A PHASE 2 DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED STUDY TO EVALUATE THE EFFICACY, SAFETY, AND TOLERABILITY OF PF-06823859 IN ADULT SUBJECTS WITH DERMATOMYOSITIS

Investigational Product Number:	PF-06823859
Investigational Product Name:	Not Applicable (N/A)
United States (US) Investigational New Drug (IND) Number:	CCI
European Clinical Trials Database (EudraCT) Number:	2020-004228-41
Protocol Number:	C0251002
Phase:	2

Document History

Document	Version Date	Summary of Changes and Rationale
Amendment 6	20 September 2021	The overall rationale for the amendment is to permit participants actively enrolled in the C0251002 study to have the option to continue active treatment into a long term open label extension study, known as protocol C0251008. This study is An Open Label, Extension Study for Study Participants who have completed the full treatment period in one of the qualifying parent studies (eg, protocol C0251002) utilizing the PF-06823859 compound in adult participants with Dermatomyositis. Participants will be enrolled per investigator discretion and eligibility. If participants do not continue in the open label extension study due to any reason, they will continue into the follow up portion of the C0251002 study. Added throughout protocol: All participants who complete the treatment period in this study up through and including (Visit 9, Week 24), will have the opportunity to continue treatment in the open label extension C0251008 protocol. Participants who have completed the treatment period and have not had any significant protocol deviations, or safety events will be eligible. SOA: Footnote added to Visit 9, Week 24 on the amended stage 2 and stage 3. This footnote was added to note that if patients are eligible and if per the investigator discretion, they may enter into the long term open lable extension study. SOA: Amended Stage 2, added hsCRP to the early withdraw visit. Rationale: To make consistent between Stage 3 and Amended Stage 2. SOA: For amended Stage 2 and Stage 3, collection of height was added at Week 24, Visit 9, so that these assessments are completed for anyone moving into the open label extension

		study. All participants will have height assessed at Week 24. Also removed height from the early termination visits as not needed and to make both muscle and skin assessments consistent. Rationale: Allow participants the opportunity to enroll into the open label extension study. All pariticipants will have height recorded at Week 24. This will allow the participants moving into the open label extension a complete baseline. Section 3.1: Study Design: Added rationale for Amendment 5 and Amendment 6; Added that current participants upon completing Visit 9, Week 24 will have the opportunity to enroll into an open label extension study. New Figures added to reflect OLE Section 4.1, 4.2, 4.3, 4.4, 4.5 and 4.6: Inclusion and exclusion criteria associated with use of contraception has been updated. Section 4.2 and 4.6: exclusion criteria have been updated. • Clarified that oral tacrolimus within 30 days of the Day 1 visit is an exclusion. • Clarified that topical calcicneurin inhibitors within 14 days of the Day 1 visit is an exclusion. Section 4.8.2: Contraception section was updated with the bullets above. Section 5.8.5: Corticosteroids: Added under amended stage 2 and stage 3 steroid taper should not be started if the participant is continuing into the open label extension study.

		Rationale: Participants going into the open label extension study require a stable corticosteroid dose at baseline. Section 5.8.5: Removed oral corticosteroids will be recorded on a separate CRF. Rationale: Corticosteroids will be recorded on the concomitant medication page. Appendix 15 and 16: Clarification made that oral tacrolimus requires a 30 day washout period, topical calcineurin inhibitors require a 14 day washout period, and topical calcineurin inhibitors are prohibited throughout the treatment period. Rationale: Clarification. Added Appendix 25 Contraceptive and Barrier use. • Clarified that due to the half life of the study drug, males should not donate sperm during the study. • Provided the definition of user dependent vs. non user dependent birth control. • Defined highly effective contraception. Rationale: Updated to most current protocol template. Section 7.5.6: Height and Weight; updated height to be completed at times in the SOA. Rationale: Height will be collected at Week 24 with weight for a robust baseline in the extension study. Section 7.10: Laboratory tests; upated anc corrected footnotes in Table 1.
Amendment 5	04 May 2021	Country Specific Amendment Germany: Rationale: The purpose of the amendment is to address changes requested from German

		Health Authority and is only applicable to sites participating in Germany. Section 4.8.2: Contraception section was updated for clarification and for participants from Germany to see Appendix 24, CTFG guidelines, for permitted contraceptive methods. Section 5.2: Breaking the Blind section was further clarified that blinding codes can be broken by the investigator at any time. Rationale: In Section 5.2 investigators are encouraged to discuss with the sponsor's medical monitor if they believe unblinding is necessary, however, under no circumstances should unblinding be delayed in an emergency situation. Appendix 14: Guidelines for Participant Safety Monitoring and Discontinuation were, further clarified by adding "Please see Appendix 16, prohibited medications". Rationale: Discontinuation criteria in Appendix 14 did not specify if a prohibited medication was taken during the treatment period, the participant should be discontinued from treatment and proceed to the follow-up period. Added contraception guidelines from Clinical Trials Facilitation and Coordination Group, CTFG version 1.1 in Appendix 24. Rationale: Contraception language was updated throughout the protocol to "Participants from Germany please see Appendix 24". Administrative changes to Amended stage 2 and stage 3 schedule of activities which apply to sites in all countries. Rationale: Two Protocol administration letters, one dated 03 February 2021 and another dated 01 March 2021 were sent out

		to all investigative sites with updates to the Schedule of Activities for amended stage 2 and stage 3 regarding assessments that were omitted during the formatting of the protocol. The additions corrections are: Feb 2, 2021: In the Schedule of Activities (SOA) for amended Stage 2 of the study, vital signs are collected at every visit. In the previous version of the protocol, an, X" for collection of vital signs on days 10, 12 and 13 was missing ". This error was corrected. In the SOA for Stage 3, lab assessments for,Viral Surveillance (CMV, VZV, EBV, HHV6, HSV-1/2) should be collected at Visit 11 and not Visit 10. Correction: Please note: An "X" was added at Visit 11, and removed from Visit 10. In the SOA for Stage 3, the C-SSRS assessment should be collected at the early termination visit. Correction: An "X" was added at the Early termination visit for CSSR-S. In the SOA for amended study Stage 2 and Stage 3, an "X" was removed from the SOA at visit 3 for infusion site reaction, as no infusion site reaction is collected at this visit. Moved footnotes "u, v, w" to corresponding visits associated with biomarker collection, Day 1 drug administration and monitoring time after drug administration. 01 March 2021: (Stage 3 SOA) Please note: An "X" should be marked at Screening for the PtGA, as this assessment is required at Screening to derive inclusion criteria #3, (Section 4.5).
Amendment 4	20 Nov 2020	The C0251002 protocol was amended to add a moderate muscle disease cohort of approximately 8-16 participants, known as Stage 3. This cohort was added to further investigate PF-06823859 and placebo in DM participants with moderate muscle disease. The Stage 2, skin disease cohort,

		was amended to allow placebo participants the opportunity to receive active study drug, which extended the study duration for 12 weeks. The following sections have been updated: Cover Page: Added (Eudra CT Number). Rationale: Study will be conducted in Europe. Added SOA for Amended Stage 2, and Stage 3. Rationale: Study extended for Amended Stage 2 and Stage 3. All participants will receive 12 weeks active study drug. This will allow placebo participants to receive active treatment during the study. Stage 3 SoA: Added a cohort of 8-16 Dermatomyositis participants with moderate muscle disease. Section 1.6 Dose Selection Rationale. Updated to add additional dosing information for Amended Stage 2 and Stage 3 participants. Rationale: The published clinical type I interferon gene signature model for the IFNAR1 inhibitor, anifrolumab, was adapted to project a gene signature suppression by PF-06823859 in DM participants. Specifically, the published model was modified to include IFN-β and a biologically relevant mechanism for gene signature production and incorporated the PK data from C0251001. The modified model provided the rationale for doses to be considered in treatment of DM participants with clinical manifestations of skin disease and muscle disease. The efficacious dose was defined as the dose required to suppress gene signature by ≥80% in participants at trough for a duration of 4 weeks after the third dose in Study C0251002 (with IV doses once every 4 weeks for a total of 3 doses). Using this approach, the predicted efficacious

		dose of PF-06823859 in DM participants with skin and muscle was estimated to be 600 mg. Since this is the first evaluation of PF-06823859 in adult DM participants with muscle disease, the highest 600 mg Q4W dose with estimated gene suppression ≥80% at trough will be investigated. Section 2. Study Objectives and Endpoints: Section 2.3 and 2.4 added, Amended Stage 2 and Stage 3 Objectives and Endpoints. Rationale: Stage 2 was amended to provide all participants 3 consecutive doses of active study drug and 3 doses of placebo during the study. Objectives and endpoints were added for the Stage 3 participants enrolling into the muscle disease cohort. Section 3, Study Design: Updated the duration of the study to 69 months from FSFV to LSLV. Also increased the number of investigative sites to approximately 35 to 40. Rationale: Changes reflect the increased duration of the study and the need to utilize additional investigative sites. Section 3.1 Study Design updates updated to include details on the study design for Amended Stage 2 and Stage 3). Study Schematic Figures 3 and 4 added under Study Design. Rationale: To support Amended Stage 2 and Stage 3 study designs. Section 4.0 Participant Eligibility:

		Updated eligibility for Amended Stage 2 and Stage 3. Inclusion and exclusion criteria added for Amended Stage 2 and stage 3. Rationale: Due to the study being extended for 12 weeks, added additional assessments under Amended Stage 2 and new assessments for Stage 3. Exclusion criterion #7; lab values lowered for Hgb and Creatine Clearance for Amended Stage 2 and Stage 3. Rationale: DM can cause an anemia of chronic disease in which a Hgb of <9.0 g/dL is acceptable. Creatinine clearance decreases with age. Study inclusion age limit is 80 years in which a creatine clearance of 50 ml/minute is acceptable. Section 5.8.5.: Updated permitted doses of corticosteroids for Stage 3 vs. Stage 2 and Amended Stage 2. Rationale: Muscle disease may require a higher permitted dose of steroids. Added tapering of steroids may occur after Week 12 for Stage 2. Amended Stage 2 and Stage 3 tapering can occur after Week 24. Tapering is per the investigator's discretion. Rationale: Tapering steroids per the investigator's discretion is common practice. Section 6. Added Treatment Period assessments for Amended Stage 2, and Stage 3. Rationale: Clarification. Section 6. Added Follow-up Visits for Amended Stage 2, and Stage 3. Rationale: Added 3 additional visits during the treatment period for placebo participants

		to receive active study drug, therefore additional follow up visits required. Section 7.5.10 Biopsies. Added that all participants in Amended Stage 2 will have 2 additional punch biopsies due to the study being extended so that all participants receive active study drug. Added types of analysis on the biopsy tissue. Rationale: To ensure all participants receive active study drug, two additional biopsies will be collected at week 24 when the treatment period is over. Section 7.6: Rater Qualifications: Added MMT-8 and the MDAAT. Rationale: Training is required in order to complete these assessments. Section 7.7: Patient Reported Outcomes, added HAQ-DI, PtGA, EQ-5D-5L, CCI [redacted], FACIT-F and then added the order for completion for Amended Stage 2 and Stage 3. Rationale: Added several different patient reported outcomes and listed them in the order that is required for the different cohorts. These assessments were added for additional collection of information. Section 7.9: Added Total Improvement Score description and definition. Rationale: This tool is required for the Stage 3 cohort as the TIS is the secondary endpoint being measured in Stage 3. Section 9.0: Added Stage 1 data, (preliminary draft) may be shared externally and internally at a high level.

		Section 9.1.3: Added Sample Size Determination for Stage 3. Rationale: Clarification on sample size. Section 9.2.2.2: Added supportive analysis for CDASI data in Stage 2. This includes data from Day 1 through Week 12 and supportive data from Week 12 through Week 24. Section 9.2.1.3, 9.2.2.3, 9.2.3.3: Added description of analyses for primary, secondary, and CCI [redacted] for Stage 3. Rationale: Overview of the major analyses and summaries to be performed. Section 9.3: Added Pharmacokinetic Analysis for Amended Stage 2, and Stage 3. Rationale: Clarification. Section 9.5: Added that an additional interim analysis for the Stage 3 "may be conducted" depending on the enrollment rate. Rationale: Related to internal decision making. Section 16: Added references related to the newly added patient reported outcomes and additional information related to muscle disease and measurement over time. Rationale: Clarification. Appendix 1: Added abbreviations Rationale: Clarification. Added the following Appendices: Appendix 10, EQ-5D-5L, Appendix 11, FACIT-F Scale, Appendix 12, HAQ-DI scale, Appendix 13, PtGA, Appendix 18, CCI [redacted], Appendix 19 Muscle Enzymes Measurement, Appendix 20, MDAAT, Appendix 21, MMT-8,

		Appendix 22, TIS using core set measures in DM. Rationale: To provide clarification and additional information related to the Stage 3. Appendix 16: Updated corticosteroid doses for Stage 3, and that tapering of steroids is permitted after week 12 for stage 2 per investigator discretion. For Amended Stage 2 and Stage 3, tapering of steroids may occur after Week 24. Rationale: Decreasing steroids or equivalent if not needed is a health benefit. Administrative spelling errors corrected throughout the protocol.
Amendment 3	01 July 2020	The C0251002 protocol was amended after an interim analysis of the data was conducted on 32 participants. An internal review committee, separate from the blinded study team, determined to continue the study and enroll approximately 20 additional participants to evaluate an additional lower dose of PF-06823859, (150 mg) in addition to the 600 mg and placebo dose. This dose was added to explore the exposure response relationship. The primary objective, To evaluate the efficacy of PF-06823859 dose in adult participants with moderate to severe DM was changed to "doses" due to adding 1 additional dose. The terminology "Subjects" replaced with participants throughout the protocol. Updated to support the latest template language. Section 1.6 Dose Selection Rationale updated to include justification for the addition of the 150 mg Q4W IV dose to characterize exposure-response. Section 2.2 added under objectives and endopoints. Study was split into 2 Stages, endpoints and objectives added for stage 2.

		Section 3.1 Study Overview updated to a Phase 2 dose-finding study. Added the number of additional participants to be enrolled, the additional dose to be studied, the number of participants required were increased and the duration of the study was extended. Section 3.1: Removed study to be conducted in the US. Rationale: Study may be conducted in the US, and outside the US. Added Figure 2 to show the revisions to the original study schematic. Section 4.2 Exclusion criteria: Excluded participants previously exposed to anti-beta Interferon. Rationale: Study is continuing, previously enrolled participants are excluded. Section 5.2: Breaking the Blind: Noted that an additional interim analysis may be conducted for internal decision making. Section 5.4.1: Dosage Forms and Packaging: Removed duplicate information. Added vials will be boxed as 6 vials per package. Section 5.4.2: Preparation and Dispensing: Updated to note doses. Section 6.2.3 Added information regarding Alternative measures during public emergencies. At this time detailed information will be provided under separate cover for this study. Also added Appendix 12 for some of the options that may be implemented, during a public emergency. Rationale: Due to COVID-19. Section 7.1 Photography: clarification made to the wording. Section 9.1 Sample Size Determination: split into 2 subsections for Stage 1 and Stage 2. Added sample size rationale for Stage 2. Section 9.2: Added, After the treatment period is completed for all the participants, some members

		of the study team will be unblinded so that a report for the corresponding data can be generated. Rationale: To continue business planning. Section 9.2.1: Split into 2 subsections for Stage 1 and Stage 2. In Section 9.2.1.2, added description for analyses of primary endpoints for Stage 2. Section 9.2.2: Split into 2 subsections for Stage 1 and Stage 2. In Section 9.2.2.2, added description for analyses of secondary endpoints for Stage 2. Section 9.2.3: Added additional CCI [redacted]; also split into 2 subsections for Stage 1 and Stage 2. Added description of other endpoints for Stage 2. Section 9.3: Split into 2 subsections for Stage 1 and Stage 2. Section 9.4: Added text: "Safety analyses will be reported for Stage 1 and for Stage 1 and 2 combined as described in Section 2." Section 9.5.1: Interim Analysis Section updated to allow for potential additional interim analysis at a future date for business decision planning. Section 9.6: Data Monitoring Committee: Updated language that if an interim analysis occurs, the unblinded internal review committee will be responsible for reviewing the data. Appendix 12 Added: Alternative Measures During Public Emergencies: Added appendix for collecting protocol procedures during public emergencies.
Amendment 2	18 December 2019	Protocol amended to add an interim analysis after the last subject randomized completes study Visit 6, Week 12, (primary endpoint) for the purpose of early internal decision making.

		Section 5.2: Breaking the blind: added information to this section that an interim analysis will be performed, and a separate internal review committee will be reviewing unblinded data separate from the study team. Section 9.5: Added sub headers 9.5.1 and 9.5.2. 9.5.1 Analysis for Internal Decision Making: Added that an interim analysis will occur after the last subject randomized completes study Visit 6, Week 12, (primary endpoint). Added that an internal review committee separate from the blinded study team will review efficacy and safety data for internal decision making. CCI [redacted] CCI [redacted]
Amendment 1	12 March 2018	The title of 5D itch scale was changed to 5D Pruritus Scale throughout the document Rationale: Incorrect title was previously recorded. <u>SOA:</u> ECG added to screening in addition to baseline ECG. Rationale: Results needed for inclusion/exclusion criteria. Footnote "S" revised from one hour post dose to "post dose" for PK collection, and also clarified that the PK collection should be taken from the opposite arm of administration of drug.

		Rationale: Clarified time of PK collection after study drug administration. 4.1 Inclusion Criteria: Inclusion criteria #2 revised; changed the age from ≤75 to ≤80 years of age. Rationale: To include more dermatomyositis subjects. 4.2 Exclusion Criteria: Exclusion criteria #15, added (with the exception of topical calcineurin inhibitors). Section 4.4.2: Modified Contraception language per Global approved SOP deviation dated 7/18/17. Section 5.1: Un-blinded personnel was changed to blinded personnel. Rationale: For this study, the study coordinator who is blinded will randomize the subject. No un-blinded information is available to the blinded study coordinator. Section 5.5: Added "approximately" to the sentence, Blinded IV PF-06823859 or placebo will be administered at the investigative site or clinic over the course of "**approximately**" 60 minutes as an IV infusion. Rationale: To reduce protocol deviations. Section 5.8.5: Added on the day of IVIG dose administration, pre-medication to prevent hypersensitivity reaction to IVIG is permitted. The steroid dose that was previously used for pre-medication will be permitted (on IVIG dosing day only). After IVIG dosing day, steroid dosing should remain less than or equal to 15 mg or equivalent per day as per protocol Section 5.8.4.1. Also added: There is no need to change the IVIG dosing schedule or adjust the IVIG dosing schedule related to investigational product administration.

		Rationale: Clarification provided on whether or not pre dosing with steroids was permitted related to IVIG dosing, and to note that IVIG dosing schedule should not be revised according to investigational drug administration. Section 5.8.5.1: Removed recording of steroid usage in a diary. Rationale: Subjects are required to be on a stable dose of steroids, no justification for a subject diary. Section 6.1: Added screening ECG in addition to Day 1 visit. Rationale: ECG added to screening to ensure eligibility criteria were met, prior to Day 1. Section 6.2.1: Added "ECG (Day 1, Visits 4, 5, 6, EOS and ET only)": Rationale: Updated to align with the Schedule of Assessments. Section 7.1: Added Photography. Rationale: Many research offices use photography in their standard of practice. Section 7.5.10: Typo corrected, (3 mm and 5 mm) to (3 mm to 5 mm) Rationale: Typo. Section 7.9: Removed lipid profile panel requires a minimum fast of 8 hours. Rationale: Per team discussion, fasting is not required for the lipid panel. Appendix 11: Added under thalidomide, tacrolimus or mizoribine…Prohibited; any form of tacrolimus

		or any form of topical calcineurin inhibitors (TCI). Rationale: This class of medication is prohibited. Appendix 11: Pre medication with corticosteroids for IVIG is permitted. Rationale: to align with Section 5.8.5. Appendix 6: Added the acute version of the SF36. Rationale: The non-acute version was previously placed in the protocol by error. Several additional minor changes and sentence revisions were made throughout the document. Rationale: Revisions were made for the purposes of clarification and to correct minor grammatical or spelling errors."
Original protocol	10 May 2017	Not applicable (N/A)

This amendment incorporates all revisions to date, including amendments made at the request of country health authorities and IRBs/ECs.

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SCHEDULE OF ACTIVITIES (STAGE 1 AND STAGE 2)

This SoA pertains to the DM population with focus on skin disease. Stage 1 enrolled participants to 600 mg or placebo. Stage 2 enrolled participants to 600 mg, 150 mg or placebo.

The schedule of activities table provides an overview of the protocol visits and procedures. Refer to the STUDY PROCEDURES and ASSESSMENTS sections of the protocol for detailed information on each procedure and assessment required for compliance with the protocol.

The investigator may schedule visits (unplanned visits) in addition to those listed on the schedule of activities table, in order to conduct evaluations or assessments required to protect the well-being of the participant.

Protocol Activity	**Screening**	**Treatment**				**Follow-up**					
Visit identifier (Study Visit)	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**Participant withdrawal or Early Termination[a]**
Study Day/Week	**Days -35 to -1**	**Baseline Day 1**	**Week 1 Day 8**	**Week 4 Day 29**	**Week 8 Day 57**	**Week 12 Day 85**	**Week 16 Day 113**	**Week 20 Day 141**	**Week 24 Day 169**	**Week 28 Day 197 EOS**	**N/A**
Visit Window	**None**	**None**	**±3 days**								
Screening Assessments											
Informed consent	X										
Inclusion/exclusion criteria	X	X									
Demography	X										
Medical history	X	X[b]									
DM History	X										
Prior DM medication history	X	X[b]									
Prior Non DM medications	X	X[b]									
Clinical reported outcomes											
CDASI Score	X	X	X	X	X	X	X	X	X		X
PHQ-8 assessment[c]	X										
CCI [redacted]		[redacted]		[redacted]		[redacted]					[redacted]
Physician global assessment, (PhGA)[e]		X	X	X	X	X	X	X	X	X	X
Patient Reported Outcomes											
5D Pruritus Scale[f]		X	X	X	X	X	X	X	X	X	X
SF36 V2 Acute[f]		X	X	X		X				X	X
DLQI[f]		X	X	X		X				X	X

Protocol Activity	Screening	Treatment				Follow-up					
Visit identifier (Study Visit)	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**Participant withdrawal or Early Termination[a]**
Study Day/Week	**Days -35 to -1**	**Baseline Day 1**	**Week 1 Day 8**	**Week 4 Day 29**	**Week 8 Day 57**	**Week 12 Day 85**	**Week 16 Day 113**	**Week 20 Day 141**	**Week 24 Day 169**	**Week 28 Day 197 EOS**	**N/A**
Visit Window	**None**	**None**	**±3 days**								
Medical Assessments											
Vital Signs (BP, HR, Pulse, Respirations and temperature)[g]	X	X	X	X	X	X	X	X	X	X	X
Weight[h]	X	X				X				X	X
Height[h]	X										
Complete physical examination[i]	X					X				X	X
Targeted physical examination[i]		X	X	X	X		X	X	X		
ECG	X	X		X	X	X				X	X
Chest X-Ray[j]	X										
Skin Biopsies[k]		X				X					
Contraception check	X	X	X	X	X	X	X	X	X	X	X
Laboratory Safety Assessments											
Safety Labs/Urine[l]	X	X		X	X	X	X	X	X	X	X
Urine β-hCG (conducted at site)[m]		X	X	X	X	X	X	X	X	X	X
Serum β-hCG[m]	X										
Follicle stimulating hormone FSH (WONCBP only)	X										
Viral surveillance (eg, CMV, VZV, EBV, HHV6, HSV-1/2)[n]	X	X		X	X					X	X
HIV, HBsAg, HBcAb, HCVAb[o]	X										
Quantiferon® TB Gold test[p]	X										
CCI [redacted]		[redacted]		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]		[redacted]	[redacted]
Pharmacokinetic (PK)/serum		X[s]	X	X[s]	X[s]	X	X	X	X	X	X
IVIG sample collection		X[x]		X[x]	X[x]						
Banked Biospecimens											
Prep B1.5 plasma		X		X	X					X	
Banked Prep B2 serum		X		X	X					X	
Banked Prep DI genomic sample[t]		X									
Banked Prep R1 whole blood		X		X	X					X	

Protocol Activity	Screening	Treatment				Follow-up					
Visit identifier (Study Visit)	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**Participant withdrawal or Early Termination[a]**
Study Day/Week	**Days -35 to -1**	**Baseline Day 1**	**Week 1 Day 8**	**Week 4 Day 29**	**Week 8 Day 57**	**Week 12 Day 85**	**Week 16 Day 113**	**Week 20 Day 141**	**Week 24 Day 169**	**Week 28 Day 197 EOS**	**N/A**
Visit Window	**None**	**None**	**±3 days**								
Biomarkers[u]											
Blood for Muscle and Bone Biomarkers		X		X	X		X			X	
CCI [redacted]		[redacted]			[redacted]		[redacted]			[redacted]	
IP-10		X	X	X	X	X	X	X	X	X	
MX-A		X	X	X	X	X	X	X	X	X	
CCI [redacted]		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
hsCRP		X	X	X	X	X	X	X	X	X	
Gene signature panel		X	X	X	X	X	X	X	X	X	
Investigational administration											
Investigational treatment administration		X[v,w]		X	X						
Infusion Site Reaction		X	X	X	X						
Medications and Adverse events											
DM concomitant medications		X	→	→	→	→	→	→	→	X	X
Concomitant Medications and Treatment(s)		X	→	→	→	→	→	→	→	X	X
Serious and non-serious adverse event monitoring	X	X	→	→	→	→	→	→	→	X	X

Abbreviations: →= ongoing/continuous event; CCI [redacted]; AE = adverse event; β-hCG = beta-human chorionic gonadotropin; BP = blood pressure; CDASI = Cutaneous Dermatomyositis Disease Area and Severity Index; CMV = cytomegalovirus; CRF = Case Report Form; CCI [redacted]; CT = computed tomography;DLQI=Dermatology and Life Quality Index; DM = Dermatomyositis; EBV = Epstein-Barr virus; ECG = electrocardiogram; EOS = end of study; EOT = end of treatment; EW = Early Withdrawal; FSH = follicle stimulating hormone; HEENT = head, eyes, ears, nose and throat; Hep B = Hepatitis B; HBcAb = hepatitis B core antibody; HBsAg = hepatitis B surface antigen; HCVAb = hepatitis C virus antibody; HHV6= human herpes Virus; HIV = human immunodeficiency virus; HR = heart rate; hsCRP = high-sensitivity C-reactive protein; HSV-1 = herpes simplex virus type 1; HSV-2 = herpes simplex virus type 2; CCI [redacted] beta; IP = investigational product;IP-10 = Interferon gamma-induced protein 10; IRT = interactive response technology; IVIG =intravenous immune globulin; MRI = magnetic resonance imaging; N/A=Not Applicable; CCI [redacted]; PD = Pharmacodynamic; PE=Physical Exam; PhGA = Physician Global Assessment; PHQ-8 = Patient Health Questionnaire 8-Item Depression Measure; PK = pharmacokinetic; SF-36 = The Short Form (36) Health Survey; TB = tuberculosis; VZV = varicella zoster virus; WOCBP = women of childbearing potential; WONCBP = women of non-childbearing potential.

a. Any participant who prematurely withdraws from the treatment period should undergo the procedures for an early termination visit and return for follow up visits. At the time of the early termination visit, blood samples will be collected for PK and PD analysis. As with all PK and PD assessments, the date and time of the last dose and time of the sample collection should be captured and reported.

b. Review and collect any changes from screening.

c. The PHQ-8 will be used at the screening visit only. If the PHQ-8 total score is ≥15 at screening the participant will be excluded from the study.

d. CCI [redacted] Section 7.4.

e. Physician's Global Assessment (PhGA); This assessment should be completed by the same physician completing the CDAI.

f. Patient reported outcomes (5D Pruritus Scale, SF-36 v2, DLQI) are to be completed at the clinic prior to other clinical assessments. These need to be completed in the following order, 5D Pruritus Scale; SF-36 v2; and last DLQI.

g. Vital Signs include blood pressure, heart rate (pulse), respirations and temperature measured after approximately 5 minutes of rest. Participants should be seated in a chair, back supported, and arms bared (free of restrictions such as rolled-up sleeves, etc) and supported at the level of the heart. Measurements should be taken on the same arm (preferably the non-dominant arm) at each visit throughout the study after 5 minutes of rest and recorded to the nearest mm Hg. Participants should refrain from smoking or ingesting caffeine during the 30 minutes prior to the measurements.

h. Weight and height will be measured without shoes.

i. Complete PE consists of general appearance, skin, HEENT, heart, lungs, breast (optional), abdomen, external genitalia optional, extremities, neurologic function, back, and lymph nodes. Targeted PE consists of skin, heart, lungs, abdomen, and examination of body systems where there are symptom complaints by the participant. Targeted physical exam should be completed prior to dosing.

j. Chest x-ray; or other appropriate diagnostic image already collected (ie, CT scan with or without contrast or MRI) may be accepted if completed within 12 weeks prior to Day 1). Official reading must be located in the source documentation.

k. Refer to lab manual for preparation of punch skin biopsies.

l. Laboratory tests may be repeated once during the 5-week screening period; the last value will be used to determine participant eligibility.

m. Serum/urine pregnancy tests for WOCBP; serum pregnancy test must be performed at screening for all WOCBP as defined in the eligibility criteria (if serum pregnancy test is borderline positive, the central laboratory will run a FSH test to confirm menopause if the participant has missed her periods <12 months); urine pregnancy test must be performed at baseline for all WOCBP prior to dosing with investigational product and at all subsequent visits.

n. In addition to time points specified, a blood sample for viral surveillance may also be taken at the time of an AE, as clinically appropriate.

o. Confirmation and documentation of negative HIV test result within 3 months prior to screening is acceptable.

p. Additional TB testing is allowed at any time if requested by the Investigator, the Sponsor and/or if there is a suspicion of TB reactivation or new TB infection. The following are acceptable IGRA assays: In-Tube test (QFT-GIT), and QuantiFERON®-TB Gold test, (QFT-G).

q. CCI [redacted]

r. Participants who experience AEs which are considered attributable to immunogenicity and have ADA will be requested to return for additional follow-up for up to 3 months after the follow-up/EOS visit and will have PK and ADA samples drawn for analysis. This will be recorded as an unscheduled visit.

s. At dosing visits, PK samples will be collected preferably after vital signs data and within approximately 30 minutes prior to dosing and post-dose (at the end of infusion in the opposite arm that the infusion was administered).

t. If not collected on the designated collection day, collect at the next available time point when biospecimens are being collected in conjunction with a participant visit (For PREP D-1).

u. On the days of investigational drug administration, (Day 1, Week 4 and Week 8) biomarkers will be collected prior to investigational drug administration.

v. All Day 1 procedures should be completed prior to investigational treatment administration, with the exception of the infusion site reaction.

w. Once the infusion has completed, all participants will be monitored for an additional 60 minutes post investigational treatment administration.

x. All participants who are on IVIG concomitantly will have a pre-dose blood sample collected. See Section 7.15.

SCHEDULE OF ACTIVITIES (AMENDED STAGE 2)

This SoA focuses on DM participants with skin disease. The difference from Stage 2 is that in the Amended Stage 2, all participants receive 12 weeks of active study drug, and provide 2 additional skin biopsies at Week 24. Study participation is approximately 45 weeks in duration, including the screening period.

The schedule of activities table provides an overview of the protocol visits and procedures. Refer to the STUDY PROCEDURES and ASSESSMENTS sections of the protocol for detailed information on each procedure and assessment required for compliance with the protocol. The investigator may schedule visits (unplanned visits) in addition to those listed on the schedule of activities table, in order to conduct evaluations or assessments required to protect the well-being of the participant.

Protocol Activity	**Screening**	**Treatment Period**								**Follow-up Period**				
Visit identifier (Study Visit)	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9[y]**	**10**	**11**	**12**	**13[r]**	**Participant withdrawal or Early Termination[a]**
Study Day/Week	**Days -35 to -1**	**Baseline Day 1**	**Week 1 Day 8**	**Week 4 Day 29**	**Week 8 Day 57**	**Week 12 Day 85**	**Week 16 Day 113**	**Week 20 Day 141**	**Week 24[y] Day 169**	**Week 28 Day 197**	**Week 32 Day 225**	**Week 36 Day 253**	**Week 40 Day 281 EOS**	**N/A**
Visit Window	**None**	**None**	**±3 days**											
Screening Assessments														
Informed consent	X													
Inclusion/exclusion criteria	X	X												
Demography	X													
Medical history	X	X[b]												
DM History	X													
Prior DM medication history	X	X[b]												
Prior Non DM medications	X	X[b]												
Clinical Reported Outcomes														
CDASI Score	X	X	X	X	X	X	X	X	X	X	X	X	X	X
PHQ-8 assessment[c]	X													
CCI [redacted]		[redacted]		[redacted]		[redacted]			[redacted]				[redacted]	[redacted]
Physician Global Assessment, (PhGA, VAS)[e]		X	X	X	X	X	X	X	X	X	X	X	X	X
Patient Reported Outcomes[f]														
PtGA		X	X	X	X	X	X	X	X	X	X		X	X

Protocol Activity	Screening	Treatment Period								Follow-up Period				
Visit identifier (Study Visit)	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9[y]**	**10**	**11**	**12**	**13[r]**	**Participant withdrawal or Early Termination[a]**
Study Day/Week	**Days -35 to -1**	**Baseline Day 1**	**Week 1 Day 8**	**Week 4 Day 29**	**Week 8 Day 57**	**Week 12 Day 85**	**Week 16 Day 113**	**Week 20 Day 141**	**Week 24[y] Day 169**	**Week 28 Day 197**	**Week 32 Day 225**	**Week 36 Day 253**	**Week 40 Day 281 EOS**	**N/A**
Visit Window	**None**	**None**	**±3 days**											
HAQ-DI		X	X	X	X	X	X	X	X	X	X		X	X
5-D Pruritus Scale		X	X	X	X	X	X	X	X	X	X		X	X
CCI		[redacted]												
SF-36 v2 Acute		X	X	X		X	X		X				X	X
DLQI		X	X	X		X	X		X	X			X	X
EQ-5D-5L & EQ-VAS		X	X	X			X			X			X	
Medical Assessments														
Vital Signs (BP, HR, Pulse, Respirations and temperature)[g]	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Weight[h]	X	X				X			X				X	X
Height[h]	X								X				X	
Complete physical examination[i]	X					X			X				X	X
Targeted physical examination[i]		X	X	X	X		X	X		X	X	X		
ECG	X	X		X	X	X	X	X	X				X	X
Chest X-Ray[j]	X													
Skin Punch Biopsies[k]		X				X			X					
Contraception check	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Laboratory Assessments														
Safety Labs/Urine[l]	X	X		X	X	X	X	X	X[z]	X	X	X	X	X
Urine β-hCG (conducted at site)[m]		X	X	X	X	X	X	X	X	X	X	X	X	X
Serum β-hCG[m]	X													
Follicle stimulating hormone FSH (WONCBP only)	X													
Viral surveillance (eg, CMV, VZV, EBV, -HHV6, HSV-1/2)[n]	X	X		X	X		X	X			X		X	X
HIV, HBsAg, HBcAb, HCVAb[o]	X													
Quantiferon® TB Gold test[p]	X													
CCI		[redacted]												

Protocol Activity	Screening	Treatment Period								Follow-up Period				
Visit identifier (Study Visit)	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9[y]**	**10**	**11**	**12**	**13[r]**	**Participant withdrawal or Early Termination[a]**
Study Day/Week	**Days -35 to -1**	**Baseline Day 1**	**Week 1 Day 8**	**Week 4 Day 29**	**Week 8 Day 57**	**Week 12 Day 85**	**Week 16 Day 113**	**Week 20 Day 141**	**Week 24[y] Day 169**	**Week 28 Day 197**	**Week 32 Day 225**	**Week 36 Day 253**	**Week 40 Day 281 EOS**	**N/A**
Visit Window	**None**	**None**	**±3 days**											
Pharmacokinetic (PK)/serum[s]		X	X	X	X	X	X	X	X[z]	X	X	X	X	X
IVIG sample collection[x]		X		X	X	X	X	X						
Banked Biospecimens														
Prep B1.5 plasma		X		X	X		X	X	X		X		X	
Banked Prep B2 serum		X		X	X		X	X	X		X		X	
Banked Prep D1 genomic sample[t]		X												
Banked Prep R1 whole blood		X		X	X		X	X	X		X		X	
Biomarkers[u]														
Blood for Muscle and Bone Biomarkers		X		X	X		X	X	X		X		X	
CCI		[redacted]		[redacted]	[redacted]		[redacted]		[redacted]		[redacted]		[redacted]	
IP-10		X	X	X	X	X	X	X	X	X	X	X	X	
MX-A		X	X	X	X	X	X	X	X	X	X	X	X	
CCI		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
hsCRP		X	X	X	X	X	X	X	X[z]	X	X	X	X	X
Gene signature panel		X	X	X	X	X	X	X	X	X	X	X	X	X
Investigational Treatment Administration														
Investigational treatment administration[w]		X[u,v]		X[u]	X[u]	X[u]	X[u]	X[u]						
Infusion Site Reaction		X		X	X	X	X	X						
Medications and Adverse Events														
DM concomitant medications		X	→	→	→	→	→	→	→	→		→	X	X
Concomitant Medications and Treatment(s)		X	→	→	→	→	→	→	→	→		→	X	X
Serious and non-serious adverse event monitoring	X	X	→	→	→	→	→	→	→	→	→	→	X	X

Abbreviations: →= See (Stage 2): Additional assessments added: 5-D Pruritus Scale = 5-Dimensions Pruritus Scale; EQ-5D-5L =European Quality of Life Five Dimension, Five Level Scale; EQ-VAS = EuroQol Visual Analogue Scale; FACIT-F = Functional Assessment of Chronic Illness Therapy – Fatigue; HAQ-DI = Health Assessment Questionnaire Disability Index; PtGA = Patient Global Assessment; CCI [redacted]

a. Any participant who prematurely withdraws from the treatment period should undergo the procedures for an early termination visit and return for follow up visits. At the time of the early termination visit, blood samples will be collected for PK and PD analysis. As with all PK and PD assessments, the date and time of the last dose and time of the sample collection should be captured and reported.

b. Review and collect any changes from screening.

c. The PHQ-8 will be used at the screening visit only. If the PHQ-8 total score is ≥15 at screening the participant will be excluded from the study.

d. CCI [redacted]

e. Physician's Global Assessment (PhGA, VAS); This assessment should be completed by the same physician completing the CDASI.

f. Patient reported outcomes (PtGA, HAQ-DI, 5-D Pruritus Scale, CCI [redacted], SF 36 v2 acute, DLQI, and EQ-5D-5L & EQ-VAS) are to be completed at the clinic prior to other clinical assessments. These need to be completed in the following order, PtGA, HAQ-DI, 5-D Pruritus Scale, CCI [redacted], SF 36 v2 acute, DLQI, EQ-5D-5L & EQ-VAS.

g. Vital Signs include blood pressure, heart rate (pulse), respirations and temperature measured after approximately 5 minutes of rest. Participants should be seated in a chair, back supported, and arms bared (free of restrictions such as rolled-up sleeves, etc.) and supported at the level of the heart. Measurements should be taken on the same arm (preferably the non-dominant arm) at each visit throughout the study after 5 minutes of rest and recorded to the nearest mm Hg. Participants should refrain from smoking or ingesting caffeine during the 30 minutes prior to the measurements.

h. Weight and height will be measured without shoes.

i. Complete PE consists of general appearance, skin, HEENT, heart, lungs, breast (optional), abdomen, external genitalia optional, extremities, neurologic function, back, and lymph nodes. Targeted PE consists of skin, heart, lungs, abdomen, and examination of body systems where there are symptom complaints by the participant. Targeted physical exam should be completed prior to dosing.

j. Chest x-ray; or other appropriate diagnostic image already collected (ie, CT scan with or without contrast or MRI) may be accepted if completed within 12 weeks prior to Day 1). Official reading must be located in the source documentation.

k. Refer to lab manual for preparation of punch skin biopsies. There is a -6 day screening window at Day 1 for punch biopsies. At Week 12 and Week 24, a -/+ 6 day window is permitted to obtain skin punch biopsies.

l. Laboratory tests may be repeated once during the 5-week screening period; the last value will be used to determine participant eligibility.

m. Serum/urine pregnancy tests for WOCBP; serum pregnancy test must be performed at screening for all WOCBP as defined in the eligibility criteria (if serum pregnancy test is borderline positive, the central laboratory will run a FSH test to confirm menopause if the participant has missed her periods <12 months); urine pregnancy test must be performed at baseline for all WOCBP prior to dosing with investigational product and at all subsequent visits.

n. In addition to time points specified, a blood sample for viral surveillance may also be taken at the time of an AE, as clinically appropriate.

o. Confirmation and documentation of negative HIV test result within 3 months prior to screening is acceptable.

p. Additional TB testing is allowed at any time if requested by the Investigator, the Sponsor and/or if there is a suspicion of TB reactivation or new TB infection. The following are acceptable IGRA assays: In-Tube test (QFT-GIT), and QuantiFERON®-TB Gold test, (QFT-G).

q. On the days of investigational drug administration, ADA and Nab will be collected prior to investigational drug administration.

r. Participants who experience AEs which are considered attributable to immunogenicity and have ADA will be requested to return for additional follow-up for up to 3 months after the follow-up/EOS visit and will have PK and ADA samples drawn for analysis. This will be recorded as an unscheduled visit.

s. At dosing visits, PK samples will be collected preferably after vital signs data and within approximately 30 minutes prior to dosing and post-dose (at the end of infusion in the opposite arm that the infusion was administered).

t. If not collected on the designated collection day, collect at the next available time point when biospecimens are being collected in conjunction with a participant visit (For PREP D-1).

u. On the days of investigational drug administration, biomarkers will be collected prior to investigational drug administration.

v. All Day 1 procedures should be completed prior to investigational treatment administration, with the exception of the infusion site reaction.

w. Once the infusion has completed, all participants will be monitored for an additional 60 minutes post investigational treatment administration.

x. All participants who are on IVIG concomitantly will have a pre-dose blood sample collected. See Section 7.15.

y. All participants who complete the treatment period in this study up through and including (Visit 9, Week 24), will have the opportunity to continue treatment in the open label extension C0251008 protocol. Participants whom have completed the treatment period and have not had any significant protocol deviations, or safety events will be eligible. Participants will also have the opportunity to continue into the follow up period and complete the C0251002 study instead of enrolling into open label extension C0251008.

z. All participants continuing to the open label extension C0251008 study should use the DAY 1 C0251008 Lab kit. Please see lab manual for specific instructions.

SCHEDULE OF ACTIVITIES (STAGE 3)

This SoA focuses on DM participants with moderate muscle disease. The approximate study duration is 45 weeks including the screening period. Participants enrolling in Stage 3 will not provide any skin or muscle biopsies.

The schedule of activities table provides an overview of the protocol visits and procedures. Refer to the STUDY PROCEDURES and ASSESSMENTS sections of the protocol for detailed information on each procedure and assessment required for compliance with the protocol. The investigator may schedule visits (unplanned visits) in addition to those listed on the schedule of activities table, in order to conduct evaluations or assessments required to protect the well-being of the participant.

Protocol Activity	**Screening**	**Treatment Period**								**Follow-up Period**				
Visit identifier (Study Visit)	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9[y]**	**10**	**11**	**12**	**13**	**Participant withdrawal or Early Termination[a]**
Study Day/Week	**Days -35 to -1**	**Baseline Day 1**	**Week 1 Day 8**	**Week 4 Day 29**	**Week 8 Day 57**	**Week 12 Day 85**	**Week 16 Day 113**	**Week 20 Day 141**	**Week 24[y] Day 169**	**Week 28 Day 197**	**Week 32 Day 225**	**Week 36 Day 253**	**Week 40 Day 281 EOS[r]**	**N/A**
Visit Window	**None**	**None**	**±3 days**											
Screening Assessments														
Informed consent	X													
Inclusion/exclusion criteria	X	X												
Demography	X													
Medical history	X	X[b]												
DM History	X													
Prior DM medication history	X	X[b]												
Prior Non DM medications	X	X[b]												X
Clinical Reported Outcomes														
CDASI Score	X	X	X	X	X	X	X	X	X	X	X	X	X	X
PHQ-8 assessment[c]	X													

Protocol Activity	Screening	Treatment Period								Follow-up Period				
Visit identifier (Study Visit)	1	2	3	4	5	6	7	8	9[y]	10	11	12	13	Participant withdrawal or Early Termination[a]
Study Day/Week	Days -35 to -1	Baseline Day 1	Week 1 Day 8	Week 4 Day 29	Week 8 Day 57	Week 12 Day 85	Week 16 Day 113	Week 20 Day 141	Week 24[y] Day 169	Week 28 Day 197	Week 32 Day 225	Week 36 Day 253	Week 40 Day 281 EOS[r]	N/A
Visit Window	None	None	±3 days											
CCI [redacted]		[redacted]		[redacted]		[redacted]			[redacted]				[redacted]	[redacted]
Physician Global Assessment, (PhGA, VAS, VAS)[e]	X	X	X	X	X	X	X	X	X	X	X	X	X	X
MMT-8 Score	X	X		X	X	X	X	X	X	X	X	X	X	X
MDI	X													
Myositis Disease Activity Assessment Tool (MDAAT)	X	X		X	X	X	X	X	X	X	X	X	X	X
Patient Reported Outcomes[f]														
PtGA	X	X	X	X	X	X	X	X	X	X	X		X	X
HAQ-DI		X	X	X	X	X	X	X	X	X	X		X	X
5-D Pruritus Scale		X	X	X	X	X	X	X	X	X	X		X	X
CCI [redacted]		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]		[redacted]	[redacted]
FACIT-F		X	X	X		X	X			X	X		X	X
SF-36 v2 Acute		X	X	X		X	X		X				X	X
EQ-5D-5L & EQ-VAS		X	X	X			X			X			X	

Protocol Activity	Screening	Treatment Period								Follow-up Period				
Visit identifier (Study Visit)	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9[y]**	**10**	**11**	**12**	**13**	**Participant withdrawal or Early Termination[a]**
Study Day/Week	**Days -35 to -1**	**Baseline Day 1**	**Week 1 Day 8**	**Week 4 Day 29**	**Week 8 Day 57**	**Week 12 Day 85**	**Week 16 Day 113**	**Week 20 Day 141**	**Week 24[y] Day 169**	**Week 28 Day 197**	**Week 32 Day 225**	**Week 36 Day 253**	**Week 40 Day 281 EOS[r]**	**N/A**
Visit Window	**None**	**None**	**±3 days**											
Medical Assessments														
Vital Signs (BP, HR, Pulse, Respirations and temperature)[g]	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Weight[h]	X	X				X			X				X	X
Height[h]	X								X				X	
Complete physical examination[i]	X					X			X				X	X
Targeted physical examination[i]		X	X	X	X		X	X		X	X	X		X
ECG	X	X		X	X	X	X	X	X				X	X
Chest X-Ray[j]	X													
Contraception check[k]	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Laboratory Safety Assessments														
Safety Labs/Urine[l]	X	X		X	X	X	X	X	X[z]	X	X	X	X	X
Urine β-hCG (conducted at site)[m]		X	X	X	X	X	X	X	X	X	X	X	X	X
Serum β-hCG[m]	X													

Protocol Activity	Screening	Treatment Period								Follow-up Period				
Visit identifier (Study Visit)	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9[y]**	**10**	**11**	**12**	**13**	**Participant withdrawal or Early Termination[a]**
Study Day/Week	**Days -35 to -1**	**Baseline Day 1**	**Week 1 Day 8**	**Week 4 Day 29**	**Week 8 Day 57**	**Week 12 Day 85**	**Week 16 Day 113**	**Week 20 Day 141**	**Week 24[y] Day 169**	**Week 28 Day 197**	**Week 32 Day 225**	**Week 36 Day 253**	**Week 40 Day 281 EOS[r]**	**N/A**
Visit Window	**None**	**None**	**±3 days**											
Follicle stimulating hormone FSH[m] (WONCBP only)	X													
Viral surveillance (eg, CMV, VZV, EBV, HHV6, HSV-1/2)[n]	X	X		X	X		X	X			X		X	X
HIV, HBsAg, HBcAb, HCVAb[o]	X													
Quantiferon® TB Gold test[p]	X													
CCI [redacted]		[redacted]		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Pharmacokinetic (PK)/serum[s]		X	X	X	X	X	X	X	X[z]	X	X	X	X	X
IVIG sample collection[x]		X		X	X	X	X	X						
Banked Biospecimens														
Prep B1.5 plasma		X		X	X		X	X	X		X		X	
Banked Prep B2 serum		X		X	X		X	X	X		X		X	

Protocol Activity	Screening	Treatment Period								Follow-up Period				
Visit identifier (Study Visit)	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9[y]**	**10**	**11**	**12**	**13**	**Participant withdrawal or Early Termination[a]**
Study Day/Week	**Days -35 to -1**	**Baseline Day 1**	**Week 1 Day 8**	**Week 4 Day 29**	**Week 8 Day 57**	**Week 12 Day 85**	**Week 16 Day 113**	**Week 20 Day 141**	**Week 24[y] Day 169**	**Week 28 Day 197**	**Week 32 Day 225**	**Week 36 Day 253**	**Week 40 Day 281 EOS[r]**	**N/A**
Visit Window	**None**	**None**	**±3 days**											
Banked Prep D1 genomic sample[t]		X												
Banked Prep R1 whole blood		X		X	X		X	X	X		X		X	
Biomarkers[u]														
Blood for Muscle and Bone Biomarkers		X		X	X		X	X	X		X		X	
CCI [redacted]		[redacted]		[redacted]	[redacted]		[redacted]		[redacted]		[redacted]		[redacted]	
IP-10		X	X	X	X	X	X	X	X	X	X	X	X	
MX-A		X	X	X	X	X	X	X	X	X	X	X	X	
CCI [redacted]		[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]	
hsCRP		X	X	X	X	X	X	X	X[z]	X	X	X	X	X
Gene signature panel		X	X	X	X	X	X	X	X	X	X	X	X	X
Investigational administration														
Investigational treatment administration[w]		X[u,v]		X[u]	X[u]	X[u]	X[u]	X[u]						
Infusion Site Reaction		X		X	X	X	X	X						

Protocol Activity	Screening	Treatment Period								Follow-up Period				
Visit identifier (Study Visit)	1	2	3	4	5	6	7	8	9[y]	10	11	12	13	Participant withdrawal or Early Termination[a]
Study Day/Week	Days -35 to -1	Baseline Day 1	Week 1 Day 8	Week 4 Day 29	Week 8 Day 57	Week 12 Day 85	Week 16 Day 113	Week 20 Day 141	Week 24[y] Day 169	Week 28 Day 197	Week 32 Day 225	Week 36 Day 253	Week 40 Day 281 EOS[r]	N/A
Visit Window	None	None	±3 days											
Medications and Adverse events														
DM concomitant medications		X	→	→	→	→	→	→	→	→	→	→	X	X
Concomitant Medications and Treatment(s)		X	→	→	→	→	→	→	→	→	→	→	X	X
Serious and non-serious adverse event monitoring	X	X	→	→	→	→	→	→	→	→	→	→	X	X

Abbreviations: See Stage 1 and Stage 2 and Amended Stage 2 SoA; HAQ-D1-Health Assessment Questionnaire and Disease Index, MDAAT- Myositis Disease Activity Assessment Tool, MMT-8- Manual Muscle Testing-8 designated muscles, PtGA-Patient Global Assessment.

a. Any participant who prematurely withdraws from the treatment period should undergo the procedures for an early termination visit and return for follow up visits. At the time of the early termination visit, blood samples will be collected for PK and PD analysis. As with all PK and PD assessments, the date and time of the last dose and time of the sample collection should be captured and reported.

b. Review and collect any changes from screening.

c. The PHQ-8 will be used at the screening visit only. If the PHQ-8 total score is ≥15 at screening the participant will be excluded from the study.

d. The CSSRS will be used to assess suicidal ideation and behavior during the conduct of the study. The first assessment will be completed on Day 1 of the study prior to dosing to obtain a baseline assessment. At any postday 1 visits, if there are "yes" answers on items 4, 5 or on any suicidal behavior question of the CSSRS, the participant will be discontinued from treatment and referred to a mental health professional for appropriate evaluation and treatment. Please see Section 7.4.

e. Physician's Global Assessment (PhGA, VAS); This assessment should be completed by the same physician completing the CDASI, MMT-8, and the MDAAT.

f. Patient reported outcomes (PtGA, HAQ-DI, 5-D Pruritus Scale, CCI [redacted] FACIT-F, SF-36 v2 acute, and EQ-5D-5L & EQ-VAS) are to be completed at the clinic prior to other clinical assessments. These need to be completed in the following order, PtGA, HAQ-DI, 5-D Pruritus Scale, CCI [redacted] FACIT-F, SF-36 v2 acute, EQ-5D-5L & EQ-VAS.

g. Vital Signs include blood pressure, heart rate (pulse), respirations and temperature measured after approximately 5 minutes of rest. Participants should be seated in a chair, back supported, and arms bared (free of restrictions such as rolled-up sleeves, etc) and supported at the level of the heart. Measurements should be taken on the same arm (preferably the non-dominant arm) at each visit throughout the study after 5 minutes of rest and recorded to the nearest mm Hg. Participants should refrain from smoking or ingesting caffeine during the 30 minutes prior to the measurements.

h. Weight and height will be measured without shoes.

i. Complete PE consists of general appearance, skin, HEENT, heart, lungs, breast (optional), abdomen, external genitalia (optional), extremities, neurologic function, back, and lymph nodes. Targeted PE consists of skin, heart, lungs, abdomen, and examination of body systems where there are symptom complaints by the participant. Targeted physical exam should be completed prior to dosing.

j. Chest x-ray; or other appropriate diagnostic image already collected (ie, CT scan with or without contrast or MRI) may be accepted if completed within 12 weeks prior to Day 1). Official reading must be located in the source documentation.

k. Contraception check should be completed and documented in source.

l. Laboratory tests may be repeated once during the 5-week screening period; the last value will be used to determine participant eligibility.

m. Serum/urine pregnancy tests for WOCBP; serum pregnancy test must be performed at screening for all WOCBP as defined in the eligibility criteria (if serum pregnancy test is borderline positive, the central laboratory will run a FSH test to confirm menopause if the participant has missed her periods <12 months); urine pregnancy test must be performed at baseline for all WOCBP prior to dosing with investigational product and at all subsequent visits.

n. In addition to time points specified, a blood sample for viral surveillance may also be taken at the time of an AE, as clinically appropriate.

o. Confirmation and documentation of negative HIV test result within 3 months prior to screening is acceptable.

p. Additional TB testing is allowed at any time if requested by the Investigator, the Sponsor and/or if there is a suspicion of TB reactivation or new TB infection. The following are acceptable IGRA assays: In-Tube test (QFT-GIT), and QuantiFERON®-TB Gold test, (QFT-G).

q. On the days of investigational drug administration, (Day 1, Week 4, Week 8, Week 12, and Week 20) ADA and Nab will be collected prior to investigational drug administration.

r. Participants who experience AEs which are considered attributable to immunogenicity and have ADA will be requested to return for additional follow-up for up to 3 months after the follow-up/EOS visit and will have PK and ADA samples drawn for analysis. This will be recorded as an unscheduled visit.

s. At dosing visits, PK samples will be collected preferably after vital signs data and within approximately 30 minutes prior to dosing and post-dose (at the end of infusion in the opposite arm that the infusion was administered).

t. If not collected on the designated collection day, collect at the next available time point when biospecimens are being collected in conjunction with a participant visit (For PREP D-1).

u. On the days of investigational drug administration, (Day 1, Week 4, Week 8, Week 12, Week 16 and Week 20) biomarkers will be collected prior to investigational drug administration.

v. All Day 1 procedures should be completed prior to investigational treatment administration, with the exception of the infusion site reaction.

w. Once the infusion has completed, all participants will be monitored for an additional 60 minutes post investigational treatment administration.

x. All participants who are on IVIG concomitantly will have a pre-dose blood sample collected. See Section 7.15.

y. All participants who complete the treatment period in this study up through and including (Visit 9, Week 24), will have the opportunity to continue treatment in the open label extension C0251008 protocol. Participants whom have completed the treatment period and have not had any significant protocol deviations, or safety events will be eligible. Participants will also have the opportunity to continue into the follow up period and complete the C0251002 study instead of enrolling into open label extension C0251008.

z. All participants continuing to the open label extension C0251008 study should use the DAY 1 C0251008 Lab kit. Please see lab manual for specific instructions.

1. INTRODUCTION

Dermatomyositis, (DM) is an acquired rare inflammatory disease classified as both a neuromuscular disease and an autoimmune disease. DM is characterized by a distinctive skin rash and muscle weakness or inflamed muscles. Symptoms can come on suddenly or gradually over time. It is thought that the inflammation resulting in cell damage is created when the immune system attacks healthy muscle tissue and blood vessels under the skin. DM is idiopathic, however some individuals may have a genetic predisposition that is triggered by medications, viruses, bacteria, trauma, toxins, cancer or other illness. DM symptoms often wax and wane for no apparent reason and females are affected twice as often as males.[1,2]

DM has no known cure and there are no widely approved treatments. Patients typically use a combination of drugs to seek relief for their inflammatory symptoms. Typically the first line of treatment for the muscle disease is corticosteroids to address the inflammation as well as suppress the immune system. Other immunosuppressive drugs, notably azathioprine, methotrexate, mycophenolate mofetil, (MMF), and cyclophosphamide are used as subsequent lines of therapies in refractory cases or as steroid-sparing agents. However, complications of long-term steroid and immunosuppressive therapies are well documented. Other novel approaches have emerged as potential treatment, including tacrolimus (broadly immunosuppressive drug developed for transplant use), intravenous immunoglobulin, and rituximab, following positive outcomes in some case studies. However, additional randomized controlled trials with these treatments are needed to guide clinical practice.[3] Consequently, DM remains a disease with very high unmet medical need, and development of safe and effective therapies is warranted.

1.1. Mechanism of Action/Indication

PF-06823859 is a potent, selective, humanized immunoglobulin G1(IgG1) neutralizing antibody directed against the human soluble cytokine interferon-beta (IFNβ), a member of the type I interferon (IFN) family of cytokines. PF-06823859 is in development for the treatment systemic lupus erythematous (SLE) with added potential for therapeutic benefit in DM.

1.2. Background and Rationale

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1.3. Nonclinical Pharmacokinetics

After single intravenous (IV) doses of PF-06823859 at 10 and 200 mg/kg administered to cynomolgus monkeys, serum exposures were typical for an IgG1 monoclonal antibodies, (mAb) dosed to monkeys. The mean plasma clearance (CL) ranged from 0.00439 to 0.00502 L/day/kg, the mean volume at steady state (V_{ss}) ranged from 0.0747 to 0.0823 L/kg, and the mean apparent half-life ranged from 11.4 to 14.0 days. Subcutaneous (SC) bioavailability was approximately 87% following a single 10 mg/kg dose of PF-06823859. The pharmacokinetic (PK) profiles of PF-06823859 in the cynomolgus monkey were typical for a human IgG mAb in monkeys. In the pivotal repeat dose monkey toxicity study with 20 mg/kg SC, 100 mg/kg SC or 500 mg/kg IV doses of PF-06823859, there were no apparent sex-related- differences observed in systemic exposure. Systemic exposures were higher on Day 85 compared to Day 1 for all dose groups, and exposures increased with increasing dose in the SC dose groups. The incidence of Anti-Drug Antibody (ADA) induction across all dose groups administered PF-06823859 via either repeat IV or SC dosing in cynomolgus monkeys was 36%.

Additional information for this compound may be found in the single reference safety document (SRSD), which for this study is the Investigator's Brochure (IB).

1.4. Nonclinical Safety Data

In the in vitro Fc receptor (FcR) and complement protein C1q binding assays, PF-06832859 did not bind to C1q, suggesting an inability to activate the classical complement pathway and induce complement dependent cytotoxicity (CDC), and the FcR binding data demonstrated that PF-06823859 had low potential to elicit antibody-dependent cell-mediated cytotoxicity (ADCC) activity. PF-06823859 did not elicit test article-related release of 3 human pro inflammatory cytokines tumor necrosis factor alpha, (TNFα), Interleukin 6, (IL6), and Interferon gamma, (IFNγ) in the in vitro soluble phase cytokine release assay. PF-06823859 did not cause suppression of the influenza antigen-specific proliferative response in the human lymphocyte activation (HuLA) assay. In the herpes simplex virus-1 (HSV-1) assay, incubation of human dermal fibroblasts with PF-06823859 resulted in a dose dependent inhibition of IFNβ-mediated suppression of HSV-1 replication. In the good laboratory practice (GLP) compliant tissue cross-reactivity study, staining patterns with PF-06823859 overlapped between cynomolgus and human tissues, with some exceptions primarily in epithelial subtypes. The majority of staining observed was cytoplasmic, which is not expected to be accessible to the test article in vivo.

Based on binding and functional assessments across species (ie, mice, rats, rabbits, & cynomolgus monkeys), the only pharmacologically relevant species for toxicity testing is the cynomolgus monkey. In a GLP-compliant toxicity study, PF-06823859 was not associated with any adverse test article-related findings when administered to sexually-mature male and female cynomolgus monkeys once weekly via IV or SC routes up to 500 mg/kg/dose for up to 14 weeks. There were no test article-related effects on the cardiovascular system based on electrocardiography and heart rate evaluations, nor were there any test-article related effects in male or female reproductive tissues evaluated in the repeat-dose toxicity study in sexually-mature cynomolgus monkeys.

Compared with baseline, test article-related, nonadverse increases in serum globulin and subsequent nonadverse decreases in albumin:globulin ratio were noted on Days 29 and 92 in animals administered 500 mg/kg/dose (IV). This increase in serum globulin was attributed to the presence of high concentrations of PF-06823859 (an immunoglobulin) and was no longer present at the end of the 8-week recovery phase, consistent with the low concentrations of PF-06823859 in the serum at this time. The no observed adverse effect level (NOAEL) in this 14 week GLP-compliant repeat-dose toxicity study was 500 mg/kg/dose (IV). In the 500 mg/kg/dose group (IV), the mean serum concentration maximum, (C_{max}) (males and females combined) was 25,600 µg/mL and the mean area under the curve, $(AUC)_{168}$ (males and females combined) was 2,430,000 µg•h/mL on Day 85 (Week 13). The mean average concentration (C_{av}) was 14,500 µg/mL. There were no sex-related differences in systemic exposure. In conclusion, the nonclinical safety profile of PF-06823859 has been adequately characterized in vitro and in vivo in cynomolgus monkey to support progression into clinical trials up to 3 months in duration.

Additional information for this compound may be found in the single reference safety document (SRSD), which for this study is the Investigator's Brochure (IB).

1.5. Clinical Safety Profile

1.5.1. Safety (FIH C0251001)

A first in human (FIH) study, C0251001, (Phase 1, Randomized, Double-Blind, Third-Party Open Placebo-Controlled, Dose Escalating Study to Evaluate the Safety, Tolerability, Pharmacokinetics and Pharmacodynamics of Single and Multiple Intravenous and Subcutaneous Doses of PF-06823859 in Healthy Participants) has currently completed all dosing with all participants in the follow-up period of the study and expected to complete in August 2017. This study consisted of a total of 8 dosing cohorts. There were 5 cohorts of single 30 mg IV, 100 mg IV, 300 mg IV, 900 mg IV and 2000 mg IV doses. The last 3 cohorts were multiple dose cohorts consisting of 100 mg x 3 subcutaneous (SC) doses (one dose every 2 weeks), 300 mg x 3 SC doses, (one dose every 2 weeks). The last cohort evaluated 2 dosing regimens due to a longer than expected half-life based on emerging data from the preceding cohorts. This last cohort consisted of 600 mg IV x 3 doses (one dose every 2 weeks) and 600 mg IV x 2 doses (one dose every 4 weeks).

As of 07 April 2017, a total of 48 participants have received at least one dose of PF-06823859. Preliminary data from this study suggest that PF-06823859 is generally well tolerated and safe CCI [redacted] The most common adverse events were upper respiratory tract infection and headache. These adverse events were generally mild and resolved without further intervention. No serious adverse event, (AE) or death occurred during the study.

One participant experienced an injection site reaction (ISR) after each of the 100 mg SC dosing with PF-06823859 (3 doses) administered every 2 weeks. These were characterized by mild localized erythema with induration and tenderness, but no signs or symptoms of a systemic reaction. These local reactions resolved without further intervention within a few days. This participant also had treatment-induced ADA, which had returned to baseline at the time of discharge (Section 1.5.3).

Overall, there was no apparent difference in the total rate of adverse events between the participants treated with the active investigational product (IP) compared to placebo and no apparent dose relationship with the doses of the IP. However, the rate of mild upper respiratory tract infection appears to be higher in participants treated with PF-06823859.

There were no clinically significant changes in electrocardiogram (ECG), vital signs or laboratory abnormalities.

In conclusion, PF-06823859 was generally well tolerated and safe in healthy participants and the preliminary data from this FIH study supports continued clinical development of PF-06823859. Further details are provided in the current PF-06823859 Investigator's Brochure.

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1.5.3. Immunogenicity Results for C0251001

Note the data analysis provided in this section is based on preliminary immunogenicity data. A tiered approach for screening, characterization and Anti-Drug Antibody (ADA) titer assessment of serum samples was adopted to characterize immunogenicity. As of 07 April 2017, the treatment related overall ADA incidence rate was 12% (5 of 43 participants). Following PF-06823859 administration, 3 adult healthy participants in the single dose groups (2 in 30 mg IV group and 1 in 900 mg IV group) and 2 participants in repeat dose groups (1 in 100 mg SC and 1 in 300 mg SC) were found to have treatment-related ADA responses. The ADA positive participant in 100 mg SC repeat dose group had injection site reaction after each of the 3 doses. None of the other participants experienced clinical signs or symptoms consistent with an immune response. The ADA titer in all 5 participants had returned to baseline at the time of discharge and did not result in a discernible impact on PK. Currently, neutralizing antibody (NAb) assay is under development.

1.5.4. Summary of Benefits and Risks

Based on the clinical data from the FIH study (C0251001) and the available non-clinical data, the risks and potential benefits for PF-06823859 are considered to be favorable and support continued clinical development in particpants with DM.

As previously noted, DM is a rare disease with higher prevalence in females than males. Therefore, the trial objectives cannot be met without inclusion of women of childbearing potential (WoCBP). Nonclinical data to date (Section 1.4) has not identified any risk to reproductive organs in sexually mature cynomolgus monkeys, the pharmacologically relevant species. Given that an enhanced pre- and postnatal development study (ePPND) will be conducted later in development, this protocol that allows enrollment of Women of child bearing potential, (WoCBP) has stringent requirements to mitigate unintended exposures (pregnancy testing and use of contraceptives).

There is a theoretical risk that alterations in bone may occur based on published observations of osteopenia in mice genetically deficient in IFNb.[10] The potential for bone effects was assessed in the 3-month good laboratory practice (GLP) toxicity study in sexually mature cynomolgus monkeys, and there were no microscopic findings in bone, nor alterations in circulating bone-related biomarkers. However, the potential for bone effects in developing/growing bones has not been specifically assessed in growing animals. This risk is considered to be low given the lack of observed effects in the (GLP) toxicity study as well as the limited duration of total exposure to PF-06823859 in this planned DM study. While

appropriate risk mitigation has been employed, possible risks will be communicated to study participants in the ICD.

1.6. Dose Selection Rationale

CCI [redacted]

A formal interim analysis occurred in April 2020 by an unblinded internal review committee independent from the blinded study team. An internal decision was made to add an additional dose, CCI [redacted] None of the blinded study team members were involved with the data or the decision made at the time of the interim analysis. In stage 2, following the interim analysis, participants will be randomly assigned to receive CCI [redacted] that will be administered intravenously CCI [redacted] 4 weeks, for a total of 3 doses.

All participants enrolled in the Amended Stage 2 of the study will receive active study drug with the fixed sequence design. Participants will be randomly assigned to receive CCI [redacted] every 4 weeks. Participants who start the study on CCI [redacted] will have a prespecified dose change to placebo at Week 12, and participants who are on placebo will have a prespecified dose change to active study drug at Week 12. Participants will thus CCI [redacted] during the treatment period.

Stage 3 participants will be randomly assigned to receive CCI [redacted] with the fixed sequence design. Participants who start the study on active study drug will have a prespecified dose change to placebo at Week 12, and participants who are on placebo will have a prespecified dose change to active study drug at Week 12. Participants will thus receive 3 consecutive doses of CCI [redacted] and 3 consecutive doses of placebo for a total of 6 doses during the treatment period. Doses will be administered intravenously over one hour every 4 weeks.

PK and PK/PD approaches were considered using the data available to date to guide selection of the proposed dose and dose regimen. CCI [redacted]

CCI [redacted]

A CCI [redacted] for a total of 2 doses was previously tested in healthy participants and was considered safe based on data from Study C0251001. CCI [redacted]

Additional information for this compound may be found in the single reference safety document (SRSD), which for this study is the investigator brochure (IB).

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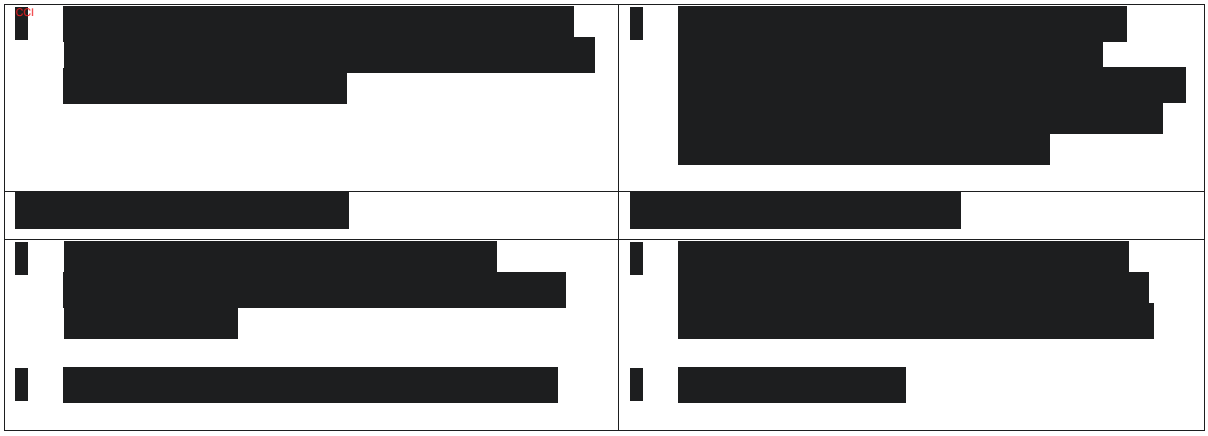
2. STUDY OBJECTIVES AND ENDPOINTS

2.1. Stage 1, Objectives and Endpoints

Primary Objective(s):	Primary Endpoint(s):
• To evaluate the efficacy of PF-06823859 in adult participants with moderate to severe DM.	• Change from baseline in CDASI activity score at Week 12.
Secondary Objective(s):	**Secondary Endpoint(s):**
• To evaluate the efficacy of PF-06823859 over time.	• Absolute values and change from baseline of CDASI activity and CDASI damage scores at all scheduled time points. (Exception: The change from baseline in CDASI activity score at Week 12 is a primary endpoint).
• To determine the safety, and tolerability, of PF-06823859.	• Incidence of adverse events (AEs) laboratory abnormalities, changes in vital signs, and electrocardiogram (ECG) findings.
Exploratory Objectives (s)	**Exploratory Endpoints(s)**
• To characterize pharmacokinetics (PK) of PF-06823859.	• Plasma concentration of PF-06823859.
• To characterize pharmacodynamics (PD) effects of PF-06823859.	• Absolute values and change from baseline in the values of selected biomarkers (Gene signature panel in blood and tissue; Human Myxovirus A (MXA), interferon gamma-induced protein 10 (IP-10), CCI highly sensitive C-reactive protein, (hsCRP), muscle and bone blood biomarkers, autoantibody concentrations in serum/plasma) at all scheduled time points.
• To evaluate the effects of PF-06823859 on patient-reported outcomes (PROs) and physician global assessment (PhGA, VAS) over time.	• Absolute values and change from baseline in the values of the PhGA, VAS, PROs (the short form (SF36) Health Survey, Dermatology and Life Quality Index (DLQI), 5D Pruritus Scale, at all scheduled time points.
• To evaluate the effects of PF-06823859 on CDASI sub-scores.	• Absolute values and change from baseline values of the sub-scores of CDASI activity and CDASI damage scores at all scheduled time points.



2.2. Stage 2, Objectives and Endpoints

Primary Objective(s):	Primary Endpoint(s):
• To estimate the efficacy of PF-06823859 in adult participants with moderate to severe DM across two stages.	• Change from baseline in CDASI activity score at Week 12.
Secondary Objective(s):	**Secondary Endpoint(s):**
• To estimate the efficacy of PF-06823859 over time across two Stages. • To determine the safety, and tolerability, of PF-06823859 across two Stages.	• Absolute values and change from baseline of CDASI activity and CDASI damage scores at all scheduled time points. (Exception: The change from baseline in CDASI activity score at Week 12 is a primary endpoint). • Incidence of adverse events (AEs) laboratory abnormalities, changes in vital signs, and electrocardiogram (ECG) findings.
Exploratory Objectives (s)	**Exploratory Endpoints(s)**
• To characterize pharmacokinetics (PK) of PF-06823859 across the two stages. • To characterize pharmacodynamics (PD) effects of PF-06823859 across the two stages. • To estimate the effects of PF-06823859 on patient-reported outcomes (PROs) and physician global assessment (PhGA, VAS) over time across the two stages. • To estimate the effects of PF-06823859 on CDASI sub-scores across the two stages.	• Plasma concentration of PF-06823859. • Absolute values and change from baseline in the values of selected biomarkers (Gene signature panel in blood and tissue; Human Myxovirus A (MXA), interferon gamma-induced protein 10 (IP-10), CCI, highly sensitive C-reactive protein, (hsCRP), muscle and bone blood biomarkers, autoantibody concentrations in serum/plasma) at all scheduled time points. • Absolute values and change from baseline in the values of the PhGA, VAS, PROs (the short form (SF36) Health Survey, Dermatology and Life Quality Index (DLQI), 5D Pruritus Scale, at all scheduled time points. • Absolute values and change from baseline values of the sub-scores of CDASI activity and

	CDASI damage scores at all scheduled time points.
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

2.3. Amended Stage 2, Objectives and Endpoints

Primary Objective(s):	**Primary Endpoint(s):**
To estimate the efficacy of PF-06823859 in adult participants with moderate to severe DM across Stage 1 and Stage 2.	• Change from baseline in CDASI activity score at Week 12.
Secondary Objective(s):	**Secondary Endpoint(s):**
• To estimate the efficacy of PF-06823859 over time across Stage 1 and Stage 2. • To determine the safety, and tolerability, of PF-06823859 across Stage 1 and Stage 2.	• Absolute values and change from baseline of CDASI activity and CDASI damage scores at all scheduled time points. (Exception: The change from baseline in CDASI activity score at Week 12 is a primary endpoint). • Incidence of adverse events (AEs) laboratory abnormalities, changes in vital signs, and electrocardiogram (ECG) findings.
Exploratory Objectives (s)	**Exploratory Endpoints(s)**
• To characterize pharmacokinetics (PK) of PF-06823859 across Stage 1 and Stage 2. • To characterize pharmacodynamics (PD) effects of PF-06823859 across Stage 1 and Stage 2. • To estimate the effects of PF-06823859 on the Physician Global Assessment (PhGA, VAS) across Stage 1 and Stage 2.	• Plasma concentration of PF-06823859. • Absolute values and change from baseline in the values of selected biomarkers (Gene signature panel in blood and tissue; Human Myxovirus A (MXA), interferon gamma-induced protein 10 (IP-10), CCI highly sensitive C-reactive protein, (hsCRP), muscle and bone blood biomarkers, autoantibody concentrations in serum/plasma) at all scheduled time points. • Absolute values and change from baseline in the values of the PhGA, VAS at all scheduled time points. • Absolute values and change from baseline in the values of PROs including the Patient

• To estimate the effects of PF-06823859 on patient-reported outcomes (PROs) over time across Stage 1 and Stage 2.	Global Assessment (PtGA), the Health Assessment Questionnaire – Disability Index (HAQ-DI), the 5-D Pruritus Scale, CCI [redacted], the Short Form (SF-36 v2 Acute), the Dermatology and Life Quality Index (DLQI) and the European Quality of Life Five Dimension, Five Level Scale (EQ-5D-5L) & EQ Visual Analogue Scale (EQ-VAS) at all scheduled time points.
• To estimate the effects of PF-06823859 on CDASI sub-scores across Stage 1 and Stage 2.	• Absolute values and change from baseline values of the sub-scores of CDASI activity and CDASI damage scores at all scheduled time points.
CCI [redacted]	[redacted]
CCI [redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

2.4. Stage 3, Objectives and Endpoints

Primary Objective(s):	**Primary Endpoint(s):**
• To evaluate the safety and tolerability of PF-06823859 in adult DM participants with moderate to severe active muscle disease.	• Incidence of adverse events (AEs) laboratory abnormalities, changes in vital signs, and electrocardiogram (ECG) findings.
Secondary Objective(s):	**Secondary Endpoint(s):**
• To evaluate the efficacy of PF-06823859 over time in adult DM participants with moderate active muscle disease.	• Total Improvement Score (TIS) at Week 12 and intermediate scheduled time points. • Change from baseline in the core Set Measures (CSM) of the TIS including PGA, PtGA, MMT, HAQ-DI, muscle enzymes, and extra-muscular activity, (MDAAT). • Absolute values and change from baseline of CDASI activity and CDASI damage scores at all scheduled time points.

Exploratory Objectives (s)	Exploratory Endpoints(s)
• To characterize PK of PF-06823859 in adult DM participants with active muscle disease.	• Plasma concentrations of PF-06823859.
• To characterize the PD of PF-06823859 in adult DM participants with active muscle disease.	• Absolute values and change from baseline in the values of selected biomarkers (Gene signature panel in blood; Human Myxovirus A (MXA), interferon gamma-induced protein 10 (IP-10), CCI highly sensitive C-reactive protein, (hsCRP), muscle and bone blood biomarkers, autoantibody concentrations in serum/plasma) at all scheduled time points.
• To estimate the effects of PF-06823859 on the physician global assessment (PhGA, VAS) over time.	• Absolute values and change from baseline in the values of the PhGA, VAS at all scheduled time points.
• To estimate the effects of PF-06823859 on patient-reported outcomes (PROs) over time.	• Absolute values and change from baseline in the values of PROs including the Patient Global Assessment (PtGA), the Health Assessment Questionnaire – Disability Index (HAQ-DI), the 5-D Pruritus Scale, CCI the Functional Assessment of Chronic Illness Therapy – Fatigue (FACIT-F), the Short Form (SF-36 v2 Acute), and the European Quality of Life Five Dimension, Five Level Scale (EQ-5D-5L) & EQ Visual Analogue Scale (EQ-VAS) at all scheduled time points.
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3. STUDY DESIGN

3.1. Study Overview

Stage 1 was a multi-center Phase 2A study planned to be conducted in approximately 30 adult participants with moderate to severe DM. Thirty two participants were randomized in order to collect data from 24 participants who completed the study. Each participant was to take part in the study for a period of approximately 9 months. After the 35 day screening period, participants who were eligible enrolled into the study and were randomized in a blinded manner, 2:1 (Active:Placebo) ratio. Investigational drug or placebo administration took place on Day 1, Week 4 and Week 8 of the study. Participants then entered a 5-month follow-up period.

In Stage 2, with the addition of 1 lower dose arm, this study then became a CCI [redacted] Participants will receive study drug, (active or placebo) on Day 1, Week 4, (Visit 4), and Week 8, (Visit 5). At Week 12, (Visit 6) is the scheduled primary endpoint of the study.

The study was further amended, and Stage 2 became "Amended Stage 2" changing the study to a fixed sequence design. In this design participants will be randomized to a treatment sequence at Day 1. The treatment sequence (Active -> Placebo or Placebo ->Active) will dictate whether the participant will receive active study drug during Day 1 to Week 12 or active study drug during Week 12 to Week 20. Although dosing is completed at Week 20, the treatment period goes through to Week 24. There is no washout in between the dose changes (Day 1 to Week 12 and Week 12 to Week 20) for this design. Another key feature is that this design will allow placebo subjects to receive active treatment at some timepoint during the study. No re-randomization will occur at Week 12. Participants who start the study on active study drug CCI [redacted] will have a prespecified dose change to placebo at Week 12, and participants who are on placebo will have a prespecified dose change to active study drug at Week 12. The placebo participants will receive prespecified doses of either CCI [redacted], in order to maintain equal distribution of these doses. There will be no unblinding or interruption of dosing during the treatment period. Each participant will receive 3 consecutive doses of active study drug and 3 consecutive doses of placebo during the trial. The dose change between active and placebo in this fixed sequence design will provide each participant 12 weeks of active drug. The participant, study doctor, or sponsor will not know what the participant is assigned to during the treatment period. The end of the treatment period is at Week 24, although the last dose is administered at the Week 20 visit (Visit 8). All participants will then enter a 4 month follow-up period (the interval between the last dose and the end of the follow-up period is 5 months).

Participants who entered Stage 2 prior to Amendment 4 will follow the design and SoA of Amendment 3, which is Stage 2. Statistical analyses including Stage 2 endpoints will involve data from the original Stage 2 of Amendment 3 and the Amended Stage 2 of Amendment 4, as appropriate.

In Amendment 4, an additional DM cohort of 8 to 16 participants with active moderate muscle involvement (MMT-8 ≤136/150) will be enrolled. This cohort is referred to as Stage 3. Participants in this cohort are allowed to have any amount of skin involvement, as no specific CDASI score is required. All participants who meet eligibility criteria for (Stage 3) will be randomized to receive either PF-06823859 600 mg active study drug or placebo. This study design is similar to the Amended Stage 2 as all participants will receive their dosing assignment at Day 1 in a fixed sequence manner for the duration of the treatment period. The treatment period will consist of 6 dosing's occurring at Day 1, Week 4, (Visit 4), Week 8, (Visit 5), Week 12 (Visit 6), Week 16 (Visit 7), and Week 20, (Visit 8). Each participant will receive 3 consecutive doses of active study drug and 3 consecutive doses of placebo. At Week 12 (Visit 6), participants will be switched to the opposite treatment arm from what they were randomly assigned to at Day 1, Week 4 and Week 8. The study design permits all participants to receive active study drug in a blinded manner. The dose change between active and placebo will provide each participant 12 weeks of active drug. The end of the treatment period is at Week 24, although the last dose is administered at the Week 20 visit (Visit 8). All participants will then enter a 4 month follow-up period (the interval between the last dose and the end of the follow-up period is 5 months).

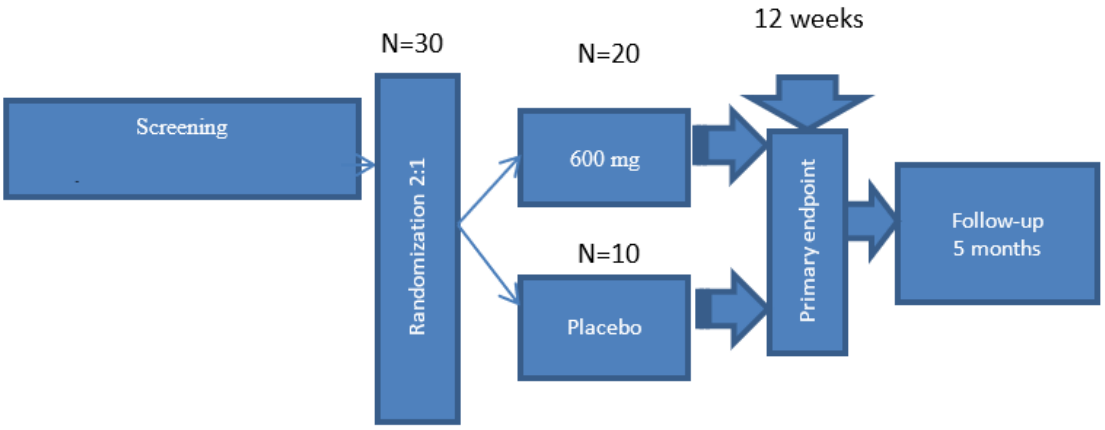
If a participant meets eligibility criteria for both Amended Stage 2 and Stage 3, the participant will be enrolled in Stage 3 unless the enrollment maximum for Stage 3 has been reached, at which point the participant would enroll in the Amended Stage 2.

Amendment 5 contained updates specific to Germany only. Germany is following the contraceptive guidelines related to CTFG guidelines, see Appendix 24.

Amendment 6; participants currently active in the C0251002 study at the time the open label extension study (C0251008) is approved, will have the opportunity to receive 24 additional weeks of treatment. Study participants will be eligible if they have completed the treatment period up through and including Visit 9, Week 24 and have not had any significant protocol deviations, or safety events. The participant can also select to continue into the follow up period of the C0251002 study for completion instead of enrolling into open label extension C0251008.

The overall duration of the C0251002 study will be approximately 69 months from first subject first visit, (FSFV) to last subject last visit, (LSLV) and will be conducted at approximately 35-40 investigative sites. Overall, approximately 76 participants will be randomized into this study.

Figure 1. Study C0251002 Design PF-06823859 (Stage 1)



* Stage 1, study randomized 32 participants.

Figure 2. Study C0251002 Design PF-06823859 Stage 2

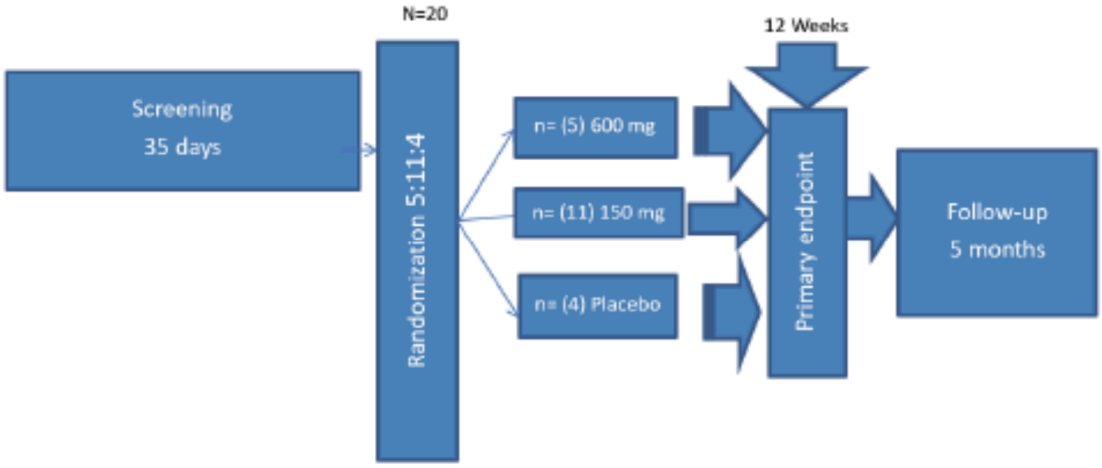


Figure 3. Study C0251002 Design PF-06823859 Amended Stage 2

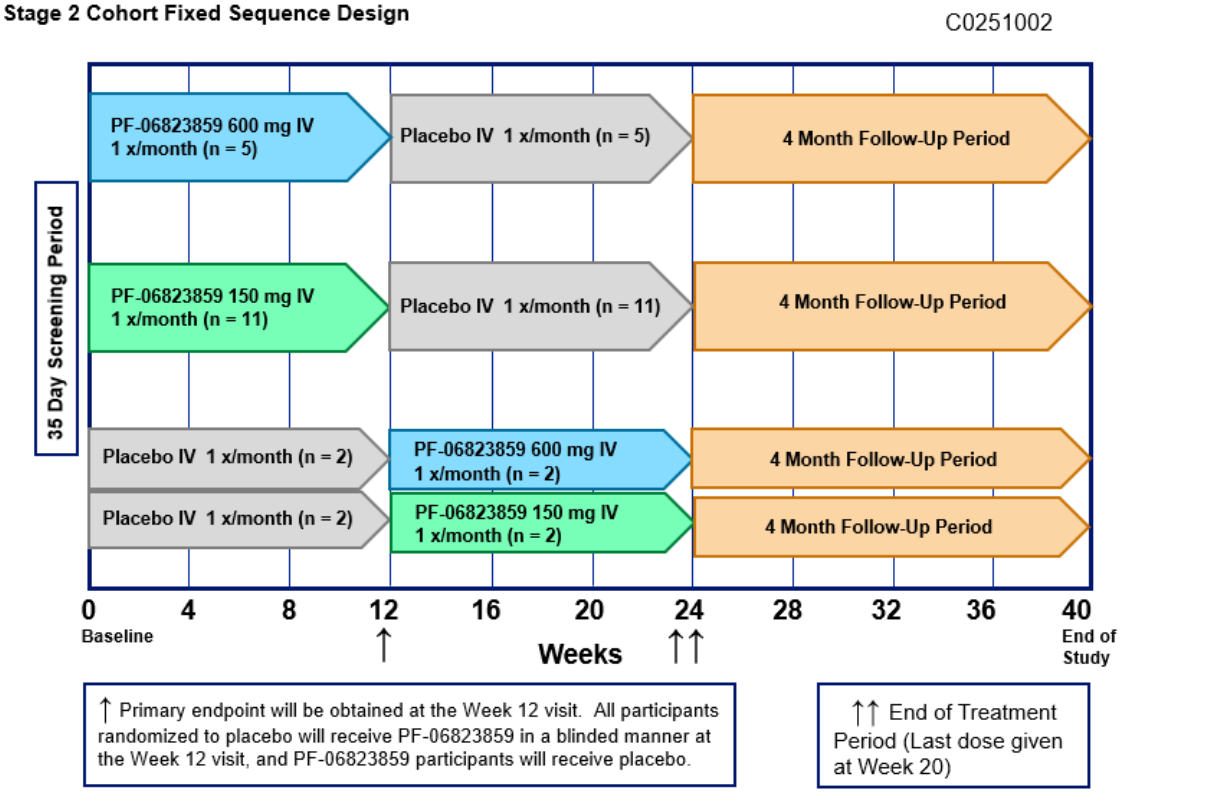


Figure 4. Study C0251002 Design PF-06823859 Stage 3

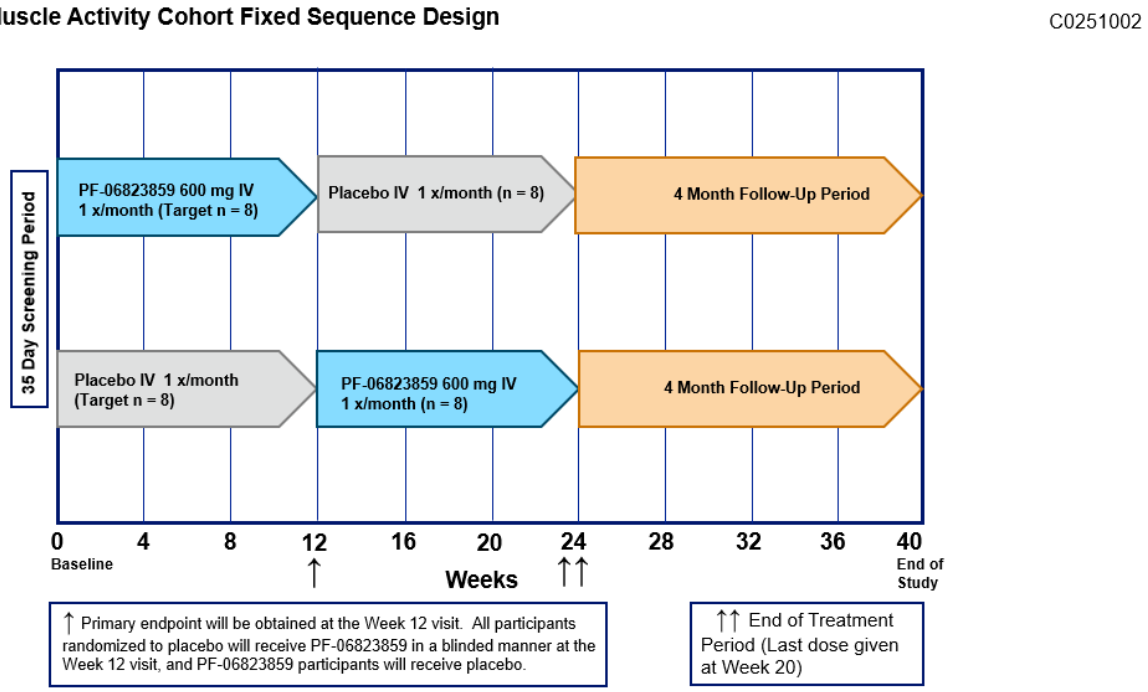


Figure 5. Amended Stage 2 with the Option of Going into the OLE Study

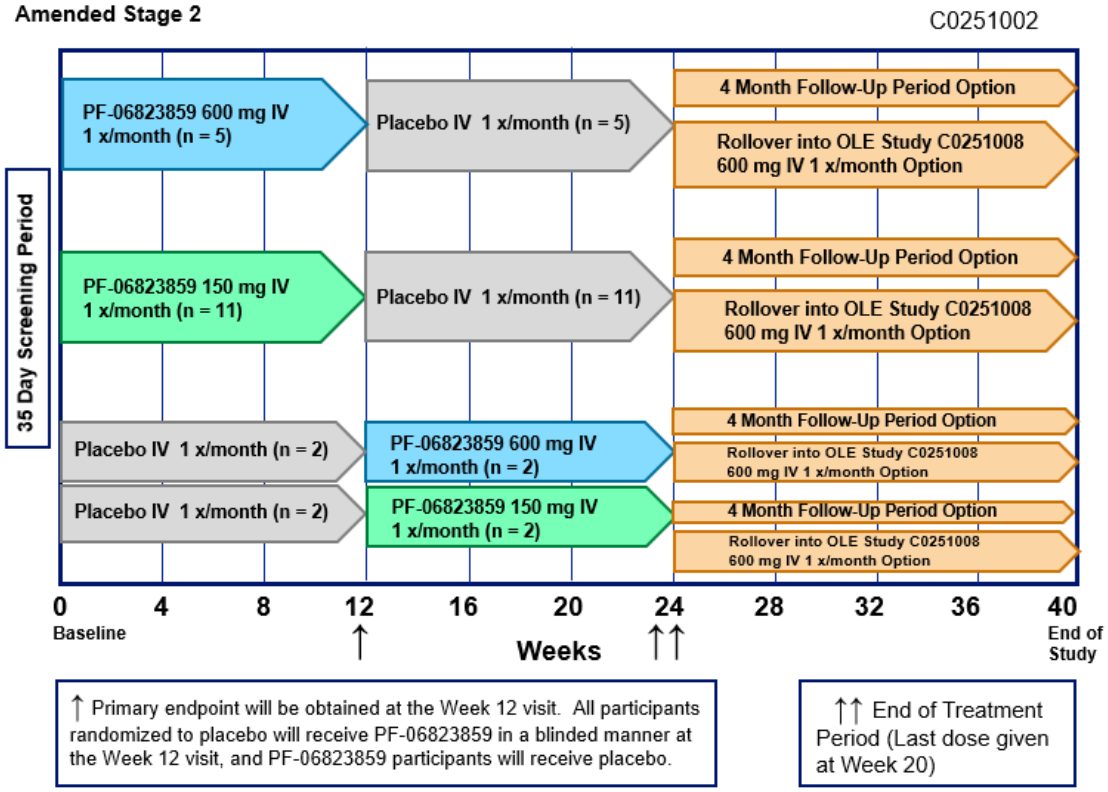
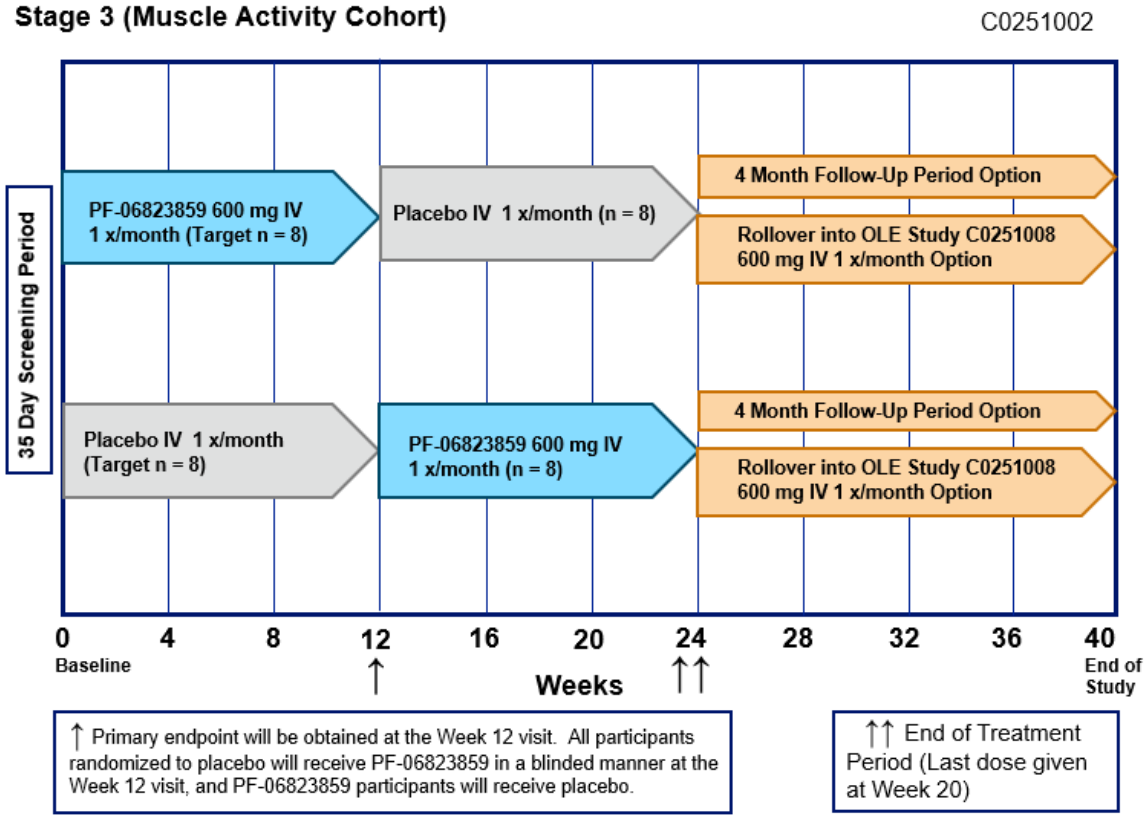


Figure 6. Stage 3 with the Option of Going into the OLE Study



4. PARTICIPANT ELIGIBILITY

This study can fulfill its objectives only if appropriate participants are enrolled. The following eligibility criteria are designed to select participants for whom participation in the study is considered appropriate. All relevant medical and nonmedical conditions should be taken into consideration when deciding whether a particular participant is suitable for this protocol.

Participant eligibility should be reviewed and documented by an appropriate member of the investigator's study team before participants are included in the study.

4.1. Inclusion Criteria, Stage 1 and Stage 2

Participants must meet all of the following inclusion criteria to be eligible for enrollment into the study:

1. Evidence of a personally signed and dated informed consent document indicating that the participant has been informed of all pertinent aspects of the study.

2. Male and or female participants between the ages of ≥18 and ≤80 years old at the time of signing the informed consent.

3. Cutaneous Dermatomyositis Disease Area and Severity Index (CDASI) Activity Score, v2-a (See Appendix 2) (Activity ≥14, and have failed at least 1 standard of care systemic treatment, (eg, corticosteroids).

4. Confirmation of DM by the investigator and two of the following:

    a. Gottron's papules;

    b. Gottron's sign;

    c. Heliotrope eruption;

    d. Nailfold changes, (dilated capillary loops, capillary dropout, cuticular hypertrophy and/or rugged cuticles;

    e. Photo distributed violaceous erythema, (skin that is exposed to sunlight and appears purplish/reddish, and patchy in appearance;

    f. Positive DM serology (eg, anti-transcriptional intermediary factor-1(TIF1-gamma), Nuclear matrix protein 2 (NXP2), Nucleosome-remodelling deacetyalse complex, (Mi2), Melanoma differentiation-associated gene 5, (MDA5), Small ubiquitin-like modifier activating enzyme ½, (SAE ½), or anti-tRNA synthetase).

Note: Concurrent myositis or a history of myositis that is in remission is permitted

5. Participant has had a standard work up for dermatomyositis (prior to) baseline.

    a. Stable interstitial lung disease related to DM that is not severe in the opinion of the investigator is allowed, ie, no supplemental oxygen permitted.

    b. If their DM diagnosis is within 2 years of the screening visit, then they must have completed either:

        - Age appropriate malignancy screening eg, computerized tomography, (CT) of the chest/abdomen/pelvis if indicated;

        or

        - PET CT of chest/abdomen/pelvis at least once by the baseline visit.

6. Willing to provide 6 skin punch biopsies; (4) skin punch biopsies at pre-dose Day 1, Visit 2, and (2) skin punch biopsies at Week 12.

7. Male participants able to father children and female participants of childbearing potential must agree to adhere to the methods of contraception listed in Appendix 25 throughout the duration of the study, including the follow-up period until the end of study.

- Participants in Germany: Please refer to guidelines for Contraceptive, located in Appendix 24.

8. Female participants of non-childbearing potential must meet at least 1 of the following criteria:

   a. Achieved postmenopausal status, defined as follows: cessation of regular menses for at least 12 consecutive months with no alternative pathological or physiological cause; status may be confirmed with a serum follicle-stimulating hormone (FSH) level confirming the postmenopausal state;

   b. Have undergone a documented hysterectomy and/or bilateral oophorectomy;

   c. Have medically confirmed ovarian failure.

   All other female participants (including female participants with tubal ligations) are considered to be of childbearing potential.

9. Willing and able to comply with scheduled visits, treatment plan, laboratory tests and other study procedures.

4.2. Exclusion Criteria, Stage 1 and Stage 2

Participants with any of the following characteristics/conditions will not be included in the study:

1. Investigator site staff members directly involved in the conduct of the study and their family members, site staff members otherwise supervised by the investigator, or participants who are Pfizer employees, including their family members, directly involved in the conduct of the study.

2. Other acute or chronic medical or psychiatric condition including recent (within the past year) or active suicidal ideation or behavior or laboratory abnormality that may increase the risk associated with study participation or investigational product administration or may interfere with the interpretation of study results and, in the judgment of the investigator, would make the participant inappropriate for entry into this study.

3. Any psychiatric condition including recent or active suicidal ideation or behavior that meets any of the following criteria:

   - Clinically significant depression by Patient Health Questionnaire 8- item depression measure (PHQ-8) total score ≥15 (Appendix 4) (completed during the screening visit).

- Suicidal ideation associated with actual intent and a method or plan in the past year: "Yes" answers on items 4 or 5 of CCI [redacted].
- Previous history of suicidal behaviors in the past 5 years: "Yes" answer CCI [redacted]
- Any lifetime history of serious or recurrent suicidal behavior.
- The presence of any current major psychiatric disorder that is not explicitly permitted in the inclusion/exclusion criteria.
- In the opinion of the investigator, exclusion is required.

4. Intake of >15 mg oral prednisone/day, or equivalent.
5. Drug induced myopathy, metabolic myopathy, muscular dystrophy, cancer associated DM, mixed connective tissue disease-associated DM, (eg, overlap syndrome).
6. Significant concurrent disease or conditions other than DM that may influence response to the study drug or safety.
7. Abnormal labs:
   - Hemoglobin <10 g/dL;
   - Neutrophils <1.0 x 109/L;
   - Lymphocytes <500 cells/uL;
   - Platelets <75 x 109/L;
   - Creatinine clearance <60 ml/min according to modified Cockcroft-Gault equation;
   - Alkaline phosphatase >2.5 x upper normal limit;
   - Total bilirubin ≥1.5 x upper limit of normal.

     Note: Elevation of aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH) , creatinine kinase (CK) or aldolase due to muscle involvement (in the opinion of the investigator) are allowed if gamma glutamyl transferase, GGT <1.5 upper limit normal.

Note: Screening laboratory tests with abnormal results may be repeated once to confirm abnormal results within the 5-week screening period. If results return to normal within the 5-week screening period, the participant may enter the study.

8. Participation in other studies involving investigational drug(s) within 30 days prior to study entry. For biologics, 5 half-lives or 180 days preceding the first dose of the investigational product (whichever is longer). This applies prior to study entry and/or during study participation.

9. Pregnant female participants; breastfeeding female participants; fertile male participants and female participants of childbearing potential who are unwilling or unable to adhere to the methods of contraception listed in Appendix 25 for the duration of the study and for 5 months after the after the last dose of investigational product.

    - Participants in Germany: please see guidelines for Contraception Methods in Appendix 24.

10. Have received the following within 180 days of Day 1:

    - A biologic investigational agent. An investigational agent is defined as any drug not approved for sale in the country in which it is being used.

    - IV or oral cyclophosphamide, belimumab or any anti-B-Lymphocyte Stimulator (anti-BLyS or anti-B-cell activating factor [anti-BAFF] agent).

    - Required 3 or more courses of systemic corticosteroids for concomitant conditions (eg, asthma, Crohn's disease, ulcerative colitis, systemic vasculitis, atopic dermatitis).

11. Have received the following within 90 days of Day 1:

    - Anti-TNF therapy (eg, infliximab, etanercept, adalimumab).

    - High dose oral corticosteroids (>100 mg/day prednisone or equivalent) or pulse IV doses.

    - Plasmapheresis.

12. Have received the following within 60 days of Day 1:

    - Any intra muscular (IM) or IV steroid injection.

    - Tofacitinib or any other Janus kinase (JAK) inhibitors.

- Any change in dose of an immunosuppressive/immunomodulatory or antimalarial agent. Dose must be stable for 60 days prior to Day 1 and remain stable through Week 12.

- Inhaled immunosuppressive agents can be used during the study however must be on a stable dose 60 days prior to Day 1 and remain stable through Week 12. (Immunosuppressive ophthalmic drops are allowed without any restrictions).

- Disease -modifying antirheumatic drugs (DMARD)s, (methotrexate, sulfasalazine, hydroxychloroquine, and leflunomide). Less frequently used medications include gold salts, azathioprine, and cyclosporine. Dose must be stable for 60 days prior to Day 1 and remain stable through Week 12.

- Participants may be on one of the following cytotoxic agents: methotrexate, azathioprine, leflunomide, mycophenolate, or 6 MP, but not on any combination of these cytotoxic agents.

Use of IV or IM antibacterials, antivirals, antifungals, or anti-parasitic agents within 60 days of Day 1. Substitution of IM agents for oral agents because of gastro intestinal, (GI) intolerance may be acceptable, as long as it does not otherwise meet the criteria for a serious infection (requires hospitalization or use of other IV antibiotics) (See exclusion #24).

13. Have received within 6 weeks of Day 1:

    - A live (live attenuated) vaccine.

14. Have received any of the following within 30 days of Day 1:

    - Any intra-articular steroid injection.

    - Any new, or change in dose of a corticosteroid or equivalent.

    - Any new, or change in dose of intravenous immunoglobulin (IVIG); (Must be on a stable dose for 30 days).

    - Oral tacrolimus.

15. Have received any of the following within 14 days prior to Day 1:

    - Stable dose of topical immunosuppressants of any strength used on the scalp is permitted throughout the study (With the exception of topical calcineurin inhibitors).

    - Use of oral antibiotics to treat an active infection within 14 days of Day 1.

    - Topical calcineurin inhibitors.

16. Have been treated with any B-cell depleting agents such as rituximab (or other CD20+ directed therapies, or epratuzumab, or anti-CD52 [alemtuzumab]), or Transmembrane Activator and CAML Interactor (TACI)-Ig, within 12 months prior to Day 1. In addition, participants that have been treated with rituximab, or TACI-Ig, serum total immunoglobulins should be checked prior to study entry.

17. Have a history of a major organ transplant (eg, heart, lung, kidney, liver) or hematopoietic stem cell/marrow transplant.

18. Active bacterial, viral, fungal, mycobacterial or other infections (including but not limited to tuberculosis [TB] and atypical mycobacterial disease, granulomatous disease on chest x-ray). History of recurrent bacterial, viral, fungal, mycobacterial or other infections (including but not limited to TB and atypical mycobacterial disease, granulomatous disease on chest x-ray) that would substantially increase the risk to the participant if he or she participates in the study.

19. Have clinically significant finding on a chest radiograph (or other appropriate diagnostic imaging study previously completed within 12 weeks prior to Day 1 such as computed tomography [CT] or magnetic resonance imaging [MRI]) such as the presence of TB, general infection, heart failure or malignancy. Chest imaging must be performed during the 5-week screening period or if diagnostic imaging was previously completed within 12 weeks prior to Day 1.

20. Infected with Mycobacterium tuberculosis (TB) as defined by any of the following:

    A positive Interferon Gamma Release Assay (IGRA) test performed at or within the 12 weeks prior to Day 1 is exclusionary; a negative test is required for eligibility. The following are acceptable IGRA assays: QuantiFERON® TB Gold In-Tube test (QFT-GIT) and QuantiFERON® - TB Gold test (QFT-G), and T-spot® TB test. If T-spot® TB test was completed within 12 weeks prior to Day 1, this is acceptable, however this test type cannot be offered for participants requiring the test during screening, or at any time during the study.

    - In participants with a history of Bacillus Calmette-Guérin (BCG) vaccination, the IGRA test is strongly recommended since the Mantoux test (tuberculin, purified protein derivative [PPD] skin test) may be positive due to vaccination.

    - If the results of the IGRA are indeterminate, the test may be repeated, and if a negative result is obtained, enrollment may proceed. A positive test on repeat is exclusionary.

    - Participants with repeat indeterminate IGRA results may be enrolled after consultation with an infectious disease and/or pulmonary specialist who determines that the risk of infection is low (ie, participant would be acceptable for immunosuppressant treatment without additional action).

- Participants who test positive for IGRA, but in the opinion of the principal investigator (PI) are at low risk of TB infection, may be referred to an infectious disease and/or pulmonary specialist for consultation and potential IGRA test repeated once. Participants will be eligible if the repeat test is negative before the randomization and an infectious disease and/or pulmonary specialist determines that the risk of infection is low (ie, participant would be acceptable for immunosuppressant treatment without additional action).

- Chest radiograph taken at screening with changes suggestive of active TB infection, unless previously performed and documented within 12 weeks prior to Day 1.

- A participant who has been treated or is currently being treated for active or latent TB infection is to be excluded.

- A participant with a history of either untreated or inadequately treated latent or active TB infection is to be excluded.

21. Have a history of any lymphoproliferative disorder such as Epstein Barr Virus (EBV) related lymphoproliferative disorder, history of lymphoma, leukemia, or signs and symptoms suggestive of current lymphatic or lymphoid disease.

22. Have a history (single episode) of disseminated herpes zoster or disseminated herpes simplex, or recurrent (more than 1 episode of) localized, dermatomal herpes zoster.

23. Known history of the following viruses:

    - Human immunodeficiency (HIV) based on documented history with positive serological test, or positive HIV serological test at screening.

      Note: a documented negative HIV test within 3 months of screening is acceptable and does not need to be repeated.

    - Have positive test for hepatitis B surface antigen (HBsAg), total hepatitis B core antibody (anti-HBcAb; also called anti-HBc), hepatitis B surface antibody (HBsAb), and/or HCV Ab.

    - All participants will be screened for HBsAg and HBcAb; participants who are HBsAg positive will be screen-failed. Participants who are HBsAg negative but HBcAb positive will be reflex-tested for HBsAb and, if HBsAb positive, may enroll; if hepatitis B surface antibody test, (HBsAb) negative, they will be screen-failed. Participants who are positive for HCV Ab will be screen-failed.

24. Have required management of acute or chronic infections as follows:

    - Currently on any suppressive therapy for a chronic infection (such as pneumocystis, cytomegalovirus [CMV], and atypical mycobacteria) that, in the opinion of the investigator and sponsor, would place the participant at risk for reactivation. Participants receiving prophylactic therapy for prior outbreaks of herpes simplex virus or herpes zoster may be enrolled with the expectation that this treatment will continue for the duration of the study.

    - Hospitalization for treatment of serious infections within 60 days of Day 1, see exclusion (#12).

25. Have acute coronary syndrome (eg, myocardial infarction, unstable angina pectoris) or any history of significant cerebrovascular disease within 24 weeks of screening. A screening 12-lead electrocardiogram (ECG) that demonstrates clinically significant abnormalities requiring treatment (eg, acute myocardial infarction, serious tachy- or brady- arrhythmias) or that is indicative of serious underlying heart disease (eg, cardiomyopathy, major congenital heart disease, low voltage in all leads, Wolff-Parkinson-White syndrome).

26. Have cancer or a history of cancer within 5 years of screening (other than adequately treated cutaneous basal cell, squamous cell carcinoma, or carcinoma in situ of the uterine cervix with no evidence of recurrence within the previous 5 years).

27. Have pre-existing demyelinating disorder such as multiple sclerosis, or other severe neurological deficits.

28. Have current alcohol and/or drug abuse, or a history of, in the past 2 years which, in the opinion of the investigator, could create a risk for the participant's health or protocol adherence.

29. Have had major surgery within 4 weeks of screening, or scheduled to occur during the study, excluding diagnostic surgery.

30. Previous treatment with total lymphoid irradiation.

31. Grade 3 or greater laboratory abnormality based on the Common Terminology Criteria for Adverse Events (CTCAE) v 4.03 (Appendix 14) except the following that are allowed: Participants with abnormal aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), aldolase, and CK lab values if these values are determined by the investigator to be related to muscle involvement, and if γ glutamyl transferase (GGT) <1.5 upper limit normal.

32. Known exposure to anti-beta Interferon, (PF-06823859) or any type of anti-beta interferon therapy.

4.3. Inclusion Criteria, Amended Stage 2

If a participant meets eligibility for both the Stage 2, (skin focused cohort) and the Stage 3, (muscle disease cohort) the patient should be placed in the Stage 3 muscle disease cohort.

All inclusion criteria is the same as Stage 1 and Stage 2 with the exception to Inclusion Criteria #6.

6. Willing to provide at least (8) vs. 6 skin punch biopsies; (4) skin punch biopsies at pre-dose Day 1 Visit 2, (2) skin punch biopsies at Week 12, Visit 6 and (2) skin punch biopsies at Week 24 Visit 9.

4.4. Exclusion Criteria, Amended Stage 2

All exclusion criteria is the same as Stage 1 and Stage 2 with the exception of Exclusion Criterion #7 Abnormal labs and Exclusion Criterion #12 related to stable dosing of concomitant medications:

Exclusion Criterion #7:

- Hemoglobin <9 g/dL;
- Creatinine clearance <50 mL/min according to modified Cockcroft-Gault equation.

Exclusion Criterion #12:

- Any change in dose of an immunosuppressive/immunomodulatory or antimalarial agent. Dose must be stable for 60 days prior to Day 1 and remain stable through Week 24.
- Inhaled immunosuppressive agents can be used during the study however must be on a stable dose 60 days prior to Day 1 and remain stable through Week 24. (Immunosuppressive ophthalmic drops are allowed without any restrictions).
- Disease -modifying antirheumatic drugs (DMARD)s, (methotrexate, sulfasalazine, hydroxychloroquine, and leflunomide). Less frequently used medications include gold salts, azathioprine, and cyclosporine. Dose must be stable for 60 days prior to Day 1 and remain stable through Week 24.

4.5. Inclusion Criteria, Stage 3

1. Evidence of a personally signed and dated informed consent document indicating that the participant has been informed of all pertinent aspects of the study.
2. Male and or female participants between the ages of ≥18 and ≤80 years old at the time of signing the informed consent.
3. Meets one of the following two criteria:

- MMT-8 ≤136/150 and PhGA, VAS ≥3 cm (0-10 cm) by visual analog scale (VAS) (Appendix 21).

- Sum of PhGA, VAS, PtGA, and extramuscular global assessment VAS scores (Appendix 20) is ≥10 cm (0-10 cm) VAS for each).

4. Participant has failed at least two or more adequate courses of an immunosuppressive agent or immunomodulatory agent, including IVIG, at a dose known to be effective for rheumatologic diseases.

5. Participant has had a standard work up for dermatomyositis (prior to) baseline.

   a. Stable interstitial lung disease related to DM that is not severe in the opinion of the investigator is allowed, ie, no supplemental oxygen permitted.

   b. If their DM diagnosis is within 2 years of the screening visit, then they must have completed either:

      - Age appropriate malignancy screening eg, computerized tomography, (CT) of the chest/abdomen/pelvis if indicated;

      or

      - PET CT of chest/abdomen/pelvis at least once by the baseline visit.

6. Male participants able to father children and female participants of childbearing potential must agree to adhere to the methods of contraception. See Appendix 25 throughout the duration of the study, including the follow-up period until the end of study.

   - Participants in Germany: please see guidelines for Contraception Methods in Appendix 24.

7. Female participants of non-childbearing potential must meet at least 1 of the following criteria:

   a. Achieved postmenopausal status, defined as follows: cessation of regular menses for at least 12 consecutive months with no alternative pathological or physiological cause; status may be confirmed with a serum follicle-stimulating hormone (FSH) level confirming the postmenopausal state.

   b. Have undergone a documented hysterectomy and/or bilateral oophorectomy.

   c. Have medically confirmed ovarian failure.

   d. All other female participants (including female participants with tubal ligations) are considered to be of childbearing potential.

8. Willing and able to comply with scheduled visits, treatment plan, laboratory tests and other study procedures.

4.6. Exclusion Criteria, Stage 3

1. Investigator site staff members directly involved in the conduct of the study and their family members, site staff members otherwise supervised by the investigator, or participants who are Pfizer employees, including their family members, directly involved in the conduct of the study.

2. Other acute or chronic medical or psychiatric condition including recent (within the past year) or active suicidal ideation or behavior or laboratory abnormality that may increase the risk associated with study participation or investigational product administration or may interfere with the interpretation of study results and, in the judgment of the investigator, would make the participant inappropriate for entry into this study.

3. Any psychiatric condition including recent or active suicidal ideation or behavior that meets any of the following criteria:

   - Clinically significant depression by Patient Health Questionnaire 8- item depression measure (PHQ-8) total score ≥15 (Appendix 4) (completed during the screening visit).

   - Suicidal ideation associated with actual intent and a method or plan in the past year: "Yes" answers on items 4 or 5 of Columbia-Suicide Severity Rating Scale during the conduct of the study (C-SSRS; Appendix 5) (completed prior to Day 1 Dosing).

   - Previous history of suicidal behaviors in the past 5 years: "Yes" answer (for events that occurred in the past 5 years) to any of the suicidal behavior items of the C-SSRS; Appendix 6).

   - Any lifetime history of serious or recurrent suicidal behavior.

   - The presence of any current major psychiatric disorder that is not explicitly permitted in the inclusion/exclusion criteria.

   - In the opinion of the investigator, exclusion is required.

4. Intake of >20 mg oral prednisone/day, or equivalent.

5. Drug induced myopathy, metabolic myopathy, muscular dystrophy, cancer associated DM, mixed connective tissue disease-associated DM, (eg, overlap syndrome) and polymyositis.

6. Significant concurrent disease or conditions other than DM that may influence response to the study drug or safety.

7. Abnormal labs:

   - Hemoglobin <9 g/dL;
   - Neutrophils <1.0 x 10^9/L;
   - Lymphocytes <500 cells/uL;
   - Platelets <75 x 10^9/L;
   - Creatinine clearance <50 ml/min according to modified Cockcroft-Gault equation;
   - Alkaline phosphatase >2.5 x upper normal limit;
   - Total bilirubin ≥1.5 x upper limit of normal.

     Note: Elevation of aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), creatinine kinase (CK) or aldolase due to muscle involvement (in the opinion of the investigator) are allowed if gamma glutamyl transferase, GGT <1.5 upper limit normal.

     Note: Screening laboratory tests with abnormal results may be repeated once to confirm abnormal results within the 5-week screening period. If results return to normal within the 5-week screening period, the participant may enter the study.

8. Participation in other studies involving investigational drug(s) within 30 days prior to study entry. For biologics, 5 half-lives or 180 days preceding the first dose of the investigational product (whichever is longer). This applies prior to study entry and/or during study participation.

9. Pregnant female participants; breastfeeding female participants; fertile male participants and female participants of childbearing potential who are unwilling or unable to adhere to the methods of contraception. See Appendix 25 as outlined in this protocol for the duration of the study and for 5 months after the after the last dose of investigational product.

10. Have received the following within 180 days of Day 1: (See Appendix 15 and Appendix 16).

    - A biologic investigational agent. An investigational agent is defined as any drug not approved for sale in the country in which it is being used.

- IV or oral cyclophosphamide, belimumab or any anti-B-Lymphocyte Stimulator (anti-BLyS or anti-B-cell activating factor [anti-BAFF] agent).

- Required 3 or more courses of systemic corticosteroids for concomitant conditions (eg, asthma, Crohn's disease, ulcerative colitis, systemic vasculitis, atopic dermatitis).

11. Have received the following within 90 days of Day 1: (See Appendix 15 and Appendix 16).

    - Anti-TNF therapy (eg, infliximab, etanercept, adalimumab).

    - High dose oral corticosteroids (>100 mg/day prednisone or equivalent) or pulse IV doses.

    - Plasmapheresis.

12. Have received the following within 60 days of Day 1: (See Appendix 15 and Appendix 16).

    - Any intra muscular (IM) or IV steroid injection. (same as above).

    - Tofacitinib or any other Janus kinase (JAK) inhibitors.

    - Any change in dose of an immunosuppressive/immunomodulatory or antimalarial agent. Dose must be stable for 60 days prior to Day 1 and remain stable through Week 24.

    - Inhaled immunosuppressive agents can be used during the study for ILD related to DM; however, must be on a stable dose 60 days prior to Day 1 and remain stable through Week 24. (Immunosuppressive ophthalmic drops are allowed without any restrictions).

    - Disease -modifying antirheumatic drugs (DMARD)s, (methotrexate, sulfasalazine, hydroxychloroquine, and leflunomide). Less frequently used medications include gold salts, azathioprine, and cyclosporine. Dose must be stable for 60 days prior to Day 1 and remain stable through Week 24.

    - Participants may be on one of the following cytotoxic agents: methotrexate, azathioprine, leflunomide, mycophenolate, or 6 MP, but not on any combination of these cytotoxic agents.

Use of IV or IM antibacterials, antivirals, antifungals, or anti-parasitic agents within 60 days of Day 1. Substitution of IM agents for oral agents because of gastro intestinal, (GI) intolerance may be acceptable, as long as it does not otherwise meet the criteria for a serious infection (requires hospitalization or use of other IV antibiotics) (See exclusion #24).

13. Have received within 6 weeks of Day 1: (See Appendix 15 and Appendix 16).

    - A live (live attenuated) vaccine.

14. Have received any of the following within 30 days of Day 1: (See Appendix 15 and Appendix 16).

    - Any intra-articular steroid injection.
    - Any new, or change in dose of a corticosteroid or equivalent.
    - Any new, or change in dose of intravenous immunoglobulin (IVIG); (Must be on a stable dose for 30 days).
    - Oral tacrolimus.

15. Have received any of the following within 14 days prior to Day 1: (See Appendix 15 and Appendix 16).

    - Use of oral antibiotics to treat an active infection within 14 days of Day 1.
    - Topical calcineurin inhibitors.

16. Have been treated with any B-cell depleting agents such as rituximab (or other CD20+ directed therapies, or epratuzumab, or anti-CD52 [alemtuzumab]), or Transmembrane Activator and CAML Interactor (TACI)-Ig, within 12 months prior to Day 1. In addition, participants that have been treated with rituximab, or TACI-Ig, serum total immunoglobulin should be checked prior to study entry.

17. Have a history of a major organ transplant (eg, heart, lung, kidney, liver) or hematopoietic stem cell/marrow transplant.

18. Active bacterial, viral, fungal, mycobacterial or other infections (including but not limited to tuberculosis [TB] and atypical mycobacterial disease, granulomatous disease on chest x-ray). History of recurrent bacterial, viral, fungal, mycobacterial or other infections (including but not limited to TB and atypical mycobacterial disease, granulomatous disease on chest x-ray) that would substantially increase the risk to the participant if he or she participates in the study.

19. Have clinically significant finding on a chest radiograph (or other appropriate diagnostic imaging study previously completed within 12 weeks prior to Day 1 such as computed tomography [CT] or magnetic resonance imaging [MRI]) such as the presence of TB, general infection, heart failure or malignancy. Chest imaging must be performed during the 5-week screening period or if diagnostic imaging was previously completed within 12 weeks prior to Day 1.

20. Infected with Mycobacterium tuberculosis (TB) as defined by any of the following:

    A positive Interferon Gamma Release Assay (IGRA) test performed at or within the 12 weeks prior to Day 1 is exclusionary; a negative test is required for eligibility. The following are acceptable IGRA assays: QuantiFERON® TB Gold In-Tube test (QFT-GIT) and QuantiFERON® - TB Gold test (QFT-G), and T-spot® TB test. If T-spot® TB test was completed within 12 weeks prior to Day 1, this is acceptable, however this test type cannot be offered for participants requiring the test during screening, or at any time during the study.

    - In participants with a history of Bacillus Calmette-Guérin (BCG) vaccination, the IGRA test is strongly recommended since the Mantoux test (tuberculin, purified protein derivative [PPD] skin test) may be positive due to vaccination.

    - If the results of the IGRA are indeterminate, the test may be repeated, and if a negative result is obtained, enrollment may proceed. A positive test on repeat is exclusionary.

    - Participants with repeat indeterminate IGRA results may be enrolled after consultation with an infectious disease and/or pulmonary specialist who determines that the risk of infection is low (ie, participant would be acceptable for immunosuppressant treatment without additional action).

    - Participants who test positive for IGRA, but in the opinion of the principal investigator (PI) are at low risk of TB infection, may be referred to an infectious disease and/or pulmonary specialist for consultation and potential IGRA test repeated once. Participants will be eligible if the repeat test is negative before the randomization and an infectious disease and/or pulmonary specialist determines that the risk of infection is low (ie, participant would be acceptable for immunosuppressant treatment without additional action).

    - Chest radiograph taken at screening with changes suggestive of active TB infection, unless previously performed and documented within 12 weeks prior to Day 1.

    - A participant who has been treated or is currently being treated for active or latent TB infection is to be excluded.

    - A participant with a history of either untreated or inadequately treated latent or active TB infection is to be excluded.

21. Have a history of any lymphoproliferative disorder such as Epstein Barr Virus (EBV) related lymphoproliferative disorder, history of lymphoma, leukemia, or signs and symptoms suggestive of current lymphatic or lymphoid disease.

22. Have a history (single episode) of disseminated herpes zoster or disseminated herpes simplex, or recurrent (more than 1 episode of) localized, dermatomal herpes zoster.

23. Known history of the following viruses:

    - Human immunodeficiency (HIV) based on documented history with positive serological test, or positive HIV serological test at screening.

      Note: a documented negative HIV test within 3 months of screening is acceptable and does not need to be repeated.

    - Have positive test for hepatitis B surface antigen (HBsAg), total hepatitis B core antibody (anti-HBcAb; also called anti-HBc), hepatitis B surface antibody (HBsAb), and/or HCV Ab.

    - All participants will be screened for HBsAg and HBcAb; participants who are HBsAg positive will be screen-failed. Participants who are HBsAg negative but HBcAb positive will be reflex-tested for HBsAb and, if HBsAb positive, may enroll; if hepatitis B surface antibody test, (HBsAb) negative, they will be screen-failed. Participants who are positive for HCV Ab will be screen-failed.

24. Have required management of acute or chronic infections as follows:

    - Currently on any suppressive therapy for a chronic infection (such as pneumocystis, cytomegalovirus [CMV], and atypical mycobacteria) that, in the opinion of the investigator and sponsor, would place the participant at risk for reactivation. Participants receiving prophylactic therapy for prior outbreaks of herpes simplex virus or herpes zoster may be enrolled with the expectation that this treatment will continue for the duration of the study.

    - Hospitalization for treatment of serious infections within 60 days of Day 1, see exclusion (#12).

25. Have acute coronary syndrome (eg, myocardial infarction, unstable angina pectoris) or any history of significant cerebrovascular disease within 24 weeks of screening. A screening 12-lead electrocardiogram (ECG) that demonstrates clinically significant abnormalities requiring treatment (eg, acute myocardial infarction, serious tachy- or brady- arrhythmias) or that is indicative of serious underlying heart disease (eg, cardiomyopathy, major congenital heart disease, low voltage in all leads, Wolff-Parkinson-White syndrome).

26. Have cancer or a history of cancer within 5 years of screening (other than adequately treated cutaneous basal cell, squamous cell carcinoma, or carcinoma in situ of the uterine cervix with no evidence of recurrence within the previous 5 years).

27. Have pre-existing demyelinating disorder such as multiple sclerosis, or other severe neurological deficits.

28. Have current alcohol and/or drug abuse, or a history of, in the past 2 years which, in the opinion of the investigator, could create a risk for the participant's health or protocol adherence.

29. Have had major surgery within 4 weeks of screening, or scheduled to occur during the study, excluding diagnostic surgery.

30. Previous treatment with total lymphoid irradiation.

31. Grade 3 or greater laboratory abnormality based on the Common Terminology Criteria for Adverse Events (CTCAE) v 4.03 (See Appendix 14) except the following that are allowed: Participants with abnormal aspartate aminotransferase (AST), alanine aminotransferase (ALT), lactate dehydrogenase (LDH), aldolase, and CK lab values if these values are determined by the investigator to be related to muscle involvement, and if γ glutamyl transferase (GGT) <1.5 upper limit normal.

32. Known exposure to anti-beta Interferon, (PF-06823859) or any type of anti-beta interferon therapy.

33. Participant has severe muscle damage defined as a global muscle damage score >5 on a 10 cm VAS scale which is a component on the Myositis Damage Index (MDI) Appendix 23.

4.7. Randomization Criteria

Participants will be randomized after successfully meeting all eligibility requirements.

4.8. Lifestyle Requirements

In order to participate in the study, participants must be aware of the life style guidelines and restrictions that apply during and after the study period described in Section 4.8.2 and Appendix 25.

4.8.1. Surgery

During the study, no elective surgery should occur without first consulting with the sponsor. Preferably, elective surgery should occur 4 weeks before the study screening visit or be delayed until participation in the study is completed.

The sponsor should be notified if a participant requires surgery (including dental surgery) during the study to determine whether the participant should discontinue from the study and/or discontinue the investigational product prior to the surgical procedure. In general, planned surgical procedures should not be performed unless the investigational product has been discontinued for at least 28 days (unless otherwise advised by the sponsor). In addition, the sponsor should be notified as soon as possible if a participant undergoes a surgical procedure without first informing the study staff.

4.8.2. Contraception

Studies to evaluate the development toxicity of PF-06823859 have not been conducted. Therefore, the use of a highly effective method of contraception is required (see Appendix 25 and study sites participating in Germany please see Appendix 24).

The investigator or his or her designee, in consultation with the participant, will confirm that the participant has selected an appropriate method of contraception for the individual participant and his or her partner(s) from the permitted list of contraception methods (see Appendix 25 and study sites from Germany see Appendix 24) and will confirm that the participant has been instructed in its consistent and correct use. At time points indicated in the SoA, the investigator or designee will inform the participant of the need to use highly effective contraception consistently and correctly and document the conversation and the participant's affirmation in the participant's chart (participants need to affirm their consistent and correct use of at least 1 of the selected methods of contraception) considering that their risk for pregnancy may have changed since the last visit. In addition, the investigator or designee will instruct the participant to call immediately if the selected contraception method is discontinued or if pregnancy is known or suspected in the participant or partner.

In Germany, CTFG guidelines will be followed, where one highly effective method of contraception must be used, see Appendix 24. The investigator will document the conversation, and the participant's affirmation, in the participant's chart.

4.9. Sponsor's Qualified Medical Personnel

The contact information for the sponsor's appropriately qualified medical personnel for the study is documented in the study contact list located in Study Team on Demand (STOD), STOD@pfizer.com.

To facilitate access to appropriately qualified medical personnel on study-related medical questions or problems, participants are provided with a contact card. The contact card contains, at a minimum, protocol and investigational product identifiers, participant study numbers, contact information for the investigator site, and contact details for a contact center in the event that the investigator site staff cannot be reached to provide advice on a medical question or problem originating from another healthcare professional not involved in the participant's participation in the study. The contact number can also be used by investigator staff if they are seeking advice on medical questions or problems; however, it should be used only in the event that the established communication pathways between the investigator site and the study team are not available. It is therefore intended to augment, but not replace, the established communication pathways between the investigator site and the study team for advice on medical questions or problems that may arise during the study. The contact number is not intended for use by the participant directly, and if a participant calls that number, he or she will be directed back to the investigator site.

5. STUDY TREATMENTS

For the purposes of this study, and per International Conference on Harmonisation (ICH) guidelines, investigational product is defined as a pharmaceutical form of an active ingredient or placebo being tested or used as a reference/comparator in a clinical trial, including a product with a marketing authorization when used or assembled (formulated or packaged) in a way different from the approved form, or when used for an unapproved indication, or when used to gain further information about an approved use (ICH E6 1.33).

For this study, the investigational product will be administered intravenously over approximately one hour. Investigational product will be administered every 4 weeks, each participant receiving 3 doses of investigational product.

5.1. Allocation to Treatment

Allocation of participants to treatment/ or placebo will proceed through the use of an interactive response technology (IRT) system or (interactive Web-based response [IWR]. The blinded personnel will be required to enter or select information including but not limited to the user's identification (ID) and password, the protocol number and the participant number. The blinded person will then be provided with a randomization number, and dispensable unit (DU) or container number when investigational product is being supplied via the IRT system. It is noted that all of the information shown in the IRT system during drug assignment, and on the relevant confirmation report, is blinded information. The IRT system will provide a confirmation report containing the participant number, randomization number, and DU or container number assigned.

The study specific IRT reference manual will provide the contact information and further details on the use of the IRT system.

5.2. Breaking the Blind

This study will be double blinded, (Sponsor, Investigator and participant will all be and remain blinded throughout the duration of the study). An interim analysis may be conducted for internal decision making. An internal review committee, (IRC) separate from the blinded study team will review safety and efficacy data.

At the initiation of the study, the investigator site will be instructed on the method for breaking the blind. The method will be an electronic process. Blinding codes are able to be broken in exceptional circumstances when knowledge of the actual treatment code is absolutely essential for further management of the participant. If the situation allows, investigators are encouraged to discuss with the sponsor's medical monitor if they believe unblinding is necessary, however, under no circumstances should unblinding be delayed in an emergency situation. When the blinding code is broken, the reason must be fully documented and entered on the case report form (CRF).

5.3. Participant Compliance

All doses of investigational product will be administered by the appropriately designated study staff at the investigator site.

5.4. Investigational Product Supplies

5.4.1. Dosage Form(s) and Packaging

CCI [redacted]

Placebo for CCI [redacted] sealed with a stopper and a flip off aluminum seal.

The vials will be packed into cartons containing 6 vials per carton.

5.4.2. Preparation and Dispensing

Once eligibility has been confirmed through the screening period process, each participant will be randomized. The investigational product will be dispensed using an interactive response technology, (IRT) drug management system at each dispensing visit. A qualified staff member will dispense the investigational product via unique container numbers on the label provided, in quantities appropriate for the dose assignment.

See the IP manual for instructions on how to prepare the investigational product for administration. Investigational product should be prepared and dispensed by an appropriately qualified and experienced member of the study staff (eg, physician, nurse, physician's assistant, nurse practitioner, pharmacy assistant/technician, or pharmacist) as allowed by local, state, and institutional guidance.

PF-06823859 doses and placebo will be prepared by qualified unblinded site personnel according to the IP manual. The investigational product will be administered to participants in a blinded manner.

5.5. Administration

Blinded IV PF-06823859 or placebo will be administered at the investigative site or clinic over the course of CCI [redacted] has completed, all participants will be monitored for an additional 60 minutes post investigational treatment administration.

5.5.1. Infusion Discontinuation

- If a participant experiences symptoms typical of an allergic reaction, the study drug administration should be discontinued immediately and permanently.

- If a participant experiences symptoms typical of infusion reactions (eg, lightheadedness, nausea, chills, fever), the study drug infusion should be stopped. At the discretion of the investigator, the infusion can be restarted at a slower rate if symptoms are resolved within 1 hour after the stop of infusion. If symptoms return,

then the study drug administration should be discontinued immediately and permanently.

- In the event that there is an infusion interruption, the entire duration of drug infusion, from the initial start of infusion to the completion of infusion, should not exceed 3 hours. Participants will receive appropriate treatment at the discretion of the investigator.

5.6. Investigational Product Storage

The investigator, or an approved representative, eg, pharmacist, will ensure that all investigational products are stored in a secured area with controlled access under required storage conditions and in accordance with applicable regulatory requirements.

Investigational product should be stored in its original container and in accordance with the label.

See the IP manual for complete information on storage conditions, handling and stability of the product.

Any storage conditions stated in the single reference safety document (SRSD) (eg, Investigator's Brochure [IB]) will be superseded by the storage conditions stated on the product label.

Site systems must be capable of measuring and documenting (for example, via a log), at a minimum, daily minimum and maximum temperatures for all site storage locations (as applicable, including frozen, refrigerated, and/or room temperature products). This should be captured from the time of investigational product receipt throughout the study. Even for continuous monitoring systems, a log or site procedure that ensures daily evaluation for excursions should be available. The intent is to ensure that the minimum and maximum temperature is checked each business day to confirm that no excursion occurred since the last evaluation and to provide the site with the capability to store or view the minimum/maximum temperature for all nonworking days upon return to normal operations. The operation of the temperature monitoring device and storage unit (for example, refrigerator), as applicable, should be regularly inspected to ensure it is maintained in working order.

Any excursions from the product label storage conditions should be reported to Pfizer upon discovery. The site should actively pursue options for returning the product to the storage conditions as described in the labeling, as soon as possible. Deviations from the storage requirements, including any actions taken, must be documented and reported to Pfizer.

Once an excursion is identified, the investigational product must be quarantined and not used until Pfizer provides documentation of permission to use the investigational product. It will not be considered a protocol deviation if Pfizer approves the use of the investigational product after the temperature excursion. Use of the investigational product prior to Pfizer approval will be considered a protocol deviation. Specific details regarding information the site should report for each excursion will be provided to the site.

Receipt of materials, door opening and closing, and other routine handling operations where the product(s) are briefly out of the temperature range described in the labeling are not considered excursions.

5.7. Investigational Product Accountability

The investigator site must maintain adequate records documenting the receipt, use, loss, or other disposition of the investigational product supplies. All investigational products will be accounted for using a drug accountability form/record.

5.7.1. Destruction of Investigational Product Supplies

The sponsor or designee will provide guidance on the destruction of unused investigational product (eg, at the site). If destruction is authorized to take place at the investigator site, the investigator must ensure that the materials are destroyed in compliance with applicable environmental regulations, institutional policy, and any special instructions provided by Pfizer, and all destruction must be adequately documented.

All used glass vials should be maintained at the investigative site for accountability. The investigator will maintain the unused supply until destruction is authorized. Pfizer will provide instructions as to the disposition of any unused investigational product.

5.8. Concomitant Treatment(s)

5.8.1. Prior Treatments

The indication for use, total daily dose, route of administration, and start and stop dates for all prior medications (including prescription medications and treatments, vaccinations, nonprescription medications, nondrug treatments and dietary supplements) received within 30 days prior to obtaining informed consent for the study will be recorded on the CRF.

For a list of prohibited and permitted concomitant medications refer to Appendix 15 and Appendix 16 Concomitant Treatment(s)

Participants will abstain from concomitant treatments as described in the Inclusion and Exclusion sections of the protocol.

Participants enrolling in the study are permitted to be on a stable DM treatment prior to Day 1 investigational treatment, as long as it is permitted treatment. All concomitant treatments taken during the study must be recorded in study records with indication for use, total daily dose, and start and stop dates of administration.

All participants will be questioned about concomitant treatment at each site visit.

Medications that are taken during the 5-week screening period (after informed consent is obtained and before the first dose of investigational product) will be documented as prior medications. Medications taken after the first dose of investigational product has been administered will be documented as concomitant medications.

Participants will be asked about all concomitant treatments (including prescription medications and treatments, vaccinations, nonprescription medications, nondrug treatments, dietary supplements and herbal preparations) at each study visit. Any new concomitant medications or dose changes to current concomitant medications should be evaluated for potential new or worsening AEs.

For the purposes of this protocol, dietary supplements are defined as vitamins, minerals, purified food substances, and herbals with pharmaceutical properties. Vitamins, minerals, purified food substances, and herbals with pharmaceutical properties are allowed in amounts not known to be associated with adverse effects (such as hypervitaminosis). Herbals with unknown properties or those herbals that are known to have an effect on drug metabolism (eg, St. John's Wort) must be discontinued at least 1 week or 5 half-lives (whichever is longer) before the first dose of investigational product.

5.8.2. Prohibited Concomitant Medications

Please See Appendix 15 and Appendix 16.

5.8.3. Permitted Concomitant Medications

Please See Appendix 15 and Appendix 16.

5.8.4. Pre Medication use on the day of IVIG Administration

For participants who enroll in the study who are on IVIG: On the day of IVIG dose administration, pre-medication to prevent hypersensitivity reaction to IVIG is permitted. The steroid dose that was previously used for pre-medication will be permitted (on IVIG dosing day only). After IVIG dosing day, steroid dosing should remain less than or equal to 15 mg or equivalent per day as per protocol Section 5.8.5.

There is no need to change the IVIG dosing schedule or adjust the IVIG dosing schedule related to investigational product administration.

5.8.5. Corticosteroids

For Stage 1, 2, a stable dose of ≤15 mg/day of corticosteroids or equivalent are permitted during the study through Week 12, Visit 6. After Week 12 as per the investigator's discretion tapering of steroids may occur. The decision of tapering the steroids is entirely up to the study investigator and any change in the steroid dose should be recorded on the concomitant steroid page.

For Amended Stage 2, a stable dose of ≤15 mg/day of corticosteroids or equivalent are permitted during the study through Week 24, Visit 9. After Week 24 as per the investigator's discretion tapering of steroids may occur. The decision of tapering the steroids is entirely up to the study investigator and any change in the steroid dose should be recorded on the concomitant steroid page. Please note if the participant is considering entering the open label extension study, please refrain from tapering steroids until the participant has been in the open label study for 4 weeks.

For Stage 3, a stable dose of ≤20 mg/day of corticosteroid's or equivalent are permitted during the study through Week 24, Visit 9. After Week 24 as per the investigator's discretion tapering of steroids may occur. The decision of tapering the steroids is entirely up to the study investigator and any change in the steroid dose should be recorded on the concomitant steroid page. Please note if the participant is considering entering the open label extension study, please refrain from tapering steroids until the participant has been in the open label study for 4 weeks.

All concomitant treatments including corticosteroids or equivalent taken during the study must be recorded in study records with indication for use, total daily dose, and start and stop dates of administration.

5.8.6. Guidance for Investigators

During the course of the study, those participant who experience a severe flare requiring new or increased doses of immunosuppressants (including new or increased doses of corticosteroids beyond what is permitted or hospitalization), will be discontinued from the treatment period of the study and placed in the follow-up period, and therefore, will receive no further investigational product. Rescue therapy may be administered as clinically necessary.

5.9. Rescue Medication

After a participant enters the follow up period, or prematurely withdrawn from the study for any reason, medically necessary treatments for DM will be allowed. The previous prohibited medications will no longer apply.

6. STUDY PROCEDURES

6.1. Screening

For screening procedures, see Schedule of Activities and ASSESSMENTS section.

Participants will be screened within 35 days prior to administration of investigational product to confirm that they meet the participant eligibility criteria for the study. The investigator (or appropriate delegate at the investigator site) will obtain informed consent from each participant in accordance with the procedures described in Section 12.3. Screening visits may occur over multiple visits to achieve all of the required testing.

Screening laboratory tests with abnormal results may be repeated once to confirm abnormal results. The last value (most recent value obtained) will be used to determine eligibility. If results return to normal within the 5-week screening period, the participant may enter the study.

Rescreening:

Participants who do not meet the eligibility criteria (ie, screen failure) may be re-screened once at a later date. Any participant who is re-screened must be re-consented and receive a new participant number. All activities required for the screening visit must be repeated.

6.2. Study Period

6.2.1. Treatment Period (Stage 1 and 2)

The treatment period will begin on Day 1 and consist of 4 scheduled visits, (Visits 2-5). From Day 1, where investigational treatment or placebo is received, a scheduled visit will occur in 7 days (±) 3 days, to follow up with the participant after the first investigational drug/placebo administration. For all other visits the participant will be seen every 4 weeks from Day 1. Investigational treatment will be received at Visits 2 (Day 1), Visits 4 and 5. During the treatment period visits, the following assessments may occur:

- Investigational drug or placebo administered.
- Skin biopsy (4). (*After randomization prior to first dose of investigational/placebo treatment*) Day 1, Visit 2.
- CDASI assessment.
- CCI [redacted]
- Physicians Global Assessment.
- Vital signs, (Blood pressure, (BP), Heart Rate, (HR), Pulse, respirations and temperature).
- Weight.
- Targeted Physical examination.
- ECG, (Day 1, Visits 4, 5, 6, End of Study or Early termination).
- Blood & urine collection for safety laboratory testing.
- Males and females, (contraception check).
- All females Urine Pregnancy test.
- Blood collection for various biomarkers, (IP-10, MX-A, CCI [redacted] hsCRP, Gene signature panel).
- CCI [redacted]
- CCI [redacted]
- Patient reported outcomes, 5D Pruritus Scale, SF36 V2 Acute, and DLQI.
- Recording of any new concomitant medications, DM concomitant medications or changes in ongoing concomitant medications, or DM concomitant medications.

- Collection for Viral Surveillance.
- Check for Infusion site reactions.
- Collection of any serious and non-serious adverse events.
- Genomic Banked biospecimen (Prep D1) If missed, the site may collect at the next available time point when biospecimens are being collected in conjunction with a participant visit.

Please see the Schedule of Assessments for specific details on which procedures will occur at each visit.

6.2.2. Treatment Period (Amended Stage 2)

The treatment period will begin on Day 1 and consist of 8 scheduled treatment visits, (Visits 2-8). The first dose of investigational treatment or placebo will be administered on Day 1. Following Day 1, a scheduled visit will occur in 7 days (±) 3 days. Otherwise, monthly visits will occur to the end of the follow-up period after the first dose administration. Investigational treatment will be received at Visit 2 (Day 1), Visit 4 (Week 4), Visit 5 (Week 8), Visit 6 (Week 12), Visit 7 (Week 16) and Visit 8 (Week 20). The end of the treatment period is at Week 24. Once Week 24 has been completed, eligible participants will have the opportunity to enter the open label extension study or may continue into the follow up period.

During the treatment period visits, the following assessments may occur: For more details please follow the SoA.

- Investigational drug or placebo administered through Visit 8.
- Punch Skin biopsy (4), (-6 days prior to randomization Day 1, Visit 2).
- Punch Skin biopsy (2), (±6 days, Week 12, Visit 6).
- Punch Skin biopsy (2), (±6 days, Week 24, Visit 9).
- CDASI assessment.
- CCI [redacted]
- Physicians Global Assessment.
- Vital signs, (Blood pressure, (BP), Heart Rate, (HR), Pulse, respirations and temperature).
- Weight.

- Targeted Physical examination.
- Complete Physical examination.
- ECG, (Day 1, Visits 4, 5, 6, 7, 8, 9, End of Study Visit 13, or Early termination).
- Blood & urine collection for safety laboratory testing.
- Males and females, (contraception check).
- All females Urine Pregnancy test.
- Blood collection for various biomarkers, (IP-10, MX-A, CCI [redacted] hsCRP, Gene signature panel).
- CCI [redacted]
- CCI [redacted]
- Patient reported outcomes, PtGA, HAQ-DI, DLQI, 5D Pruritus Scale, CCI [redacted], SF36 V2 Acute, and EQ-5D-5L, EQ-VAS.
- Recording of any new concomitant medications, DM concomitant medications or changes in ongoing concomitant medications.
- Collection for Viral Surveillance.
- Check for Infusion site reactions.
- Collection of any serious and non-serious adverse events.
- CCI [redacted] If missed, the site may collect at the next available time point when biospecimens are being collected in conjunction with a participant visit. For more details please follow the SoA.

6.2.3. Treatment Period for Stage 3

The treatment period will begin on Day 1 and consist of 8 scheduled visits, (Visits 2-8). The first dose of investigational treatment or placebo will be administered on Day 1. Following Day 1, a scheduled visit will occur in 7 days (±) 3 days. Otherwise, monthly visits will occur to the end of the follow-up period after the first dose administration. Investigational treatment will be received at Visit 2 (Day 1), Visit 4 (Week 4), Visit 5 (Week 8), Visit 6 (Week 12), Visit 7 (Week 16) and Visit 8 (Week 20). The end of the treatment period is at Week 24. Once Week 24 has been completed, eligible participants will have the opportunity to enter the open label extension study or they may continue into the follow up period.

During the treatment period visits, the following assessments may occur: For more details please follow the SoA.

- Investigational drug or placebo administered through Visit 8.
- CDASI assessment.
- CCI [redacted]
- MMT-8 assessment (See Appendix 21).
- Physicians Global Assessment, PhGA, VAS (See Appendix 3).
- Myositis Disease Activity Assessment Test, MDAAT(See Appendix 20).
- Recording of Muscle Enzymes (See Appendix 19).
- Vital signs, (Blood pressure, (BP), Heart Rate, (HR), Pulse, respirations and temperature).
- Weight.
- Complete Physical Exam.
- Targeted Physical Exam.
- ECG, (Day 1, Visits 4, 5, 6, 7, 8, 9, End of Study Visit 13, or Early termination).
- Blood & urine collection for safety laboratory testing, (including muscle enzymes).
- Males and females, (contraception check).
- All females Urine Pregnancy test.
- Blood collection for various biomarkers, (IP-10, MX-A, CCI [redacted] hsCRP, Gene signature panel).
- CCI [redacted]
- CCI [redacted]
- Patient reported outcomes in the following order, PtGA, HAQ-DI, 5D Pruritus Scale, CCI [redacted] FACIT-F, SF36 V2 Acute, and EQ-5D-5L, EQ-VAS.
- Recording of any new concomitant medications, DM concomitant medications or changes in ongoing concomitant medications.

- Collection for Viral Surveillance.
- Check for Infusion site reactions.
- Collection of any serious and non-serious adverse events.

6.2.4. Follow-up Visits for Stage 2

Due to the investigational drug's half-life of approximately 28 days, 5 follow-up visits, (Visits 6-10) will be conducted monthly. During the follow up period, the participant will have the following assessments and procedures completed. Please see Schedule of Assessments for specific details on which procedures will occur at each visit.

- Punch Skin biopsy (2), (Week 12, Visit 6).
- CDASI assessment.
- CCI [redacted]
- Physicians Global Assessment.
- Vital signs, (Blood pressure, (BP), Heart Rate, (HR), Pulse, respirations and temperature).
- Weight.
- Targeted Physical examination.
- Complete Physical examination.
- ECG, (Visit 12, End of Study Visit 10), or Early termination).
- Blood & urine collection for safety laboratory testing.
- Males and females, (contraception check).
- All females Urine Pregnancy test.
- Blood collection for various biomarkers, (IP-10, MX-A, CCI [redacted], hsCRP, Gene signature panel).
- CCI [redacted]
- CCI [redacted]
- Patient reported outcomes, 5D Pruritus Scale, SF36 V2 Acute, DLQI and EQ-5D-5L.

- Recording of any new concomitant medications, DM concomitant medications or changes in ongoing concomitant medications,
- Collection for Viral Surveillance.
- Collection of any serious and non-serious adverse events.
- Genomic Banked biospecimen (Prep D1) If missed, the site may collect at the next available time point when biospecimens are being collected in conjunction with a participant visit.

6.2.5. Follow-up Visits for Amended Stage 2

Due to the investigational drug's half-life of approximately 28 days, 4 follow-up visits will occur after completing the treatment period, Week 24, (Visit 9) and will be conducted every 4 weeks. The last dose is administered at Week 20 which provides a 5 month interval to the end of the study. During the follow up period, the participant will have the following assessments and procedures completed. Please see Schedule of Assessments for specific details on which procedures will occur at each visit.

- Punch Skin biopsy (2), (± 6 days, Week 24, Visit 9).
- CDASI assessment.
- CCI [redacted]
- Physicians Global Assessment.
- Vital signs, (Blood pressure, (BP), Heart Rate, (HR), Pulse, respirations and temperature).
- Weight.
- Height.
- Targeted Physical examination.
- Complete Physical examination.
- ECG, (Visit 9, End of Study Visit 13), or Early termination).
- Blood & urine collection for safety laboratory testing.
- Males and females, (contraception check).
- All females Urine Pregnancy test.

- Blood collection for various biomarkers, (IP-10, MX-A, CCI [redacted], hsCRP, Gene signature panel).
- CCI [redacted]
- CCI [redacted]
- Patient reported outcomes, PtGA, HAQ-DI, DL,QI, Pruritus Scale, CCI [redacted], SF36 V2 Acute, and EQ-5D-5L, EQ-VAS.
- Recording of any new concomitant medications, DM concomitant medications or changes in ongoing concomitant medications.
- Collection for Viral Surveillance.
- Collection of any serious and non-serious adverse events.

6.2.6. Follow-up Visits for Stage 3

Due to the investigational drug's half-life of approximately 28 days, 4 follow-up visits will occur after completing the treatment period, Week 24,(Visit 9) and will be conducted every 4 weeks. The last dose is administered at Week 20 which provides a 5 month interval to the end of the study. During the follow up period, the participant will have the following assessments and procedures completed. Please see Schedule of Assessments for specific details on which procedures will occur at each visit.

- CDASI assessment (See Appendix 2).
- CCI [redacted]
- MMT-8 assessment (See Appendix 21).
- Pt Global Assessment (PtGA) (See Appendix 13).
- Physicians Global Assessment, (PhGA, VAS) (See Appendix 3).
- Myositis Disease Activity Assessment Test, (MDAAT) (See Appendix 20).
- Recording of Muscle Enzymes (See Appendix 19).
- Vital signs, (Blood pressure, (BP), Heart Rate, (HR), Pulse, respirations and temperature).
- Weight.
- Height

- Complete Physical Exam.
- Targeted Physical Exam.
- ECG, (Visit 9, End of Study Visit 13, or Early Termination).
- Blood & urine collection for safety laboratory testing, (including muscle enzymes).
- Males and females, (contraception check).
- All females Urine Pregnancy test.
- Blood collection for various biomarkers, (IP-10, MX-A, CCI [redacted] hsCRP, Gene signature panel).
- CCI [redacted]
- CCI [redacted]
- Patient reported outcomes in the following order, PtGA, HAQ-DI, 5-D Pruritus Scale, CCI [redacted] FACIT-F, SF36 V2 Acute, and EQ-5D-5L and EQ-VAS.
- Recording of any new concomitant medications, DM concomitant medications or changes in ongoing concomitant medications.
- Collection for Viral Surveillance.
- Collection of any serious and non-serious adverse events.

6.2.7. Unscheduled Visits

At any time during the conduct of the study a participant may be brought in for an unscheduled study visit. This may be related to a lab value, or per the investigator's discretion.

6.2.8. Alternative Measures During a Public Emergency

The implementation of alternative measures during public emergencies should be consistent with the protocol to the extent possible if feasible. A separate document will be provided which outlines specific details in collecting procedures according to this protocol. Please also reference Appendix 17 for options that may be available to continue the conduct of the study.

Participant Withdrawal (Early Termination) The early termination visit only applies to participant who are randomized and then are prematurely withdrawn from the study. Contraception should also be continued for a minimum of 5 months from the last dose of investigational product.

It may be appropriate for the participant to return to the clinic for final safety assessments to be scheduled as early as practically feasible following the decision to withdraw from the study. Participants should be questioned regarding their reason for withdrawal. At the early withdrawal visit, every effort must be made to complete the assessments according to the early withdraw visit in the SOA. The site should follow the applicable SOA the participant has been following during their participation in the study.

Lack of completion of all or any of the early termination procedures will not be viewed as protocol deviations so long as the participant safety was preserved.

Withdrawal of consent

Participants who request to discontinue receipt of study treatment will remain in the study and must continue to be followed for protocol specified follow-up procedures. The only exception to this is when a participant specifically withdraws consent for any further contact with him or her or persons previously authorized by the participant to provide this information. Participants should notify the investigator in writing of the decision to withdraw consent from future follow-up, whenever possible. The withdrawal of consent should be explained in detail in the medical records by the investigator, as to whether the withdrawal is only from further receipt of investigational product or also from study procedures and/or post treatment study follow-up, and entered on the appropriate CRF page. In the event that vital status (whether the participant is alive or dead) is being measured, publicly available information should be used to determine vital status only as appropriately directed in accordance with local law.

Lost to follow-up:

All reasonable efforts must be made to locate participants to determine and report their ongoing status. This includes follow-up with persons authorized by the participant as noted above. Lost to follow-up is defined by the inability to reach the participant after a minimum of 2 documented phone calls, faxes, or e-mails as well as lack of response by the participant to 1 registered mail letter. All attempts should be documented in the participant's medical records. If it is determined that the participant has died, the site will use locally permissible methods to obtain the date and cause of death. If the investigator's use of a third-party representative to assist in the follow-up portion of the study has been included in the participant's informed consent, then the investigator may use a sponsor-retained third-party representative to assist site staff with obtaining the participant's contact information or other public vital status data necessary to complete the follow-up portion of the study. The site staff and representative will consult publicly available sources, such as public health registries and databases, in order to obtain updated contact information. If, after all attempts, the participant remains lost to follow-up, then the last-known-alive date as determined by the investigator should be reported and documented in the participant's medical records.

Participants may withdraw from the study at any time at their own request, or they may be withdrawn at any time at the discretion of the investigator or sponsor for safety (see also the Withdrawal From the Study Due to Adverse Events section) or behavioral reasons, or the inability of the participant to comply with the protocol-required schedule of study visits or procedures at a given study site.

If a participant does not return for a scheduled visit, every effort should be made to contact the participant. The Investigator or designee should attempt to contact the participant twice. After two attempts, study site staff may send a registered letter. If no response is received from the participant, the participant will be considered lost to follow up. All attempts to contact the participant and information received during contact attempts must be documented in the participant's medical record. In any circumstance, every effort should be made to document participant outcome, if possible. The investigator should inquire about the reason for withdrawal, request that the participant return for a final visit, if applicable, and follow-up with the participant regarding any unresolved adverse events (AEs).

If the participant withdraws from the study, and also withdraws consent for disclosure of future information, no further evaluations should be performed, and no additional data should be collected. The sponsor may retain and continue to use any data collected before such withdrawal of consent.

Participants who withdraw from the study may be replaced at the discretion of the investigator upon consultation with the sponsor.

7. ASSESSMENTS

Every effort should be made to ensure that the protocol-required tests and procedures are completed as described. However, it is anticipated that from time to time there may be circumstances outside of the control of the investigator that may make it unfeasible to perform the test. In these cases the investigator will take all steps necessary to ensure the safety and well-being of the participant. When a protocol-required test cannot be performed, the investigator will document the reason for this and any corrective and preventive actions that he or she has taken to ensure that normal processes are adhered to as soon as possible. The study team will be informed of these incidents in a timely manner.

For samples being collected and shipped, detailed collection, processing, storage, and shipment instructions and contact information will be provided to the investigator site prior to initiation of the study.

7.1. Photography

During the study, photographic images may be taken of the participant's skin. The photographs taken for this study are for source documentation purposes only and will not be evaluated, nor included in the clinical study report.

7.2. Pregnancy Testing

All pregnancy tests used in this study, either urine or serum, must have a sensitivity of at least 5 mIU/ml and must be performed by a certified laboratory. For female participants of childbearing potential, 2 negative pregnancy tests are required before receiving investigational product (1 negative pregnancy test at screening and 1 at the baseline visit immediately before investigational product administration). Following a negative pregnancy test result at screening, appropriate contraception according to Appendix 25 or Appendix 24 for participants from Germany must be commenced and the second negative pregnancy test result will then be required at the baseline visit and within 5 days after the first day of the menstrual period (counting the first day of the menstrual period as Day 1) before the participant may receive the investigational product. In the absence of regular menstrual bleeding, the study candidate should have used contraception according to Appendix 25 or Appendix 24 for Germany participants for at least 1 month before the second pregnancy test. Pregnancy tests will be repeated at every visit including treatment and follow-up visits, and at the end of the study to confirm that the participant has not become pregnant during the study. Pregnancy tests will also be conducted whenever 1 menstrual cycle is missed during the active treatment period and/or when potential pregnancy is otherwise suspected, and may be repeated if requested by institutional review boards (IRBs)/ethics committees (ECs) or if required by local regulations. In the case of a confirmed pregnancy, the participant will be withdrawn from administration of investigational product but should remain in the study for the early withdrawal visit.

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7.5. Safety Assessments

Safety will be assessed by the spontaneous reporting of AEs, physical examinations and clinical laboratory results. Unscheduled safety assessments may be performed at any time during the study to assess any perceived safety concerns. Investigators and Pfizer Clinicians will review individual participant data throughout the conduct of the study to ensure the well-being of study participants.

7.5.1. Chest X-RAY

Chest radiograph (posterior-anterior and lateral views are recommended, however, local guidelines should be followed). If another diagnostic image (ie, CT or MRI was already completed within 12 weeks prior to Day 1, this may be accepted). The image will show no evidence of current, active TB or previous inactive TB, general infections, heart failure or malignancy, and must be read by a qualified radiologist. Documentation of the official reading must be located and available in the source documentation.

7.5.2. Electrocardiogram

Single 12-lead ECGs should be collected at times specified in the Schedule of Activities.

All scheduled ECGs should be performed after the participant has rested quietly for at least 10 minutes in a supine position and prior to any blood collection procedures.

The Day 1 pre- dose ECG values will serve as each participant's baseline values. To ensure safety of the participants, a qualified individual (investigator or sub-investigator) at the investigator site will make comparisons to baseline measurements. A paper or digital copy of the ECG should be filed in the participant's chart and must be available to the sponsor upon request. Any clinically significant changes will be recorded as AEs and evaluated further, as clinically warranted. In some cases, it may be appropriate to repeat abnormal ECGs to rule out improper lead placement as contributing to the ECG abnormality.

7.5.3. Vital Signs

Vital signs (blood pressure, heart rate [pulse], respirations and temperature) will be measured after approximately 5 minutes of rest as indicated in the Schedule of Activities.

Blood pressure (BP) will be measured using a standard calibrated blood pressure measuring device. A BP device that uses multiple cuff sizes for the participant based on the arm circumference is required. The arm circumference at the midpoint of the length of the upper arm should be measured to determine the appropriate cuff size in accordance with the specifications of the BP measuring device. The same properly sized and calibrated blood pressure cuff will be used to measure blood pressure each time. The use of automated devices for measuring BP and heart rate (pulse) are acceptable, although, when done manually, heart rate will be measured in the brachial/radial artery for at least 30 seconds.

Participants should be seated in a chair, back supported, and arms bared (free of restrictions such as rolled-up sleeves, etc) and supported at the level of the heart. Measurements should be taken on the same arm (preferably the non-dominant arm) at each visit throughout the study after 5-10 minutes of rest and recorded to the nearest mm Hg. Participants should refrain from smoking or ingesting caffeine during the 30 minutes prior to the measurements.

Heart rate should be measured at approximately the same time as BP for a minimum of 30 seconds. When the timing of BP and heart rate measurements coincides with a blood collection or other study procedure, BP and heart rate should be obtained first.

It is preferred that body temperature be collected using the tympanic or oral methods and that the same method be used consistently throughout the study.

7.5.4. Medical History

A complete medical history will be taken including onset of DM disease. The clinical involvement of additional organs, (ie, lung, heart, liver) and prior DM treatments will be recorded. Participants should have had a standard work up for dermatomyositis (prior to) baseline. Stable interstitial lung disease related to DM that is not severe in the opinion of the investigator is allowed, ie, no supplemental oxygen permitted. If their DM diagnosis is within 2 years of the screening visit, then they must have completed either age appropriate malignancy screening and a CT of the chest/abdomen/pelvis; or Positron emission tomography (PET) CT of chest/abdomen/pelvis at least once prior to the baseline visit.

7.5.5. Physical Examinations

Complete physical examination (PE) must be performed by the investigator, sub-investigator or a qualified health professional per local guidelines. Complete PE consists of assessments of general appearance, skin, head, eyes, ears, nose and throat (HEENT), heart, lungs, breast (optional), abdomen, external genitalia (optional), extremities, neurologic function, back, and lymph nodes.

Targeted PE must be performed by the investigator, sub-investigator or a qualified health professional per local guidelines. Targeted PE consists of assessments of skin, heart, lungs, abdomen, and examination of body systems where there are symptom complaints by the participant. Target physical exam should be completed prior to dosing.

Complete and targeted physical examinations are performed at various time points, see Schedules of Activities.

7.5.6. Height and Weight

Height and weight will be measured without the participant wearing shoes. Height (inches or centimeters) and weight (pounds or kilograms) will be measured up to one decimal place and recorded in the source document at the baseline visit.

Height (inches or centimeters) will be measured at times according to the SOA. Weight will continue to be assessed and recorded at various time points, see Schedules of Activities.

7.5.7. Tuberculosis (TB) Screening and Monitoring

7.5.7.1. Interferon Gamma Release Assay (IGRA) Tuberculin Test

Participants should be screened for TB using an Interferon gamma release assay (IGRA) per local guidelines. IGRA will be tested during screening or within 12 weeks prior to Day 1. The following are acceptable IGRA assays: In-Tube test (QFT-GIT) and QuantiFERON®-TB Gold test (QFT-G). If T-spot®TB test was completed within 12 weeks prior to Day 1, this is acceptable, however this test type cannot be offered for participants requiring the test during screening, or treatment.

Site personnel should follow the processing and analyses steps based on the assay chosen. Ensure incubation steps are followed as appropriate. Documentation of IGRA product used and the test result must be in the participant's source documentation.

If the results of the IGRA are indeterminate, the test may be repeated, and if a negative result is obtained, enrollment may proceed. A positive test on repeat is exclusionary.

Participants with repeat indeterminate IGRA results may be enrolled after consultation with an infectious disease and/or pulmonary specialist who determines that the risk of infection is low (ie, participant would be acceptable for immunosuppressant treatment without additional action).

There is no additional scheduled testing for TB after screening. However, if at any time the participant has signs or symptoms associated with TB, the investigator should complete additional TB testing to ensure TB activation has not occurred.

Refer to lab manual for any additional processing information and shipping instructions.

7.5.8. Monitoring for Infections

Participants will be monitored for development of any infection (viral, bacterial, and fungal). Infections will be classified as either treated or non-treated infections. All treated infections occurring during the study require identification of the causative organism, if feasible, whether by culture, antigen assay, serology, etc. (as appropriate) and the results (eg, any identified organisms or absence of growth) recorded in the CRF.

Treated infections are infections that:

- Require antimicrobial therapy by any route of administration or;
- Require any surgical intervention (eg, incision and drainage).

Treated infections will be further classified as serious or non-serious. Serious infections are treated infections that:

- Require parenteral antimicrobial therapy or;
- Required hospitalization for treatment or;
- Meet other criteria that require the infection to be classified as a SAE.

A participant who experiences a serious infection should be discontinued from treatment. A serious infection should be reported as a SAE and should be listed as the reason for discontinuation in the CRF. All serious infections occurring during the study should undergo appropriate laboratory investigations, including culture, and the results (eg, any identified organisms or absence of growth) be recorded in the CRF.

7.5.9. Viral Surveillance

Blood sample for possible analysis of cytomegalovirus (CMV), Epstein-Barr virus (EBV), herpes simplex virus type 1 (HSV-1), herpes simplex virus type 2 (HSV-2) and varicella-zoster virus (VZV), Human Herpes Virus 6 (HHV6) and other viruses will be collected according to the times outlined in the Schedule of Activities. Additional sample collection instructions will be provided in the laboratory manual.

Note: Due to long turnaround time, the retrospective nature of these labs might make their reporting time quite delayed.

In addition to time points specified, a blood sample for viral surveillance sample may also be taken at the time of an AE, as clinically appropriate.

7.5.10. Biopsies

Punch biopsy is considered the primary technique for obtaining diagnostic full -thickness skin specimens. During this study punch biopsies (4 mm each) will be collected from all participants in the Stage 1, 2, and Amended Stage 2 of the study. Four punch biopsies will be collected at baseline Day 1. Two biopsies from an active skin lesion and two biopsies from skin that is healthy and free of any skin lesions, or discoloration. At Week 12, two biopsies will be collected from the same area as the baseline biopsies for the active lesion. For additional information on acceptable body locations for punch biopsy, please see the lab manual.

For participants enrolled in the Amended Stage 2 part of the study, an additional 2 biopsies will be collected at Week 24, Visit 9. Biopsies should be collected from the same active lesion area as previously collected. All biopsies will be analyzed to see if there are any changes from the baseline biopsies in an CCI manner, after study treatment.

Additional information on the collection and processing of the skin biopsies will be provided in the lab manual under separate cover. Histology and immunohistochemistry will be performed on tissue slices to understand changes in tissue morphology. RNA will be extracted to understand gene expression changes following treatment.

7.5.11. Infusion Site Reaction Assessment

Infusion site reactions will be assessed according to the Schedule of Activities. Infusion site reactions may include but are not limited to erythema, induration, ecchymosis, pain, and pruritus.

Any signs or symptoms related to an infusion site reaction should be treated according to the investigator's standard of care and reported as adverse events.

7.6. Rater Qualifications

7.6.1. CDASI

The primary and secondary endpoints for this study assess changes in the modified CDASI,[14] activity score as well as the individual components.

To ensure uniform conduct of the CDASI in participants with DM, investigators or other qualified site personnel will be required to go through training session(s) led by a qualified individual. Personnel responsible for conducting the CDASI will be permitted to complete CDASI assessments once training is completed and proper documentation of training is issued. It is highly recommended that the same individual conduct the CDASI assessment from visit to visit to decrease variability. It is also highly recommended that the same individual complete the Physician Global Assessment (PhGA, VAS) for consistency (See Appendix 3).

7.6.2. MMT-8 Stage 3

This partially validated tool assesses muscle strength using manual muscle testing (MMT). A 0 - 10 point scale is proposed for use. An abbreviated group of 8 proximal, distal, and axial muscles performs similarly to a total of 24 muscle groups, and is also proposed for use for research studies.

To ensure uniform conduct of the MMT-8 in participants with DM, investigators or other qualified site personnel will be required to go through training session(s) led by a qualified individual, or video training. Personnel responsible for conducting the MMT-8 will be permitted to complete MMT-8 assessments once training is completed and proper documentation of training is issued. It is highly recommended that the same individual conduct the CDASI assessment from visit to visit to decrease variability. (See Appendix 21).

7.6.3. MDAAT Stage 3

Global extramuscular disease activity is measured by the MDAAT, a tool with a comprehensive approach that assesses constitutional, cutaneous, skeletal, gastrointestinal, pulmonary, and cardiovascular activity. To ensure uniform conduct of the MDAAT in participants with DM, investigators or other qualified site personnel will be required to go through training session(s) led by a qualified individual, or video training. (See Appendix 20)

7.7. Patient Reported Outcomes

When the participant reports to the clinic for a visit, the order in which the patient reported outcomes are completed is important, and these assessments should be completed at every visit in the same consistent order. Please find the following descriptions of all patient reported outcomes used in this study.

7.7.1. The Short Form -36 Version 2, Acute (SF-36 v2 acute)

The Short Form (36) Health Survey (SF-36) version 2, acute is a 36 item generic health status measure.[15,16,17] It measures 8 health domains: physical function, role physical, bodily pain, general health, vitality, social functioning, role emotional, and mental health. These domains can be summarized as physical component scores (PCS) and mental component scores (MCS). The SF-36 acute version uses a one-week recall and is suitable for use when the measure is administered repeatedly on a weekly basis. The SF-36 will be collected as indicated in the Schedule of Activities. A copy of the SF-36 version 2, acute questionnaire can be found in Appendix 7.

7.7.2. 5-D Pruritus Scale

The 5-D Pruritus Scale measures five dimensions of itch: degree, duration, direction, disability and distribution.[18] This patient-reported questionnaire is a multidimensional Likert response instrument designed to evaluate several components of chronic pruritus, including the areas of the body affected, itch intensity, course of itch through the day, impact on sleep and activities of daily living and disability induced by the pruritus and whether or not the symptom has changed in the past two weeks and would provide pruritus assessments

complementary to the unidimensional itch instruments, which for example measure intensity without impact on quality of life daily.[19,20,21,22,23] The 5-D Pruritus Scale was validated in participants with dermatological and systemic diseases and has a recall period of two weeks.[22] The 5-D Pruritus Scale will be collected as indicated in the Schedule of Activities. A copy of the scale can be found in Appendix 9.

7.7.3. Dermatology and Life Quality Index (DLQI)

The DLQI (Dermatology and Life Quality Index) is a 10-item, validated patient-reported questionnaire used in clinical practice and clinical trials to assess the impact of skin conditions on quality of life. This 10-item questionnaire is applicable to participants with various skin diseases and has a recall period of one Week24. The DLQI is calculated by summing the score of each question resulting in a minimum of 0 to maximum of 30, with a higher score indicating a greater QoL impairment. Using a Likert scale, this questionnaire assesses symptoms and feelings, daily activities, leisure, work and school, personal relationships, and distress as related to the participant's skin condition. The DLQI will be collected as indicated in the Schedule of Activities. A copy of the DLQI can be found in Appendix 8.

7.7.4. Health Assessment Questionnaire – Disability Index (HAQ-DI) start

Participants will complete the HAQ-DI that assesses the degree of difficulty a patient has experienced during the past week in 8 domains of daily living activities: dressing and grooming, arising, eating, walking, hygiene, reach, grip, and other activities.[25]

- For each of these eight domains, the patient reports the amount of difficulty they have in performing specific activities. For each question, the level of difficulty is scored from 0 to 3 with 0 representing "without any difficulty," and 3 as "unable to do." Participants should complete the section on activities that require them to use aids and/or devices or if they need help from another person. These sections may be left blank if no aids or devices are required or no help from another person is needed. The HAQ-DI will be collected as indicated in the Schedule of Activities. A copy of the HAQ-DI questionnaire can be found in Appendix 12.

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7.7.6. Patient's Global Assessment (PtGA)

The Patient's Global Assessment (PtGA) is a single item question to measure the global evaluation as reported by the patient. The PtGA question assesses the patient's overall activity at the time of assessment using a 10 cm visual analog scale (VAS) by asking the patient to answer: "Your myositis is the result of the combined effects of many disease processes. One of these is disease activity, which is active inflammation in your muscles, skin, joints, intestines, heart, lungs or other parts of your body, which can improve when treated with medicines. Considering all the ways that myositis affects you, please rate the overall activity of your disease today by placing a mark on the line below." Higher scores indicate extremely active or severe disease activity.[29,30] The PtGA will be collected as indicated in the Schedule of Activities. A copy of PtGA questionnaire can be found in Appendix 13.

7.7.8. Functional Assessment of Chronic Illness Therapy - fatigue (FACIT-F)

The Functional Assessment of Chronic Illness Therapy - fatigue (FACIT-F) scale is a 13-item instrument to measure fatigue or tiredness and its impact on a patient's daily activities and functioning. The FACIT-F includes items such as tiredness, weakness, lack of energy, and the impact of these feelings on daily functioning (eg, sleeping, and social activities). The content validity and psychometric properties of the instrument have been established in different chronic conditions including rheumatoid arthritis, psoriatic arthritis, systemic lupus erythematosus etc. Each item is scored from 0 to 4 with 0 representing "Not at all" to 4 as "Very much". To score the FACIT-F, all items are summed to create a single fatigue score with a range from 0 to 52. Items are reverse scored when appropriate to provide a scale in which higher scores represent better functioning or less fatigue. The FACIT-F will be collected as indicated in the Schedule of Activities. A copy of the FACIT-F can be found in Appendix 11.

For this study, participants in Stage 2, the Amended Stage 2, and Stage 3 will complete the patient reported outcomes in the following order, prior to any other clinical assessments:

7.7.9. Stage 2 PRO Measures

1. 5D Pruritus Scale.

2. SF-36 v2 acute.

3. DLQI.

7.7.10. Amended Stage 2 PRO Measures

1. PtGA.
2. HAQ-DI.
3. 5-D Pruritus Scale.

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5. SF-36 v2 acute.
6. DLQI.

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7.7.11. Stage 3 PRO Measures

1. PtGA.
2. HAQ-DI.
3. 5-D Pruritus Scale.

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5. FACIT-F.
6. SF-36 v2 acute.

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The DLQI and the FACIT-F need to be assessed only in the skin cohort and the muscle cohort, respectively. When the participant reports to the clinic for a visit, the order in which the patient reported outcomes are completed is important, and these assessments should be completed **at every visit in the chronological order for both the cohorts as listed above. These patient reported outcomes should be completed prior to any other clinical activities and checked by site staff for completeness.**

7.8. Physician Clinician Assessment

7.8.1. Physician Global Assessment (PhGA, Visual Analogue Scale VAS)

The Physician Global Assessment (PhGA, VAS) is an assessment of the participant's general health status rather than the disease activity in a specific organ (Appendix 3). The investigator will be asked to make a mark on a visual analog scale answering the question "The patient's DM at this time is". The scale uses a 100 mm VAS which has verbal anchors

at 0 (very good) and 100 (very poor). The investigator is asked to evaluate the participant's overall disease activity and response to treatment at the time of the clinic visit.

This assessment should be completed by the same physician completing the CDASI.

7.9. Total Improvement Score for Stage 3

There are 6 core set measures that comprise the total improvement score. These components are the physician global activity assessment, the patient global activity assessment, MMT-8 score, HAQ- DI score, the myositis disease activity assessment tool, (MDAAT), and the participant's most elevated muscle enzymes. The total improvement score is the sum of all 6 improvement scores associated with the change in each core set measure. See Appendix 22.

7.10. Clinical Laboratory Tests

The following laboratory tests will be performed at time points defined in the Schedule of Activities. Sample collection, labeling, storage and shipping instructions can be found in the laboratory manual.

Additional blood samples may need to be collected at times not specified in the protocol (eg, replacement of clotted or compromised specimens, or repeat of clinically significant out of range laboratory results.

Laboratory tests may be repeated once during screening; the last value will be used to determine participant eligibility. Unscheduled clinical labs may be obtained at any time during the study to assess any perceived safety concerns at the investigator's discretion. All laboratory tests with clinically important changes from baseline identified after administration of investigational product will be followed until the value stabilizes.

For samples that are collected for safety labs or pharmacokinetics, sample that remains after the intended analysis may be used to better understand potential adverse events.

Table 1. Laboratory Tests

Hematology	Chemistry	Urinalysis	Other
Hemoglobin	BUN and Creatinine	pH	HBsAg[c]
Hematocrit	Creatine Phosphokinase	Glucose (qual)	HBcAb[c]
RBC count	Glucose (fasting & non fasting)	Protein (qual)	HCVAb[c]
Platelet count	Sodium	Blood (qual)	HIV[c]
WBC count with differential	Potassium	Ketones	HepB reflex,[c] *if applicable*
Total neutrophils (%, Abs)	Chloride	Nitrites	
Eosinophils (%, Abs)	Calcium	Leukocyte esterase	β-hCG[d]
Basophils (%, Abs)	Total CO_2 (Bicarbonate)	Microscopy[b]	FSH[d]
Lymphocytes (%, Abs)	AST, ALT	Spot Urine (Upr:Ucr)[e]	(QFT-GIT or QFT-G)
Monocytes (%, Abs)	LDH		Viral surveillance (may include)
Reticulocyte count (%, Abs)	Aldolase		*CMV*
PT/PTT	CKMB (Only if CPK is elevated)		*EBV*
	Total Indirect and Direct Bilirubin		*HSV-1 and HSV-2*
	Alkaline phosphatase		*VZV, HHV6*
	Uric acid		
	Albumin Total protein		
	Lipid Profile Panel:[a]		
	Total Cholesterol		
	LDL-Cholesterol (direct)		
	HDL-Cholesterol		
	Triglycerides		

a. Lipid profile panel will be completed on Day 1, Week 4, Week 8, Week 12, Week 16, Week 20, Week 24, and Week 28 (and if applicable, at participant withdrawal/early withdrawal and post-withdrawal visits).

b. Only if urine dipstick is positive for blood or protein.

c. At screening only; confirmation and documentation of negative HIV test result within 3 months prior to screening is acceptable.

d. Serum/urine pregnancy tests for (WOCBP); serum pregnancy test must be performed at screening for all WOCBP as defined in the eligibility criteria (if serum pregnancy test is borderline positive, the central laboratory will run a FSH test to confirm menopause if the participant has missed her periods <12 months); urine pregnancy test must be performed at baseline for all WOCBP prior to dosing with investigational product and at all subsequent visits. FSH for women of non-child bearing potential, (WONCBP) only; at screening only.

e. Spot Urine Protein and creatinine.

Table 2. Additional Lab Testing

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Gene signature panel
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Refer to the schedule of activities for collection times.

a. Several exploratory biomarkers will be collected at specified time points. Some will be evaluated in real time; others stored for future analysis.

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7.11.1. Samples for IP-10 Analysis

Blood samples to provide serum for the analysis of IP-10 will be collected into appropriately labeled tubes according to the times outlined in the Schedule of Activities.

7.11.2. Samples for hsCRP Analysis

Blood samples to provide serum for the analysis of hsCRP will be collected into appropriately labeled tubes according to the times outlined in the Schedule of Activities.

7.11.3. Samples for MX-A Analysis

Whole blood samples for the analysis of MXA will be collected into appropriately labeled tubes according to the times outlined in the Schedule of Activities.

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7.11.6. Gene Signature Panel

Blood samples to be assayed with a gene signature panel will be collected into appropriately labeled tubes according to the times outlined in the Schedule of Activities.

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7.13. Shipment of Pharmacokinetic Samples

The shipment address and contact information will be provided to the investigator site prior to the initiation of the study. The central laboratory will provide collection materials and directions for packaging and shipment of samples and will forward samples to the contract analytical laboratory. The contract analytical laboratory will be provided with randomization codes so that only samples in the PF-06823859 treatment groups are assayed. Placebo samples may be assayed in the event of suspected error in participant randomization. Refer to the central laboratory manual for further information.

7.14. Immunogenicity

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8. ADVERSE EVENT REPORTING

8.1. Requirements

The table below summarizes the requirements for recording safety events on the CRF and for reporting safety events on the Clinical Trial (CT) Serious Adverse Event (SAE) Report Form to Pfizer Safety. These requirements are delineated for 3 types of events: (1) SAEs; (2) non-serious adverse events (AEs); and (3) exposure to the investigational product under study during pregnancy or breastfeeding, and occupational exposure.

Safety Event	Recorded on the CRF	Reported on the CT SAE Report Form to Pfizer Safety Within 24 Hours of Awareness
SAE	All	All
Non-serious AE	All	None
Exposure to the investigational product under study during pregnancy or breastfeeding, and occupational exposure	All (regardless of whether associated with an AE), **except occupational exposure**	Exposure during pregnancy, exposure via breastfeeding, occupational exposure (regardless of whether associated with an AE)

All observed or volunteered events regardless of treatment group or suspected causal relationship to the investigational product(s) will be reported as described in the following paragraphs.

Events listed in the table above that require reporting to Pfizer Safety on the CT SAE Report Form within 24 hours of awareness of the event by the investigator **are to be reported regardless of whether the event is determined by the investigator to be related to an investigational product under study**. In particular, if the SAE is fatal or life-threatening, notification to Pfizer Safety must be made immediately, irrespective of the extent of available event information. This time frame also applies to additional new (follow-up) information on previously forwarded reports. In the rare situation that the investigator does not become immediately aware of the occurrence of an event, the investigator must report the event within 24 hours after learning of it and document the time of his/her first awareness of the event.

For each event, the investigator must pursue and obtain adequate information both to determine the outcome and to assess whether it meets the criteria for classification as an SAE (see Section 8.2.3). In addition, the investigator may be requested by Pfizer Safety to obtain specific follow-up information in an expedited fashion. This information is more detailed than that recorded on the CRF. In general, this will include a description of the event in sufficient detail to allow for a complete medical assessment of the case and independent determination of possible causality. Any information relevant to the event, such as concomitant medications and illnesses, must be provided. In the case of a participant death, a summary of available autopsy findings must be submitted as soon as possible to Pfizer Safety. Any pertinent additional information must be reported on the CT SAE Report Form; additional source documents (eg, medical records, CRF, laboratory data) are to be sent to Pfizer Safety ONLY upon request.

As part of ongoing safety reviews conducted by the sponsor, any non-serious AE that is determined by the sponsor to be serious will be reported by the sponsor as an SAE. To assist in the determination of case seriousness, further information may be requested from the investigator to provide clarity and understanding of the event in the context of the clinical study.

8.1.1. Additional Details on Recording Adverse Events on the CRF

All events detailed in the table above will be recorded on the AE page(s) of the CRF. It should be noted that the CT SAE Report Form for reporting of SAE information is not the same as the AE page of the CRF. When the same data are collected, the forms must be completed in a consistent manner. AEs should be recorded using concise medical terminology and the same AE term should be used on both the CRF and the CT SAE Report Form for reporting of SAE information.

8.1.2. Eliciting Adverse Event Information

The investigator is to record on the CRF all directly observed AEs and all AEs spontaneously reported by the study participant. In addition, each study participant will be questioned about the occurrence of AEs in a non-leading manner.

8.1.3. Withdrawal from the Study Due to Adverse Events (see also the Participant Withdrawal (Early Termination) section)

Withdrawal due to AEs should be distinguished from withdrawal due to other causes, according to the definition of AE noted below, and recorded on the CRF.

When a participant withdraws from the study because of an SAE, the SAE must be recorded on the CRF and reported, as appropriate, on the CT SAE Report Form, in accordance with the Requirements section above.

8.1.4. Time Period for Collecting AE/SAE Information

The time period for actively eliciting and collecting AEs and SAEs ("active collection period") for each participant begins from the time the participant provides informed consent, which is obtained before the participant's participation in the study (ie, before undergoing any study-related procedure and/or receiving investigational product), through and including a minimum of 5 months after the last administration of the investigational product.

For participants who are screen failures, the active collection period ends when screen failure status is determined.

8.1.4.1. Reporting SAEs to Pfizer Safety

All SAEs occurring in a participant during the active collection period are reported to Pfizer Safety on the CT SAE Report Form.

SAEs occurring in a participant after the active collection period has ended are reported to Pfizer Safety if the investigator becomes aware of them; at a minimum, all SAEs that the investigator believes have at least a reasonable possibility of being related to investigational product must be reported to Pfizer Safety.

Follow up by the investigator continues throughout and after the active collection period and until the event or its sequelae resolve or stabilize at a level acceptable to the investigator, and Pfizer concurs with that assessment.

8.1.4.2. Recording Non-serious AEs and SAEs on the CRF

During the active collection period, both non-serious AEs and SAEs are recorded on the CRF.

Follow-up by the investigator may be required until the event or its sequelae resolve or stabilize at a level acceptable to the investigator, and Pfizer concurs with that assessment.

8.1.5. Causality Assessment

The investigator's assessment of causality must be provided for all AEs (serious and non-serious); the investigator must record the causal relationship on the CRF, and report such an assessment in accordance with the SAE reporting requirements, if applicable. An investigator's causality assessment is the determination of whether there exists a reasonable possibility that the investigational product caused or contributed to an AE; generally the facts (evidence) or arguments to suggest a causal relationship should be provided. If the investigator does not know whether or not the investigational product caused the event, then the event will be handled as "related to investigational product" for reporting purposes, as defined by the sponsor. If the investigator's causality assessment is "unknown but not related" to investigational product, this should be clearly documented on study records.

In addition, if the investigator determines that an SAE is associated with study procedures, the investigator must record this causal relationship in the source documents and CRF, and report such an assessment in the dedicated section of the CT SAE Report Form and in accordance with the SAE reporting requirements.

8.1.6. Sponsor's Reporting Requirements to Regulatory Authorities

AE reporting, including suspected unexpected serious adverse reactions, will be carried out in accordance with applicable local regulations.

8.2. Definitions

8.2.1. Adverse Events

An AE is any untoward medical occurrence in a study participant administered a product or medical device; the event need not necessarily have a causal relationship with the treatment or usage. Examples of AEs include, but are not limited to:

- Abnormal test findings;

- Clinically significant signs and symptoms;
- Changes in physical examination findings;
- Hypersensitivity;
- Progression/worsening of underlying disease;
- Drug abuse;
- Drug dependency.

Additionally, AEs may include signs and symptoms resulting from:

- Drug overdose;
- Drug withdrawal;
- Drug misuse;
- Drug interactions;
- Extravasation;
- Exposure during pregnancy (EDP);
- Exposure via breastfeeding;
- Medication error;
- Occupational exposure.

8.2.2. Abnormal Test Findings

Abnormal objective test findings should be recorded as AEs when any of the following conditions are met:

- Test result is associated with accompanying symptoms; and/or
- Test result requires additional diagnostic testing or medical/surgical intervention; and/or
- Test result leads to a change in study dosing (outside of any protocol-specified dose adjustments) or discontinuation from the study, significant additional concomitant drug treatment, or other therapy; and/or
- Test result is considered to be an AE by the investigator or sponsor.

Merely repeating an abnormal test, in the absence of any of the above conditions, does not constitute an AE. Any abnormal test result that is determined to be an error does not require recording as an AE.

8.2.3. Serious Adverse Events

A serious adverse event is any untoward medical occurrence at any dose that:

- Results in death;
- Is life-threatening (immediate risk of death);
- Requires inpatient hospitalization or prolongation of existing hospitalization;
- Results in persistent or significant disability/incapacity (substantial disruption of the ability to conduct normal life functions);
- Results in congenital anomaly/birth defect.

Or that is considered to be:

- An important medical event.

Medical and scientific judgment is exercised in determining whether an event is an important medical event. An important medical event may not be immediately life-threatening and/or result in death or hospitalization. However, if it is determined that the event may jeopardize the participant or may require intervention to prevent one of the other AE outcomes, the important medical event should be reported as serious.

Examples of such events are intensive treatment in an emergency room or at home for allergic bronchospasm; blood dyscrasias or convulsions that do not result in hospitalization; or development of drug dependency or drug abuse.

8.2.4. Hospitalization

Hospitalization is defined as any initial admission (even less than 24 hours) in a hospital or equivalent healthcare facility, or any prolongation of an existing admission. Admission also includes transfer within the hospital to an acute/intensive care unit (eg, from the psychiatric wing to a medical floor, medical floor to a coronary care unit, or neurological floor to a tuberculosis unit). An emergency room visit does not necessarily constitute a hospitalization; however, the event leading to the emergency room visit is assessed for medical importance.

Hospitalization does not include the following:

- Rehabilitation facilities;
- Hospice facilities;

- Respite care (eg, caregiver relief);
- Skilled nursing facilities;
- Nursing homes;
- Same-day surgeries (as outpatient/same-day/ambulatory procedures).

Hospitalization or prolongation of hospitalization in the absence of a precipitating clinical AE is not in itself an SAE. Examples include:

- Admission for treatment of a preexisting condition not associated with the development of a new AE or with a worsening of the preexisting condition (eg, for workup of a persistent pretreatment laboratory abnormality);
- Social admission (eg, participant has no place to sleep);
- Administrative admission (eg, for yearly physical examination);
- Protocol-specified admission during a study (eg, for a procedure required by the study protocol);
- Optional admission not associated with a precipitating clinical AE (eg, for elective cosmetic surgery);
- Hospitalization for observation without a medical AE;
- Preplanned treatments or surgical procedures. These should be noted in the baseline documentation for the entire protocol and/or for the individual participant.

Diagnostic and therapeutic noninvasive and invasive procedures, such as surgery, should not be reported as SAEs. However, the medical condition for which the procedure was performed should be reported if it meets the definition of an SAE. For example, an acute appendicitis that begins during the reporting period should be reported if the SAE requirements are met, and the resulting appendectomy should be recorded as treatment of the AE.

8.3. Severity Assessment

If required on the AE page of the CRF, the investigator will use the adjectives MILD, MODERATE, or SEVERE to describe the maximum intensity of the AE. For purposes of consistency, these intensity grades are defined as follows:	
MILD	Does not interfere with participant's usual function.
MODERATE	Interferes to some extent with participant's usual function.
SEVERE	Interferes significantly with participant's usual function.

Note the distinction between the severity and the seriousness of an AE. A severe event is not necessarily an SAE. For example, a headache may be severe (interferes significantly with the participant's usual function) but would not be classified as serious unless it met one of the criteria for SAEs, listed above.

8.4. Special Situations

8.4.1. Protocol -Specified Serious Adverse Events

There are no protocol -specified SAEs in this study. All SAEs will be reported to Pfizer Safety by the investigator as described in previous sections, and will be handled as SAEs in the safety database.

8.4.2. Potential Cases of Drug -Induced Liver Injury

Humans exposed to a drug who show no sign of liver injury (as determined by elevations in transaminases) are termed “tolerators,” while those who show transient liver injury, but adapt are termed “adaptors.” In some participants, transaminase elevations are a harbinger of a more serious potential outcome. These participants fail to adapt and therefore are "susceptible" to progressive and serious liver injury, commonly referred to as drug -induced liver injury (DILI). Participants who experience a transaminase elevation above 3 times the upper limit of normal (× ULN) should be monitored more frequently to determine if they are an “adaptor” or are “susceptible.”

In the majority of DILI cases, elevations in aspartate aminotransferase (AST) and/or alanine aminotransferase (ALT) precede total bilirubin (TBili) elevations (>2 × ULN) by several days or weeks. The increase in TBili typically occurs while AST/ALT is/are still elevated above 3 × ULN (ie, AST/ALT and TBili values will be elevated within the same lab sample). In rare instances, by the time TBili elevations are detected, AST/ALT values might have decreased. This occurrence is still regarded as a potential DILI. Therefore, abnormal elevations in either AST OR ALT in addition to TBili that meet the criteria outlined below are considered potential DILI (assessed per Hy’s law criteria) cases and should always be considered important medical events, even before all other possible causes of liver injury have been excluded.

The threshold of laboratory abnormalities for a potential DILI case depends on the participant’s individual baseline values and underlying conditions. Participants who present with the following laboratory abnormalities should be evaluated further as potential DILI (Hy’s law) cases to definitively determine the etiology of the abnormal laboratory values:

- Participants with AST/ALT and TBili baseline values within the normal range who subsequently present with AST OR ALT values >3 × ULN AND a TBili value >2 × ULN with no evidence of hemolysis and an alkaline phosphatase value <2 × ULN or not available;

- For participants with baseline AST OR ALT OR TBili values above the ULN, the following threshold values are used in the definition mentioned above, as needed, depending on which values are above the ULN at baseline:

- Preexisting AST or ALT baseline values above the normal range: AST or ALT values >2 times the baseline values AND >3 × ULN; or >8 × ULN (whichever is smaller).

- Preexisting values of TBili above the normal range: TBili level increased from baseline value by an amount of at least 1 × ULN or if the value reaches >3 × ULN (whichever is smaller).

Rises in AST/ALT and TBili separated by more than a few weeks should be assessed individually based on clinical judgment; any case where uncertainty remains as to whether it represents a potential Hy's law case should be reviewed with the sponsor.

The participant should return to the investigator site and be evaluated as soon as possible, preferably within 48 hours from awareness of the abnormal results. This evaluation should include laboratory tests, detailed history, and physical assessment.

In addition to repeating measurements of AST and ALT and TBili, laboratory tests should include albumin, creatine kinase (CK), direct and indirect bilirubin, gamma-glutamyl transferase (GGT), prothrombin time (PT)/international normalized ratio (INR), total bile acids, alkaline phosphatase and acetaminophen drug and/or protein adduct levels. Consideration should also be given to drawing a separate tube of clotted blood and an anticoagulated tube of blood for further testing, as needed, for further contemporaneous analyses at the time of the recognized initial abnormalities to determine etiology. A detailed history, including relevant information, such as review of ethanol, acetaminophen (either by itself or as a co formulated product in prescription or over-the-counter medications), recreational drug, supplement (herbal) use and consumption, family history, sexual history, travel history, history of contact with a jaundiced person, surgery, blood transfusion, history of liver or allergic disease, and potential occupational exposure to chemicals, should be collected. Further testing for acute hepatitis A, B, C, D, and E infection and liver imaging (eg, biliary tract) may be warranted.

All cases demonstrated on repeat testing as meeting the laboratory criteria of AST/ALT and TBili elevation defined above should be considered potential DILI (Hy's law) cases if no other reason for the liver function test (LFT) abnormalities has yet been found. **Such potential DILI (Hy's law) cases are to be reported as SAEs, irrespective of availability of all the results of the investigations performed to determine etiology of the LFT abnormalities.**

A potential DILI (Hy's law) case becomes a confirmed case only after all results of reasonable investigations have been received and have excluded an alternative etiology.

Please Note:

For Participants with DM who experience elevated AST, ALT, LDH, aldolase, and CK, due to muscle involvement the investigator should determine whether or not these are related to the existing condition of DM or if these lab abnormalities are related to another condition. Information should be provided in the source documentation with rationale related to any lab abnormalities.

8.4.3. Exposure to the Investigational Product During Pregnancy or Breastfeeding, and Occupational Exposure

Exposure to the investigational product under study during pregnancy or breastfeeding and occupational exposure are reportable to Pfizer Safety within 24 hours of investigator awareness.

8.4.3.1. Exposure during Pregnancy

For both unapproved/unlicensed products and for marketed products, an exposure during pregnancy (EDP) occurs if:

- A female becomes, or is found to be, pregnant either while receiving or having been exposed (eg, because of treatment or environmental exposure) to the investigational product; or the female becomes or is found to be pregnant after discontinuing and/or being exposed to the investigational product;
    - An example of environmental exposure would be a case involving direct contact with a Pfizer product in a pregnant woman (eg, a nurse reports that she is pregnant and has been exposed to chemotherapeutic products).
    - A male has been exposed (eg, because of treatment or environmental exposure) to the investigational product prior to or around the time of conception and/or is exposed during his partner's pregnancy.

If a participant or participant's partner becomes or is found to be pregnant during the participant's treatment with the investigational product, the investigator must report this information to Pfizer Safety on the CT SAE Report Form and an EDP supplemental form, regardless of whether an SAE has occurred. In addition, the investigator must submit information regarding environmental exposure to a Pfizer product in a pregnant woman (eg, participant reports that she is pregnant and has been exposed to a cytotoxic product by inhalation or spillage) to Pfizer Safety using the EDP supplemental form. This must be done irrespective of whether an AE has occurred and within 24 hours of awareness of the exposure. The information submitted should include the anticipated date of delivery (see below for information related to termination of pregnancy).

Follow-up is conducted to obtain general information on the pregnancy and its outcome for all EDP reports with an unknown outcome. The investigator will follow the pregnancy until completion (or until pregnancy termination) and notify Pfizer Safety of the outcome as a follow-up to the initial EDP supplemental form. In the case of a live birth, the structural

integrity of the neonate can be assessed at the time of birth. In the event of a termination, the reason(s) for termination should be specified and, if clinically possible, the structural integrity of the terminated fetus should be assessed by gross visual inspection (unless pre-procedure test findings are conclusive for a congenital anomaly and the findings are reported).

If the outcome of the pregnancy meets the criteria for an SAE (ie, ectopic pregnancy, spontaneous abortion, intrauterine fetal demise, neonatal death, or congenital anomaly [in a live-born baby, a terminated fetus, an intrauterine fetal demise, or a neonatal death]), the investigator should follow the procedures for reporting SAEs.

Additional information about pregnancy outcomes that are reported to Pfizer Safety as SAEs follows:

- Spontaneous abortion includes miscarriage and missed abortion;
- Neonatal deaths that occur within 1 month of birth should be reported, without regard to causality, as SAEs. In addition, infant deaths after 1 month should be reported as SAEs when the investigator assesses the infant death as related or possibly related to exposure to the investigational product.

Additional information regarding the EDP may be requested by the sponsor. Further follow-up of birth outcomes will be handled on a case-by-case basis (eg, follow-up on preterm infants to identify developmental delays). In the case of paternal exposure, the investigator will provide the participant with the Pregnant Partner Release of Information Form to deliver to his partner. The investigator must document in the source documents that the participant was given the Pregnant Partner Release of Information Form to provide to his partner.

8.4.3.2. Exposure during Breastfeeding

Scenarios of exposure during breastfeeding must be reported, irrespective of the presence of an associated SAE, to Pfizer Safety within 24 hours of the investigator's awareness, using the CT SAE Report Form. An exposure during breastfeeding report is not created when a Pfizer drug specifically approved for use in breastfeeding women (eg, vitamins) is administered in accord with authorized use. However, if the infant experiences an SAE associated with such a drug's administration, the SAE is reported together with the exposure during breastfeeding.

8.4.3.3. Occupational Exposure

An occupational exposure occurs when, during the performance of job duties, a person (whether a healthcare professional or otherwise) gets in unplanned direct contact with the product, which may or may not lead to the occurrence of an AE.

An occupational exposure is reported to Pfizer Safety within 24 hours of the investigator's awareness, using the CT SAE Report Form, regardless of whether there is an associated SAE. Since the information does not pertain to a participant enrolled in the study, the information is not recorded on a CRF; however, a copy of the completed CT SAE Report Form is maintained in the investigator site file.

8.4.4. Medication Errors

Other exposures to the investigational product under study may occur in clinical trial settings, such as medication errors.

Safety Event	Recorded on the CRF	Reported on the CT SAE Report Form to Pfizer Safety Within 24 Hours of Awareness
Medication errors	All (regardless of whether associated with an AE)	Only if associated with an SAE

8.5. Medication Errors

Medication errors may result from the administration or consumption of the investigational product by the wrong participant, or at the wrong time, or at the wrong dosage strength Medication errors include:

- Medication errors involving participant exposure to the investigational product;
- Potential medication errors or uses outside of what is foreseen in the protocol that do or do not involve the participating participant.

Such medication errors occurring to a study participant are to be captured on the medication error page of the CRF, which is a specific version of the AE page.

In the event of a medication dosing error, the sponsor should be notified immediately.

Whether or not the medication error is accompanied by an AE, as determined by the investigator, the medication error is recorded on the medication error page of the CRF and, if applicable, any associated AE(s), serious and non-serious, are recorded on an AE page of the CRF.

Medication errors should be reported to Pfizer Safety within 24 hours on a CT SAE Report Form **only when associated with an SAE**.

9. DATA ANALYSIS/STATISTICAL METHODS

Detailed methodology for summary and statistical analyses of the data collected in this study is outlined here and further detailed in a statistical analysis plan (SAP), which will be maintained by the sponsor. The SAP may modify what is outlined in the protocol where appropriate; however, any major modifications of the primary endpoint definitions or their analyses will also be reflected in a protocol amendment.

At the completion of Stage 1, the team may provide limited summary level (but not patient level) data that may be shared externally and internally. This will be considered preliminary data and the timing of the data release will be contingent on internal Pfizer procedures to maintain data integrity. During this time, the investigators and select list of individuals from the sponsor who interact with the investigators and monitor safety will continue to be blinded to individual study treatments through the query resolution of the Stage 1 data. Patient level data will not be shared with the investigators until the entire study is complete.

9.1. Sample Size Determination

9.1.1. Sample Size Determination in Stage 1

The primary endpoint is the change from baseline in CDASI activity score at Week 12. The treatment effect is defined as the difference (mean change from baseline at Week 12 in the active treatment group minus the mean change from baseline at Week 12 in the placebo group) in the mean change of CDASI activity score from baseline at Week 12. A successful treatment should *decrease* CDASI activity score and therefore the desirable value of the treatment effect is negative. The value -5 is viewed as the minimal clinically important value of the treatment effect.

In the comparison of the active treatment arm to placebo, the treatment is declared efficacious if both of the following conditions are satisfied:

- C1: Estimated value of the treatment effect is lower than -5.
- C2: An upper limit of 2-sided 90% confidence interval for the treatment effect is below zero.

The standard deviation of the change from baseline in CDASI activity score is assumed to be equal to 8 units. This assumption is based on the analysis of the observational data sets collected by the researchers at Pfizer's Center of Therapeutic Innovation and University of Pennsylvania.

A sample size of 24 participants (16 participants in the active and 8 participants in the placebo treatment groups) with complete response is expected to provide 80% probability of declaring efficacy (satisfying both of the conditions C1 and C2) for the reference value of the true treatment effect equal to -8.6 units.

It is assumed that 80% of randomized participants will provide complete responses of CDASI activity score at Week 12.

9.1.2. Sample Size Determination in Stage 2

The primary endpoint is the change from baseline in CDASI activity score at Week 12. Baseline is defined as Day 1. For each active treatment group, the treatment effect is defined as the difference (between the active treatment group and the placebo group across the two stages) in the mean change of CDASI activity score from baseline at Week 12. The standard deviation of the change from baseline CDASI activity score is assumed to be 8 units.

For the comparison of 150 mg PF-06823859 and placebo, assuming a SD of 8 and assuming a pooled sample size of approximately 10 and 11 completers respectively across the two Stages, we expect the half length of the 90% CI to be 5.75. For the comparison of 600 mg PF-06823859 and placebo, assuming a SD of 8 and assuming a pooled sample size of approximately 21 and 11 completers respectively across the two Stages, we expect the half length of the 90% CI to be 4.90.

No p-values will be presented for the comparisons listed in the objectives and endpoints of Section 2.2 for Stage 2.

9.1.3. Sample Size Determination in Stage 3

The major efficacy endpoint of interest in Stage 3 is the TIS,[31] which is a continuous measure ranging from 0 to 100. The treatment effect is defined as the difference in mean TIS between the active and placebo treatment groups at Week 12. The standard deviation in TIS at Week 12 is estimated to be between 15 and 25 units.[32,33]

The DM muscle disease cohort will enroll between 8 and 16 participants randomized 1:1 to active and placebo. Table 3 shows the estimated half widths of the 90% confidence intervals for the difference in mean TIS between the PF-06823859 600 mg arm and the placebo arm at Week 12 across a range of standard deviations and number of completers. For example, if 10 participants (5 active, 5 placebo) complete the Week 12 assessment and the SD of the TIS is 20, the estimated half width of the 90% confidence interval is approximately 20.8.

No p-values will be presented for the comparisons listed in the objectives and endpoints of Section 2.4 for the DM muscle cohort.

Table 3. Estimated Half-widths of 90% Confidence Intervals for the Difference in TIS between Active and Placebo at Week 12

Number of completers (active: placebo)	Assumed SD of TIS	Half width of 90% CI
8 (4:4)	15	17.4
	20	23.3
	25	29.1
10 (5:5)	15	15.6
	20	20.8
	25	26.0
12 (6:6)	15	14.2
	20	19.0
	25	23.7
14 (7:7)	15	13.2
	20	17.6
	25	22.0
16 (8:8)	15	12.3
	20	16.4
	25	20.6

9.2. Efficacy Analysis

The primary efficacy analysis of Stage 1 and Stage 2 is based on the CDASI activity scores at Week 12. The primary efficacy analysis in Stage 3 is based on the TIS at Week 12. Analysis of efficacy endpoints will be performed for the modified intenttotreat (mITT) population, defined as all randomized participants who receive at least 1 dose of investigational product. Formal statistical testing for efficacy will be based on Stage 1 data only.

All treatment periods in this study will be conducted in a double blinded fashion. During this period, the participants, investigators and sponsor (or designee) will be blinded to randomized study treatments. After the treatment period is completed for all the participants, some members of the study team will be unblinded so that a report for the corresponding data can be generated. The participants, investigators, and individuals from the sponsor (or designee) who interact with the investigators and monitor safety will continue to be blinded to individual study treatments throughout the follow up period of the study. The official database release will occur after the last participant completes the last visit. The Clinical Study Report (CSR) will be based on the data generated following the database release.

9.2.1. Analysis of the Primary Endpoint

9.2.1.1. Analysis of Primary Endpoint in Stage 1

The treatment effect is defined as the difference (mean change from baseline at Week 12 in the active treatment group minus the mean change from baseline at Week 12 in the placebo group) in the mean change of CDASI activity score from baseline at Week 12.

The estimates for treatment effect will be obtained by fitting the longitudinal analysis of covariance (LANCOVA) model to the CDASI activity score change from baseline. The model will include treatment (active dose and placebo), week and treatment by week interaction as fixed effects and baseline value as a covariate. An unstructured variance-covariance matrix will be allowed.

A sensitivity analysis will be based on the analysis of covariance (ANCOVA). The ANCOVA-based estimation of the treatment effect will use the observations collected at baseline and Week 12 visits only and will eliminate the complexity of modeling the covariance between the repeated measures of outcome observed at different visits. The resulting estimate may be slightly less precise than the LANCOVA-based estimate.

Estimates and the confidence intervals for treatment effect will be presented for each of these methods.

9.2.1.2. Analysis of Primary Endpoint in Stage 2

The treatment effect is defined as the difference (between each active treatment group and placebo group across the two stages) in the mean change of CDASI activity score from baseline at Week 12. Baseline is defined as Day 1.

Estimates and 90% CI will be computed. No p-values will be computed for the analysis in this stage.

The estimates will be obtained using the same LANCOVA model as described in Section 9.2.2.1.

Data permitting, the secondary analysis for the primary endpoint in Stage 2 will be the PF-06823859 exposure-response analysis of the combined data from Stage 1 and Stage 2. The Population Modeling Analysis Plan, (PMAP) will describe the evaluation of the relationship between PF-06823859 exposures and response at Week 12. Analyses developed to characterize this exposure-response relationship will not be part of the Clinical Study Report (CSR) and may be reported separately.

Additional sensitivity analysis will be described in the SAP.

9.2.1.3. Analysis of Primary Endpoint in Stage 3

The primary objective in Stage 3 is to determine the safety and tolerability of PF-06823859 in adult DM participants with moderate muscle disease. No efficacy analyses will be performed for the primary endpoint. All safety data will be reported according to sponsor standards consistent with the previous stages.

9.2.2. Analysis of Secondary Endpoints

9.2.2.1. Analysis of the Secondary Endpoints in Stage 1

The values of CDASI activity and damage scores at each visit will be summarized by descriptive statistics. The estimates for treatment effect will be obtained by LANCOVA and ANCOVA methods described in Section 9.2.1 where the change from baseline of a corresponding score (ie, activity or damage score) will be used as a dependent variable. The ANCOVA analysis will be used as supportive analysis. Estimates and the confidence intervals for treatment effect will be presented for each of these methods.

9.2.2.2. Analysis of the Secondary Endpoints in Stage 2

The analyses and summaries of the secondary endpoints in Stage 2 will be the same as those in Section 9.2.2.1 except that they will be conducted for the data across the two Stages. No p-values will be presented for these analyses.

As a supportive analysis, summaries will also be presented for change from baseline in CDASI activity score after 12 weeks of active treatment, which includes pooled data from participants who received active treatment from Day 1 to Week 12 (CDASI measured at Week 12) and participants who received active treatment from Week 12 to Week 24 (CDASI measured at Week 24). This may be compared to the participants receiving placebo during the first 12 weeks. Baseline is defined as Day 1 for participants who received active treatment from Day 1 to Week 12. Baseline is defined as Week 12 for participants who received active treatment from Week 12 to Week 24. Further details will be provided in the SAP.

9.2.2.3. Analysis of the Secondary Endpoints in Stage 3

The TIS at baseline is 0 indicating no change. The TIS at post baseline visits is scored as relative change from baseline. The absolute value of the TIS at each post baseline visit will be summarized by descriptive statistics. The estimates of the treatment effect from Baseline to Week 12 will be obtained by LANCOVA where the TIS will be used as a dependent variable. The model will include treatment (active dose and placebo), week and treatment by week interaction as fixed effects. An unstructured variance-covariance matrix will be allowed.

Estimates and the 90% confidence intervals for treatment effect will be presented. No p-values will be presented for these analyses.

As a supportive analysis, the mean TIS after receiving 12 weeks of active treatment will also be estimated among all participants who completed or had the chance to complete the fixed sequence using pooled data from participants who received active treatment from Day 1 to Week 12 (TIS measured at Week 12) and participants who received active treatment from Week 12 to Week 24 (TIS measured at Week 24). This may be compared to the placebo during the first 12 weeks. Baseline is defined as Day 1 for participants who received active treatment from Day 1 to Week 12. Baseline is defined as Week 12 for participants who received active treatment from Week 12 to Week 24. Further details will be provided in the SAP.

The CSM of the TIS, including PGA, PtGA, MMT, HAQ-DI, muscle enzymes, and extra-muscular activity, at each visit will also be summarized by descriptive statistics on the absolute scale and change from baseline.

Additionally, the absolute values and change from baseline of CDASI activity and CDASI damage scores at all scheduled time points will be summarized by descriptive statistics per Section 9.2.2.1.

Further details will be provided in the SAP.

9.2.3. Analysis of Other Endpoints

9.2.3.1. Analysis of Other Endpoints in Stage 1

The values of patient reported outcomes (SF36, DLQI and 5D Pruritus Scale, Severity Score) at each visit will be summarized by descriptive statistics. The estimates for treatment effect will be obtained by LANCOVA method described in Section 9.2.1 where the change from baseline of a corresponding score will be used as a dependent variable.

The individual items of the CDASI will be summarized by descriptive statistics.

CCI [redacted]

The detailed analysis of gene signature data and other biomarkers will be described in the exploratory analysis plan.

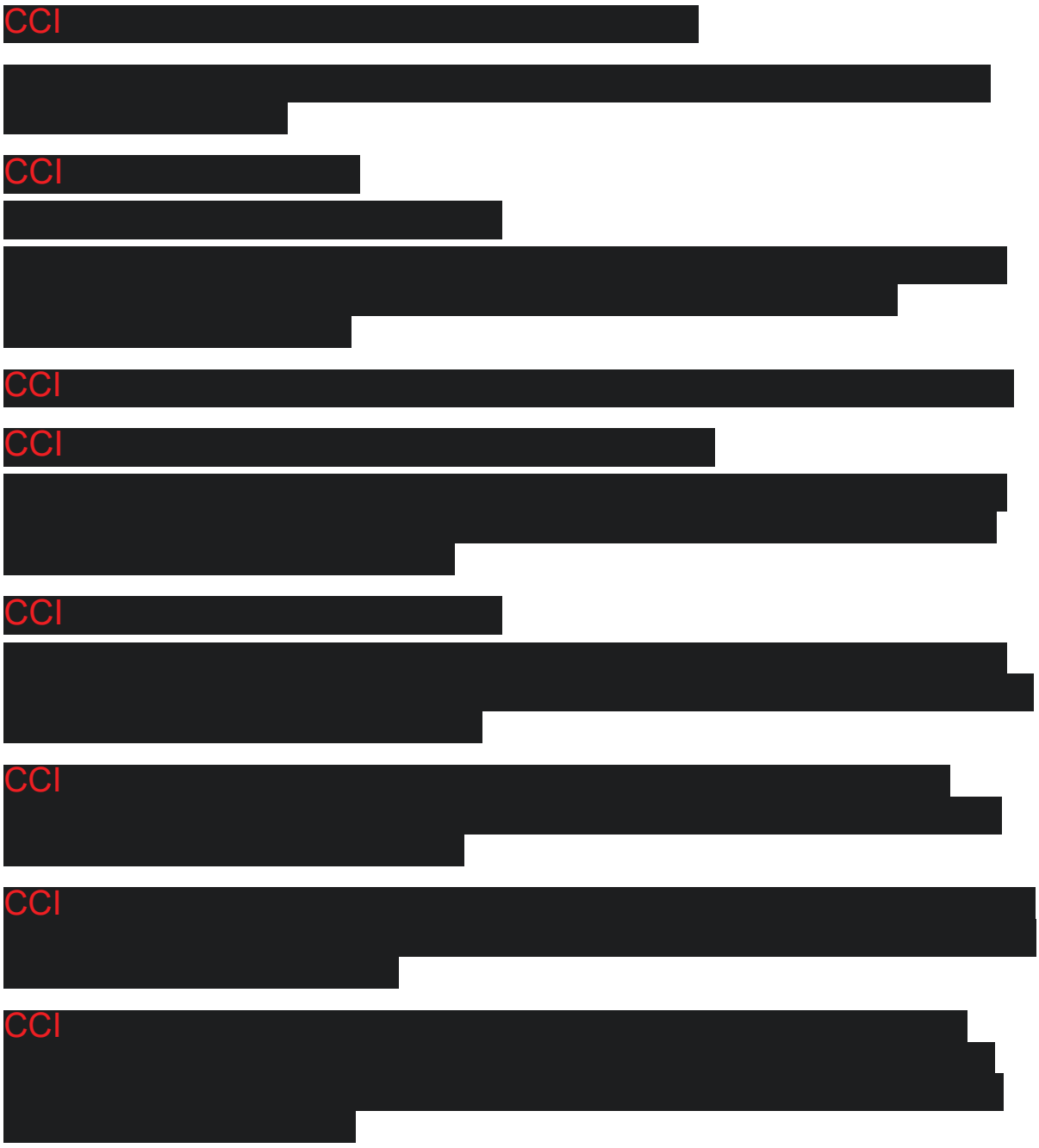
CCI [redacted]

[redacted]

[redacted]

9.2.3.3. Analysis of Other Endpoints in Stage 3

The values of PROs (PtGA, HAQ-Di, 5D Puritus, CCI [redacted], FACIT-F, SF-36V2, and EQ-5D-5L) and PhGA, VAS at each visit will be summarized by descriptive statistics.



9.4. Safety Analysis

The safety analysis population will include all participants who have received at least one dose of study drug or placebo. Safety data will be presented in tabular and/or graphical format and summarized descriptively, where appropriate. All safety endpoints will be listed and summarized in accordance with Pfizer Data Standards. Categorical outcomes (eg, AEs) will be summarized by participant counts and percentage. Continuous outcome (eg, BP, heart rate) will be summarized using N, mean, median, standard deviation. Change from baseline in laboratory data and vital signs will also be summarized according to sponsor Data Standards. Participant listings will be produced for these safety endpoints accordingly.

Safety analyses will be reported for Stage 1, Stage 1 and 2 combined, and Stage 3 as described in Section 2.

9.4.1. Adverse Events and Suicidality Assessments

The safety analyses will be carried out in the safety population and detailed analyses will be described in the SAP.

Data relevant to the assessment of suicidality will be mapped to the Columbia Classification Algorithm of Suicide Assessment (C CASA) codes. Baseline and post baseline C SSRS data (mapped to C CASA scores) will be summarized descriptively by treatment group at baseline and each post baseline visit. The safety analyses will be carried out in the safety population, detailed analyses will be described in the SAP.

9.4.2. Electrocardiogram

Changes from baseline for the ECG parameters (QT interval, heart rate, corrected QT interval QTc (QTcB and QTcF versions) and QRS interval will be summarized by treatment and time. The Day 1 pre-dose ECG measurements will be used as a participant's baseline. The number (%) of participants with maximum post dose QTc values (QTcB or QTcF) and maximum increases from baseline in the following categories will be tabulated by treatment:

	Borderline (msec)	**Prolonged (msec)**
Absolute Value	≥450 - <480	≥480
Absolute Change	30-<60	≥60

In addition, the number of participants with absolute QTc values ≥500 msec will be listed.

9.5. Interim Analyses

9.5.1. Analysis for Internal Decision Making

In stage 1 of the study, an interim analysis was performed when 32 participants were randomized and completed Visit 6 (Week 12). Additional interim analyses in later study stages *may b*e conducted depending on the enrollment rate. If an additional interim analysis is done in the future, an internal review committee (IRC), independent from the blinded study team will review efficacy and safety data for business decision planning, if applicable. No changes to the conduct of the study will occur. The results of the interim analysis will not be shared with the study team, participants, or investigators.

CCI [redacted]

CCI [redacted]

CCI [redacted]

10. QUALITY CONTROL AND QUALITY ASSURANCE

Pfizer or its agent will conduct periodic monitoring visits during study conduct to ensure that the protocol and Good Clinical Practices (GCPs) are being followed. The monitors may review source documents to confirm that the data recorded on CRFs are accurate. The investigator and institution will allow Pfizer monitors/auditors or its agents and appropriate regulatory authorities direct access to source documents to perform this verification. This verification may also occur after study completion.

During study conduct and/or after study completion, the investigator site may be participant to review by the IRB/EC, and/or to quality assurance audits performed by Pfizer, or companies working with or on behalf of Pfizer, and/or to inspection by appropriate regulatory authorities.

The investigator(s) will notify Pfizer or its agents immediately of any regulatory inspection notification in relation to the study. Furthermore, the investigator will cooperate with Pfizer or its agents to prepare the investigator site for the inspection and will allow Pfizer or its agent, whenever feasible, to be present during the inspection. The investigator site and investigator will promptly resolve any discrepancies that are identified between the study data and the participant's medical records. The investigator will promptly provide copies of the inspection findings to Pfizer or its agent. Before response submission to the regulatory authorities, the investigator will provide Pfizer or its agents with an opportunity to review and comment on responses to any such findings.

It is important that the investigator(s) and their relevant personnel are available during the monitoring visits and possible audits or inspections and that sufficient time is devoted to the process.

11. DATA HANDLING AND RECORD KEEPING

11.1. Case Report Forms/Electronic Data Record

As used in this protocol, the term CRF should be understood to refer to either a paper form or an electronic data record or both, depending on the data collection method used in this study.

A CRF is required and should be completed for each included participant. The completed original CRFs are the sole property of Pfizer and should not be made available in any form to third parties, except for authorized representatives of Pfizer or appropriate regulatory authorities, without written permission from Pfizer.

The investigator has ultimate responsibility for the collection and reporting of all clinical, safety, and laboratory data entered on the CRFs and any other data collection forms (source documents) and ensuring that they are accurate, authentic/original, attributable, complete, consistent, legible, timely (contemporaneous), enduring, and available when required. The CRFs must be signed by the investigator or by an authorized staff member to attest that the data contained on the CRFs are true. Any corrections to entries made in the CRFs or source documents must be dated, initialed, and explained (if necessary) and should not obscure the original entry.

In most cases, the source documents are the hospital or the physician participant chart. In these cases, data collected on the CRFs must match the data in those charts.

In some cases, the CRF may also serve as the source document. In these cases, a document should be available at the investigator site and at Pfizer that clearly identifies those data that will be recorded on the CRF, and for which the CRF will stand as the source document.

11.2. Record Retention

To enable evaluations and/or inspections/audits from regulatory authorities or Pfizer, the investigator agrees to keep records, including the identity of all participating participants (sufficient information to link records, eg, CRFs and hospital records), all original signed informed consent documents, copies of all CRFs, safety reporting forms, source documents, and detailed records of treatment disposition, and adequate documentation of relevant correspondence (eg, letters, meeting minutes, and telephone call reports). The records should be retained by the investigator according to the ICH guidelines, according to local regulations, or as specified in the clinical study agreement (CSA), whichever is longer.

If the investigator becomes unable for any reason to continue to retain study records for the required period (eg, retirement, relocation), Pfizer should be prospectively notified. The study records must be transferred to a designee acceptable to Pfizer, such as another investigator, another institution, or an independent third party arranged by Pfizer.

Investigator records must be kept for a minimum of 15 years after completion or discontinuation of the study or for longer if required by applicable local regulations.

The investigator must obtain Pfizer's written permission before disposing of any records, even if retention requirements have been met.

12. ETHICS

12.1. Institutional Review Board/Ethics Committee

It is the responsibility of the investigator to have prospective approval of the study protocol, protocol amendments, informed consent documents, and other relevant documents, eg, recruitment advertisements, if applicable, from the IRB/EC. All correspondence with the IRB/EC should be retained in the investigator file. Copies of IRB/EC approvals should be forwarded to Pfizer.

The only circumstance in which an amendment may be initiated prior to IRB/EC approval is where the change is necessary to eliminate apparent immediate hazards to the participants. In that event, the investigator must notify the IRB/EC and Pfizer in writing immediately after the implementation.

12.2. Ethical Conduct of the Study

The study will be conducted in accordance with the protocol, legal and regulatory requirements and the general principles set forth in the International Ethical Guidelines for Biomedical Research Involving Human Participants (Council for International Organizations of Medical Sciences 2002), ICH Guideline for Good Clinical Practice, and the Declaration of Helsinki.

12.3. Participant Information and Consent

All parties will ensure protection of participant personal data and will not include participant names or other identifiable data in any reports, publications, or other disclosures, except where required by law.

When study data are compiled for transfer to Pfizer and other authorized parties, participant names, addresses, and other identifiable data will be replaced by numerical codes based on a numbering system provided by Pfizer in order to de-identify study participants. The investigator site will maintain a confidential list of participants who participated in the study, linking each participant’s numerical code to his or her actual identity. In case of data transfer, Pfizer will maintain high standards of confidentiality and protection of participants’ personal data consistent with applicable privacy laws.

The informed consent documents and any participant recruitment materials must be in compliance with ICH GCP, local regulatory requirements, and legal requirements, including applicable privacy laws.

The informed consent documents used during the informed consent process and any participant recruitment materials must be reviewed and approved by Pfizer, approved by the IRB/EC before use, and available for inspection.

The investigator must ensure that each study participant is fully informed about the nature and objectives of the study and possible risks associated with participation.

The investigator, or a person designated by the investigator, will obtain written informed consent from each participant before any study-specific activity is performed. The investigator will retain the original of each participant's signed consent document.

12.4. Reporting of Safety Issues and Serious Breaches of the Protocol or ICH GCP

In the event of any prohibition or restriction imposed (ie, clinical hold) by an applicable regulatory authority in any area of the world, or if the investigator is aware of any new information that might influence the evaluation of the benefits and risks of the investigational product, Pfizer should be informed immediately.

In addition, the investigator will inform Pfizer immediately of any urgent safety measures taken by the investigator to protect the study participants against any immediate hazard, and of any serious breaches of this protocol or of ICH GCP that the investigator becomes aware of.

13. DEFINITION OF END OF TRIAL

13.1. End of the Trial

Last participant last visit (LSLV) is defined as the date the investigator reviews the last participant’s final safety data and determines that no further evaluation is required for the participant to complete the trial.

14. SPONSOR DISCONTINUATION CRITERIA

Premature termination of this study may occur because of a regulatory authority decision, change in opinion of the IRB/EC, or investigational product safety problems, or at the discretion of Pfizer. In addition, Pfizer retains the right to discontinue development of PF-06823859 at any time.

If a study is prematurely terminated, Pfizer will promptly notify the investigator. After notification, the investigator must contact all participating participants and the hospital pharmacy (if applicable) within 7 days. As directed by Pfizer, all study materials must be collected and all CRFs completed to the greatest extent possible.

15. PUBLICATION OF STUDY RESULTS

15.1. Communication of Results by Pfizer

Pfizer fulfills its commitment to publicly disclose clinical trial results through posting the results of studies on www.clinicaltrials.gov (ClinicalTrials.gov), the European Clinical Trials Database (EudraCT), and/or www.pfizer.com, and other public registries in accordance with applicable local laws/regulations.

In all cases, study results are reported by Pfizer in an objective, accurate, balanced, and complete manner and are reported regardless of the outcome of the study or the country in which the study was conducted.

www.clinicaltrials.gov

Pfizer posts clinical trial US Basic Results on www.clinicaltrials.gov for Pfizer-sponsored interventional studies (conducted in participants) that evaluate the safety and/or efficacy of a Pfizer product, regardless of the geographical location in which the study is conducted. US Basic Results are submitted for posting within 1 year of the primary completion date (PCD) for studies in adult populations or within 6 months of the PCD for studies in pediatric populations.

PCD is defined as the date that the final participant was examined or received an intervention for the purposes of final collection of data for the primary outcome, whether the clinical study concluded according to the prespecified protocol or was terminated.

EudraCT

Pfizer posts European Union (EU) Basic Results on EudraCT for all Pfizer-sponsored interventional studies that are in scope of EU requirements. EU Basic Results are submitted for posting within 1 year of the PCD for studies in adult populations or within 6 months of the PCD for studies in pediatric populations.

www.pfizer.com

Pfizer posts Public Disclosure Synopses (clinical study report synopses in which any data that could be used to identify individual participants has been removed) on www.pfizer.com for Pfizer-sponsored interventional studies at the same time the US Basic Results document is posted to www.clinicaltrials.gov.

15.2. Publications by Investigators

Pfizer supports the exercise of academic freedom and has no objection to publication by the principal investigator (PI) of the results of the study based on information collected or generated by the PI, whether or not the results are favorable to the Pfizer product. However, to ensure against inadvertent disclosure of confidential information or unprotected inventions, the investigator will provide Pfizer an opportunity to review any proposed publication or other type of disclosure of the results of the study (collectively, “publication”) before it is submitted or otherwise disclosed.

The investigator will provide any publication to Pfizer at least 30 days before it is submitted for publication or otherwise disclosed. If any patent action is required to protect intellectual property rights, the investigator agrees to delay the disclosure for a period not to exceed an additional 60 days.

The investigator will, on request, remove any previously undisclosed confidential information before disclosure, except for any study- or Pfizer product-related information necessary to the appropriate scientific presentation or understanding of the study results.

If the study is part of a multicenter study, the investigator agrees that the first publication is to be a joint publication covering all investigator sites, and that any subsequent publications by the PI will reference that primary publication. However, if a joint manuscript has not been submitted for publication within 12 months of completion or termination of the study at all participating sites, the investigator is free to publish separately, participant to the other requirements of this section.

For all publications relating to the study, the institution will comply with recognized ethical standards concerning publications and authorship, including Section II - "Ethical Considerations in the Conduct and Reporting of Research" of the Uniform Requirements for Manuscripts Submitted to Biomedical Journals, http://www.icmje.org/index.html#authorship, established by the International Committee of Medical Journal Editors.

Publication of study results is also provided for in the CSA between Pfizer and the institution. In this section entitled Publications by Investigators, the defined terms shall have the meanings given to them in the CSA.

If there is any conflict between the CSA and any attachments to it, the terms of the CSA control. If there is any conflict between this protocol and the CSA, this protocol will control as to any issue regarding treatment of study participants, and the CSA will control as to all other issues.

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Appendix 1. Abbreviations

This following is a list of abbreviations that may be used in the protocol.

Abbreviation	Term
%CV	percent coefficient of variation
ADA	Anti-Drug antibody
ADCC	Antibody-dependent cell-mediated cytotoxicity
AE	adverse event
ALC	absolute lymphocyte count
ALT	alanine aminotransferase
ANC	absolute neutrophil count
ANCOVA	Analysis of covariance
anti-TNF	anti-tumor necrosis factor
anti-IFN a	anti-interferon alpha
AST	aspartate aminotransferase
ATP	adenosine tri-phosphate
AUC	area under the curve
AZA	Azathioprine
β	Beta
β-hCG	beta-human chorionic gonadotropin
BA	Bioavailability
BAFF	B-cell activating factor
BBS	Biospecimen Banking System
BCD	Bacille Calmette Guerin
BID	twice a day
BLyS	B-lymphocyte stimulator
BP	blood pressure
C_{max}	maximum (or peak) serum concentration
C_{AV}	Concentration average
CDC	Centers for Disease Control
CDASI	Cutaneous Dermatomyositis Disease Area and Severity Index
CDS	core data sheet
CI	confidence interval
CK	creatine kinase
Cl	chlorine
Clq	Chloroquine
CMV	Cytomegalovirus
CNS	central nervous system
COVID-19	Corona Virus Disease 2019
CRF	case report form
CSA	clinical study agreement
CSM	Core Set Measure
CSR	Clinical Study Report
C-SSRS	Columbia-Suicide Severity Rating Scale

Abbreviation	Term
CT	clinical trial
CT	Computed tomography
CTCAE	Common Terminology Criteria for Adverse Events
CTFG	Clinical Trial Facilitation and Coordination Group
CVA	cerebrovascular accident
DAI	dosage and administration instructions
DDI	drug-drug interaction
DILI	drug-induced liver injury
DLQI	Dermatology and Life Quality Index
DM	Dermatomyositis
DMARDs	disease-modifying antirheumatic drugs
DNA	deoxyribonucleic acid
DU	dispensable unit
EBV	Epstein-Barr virus
EC	ethics committee
ECG	electrocardiogram
EDP	exposure during pregnancy
EDTA	edetic acid (ethylenediaminetetraacetic acid)
EFD	Embryo-Fetal Development
EOS	end of study
EPO	Erythropoietin
ePPND	enhanced pre and postnatal development
EQ-5D-5L & EQ VAS	European Quality of Life, 5 Dimenstion, 5 Level Scale and Visual Analogue Scale
ET	Early termination
Eudra CT	European Union Drug Regulating Authorities Clinical Trials
EW	early withdrawal
FACIT-F	Functional Assessment of Chronic Illness Therapy Fatigue Scale
FcR	Fc Receptor
FDA	Food and Drug Administration
FIH	first in human
FSFV	first subject first visit
FSH	follicle-stimulating hormone
GCP	Good Clinical Practice
GGT	gamma-glutamyl transferase
GI	Gastrointestinal
GLMM	generalized linear mixed model
GLP	Good laboratory practice
HAQ-DI	Health Assessment Questionnaire and Disease Index
HBcAb	hepatitis B core antibody
HBsAb	hepatitis B surface antibody test
HBsAg	hepatitis B surface antigen
HCVAb	hepatitis C virus antibody

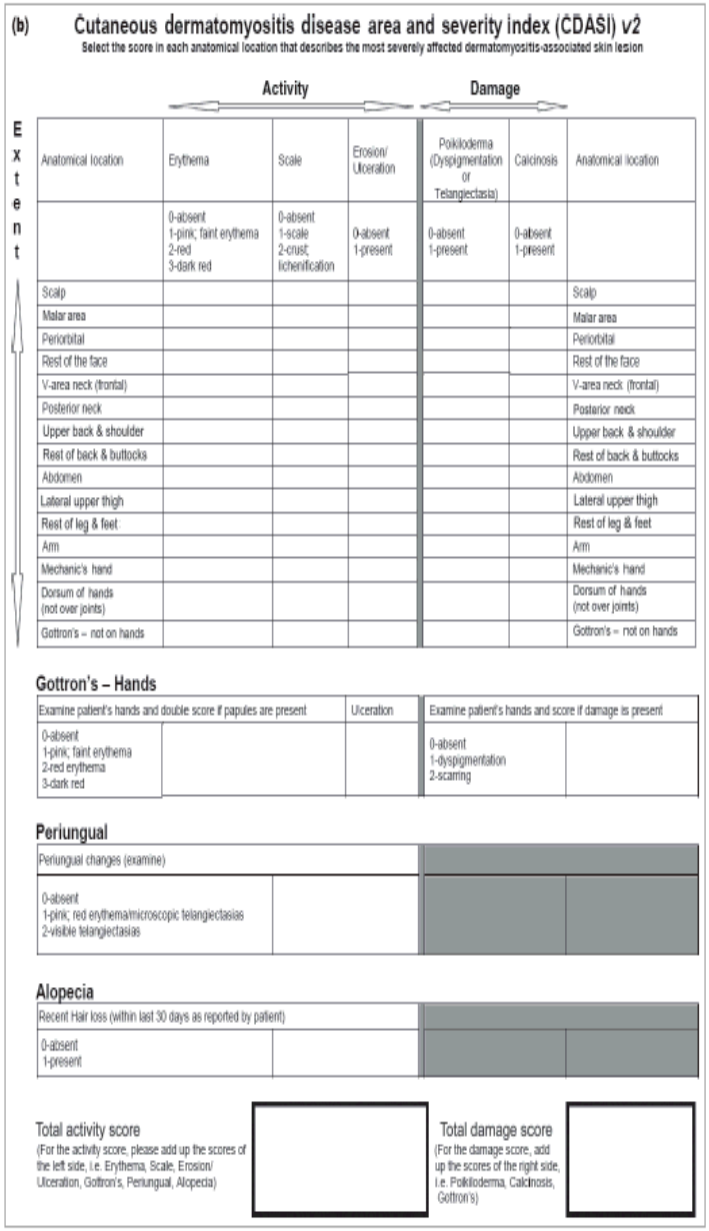
Abbreviation	Term
HEENT	head, eyes, ears, nose and throat
Hep B	hepatitis B
HHV6	Human Herpes Virus 6
HIV	human immunodeficiency virus
HR	heart rate
HRT	hormone replacement therapy
hsCRP	high-sensitivity C-reactive protein
HSV-1	herpes simplex virus type 1
HSV-2	herpes simplex virus type 2
IA	Intra-articular
IB	Investigator's Brochure
ICF	informed consent form
ICH	International Conference on Harmonisation
ID	Identification
IFN-	Interferon beta
IFNAR	interferon-α/β receptor
Ig	Immunoglobulin
IgG1	Immunoglobulin G1
IGRA	Interferon-Gamma Release Assays
IL-6	Interlukin 6
IM	Intramuscular
IMACS	International Myostits Assessment & Clinical Studies
IMP	investigational medicinal product
IND	investigational new drug application
INF	Interferon
INR	international normalized ratio
IP	investigational product
IP-10	interferon gamma-induced protein 10
IRB	institutional review board
IRC	internal review committee
IRT	interactive response technology
IRG	Interferon regulated gene
ISR	Injection site reaction
IUD	intrauterine device
IUS	Intrauterine system
IV	intravenous
IVIG	intravenous immunoglobulin
IVR	interactive voice-based response
IWR	interactive web-based response
JAK	Janus kinase
K_2EDTA	anticoagulant
LANCOVA	longitudinal analysis of covariance
LDH	lactate dehydrogenase

Abbreviation	Term
LFT	liver function test
LLN	lower limit of normal
LSLV	last subject last visit
MAb	Monoclonal antibody
MAD	multiple ascending dose
MPV	mean platelet volume
MCS	Multiple chemical sensitivity
MDAAT	Myositis Disease Activity Assessment Tool
MDA5	melanoma differentiation-associated gene 5
MDI	Muscle Disease Index
Mi2	myositis specific Autoantibody
mITT	Modified intent to treat
MMF	Mycophenolic acid
MMT-8	Manual Muscle Testing-8 designated muscle groups
MP	Mycoplasma Pneumoniae
MRI	magnetic resonance imaging
MTX	Methotrexate
MXA-1	Human myxovirus resistance protein 1
N/A	not applicable
NAb	Neutralizing Anti-body
NOAEL	no-observed-adverse-effect-level
NXP2	Nuclear matrix protein
OLE	open label extension
PCD	primary completion date
PCS	physical component scores
PD	Pharmacodynamics
PE	physical examination
PET	positron emission tomography
pH	Potential of Hydrogen
PhGA, VAS	physician global assessment
PHQ-8	Patient Health Questionnaire 8-item depression measure
PI	Principal Investigator
PK	Pharmacokinetics
PMAP	Population Modeling Analysis Plan
PoC	proof-of-concept
PoM	proof-of-mechanism
PPD	purified protein derivative
PR interval	period, in milliseconds, that extends from beginning of P wave until beginning of QRS complex
PROMIS	Patient Reported Outcome Measurement Information System
PT	prothrombin time
PtGA	Patient global assessment
PTT	partial thromboplastin time

Abbreviation	Term
PPT	partial prothrombin time
PRO	patient reported outcome
QD	once a day
QFT-GIT	QuantiFERON-TB Gold In-Tube
QoL	quality of life
QRS complex	combination of the Q wave, R wave and S wave
QT interval	measure between Q wave and T wave
QT_cF	QT interval calculated by Fridericia's formula
Q4W	Every 4 weeks
RNA	ribonucleic acid
RR	respiratory rate
R-R interval	time between beats on ECG
SAD	single ascending dose
SAE	serious adverse event
SAP	statistical analysis plan
SC	Subcutaneous
SCL	Supply Chain Lead
SD	Standard deviation
SF-36	The Short Form (36) Health Survey
SGOT	serum glutamic-oxaloacetic transaminase
SGPT	serum glutamic-pyruvic transaminase
SIB	suicidal ideation and behavior
SoA/SOA	Schedule of Assessments
SoC	standard of care
SLE	Systemic lupus erythematous
SOC	System Organ Class
SOP	standard operating procedure
SRSD	single reference safety document
TACI	transmembrane activator and CAML interactor
T_{max}	time drug is present at maximum concentration in serum
TB	Tuberculosis
TBili	Total Bilirubin
TEAE	treatment-emergent adverse event
TIS	Total Improvement Score
TIF	Transcription intermediary factor
TNF	tumor necrosis factor
ULN	upper limit of normal
US	United States
VAS	visual analog scale
Vss	Volume at steady state
VZV	varicella zoster virus
WBC	white blood cell
WOCBP	women of child bearing potential

Abbreviation	Term
WONCBP	women of non-child bearing potential

Appendix 2. CDASI



(b) Cutaneous dermatomyositis disease area and severity index (CDASI) v2

Select the score in each anatomical location that describes the most severely affected dermatomyositis-associated skin lesion

Extent	Activity			Damage		
Anatomical location	Erythema	Scale	Erosion/ Ulceration	Poikiloderma (Dyspigmentation or Telangiectasia)	Calcinosis	Anatomical location
	0-absent 1-pink; faint erythema 2-red 3-dark red	0-absent 1-scale 2-crust; lichenification	0-absent 1-present	0-absent 1-present	0-absent 1-present	
Scalp						Scalp
Malar area						Malar area
Periorbital						Periorbital
Rest of the face						Rest of the face
V-area neck (frontal)						V-area neck (frontal)
Posterior neck						Posterior neck
Upper back & shoulder						Upper back & shoulder
Rest of back & buttocks						Rest of back & buttocks
Abdomen						Abdomen
Lateral upper thigh						Lateral upper thigh
Rest of leg & feet						Rest of leg & feet
Arm						Arm
Mechanic's hand						Mechanic's hand
Dorsum of hands (not over joints)						Dorsum of hands (not over joints)
Gottron's – not on hands						Gottron's – not on hands

Gottron's – Hands

Examine patient's hands and double score if papules are present		Ulceration	Examine patient's hands and score if damage is present	
0-absent 1-pink; faint erythema 2-red erythema 3-dark red			0-absent 1-dyspigmentation 2-scarring	

Periungual

Periungual changes (examine)			
0-absent 1-pink; red erythema/microscopic telangiectasias 2-visible telangiectasias			

Alopecia

Recent Hair loss (within last 30 days as reported by patient)			
0-absent 1-present			

Total activity score
(For the activity score, please add up the scores of the left side, i.e. Erythema, Scale, Erosion/ Ulceration, Gottron's, Periungual, Alopecia)

Total damage score
(For the damage score, add up the scores of the right side, i.e. Poikiloderma, Calcinosis, Gottron's)

Appendix 3. Physician Global Assessment (PhGA, VAS)

THE PATIENT'S DERMATOMYOSITIS AT THIS TIME IS:

(PLEASE PLACE A VERTICLE LINEON THE LINE BELOW.)

Very _____ Very
Good Poor

[Note: Scale will be 100 mm in length]

Appendix 4. Personal Health Questionnaire Eight-Item Depression Measure (PHQ-8)

PHQ-8

Over the last 2 weeks, how often have you been bothered by any of the following problems? (Use "✔" to indicate your answer)	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself – or that you are a failure or have let yourself or your family down	0	1	2	3
7. Troubleconcentratingonthings,suchas reading thenewspaperorwatchingtelevision.	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed? Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3

(For office coding: Total Score _____ = ___ + ___ + ___)

From the Primary Care Evaluation of Mental Disorders Patient Health Questionnaire (PRIME-MDPHQ). The PHQ was developed by Drs. Robert L. Spitzer, Janet B.W. Williams, Kurt Kroenke and colleagues. For research in formation, contact Dr. Spitzera trls8@columbia.edu. PRIME-MD® is a trademark of Pfizer Inc. Copyright© 1999 Pfizer Inc. All rights reserved. Reproduced with permission

PHQ-8

Over the last 2 weeks, how often have you been bothered by any of the following problems? (Use "✔" to indicate your answer)	Not at all	Several days	More than half the days	Nearly every day
1. Little interest or pleasure in doing things	0	1	2	3
2. Feeling down, depressed, or hopeless	0	1	2	3
3. Trouble falling or staying asleep, or sleeping too much	0	1	2	3
4. Feeling tired or having little energy	0	1	2	3
5. Poor appetite or overeating	0	1	2	3
6. Feeling bad about yourself – or that you are a failure or have let yourself or your family down	0	1	2	3
7. Troubleconcentratingonthings,suchas reading thenewspaperorwatchingtelevision.	0	1	2	3
8. Moving or speaking so slowly that other people could have noticed? Or the opposite – being so fidgety or restless that you have been moving around a lot more than usual	0	1	2	3

(For office coding: Total Score _____ = ___ + ___ + ___)

From the Primary Care Evaluation of Mental Disorders Patient Health Questionnaire (PRIME-MDPHQ). The PHQ was developed by Drs. Robert L. Spitzer, Janet B.W. Williams, Kurt Kroenke and colleagues. For research in formation, contact Dr. Spitzera trls8@columbia.edu. PRIME-MD® is a trademark of Pfizer Inc. Copyright© 1999 Pfizer Inc. All rights reserved. Reproduced with permission

Kroenke K, Strine TW, Spitzer RL, et al. The PHQ-8 as a measure of current depression in the general population. J Affect Disord 2009;114(1-3):163-173.

Appendix 5. CCI [redacted]

[redacted]

[redacted]

SUICIDAL IDEATION *Ask questions 1 and 2. If both are negative, proceed to "Suicidal Behavior" section. If the answer to question 2 is "yes", ask questions 3, 4 and 5. If the answer to question 1 and/or 2 is "yes", complete "Intensity of Ideation" section below.*	**Lifetime: Time He/She Felt Most Suicidal**	**Past __ Months**
1. Wish to be Dead Subject endorses thoughts about a wish to be dead or not alive anymore, or wish to fall asleep and not wake up. ***Have you wished you were dead or wished you could go to sleep and not wake up?*** If yes, describe:	Yes ☐ No ☐	Yes ☐ No ☐
2. Non-Specific Active Suicidal Thoughts General non-specific thoughts of wanting to end one's life/commit suicide (e.g., *"I've thought about killing myself"*) without thoughts of ways to kill oneself/associated methods, intent, or plan during the assessment period. ***Have you actually had any thoughts of killing yourself?*** If yes, describe:	Yes ☐ No ☐	Yes ☐ No ☐
3. Active Suicidal Ideation with Any Methods (Not Plan) without Intent to Act Subject endorses thoughts of suicide and has thought of at least one method during the assessment period. This is different than a specific plan with time, place or method details worked out (e.g. thought of method to kill self but not a specific plan). Includes person who would say, *"I thought about taking an overdose but I never made a specific plan as to when, where or how I would actually do it…and I would never go through with it."* ***Have you been thinking about how you might do this?*** If yes, describe:	Yes ☐ No ☐	Yes ☐ No ☐
4. Active Suicidal Ideation with Some Intent to Act, without Specific Plan Active suicidal thoughts of killing oneself and subject reports having some intent to act on such thoughts, as opposed to *"I have the thoughts but I definitely will not do anything about them."* ***Have you had these thoughts and had some intention of acting on them?*** If yes, describe:	Yes ☐ No ☐	Yes ☐ No ☐
5. Active Suicidal Ideation with Specific Plan and Intent Thoughts of killing oneself with details of plan fully or partially worked out and subject has some intent to carry it out. ***Have you started to work out or worked out the details of how to kill yourself? Do you intend to carry out this plan?*** If yes, describe:	Yes ☐ No ☐	Yes ☐ No ☐
INTENSITY OF IDEATION *The following features should be rated with respect to the most severe type of ideation (i.e., 1-5 from above, with 1 being the least severe and 5 being the most severe). Ask about time he/she was feeling the most suicidal.* Lifetime - ***Most Severe Ideation:*** _____ *Type # (1-5)* _____ *Description of Ideation* Past X Months - ***Most Severe Ideation:*** _____ *Type # (1-5)* _____ *Description of Ideation*	Most Severe	Most Severe
Frequency ***How many times have you had these thoughts?*** (1) Less than once a week (2) Once a week (3) 2-5 times in week (4) Daily or almost daily (5) Many times each day	____	____
Duration ***When you have the thoughts how long do they last?*** (1) Fleeting - few seconds or minutes (2) Less than 1 hour/some of the time (3) 1-4 hours/a lot of time (4) 4-8 hours/most of day (5) More than 8 hours/persistent or continuous	____	____
Controllability ***Could/can you stop thinking about killing yourself or wanting to die if you want to?*** (1) Easily able to control thoughts (2) Can control thoughts with little difficulty (3) Can control thoughts with some difficulty (4) Can control thoughts with a lot of difficulty (5) Unable to control thoughts (0) Does not attempt to control thoughts	____	____
Deterrents ***Are there things - anyone or anything (e.g., family, religion, pain of death) - that stopped you from wanting to die or acting on thoughts of committing suicide?*** (1) Deterrents definitely stopped you from attempting suicide (2) Deterrents probably stopped you (3) Uncertain that deterrents stopped you (4) Deterrents most likely did not stop you (5) Deterrents definitely did not stop you (0) Does not apply	____	____
Reasons for Ideation ***What sort of reasons did you have for thinking about wanting to die or killing yourself? Was it to end the pain or stop the way you were feeling (in other words you couldn't go on living with this pain or how you were feeling) or was it to get attention, revenge or a reaction from others? Or both?*** (1) Completely to get attention, revenge or a reaction from others (2) Mostly to get attention, revenge or a reaction from others (3) Equally to get attention, revenge or a reaction from others and to end/stop the pain (4) Mostly to end or stop the pain (you couldn't go on living with the pain or how you were feeling) (5) Completely to end or stop the pain (you couldn't go on living with the pain or how you were feeling) (0) Does not apply	____	____

SUICIDAL BEHAVIOR *(Check all that apply, so long as these are separate events; must ask about all types)*	**Lifetime**	**Past _ Years**
Actual Attempt: A potentially self-injurious act committed with at least some wish to die, *as a result of act.* Behavior was in part thought of as method to kill oneself. Intent does not have to be 100%. If there is ***any*** intent/desire to die associated with the act, then it can be considered an actual suicide attempt. ***There does not have to be any injury or harm***, just the potential for injury or harm. If person pulls trigger while gun is in mouth but gun is broken so no injury results, this is considered an attempt. Inferring Intent: Even if an individual denies intent/wish to die, it may be inferred clinically from the behavior or circumstances. For example, a highly lethal act that is clearly not an accident so no other intent but suicide can be inferred (e.g., gunshot to head, jumping from window of a high floor/story). Also, if someone denies intent to die, but they thought that what they did could be lethal, intent may be inferred. ***Have you made a suicide attempt?*** ***Have you done anything to harm yourself?*** ***Have you done anything dangerous where you could have died?*** ***What did you do?*** ***Did you_____ as a way to end your life?*** ***Did you want to die (even a little) when you_____?*** ***Were you trying to end your life when you _____?*** ***Or Did you think it was possible you could have died from_____?*** ***Or did you do it purely for other reasons / without ANY intention of killing yourself (like to relieve stress, feel better, get sympathy, or get something else to happen)?*** (Self-Injurious Behavior without suicidal intent) If yes, describe:	Yes ☐ No ☐ Total # of Attempts _____	Yes ☐ No ☐ Total # of Attempts _____
Has subject engaged in Non-Suicidal Self-Injurious Behavior?	Yes ☐ No ☐	Yes ☐ No ☐
Interrupted Attempt: When the person is interrupted (by an outside circumstance) from starting the potentially self-injurious act *(if not for that, actual attempt would have occurred).* Overdose: Person has pills in hand but is stopped from ingesting. Once they ingest any pills, this becomes an attempt rather than an interrupted attempt. Shooting: Person has gun pointed toward self, gun is taken away by someone else, or is somehow prevented from pulling trigger. Once they pull the trigger, even if the gun fails to fire, it is an attempt. Jumping: Person is poised to jump, is grabbed and taken down from ledge. Hanging: Person has noose around neck but has not yet started to hang - is stopped from doing so. ***Has there been a time when you started to do something to end your life but someone or something stopped you before you actually did anything?*** If yes, describe:	Yes ☐ No ☐ Total # of interrupted _____	Yes ☐ No ☐ Total # of interrupted _____
Aborted Attempt: When person begins to take steps toward making a suicide attempt, but stops themselves before they actually have engaged in any self-destructive behavior. Examples are similar to interrupted attempts, except that the individual stops him/herself, instead of being stopped by something else. ***Has there been a time when you started to do something to try to end your life but you stopped yourself before you actually did anything?*** If yes, describe:	Yes ☐ No ☐ Total # of aborted _____	Yes ☐ No ☐ Total # of aborted _____
Preparatory Acts or Behavior: Acts or preparation towards imminently making a suicide attempt. This can include anything beyond a verbalization or thought, such as assembling a specific method (e.g., buying pills, purchasing a gun) or preparing for one's death by suicide (e.g., giving things away, writing a suicide note). ***Have you taken any steps towards making a suicide attempt or preparing to kill yourself (such as collecting pills, getting a gun, giving valuables away or writing a suicide note)?*** If yes, describe:	Yes ☐ No ☐	Yes ☐ No ☐
Suicidal Behavior: Suicidal behavior was present during the assessment period?	Yes ☐ No ☐	Yes ☐ No ☐

Answer for Actual Attempts Only	Most Recent Attempt Date:	Most Lethal Attempt Date:	Initial/First Attempt Date:
Actual Lethality/Medical Damage: 0. No physical damage or very minor physical damage (e.g., surface scratches). 1. Minor physical damage (e.g., lethargic speech; first-degree burns; mild bleeding; sprains). 2. Moderate physical damage; medical attention needed (e.g., conscious but sleepy, somewhat responsive; second-degree burns; bleeding of major vessel). 3. Moderately severe physical damage; *medical* hospitalization and likely intensive care required (e.g., comatose with reflexes intact; third-degree burns less than 20% of body; extensive blood loss but can recover; major fractures). 4. Severe physical damage; *medical* hospitalization with intensive care required (e.g., comatose without reflexes; third-degree burns over 20% of body; extensive blood loss with unstable vital signs; major damage to a vital area). 5. Death	*Enter Code* _____	*Enter Code* _____	*Enter Code* _____
Potential Lethality: Only Answer if Actual Lethality=0 Likely lethality of actual attempt if no medical damage (the following examples, while having no actual medical damage, had potential for very serious lethality: put gun in mouth and pulled the trigger but gun fails to fire so no medical damage; laying on train tracks with oncoming train but pulled away before run over). 0 = Behavior not likely to result in injury 1 = Behavior likely to result in injury but not likely to cause death 2 = Behavior likely to result in death despite available medical care	*Enter Code* _____	*Enter Code* _____	*Enter Code* _____

CCI [redacted]

[redacted]

SUICIDAL IDEATION	
Ask questions 1 and 2. If both are negative, proceed to "Suicidal Behavior" section. If the answer to question 2 is "yes", ask questions 3, 4 and 5. If the answer to question 1 and/or 2 is "yes", complete "Intensity of Ideation" section below.	**Since Last Visit**
1. Wish to be Dead Subject endorses thoughts about a wish to be dead or not alive anymore, or wish to fall asleep and not wake up. ***Have you wished you were dead or wished you could go to sleep and not wake up?*** If yes, describe:	**Yes** ☐ **No** ☐
2. Non-Specific Active Suicidal Thoughts General, non-specific thoughts of wanting to end one's life/commit suicide (e.g., *"I've thought about killing myself"*) without thoughts of ways to kill oneself/associated methods, intent, or plan during the assessment period. ***Have you actually had any thoughts of killing yourself?*** If yes, describe:	**Yes** ☐ **No** ☐
3. Active Suicidal Ideation with Any Methods (Not Plan) without Intent to Act Subject endorses thoughts of suicide and has thought of at least one method during the assessment period. This is different than a specific plan with time, place or method details worked out (e.g., thought of method to kill self but not a specific plan). Includes person who would say, *"I thought about taking an overdose but I never made a specific plan as to when, where or how I would actually do it...and I would never go through with it."* ***Have you been thinking about how you might do this?*** If yes, describe:	**Yes** ☐ **No** ☐
4. Active Suicidal Ideation with Some Intent to Act, without Specific Plan Active suicidal thoughts of killing oneself and subject reports having some intent to act on such thoughts, as opposed to *"I have the thoughts but I definitely will not do anything about them."* ***Have you had these thoughts and had some intention of acting on them?*** If yes, describe:	**Yes** ☐ **No** ☐
5. Active Suicidal Ideation with Specific Plan and Intent Thoughts of killing oneself with details of plan fully or partially worked out and subject has some intent to carry it out. ***Have you started to work out or worked out the details of how to kill yourself? Do you intend to carry out this plan?*** If yes, describe:	**Yes** ☐ **No** ☐
INTENSITY OF IDEATION	
The following features should be rated with respect to the most severe type of ideation (i.e., 1-5 from above, with 1 being the least severe and 5 being the most severe). ***Most Severe Ideation:*** ____ _____ ***Type # (1-5)*** ***Description of Ideation***	Most Severe
Frequency ***How many times have you had these thoughts?*** (1) Less than once a week (2) Once a week (3) 2-5 times in week (4) Daily or almost daily (5) Many times each day	____
Duration ***When you have the thoughts, how long do they last?*** (1) Fleeting - few seconds or minutes (2) Less than 1 hour/some of the time (3) 1-4 hours/a lot of time (4) 4-8 hours/most of day (5) More than 8 hours/persistent or continuous	____
Controllability ***Could/can you stop thinking about killing yourself or wanting to die if you want to?*** (1) Easily able to control thoughts (2) Can control thoughts with little difficulty (3) Can control thoughts with some difficulty (4) Can control thoughts with a lot of difficulty (5) Unable to control thoughts (0) Does not attempt to control thoughts	____
Deterrents ***Are there things - anyone or anything (e.g., family, religion, pain of death) - that stopped you from wanting to die or acting on thoughts of committing suicide?*** (1) Deterrents definitely stopped you from attempting suicide (2) Deterrents probably stopped you (3) Uncertain that deterrents stopped you (4) Deterrents most likely did not stop you (5) Deterrents definitely did not stop you (0) Does not apply	____
Reasons for Ideation ***What sort of reasons did you have for thinking about wanting to die or killing yourself? Was it to end the pain or stop the way you were feeling (in other words you couldn't go on living with this pain or how you were feeling) or was it to get attention, revenge or a reaction from others? Or both?*** (1) Completely to get attention, revenge or a reaction from others (2) Mostly to get attention, revenge or a reaction from others (3) Equally to get attention, revenge or a reaction from others and to end/stop the pain (4) Mostly to end or stop the pain (you couldn't go on living with the pain or how you were feeling) (5) Completely to end or stop the pain (you couldn't go on living with the pain or how you were feeling) (0) Does not apply	____

SUICIDAL BEHAVIOR *(Check all that apply, so long as these are separate events; must ask about all types)*	**Since Last Visit**
Actual Attempt: A potentially self-injurious act committed with at least some wish to die, *as a result of act.* Behavior was in part thought of as method to kill oneself. Intent does not have to be 100%. If there is ***any*** intent/desire to die associated with the act, then it can be considered an actual suicide attempt. ***There does not have to be any injury or harm***, just the potential for injury or harm. If person pulls trigger while gun is in mouth but gun is broken so no injury results, this is considered an attempt. Inferring Intent: Even if an individual denies intent/wish to die, it may be inferred clinically from the behavior or circumstances. For example, a highly lethal act that is clearly not an accident so no other intent but suicide can be inferred (e.g., gunshot to head, jumping from window of a high floor/story). Also, if someone denies intent to die, but they thought that what they did could be lethal, intent may be inferred. ***Have you made a suicide attempt?*** ***Have you done anything to harm yourself?*** ***Have you done anything dangerous where you could have died?*** ***What did you do?*** ***Did you_____ as a way to end your life?*** ***Did you want to die (even a little) when you_____?*** ***Were you trying to end your life when you _____?*** ***Or did you think it was possible you could have died from_____?*** ***Or did you do it purely for other reasons / without ANY intention of killing yourself (like to relieve stress, feel better, get sympathy, or get something else to happen)?*** (Self-Injurious Behavior without suicidal intent) If yes, describe: **Has subject engaged in Non-Suicidal Self-Injurious Behavior?**	**Yes No** ☐ ☐ Total # of Attempts _____ **Yes No** ☐ ☐
Interrupted Attempt: When the person is interrupted (by an outside circumstance) from starting the potentially self-injurious act *(if not for that, actual attempt would have occurred).* Overdose: Person has pills in hand but is stopped from ingesting. Once they ingest any pills, this becomes an attempt rather than an interrupted attempt. Shooting: Person has gun pointed toward self, gun is taken away by someone else, or is somehow prevented from pulling trigger. Once they pull the trigger, even if the gun fails to fire, it is an attempt. Jumping: Person is poised to jump, is grabbed and taken down from ledge. Hanging: Person has noose around neck but has not yet started to hang - is stopped from doing so. ***Has there been a time when you started to do something to end your life but someone or something stopped you before you actually did anything?*** If yes, describe:	**Yes No** ☐ ☐ Total # of interrupted _____
Aborted Attempt: When person begins to take steps toward making a suicide attempt, but stops themselves before they actually have engaged in any self-destructive behavior. Examples are similar to interrupted attempts, except that the individual stops him/herself, instead of being stopped by something else. ***Has there been a time when you started to do something to try to end your life but you stopped yourself before you actually did anything?*** If yes, describe:	**Yes No** ☐ ☐ Total # of aborted _____
Preparatory Acts or Behavior: Acts or preparation towards imminently making a suicide attempt. This can include anything beyond a verbalization or thought, such as assembling a specific method (e.g., buying pills, purchasing a gun) or preparing for one's death by suicide (e.g., giving things away, writing a suicide note). ***Have you taken any steps towards making a suicide attempt or preparing to kill yourself (such as collecting pills, getting a gun, giving valuables away or writing a suicide note)?*** If yes, describe:	**Yes No** ☐ ☐
Suicidal Behavior: Suicidal behavior was present during the assessment period?	**Yes No** ☐ ☐
Suicide:	**Yes No** ☐ ☐
Answer for Actual Attempts Only	Most Lethal Attempt Date:
Actual Lethality/Medical Damage: 0. No physical damage or very minor physical damage (e.g., surface scratches). 1. Minor physical damage (e.g., lethargic speech; first-degree burns; mild bleeding; sprains). 2. Moderate physical damage; medical attention needed (e.g., conscious but sleepy, somewhat responsive; second-degree burns; bleeding of major vessel). 3. Moderately severe physical damage; *medical* hospitalization and likely intensive care required (e.g., comatose with reflexes intact; third-degree burns less than 20% of body; extensive blood loss but can recover; major fractures). 4. Severe physical damage; *medical* hospitalization with intensive care required (e.g., comatose without reflexes; third-degree burns over 20% of body; extensive blood loss with unstable vital signs; major damage to a vital area). 5. Death	*Enter Code* _____
Potential Lethality: Only Answer if Actual Lethality=0 Likely lethality of actual attempt if no medical damage (the following examples, while having no actual medical damage, had potential for very serious lethality: put gun in mouth and pulled the trigger but gun fails to fire so no medical damage; laying on train tracks with oncoming train but pulled away before run over). 0 = Behavior not likely to result in injury 1 = Behavior likely to result in injury but not likely to cause death 2 = Behavior likely to result in death despite available medical care	*Enter Code* _____

Posner K, Oquendo MA, Gould M, et al. Columbia classification algorithm of suicide assessment (C-CASA): classification of suicidal events in the FDA's pediatric suicidal risk analysis of antidepressants. Am J Psychiatry 2007;164(7):1035-43.

CCI

SF36v2™ HEALTH SURVEY - Page 1 of 6

☐ (1) NOT DONE Language Administered: ☒ (44) English for USA

Your Health and Well-Being

This survey asks for your views about your health. This information will help keep track of hov you feel and how well you are able to do your usual activities. *Thank you for completing this survey!*

For each of the following questions, please mark an [X] in the one box that best describes you answer.

1. In general, would you say your health is:

Excellent	Very good	Good	Fair	Poor
W	W	W	W	W
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

2. <u>Compared to one week ago</u>, how would you rate your health in general <u>now</u>?

Much better now than one week ago	Somewhat better now than one week ago	About the same as one week ago	Somewhat worse now than one week ago	Much worse now than one week ago
W	W	W	W	W
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

SF36v2™ HEALTH SURVEY - Page 2 of 6

3. The following questions are about activities you might do during a typical day. Does <u>your health now limit you</u> in these activities? If so, how much?

	Yes, limited a lot	Yes, limited a little	No, not limited at all
	W	W	W
a. <u>Vigorous activities</u>, such as running, lifting heavy objects, participating in strenuous sports	☐ 1	☐ 2	☐ 3
b. <u>Moderate activities</u>, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf	☐ 1	☐ 2	☐ 3
c. Lifting or carrying groceries	☐ 1	☐ 2	☐ 3
d. Climbing <u>several</u> flights of stairs	☐ 1	☐ 2	☐ 3
e. Climbing <u>one</u> flight of stairs	☐ 1	☐ 2	☐ 3
f. Bending, kneeling, or stooping	☐ 1	☐ 2	☐ 3
g. Walking <u>more than a mile</u>	☐ 1	☐ 2	☐ 3
h. Walking <u>several hundred yards</u>	☐ 1	☐ 2	☐ 3
i. Walking <u>one hundred yards</u>	☐ 1	☐ 2	☐ 3
j. Bathing or dressing yourself	☐ 1	☐ 2	☐ 3

SF36v2™ HEALTH SURVEY - Page 3 of 6

4. During the past week, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of your physical health?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
	W	W	W	W	W
a. Cut down on the amount of time you spent on work or other activities	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b. Accomplished less than you would like	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c. Were limited in the kind of work or other activities	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
d. Had difficulty performing the work or other activities (for example, it took extra effort)	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

5. During the past week, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)?

	All of the time	Most of the time	Some of the time	A little of the time	None of the time
	W	W	W	W	W
a. Cut down on the amount of time you spent on work or other activities	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b. Accomplished less than you would like	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c. Did work or other activities less carefully than usual	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

SF36v2™ HEALTH SURVEY - Page 4 of 6

6. **During the <u>past week</u>, to what extent has your <u>physical health or emotional problems</u> interfered with your normal social activities with family, friends, neighbors, or groups?**

Not at all	Slightly	Moderately	Quite a bit	Extremely
W ☐ 1	W ☐ 2	W ☐ 3	W ☐ 4	W ☐ 5

7. **How much <u>bodily</u> pain have you had during the <u>past week</u>?**

None	Very mild	Mild	Moderate	Severe	Very Severe
W ☐ 1	W ☐ 2	W ☐ 3	W ☐ 4	W ☐ 5	W ☐ 6

8. **During the <u>past week</u>, how much did <u>pain</u> interfere with your normal work (including both work outside the home and housework)?**

Not at all	A Little Bit	Moderately	Quite a bit	Extremely
W ☐ 1	W ☐ 2	W ☐ 3	W ☐ 4	W ☐ 5

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9. These questions are about how you feel and how things have been with you during the past week. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past week...

	All of the time W	Most of the time W	Some of the time W	A little of the time W	None of the time W
a. Did you feel full of life?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b. Have you been very nervous?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c. Have you felt so down in the dumps that nothing could cheer you up?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
d. Have you felt calm and peaceful?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
e. Did you have a lot of energy?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
f. Have you felt downhearted and depressed?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
g. Did you feel worn out?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
h. Have you been happy?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
i. Did you feel tired?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

10. During the past week, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting friends, relatives, etc.)?

All of the time W	Most of the time W	Some of the time W	A little of the time W	None of the time W
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

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11. How TRUE or FALSE is <u>each</u> of the following statements for you?

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
	W	W	W	W	W
a. I seem to get sick a little easier than other people	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b. I am as healthy as anybody I know	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c. I expect my health to get worse	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
d. My health is excellent	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

THANK YOU FOR COMPLETING THESE QUESTIONS!

SF36v2™ HEALTH SURVEY - Page 6 of 6

11. How TRUE or FALSE is <u>each</u> of the following statements for you?

	Definitely true	Mostly true	Don't know	Mostly false	Definitely false
	W	W	W	W	W
a. I seem to get sick a little easier than other people	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
b. I am as healthy as anybody I know	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
c. I expect my health to get worse	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
d. My health is excellent	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

THANK YOU FOR COMPLETING THESE QUESTIONS!

(SF-36v2 Standard, US Version 2.0).

McHorney CA, Ware JE, Lu JFR, et al. The MOS 36Item ShortForm Health Survey (SF36®): III. tests of data quality, scaling assumptions and reliability across diverse patient groups. Med Care 1994; 32(4):4066. Ware JE, Snow KK, Kosinski M, et al. 36® Health Survey Manual and Interpretation Guide. Boston, MA: New England Medical Center, The Health Institute, 1993.Ware JE and Sherbourne CD. The MOS 36Item.

Appendix 8. Dermatology Life Quality Index

DERMATOLOGY LIFE QUALITY INDEX

DLQI

The aim of this questionnaire is to measure how much your skin problem has affected your life OVER THE LAST WEEK. Please tick one box for each question.

1.	Over the last week, how **itchy**, **sore**, **painful** or **stinging** has your skin been?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	
2.	Over the last week, how **embarrassed** or **self conscious** have you been because of your skin?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	
3.	Over the last week, how much has your skin interfered with you going **shopping** or looking after your **home** or **garden?**	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
4.	Over the last week, how much has your skin influenced the **clothes** you wear?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
5.	Over the last week, how much has your skin affected any **social** or **leisure** activities?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
6.	Over the last week, how much has your skin made it difficult for you to do any **sport**?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
7.	Over the last week, has your skin prevented you from **working** or **studying**?	yes no	☐ ☐	Not relevant ☐
	If "No", over the last week how much has your skin been a problem at **work** or **studying**?	A lot A little Not at all	☐ ☐ ☐	
8.	Over the last week, how much has your skin created problems with your **partner** or any of your **close friends** or **relatives**?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
9.	Over the last week, how much has your skin caused any **sexual difficulties**?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐
10.	Over the last week, how much of a problem has the **treatment** for your skin been, for example by making your home messy, or by taking up time?	Very much A lot A little Not at all	☐ ☐ ☐ ☐	Not relevant ☐

Please check you have answered EVERY question. Thank you.

Appendix 9. 5D Pruritus Scale

5-D Pruritus Scale

1. **Duration**: During the last 2 weeks, how many hours a day have you been itching?

Less than 6hrs/day	6-12 hrs/day	12-18 hrs/day	18-23 hrs/day	All day
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

2. **Degree**: Please rate the intensity of your itching over the past 2 weeks

Not present	Mild	Moderate	Severe	Unbearable
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

3. **Direction**: Over the past 2 weeks has your itching gotten better or worse compared to the previous month?

Completely resolved	Much better, but still present	Little bit better, but still present	Unchanged	Getting worse
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

4. **Disability**: Rate the impact of your itching on the following activities over the last 2 weeks

	Never affects sleep	Occasionally delays falling asleep	Frequently delays falling asleep	Delays falling asleep and occasionally wakes me up at night	Delays falling asleep and frequently wakes me up at night
Sleep	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

	N/A	Never affects this activity	Rarely affects this activity	Occasionally affects this activity	Frequently affects this activity	Always affects this activity
Leisure/Social	☐	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Housework/ Errands	☐	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
Work/School	☐	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

5. **Distribution:** Mark whether itching has been present in the following parts of your body over the last 2 weeks. If a body part is not listed, choose the one that is closest anatomically.

	Present		Present
Head/Scalp	☐	Soles	☐
Face	☐	Palms	☐
Chest	☐	Tops of Hands/Fingers	☐
Abdomen	☐	Forearms	☐
Back	☐	Upper Arms	☐
Buttocks	☐	Points of Contact w/ Clothing	
Thighs	☐	(e.g waistband, undergarment)	☐
Lower legs	☐	Groin	☐
Tops of Feet/Toes	☐		

Appendix 10. EQ-5D-5L AND EQ-VAS

Health Questionnaire

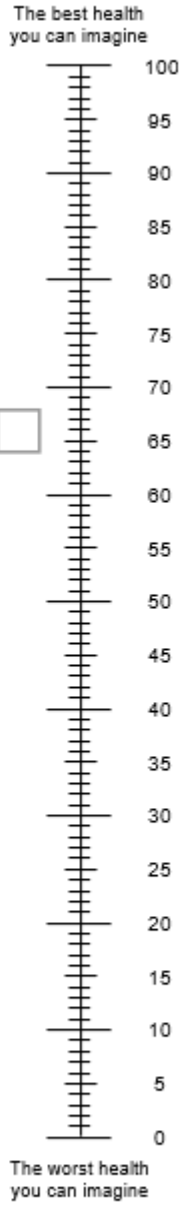
English version for the USA

Under each heading, please check the ONE box that best describes your health TODAY.	
MOBILITY	
I have no problems walking	❑
I have slight problems walking	❑
I have moderate problems walking	❑
I have severe problems walking	❑
I am unable to walk	❑
SELF-CARE	
I have no problems washing or dressing myself	❑
I have slight problems washing or dressing myself	❑
I have moderate problems washing or dressing myself	❑
I have severe problems washing or dressing myself	❑
I am unable to wash or dress myself	❑
USUAL ACTIVITIES *(e.g. work, study, housework, family or leisure activities)*	
I have no problems doing my usual activities	❑
I have slight problems doing my usual activities	❑
I have moderate problems doing my usual activities	❑
I have severe problems doing my usual activities	❑
I am unable to do my usual activities	❑
PAIN / DISCOMFORT	
I have no pain or discomfort	❑
I have slight pain or discomfort	❑
I have moderate pain or discomfort	❑
I have severe pain or discomfort	❑
I have extreme pain or discomfort	❑
ANXIETY / DEPRESSION	
I am not anxious or depressed	❑
I am slightly anxious or depressed	❑
I am moderately anxious or depressed	❑
I am severely anxious or depressed	❑
I am extremely anxious or depressed	❑

2

- We would like to know how good or bad your health is TODAY.
- This scale is numbered from 0 to 100.
- 100 means the best health you can imagine.
  0 means the worst health you can imagine.
- Mark an X on the scale to indicate how your health is TODAY.
- Now, please write the number you marked on the scale in the box below.

YOUR HEALTH TODAY = ☐



3

Appendix 11. FACIT-F Scale

FACIT Fatigue Scale (Version 4)

Below is a list of statements that other people with your illness have said are important. **Please circle or mark one number per line to indicate your response as it applies to the past 7 days.**

		Not at all	A little bit	Some-what	Quite a bit	Very much
HI7	I feel fatigued	0	1	2	3	4
HI12	I feel weak all over	0	1	2	3	4
An1	I feel listless ("washed out")	0	1	2	3	4
An2	I feel tired	0	1	2	3	4
An3	I have trouble starting things because I am tired	0	1	2	3	4
An4	I have trouble finishing things because I am tired	0	1	2	3	4
An5	I have energy	0	1	2	3	4
An7	I am able to do my usual activities	0	1	2	3	4
An8	I need to sleep during the day	0	1	2	3	4
An12	I am too tired to eat	0	1	2	3	4
An14	I need help doing my usual activities	0	1	2	3	4
An15	I am frustrated by being too tired to do the things I want to do	0	1	2	3	4
An16	I have to limit my social activity because I am tired	0	1	2	3	4

Appendix 12. 12 HAQ

IMACS FORM 05a: HEALTH ASSESSMENT QUESTIONNAIRE

Subject's IMACS number_____
Person Completing: ☐ Patient ☐ Other: Relationship_____
Date of assessment (mm/dd/yy)_____ Assessment number_____

In this section we are interested in learning how your illness affects your ability to function in daily life. Please feel free to add any comments on the back of this page.
Please check the response which best describes your usual abilities OVER THE PAST WEEK:

	Without ANY difficulty[0]	With SOME difficulty[1]	With MUCH difficulty[2]	UNABLE to do[3]
DRESSING & GROOMING				
Are you able to:				
-Dress yourself, including tying shoelaces, and doing buttons?	☐	☐	☐	☐
-Shampoo your hair?	☐	☐	☐	☐
ARISING				
Are you able to:				
-Stand up from a straight chair?	☐	☐	☐	☐
-Get in and out of bed?	☐	☐	☐	☐
EATING				
Are you able to:				
-Cut your meat?	☐	☐	☐	☐
-Lift a full cup or glass to your mouth?	☐	☐	☐	☐
-Open a milk carton?	☐	☐	☐	☐
WALKING				
Are you able to:				
-Walk outdoors on flat ground?	☐	☐	☐	☐
-Climb up five steps?	☐	☐	☐	☐

Please check any AIDS OR DEVICES that you usually use for any if these activities:

- ☐ Cane
- ☐ Walker
- ☐ Crutches
- ☐ Wheelchair
- ☐ Devices used for dressing (button hook, zipper pull, shoe horn, etc.)
- ☐ Special or built up utensils
- ☐ Special or built up chair
- ☐ Other (specify:_____)

Please check any categories for which you usually need HELP FROM ANOTHER PERSON:

- ☐ Dressing and Grooming
- ☐ Arising
- ☐ Eating
- ☐ Walking

IMACS FORM 05a: HEALTH ASSESSMENT QUESTIONNAIRE 1

Subject's IMACS number_____ Person Completing: ☐ Patient ☐ Other
Date of assessment (mm/dd/yy)_____ Assessment number_____

Please check the response which best describes your usual abilities OVER THE PAST WEEK:

	Without ANY difficulty[0]	With SOME difficulty[1]	With MUCH difficulty[2]	UNABLE to do[3]
HYGENE				
Are you able to:				
-Wash and dry your body?	☐	☐	☐	☐
-Take a tub bath	☐	☐	☐	☐
-Get on and off the toilet	☐	☐	☐	☐
REACH				
Are you able to:				
-Reach and get down a 5-pound object (such as a bag of sugar) from just above your head?	☐	☐	☐	☐
-Bend down to pick up clothing from floor?	☐	☐	☐	☐
GRIP				
Are you able to:				
-Open car doors?	☐	☐	☐	☐
-Open jars which have been previously opened?	☐	☐	☐	☐
-Turn faucets on and off?	☐	☐	☐	☐
ACTIVITIES				
Are you able to:				
-Run errands and shop?	☐	☐	☐	☐
-Get in and out of a car?	☐	☐	☐	☐
-Do chores such as vacuuming or yardwork?	☐	☐	☐	☐

Please check any AIDS or DEVICES that you usually use for any activities:

☐ Raised toilet seat
☐ Bathtub bar
☐ Bathtub seat
☐ Long-handled appliances for reach
☐ Jar opener (for jars previously opened)
☐ Long-handled appliances in bathroom
☐ Other (specify_____)

Please check any categories for which you usually need HELP FROM ANOTHER PERSON:

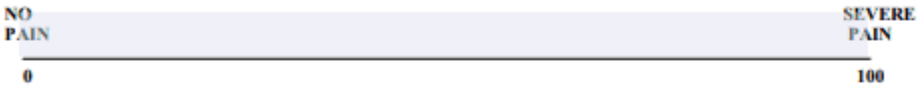
☐ Hygiene
☐ Gripping and opening things
☐ Reach
☐ Errands and chores

IMACS FORM 05a: HEALTH ASSESSMENT QUESTIONNAIRE 2

We are also interested in learning whether or not you are affected by pain because of your illness.

How much pain have you had because of your illness IN THE PAST WEEK:

PLACE A VERTICAL (|) MARK ON THE LINE TO INDICATE THE SEVERITY OF PAIN



IMACS FORM 05a: HEALTH ASSESSMENT QUESTIONNAIRE 3

Appendix 13. Patient Global Assessment (PtGA)

IMACS FORM 03: PATIENT/PARENT GLOBAL ACTIVITY ASSESSMENT

Subject's IMACS number _____

Assessor _____ _____

Assessor's relationship to subject: ◯Patient; ◯Mother; ◯Father; ◯Other (specify):_____

Date of assessment (mm/dd/yy) _____

Assessment number _____

Your myositis is the result of the combined effects of many disease processes. One of these is disease activity, which is active inflammation in your/your child's muscles, skin, joints, intestines, heart, lungs or other parts of your body, which can improve when treated with medicines.

1. Considering all the ways that myositis affects you/your child, please rate the overall activity of your/your child's disease today by placing a mark on the line below.

No evidence of disease activity

Extremely active or severe disease activity

Appendix 14. Guidelines for Participant Safety Monitoring and Discontinuation

These guidelines for participant safety monitoring and discontinuation are to be applied to all participants in study C0251002. Additional individual participant monitoring is at the discretion of the investigator and dependent on any perceived safety concerns. Unscheduled clinical labs may be obtained at any time during the study to assess such concerns, and a participant may be withdrawn at any time at the discretion of the investigator.

Monitoring

Please Note: For Participants with DM who experience elevated AST, ALT, LDH, Aldolase, and CK, due to muscle involvement the investigator should determine whether or not these are related to the existing condition of DM or if these lab abnormalities are related to another condition. (If related to DM, GGT should be <1.5 ULN) Information should be provided in the source documentation with rationale related to any lab abnormalities.

The following laboratory abnormalities require re-testing within 1 week:

- Any single AST and/or ALT elevation ≥3 times the upper limit of normal (repeat laboratory testing should include albumin, creatine kinase, total bilirubin, direct and indirect bilirubin, GGT, PT [prothrombin time] with INR [international normalized ratio], and alkaline phosphatase), regardless of the total bilirubin. (Please note that 3 times the upper limit of normal increases in ALT, AST need confirmation on separate blood draw before undertaking thorough evaluation for liver injury);

- For women of child-bearing potential with any positive urine β-hCG test, the participant will have study drug interrupted and a serum sample submitted to the central laboratory for β-hCG testing.

Discontinuation

Investigators are encouraged to discuss with the sponsor's Clinical team as soon as possible, and participants are to be discontinued from treatment if any of the following occur during the study:

- Serious infections defined as any infection (viral, bacterial, and fungal) requiring parenteral antimicrobial therapy, hospitalization for treatment, or meeting other criteria that require the infection to be classified as serious adverse event;

- Other serious or severe AEs, at the discretion of the investigator or sponsor;

- If there are "yes" answers on items 4, 5, or on any behavior question of the C-SSRS, the participant will be discontinued from treatment and referred to a mental health professional for appropriate evaluation and treatment (if the participant cannot be seen by a mental health professional within 24 hours, then the participant should be sent to a local emergency room for psychiatric assessment);

- All of the following laboratory abnormalities require discontinuation if they are confirmed (confirmation through re-testing is expected to occur within 1 week):
  - Two sequential AST or ALT elevation ≥3 times the upper limit of normal with at least one total bilirubin value ≥2 times the upper limit of normal;[a]
  - Two sequential AST or ALT elevation ≥3 times the upper limit of normal accompanied by signs or symptoms consistent with hepatic injury;[a]
  - Two sequential AST or ALT elevation ≥5 times the upper limit of normal, regardless of total bilirubin or accompanying signs or symptoms;[a]
  - Female participants found to be pregnant during the study;
  - Other serious or severe AEs, after consultation with the Pfizer medical monitor or designee.

a. In each case, there is a need for additional investigations, such as review of ethanol, recreational drug and dietary supplement consumption; testing for acute hepatitis A, B or C infection and biliary tract imaging should be promptly discussed with the Pfizer medical monitor or designee.

Use of prohibited medications require participant discontinuation as reflected in Appendix 16:

Please refer to Appendix 16 for all inclusive prohibited medication listing.

Any participant meeting discontinuation criteria must enter follow-up with their first follow-up visit occurring 1 week after their last dose whenever possible, until the event has returned to normal or baseline levels or is deemed clinically stable. The procedures scheduled for the early withdrawal visit will be performed on the last day the participant takes the IP or as soon as possible thereafter. The only exception to this is when a participant specifically withdraws consent for any further contact with him/her or persons previously authorized by the participant to provide this information.

Participants will be followed post drug discontinuation for 5 months. Additional follow-up visits may occur as needed until any clinically relevant abnormalities or adverse events have resolved, returned to a baseline state, or are deemed clinically stable.

Appendix 15. Time needed for Washout of Prohibited Medication or Medication Stabilization Prior to Day 1

180 days (6 months) prior to DAY 1
• B-cell depleting agents, (rituximab, epratuzumab, alemtuzumab, or TACI-Ig). In addition, participants that have been treated with rituximab, or TACI-g, (serum total immunoglobulin should be checked prior to study entry); • Investigational biologic agent; • IV or Oral Cyclophosphamide; • Belimumab; or • Any B-Lymphocyte Stimulator, (BLys or anti BAFF agent).
90 Days (3 months) prior to DAY 1
• Anti-TNF therapy, (infliximab, etanercept, adalimumab). • High dose oral corticosteroids (>100 mg/day prednisone, or equivalent) or pulse IV doses. • Plasmapheresis.
60 Days (2 months) prior to DAY 1
• Any IV or IM steroid injection • Tofacitinib or any other JAK inhibitor • Stable dose of antimalarial agent 60 days, • Stable dose of immunosuppressive/immunomodulatory agent (60 days) • INHALED immunosuppressive agents (STABLE 60 days prior to Day 1, dose must remain stable during the study) • DMARDs, (methotrexate, sulfasalazine, hydroxychloroquine, and leflunomide. Less frequently used medications include gold salts, azathioprine, and cyclosporine) Dose must be stable for 60 days and remain stable during the treatment. • Participants may be on one of the following cytotoxic agents: Methotrexate,(MTX), Azathioprine, (AZA), leflunominde, mycophenolate, or 6- Mercaptopurine (MP), but not on any combination of these cytotoxic agents.   • Replacement of one immunosuppressive medication or antimalarial drug for another may be permitted for safety related issues after discussion with the sponsor.

42 Days (6 weeks prior to Day 1)
• Live or attenuated vaccine.
30 Days (1 month prior to Day 1)
• Intra articular steroid injection. • Must be on a stable dose of corticosteroid or equivalent for 30 days. • Must be on a stable dose of IVIG for 30 days. • Oral Tacrolimus requires a 30 day washout prior to Day 1 and is prohibited throughout the treatment period.
14 Days (2 weeks prior to Day 1)
• Topical calcineurin inhibitors, (eg, topical tacrolimus, pimecrolimus) require a 14 day washout prior to Day 1 and are prohibited throughout the treatment period. • A stable dose of topical immunosuppressant of any strength used on the scalp is permitted throughout the study, with the exception of prohibited medications.
Marketed Biologics (prior to Day 1)
• Marketed Biologics require a five half-life washout period.

Appendix 16. List of Prohibited and Permitted Concomitant Medications

Medications		C0251002 **Treatment Period Day 1-Week 12 (Stage 2)** **Treatment Period Day 1-Week 24 (Amended Stage 2** **(Amended Stage 3)**	Follow-up Period
Corticosteroids	Parenteral injections (intra-articular) IA, IM, or IV)	Prohibited	Permitted
	Oral (prednisone or equivalent)	Permitted (Stage 2) • Prednisone ≤15 mg/day or equivalent provided dose is stable for at least 30 days prior to Day 1. Permitted (Stage 3) • Prednisone ≤20 mg/day or equivalent provided dose is stable for at least 30 days prior to Day 1. • Tapering of steroids is permitted after Week 24, in Amended Stage 2 and Stage 3.	Permitted
Immunosuppressive or immunomodulatory agents including methotrexate (MTX), azathioprine (AZA), leflunomide, mycophenolate (including mycophenolate mofetil, mycophenolate mofetil hydrochloride, and mycophenolate sodium), or 6-mercaptopurine (6-MP).		Permitted • Provided pre-existing dose is stable for at least 60 days prior to Day 1. • No new immunosuppressives or increase in dose is allowed during the treatment period. • Participants can be on 1 of the following cytotoxic agents: MTX, AZA, leflunomide, mycophenolate, or 6-MP, but not on any combination of these cytotoxic agents.	Permitted
Antimalarials (eg, hydroxychloroquine, chloroquine, quinacrine)		Permitted • Provided pre-existing dose is stable for at least 60 days prior to Day 1. • No new antimalarial drugs or increase in dose is allowed during the treatment period.	Permitted
Thalidomide, tacrolimus, or mizoribine		Prohibited • Any form of tacrolimus or any form of a topical calcineurin inhibitor, (TCI) is not allowed.	Permitted
Immunosuppressive topical		Permitted • Immunosuppressive ointment for the scalp. Stable dose for 14 days prior to Day 1.	Permitted
Topical calcineurin inhibitors		Prohibited	Permitted
Immunosuppressive eye drops		Permitted	Permitted

Medications	C0251002 Treatment Period Day 1-Week 12 (Stage 2) Treatment Period Day 1-Week 24 (Amended Stage 2 (Amended Stage 3)	Follow-up Period
Investigational or marketed biologics (eg, abatacept, tocilizumab, TNF inhibitors)	Prohibited	Prohibited
Cyclophosphamide or chlorambucil	Prohibited	Permitted
Cyclosporine	Prohibited	Permitted
Other investigational drugs or investigational combinations	Prohibited	Prohibited
B-cell depleting therapy (eg, rituximab, belimumab, epratuzumab)	Prohibited	Prohibited
Any live (live attenuated) vaccines	Prohibited	Prohibited
Inactivated vaccine and boosters	Permitted	Permitted
Kinase inhibitors (eg, tofacitinib, ruxolitinib)	Prohibited	Permitted
IVIG	Permitted	Permitted
Pre- Medication with corticosteroids for IVIG administration: On the day of the IVIG dose administration, pre-medication to prevent hypersensitivity reaction to IVIG is permitted. Steroid dose that was previously used for pre- medication will be permitted (on IVIG dosing day only). After IVIG dosing day, steroid dosing should remain less than or equal to 15 mg or equivalent per day as per protocol Section 5.8.5.	Permitted	Permitted

Note: If you have any questions about the use of a drug, please contact the study team. If you see that a specific drug is not listed, but it is in the same drug class as a prohibited drug; it should be considered prohibited.

Appendix 17. Alternative Measures During Public Emergencies

The alternative study measures described in this section are to be followed during public emergencies, including the COVID-19 pandemic. This appendix applies for the duration of the COVID-19 pandemic globally and will become effective for other public emergencies only upon written notification from Pfizer.

Use of these alternative study measures are expected to cease upon the return of business as usual circumstances (including the lifting of any quarantines and travel bans/advisories).

Appendix 17.1. **Telehealth Visits (if applicable)**

In the event that in-clinic study visits cannot be conducted, every effort should be made to follow up on the safety of study participants at scheduled visits per the Schedule of Activities or unscheduled visits. Telehealth visits may be used to continue to assess participant safety and collect data points. Telehealth includes the exchange of healthcare information and services via telecommunication technologies (eg, audio, video, video-conferencing software) remotely, allowing the participant and the investigator to communicate on aspects of clinical care, including medical advice, reminders, education, and safety monitoring.

The following assessments may be performed during a telehealth visit:

- Review and record any AEs and SAEs since the last contact. Refer to Section 8.3, and Section 12.4.
- Review and record any new concomitant medications or changes in concomitant medications since the last contact.
- Review and record contraceptive method. Confirm that the participant is adhering to the contraception method(s) required in the protocol. Refer to Section 4.8.2 and Appendix 25. German participants will follow Appendix 24.
- PGA.
- CDASI (if applicable).
- CSSRS (if applicable).
- Patient Reported Outcomes (if applicable).
- Study participants must be reminded to promptly notify site staff about any change in their health status.

Appendix 17.2. **Home Health Visits (If applicable)**

A home health care service will be utilized to facilitate scheduled visits per the Schedule of Activities. Home health visits include a healthcare provider conducting an in-person study visit at the participant's location, rather than an in-person study visit at the site. The following may be performed during a home health visit:

- Lab Collection;
- Physical assessment;
- Vital signs.

Appendix 17.3. **Laboratory Testing: (If applicable)**

- If a study participant is unable to visit the site for protocol-specified safety laboratory evaluations, testing may be conducted at a local laboratory if permitted by local regulations. The local laboratory may be a standalone institution or within a hospital. The following safety laboratory evaluations may be performed at a local laboratory:

  Please refer to Table 1 of the protocol; not all laboratory collections may be possible.

  - Hematology;
  - Chemistry;
  - Urinalysis;
  - Viral Surveillance (if applicable);
  - Pregnancy testing (if applicable);
  - PK (if applicable).

- If a participant requiring pregnancy testing cannot visit a local laboratory for pregnancy testing, a home urine pregnancy testing kit with a sensitivity of at least 25 IU/mL may be used by the participant to perform the test at home, if compliant with local regulatory requirements. The pregnancy test outcome should be documented in the participant's source documents/medical records and relevant data recorded on the CRF. Confirm that the participant is adhering to the contraception method(s) required in the protocol.

- If a local laboratory is used, qualified study site personnel must order, receive, and review results. Site staff must collect the local laboratory reference ranges and certifications/accreditations for filing at the site. Laboratory test results are to be provided to the site staff as soon as possible. The local laboratory reports should

be filed in the participant's source documents/medical records. Relevant data from the local laboratory report should be recorded on the CRF.

Appendix 17.4. **Electrocardiograms (If applicable)**

- If the participant is unable to visit the study site for ECGs, the participant may visit an alternative facility to have the ECGs performed. Qualified study site personnel must order, receive, and review results.

Appendix 17.5. **Adverse Events and Serious Adverse Events**

- If a participant has COVID-19 during the study, this should be reported as an adverse event (AE) or serious adverse events (SAE) and appropriate medical intervention provided. There is a potential risk of increased susceptibility to viral infections with IFNβ blockade as with any antagonist of Type 1 interferon signaling (eg, anti-IFNAR1, anti-IFNα, JAK inhibitors). Viral monitoring will be conducted as a precautionary measure to ensure participant safety. Details can be found in the trial protocol as well as the investigators brochure. Temporary discontinuation of the study intervention may be medically appropriate until the participant has recovered from COVID-19.

- It is recommended that the investigator discuss temporary or permanent discontinuation of study intervention with the study medical monitor.

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Appendix 19. Muscle Enzymes

IMACS FORM 06: SERUM LEVELS OF MUSCLE ENZYMES

Subject's IMACS number _____
Date of assessment (mm/dd/yy) _____
Assessment number _____

Blood laboratories:	Result	Normal Range
Creatine kinase (IU/L)		
Aldolase (IU/L)		
SGOT (IU/L)		
SGPT (IU/L)		
LDH (IU/L)		
Creatinine (mg/dl)		

Appendix 20. MDAAT

IMACS FORM 07a: MYOSITIS DISEASE ACTIVITY ASSESSMENT TOOL – 2005, Version 2

Subject's IMACS number: _____ **ASSESSOR:** _____ **Date Assessed:** _____ **Assessment number:** _____

Constitutional Disease Activity	(Absent) (Maximum) __ __. __ cm	Examples of maximal score: Severe fatigue or malaise resulting in being bed bound and an inability to perform self care					
1. Pyrexia – documented fever > 38° Celsius		0	1	2	3	4	NA
2. Weight loss – unintentional > 5%		0	1	2	3	4	NA
3. Fatigue/malaise/lethargy		0	1	2	3	4	NA

Cutaneous Disease Activity	(Absent) (Maximum) __ __. __ cm	Examples of maximal score: - Ulceration to muscle, tendon or bone; - Extensive erythroderma					
4. Cutaneous ulceration		0	1	2	3	4	NA
5. Erythroderma		0	1	2	3	4	NA
6. Panniculitis		0	1	2	3	4	NA
7. Erythematous rashes:							
a. **with** secondary changes (e.g. accompanied by erosions, vesiculobullous change or necrosis)		0	1	2	3	4	NA
b. **without** secondary changes		0	1	2	3	4	NA
8. Heliotrope rash		0	1	2	3	4	NA
9. Gottron's papules/sign		0	1	2	3	4	NA
10. Periungual capillary changes		0	1	2	3	4	NA
11. Alopecia:							
a. Diffuse hair loss		0	1	2	3	4	NA
b. Focal, patchy with erythema		0	1	2	3	4	NA
12. Mechanics hands		0	1	2	3	4	NA

IMACS Form 07a: Myositis Disease Activity Assessment Tool – 2005, Version 2, updated 2015 Page 1 of 3

Skeletal Disease Activity	(Absent) — (Maximum) __ __ . __ cm	**Examples of maximal score** Severe arthritis with extreme loss of function (bedridden, inability for self care)

13. Arthritis:						
a. Severe active polyarthritis	0	1	2	3	4	NA
b. Moderately active arthritis	0	1	2	3	4	NA
c. Mild arthritis	0	1	2	3	4	NA
14. Arthralgia	0	1	2	3	4	NA

Gastrointestinal Disease Activity	(Absent) — (Maximum) __ __ . __ cm	**Examples of maximal score** Major abdominal crisis requiring surgery or intensive care

15. Dysphagia:						
a. Moderate/severe dysphagia	0	1	2	3	4	NA
b. Mild dysphagia	0	1	2	3	4	NA
16. Abdominal pain related to the myositis disease process:						
a. Severe	0	1	2	3	4	NA
b. Moderate	0	1	2	3	4	NA
c. Mild	0	1	2	3	4	NA

Pulmonary Disease Activity	(Absent) — (Maximum) __ __ . __ cm	**Examples of maximal score** Active interstitial lung disease or respiratory muscle weakness requiring ventilatory support

17. Respiratory muscle weakness **without** interstitial lung disease (ILD):						
a. Dyspnea at rest	0	1	2	3	4	NA
b. Dyspnea on exertion	0	1	2	3	4	NA
18. **Active reversible ILD** (i.e. not just ventilatory abnormalities due to pulmonary fibrosis): *Read glossary for scoring pulmonary function tests and score each item below (a,b and c).*						
a. Dyspnea or cough due to ILD	0	1	2	3	4	NA
b. Parenchymal abnormalities on chest x-ray or high resolution CT scan (HRCT) and/or ground glass shadowing on HRCT	0	1	2	3	4	NA
c. Pulmonary Function Tests: ≥ 10% change in FVC OR ≥ 15% change in DLCO	0	1	2	3	4	NA
19. Dysphonia:						
a. Moderate to severe	0	1	2	3	4	NA
b. Mild	0	1	2	3	4	NA

IMACS Form 07a: Myositis Disease Activity Assessment Tool – 2005, Version 2, updated 2015

Page 2 of 3

Cardiovascular Disease Activity	(Absent) — (Maximum) ___.__ cm	Examples of maximal score: Myocarditis, pericarditis or severe arrhythmia requiring intensive care unit

20. Pericarditis	0	1	2	3	4	NA
21. Myocarditis	0	1	2	3	4	NA
22. Arrhythmia:						
a. Severe arrhythmia	0	1	2	3	4	NA
b. Other arrhythmia, except sinus tachycardia	0	1	2	3	4	NA
23. Sinus tachycardia	0	1	2	3	4	NA

Other Disease Activity	(Absent) — (Maximum) ___.__ cm	Examples of maximal score: Extreme disease activity with major impact on function

24. Specify:_____	0	1	2	3	4	NA

Extramuscular Global Assessment	(Absent) — (Maximum) ___.__ cm	Overall evaluation for disease activity in all extramuscular systems **(EXCLUDING MUSCLE DISEASE ACTIVITY)**

Muscle Disease Activity	(Absent) — (Maximum) ___.__ cm	Examples of maximal score: Severe muscle weakness resulting in being bed bound and an inability to perform self care

25. Myositis:						
a. Severe muscle inflammation	0	1	2	3	4	NA
b. Moderate muscle inflammation	0	1	2	3	4	NA
c. Mild muscle inflammation	0	1	2	3	4	NA
26. Myalgia	0	1	2	3	4	NA

Global Disease Activity	(Absent) — (Maximum) ___.__ cm	Overall evaluation for the totality of disease activity in ALL systems, **(INCLUDING MUSCLE DISEASE ACTIVITY)**

IMACS Form 07a: Myositis Disease Activity Assessment Tool – 2005, Version 2, updated 2015 Page 3 of 3

Appendix 21. MMT-8

IMACS FORM 04: Manual Muscle Testing Scoring Sheet

Subject's IMACS number _____

Assessor _____

Date of assessment (mm/dd/yy) _____

Assessment number _____

Muscle Groups	Right (0 – 10)	Left (0 – 10)	Axial (0 – 10)
Axial Muscles (0 – 20)			
Neck Flexors**	-	-	
Neck Extensors	-	-	
Proximal Muscles (0 – 160)			
Trapezius			-
Deltoid middle**			-
Biceps brachii**			-
Gluteus maximus**			-
Gluteus medius**			-
Iliopsoas			-
Hamstrings			-
Quadriceps**			-
Distal Muscles (0 – 80)			-
Wrist Extensors**			-
Wrist Flexors			-
Ankle dorsiflexors**			-
Ankle plantar flexors			-
MMT8 score (0 – 80)**			
Total MMT26 score (0 – 260)			

****MMT8** is a set of 8 designated muscles tested unilaterally (potential score 0 – 80), generally on right side (unless cannot be tested on right, then use left side)
Axial score: 0 – 20 potential range: sum of neck flexors and extensors
Proximal score: 0 - 160 potential range; 8 muscle groups tested bilaterally
Distal score: 0 - 80 potential range; 4 muscle groups tested bilaterally
Total score (MMT26): 0 - 260 potential range; sum of axial, proximal and distal scores

IMACS Form 04: Manual Muscle Testing Scoring Sheet

Appendix 22. TIS using Core Set Measures in DM

The **total improvement score** is the sum of all 6 improvement scores associated with the change in each core set measure. A total improvement score of ≥**20** represents **minimal improvement**, a score of ≥**40** represents **moderate improvement**, and a score of ≥**60** represents **major improvement**.[31]

ACR/EULAR CRITERIA FOR CLINICAL RESPONSE IN ADULT DERMATOMYOSITIS AND POLYMYOSITIS

Table 3. Final myositis response criteria for minimal, moderate, and major improvement in adult dermatomyositis/polymyositis (DM/PM) and combined adult DM/PM and juvenile DM clinical trials and studies*

Core set measure, level of improvement based on absolute percent change	Improvement score
Physician global activity	
Worsening to 5% improvement	0
>5% to 15% improvement	7.5
>15% to 25% improvement	15
>25% to 40% improvement	17.5
>40% improvement	20
Patient global activity	
Worsening to 5% improvement	0
>5% to 15% improvement	2.5
>15% to 25% improvement	5
>25% to 40% improvement	7.5
>40% improvement	10
Manual muscle testing	
Worsening to 2% improvement	0
>2% to 10% improvement	10
>10% to 20% improvement	20
>20% to 30% improvement	27.5
>30% improvement	32.5
Health Assessment Questionnaire	
Worsening to 5% improvement	0
>5% to 15% improvement	5
>15% to 25% improvement	7.5
>25% to 40% improvement	7.5
>40% improvement	10
Enzyme (most abnormal)	
Worsening to 5% improvement	0
>5% to 15% improvement	2.5
>15% to 25% improvement	5
>25% to 40% improvement	7.5
>40% improvement	7.5
Extramuscular activity	
Worsening to 5% improvement	0
>5% to 15% improvement	7.5
>15% to 25% improvement	12.5
>25% to 40% improvement	15
>40% improvement	20

The **total improvement score** is the sum of all 6 improvement scores associated with the change in each core set measure. A total improvement score of **≥20** represents **minimal improvement**, a score of **≥40** represents **moderate improvement**, and a score of **≥60** represents **major improvement**.

* Note that these response criteria are also proposed for use in combined adult DM/PM and juvenile DM trials (20). For comparison, the thresholds of improvement in the total improvement score for juvenile DM are ≥30 for minimal improvement, ≥45 for moderate improvement, and ≥70 for major improvement. Also note that the criteria for major improvement for adult DM/PM are preliminary.

How to calculate the improvement score: The absolute percent change ([final value − baseline value]/range × 100) is calculated for each core set measure. For muscle enzymes, the most abnormal serum muscle enzyme level at baseline (creatine kinase, aldolase, alanine transaminase, aspartate aminotransferase, lactate dehydrogenase) is used. The enzyme range was calculated based on a 90% range of enzymes from natural history data (34,46), which for creatine kinase is 15 times the upper limit of normal (ULN), for aldolase is 6 times the ULN, and for lactate dehydrogenase, aspartate aminotransferase, and alanine transaminase is 3 times the ULN. The ULN is determined according to the individual laboratories in the participating centers. The ranges for physician global activity, patient global activity, manual muscle testing, Health Assessment Questionnaire, and extramuscular global activity are based on the instrument scale used (3,26). An improvement score is assigned for each core set measure based on the absolute percent change in the core set measure according to the definition. These individual core set measure improvement scores are then totaled among the 6 core set measures to give the total improvement score. The thresholds for minimal, moderate, and major improvement are provided. The total improvement score itself may also be compared among treatment arms in a trial. A total improvement score between 0 and 100 corresponds to the degree of improvement, with higher scores corresponding to a greater degree of improvement.

Appendix 23. Muscle Damage Index, MDI

IMACS FORM 08: MYOSITIS DAMAGE INDEX (MDI) - 2001

Please see the instructions and Myositis Damage Index Glossary of Terms Prior to Assessment (pp. 5-8).

Subject's IMACS number:_____ **ASSESSOR:**_____ **Date Assessed:**_____**Assessment number:**_____

MUSCLE DAMAGE	(Absent) (Maximum)	**Maximum Value Guidelines (Examples of maximal score)** Severe muscle atrophy or weakness resulting in being bed bound and an inability to perform self care

Please assess the severity and extent of damage exhibited by the patient at this time. To assess the severity, please rate your overall assessment of the current disease damage for by drawing a vertical mark on the 10cm. line according to the following scale: Left end of line = no evidence of disease damage, Midpoint of line = moderate disease damage, and -Right end of line = extreme or maximum disease damage. Please write in NA if the system cannot be assessed.

Appendix 24. CTFG Guidelines[34] Regarding Contraception for Germany

Birth control methods which may be considered as highly effective:

For the purpose of this guidance, methods that can achieve a failure rate of less than 1% per year when used consistently and correctly are considered as highly effective birth control methods. Such methods include:

1. Combined (estrogen and progestogen containing) hormonal contraception associated with inhibition of ovulation:[1]
   - Oral;
   - Intravaginal;
   - Transdermal.
2. progestogen-only hormonal contraception associated with inhibition of ovulation:[1]
   - oral
   - injectable
   - implantable.[2]
3. intrauterine device (IUD).[2]
4. intrauterine hormone-releasing system (IUS).[2]
5. bilateral tubal occlusion.[2]
6. vasectomised partner.[2,3]
7. sexual abstinence.[4]

1. Hormonal contraception may be susceptible to interaction with the IMP, which may reduce the efficacy of the contraception method.
2. Contraception methods that in the context of this guidance are considered to have low user dependency.
3. Vasectomised partner is a highly effective birth control method provided that partner is the sole sexual partner of the WOCBP trial participant and that the vasectomised partner has received medical assessment of the surgical success.
4. In the context of this guidance sexual abstinence is considered a highly effective method only if defined as refraining from heterosexual intercourse during the entire period of risk associated with the study treatments. The reliability of sexual abstinence needs to be evaluated in relation to the duration of the clinical trial and the preferred and usual lifestyle of the subject.

Appendix 25. Contraceptive and Barrier Guidance

Appendix 25.1. **Male Participant Reproductive Inclusion Criteria**

Male participants are eligible to participate if they agree to the following requirements during the intervention period and for at least 5 months after the last dose of study intervention, which corresponds to the time needed to eliminate reproductive safety risk of the study intervention.

- Refrain from donating sperm.

PLUS either:

- Be abstinent from heterosexual intercourse with a female of childbearing potential as their preferred and usual lifestyle (abstinent on a long-term and persistent basis) and agree to remain abstinent.

OR

- Must agree to use contraception/barrier as detailed below:
    - Agree to use a male condom and should also be advised of the benefit for a female partner to use a highly effective method of contraception as a condom may break or leak when having sexual intercourse with a woman of childbearing potential who is not currently pregnant.
- In addition to male condom use, a highly effective method of contraception may be considered in WOCBP partners of male participants (refer to the list of highly effective methods below in Appendix 25.4.

Appendix 25.2. **Female Participant Reproductive Inclusion Criteria**

Female Participant Options:

A female participant is eligible to participate if she is not pregnant or breastfeeding, and at least 1 of the following conditions apply.

- Is not a WOCBP (see definitions below in Appendix 25.3.

OR

- Is a WOCBP and using a contraceptive method that is highly effective (with a failure rate of <1% per year), ***preferably*** with low user dependency, as described below during the intervention period and for at least 5 months after the last dose of study intervention, which corresponds to the time needed to eliminate any reproductive safety risk of the study intervention. The investigator should evaluate the

effectiveness of the contraceptive method in relationship to the first dose of study intervention.

- Is a WOCBP and using a contraceptive method that is highly effective (with a failure rate of <1% per year), with high user dependency, as described below during the intervention period and for at least 5 months after the last dose of study intervention, which corresponds to the time needed to eliminate any reproductive safety risk of the study intervention. In addition, a second effective method of contraception, as described below, must be used. The investigator should evaluate the effectiveness of the contraceptive method in relationship to the first dose of study intervention.

The investigator is responsible for review of medical history, menstrual history, and recent sexual activity to decrease the risk for inclusion of a woman with an early undetected pregnancy.

Appendix 25.3. **Women of Childbearing Potential**

A woman is considered fertile following menarche and until becoming post menopausal unless permanently sterile (see below).

If fertility is unclear (eg, amenorrhea in adolescents or athletes) and a menstrual cycle cannot be confirmed before the first dose of study intervention, additional evaluation should be considered.

Women in the following categories are not considered WOCBP:

1. Premenopausal female with 1 of the following:

    - Documented hysterectomy;
    - Documented bilateral salpingectomy;
    - Documented bilateral oophorectomy.

    For individuals with permanent infertility due to an alternate medical cause other than the above, (eg, mullerian agenesis, androgen insensitivity), investigator discretion should be applied to determining study entry.

    Note: Documentation for any of the above categories can come from the site personnel's review of the participant's medical records, medical examination, or medical history interview. The method of documentation should be recorded in the participant's medical record for the study.

2. Postmenopausal female:

    - A postmenopausal state is defined as no menses for 12 months without an alternative medical cause. In addition:

- A high FSH level in the postmenopausal range must be used to confirm a postmenopausal state in women under 60 years of age and not using hormonal contraception or HRT.

- A female on HRT and whose menopausal status is in doubt will be required to use one of the nonestrogen hormonal highly effective contraception methods if they wish to continue their HRT during the study. Otherwise, they must discontinue HRT to allow confirmation of postmenopausal status before study enrollment.

Appendix 25.4. **Contraception Methods**

Contraceptive use by men or women should be consistent with local availability/regulations regarding the use of contraceptive methods for those participating in clinical trials.

Highly Effective Methods That Have Low User Dependency

1. Implantable progestogen-only hormone contraception associated with inhibition of ovulation.

2. Intrauterine device.

3. Intrauterine hormone-releasing system.

4. Bilateral tubal occlusion (eg, bilateral tubal ligation).

5. Vasectomized partner.

    - A vasectomized partner is a highly effective contraceptive method provided that the partner is the sole sexual partner of the WOCBP and the absence of sperm has been confirmed. If not, an additional highly effective method of contraception should be used. The spermatogenesis cycle is approximately 90 days.

Highly Effective Methods That Are User Dependent

6. Combined (estrogen- and progestogen-containing) hormonal contraception associated with inhibition of ovulation:

    - Oral;

    - Intravaginal;

    - Transdermal.

7. Progestogen-only hormone contraception associated with inhibition of ovulation:

    - Oral;

- Injectable.

8. Sexual abstinence:

    - Sexual abstinence is considered a highly effective method only if defined as refraining from heterosexual intercourse during the entire period of risk associated with the study intervention. The reliability of sexual abstinence needs to be evaluated in relation to the duration of the study and the preferred and usual lifestyle of the participant.

One of the following effective barrier methods must be used in addition to the highly effective methods listed above that are user dependent:

- Male or female condom with or without spermicide;
- Cervical cap, diaphragm, or sponge with spermicide;
- A combination of male condom with either cervical cap, diaphragm, or sponge with spermicide (double-barrier methods).