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GENERIC NAME and/or COMPOUND NUMBER: MYO-029 (Stamulumab) / WAY-210757

PROTOCOL NO.: 3147K2-101-WW

PROTOCOL TITLE: A Double-Blind, Placebo-Controlled, Randomized, Multiple Ascending Dose, Safety Study of MYO-029 Administered to Adult Patients With Becker, Facioscapulohumeral, and Limb-Girdle Muscular Dystrophy

Study Centers: Ten (10) centers took part in the study and randomized subjects; 9 in the United States of America, 1 in the United Kingdom.

Study Initiation and Final Completion Dates: 15 February 2005 to 31 January 2007.

The study was terminated prematurely on 31 January 2007 due to safety concerns.

Phase of Development: Phase 1/2

Study Objectives:

Primary Objective:

- To evaluate the safety of MYO-029 in adult subjects with muscular dystrophy (MD)

Secondary Objectives:

- To evaluate the biological activity of MYO-029 in adult subjects with MD by evaluating muscle mass, volume, strength, histopathology findings, subject-reported outcomes, and functional measurements
- To explore associations between gene expression patterns, test article administration, and clinical variables
- To evaluate the pharmacokinetics (PK) of MYO-029 in adult subjects with MD

METHODS

Study Design: This was a randomized, double-blind, placebo-controlled, multiple ascending dose study in subjects with becker muscular dystrophy (BMD), facioscapulohumeral muscular dystrophy (FSHD), or limb-girdle muscular dystrophy (LGMD). Single intravenous (IV) doses of MYO-029 (1, 3, 10, or 30 mg/kg) or placebo were administered

every 2 weeks for 24 weeks, for a total of 13 doses. This study was not completed as planned due to safety concerns. The study activities are presented in Table 1.

Table 1. Study Flowchart

Study Visit	V 1	V 2	V 3	V 4	V 5	V 6	V 7	V 8	V 9	V 10	V 11	V 12	V 13	V 14	V 15/89	V 16
Study Interval	**S/B**	**Active Phase**													**FU**	
		Do 1	**Do 2**	**Do 3**	**Do 4**	**Do 5**	**Do 6**	**Do 7**	**Do 8**	**Do 9**	**Do 10**	**Do 11**	**Do 12**	**Do 13**	**FU 1/ET**	**FU 2**
Study Procedures	**D -28 to -1**	**D 1**	**W 2 D 15**	**W 4 D 29**	**W 6 D 43**	**W 8 D 57**	**W 10 D 71**	**W 12 D 85**	**W 14 D 99**	**W 16 D 113**	**W 18 D 127**	**W 20 D 141**	**W 22 D 155**	**W 24 D 169**	**W 26 D 183**	**W 36 D 253**
Informed consent	X															
CORE II[a]	X	X														
Demographics	X															
Medical history	X															
Muscular dystrophy history	X															
Prior medications	X															
Prior treatment non-pharmacologic	X															
Height	X															
Weight	X	X		X		X		X		X		X		X	X	X
Vital signs	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Physical examination[b]	X				X			X							X	
Neuromuscular examination	X				X			X							X	
Muscle circumference	X							X							X	
Hematology	X	X	X		X			X			X				X	X
Serum chemistry	X	X	X		X			X			X				X	X
Urinalysis	X	X	X		X			X			X				X	X
Blood sample for gene expression and, potentially, metabolomics[c]		X		X											X	X
Blood sample for anti-MYO-029 antibody	X				X			X								X
Blood sample for MYO-029 levels[d]		X,Y			X			X						X,Y	X	X
Blood sample for myostatin levels	X				X											X
ECG	X														X	
Echocardiogram	X														X	X

Table 1. Study Flowchart

Study Visit	**V 1**		**V 2**	**V 3**	**V 4**	**V 5**	**V 6**	**V 7**	**V 8**	**V 9**	**V 10**	**V 11**	**V 12**	**V 13**	**V 14**	**V 15/89**	**V 16**
Study Interval	**S/B**		**Active Phase**													**FU**	
			Do 1	**Do 2**	**Do 3**	**Do 4**	**Do 5**	**Do 6**	**Do 7**	**Do 8**	**Do 9**	**Do 10**	**Do 11**	**Do 12**	**Do 13**	**FU 1/ET**	**FU 2**
Study Procedures	**D -28 to -1**		**D 1**	**W 2 D 15**	**W 4 D 29**	**W 6 D 43**	**W 8 D 57**	**W 10 D 71**	**W 12 D 85**	**W 14 D 99**	**W 16 D 113**	**W 18 D 127**	**W 20 D 141**	**W 22 D 155**	**W 24 D 169**	**W 26 D 183**	**W 36 D 253**
Audiogram (FSHD only)	X															X	
Eye exam (FSHD only)	X															X	
MMT[e]	X	X				X			X							X	X
QMT[f]		X				X			X							X	X
PFT	X[g]	X				X			X							X	X
Timed function tests	X[h]	X[i]				X[i]			X[i]							X[i]	X[i]
SF-36 health survey	X								X							X	
ADL instrument	X									X						X	
INQoL	X									X						X	
Health thermometer	X									X						X	
DEXA	X															X	
MRI	X															X	
Muscle biopsy[j] (optional)	X															X	
Test article administration			X	X	X	X	X	X	X	X	X	X	X	X	X		
Physical activity assessment			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Dietary intake assessment			X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Adverse events	Collected from time consent was signed until 14 days following the last visit																
Concomitant medications	Ccollected from time consent was signed until 14 days following the last visit																
Concomitant treatment non-pharmacologic	Collected from time consent was signed until 14 days following the last visit																

Table 1. Study Flowchart

Study Visit	V 1	V 2	V 3	V 4	V 5	V 6	V 7	V 8	V 9	V 10	V 11	V 12	V 13	V 14	V 15/89	V 16
Study Interval	S/B	Active Phase													FU	
		Do 1	Do 2	Do 3	Do 4	Do 5	Do 6	Do 7	Do 8	Do 9	Do 10	Do 11	Do 12	Do 13	FU 1/ET	FU 2
Study Procedures	D -28 to -1	D 1	W 2 D 15	W 4 D 29	W 6 D 43	W 8 D 57	W 10 D 71	W 12 D 85	W 14 D 99	W 16 D 113	W 18 D 127	W 20 D 141	W 22 D 155	W 24 D 169	W 26 D 183	W 36 D 253

ADL = activity of daily living; B = baseline; CORE II = Computerized Randomization and Enrollment System II; D = day; DEXA = dual energy x-ray absorptiometer; Do = dose; ECG = electrocardiogram; ET = early term; FSHD = facioscapulohumeral muscular dystrophy; FU = follow-up; INQoL = individualised neuromuscular quality of life; MMT = manual muscle testing; MRI = magnetic resonance imaging PFT = pulmonary function test; QMT = quantitative muscle test; S = screening; SF-36 = Short Form (36) health survey; V = visit; W = week; X = dosing; Y = test article administration.

a. A subject number was required to complete the laboratory requisitions for the screening samples. Subjects must have registered in the CORE II system at the beginning of the screening period (V 1), after signing the informed consent. If the subject met eligibility requirements, a randomization number was given to the subject at V 2, by using the CORE II system.
b. A full physical examination, except for gynecologic and rectal examination, was performed at V 1 and V 15. A physical examination including at a minimum, a review of general appearance, skin, heart, and the lungs was performed at V 5 and V 8.
c. Collection of blood sample for gene expression and, potentially, metabolomics must have been completed within 2 hours before test article administration.
d. At V 2 and V 14, blood samples must have been collected within 2 hours before dosing (X) and at the end of test article administration (Y).
e. For V 1 only, 2 sets of MMT evaluations were required and must have been performed on different calendar days >20 hours and <7 days apart.
f. Performed only at sites with the appropriate QMT equipment.
g. A seated PFT must have been performed to confirm eligibility.
h. At Screening, subjects must have been traversed 9-meters to confirm eligibility. Timing of this test was not required to meet eligibility. A 4-stair climb and stand from a seated position in a chair should have not been performed at Screening.
i. At Baseline and subsequent evaluations, timing of the following function tests should have been recorded: traverse 9-meters, complete a 4-stair climb and stand from a seated position in a chair.
j. The open muscle biopsy must have been performed after the strength evaluations (MMT, QMT, PFT, and timed function tests), DEXA, and MRI if obtained at V 1. If obtained at V 2, the biopsy must have been performed before test article administration.

Number of Subjects (Planned and Analyzed): One hundred thirty six (136) subjects were planned to enroll in the study. A total of 116 subjects (36 subjects with BMD, 42 subjects with FSHD, and 38 subjects with LGMD) were enrolled in the study; 29 subjects received placebo, 27 subjects each received MYO-029 1 mg/kg, MYO-029 3 mg/kg or MYO-029 10 mg/kg, and 6 subjects received MYO-029 30 mg/kg.

Diagnosis and Main Criteria for Inclusion: Male or female subjects aged ≥18 years, with confirmed clinical and molecular diagnosis of BMD, FSHD, or LGMD and independently ambulatory were included in the study.

Exclusion Criteria: Subjects with certain clinical conditions, using steroids or other medications/treatments with the potential to affect muscle function, and history of sensitivity to monoclonal antibodies or to protein pharmaceuticals were excluded.

Study Treatment: The IV doses of MYO-029 (1, 3, 10, or 30 mg/kg) or placebo were administered every 2 weeks for 24 weeks, for a total of 13 doses.

Pharmacokinetics, Pharmacodynamic, Pharmacogenomic and Safety Endpoints:

- Safety of MYO-029 in adult subjects with MD
- Biological activity of MYO-029 (changes in body composition, muscle strength and mucle histopathology, subject-reported outcomes, and functional measurements)
- PK, bioanalytics and pharmacogenomics of MYO-029

The study was not completed as planned; therefore, no PK, pharmacodynamic or pharmacogenomic analyses were reported**.**

No efficacy evaluations were performed for this study.

Safety Evaluations: Safety evaluations included adverse events (AEs) monitoring and laboratory findings.

Statistical Methods: Safety analyses were conducted on an intent-to-treat population, defined as all subjects randomized who received at least 1 dose of STAMULUMAB or placebo. The study was not completed as planned; descriptive analyses of safety evaluations and differentiation factor-8 (GDF-8) levels were reported.

RESULTS

Subject Disposition and Demography: Table 2 provides the reasons for conclusion of subject participation in the study. Twenty-seven (27) subjects were discontinued from the study, 15 subjects were withdrawn by the Sponsor and 4 subjects withdrew because of AEs.

Table 2. Conclusion of Subject Participation: Intent-to-Treat Population

Conclusion Status Reason[a]	Placebo n=29	MYO-029				Total N=116
		1 mg/kg n=27	3 mg/kg n=27	10 mg/kg n=27	30 mg/kg n=6	
Total	29 (100)	27 (100)	27 (100)	27 (100)	6 (100)	116 (100)
Completed	24 (82.8)	25 (92.6)	26 (96.3)	14 (51.9)	0	89 (76.7)
Study completed	24 (82.8)	25 (92.6)	26 (96.3)	14 (51.9)	0	89 (76.7)
Discontinued	5 (17.2)	2 (7.4)	1 (3.7)	13 (48.1)	6 (100)	27 (23.3)
Discontinuation of study by Sponsor	4 (13.8)	0	0	5 (18.5)	6 (100)	15 (12.9)
Adverse event	1 (3.4)	0	0	3 (11.1)	0	4 (3.4)
Other	0	0	0	3 (11.1)	0	3 (2.6)
Failed to return	0	0	1 (3.7)	0	0	1 (0.9)
Investigator request	0	1 (3.7)	0	0	0	1 (0.9)
Subject request	0	1 (3.7)	0	0	0	1 (0.9)
Protocol violation	0	0	0	1 (3.7)	0	1 (0.9)
Unsatisfactory response-efficacy	0	0	0	1 (3.7)	0	1 (0.9)

n = number of subjects in each treatment group; N = total number of subjects.
a. Total discontinued was the sum of individual reasons because they were mutually exclusive by subject.

The summary of demographic characteristics is presented in Table 3.

Table 3. Demographic Characteristics: Intent-to-Treat Population

Characteristics	Placebo n=29	MYO-029				Total N=116
		1 mg/kg n=27	3 mg/kg n=27	10 mg/kg n=27	30 mg/kg n=6	
Age (years)						
Mean	39.28	37.19	37.07	40.19	44.33	38.75
Standard deviation	13.32	9.45	13.60	11.46	10.23	11.95
Minimum	18.00	21.00	18.00	19.00	29.00	18.00
Maximum	67.00	59.00	70.00	62.00	55.00	70.00
Median	38.00	35.00	39.00	40.00	45.50	38.00
Sex, n (%)						
Female	8 (27.6)	7 (25.9)	5 (18.5)	7 (25.9)	1 (16.7)	28 (24.1)
Male	21 (72.4)	20 (74.1)	22 (81.5)	20 (74.1)	5 (83.3)	88 (75.9)

n = number of subjects in each treatment group; N = total number of subjects.

Pharmacokinetic Results:

Pharmacokinetic Results: Of 296 serum samples analyzed for free and total GDF-8, 189 samples showed free GDF-8 concentration less than the lower limit of quantitation and no samples showed total GDF-8 below the lower limit of quantitation.

No efficacy analysis could be conducted because the study was terminated prematurely due to safety concerns (diplopia/aseptic meningitis/hypersensitivity reactions).

Safety Results: A total of 109 subjects reported AEs, of which 104 were considered to be treatment-emergent adverse events (TEAEs). The most common TEAEs were headache, experienced by 41 (35.3%) subjects, followed by accidental injury (36, 31.0%); infection

(22, 19%); back pain (20, 17.2%); asthenia (18, 15.5%); pain (16, 13.8%); arthralgia (16, 13.8%); dizziness (15, 12.9%); nausea (13, 11.2%); myalgia (12, 10.3%); and diarrhea (11, 9.5%). One (1) subject from the 10 mg/kg cohort reported urticaria and hives, which were considered to be definitely related to the test article. The number (%) of subjects experiencing TEAEs in descending order of incidence, intent-to-treat population, for events occurring in ≥5% of subjects in any treatment group, including the total group is presented in Table 4.

Table 4. Number (%) of Subjects Experiencing TEAEs in Descending Order of Incidence, ITT Population, for Events Occurring in ≥5% of Subjects in Any Treatment Group, Including the Total Group

Body System[a] Adverse Event	Overall p-Value	Placebo n=29	MYO-029				Total N=116
			1 mg/kg n=27	3 mg/kg n=27	10 mg/kg n=27	30 mg/kg n=27	
Any adverse event	0.129	28 (96.6)	25 (92.6)	25 (92.6)	22 (81.5)	4 (66.7)	104 (89.7)
Body as a whole	0.686	21 (72.4)	21 (77.8)	20 (74.1)	18 (66.7)	3 (50.0)	83 (71.6)
Headache	0.341	14 (48.3)	11 (40.7)	7 (25.9)	7 (25.9)	2 (33.3)	41 (35.3)
Accidental injury	0.026*	8 (27.6)	13 (48.1)	11 (40.7)	4 (14.8)	0	36 (31.0)
Infection	0.221	6 (20.7)	4 (14.8)	9 (33.3)	3 (11.1)	0	22 (19.0)
Back pain	0.749	4 (13.8)	6 (22.2)	6 (22.2)	3 (11.1)	1 (16.7)	20 (17.2)
Asthenia	1.000	5 (17.2)	4 (14.8)	4 (14.8)	4 (14.8)	1 (16.7)	18 (15.5)
Pain	0.727	5 (17.2)	5 (18.5)	4 (14.8)	2 (7.4)	0	16 (13.8)
Neck pain	0.915	2 (6.9)	3 (11.1)	2 (7.4)	1 (3.7)	0	8 (6.9)
Flu syndrome	0.097	0	1 (3.7)	4 (14.8)	1 (3.7)	1 (16.7)	7 (6.0)
Injection site pain	0.449	1 (3.4)	3 (11.1)	0	2 (7.4)	0	6 (5.2)
Chest pain	0.950	1 (3.4)	2 (7.4)	1 (3.7)	1 (3.7)	0	5 (4.3)
Fever	0.950	1 (3.4)	1 (3.7)	1 (3.7)	2 (7.4)	0	5 (4.3)
Injection site reaction	0.667	1 (3.4)	2 (7.4)	0	2 (7.4)	0	5 (4.3)
Abdominal pain	0.142	0	1 (3.7)	0	1 (3.7)	1 (16.7)	3 (2.6)
Allergic reaction	0.259	0	2 (7.4)	0	0	0	2 (1.7)
Hernia	0.259	0	0	0	2 (7.4)	0	2 (1.7)
Cardiovascular system	0.234	6 (20.7)	6 (22.2)	1 (3.7)	3 (11.1)	1 (16.7)	17 (14.7)
Hypotension	0.920	2 (6.9)	1 (3.7)	0	1 (3.7)	0	4 (3.4)
Migraine	0.542	1 (3.4)	2 (7.4)	0	0	0	3 (2.6)
Vasodilatation	0.422	0	1 (3.7)	0	2 (7.4)	0	3 (2.6)
Tachycardia	0.052	0	0	0	0	1 (16.7)	1 (0.9)
Digestive system	0.383	10 (34.5)	12 (44.4)	9 (33.3)	10 (37.0)	0	41 (35.3)
Nausea	0.052	1 (3.4)	4 (14.8)	1 (3.7)	7 (25.9)	0	13 (11.2)
Diarrhea	0.430	3 (10.3)	5 (18.5)	1 (3.7)	2 (7.4)	0	11 (9.5)
Dyspepsia	0.541	2 (6.9)	2 (7.4)	3 (11.1)	0	0	7 (6.0)
Tooth caries	0.672	2 (6.9)	0	1 (3.7)	0	0	3 (2.6)
Constipation	0.259	0	0	2 (7.4)	0	0	2 (1.7)
Hemic and lymphatic System	0.517	3 (10.3)	1 (3.7)	0	1 (3.7)	0	5 (4.3)
Ecchymosis	0.672	2 (6.9)	1 (3.7)	0	0	0	3 (2.6)
Metabolic and nutritional	0.039*	7 (24.1)	3 (11.1)	2 (7.4)	0	1 (16.7)	13 (11.2)
Peripheral edema	0.811	2 (6.9)	2 (7.4)	1 (3.7)	0	0	5 (4.3)
Hypokalemia	0.796	1 (3.4)	1 (3.7)	2 (7.4)	0	0	4 (3.4)
Hyperglycemia	0.090	3 (10.3)	0	0	0	0	3 (2.6)
Hyperlipemia	0.052	0	0	0	0	1 (16.7)	1 (0.9)
Musculoskeletal system	0.134	10 (34.5)	14 (51.9)	8 (29.6)	5 (18.5)	2 (33.3)	39 (33.6)
Arthralgia	0.547	3 (10.3)	6 (22.2)	4 (14.8)	2 (7.4)	1 (16.7)	16 (13.8)
Myalgia	0.260	2 (6.9)	6 (22.2)	1 (3.7)	3 (11.1)	0	12 (10.3)
Musculoskeletal stiffness	0.599	0	2 (7.4)	2 (7.4)	2 (7.4)	0	6 (5.2)
Joint disorder	0.920	2 (6.9)	0	1 (3.7)	1 (3.7)	0	4 (3.4)
Muscle spasms	0.566	0	1 (3.7)	2 (7.4)	1 (3.7)	0	4 (3.4)
Muscle cramp	0.198	1 (3.4)	1 (3.7)	0	0	1 (16.7)	3 (2.6)
Myasthenia	0.672	2 (6.9)	1 (3.7)	0	0	0	3 (2.6)
Nervous system	0.451	7 (24.1)	11 (40.7)	5 (18.5)	7 (25.9)	1 (16.7)	31 (26.7)
Dizziness	1.000	4 (13.8)	4 (14.8)	3 (11.1)	4 (14.8)	0	15 (12.9)
Insomnia	0.809	1 (3.4)	2 (7.4)	3 (11.1)	2 (7.4)	0	8 (6.9)
Anxiety	0.467	1 (3.4)	3 (11.1)	0	1 (3.7)	0	5 (4.3)
Depression	0.346	0	2 (7.4)	0	2 (7.4)	0	4 (3.4)
Hypotonia	0.259	0	0	2 (7.4)	0	0	2 (1.7)
Hyperesthesia	0.052	0	0	0	0	1 (16.7)	1 (0.9)
Respiratory system	0.277	9 (31.0)	10 (37.0)	11 (40.7)	6 (22.2)	0	36 (31.0)

Table 4. Number (%) of Subjects Experiencing TEAEs in Descending Order of Incidence, ITT Population, for Events Occurring in ≥5% of Subjects in Any Treatment Group, Including the Total Group

Body System[a] Adverse Event	Overall p-Value	Placebo n=29	MYO-029 1 mg/kg n=27	MYO-029 3 mg/kg n=27	MYO-029 10 mg/kg n=27	MYO-029 30 mg/kg n=27	Total N=116
Upper respiratory infection	0.267	4 (13.8)	0	4 (14.8)	3 (11.1)	0	11 (9.5)
Pharyngitis	0.080	1 (3.4)	5 (18.5)	1 (3.7)	0	0	7 (6.0)
Sinusitis	0.072	0	1 (3.7)	5 (18.5)	1 (3.7)	0	7 (6.0)
Cough increased	1.000	2 (6.9)	2 (7.4)	1 (3.7)	1 (3.7)	0	6 (5.2)
Dyspnea	0.796	1 (3.4)	2 (7.4)	0	1 (3.7)	0	4 (3.4)
Rhinitis	0.236	1 (3.4)	0	3 (11.1)	0	0	4 (3.4)
Sinus congestion	0.542	1 (3.4)	0	2 (7.4)	0	0	3 (2.6)
Skin and appendages	0.778	7 (24.1)	7 (25.9)	4 (14.8)	7 (25.9)	2 (33.3)	27 (23.3)
Rash	0.268	2 (6.9)	3 (11.1)	1 (3.7)	0	1 (16.7)	7 (6.0)
Urticaria	0.076	0	0	0	3 (11.1)	0	3 (2.6)
Pruritic rash	0.075	0	0	0	1 (3.7)	1 (16.7)	2 (1.7)
Special senses	0.869	2 (6.9)	4 (14.8)	3 (11.1)	3 (11.1)	0	12 (10.3)
Conjunctivitis	0.320	2 (6.9)	0	0	0	0	2 (1.7)
Taste loss	0.259	0	0	0	2 (7.4)	0	2 (1.7)
Urogenital system	0.727	5 (17.2)	2 (7.4)	5 (18.5)	4 (14.8)	0	16 (13.8)
Hematuria	0.320	2 (6.9)	0	0	0	0	2 (1.7)
Urine abnormality	0.259	0	0	2 (7.4)	0	0	2 (1.7)
AEs associated with miscellaneous factors	0.507	5 (17.2)	4 (14.8)	4 (14.8)	1 (3.7)	0	14 (12.1)
Local reaction to procedure	0.778	4 (13.8)	2 (7.4)	3 (11.1)	1 (3.7)	0	10 (8.6)
Allergic reaction other than drug	0.236	1 (3.4)	3 (11.1)	0	0	0	4 (3.4)

Overall p-value: Fisher exact test (2 tailed).
Statistical significance at the 0.05 levels is denoted by *.
Dictionary used to code: Coding Symbols for a Thesaurus of Adverse Reaction Terms (COSTART).
AEs = adverse events; ITT = intent-to-treat; n = number of subjects in each treatment group; N = total number of subjects; TEAEs = treatment-emergent adverse events.
a. Body system totals were not necessarily the sum of the individual AEs because a subject could have reported ≥2 different AEs in the same body system.

Serious Adverse Events (SAEs): Altogether, 7 (6%) subjects reported SAEs during the study period. Two (2, 6.9%) of the 29 subjects in the placebo group experienced at least 1 SAE: dyspnea and upper respiratory tract infection (1 subject) and unintended pregnancy (1 subject). Of the 27 subjects in the 3-mg/kg cohort, 2 subjects had SAEs: dementia (1 subject) and depression followed by a suicide attempt (1 subject). Of the 27 subjects in the 10-mg/kg cohort, 3 subjects had SAEs: diplopia and aseptic meningitis (1 subject), diarrhea (1 subject), and chest pain (1 subject). No SAEs were reported in the 1-mg/kg (27 subjects) and 30-mg/kg (6 subjects) cohorts. A summary of SAEs is presented in Table 5.

Table 5. Serious Adverse Events: Intent-to-Treat Population

Treatment	Subject Serial No.	Age (Y)/ Sex/Disease	Body System/Adverse Event/Verbatim	TEAE	Sev	Test Article Related	Action	Outcome	SAE	Study Day (Start)	Study Day (Stop)
Placebo	1	36/F/FSHD	Respiratory system/dyspnea/ shortness of breath	Yes	2	PNOT	N, ER, C	Res	Yes	156	168
			Respiratory system/upper respiratory infection/viral upper respiratory infection	Yes	2	PNOT	ER, C	Res	Yes	156	168
Placebo	2	18/F/BMD	Urogenital system/ unintended pregnancy/ pregnancy	No	2	DNOT	W	Per	Yes	64	-
MYO-029 3 mg/kg	3	52/M/BMD	Nervous system/dementia/ dementia	No	3	PNOT	N	Per	Yes	-	-
MYO-029 3 mg/kg	4	23/M/FSHD	Nervous system/depression/ increased depression	No	4	DNOT	H	Res	Yes	250	263
MYO-029 3 mg/kg			Body as a whole/suicide attempt/ suicide attempt	No	4	DNOT	H	Res	Yes	250	263
MYO-029 10 mg/kg	5	35/M/LGMD	Special senses/diplopia/ diplopia	No	2	PNOT	H, UT, P	Res	Yes	24	125
MYO-029 10 mg/kg			Nervous system/meningitis/ aseptic meningitis	No	2	PNOT	H	Res	Yes	25	124
MYO-029 10 mg/kg	6	42/F/FSHD	Digestive system/diarrhea/ diarrhea	No	3	POS	C, T, UT, O, P, D	Res	Yes	59	88
MYO-029 10 mg/kg	7	44/M/FSHD	Body as a whole/chest pain/ chest pain	Yes	2	PNOT	H, ER, C, N	Res	Yes	49	90

Dictionary used to code: Coding Symbols for a Thesaurus of Adverse Reaction Terms (COSTART).
BMD = Becker muscular dystrophy; C = concomitant medication; D = discontinued test article permanently; DNOT = definitely not; ER = emergency room visit/test or procedures; F = female; FSHD = facioscapulohumeral muscular dystrophy; H = hospitalized; LGMD = limb-girdle muscular dystrophy; M = male; N = none; No. = number; P = primary reason for study withdrawal; per = persisted; O = other; PNOT = probably not; POS = possibly; Res = resolved; T = temporarily stopped test article; TEAE = treatment-emergent adverse event; SAE = serious adverse event; Sev = severity; UT = unscheduled visit/test; W = withdrawn.

Permanent or Temporary Discontinuations or Dose Reductions due to Adverse Events: Among the 4 subjects who withdrew because of AEs, 3 subjects had SAEs (unintended pregnancy [1 subject]; diplopia [1 subject]; and diarrhea [1 subject]). One (1) subject was withdrawn because of urticaria and hives, and its causality was definitely related to the treatment with MYO-029. A summary of subjects who were withdrawn from the study because of an AE is presented in Table 6.

Table 6. Adverse Events Causing Study Withdrawal: Intent-to-Treat Population

Treatment	Subject Serial No.	Age (Y)/Sex/ Disease	Body System/AEs/ Verbatim	TEAE	Sev	Test Article Related	Action	Outcome	SAE	Study Day (Start)	Study Day (Stop)
Placebo	1	18/F/BMD	Urogenital system/ unintended pregnancy/ pregnancy	No	2	DNOT	W	Per	Yes	64	-
MYO-029 10 mg/kg	2	56/M/FSHD	Skin and appendages/ urticaria/hives	Yes	3	DEF	D, C, P	Res	No	1	1
MYO-029 10 mg/kg	3	35/M/LGMD	Special senses/diplopia/ diplopia	No	2	PNOT	H, UT, P	Res	Yes	24	125
MYO-029 10 mg/kg	4	42/F/FSHD	Digestive system/ diarrhea/ diarrhea	No	3	POS	P, D, C, UT	Res	Yes	59	88

Dictionary used to code: Coding Symbols for a Thesaurus of Adverse Reaction Terms (COSTART).
AEs = adverse events; BMD = Becker muscular dystrophy; C = concomitant medication; D = discontinued test article permanently; DEF = definitely; DNOT = definitely not; F = female; FSHD = facioscapulohumeral muscular dystrophy; H = hospitalized; LGMD = limb-girdle muscular dystrophy; M = male; No. = number; P = primary reason for study withdrawal; per = persisted; PNOT = probably not; POS = possibly; Res = resolved; TEAE = treatment-emergent adverse event; SAE = serious adverse event; Sev = severity; UT = unscheduled visit/test; W = withdrawn.

Deaths: No deaths were reported in this study.

Laboratory Test, ECG and Vital Signs: Out of 116 subjects, 64 (55.2%) had laboratory test results of potential clinical importance. Statistically significant differences in the levels of calcium from Baseline were observed at Visits 8, 11 and 16 in the 1-mg/kg cohort; at Visit 16 in the 3-mg/kg cohort; at Visits 5, 8, 11, and 89 in the 10-mg/kg cohort. Statistically significant differences in the levels of basophils from Baseline were observed: at Visits 5, 8 and 11 in the 1-mg/kg cohort; at Visits 8 and 11 in the 3-mg/kg cohort; at Visits 8, 11 and 15 in the 10 mg/kg cohort. However, no consistent statistical differences or clinically meaningful changes across any of the laboratory test values were observed in any of the MYO-029 treatment groups.

CONCLUSIONS: This study was not completed as planned due to safety concerns (89.7% of subjects experienced at least 1 TEAE, 7 subjects reported SAEs [of these, 3 treatment-emergent SAEs] and 27 subjects withdrew from the study [of these, 4 for safety reasons]). Planned analyses for efficacy, pharmacodynamics, pharmacokinetics, pharmacogenomics and health outcomes could not be conducted.