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Supplementary appendix

This appendix formed part of the original submission and has been peer reviewed. We post it as supplied by the authors.

Supplement to: Mammen AL, Amato AA, Dimachkie MM, et al. Zilucoplan in immune-mediated necrotising myopathy: a phase 2, randomised, double-blind, placebo-controlled, multicentre trial. *Lancet Rheumatol* 2023; **5:** e67–76.

Protocol Amendments

The original protocol was dated 05 Apr 2019 (Version 1.0). Subsequently, 2 country-specific protocol amendments and 1 global protocol amendment were issued. All protocol amendments were reviewed by the appropriate regulatory authority and IRB/IEC prior to their implementation. The primary purpose of the global protocol amendment, including changes made in earlier country-specific protocol amendments, is provided in the following section.

Protocol Amendment (Global) Version 2.0 and country-specific protocol amendments (GB.1.1 and FR.1.1) Protocol Amendment (Global) Version 2.0 was issued on 16 Feb 2021, which consolidated changes made in earlier United Kingdom (GB.1.1; dated 25 Jul 2019) and France (FR.1.1; dated 20 Feb 2020) country-specific protocol amendments, and included the following changes:

1. The United Kingdom country-specific protocol amendment included a note that the primary and secondary efficacy endpoints evaluated in the Main Portion of the study continued to be collected during in the Extension Portion of the study to determine the long-term safety, tolerability, and efficacy of ZLP in study participants with IMNM. This change was incorporated into the global protocol amendment by including the Extension Portion objective and endpoints in the Objectives and Endpoints table. Notes were added into the global protocol amendment that the long-term safety, tolerability, and efficacy were evaluated during the open-label Extension Portion of the study.

2. Text regarding safety data review was updated.

3. For France only, the duration of study participation during the Extension Portion of this study was amended from 4 months to 18 months.

4. Added exclusion criterion 14 (hypersensitivity to IMP).

5. Footnote “a” was updated to state that if a study participant permanently discontinued IMP treatment prior to the Week 8 Visit for any reason, he/she was not eligible for the Extension Portion. For study participants who permanently discontinued treatment with IMP, a Safety Follow-up Visit was performed 40 days after the last dose to collect information on any ongoing AEs or new SAEs since the last study visit.

6. A new footnote “b” was added to the “Visits after Day Extension (E)117” to state that for France only, the duration of study participation during the Extension Portion included an open-label, single-arm, 18-month Treatment Period.

7. Revised information on contraception. In addition, for the global protocol amendment, the objectives and endpoints were revised to reflect current UCB practices for the categorization and description of study objectives based on estimand definitions (to align with the updated ICH E9 [R1] addendum). Also, the efficacy analysis presented in the protocol was updated from the 2-sided Wilcoxon rank sum test to the 2-sided stratified Wilcoxon rank sum test (Van Elteren test), and a sentence was added to state that the effect of ZLP on American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) minimal response was investigated using a binary logistic regression model with treatment and stratification included as factors. The protocol was also updated to include provisions for the COVID-19 pandemic. Finally, in addition to administrative updates, changes were made to clarify that the snapshot was taken after the Week 8 Visit (ie, the study remained double-blinded until after the data from Week 8 of the Main Portion of the study were reviewed, locked, and unblinded).

Complete Inclusion and Exclusion Criteria

In order to be considered eligible for this study, all of the following criteria must have been met:

1. Male or female ≥18 years and <75 years.

2. Were able to provide informed consent, including signing and dating the ICF.

3. Clinical diagnosis of IMNM.

4. Positive serology for anti-HMGCR or anti-SRP autoantibodies.

5. Clinical evidence of weakness (≤Grade 4 out of 5) on manual muscle testing (MMT) in at least 1 proximal limb muscle group.

6. Creatine kinase of >1000U/L at Screening.

7. No change in corticosteroid dose for at least 30 days prior to Baseline or anticipated to occur during the first 8-weeks on study.

8. No changes in immunosuppressive therapy, including dose, for at least 30 days prior to Baseline or anticipated to occur during the first 8-weeks on study.

9. Female study participants of childbearing potential must have had a negative serum pregnancy test at Screening and a negative urine pregnancy test within 24 hours prior to the first dose of the IMP.

10. Sexually active female study participants of childbearing potential (ie, women who were not postmenopausal or who had not had a hysterectomy, bilateral oophorectomy, or bilateral tubal ligation) and all male study participants (who had not been surgically sterilized by vasectomy) must have agreed to use effective contraception during the study. Postmenopausal women were defined as women who had gone 12 consecutive months without menstruation.

Study participants who met any of the following exclusion criteria were ineligible for participation in the study:

1. History of meningococcal disease.

2. Current or recent systemic infection within 2 weeks prior to Screening or infection requiring intravenous antibiotics within 4 weeks prior to Screening.

3. Pregnant, planning to become pregnant, or nursing female study participants.

4. Recent surgery requiring general anesthesia within 2 weeks prior to Screening or expected to have surgery requiring general anesthesia during the 8-week Treatment Period.

5. Treatment with a complement inhibitor or an experimental drug within 30 days or 5 half-lives of the drug (whichever was longer) prior to Baseline.

6. Statin use within 30 days prior to Baseline or anticipated to occur during study.

7. Rituximab use within 90 days prior to Baseline or anticipated to occur during study. NOTE: For study participants who received rituximab more than 90 days but less than 6 months prior to Baseline, prophylactic antibiotics (eg, ciprofloxacin, erythromycin, penicillin V) were given upon initiation of IMP until 6 months after the last rituximab dose.

8. Recent initiation of IVIG (ie, first cycle administered less than 90 days prior to Baseline).

9. Plasma exchange within 4 weeks prior to Baseline or expected to occur during the 8-week Treatment Period.

10. Active malignancy (except curatively resected squamous or basal cell carcinoma of the skin) requiring surgery, chemotherapy, or radiation within the prior 12 months (study participants with a history of malignancy who underwent curative resection or otherwise did not require treatment for at least 12 months prior to Screening with no detectable recurrence were allowed).

11. History of any significant medical, psychiatric disorder, or laboratory abnormality that in the opinion of the Investigator made the study participant unsuitable for participation in the study.

12. Participation in another concurrent clinical trial involving an experimental therapeutic intervention (participation in observational studies and/or registry studies was permitted).

13. Were unable or unwilling to comply with the requirements of the study.

14. Study participants who had a known hypersensitivity to ZLP or any of its excipients (as per

Inclusion criteria for the Extension Portion of the study

1. Completion of the Main Portion of the study.

2. Continued to meet inclusion criteria 2, 9, and 10, from the Main Portion of the study.

3. Did not start any disallowed medication per the exclusion criteria from the Main Portion of the study or alter the dose of any other concomitant medication, unless medically indicated.

4. Were able and willing to comply with the requirements of the study.

5. Did not have any new medical condition (since entry into the Main Portion) or any other reason that, in the opinion of the Investigator or Sponsor, disqualified the study participant from participation in the Extension Portion of the study.

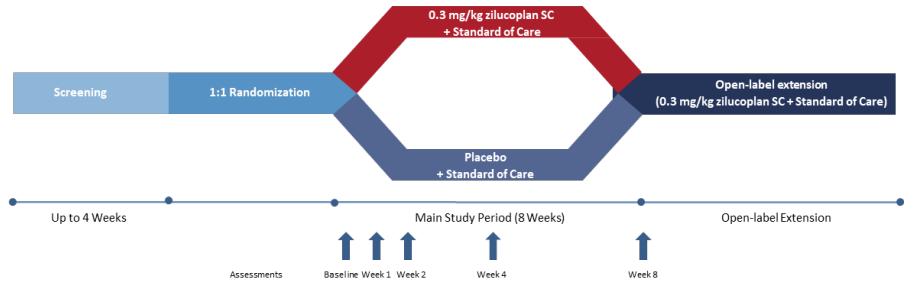
Exploratory endpoints

To assess the long-term efficacy of zilucoplan	• At least minimal response based on the ACR/EULAR Response Criteria Scale at each visit following Week 8 • Change from Baseline of 3TUG Test (in ambulatory patients only) at each visit following Week 8 • Change from Baseline of Proximal MMT at each visit following Week 8 • Change from Baseline of Physician Global Activity VAS at each visit following Week 8 • Change from Baseline of Patient Global Activity VAS at each visit following Week 8 • Change from Baseline of HAQ at each visit following Week 8 • Change from Baseline of MDAAT Extramuscular Disease Activity VAS Score at each visit following Week 8 • Change from Baseline of FACIT Fatigue Scale at each visit following Week 8
To assess the PK of zilucoplan	• Plasma concentrations of zilucoplan and its major metabolites
To assess the PD of zilucoplan	• Sheep red blood cell lysis assay for evaluation of classical complement pathway activation • Complement component 5 levels
To assess the effect of zilucoplan on biomarkers	• Mechanistic biomarkers (e.g., complement fixation, complement function, complement pathway proteins, autoantibody characterization [titer and immunoglobulin class], myocyte markers, and inflammatory markers)
To assess the effect of zilucoplan on pharmacogenomics	• Pharmacogenomic analyses (optional): Genomic studies (e.g., deoxyribonucleic acid [DNA] sequencing, including exploration of whether specific genomic features correlate with response or resistance to study drug) may be performed.

3TUG=Triple Timed Up and Go, ACR=American College of Rheumatology, EULAR=European League Against Rheumatism, FACIT= Functional Assessment of Chronic Illness Therapy, HAQ=Health Assessment

Questionnaire, MDAAT= Myositis Disease Activity Assessment Tool, MMT=manual muscle testing
PD=pharmacodynamic, PK=pharmacokinetic, VAS=visual analogue scale.

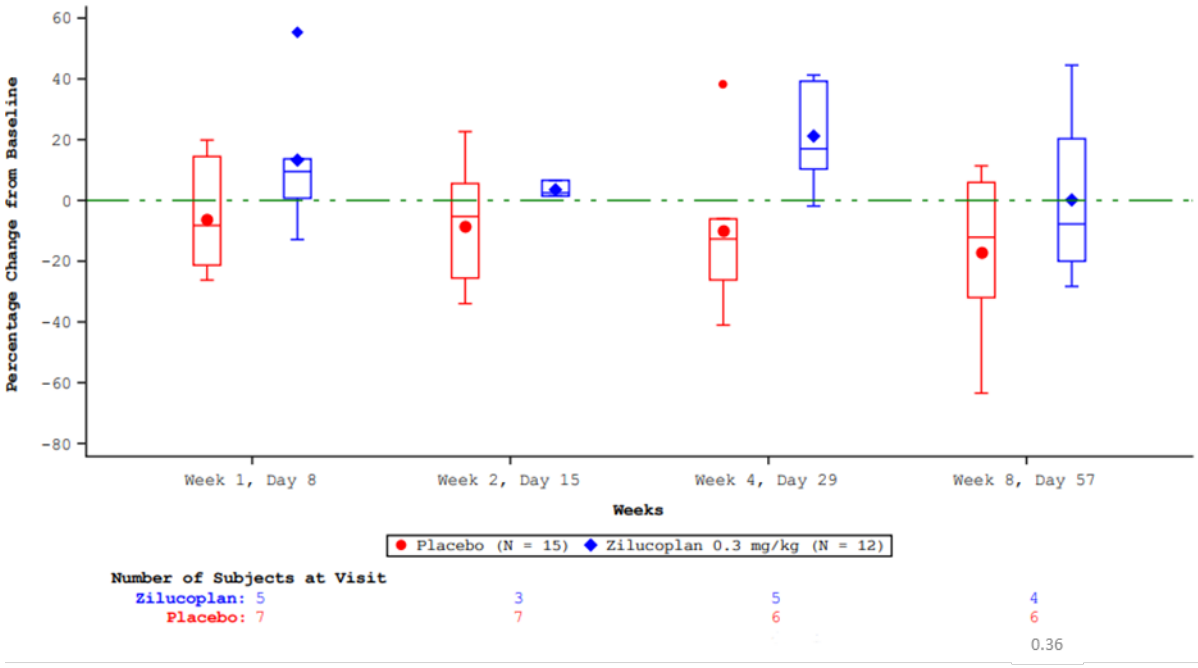
Figure S1: IMNM 01 Study Design



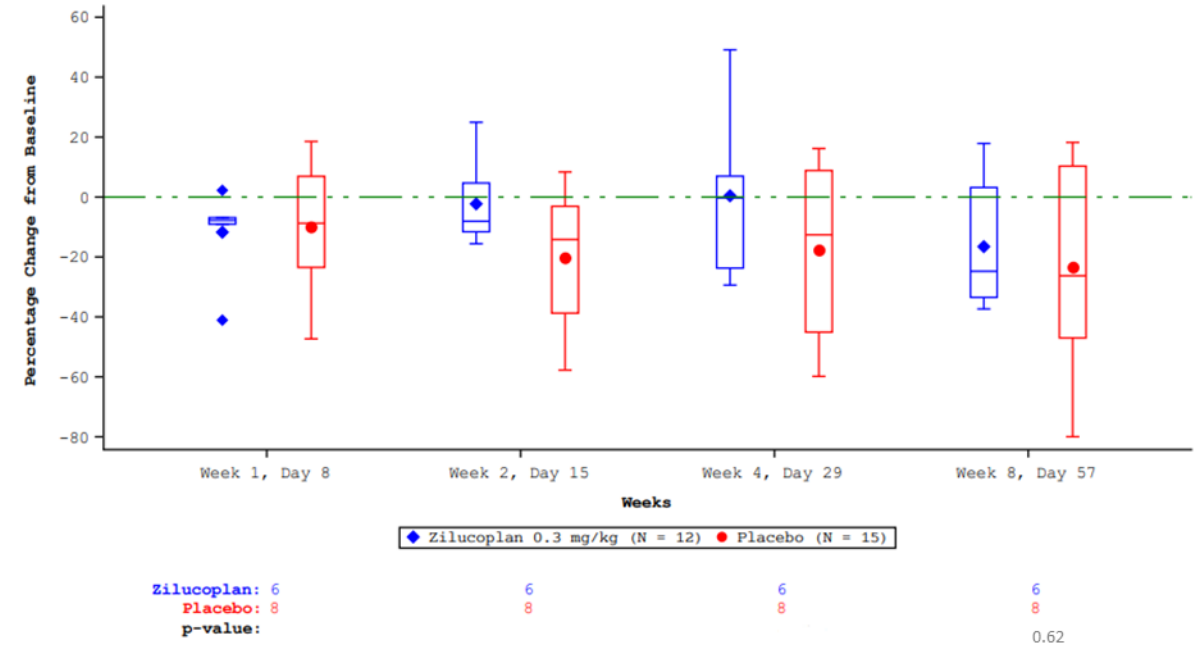
SC, subcutaneous.

Figure S2. Percent changes in Creatine Kinase Levels from Baseline to Week 8 (ITT population), by Sex

A. Female



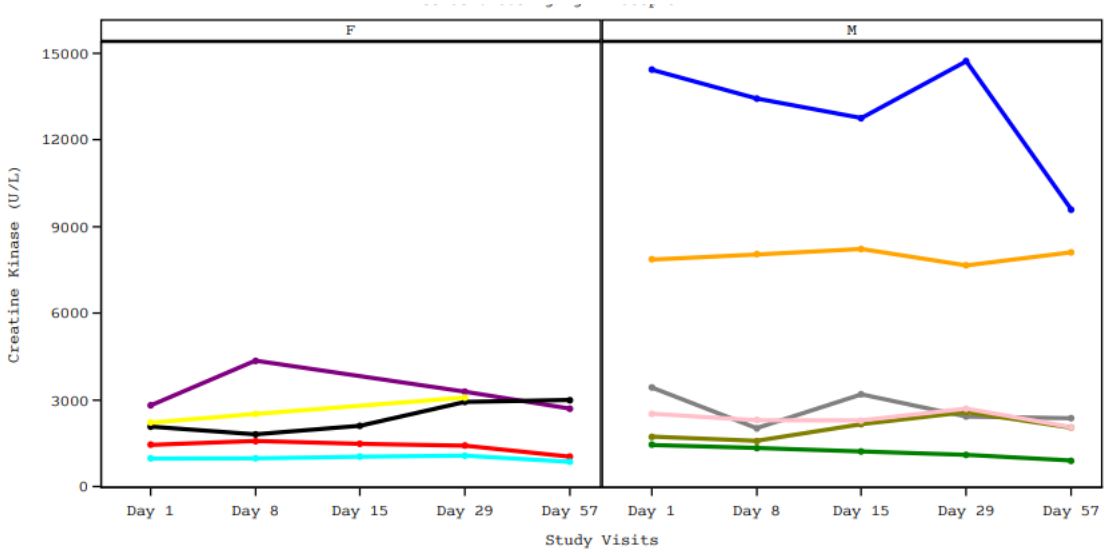
B. Male



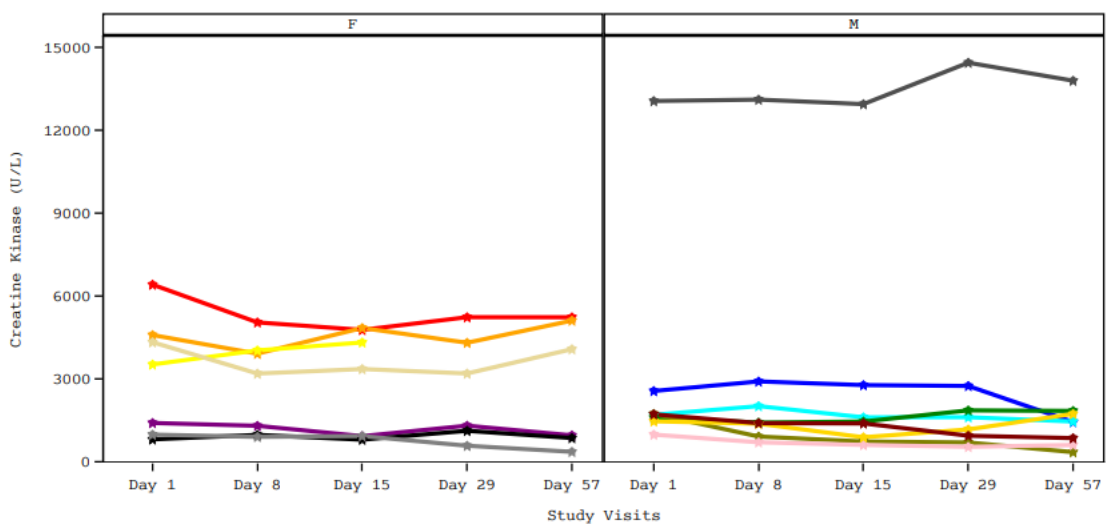
ITT=intention-to-treat

Figure S3. Individual Creatine Kinase Levels (U/L) Over the Main Study Period (ITT population) by Sex

A. Zilucoplan 0.3 mg/kg

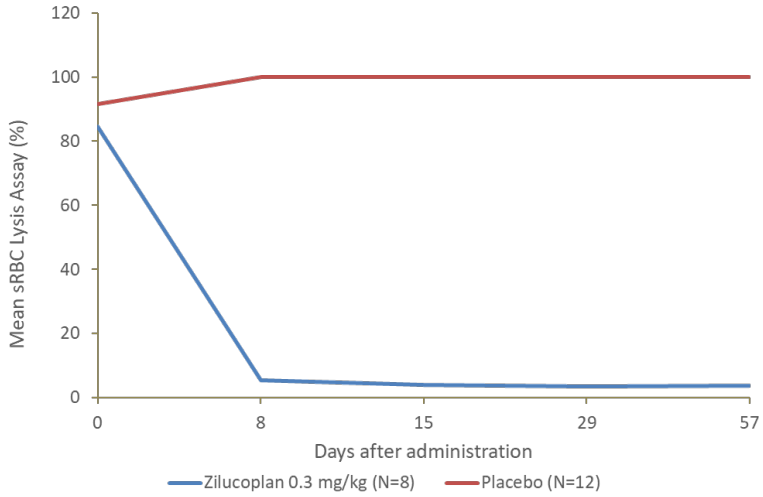


B. Placebo



ITT=intention-to-treat

Figure S4. Mean complement inhibition levels, based on sRBC lysis assay in the main study period (PD-PPS population)



PD-PPS=pharmacodynamic per-protocol set, sRBC= sheep red blood cell.

Table S1. Change from baseline to Week 8 in secondary endpoints (ITT population)

	ZLP 0·3mg/kg N=12	**PBO N=15**
ACR/EULAR Total Improvement Score		
N	11	14
Responder*, n (%)	6 (54·5)	7 (50·0)
Non-responder, n (%)	5 (45·5)	7 (50·0)
Odds ratio vs placebo* (95% CI)	1·088 (0·214, 5·535)	
p-value†	0·92	
Triple Timed Up and Go test		
N	10	10
Baseline mean	12·8	11·6
LS mean change (SE) at Week 8	-1·401 (0·788)	-0·712 (0·789)
LS mean difference (95% CI)	-0·688 (-2·781, 1·404)	
p-value‡	0·496	
Proximal MMT		
N	11	14
Baseline mean	115·3	99·5
LS mean change (SE) at Week 8	3·71 (3·81)	-0·18 (3·44)
LS mean difference (95% CI)	3·89 (-6.18, 13·95)	
p-value‡	0·431	
Physician Global Activity VAS		
N	11	15
Baseline mean	4·48	4.89
LS mean change (SE) at Week 8	-0·830 (0·671)	-0·626 (0·557)
LS mean difference (95% CI)	-0·204 (-1·855, 1·448)	
p-value‡	0·800	
Patient Global Activity VAS		
N	11	15
Baseline mean	5·94	6·71
LS mean change (SE) at Week 8	-1·966 (0·854)	-0·685 (0·707)
LS mean difference (95% CI)	-1·281 (-3·390, 0·829)	
p-value‡	0·221	
HAQ		
N	11	15
Baseline mean	1·19	1·55
LS mean change (SE) at Week 8	-0.125 (0.183)	0·022 (0·151)
LS mean difference (95% CI)	-0·147 (-0·601, 0·307)	
p-value‡	0·508	
MDAAT		
N	11	15
Baseline mean	0·55	0·73
LS mean change (SE) at Week 8	-0·287 (0·398)	-0·144 (0·336)
LS mean difference (95% CI)	-0·143 (-1·123, 0·837)	
p-value‡	0·765	
FACIT-Fatigue scale		
N	11	15
Baseline mean	27·8	27·1
LS mean change (SE) at Week 8	8·98 (4·08)	3·45 (3·41)
LS mean difference (95% CI)	5·53 (-4·49, 15·55)	
p-value‡	0·265	

*Threshold of 20 in the ACR/EULAR corresponds to a minimal response based on the criterion scale

[†]P-values for the comparison of treatment groups have been calculated using logistic regression with IMP and strata as fixed factors.

[‡]Based on a linear model with treatment and strata (anti-HMGCR+/anti-SRP+) as fixed factors with baseline Triple Timed Up and Go, baseline proximal MMT, baseline Physician Global Activity Visual Analogue Scale, Patient Global Activity Visual Analogue Scale, baseline Health Assessment Questionnaire, baseline MDAAT or baseline FACIT-Fatigue Scale as a covariate

ACR=American College of Rheumatology, CI=confidence interval, CHG= change from baseline, CK=creatinine kinase, EULAR=European League Against Rheumatism, FACIT-Fatigue=Functional Assessment of Chronic Illness Therapy, HAQ=health assessment questionnaire, LS=least square, Max=maximum, MDAAT=myositis disease activity assessment tool, Min=minimum, MMT=manual muscle testing, SD=standard deviation, SE=standard error, VAS=visual analogue scale.

Table S2. Subgroup analysis (Sex, age and stratification factor, ITT population)

	ZLP 0·3mg/kg N=12	PBO N=15	ZLP 0·3mg/kg N=12	PBO N=15	ZLP 0·3mg/kg N=12	PBO N=15	ZLP 0·3mg/kg N=12	PBO N=15	ZLP 0·3mg/kg N=12	PBO N=15	ZLP 0·3mg/kg N=12	PBO N=15
	Sex Female		Sex Male		Age <55 years		Age ≥55 years		Anti-HMGCR+		Anti-SRP+	
Percentage change from baseline in CK levels*												
N	6	5	6	8	3	7	8	7	9	10	2	4
Week 4 Mean percent change from baseline (SD)	21·2 (18·7)	-10·1 (27·0)	0·41 (27·9)	-17·7 (29·3)	7·6 (-)	-2·0 (26·4)	10·7 (22·8)	-26·8 (24·2)	13·5 (25·6)	-19·3 (23·4)	-6·7 (-)	-2·3 (36·9)
N	6	4	6	8	3	7	7	7	8	10	2	4
Week 8 Mean percent change from baseline (SD)	0·16 (31·3)	-17·1 (27·7)	-16·6 (22·4)	-23·5 (35·2)	-5·4 (-)	-18·0 (22·2)	-11·8 (27·1)	-23·5 (40·0)	-6·2 (27·4)	-24·2 (32·8)	-24·5 (-)	-11·9 (29·2)
ACR/EULAR Response Criteria Scale, TIS ≥20 at Week 4 and Week 8†												
N	6	5	6	7	3	6	9	6	10	9	2	3
Week 4 responder, n (%)	3 (50%)	3 (60%)	4 (67%)	3 (43%)	2 (67%)	2 (33%)	5 (56%)	4 (67%)	5 (50%)	5 (56%)	2 (100%)	1 (33%)
N	5	6	6	8	3	7	8	7	9	10	2	4
Week 8 responder, n (%)	2 (40%)	3 (50%)	4 (67%)	4 (50%)	2 (67%)	5 (71%)	4 (50%)	2 (29%)	5 (56%)	6 (60%)	1 (50%)	1 (25%)
Change from baseline in 3TUG‡												
N	4	4	6	5	3	3	7	6	8	8	2	1
Week 4 Mean percent change from baseline (SD)	-0·43 (2·9)	0.68 (0·97)	-0·98 (1·8)	0·18 (1·7)	-2·1 (-)	0·63 (-)	-0·19 (-2·1)	0·28 (1·4)	-0·65 (2·4)	0·45 (1·4)	-1·2 (-)	0
N	4	4	6	6	3	3	7	7	8	8	2	2
Week 8 Mean percent change from baseline (SD)	-1·7 (2·7)	-0·05 (1·2)	-0·62 (2·6)	-0·50 (2·0)	-2·4 (-)	0·13 (-)	-0·44 (2·7)	-0·51 (1·4)	-0·88 (2·8)	0·01 (1·5)	-1·7 (-)	-1·7 (-)
Change from baseline in proximal MMT‡												
N	6	5	6	7	3	6	9	6	10	9	2	3
Week 4 Mean percent change from baseline (SD)	1·3 (15·5)	3·4 (5·8)	7·8 (9·4)	5·4 (2·4)	7·0 (-)	3·3 (4·6)	3·8 (13·7)	5·8 (3·4)	5·6 (13.8))	6·1 (3·1)	-0·5 (-)	0
N	5	6	6	8	3	7	8	7	9	10	2	4

Week 8 Mean percent change from baseline (SD)	2·2 (16·6)	10·2 (13·2)	8·3 (12·7)	-0·13 (7·0)	10·3 (-)	8·3 (13·0)	3·8 (14·4)	0·29 (7·5)	7·1 (15·1)	6·6 (11·1)	-1·5 (-)	-1·5 (9·5)
Change from baseline in Physician global activity VAS[‡]												
N	6	6	6	8	3	7	9	7	10	10	2	4
Week 4 Mean percent change from baseline (SD)	-1·5 (1·3)	-1·6 (1·3)	-1·3 (1·9)	-0·51 (1·1)	-1·5 (-)	-1·3 (1·6)	-1·3 (1·2)	-0·67 (0·95)	-1·4 (1·7)	-1·2 (1·2)	-1·3 (-)	-0·55 (1·6)
N	5	7	6	8	3	7	8	8	9	11	2	4
Week 8 Mean percent change from baseline (SD)	-1·1 (2·3)	-1·5 (2·0)	-1·3 (2·8)	-0·54 (1·2)	-1·1 (-)	-1·3 (2·3)	-1·3 (2·0)	-0·69 (0·87)	-1·5 (2·3)	-1·3 (1·7)	0·05 (-)	0·03 (1.3)
Change from baseline in Patient global activity VAS[‡]												
N	6	6	6	8	3	7	9	7	10	10	2	4
Week 4 Mean percent change from baseline (SD)	-1·3 (1·1)	-1·7 (1·4)	-2·3 (2·4)	1·3 (2·0)	-3·4 (-)	0·41 (2·8)	-1·2 (1·8)	-0·39 (1·8)	-1·7 (2·0)	-0·15 (2·5)	-2·3 (-)	0·43 (2.0)
N	5	7	6	8	3	7	8	8	9	11	2	4
Week 8 Mean percent change from baseline (SD)	-1·3 (1·3)	-1·6 (2·5)	-2·4 (4·0)	-0·16 (1·4)	-4·7 (-)	-0·89 (2·9)	-0·86 (2·2)	-0·75 (1·2)	-2·0 (3·3)	-0·84 (2·1)	-1·4 (-)	-0·75 (2·2)
Change from baseline in HAQ[c]												
N	6	6	6	8	3	7	9	7	10	10	2	4
Week 4 Mean percent change from baseline (SD)	-0·13 (0·41)	-0·25 (0·37)	-0·38 (0·68)	-0·09 (0·50)	-0·83 (-)	-0·36 (0·33)	-0·06 (0·35)	0·04 (0·47)	-0·25 (0·60)	-0·29 (0·33)	-0·25 (-)	0·16 (0·56)
N	5	7	6	8	3	7	8	8	9	11	2	4
Week 8 Mean percent change from baseline (SD)	-0·10 (0·64)	-0·18 (0·79)	-0·31 (0·55)	-0·03 (0·33)	-0·67 (-)	-0·25 (0·76)	-0·05 (0·50)	0·03 (0·33)	-0·25 (0·63)	-0·25 (0·58)	0·06 (-)	0·31 (0·33)
Change from baseline in MDAAT Extramuscular Disease Activity Score[‡]												
N	6	6	6	8	3	7	9	7	10	10	2	4
Week 4 Mean percent change from baseline (SD)	-0·22 (0·33)	-0·40 (1·1)	-0·45 (0·95)	0·26 (0·53)	-0·50 (-)	-0·03 (1·2)	0·28 (0·38)	-0·01 (0·21)	-0·33 (0·73)	0·09 (0·36)	-0·35 (-)	-0·30 (1·6)
N	5	7	6	8	3	7	8	8	9	11	2	4
Week 8 Mean percent change from baseline (SD)	-0·24 (0·37)	-0·34 (2·0)	0·02 (1·6)	0·14 (0·41)	-0·70 (-)	-0·46 (1·8)	0·13 (0·96)	0·24 (0.92))	-0·06 (1·24)	0·20 (0·77)	-0·30 (-)	-0·88 (2·4)
Change from baseline in FACIT-Fatigue Scale[c]												

N	6	6	6	7	3	7	9	6	10	10	2	3
Week 4 Mean percent change from baseline (SD)	7·7 (7·8)	7·7 (7·3)	9·7 (14·4)	5·0 (5·7)	20·7 (-)	4·6 (5·4)	4·7 (7·8)	8·2 (7·3)	8·6 (12·3)	8·0 (5·6)	9·0 (-)	0·33 (-)
N	5	7	6	8	3	7	8	8	9	11	2	4
Week 8 Mean percent change from baseline (SD)	3·3 (16·3)	3·3 (10·9)	13·8 (17·5)	4·1 (7·1)	27·0 (-)	3·0 (7·7)	2·3 (12·5)	4·4 (10·1)	8·6 (19·0)	3·6 (10·1)	11·0 (-)	4·3 (4·0)

[*] The percentage change from baseline of CK levels was defined as %CHG = 100 x (Post Baseline - Baseline) / Baseline; Baseline during the Main Portion was defined as the closest non-missing value obtained prior to the first study drug administration; Baseline mean was defined as the Baseline results for those participants who were also assessed at the specified visit.

[†] Percentages are based on the number of participants with a non-missing result at the specific visit. A total improvement score of >=20 represents Minimal Improvement, a score of >=40 represents Moderate Improvement, and a score of >=60 represents Major Improvement.

[‡] The change from baseline is defined as CHG = Post Baseline - Baseline. Baseline during the Main Portion was defined as the closest non-missing value obtained prior to the first study drug administration. Baseline mean was defined as the Baseline results for those participants who were also assessed at the specified visit.

ACR=American College of Rheumatology, CI=confidence interval, CHG= change from baseline, CK=creatinine kinase, EULAR=European League Against Rheumatism, FACIT-Fatigue=Functional Assessment of Chronic Illness Therapy, HAQ=health assessment questionnaire, LS=least square, Max=maximum, MDAAT=myositis disease activity assessment tool, Min=minimum, MMT=manual muscle testing, SD=standard deviation, SE=standard error, 3TUG=triple timed up and go test, VAS=visual analogue scale.

Table S3. Summary of treatment-emergent adverse events (safety analysis population), by Sex

	Zilucoplan 0·3mg/kg n (%)*	**Placebo n (%)***
Female	**N=6**	**N=7**
Any TEAE	4 (66·7)	6 (85·7)
Most Frequent TEAE†		
Headache	3 (50·0)	2 (28·6)
Nausea	2 (33·3)	1 (14·3)
Serious TEAE	0	1 (14·3)
TEAE Resulting in Permanent Withdrawal from Study Medication	0	0
Treatment-related TEAE	1 (16·7)	2 (28·6)
Headache	0	1 (14·3)
Nausea	0	0
Vertigo	0	1 (14·3)
Treatment Related Serious TEAE	0	0
Deaths (TEAEs leading to death)	0	0
Male	**N=6**	**N=8**
Any TEAE	5 (83·3)	7 (87·5)
Most Frequent TEAE†		
Headache	1 (16·7)	2 (25·0)
Nausea	1 (16·7)	2 (25·0)
Serious TEAE	0	2 (25·0)
TEAE Resulting in Permanent Withdrawal from Study Medication	0	
Treatment-related TEAE	3 (50.0)	3 (37·5)
Headache	1 (16·7)	1 (12·5)
Nausea	1 (16·7)	1 (12·5)
Vertigo	0	1 (12·5)
Treatment Related Serious TEAE	0	0
Deaths (TEAEs leading to death)	0	0

TEAE=treatment-emergent adverse event. *n=number of participants reporting at least one TEAE in that category; †TEAEs reported in >2 participants in either treatment group.

Table S4. List of Investigators

Name	Affiliation	Country
Yves Allenbach	Hôpital Universitaire Pitié Salpêtrière	France
Olivier Benveniste*		
Nicolas Champtiaux		
Giorgia Querin		
Anneke van der Kooi*	Amsterdam Universitair Medische Centra - Academisch Medisch Centrum	Netherlands
Joost Raaphorst		
Hector Chinoy*	Salford Royal NHS Foundation Trust	United Kingdom
James Lilleker		
Andrew Snedden		
Matthew Appleby	University College London Hospitals NHS Foundation Trust	United Kingdom
Pedro Machado*		
George Ransley		
Jerrica Farias	University of South Florida Health Morsani Center for Advanced Healthcare	United States of America
Niraja Suresh*		
Tuan Vu		
Ali A. Habib	University of California Irvine	United States of America
Tahseen Mozaffar*		
Richard J Barohn	University of Kansas Medical Center	United States of America
Mazen Dimachkie*		
Constantine Farmakidis		
Mamatha Pasnoor		
Jeffrey Statland		

Miriam Freimer*	The Ohio State University Wexner Medical Center	United States of America
Samantha Lorusso		
Payam Soltanzadeh*	University of California Los Angeles	United States of America
Andrew Mammen*	National Institutes of Health	United States of America
Iago Pinal-Fernandez		
Anthony Amato*	Brigham and Women's Hospital	United States of America
Christopher Doughty		
Christyn Edmundson*	Penn Neuroscience Center	United States of America
Chafic Karam		
Suur Biliciler*	UT Physicians Neurology	United States of America
Kazim Sheikh		
Anthony Geraci*	Northwell Health Neuroscience Institute - Great Neck	United States of America
Sami Saba		
Yessar Hussain*	Austin Neuromuscular Center	United States of America

*Principal Investigator

Table S5. List of Study Co-ordinators

Name	Affiliation	Country
Saadane Kirouani	Hôpital Universitaire Pitié Salpêtrière	France
Tamar Gibson	Amsterdam Universitair Medische Centra - Academisch Medisch Centrum	Netherlands
Marie Greenhalgh	Salford Royal NHS Foundation Trust	United Kingdom
Jonathan Ogor		
Anne Keen		
Jessica Shaw	University of South Florida Health Morsani Center for Advanced Healthcare	United States of America
Beverly Brooks		
Lucy Lam		
Jeanette Overton	University of California Irvine	United States of America
Denise Davis		
Celeste Alcantara		
Vivian Li		
Katie Lillig	University of Kansas Medical Center	United States of America
Andrew Heim		
Samantha Colgan		
Ali Ciersdorff		
Marco Tellez	The Ohio State University Wexner Medical Center	United States of America
Gilda Avila	University of California Los Angeles	United States of America
Julie Thompson	National Institutes of Health	United States of America
Janet Orozco	Brigham and Women's Hospital	United States of America
Kelsey Moulton	Penn Neuroscience Center	United States of America
Pranali Ravikumar		
Estela Acosta	UT Physicians Neurology	United States of America
Carla Wilkerson		

Principal Investigator	Location Name	Country	Screened	Randomized
Andrew Mammen	National Institutes of Health	United States of America	5	4
Olivier Benveniste	Hopital Universitaire Pitie Salpetriere	France	5	4
Yessar Hussain	Austin Neuromuscular Center	United States of America	5	4
Hector Chinoy	Salford Royal NHS Foundation Trust	United Kingdom	5	3
Anthony Geraci	Northwell Health Neuroscience Institute - Great Neck	United States of America	3	1
Anthony Amato	Brigham and Womens Hospital	United States of America	2	2
Mazen Dimachkie	The University of Kansas	United States of America	2	1
Payam Soltanzadeh	University of California Los Angeles	United States of America	2	1
Niraja Suresh	University of South Florida Health Morsani Center for Advanced Healthcare	United States of America	1	1
Tahseen Mozaffar	University of California Irvine	United States of America	1	1
Miriam Freimer	The Ohio State University Wexner Medical Center	United States of America	1	1
Pedro Machado	University College London Hospitals NHS Foundation Trust	United Kingdom	1	1
Christyn Edmundson	University of Pennsylvania	United States of America	1	1
Suur Biliciler	UT Physicians Neurology	United States of America	1	1
Anneke van der Kooi	Amsterdam Academisch Medisch Centrum	Netherlands	1	1