Clinical trial results:
A 24 week off drug extension, parallel group, study assessing durability of effect on skeletal muscle strength and function following a 6-month double-blind, placebo controlled study evaluating bimagrumab in older adults with sarcopenia (InvestiGAIT extension)

Summary

EudraCT number	2015-000471-27
Trial protocol	ES BE DK
Global end of trial date	03 December 2018

Results information

Result version number	v1 (current)
This version publication date	13 November 2019
First version publication date	13 November 2019

Trial information

Trial identification

Sponsor protocol code	CBYM338E2202E1

Additional study identifiers

ISRCTN number	-
ClinicalTrials.gov id (NCT number)	NCT02468674
WHO universal trial number (UTN)	-

Notes:

Sponsors

Sponsor organisation name	Novartis Pharma AG
Sponsor organisation address	CH-4002, Basel, Switzerland,
Public contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.com
Scientific contact	Clinical Disclosure Office, Novartis Pharma AG, 41 613241111, Novartis.email@novartis.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	03 December 2018
Is this the analysis of the primary completion data?	Yes
Primary completion date	03 December 2018
Global end of trial reached?	Yes
Global end of trial date	03 December 2018
Was the trial ended prematurely?	No

Notes:

General information about the trial

Main objective of the trial:

The primary objective was to assess the durability of effect of bimagrumab (BYM338) on physical function as measured by the Short Physical Performance Battery (SPPB) total score at Week 49.

Protection of trial subjects:

The study was in compliance with the ethical principles derived from the Declaration of Helsinki and the International Conference on Harmonization (ICH) Good Clinical Practice (GCP) guidelines. All the local regulatory requirements pertinent to safety of trial subjects were also followed during the conduct of the trial.

Background therapy: -

Evidence for comparator: -

Actual start date of recruitment	22 July 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	Australia: 2
Country: Number of subjects enrolled	Belgium: 1
Country: Number of subjects enrolled	Czech Republic: 1
Country: Number of subjects enrolled	Denmark: 3
Country: Number of subjects enrolled	France: 3
Country: Number of subjects enrolled	Japan: 16
Country: Number of subjects enrolled	Korea, Republic of: 5
Country: Number of subjects enrolled	Russian Federation: 15
Country: Number of subjects enrolled	Spain: 3
Country: Number of subjects enrolled	Switzerland: 1
Country: Number of subjects enrolled	Taiwan: 5
Country: Number of subjects enrolled	United States: 105
Worldwide total number of subjects	160
EEA total number of subjects	11

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)	0
From 65 to 84 years	131
85 years and over	29

Subject disposition

Recruitment

Recruitment details: -

Pre-assignment

Screening details:

This study was conducted in 30 centers in 12 countries: Australia (1), Belgium (1), Czech Republic (1), Denmark (1), France (2), Japan (10), Russia (4), South Korea (1), Spain (2), Switzerland (1), Taiwan (1), United States (5).

Period 1

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

Arms

Are arms mutually exclusive?	Yes
Arm title	Population I: BYM338 700 mg

Arm description:

Follow-up (arm 1): Patients in Population I received 6 doses of bimagrumab 70 mg, 210 mg, 700 mg or placebo – one approximately every four weeks – over a 20-week period providing drug exposure for a total of 24 weeks.

Arm type	Experimental
Investigational medicinal product name	Bimagrumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

6 doses of bimagrumab 700 mg one approximately every four weeks – over a 20-week period providing drug exposure for a total of 24 weeks.

Arm title	Population I BYM338: 700 mg to Placebo

Arm description:

Follow-up (arm 1): Patients in Population I received 6 doses of bimagrumab 70 mg, 210 mg, 700 mg or placebo – one approximately every four weeks – over a 20-week period providing drug exposure for a total of 24 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

6 doses of bimagrumab 700 mg matching placebo one approximately every four weeks – over a 20-week period providing drug exposure for a total of 24 weeks.

Arm title	Population I: BYM338 210 mg

Arm description:

Follow-up (arm 1): Patients in Population I received 6 doses of bimagrumab 70 mg, 210 mg, 700 mg or placebo – one approximately every four weeks – over a 20-week period providing drug exposure for a total of 24 weeks.

Arm type	Experimental

Investigational medicinal product name	Bimagrumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

6 doses of bimagrumab 210 mg one approximately every four weeks – over a 20-week period providing drug exposure for a total of 24 weeks.

Arm title	Population I BYM338: 210 mg to Placebo

Arm description:

Follow-up (arm 1): Patients in Population I received 6 doses of bimagrumab 70 mg, 210 mg, 700 mg or placebo – one approximately every four weeks – over a 20-week period providing drug exposure for a total of 24 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

6 doses of bimagrumab 210 mg mg matching placebo one approximately every four weeks – over a 20-week period providing drug exposure for a total of 24 weeks.

Arm title	Population I: BYM338 70 mg

Arm description:

Follow-up (arm 1): Patients in Population I received 6 doses of bimagrumab 70 mg, 210 mg, 700 mg or placebo – one approximately every four weeks – over a 20-week period providing drug exposure for a total of 24 weeks.

Arm type	Experimental
Investigational medicinal product name	Bimagrumab
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate and solvent for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

6 doses of bimagrumab 70 mg one approximately every four weeks – over a 20-week period providing drug exposure for a total of 24 weeks.

Arm title	Population I: BYM338 70 mg to Placebo

Arm description:

Follow-up (arm 1): Patients in Population I received 6 doses of bimagrumab 70 mg, 210 mg, 700 mg or placebo – one approximately every four weeks – over a 20-week period providing drug exposure for a total of 24 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

6 doses of bimagrumab 70 mg matching placebo one approximately every four weeks – over a 20-week period providing drug exposure for a total of 24 weeks.

Arm title	Population I: Placebo

Arm description:

Follow-up (arm 1): Patients in Population I received 6 doses of bimagrumab 70 mg, 210 mg, 700 mg or placebo – one approximately every four weeks – over a 20-week period providing drug exposure for a

total of 24 weeks.

Arm type	Placebo
Investigational medicinal product name	Placebo
Investigational medicinal product code	
Other name	
Pharmaceutical forms	Concentrate for solution for infusion
Routes of administration	Intravenous use

Dosage and administration details:

6 doses of bimagrumab 70 mg, 210 mg or 700 mg matching placebo one approximately every four weeks – over a 20-week period providing drug exposure for a total of 24 weeks.

Arm title	Population: II BYM338 700 mg

Arm description:

Follow-up (arm 2): Patients in Population II received either bimagrumab 700 mg or placebo in the core study and did not receive any investigational treatment in the extension study.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Arm title	Population: II Placebo

Arm description:

Follow-up (arm 2): Patients in Population II received either bimagrumab 700 mg or placebo in the core study and did not receive any investigational treatment in the extension study.

Arm type	No intervention

No investigational medicinal product assigned in this arm

Number of subjects in period 1	Population I: BYM338 700 mg	Population I BYM338: 700 mg to Placebo	Population I: BYM338 210 mg
Started	5	5	5
Completed	4	5	5
Not completed	1	0	0
Physician decision	-	-	-
Adverse event, non-fatal	-	-	-
Patient/Guardian Decision	-	-	-
Protocol Deviation	-	-	-
Lost to follow-up	1	-	-

Number of subjects in period 1	Population I BYM338: 210 mg to Placebo	Population I: BYM338 70 mg	Population I: BYM338 70 mg to Placebo
Started	4	7	7
Completed	3	6	6
Not completed	1	1	1
Physician decision	-	-	-
Adverse event, non-fatal	1	-	1
Patient/Guardian Decision	-	1	-
Protocol Deviation	-	-	-
Lost to follow-up	-	-	-

Number of subjects in period 1	Population I: Placebo	Population: II BYM338 700 mg	Population: II Placebo
Started	15	69	43
Completed	14	65	40
Not completed	1	4	3
Physician decision	1	-	-
Adverse event, non-fatal	-	-	-
Patient/Guardian Decision	-	2	1
Protocol Deviation	-	1	1
Lost to follow-up	-	1	1

Baseline characteristics

Reporting groups	
Reporting group title	Population I: BYM338 700 mg
Reporting group description:	
Follow-up (arm 1): Patients in Population I received 6 doses of bimagrumab 70 mg, 210 mg, 700 mg or placebo – one approximately every four weeks – over a 20-week period providing drug exposure for a total of 24 weeks.	
Reporting group title	Population I BYM338: 700 mg to Placebo
Reporting group description:	
Follow-up (arm 1): Patients in Population I received 6 doses of bimagrumab 70 mg, 210 mg, 700 mg or placebo – one approximately every four weeks – over a 20-week period providing drug exposure for a total of 24 weeks.	
Reporting group title	Population I: BYM338 210 mg
Reporting group description:	
Follow-up (arm 1): Patients in Population I received 6 doses of bimagrumab 70 mg, 210 mg, 700 mg or placebo – one approximately every four weeks – over a 20-week period providing drug exposure for a total of 24 weeks.	
Reporting group title	Population I BYM338: 210 mg to Placebo
Reporting group description:	
Follow-up (arm 1): Patients in Population I received 6 doses of bimagrumab 70 mg, 210 mg, 700 mg or placebo – one approximately every four weeks – over a 20-week period providing drug exposure for a total of 24 weeks.	
Reporting group title	Population I: BYM338 70 mg
Reporting group description:	
Follow-up (arm 1): Patients in Population I received 6 doses of bimagrumab 70 mg, 210 mg, 700 mg or placebo – one approximately every four weeks – over a 20-week period providing drug exposure for a total of 24 weeks.	
Reporting group title	Population I: BYM338 70 mg to Placebo
Reporting group description:	
Follow-up (arm 1): Patients in Population I received 6 doses of bimagrumab 70 mg, 210 mg, 700 mg or placebo – one approximately every four weeks – over a 20-week period providing drug exposure for a total of 24 weeks.	
Reporting group title	Population I: Placebo
Reporting group description:	
Follow-up (arm 1): Patients in Population I received 6 doses of bimagrumab 70 mg, 210 mg, 700 mg or placebo – one approximately every four weeks – over a 20-week period providing drug exposure for a total of 24 weeks.	
Reporting group title	Population: II BYM338 700 mg
Reporting group description:	
Follow-up (arm 2): Patients in Population II received either bimagrumab 700 mg or placebo in the core study and did not receive any investigational treatment in the extension study.	
Reporting group title	Population: II Placebo
Reporting group description:	
Follow-up (arm 2): Patients in Population II received either bimagrumab 700 mg or placebo in the core study and did not receive any investigational treatment in the extension study.	

Reporting group values	Population I: BYM338 700 mg	Population I BYM338: 700 mg to Placebo	Population I: BYM338 210 mg
Number of subjects	5	5	5
Age categorical Units: Subjects			
In utero	0	0	0

Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	4	3	5
85 years and over	1	2	0
Age Continuous			
Age Continuous for Population I and Population II			
Units: years			
arithmetic mean	80.0	79.4	79.0
standard deviation	± 4.90	± 7.27	± 1.58
Sex: Female, Male			
Gender for Population I and Population II			
Units: Subjects			
Female	1	2	2
Male	4	3	3
Race/Ethnicity, Customized			
Race/Ethnicity for Population I and Population II			
Units: Subjects			
Asian	1	0	0
Black	0	0	0
Caucasian	4	5	5
Native American	0	0	0
Pacific Islander	0	0	0
Population I & II: Short Physical Performance Battery (SPPB) total score at Week 25			
Baseline Extension Visit = Week 25. SPPB evaluates lower extremities in three functional components: maintenance of standing balance, usual gait speed and chair stand. Each test yields a score on a scale from 0 to 4 (total score 0-12, with the higher score reflecting a higher level of function).			
Units: Total scores			
arithmetic mean	8.8	10.4	8.6
standard deviation	± 2.17	± 1.34	± 1.67
Population I & II: 6-minute walking distance (6MWT) at Week 25			
Baseline Extension Visit = Week 25. The 6MWT measures the distance an individual is able to walk over a total of six minutes on a hard, flat surface. The goal is for the individual to walk as far as possible in six minutes. The individual is able to self-pace and rest as needed as they traverse back and forth along a marked walkway.			
Units: meters			
arithmetic mean	302.73	353.10	313.67
standard deviation	± 130.22	± 66.17	± 71.39
Population I & II: Gait speed at Week 25			
Baseline Extension Visit = Week 25. Gait Speed was assessed as part of SPPB, over a 4 meter distance of a 6 meter course. Gait speed assesses a person's usual walking speed, which is defined as the speed a person normally walks from one place to another. Poor functional performance is measured by slow or declining gait speed.			
Units: m/sec			
arithmetic mean	0.8	0.9	0.9
standard deviation	± 0.20	± 0.13	± 0.27

Reporting group values	Population I BYM338: 210 mg to Placebo	Population I: BYM338 70 mg	Population I: BYM338 70 mg to Placebo
Number of subjects	4	7	7
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	4	6	5
85 years and over	0	1	2
Age Continuous			
Age Continuous for Population I and Population II			
Units: years			
arithmetic mean	74.8	77.6	81.6
standard deviation	± 2.63	± 6.75	± 4.58
Sex: Female, Male			
Gender for Population I and Population II			
Units: Subjects			
Female	2	3	5
Male	2	4	2
Race/Ethnicity, Customized			
Race/Ethnicity for Population I and Population II			
Units: Subjects			
Asian	1	2	2
Black	0	1	1
Caucasian	3	4	4
Native American	0	0	0
Pacific Islander	0	0	0
Population I & II: Short Physical Performance Battery (SPPB) total score at Week 25			
Baseline Extension Visit = Week 25. SPPB evaluates lower extremities in three functional components: maintenance of standing balance, usual gait speed and chair stand. Each test yields a score on a scale from 0 to 4 (total score 0-12, with the higher score reflecting a higher level of function).			
Units: Total scores			
arithmetic mean	8.5	8.9	8.0
standard deviation	± 1.91	± 2.04	± 3.27
Population I & II: 6-minute walking distance (6MWT) at Week 25			
Baseline Extension Visit = Week 25. The 6MWT measures the distance an individual is able to walk over a total of six minutes on a hard, flat surface. The goal is for the individual to walk as far as possible in six minutes. The individual is able to self-pace and rest as needed as they traverse back and forth along a marked walkway.			
Units: meters			
arithmetic mean	361.07	305.24	286.94
standard deviation	± 80.11	± 111.34	± 119.37
Population I & II: Gait speed at Week 25			
Baseline Extension Visit = Week 25. Gait Speed was assessed as part of SPPB, over a 4 meter distance			

of a 6 meter course. Gait speed assesses a person's usual walking speed, which is defined as the speed a person normally walks from one place to another. Poor functional performance is measured by slow or declining gait speed.			
Units: m/sec			
arithmetic mean	0.9	0.8	0.6
standard deviation	± 0.12	± 0.19	± 0.28

Reporting group values	Population I: Placebo	Population: II BYM338 700 mg	Population: II Placebo
Number of subjects	15	69	43
Age categorical			
Units: Subjects			
In utero	0	0	0
Preterm newborn infants (gestational age < 37 wks)	0	0	0
Newborns (0-27 days)	0	0	0
Infants and toddlers (28 days-23 months)	0	0	0
Children (2-11 years)	0	0	0
Adolescents (12-17 years)	0	0	0
Adults (18-64 years)	0	0	0
From 65-84 years	13	56	35
85 years and over	2	13	8
Age Continuous			
Age Continuous for Population I and Population II			
Units: years			
arithmetic mean	79.9	79.8	78.2
standard deviation	± 4.22	± 5.05	± 5.29
Sex: Female, Male			
Gender for Population I and Population II			
Units: Subjects			
Female	8	40	29
Male	7	29	14
Race/Ethnicity, Customized			
Race/Ethnicity for Population I and Population II			
Units: Subjects			
Asian	6	11	3
Black	1	0	0
Caucasian	8	56	40
Native American	0	1	0
Pacific Islander	0	1	0
Population I & II: Short Physical Performance Battery (SPPB) total score at Week 25			
Baseline Extension Visit = Week 25. SPPB evaluates lower extremities in three functional components: maintenance of standing balance, usual gait speed and chair stand. Each test yields a score on a scale from 0 to 4 (total score 0-12, with the higher score reflecting a higher level of function).			
Units: Total scores			
arithmetic mean	9.1	8.5	8.2
standard deviation	± 1.58	± 2.17	± 2.25
Population I & II: 6-minute walking distance (6MWT) at Week 25			
Baseline Extension Visit = Week 25. The 6MWT measures the distance an individual is able to walk over a total of six minutes on a hard, flat surface. The goal is for the individual to walk as far as possible in six minutes. The individual is able to self-pace and rest as needed as they traverse back and forth along a marked walkway.			

Units: meters			
arithmetic mean	352.18	307.84	315.61
standard deviation	± 123.55	± 99.96	± 95.74
Population I & II: Gait speed at Week 25			
Baseline Extension Visit = Week 25. Gait Speed was assessed as part of SPPB, over a 4 meter distance of a 6 meter course. Gait speed assesses a person's usual walking speed, which is defined as the speed a person normally walks from one place to another. Poor functional performance is measured by slow or declining gait speed.			
Units: m/sec			
arithmetic mean	0.8	0.8	0.8
standard deviation	± 0.19	± 0.23	± 0.22

Reporting group values	Total		
Number of subjects	160		
Age categorical			
Units: Subjects			
In utero	0		
Preterm newborn infants (gestational age < 37 wks)	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)	0		
From 65-84 years	131		
85 years and over	29		
Age Continuous			
Age Continuous for Population I and Population II			
Units: years			
arithmetic mean			
standard deviation	-		
Sex: Female, Male			
Gender for Population I and Population II			
Units: Subjects			
Female	92		
Male	68		
Race/Ethnicity, Customized			
Race/Ethnicity for Population I and Population II			
Units: Subjects			
Asian	26		
Black	3		
Caucasian	129		
Native American	1		
Pacific Islander	1		
Population I & II: Short Physical Performance Battery (SPPB) total score at Week 25			
Baseline Extension Visit = Week 25. SPPB evaluates lower extremities in three functional components: maintenance of standing balance, usual gait speed and chair stand. Each test yields a score on a scale from 0 to 4 (total score 0-12, with the higher score reflecting a higher level of function).			
Units: Total scores			
arithmetic mean			
standard deviation	-		

Population I & II: 6-minute walking distance (6MWT) at Week 25			
Baseline Extension Visit = Week 25. The 6MWT measures the distance an individual is able to walk over a total of six minutes on a hard, flat surface. The goal is for the individual to walk as far as possible in six minutes. The individual is able to self-pace and rest as needed as they traverse back and forth along a marked walkway.			
Units: meters arithmetic mean standard deviation	- 		
Population I & II: Gait speed at Week 25			
Baseline Extension Visit = Week 25. Gait Speed was assessed as part of SPPB, over a 4 meter distance of a 6 meter course. Gait speed assesses a person's usual walking speed, which is defined as the speed a person normally walks from one place to another. Poor functional performance is measured by slow or declining gait speed.			
Units: m/sec arithmetic mean standard deviation	- 		

End points

End points reporting groups

Reporting group title	Population I: BYM338 700 mg
Reporting group description:	
Follow-up (arm 1): Patients in Population I received 6 doses of bimagrumab 70 mg, 210 mg, 700 mg or placebo – one approximately every four weeks – over a 20-week period providing drug exposure for a total of 24 weeks.	
Reporting group title	Population I BYM338: 700 mg to Placebo
Reporting group description:	
Follow-up (arm 1): Patients in Population I received 6 doses of bimagrumab 70 mg, 210 mg, 700 mg or placebo – one approximately every four weeks – over a 20-week period providing drug exposure for a total of 24 weeks.	
Reporting group title	Population I: BYM338 210 mg
Reporting group description:	
Follow-up (arm 1): Patients in Population I received 6 doses of bimagrumab 70 mg, 210 mg, 700 mg or placebo – one approximately every four weeks – over a 20-week period providing drug exposure for a total of 24 weeks.	
Reporting group title	Population I BYM338: 210 mg to Placebo
Reporting group description:	
Follow-up (arm 1): Patients in Population I received 6 doses of bimagrumab 70 mg, 210 mg, 700 mg or placebo – one approximately every four weeks – over a 20-week period providing drug exposure for a total of 24 weeks.	
Reporting group title	Population I: BYM338 70 mg
Reporting group description:	
Follow-up (arm 1): Patients in Population I received 6 doses of bimagrumab 70 mg, 210 mg, 700 mg or placebo – one approximately every four weeks – over a 20-week period providing drug exposure for a total of 24 weeks.	
Reporting group title	Population I: BYM338 70 mg to Placebo
Reporting group description:	
Follow-up (arm 1): Patients in Population I received 6 doses of bimagrumab 70 mg, 210 mg, 700 mg or placebo – one approximately every four weeks – over a 20-week period providing drug exposure for a total of 24 weeks.	
Reporting group title	Population I: Placebo
Reporting group description:	
Follow-up (arm 1): Patients in Population I received 6 doses of bimagrumab 70 mg, 210 mg, 700 mg or placebo – one approximately every four weeks – over a 20-week period providing drug exposure for a total of 24 weeks.	
Reporting group title	Population: II BYM338 700 mg
Reporting group description:	
Follow-up (arm 2): Patients in Population II received either bimagrumab 700 mg or placebo in the core study and did not receive any investigational treatment in the extension study.	
Reporting group title	Population: II Placebo
Reporting group description:	
Follow-up (arm 2): Patients in Population II received either bimagrumab 700 mg or placebo in the core study and did not receive any investigational treatment in the extension study.	

Primary: Population I: Short Physical Performance Battery (SPPB) total score at Week 49

End point title	Population I: Short Physical Performance Battery (SPPB) total score at Week 49[1]
End point description:	
SPPB evaluates lower extremities in three functional components: maintenance of standing balance, usual gait speed and chair stand. Each test yields a score on a scale from 0 to 4 (total score 0-12, with	

the higher score reflecting a higher level of function).

End point type	Primary

End point timeframe:

Week 49

Notes:

[1] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: To facilitate different analysis on patients enrolled before and after the protocol amendment 1, two populations are defined as below: · Population I: Patients enrolled prior to protocol amendment 1 · Population II: Patients enrolled after protocol amendment 1.

End point values	Population I: BYM338 700 mg	Population I BYM338: 700 mg to Placebo	Population I: BYM338 210 mg	Population I BYM338: 210 mg to Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	4	5	5	3
Units: Total scores				
arithmetic mean (standard deviation)	8.8 (± 3.86)	10.2 (± 1.92)	8.0 (± 2.35)	8.0 (± 2.65)

End point values	Population I: BYM338 70 mg	Population I: BYM338 70 mg to Placebo	Population I: Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	6	6	14	
Units: Total scores				
arithmetic mean (standard deviation)	9.5 (± 2.17)	7.5 (± 3.78)	9.6 (± 1.83)	

Statistical analyses

Statistical analysis title	Population I: SPPB total score at Week 49
Comparison groups	Population I: BYM338 700 mg v Population I BYM338: 700 mg to Placebo
Number of subjects included in analysis	9
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.759
Method	t-test, 1-sided

Statistical analysis title	Population I: SPPB total score at Week 49
Comparison groups	Population I: BYM338 210 mg v Population I BYM338: 210 mg to Placebo

Number of subjects included in analysis	8
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.5
Method	t-test, 1-sided

Statistical analysis title	Population I: SPPB total score at Week 49
Comparison groups	Population I: BYM338 70 mg v Population I: BYM338 70 mg to Placebo
Number of subjects included in analysis	12
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.144
Method	t-test, 1-sided

Statistical analysis title	Population I: SPPB total score at Week 49
Comparison groups	Population I: BYM338 700 mg v Population I: Placebo
Number of subjects included in analysis	18
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.648
Method	t-test, 1-sided

Statistical analysis title	Population I: SPPB total score at Week 49
Comparison groups	Population I: BYM338 210 mg v Population I: Placebo
Number of subjects included in analysis	19
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.929
Method	t-test, 1-sided

Statistical analysis title	Population I: SPPB total score at Week 49
Comparison groups	Population I: BYM338 70 mg v Population I: Placebo
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.53
Method	t-test, 1-sided

Primary: Population II: Short Physical Performance Battery (SPPB) total score at Week 49

End point title	Population II: Short Physical Performance Battery (SPPB) total score at Week 49[2]

End point description:

SPPB evaluates lower extremities in three functional components: maintenance of standing balance, usual gait speed and chair stand. Each test yields a score on a scale from 0 to 4 (total score 0-12, with the higher score reflecting a higher level of function).

End point type	Primary

End point timeframe:

Week 49

Notes:

[2] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: To facilitate different analysis on patients enrolled before and after the protocol amendment 1, two populations are defined as below: · Population I: Patients enrolled prior to protocol amendment 1 · Population II: Patients enrolled after protocol amendment 1.

End point values	Population: II BYM338 700 mg	Population: II Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	65	40		
Units: Total scores				
arithmetic mean (standard deviation)	8.6 (± 2.40)	8.8 (± 1.55)		

Statistical analyses

Statistical analysis title	Population II: SPPB total score at Week 49
Comparison groups	Population: II BYM338 700 mg v Population: II Placebo
Number of subjects included in analysis	105
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.839
Method	ANCOVA

Secondary: Population I: 6-minute walking distance (6MWT) at Week 49

End point title	Population I: 6-minute walking distance (6MWT) at Week 49[3]

End point description:

The 6MWT measures the distance an individual is able to walk over a total of six minutes on a hard, flat surface. The goal is for the individual to walk as far as possible in six minutes. The individual is able to self-pace and rest as needed as they traverse back and forth along a marked walkway. A high 6MWT represent better physical condition.

End point type	Secondary

End point timeframe:

Week 49

Notes:

[3] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: To facilitate different analysis on patients enrolled before and after the protocol amendment 1, two populations are defined as below: · Population I: Patients enrolled prior to protocol

amendment 1 · Population II: Patients enrolled after protocol amendment 1.

End point values	Population I: BYM338 700 mg	Population I BYM338: 700 mg to Placebo	Population I: BYM338 210 mg	Population I BYM338: 210 mg to Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	5	4
Units: meters				
arithmetic mean (standard deviation)	318.2 (± 159.55)	354.1 (± 69.98)	304.1 (± 63.05)	361.5 (± 144.53)

End point values	Population I: BYM338 70 mg	Population I: BYM338 70 mg to Placebo	Population I: Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	7	15	
Units: meters				
arithmetic mean (standard deviation)	316.1 (± 97.87)	273.4 (± 154.03)	368.7 (± 108.37)	

Statistical analyses

Statistical analysis title	Population I: 6MWT at Week 49
Comparison groups	Population I: BYM338 700 mg v Population I BYM338: 700 mg to Placebo
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.669
Method	t-test, 1-sided

Statistical analysis title	Population I: 6MWT at Week 49
Comparison groups	Population I: BYM338 210 mg v Population I BYM338: 210 mg to Placebo
Number of subjects included in analysis	9
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.773
Method	t-test, 1-sided

Statistical analysis title	Population I: 6MWT at Week 49
Comparison groups	Population I: BYM338 70 mg v Population I: BYM338 70 mg to

	Placebo
Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.29
Method	t-test, 1-sided

Statistical analysis title	Population I: 6MWT at Week 49
Comparison groups	Population I: BYM338 700 mg v Population I: Placebo
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.766
Method	t-test, 1-sided

Statistical analysis title	Population I: 6MWT at Week 49
Comparison groups	Population I: BYM338 210 mg v Population I: Placebo
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.885
Method	t-test, 1-sided

Statistical analysis title	Population I: 6MWT at Week 49
Comparison groups	Population I: BYM338 70 mg v Population I: Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.84
Method	t-test, 1-sided

Secondary: Population II: 6-minute walking distance (6MWT) at Week 49

End point title	Population II: 6-minute walking distance (6MWT) at Week 49[4]

End point description:

The 6MWT measures the distance an individual is able to walk over a total of six minutes on a hard, flat surface. The goal is for the individual to walk as far as possible in six minutes. The individual is able to self-pace and rest as needed as they traverse back and forth along a marked walkway. A high 6MWT represent better physical condition.

End point type	Secondary

End point timeframe:

Week 49

Notes:

[4] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: To facilitate different analysis on patients enrolled before and after the protocol amendment 1, two populations are defined as below: · Population I: Patients enrolled prior to protocol amendment 1 · Population II: Patients enrolled after protocol amendment 1.

End point values	Population: II BYM338 700 mg	Population: II Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	43		
Units: meters				
arithmetic mean (standard deviation)	321.2 (± 105.13)	323.1 (± 96.47)		

Statistical analyses

Statistical analysis title	Population II: 6MWT at Week 49
Comparison groups	Population: II BYM338 700 mg v Population: II Placebo
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.367
Method	ANCOVA

Secondary: Population I: Gait speed at Week 49

End point title	Population I: Gait speed at Week 49[5]

End point description:

Gait Speed was assessed as part of SPPB, over a 4 meter distance of a 6 meter course. Gait speed assesses a person's usual walking speed, which is defined as the speed a person normally walks from one place to another. Poor functional performance is measured by slow or declining gait speed.

End point type	Secondary

End point timeframe:

Week 49

Notes:

[5] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: To facilitate different analysis on patients enrolled before and after the protocol amendment 1, two populations are defined as below: · Population I: Patients enrolled prior to protocol amendment 1 · Population II: Patients enrolled after protocol amendment 1.

End point values	Population I: BYM338 700 mg	Population I BYM338: 700 mg to Placebo	Population I: BYM338 210 mg	Population I BYM338: 210 mg to Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	5	4
Units: m/sec				
arithmetic mean (standard deviation)	0.8 (± 0.35)	1.0 (± 0.18)	0.9 (± 0.17)	1.1 (± 0.24)

End point values	Population I: BYM338 70 mg	Population I: BYM338 70 mg to Placebo	Population I: Placebo	
Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	7	15	
Units: m/sec				
arithmetic mean (standard deviation)	0.9 (± 0.15)	0.7 (± 0.35)	0.8 (± 0.18)	

Statistical analyses

Statistical analysis title	Population I: Gait speed at Week 49
Comparison groups	Population I: BYM338 700 mg v Population I BYM338: 700 mg to Placebo
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.875
Method	t-test, 1-sided

Statistical analysis title	Population I: Gait speed at Week 49
Comparison groups	Population I: BYM338 210 mg v Population I BYM338: 210 mg to Placebo
Number of subjects included in analysis	9
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.909
Method	t-test, 1-sided

Statistical analysis title	Population I: Gait speed at Week 49
Comparison groups	Population I: BYM338 70 mg v Population I: BYM338 70 mg to Placebo
Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.168
Method	t-test, 1-sided

Statistical analysis title	Population I: Gait speed at Week 49
Comparison groups	Population I: BYM338 700 mg v Population I: Placebo

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.632
Method	t-test, 1-sided

Statistical analysis title	Population I: Gait speed at Week 49
Comparison groups	Population I: BYM338 210 mg v Population I: Placebo
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.31
Method	t-test, 1-sided

Statistical analysis title	Population I: Gait speed at Week 49
Comparison groups	Population I: BYM338 70 mg v Population I: Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.321
Method	t-test, 1-sided

Secondary: Population II: Gait speed at Week 49

End point title	Population II: Gait speed at Week 49[6]

End point description:

Gait Speed was assessed as part of SPPB, over a 4 meter distance of a 6 meter course. Gait speed assesses a person's usual walking speed, which is defined as the speed a person normally walks from one place to another. Poor functional performance is measured by slow or declining gait speed.

End point type	Secondary

End point timeframe:

Week 49

Notes:

[6] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: To facilitate different analysis on patients enrolled before and after the protocol amendment 1, two populations are defined as below: · Population I: Patients enrolled prior to protocol amendment 1 · Population II: Patients enrolled after protocol amendment 1.

End point values	Population: II BYM338 700 mg	Population: II Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	43		
Units: m/sec				
arithmetic mean (standard deviation)	0.9 (± 0.24)	0.9 (± 0.17)		

Statistical analyses

Statistical analysis title	Population II: Gait speed at Week 49
Statistical analysis description: Population II: Gait speed at Week 49	
Comparison groups	Population: II BYM338 700 mg v Population: II Placebo
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.395
Method	ANCOVA

Secondary: Population I: Appendicular Skeletal Muscle Index (ASMI) as measured by dual energy X-ray absorptiometry (DXA) at Week 49

End point title	Population I: Appendicular Skeletal Muscle Index (ASMI) as measured by dual energy X-ray absorptiometry (DXA) at Week 49[7]

End point description:

ASMI is a core requirement for determining the presence of sarcopenia and is calculated as the sum of the appendicular lean mass (kg) of the two upper and two lower limbs quantified by DXA, divided by height (m2). Therefore, an increase in ASMI indicates an increase in the quantity of an individual's lean mass.

End point type	Secondary

End point timeframe:

Week 49

Notes:

[7] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: To facilitate different analysis on patients enrolled before and after the protocol amendment 1, two populations are defined as below: · Population I: Patients enrolled prior to protocol amendment 1 · Population II: Patients enrolled after protocol amendment 1.

End point values	Population I: BYM338 700 mg	Population I BYM338: 700 mg to Placebo	Population I: BYM338 210 mg	Population I BYM338: 210 mg to Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	5	4
Units: kg/m2				
geometric mean (geometric coefficient of variation)	6.6 (± 7.22)	6.0 (± 14.05)	6.1 (± 8.08)	5.8 (± 15.08)

End point values	Population I: BYM338 70 mg	Population I: BYM338 70 mg to Placebo	Population I: Placebo	

Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	7	15	
Units: kg/m2				
geometric mean (geometric coefficient of variation)	5.9 (± 14.19)	5.2 (± 14.85)	5.6 (± 15.21)	

Statistical analyses

Statistical analysis title	Population I: ASMI at Week 49
Comparison groups	Population I: BYM338 700 mg v Population I BYM338: 700 mg to Placebo
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.12
Method	t-test, 1-sided

Statistical analysis title	Population I: ASMI at Week 49
Comparison groups	Population I: BYM338 210 mg v Population I BYM338: 210 mg to Placebo
Number of subjects included in analysis	9
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.297
Method	t-test, 1-sided

Statistical analysis title	Population I: ASMI at Week 49
Comparison groups	Population I: BYM338 70 mg v Population I: BYM338 70 mg to Placebo
Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.074
Method	t-test, 1-sided

Statistical analysis title	Population I: ASMI at Week 49
Comparison groups	Population I: BYM338 700 mg v Population I: Placebo

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.022
Method	t-test, 1-sided

Statistical analysis title	Population I: ASMI at Week 49
Comparison groups	Population I: BYM338 210 mg v Population I: Placebo
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.106
Method	t-test, 1-sided

Statistical analysis title	Population I: ASMI at Week 49
Comparison groups	Population I: BYM338 70 mg v Population I: Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.211
Method	t-test, 1-sided

Secondary: Population II: Appendicular Skeletal Muscle Index (ASMI) as measured by dual energy X-ray absorptiometry (DXA) at Week 49

End point title	Population II: Appendicular Skeletal Muscle Index (ASMI) as measured by dual energy X-ray absorptiometry (DXA) at Week 49[8]

End point description:

ASMI is a core requirement for determining the presence of sarcopenia and is calculated as the sum of the appendicular lean mass (kg) of the two upper and two lower limbs quantified by DXA, divided by height (m2). Therefore, an increase in ASMI indicates an increase in the quantity of an individual's lean mass.

End point type	Secondary

End point timeframe:

Week 49

Notes:

[8] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: To facilitate different analysis on patients enrolled before and after the protocol amendment 1, two populations are defined as below: · Population I: Patients enrolled prior to protocol amendment 1 · Population II: Patients enrolled after protocol amendment 1.

End point values	Population: II BYM338 700 mg	Population: II Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	43		
Units: kg/m2				
geometric mean (geometric coefficient of variation)	5.6 (± 14.36)	5.5 (± 12.46)		

Statistical analyses

Statistical analysis title	Population II: ASMI at Week 49
Comparison groups	Population: II BYM338 700 mg v Population: II Placebo
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	
P-value	= 1
Method	ANCOVA

Secondary: Population I: Total Lean Body Mass (LBM) as measured by dual energy X-ray absorptiometry (DXA) at Week 49

End point title	Population I: Total Lean Body Mass (LBM) as measured by dual energy X-ray absorptiometry (DXA) at Week 49[9]

End point description:

LBM is defined as the Total soft tissue fat-free body mass. A high LBM represents better pharmacodynamic effect

End point type	Secondary

End point timeframe:

Week 49

Notes:

[9] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period. Justification: To facilitate different analysis on patients enrolled before and after the protocol amendment 1, two populations are defined as below: · Population I: Patients enrolled prior to protocol amendment 1 · Population II: Patients enrolled after protocol amendment 1.

End point values	Population I: BYM338 700 mg	Population I BYM338: 700 mg to Placebo	Population I: BYM338 210 mg	Population I BYM338: 210 mg to Placebo
Subject group type	Reporting group	Reporting group	Reporting group	Reporting group
Number of subjects analysed	5	5	5	4
Units: kg				
geometric mean (geometric coefficient of variation)	41.4 (± 21.11)	34.0 (± 17.76)	35.5 (± 15.39)	32.6 (± 25.23)

End point values	Population I: BYM338 70 mg	Population I: BYM338 70 mg to Placebo	Population I: Placebo	

Subject group type	Reporting group	Reporting group	Reporting group	
Number of subjects analysed	7	7	15	
Units: kg				
geometric mean (geometric coefficient of variation)	34.9 (± 21.16)	34.0 (± 18.47)	32.6 (± 17.95)	

Statistical analyses

Statistical analysis title	Population I: LBM at Week 49
Comparison groups	Population I: BYM338 700 mg v Population I BYM338: 700 mg to Placebo
Number of subjects included in analysis	10
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.084
Method	t-test, 1-sided

Statistical analysis title	Population I: LBM at Week 49
Comparison groups	Population I: BYM338 210 mg v Population I BYM338: 210 mg to Placebo
Number of subjects included in analysis	9
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.283
Method	t-test, 1-sided

Statistical analysis title	Population I: LBM at Week 49
Comparison groups	Population I: BYM338 70 mg v Population I: BYM338 70 mg to Placebo
Number of subjects included in analysis	14
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.323
Method	t-test, 1-sided

Statistical analysis title	Population I: LBM at Week 49
Comparison groups	Population I: BYM338 700 mg v Population I: Placebo

Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.018
Method	t-test, 1-sided

Statistical analysis title	Population I: LBM at Week 49
Comparison groups	Population I: BYM338 210 mg v Population I: Placebo
Number of subjects included in analysis	20
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.179
Method	t-test, 1-sided

Statistical analysis title	Population I: LBM at Week 49
Comparison groups	Population I: BYM338 70 mg v Population I: Placebo
Number of subjects included in analysis	22
Analysis specification	Pre-specified
Analysis type	
P-value	= 0.227
Method	t-test, 1-sided

Secondary: Population II: Total Lean Body Mass (LBM) as measured by dual energy X-ray absorptiometry (DXA) at Week 49

End point title	Population II: Total Lean Body Mass (LBM) as measured by dual energy X-ray absorptiometry (DXA) at Week 49[10]

End point description:

LBM is defined as the Total soft tissue fat-free body mass. A high LBM represents better pharmacodynamic effect

End point type	Secondary

End point timeframe:

Week 49

Notes:

[10] - The end point is not reporting statistics for all the arms in the baseline period. It is expected all the baseline period arms will be reported on when providing values for an end point on the baseline period.
Justification: To facilitate different analysis on patients enrolled before and after the protocol amendment 1, two populations are defined as below: · Population I: Patients enrolled prior to protocol amendment 1 · Population II: Patients enrolled after protocol amendment 1.

End point values	Population: II BYM338 700 mg	Population: II Placebo		
Subject group type	Reporting group	Reporting group		
Number of subjects analysed	69	43		
Units: kg				
geometric mean (geometric coefficient of variation)	34.9 (± 25.01)	33.7 (± 20.40)		

Statistical analyses

Statistical analysis title	Population II: LBM at Week 49
Comparison groups	Population: II BYM338 700 mg v Population: II Placebo
Number of subjects included in analysis	112
Analysis specification	Pre-specified
Analysis type	
P-value	= 1
Method	ANCOVA

Adverse events

Adverse events information

Timeframe for reporting adverse events:

Adverse events were collected from first dose of study treatment until end of study treatment plus 30 days post treatment, up to a maximum treatment duration of 24 weeks

Adverse event reporting additional description:

Adverse events presented below are events considered to be treatment-emergent, therefore only events occurring in Population I are summarized. Patients in Population II did not receive study medication (were followed-up of-drug), thus any events occurring in this group were not treatment-emergent and are not captured in the summary.

Assessment type	Systematic

Dictionary used

Dictionary name	MedDRA
Dictionary version	21.1

Reporting groups

Reporting group title	Population I BYM338 700 mg
Reporting group description:	
Population I BYM338 700 mg	
Reporting group title	Population I BYM338 700 mg to Placebo
Reporting group description:	
Population I BYM338 700 mg to Placebo	
Reporting group title	Population I BYM338 210 mg
Reporting group description:	
Population I BYM338 210 mg	
Reporting group title	Population I BYM338 210 mg to Placebo
Reporting group description:	
Population I BYM338 210 mg to Placebo	
Reporting group title	Population I BYM338 70 mg
Reporting group description:	
Population I BYM338 70 mg	
Reporting group title	Population I BYM338 70 mg to Placebo
Reporting group description:	
Population I BYM338 70 mg to Placebo	
Reporting group title	Population I Placebo
Reporting group description:	
Population I Placebo	
Reporting group title	Population: II BYM338 700 mg
Reporting group description:	
Population: II BYM338 700 mg	
Reporting group title	Population: II Placebo
Reporting group description:	
Population: II Placebo	

Serious adverse events	Population I BYM338 700 mg	Population I BYM338 700 mg to Placebo	Population I BYM338 210 mg
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)

number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Gallbladder cancer			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic carcinoma			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar vertebral fracture			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Seizure			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 1	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Cataract			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Osteoarthritis			

subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Population I BYM338 210 mg to Placebo	Population I BYM338 70 mg	Population I BYM338 70 mg to Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	2 / 7 (28.57%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Gallbladder cancer			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic carcinoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar vertebral fracture			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Seizure			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Cataract			

subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 1
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

Serious adverse events	Population I Placebo	Population: II BYM338 700 mg	Population: II Placebo
Total subjects affected by serious adverse events			
subjects affected / exposed	2 / 15 (13.33%)	0 / 69 (0.00%)	0 / 43 (0.00%)
number of deaths (all causes)	0	0	0
number of deaths resulting from adverse events	0	0	0
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Gallbladder cancer			
subjects affected / exposed	0 / 15 (0.00%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Pancreatic carcinoma			
subjects affected / exposed	1 / 15 (6.67%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Injury, poisoning and procedural complications			
Fall			
subjects affected / exposed	0 / 15 (0.00%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Lumbar vertebral fracture			
subjects affected / exposed	0 / 15 (0.00%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Nervous system disorders			
Seizure			

subjects affected / exposed	0 / 15 (0.00%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Eye disorders			
Cataract			
subjects affected / exposed	1 / 15 (6.67%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 1	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0
Musculoskeletal and connective tissue disorders			
Osteoarthritis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences causally related to treatment / all	0 / 0	0 / 0	0 / 0
deaths causally related to treatment / all	0 / 0	0 / 0	0 / 0

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

Non-serious adverse events	Population I BYM338 700 mg	Population I BYM338 700 mg to Placebo	Population I BYM338 210 mg
Total subjects affected by non-serious adverse events			
subjects affected / exposed	4 / 5 (80.00%)	4 / 5 (80.00%)	3 / 5 (60.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Skin papilloma			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Influenza like illness			

subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Reproductive system and breast disorders			
Prostatic dysplasia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Psychiatric disorders			
Anxiety disorder			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Product issues			
Device loosening			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Body mass index decreased			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Lipase increased			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Injury, poisoning and procedural complications			

Arthropod bite			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	1 / 5 (20.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences (all)	3	1	0
Head injury			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Muscle contusion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Bundle branch block left			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Ventricular extrasystoles			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Headache			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Presyncope			

subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Eye irritation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Macular degeneration			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Chronic gastritis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Constipation			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Large intestine polyp			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Nausea			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Vomiting			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Hepatobiliary disorders			

Hepatic function abnormal			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Renal cyst			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Back pain			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Muscle spasms			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Pain in extremity			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Tenosynovitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Infections and infestations			
Cystitis			

subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Nasopharyngitis			
subjects affected / exposed	0 / 5 (0.00%)	1 / 5 (20.00%)	0 / 5 (0.00%)
occurrences (all)	0	1	0
Pneumonia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Rhinitis			
subjects affected / exposed	1 / 5 (20.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	1	0	0
Sinusitis			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	1 / 5 (20.00%)
occurrences (all)	0	0	1
Tinea versicolour			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 5 (0.00%)	0 / 5 (0.00%)	0 / 5 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Population I BYM338 210 mg to Placebo	Population I BYM338 70 mg	Population I BYM338 70 mg to Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	2 / 4 (50.00%)	5 / 7 (71.43%)	3 / 7 (42.86%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Skin papilloma			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
General disorders and administration site conditions			
Fatigue			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Influenza like illness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Non-cardiac chest pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Peripheral swelling			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Prostatic dysplasia			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Psychiatric disorders			
Anxiety disorder			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Product issues			
Device loosening			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Body mass index decreased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Lipase increased			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Contusion			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Fall			
subjects affected / exposed	1 / 4 (25.00%)	2 / 7 (28.57%)	0 / 7 (0.00%)
occurrences (all)	2	2	0
Head injury			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Ligament sprain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Muscle contusion			

subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Skin abrasion			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	2	0	0
Cardiac disorders			
Bundle branch block left			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Ventricular extrasystoles			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Headache			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Presyncope			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Eye irritation			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Macular degeneration			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Chronic gastritis			

subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	1 / 7 (14.29%)
occurrences (all)	0	1	1
Gastrooesophageal reflux disease			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Large intestine polyp			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Vomiting			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Renal cyst			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Back pain			
subjects affected / exposed	0 / 4 (0.00%)	2 / 7 (28.57%)	1 / 7 (14.29%)
occurrences (all)	0	2	1
Muscle spasms			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Musculoskeletal pain			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Tenosynovitis			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Infections and infestations			
Cystitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Gastroenteritis			
subjects affected / exposed	1 / 4 (25.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	1	0	0
Gingivitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Herpes zoster			
subjects affected / exposed	0 / 4 (0.00%)	2 / 7 (28.57%)	0 / 7 (0.00%)
occurrences (all)	0	2	0
Nasopharyngitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Pneumonia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Rhinitis			

subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Tinea versicolour			
subjects affected / exposed	0 / 4 (0.00%)	1 / 7 (14.29%)	0 / 7 (0.00%)
occurrences (all)	0	1	0
Upper respiratory tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0
Urinary tract infection			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	1 / 7 (14.29%)
occurrences (all)	0	0	1
Metabolism and nutrition disorders			
Hyperkalaemia			
subjects affected / exposed	0 / 4 (0.00%)	0 / 7 (0.00%)	0 / 7 (0.00%)
occurrences (all)	0	0	0

Non-serious adverse events	Population I Placebo	Population: II BYM338 700 mg	Population: II Placebo
Total subjects affected by non-serious adverse events			
subjects affected / exposed	11 / 15 (73.33%)	0 / 69 (0.00%)	0 / 43 (0.00%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)			
Basal cell carcinoma			
subjects affected / exposed	0 / 15 (0.00%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Skin papilloma			
subjects affected / exposed	0 / 15 (0.00%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Vascular disorders			
Hypertension			
subjects affected / exposed	0 / 15 (0.00%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
General disorders and administration site conditions			
Fatigue			

subjects affected / exposed	1 / 15 (6.67%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Influenza like illness			
subjects affected / exposed	1 / 15 (6.67%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Non-cardiac chest pain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Peripheral swelling			
subjects affected / exposed	0 / 15 (0.00%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Reproductive system and breast disorders			
Prostatic dysplasia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Respiratory, thoracic and mediastinal disorders			
Dyspnoea			
subjects affected / exposed	1 / 15 (6.67%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Psychiatric disorders			
Anxiety disorder			
subjects affected / exposed	0 / 15 (0.00%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Product issues			
Device loosening			
subjects affected / exposed	0 / 15 (0.00%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Investigations			
Aspartate aminotransferase increased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Body mass index decreased			
subjects affected / exposed	0 / 15 (0.00%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Lipase increased			

subjects affected / exposed	0 / 15 (0.00%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Injury, poisoning and procedural complications			
Arthropod bite			
subjects affected / exposed	1 / 15 (6.67%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Contusion			
subjects affected / exposed	2 / 15 (13.33%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	2	0	0
Fall			
subjects affected / exposed	6 / 15 (40.00%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	8	0	0
Head injury			
subjects affected / exposed	1 / 15 (6.67%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Ligament sprain			
subjects affected / exposed	1 / 15 (6.67%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	2	0	0
Muscle contusion			
subjects affected / exposed	0 / 15 (0.00%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Skin abrasion			
subjects affected / exposed	0 / 15 (0.00%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Cardiac disorders			
Bundle branch block left			
subjects affected / exposed	1 / 15 (6.67%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Ventricular extrasystoles			
subjects affected / exposed	0 / 15 (0.00%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Nervous system disorders			
Dizziness			
subjects affected / exposed	0 / 15 (0.00%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Headache			

subjects affected / exposed	1 / 15 (6.67%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Presyncope			
subjects affected / exposed	1 / 15 (6.67%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Eye disorders			
Dry eye			
subjects affected / exposed	0 / 15 (0.00%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Eye irritation			
subjects affected / exposed	1 / 15 (6.67%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Macular degeneration			
subjects affected / exposed	0 / 15 (0.00%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Gastrointestinal disorders			
Abdominal discomfort			
subjects affected / exposed	0 / 15 (0.00%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Chronic gastritis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Constipation			
subjects affected / exposed	0 / 15 (0.00%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Gastrooesophageal reflux disease			
subjects affected / exposed	1 / 15 (6.67%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Large intestine polyp			
subjects affected / exposed	0 / 15 (0.00%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Nausea			
subjects affected / exposed	1 / 15 (6.67%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Vomiting			

subjects affected / exposed	0 / 15 (0.00%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Hepatobiliary disorders			
Hepatic function abnormal			
subjects affected / exposed	1 / 15 (6.67%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Skin and subcutaneous tissue disorders			
Skin ulcer			
subjects affected / exposed	1 / 15 (6.67%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Renal and urinary disorders			
Nephrolithiasis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Renal cyst			
subjects affected / exposed	0 / 15 (0.00%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal and connective tissue disorders			
Arthralgia			
subjects affected / exposed	1 / 15 (6.67%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Back pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Muscle spasms			
subjects affected / exposed	0 / 15 (0.00%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Musculoskeletal pain			
subjects affected / exposed	0 / 15 (0.00%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Pain in extremity			
subjects affected / exposed	2 / 15 (13.33%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	2	0	0
Tenosynovitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0

Infections and infestations			
Cystitis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Gastroenteritis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Gingivitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Herpes zoster			
subjects affected / exposed	1 / 15 (6.67%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Nasopharyngitis			
subjects affected / exposed	1 / 15 (6.67%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	2	0	0
Pneumonia			
subjects affected / exposed	0 / 15 (0.00%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Rhinitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Sinusitis			
subjects affected / exposed	0 / 15 (0.00%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Tinea versicolour			
subjects affected / exposed	0 / 15 (0.00%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	0	0	0
Upper respiratory tract infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Urinary tract infection			
subjects affected / exposed	1 / 15 (6.67%)	0 / 69 (0.00%)	0 / 43 (0.00%)
occurrences (all)	1	0	0
Metabolism and nutrition disorders			

Hyperkalaemia subjects affected / exposed occurrences (all)	1 / 15 (6.67%) 1	0 / 69 (0.00%) 0	0 / 43 (0.00%) 0

More information

Substantial protocol amendments (globally)

Were there any global substantial amendments to the protocol? Yes

Date	Amendment
26 April 2017	1. Re-focus of the study on assessing the durability of effect of bimagrumab over a 24 week period off drug. 2. Study was reduced to 24 weeks with site visits every 12 weeks instead of every 4 weeks and phone calls were added in between visits to promote adherence and to record falls or other associated feedback from study participants 3. Addition of a planned interim analysis 4. The need for unblinding of core treatment code for newly enrolled patients followed the core study protocol procedure 5. All IMP related sections were only applicable to those patients enrolled under the original protocol version 6. Inclusion/exclusion criteria were simplified as only patients willing and having fully completed the 24 weeks of core study treatment are eligible 7. As part of the alignment between the core and the extension studies, the following key changes were implemented in this extension study: a. The SPPB replaced the 6MWT as primary endpoint, the 6MWT changed to a secondary endpoint b. The 400 meter walk test was removed c. Echocardiography was eliminated and overall cardiac monitoring was reduced from a level of intense monitoring to one reflecting standard of care following the results of the dedicated profiling cardiac safety study d. Additional safety monitoring guidance for patients with change in body weight since the core study baseline of +/- 5% e. Removal of certain central laboratory assessments (i.e. urinalysis, coagulation measurement) f. e-devices diaries (falls and exercises) are replaced by paper diaries which are easier to use for this patient population g. Addition of the PAISs instrument, a Novartis developed PRO and the necessary battery of questionnaires to contribute to its validation (i.e. PGIC, PGIS, SF-36v2, EQ-5D-5L) h. The frequency of the DXA assessment was reduced to a final one at the EOS only

Notes:

Interruptions (globally)

Were there any global interruptions to the trial? No

Limitations and caveats

None reported