complication associated with device			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Excessive granulation tissue			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Fatigue			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Peripheral swelling			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Immune system disorders			

Seasonal allergy subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Reproductive system and breast disorders Dysmenorrhoea subjects affected / exposed occurrences (all)  Premenstrual pain subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1  1 / 3 (33.33%) 1		
Respiratory, thoracic and mediastinal disorders Epistaxis subjects affected / exposed occurrences (all)  Choking subjects affected / exposed occurrences (all)  Cough subjects affected / exposed occurrences (all)  Rhinorrhoea subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 2  1 / 3 (33.33%) 1  1 / 3 (33.33%) 1  1 / 3 (33.33%) 1		
Psychiatric disorders Restlessness subjects affected / exposed occurrences (all)  Anxiety subjects affected / exposed occurrences (all)  Sleep disorder subjects affected / exposed occurrences (all)  Abnormal behaviour subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 4  2 / 3 (66.67%) 3  2 / 3 (66.67%) 2  1 / 3 (33.33%) 1		



Breath holding subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Emotional distress subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Investigations Body temperature increased subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Injury, poisoning and procedural complications Fall subjects affected / exposed occurrences (all)  Procedural pain subjects affected / exposed occurrences (all)  Contusion subjects affected / exposed occurrences (all)  Post-traumatic pain subjects affected / exposed occurrences (all)  Scratch subjects affected / exposed occurrences (all)	3 / 3 (100.00%) 8  3 / 3 (100.00%) 4  1 / 3 (33.33%) 1  1 / 3 (33.33%) 1  1 / 3 (33.33%) 1		
Cardiac disorders Bradycardia subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Nervous system disorders Headache subjects affected / exposed occurrences (all)  Psychomotor hyperactivity	2 / 3 (66.67%) 2		

subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	2		
Dyskinesia			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	2		
Seizure			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	2		
Motor dysfunction			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Petit mal epilepsy			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		
Gastrointestinal disorders			
Vomiting			
subjects affected / exposed	3 / 3 (100.00%)		
occurrences (all)	6		
Diarrhoea			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	8		
Toothache			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	8		
Constipation			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	2		
Salivary hypersecretion			
subjects affected / exposed	2 / 3 (66.67%)		
occurrences (all)	2		
Abdominal pain upper			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	2		
Abdominal discomfort			
subjects affected / exposed	1 / 3 (33.33%)		
occurrences (all)	1		

Dysphagia subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Vomiting projectile subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Skin and subcutaneous tissue disorders Skin warm subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 2		
Application site erythema subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Excessive granulation tissue subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Hair disorder subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Skin irritation subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Urticaria subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Endocrine disorders Precocious puberty subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Musculoskeletal and connective tissue disorders Back pain subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Musculoskeletal stiffness subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		

Pain in extremity subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Infections and infestations			
Nasopharyngitis subjects affected / exposed occurrences (all)	3 / 3 (100.00%) 11		
Staphylococcal infection subjects affected / exposed occurrences (all)	2 / 3 (66.67%) 2		
Candida infection subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 2		
Ear infection subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Urinary tract infection subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		
Viral upper respiratory tract infection subjects affected / exposed occurrences (all)	1 / 3 (33.33%) 1		

## More information

### Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
07 July 2015	Amendment# 1: The purpose of this amendment was to provide further clarification on: starting dose of study drug, contraceptive methods as it pertains to inclusion criteria #3 and the stopping rules for multiple subjects who experience SAEs possible related to study drug.

Notes:

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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.

None reported.
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Notes: