Title Page

AN OPEN LABEL, LONG-TERM EXTENSION STUDY TO INVESTIGATE THE SAFETY OF PF-06823859 ADMINISTERED TO ADULT PARTICIPANTS ≥18 AND ≤80 WITH ACTIVE DERMATOMYOSITIS.

Study Intervention Number:	PF-06823859
Study Intervention Name:	N/A
US IND Number:	129230
EudraCT Number:	2021-004787-10
Protocol Number:	C0251008
Phase:	2b

Brief Title: An Open-Label Extension Study for Participants Who Have Completed the Treatment Period of a Qualifying Parent Study.

Document History

Document	Version Date
Original protocol	03 September 2021

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1. PROTOCOL SUMMARY

1.1. Synopsis

Brief Title: An Open-Label Extension Study for Participants Who Have Completed the Treatment Period of a Qualifying Parent Study.

Rationale

The purpose of the study is to evaluate the long-term safety, and tolerability of PF-06823859 in adult participants with DM from a qualifying study.

Objectives, Endpoints, and Estimands

Objectives	Endpoints	Estimands
Primary:	**Primary:**	**Primary:**
• To evaluate the long-term safety and tolerability of PF-06823859.	• Incidence of AEs, laboratory abnormalities, changes in vital signs, and ECG findings.	• There are no defined estimands for safety and tolerability endpoints; these will be analyzed using Pfizer data standards, as applicable.
Secondary:	**Secondary:**	**Secondary:**
• To evaluate the long-term efficacy of PF-06823859 in adult participants with moderate to severe DM.	• Change from baseline in CDASI activity score at Week 52.	• E1: This estimand uses a hypothetical estimand strategy (ICH E9 addendum) estimating the mean effect of PF-06823859 in the absence of intercurrent events (study withdrawal). This is the mean change from baseline to Week 52 CDASI activity score for all randomized and dosed participants with non-missing baseline score in the (a) Skin Analysis Set and (b) Muscle Analysis Set (see details in Section 9.1.1).
	• Absolute values and changes from baseline of CDASI activity and CDASI damage scores at all scheduled timepoints.	• These additional CDASI endpoints will be analyzed using E1 at all scheduled timepoints.
	• TIS score at Week 52 and at intermediate scheduled timepoints for participants who entered from Stage 3 of Protocol C0251002.	• E2: This estimand uses a hypothetical estimand strategy (ICH E9 addendum) estimating the mean effect of PF-06823859 in the absence

		of intercurrent events (study withdrawal). This is the mean TIS at Week 52 for all randomized and dosed participants included with non-missing baseline score in the Stage 3 Muscle Analysis Set (see details in Section 9.1.1).
	• Change from baseline in the CSMs of the TIS including PhGA, PtGA, MMT-8, HAQ-DI, muscle enzymes, and MDAAT at Week 52 and at intermediate scheduled timepoints.	• The endpoints for the CSMs of the TIS will be analyzed using E2 at Week 52 and all intermediate scheduled timepoints.

Overall Design

This is a Phase 2b, OLE study to evaluate the long-term safety, and tolerability, of PF-06823859 in adult participants with moderate to severe DM who have completed the treatment period of a qualifying study (including Protocol C0251002) and have agreement from their study doctor to continue active treatment. Eligible participants will not have had any significant protocol deviations, (eg, not following the protocol, taking prohibited medications, not using appropriate contraception) or have not completed all study treatment in a qualifying study. Approximately 30 participants who complete the Week 24 visit during the treatment period in Study C0251002 or equivalent in another qualifying study, may be enrolled in Protocol C0251008. The treatment duration of OLE study participation will be up to 48 weeks (treatment period is up through and including Week 52), with a 16 week follow up period.

Eligible participants will be randomized to receive open-label PF-06823859 600 mg IV every 4 weeks for up to 48 weeks, however the treatment period is up to Week 52. All participants will be followed for 16 weeks in the Follow-up Period. Participants who are discontinued from study intervention will enter the follow-up period.

Brief Summary

Based on the mechanism of action of PF-06823859 and preliminary results from the Phase 2 C0251002 clinical study in adults with DM (see Section 2.2.1.1.4), this OLE study is being conducted to provide additional data on the long-term safety and tolerability of IV PF-06823859 in adult participants with active DM.

Number of Participants

The sample size will be determined by the number of patients who enroll from Protocol C0251002 and any other future qualifying studies. It is anticipated that up to approximately 30 participants from Amended Stage 2 and Stage 3 of Protocol C0251002 will be enrolled to receive open-label study intervention.

Intervention Groups and Duration

This is an open-label study. The site will contact the IRT prior to the start of study intervention administration for each participant. The site will record the vial numbers assigned on the applicable CRF, if required.

For this study, the study intervention will be administered intravenously over approximately one hour. Study intervention will be administered every 4 weeks, each participant receiving up to 13 doses of study intervention.

Dose modification is not permitted in this study.

If study intervention is permanently discontinued, the participant will have an End of Treatment visit and enter the follow-up period to be evaluated for safety.

Data Monitoring Committee or Other Independent Oversight Committee:

Not Applicable.

Statistical Methods

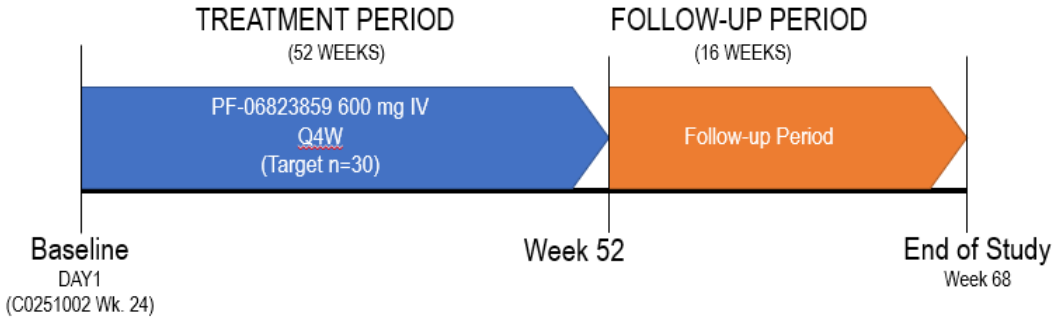
This is an extension study to assess the safety and tolerability of the long-term therapy of PF-06823859 in participants with DM. All efficacy endpoints are secondary endpoints. The primary analysis population for safety evaluations will be the safety analysis set (See Section 9.2). All efficacy evaluations will be completed separately for those originating from the skin-predominant DM cohort included in the C0251002 protocol Amended Stage 2 or the muscle-predominant DM cohort including Stage 3 of the C0251002 protocol. The respective analysis sets for these efficacy evaluations are the Skin Analysis Set and Muscle Analysis Set. Baseline will be Day 1 of study C0251008; sensitivity analyses that redefine Baseline as Day 1 of the parent study may also be performed and will be defined in the SAP.

No formal statistical hypothesis testing is planned for this study.

There are no defined estimands for the incidence of AEs, laboratory abnormalities, changes in vital signs, and ECG findings. These endpoints will be analyzed using Pfizer data standards as applicable. All participants who receive at least 1 dose of IP will be included in the safety analyses. All safety data will be summarized descriptively through appropriate data tabulations, descriptive statistics, categorical summaries, and graphical presentations.

Two estimands are defined for this study. **Estimand 1** (E1) will support specified CDASI assessments at specified timepoints for participants in the Skin Analysis Set and Muscle Analysis Set separately. **Estimand 2** (E2) will support TIS and CSM assessments at specified timepoints for participants in the Muscle Analysis Set.

1.2. Schema



1.3. Schedule of Activities

The SoA table provides an overview of the protocol visits and procedures. Refer to the STUDY ASSESSMENTS AND PROCEDURES section 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 in the SoA table, in order to conduct evaluations or assessments required to protect the well-being of the participant.

References to "baseline" in this study correspond to the Week 24 visit of the Phase 2 C0251002 study and Day 1 of this study. All study procedures will be completed for Visit 24 in the C0251002 study, and Day 1 in the current study prior to drug administration.

Table 1. DM Participants with Moderate to Severe Skin Disease

This SoA focuses on DM participants with moderate skin disease including participants from Amended Stage 2 of the Phase 2 C0251002 study. The approximate study duration is 68 weeks; 48 weeks of study treatment, (treatment period is up through and including Week 52) with a 16 week follow up period.

Protocol Activity	Treatment Period														Follow-up[s]				
Visit identifier (Study Visit)	1 Baseline	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18 EOS	Participant withdrawal or Early Termination[a]
Study Day/Week	Week 24 C0251002 DAY 1	Week 4	Week 8	Week 12	Week 16	Week 20	Week 24	Week 28	Week 32	Week 36	Week 40	Week 44	Week 48	Week 52	Week 56	Week 60	Week 64	Week 68	N/A
Visit Window	(+) 7 days*	±3 days																	
Informed consent	X																		
Inclusion/exclusion criteria[b]	X																		
Medical history[c]	X																		
Demography	X																		
Clinical Reported Outcomes																			
C-SSRS[d]	D			X			X			X			X			X		X	X
PhGA VAS[e]	D			X			X			X			X	X		X		X	X
CDASI	D			X			X			X			X	X		X		X	X

Protocol Activity	Treatment Period														Follow-up[s]				
Visit identifier (Study Visit)	1 Baseline	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18 EOS	Participant withdrawal or Early Termination[a]
Study Day/Week	Week 24 C0251002 DAY 1	Week 4	Week 8	Week 12	Week 16	Week 20	Week 24	Week 28	Week 32	Week 36	Week 40	Week 44	Week 48	Week 52	Week 56	Week 60	Week 64	Week 68	N/A
Visit Window	(+) 7 days*	±3 days																	
Patient Reported Outcomes																			
SF36 v2 Acute[f]	D			X			X			X			X			X		X	X
EQ-5D-5L & EQ-VAS[f]	X			X			X			X			X			X		X	X
Medical Assessments																			
Vital Signs (BP, HR, Pulse, and temperature)[g]	D	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Weight[h]	D						X						X					X	X
Height[h]	D																		
Complete physical examination[i]	D					X					X							X	X
Targeted physical examination[i]		X	X	X	X		X	X	X	X		X	X	X	X	X	X		
ECG	D			X			X			X			X			X		X	X
Contraception check[j]	D	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Laboratory Safety Assessments																			
Safety Labs/Urine	X			X			X			X			X	X		X		X	X
eGFR	X						X						X					X	X
Serum cystatin C	X						X						X					X	X
Urine β-hCG (conducted at site)[k]	D	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Immunogenicity (ADA, Nab) serum	X[l]			X[l]			X[l]			X[l]			X[l]	X				X	X
Pharmacokinetic (PK)/serum[m]	X			X			X			X			X	X				X	X
IVIG sample collection[n]	X			X			X			X			X						

Protocol Activity	Treatment Period														Follow-up[s]				
Visit identifier (Study Visit)	1 Baseline	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18 EOS	Participant withdrawal or Early Termination[a]
Study Day/Week	Week 24 C0251002 DAY 1	Week 4	Week 8	Week 12	Week 16	Week 20	Week 24	Week 28	Week 32	Week 36	Week 40	Week 44	Week 48	Week 52	Week 56	Week 60	Week 64	Week 68	N/A
Visit Window	(+) 7 days*	±3 days																	
Retained Research Samples																			
Prep B1.5 plasma, Prep B2.5 serum, and Prep R1 whole blood	D			X			X			X			X			X		X	
Biomarkers[o]																			
Blood for muscle biomarkers	D			X			X			X			X	X		X		X	X
Total IFNβ	X			X			X			X			X	X				X	X
hsCRP	X			X			X			X			X	X		X		X	X
Study Intervention Administration																			
Study Intervention treatment administration[q]	X[p]	X	X	X	X	X	X	X	X	X	X	X	X						
Infusion Site Reaction	X	X	X	X	X	X	X	X	X	X	X	X	X						
Ongoing Medications[r]																			
Ongoing Adverse event[s,c]																			
Concomitant Medications and Treatment(s)	D	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	X	X
AE monitoring	D	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	X	X

Note: D=Done at week 24 visit (C0251002); "X" at week 24 indicates procedure/sample needs to be completed under study C0251008 * (+7 days for baseline): Baseline date should be the same date as the last visit from the previous study. In rare circumstances, up to 7 days may occur between the last visit in the feeder study and the baseline date of this study. Sponsor approval is required.

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. Inclusion and exclusion criteria need to be reviewed to ensure participant is eligible for the study. No CRF will be completed, however source documentation is required to reflect that participant is eligible for study participation.

c. Medical History for this study is any ongoing adverse events from the previous study. Please record only ongoing adverse events from the previous study onto the medical history page, so that these can be monitored. Any AEs occurring after receiving study drug administration will be considered an AE for this study.

d. The C-SSRS will be used to assess suicidal ideation and behavior during the conduct of the study. At any visits, if there are "yes" answers on items 4, 5 or on any suicidal 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. Please see Section 8.2.10.1.

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

f. Patient reported outcomes (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 SF-36 v2 acute, EQ-5D-5L & EQ-VAS.

g. Vital Signs include blood pressure, heart rate (pulse), 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 5-10 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.

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, please record in source documentation. 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 and recorded in source documentation.

j. Contraception check should be completed and documented in source at each and every visit.

k. Urine pregnancy test must be performed at baseline for all WOCBP prior to dosing with study intervention and at all subsequent visits.

l. ADA, Nab, and INFβ will be collected prior to investigational drug administration according to the SoA.

m. At dosing visits, PK samples will be collected pre and post dose, preferably after vital signs data and within approximately 30 minutes prior to dosing. PK will also be collected at the end of the study infusion in the opposite arm of the infusion at all PK collection visits according to the SoA.

n. Only participants who are on IVIG concomitantly will have a pre-dose blood sample collected. See Section 8.4.3.

o. Biomarkers will be collected prior to study drug administration according to the SoA.

p. All Day 1 and Week 24 from previous study (eg, C0251002) procedures should be completed prior to investigational treatment administration.

q. Once the infusion has been administered over 60 minutes, all participants will be monitored for an additional 60 minutes to ensure no infusion site reactions.

r. All ongoing medications from the previous study should be re-written in the new concomitant medication page for this study.

s. Participants who experience AEs which are considered attributable to immunogenicity and have ADA may be requested to return for additional follow up for up to 5 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.

Table 2. DM Participants with Moderate Muscle Disease

This SoA focuses on DM participants with moderate muscle disease including participants from Stage 3 of the C0251002 study. The approximate study duration is 68 weeks; 48 weeks of study treatment (treatment period is up through and including Week 52) with a 16 week follow up period. Participants enrolling in the muscle cohort will not be required to provide any skin or muscle biopsies.

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

References to "baseline" in this study correspond to the Week 24 visit of the Phase 2 C0251002 Study and Day 1 of this study. All study procedures will be completed for Visit 24 in the C0251002 study and Day 1 in the current study prior to drug administration.

Protocol Activity	**Treatment Period**														**Follow-up**[s]				
Visit identifier (Study Visit)	1 Baseline	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18 EOS	Participant withdrawal or Early Termination [a]
Study Day/Week	Week 24 C0251002 DAY 1	Week 4	Week 8	Week 12	Week 16	Week 20	Week 24	Week 28	Week 32	Week 36	Week 40	Week 44	Week 48	Week 52	Week 56	Week 60	Week 64	Week 68	N/A
Visit Window	(+)7 days*	±3 days																	
Informed consent	X																		
Inclusion/exclusion criteria[b]	X																		
Medical history[c]	X																		
Demography	X																		
Clinical Reported Outcomes																			
CDASI Score	D			X			X			X			X	X		X		X	X
C-SSRS[d]	D			X			X			X			X			X		X	X
PhGA, VAS[e]	D			X			X			X			X	X		X		X	X
MMT-8 Score	D			X			X			X			X	X		X		X	X
MDAAT	D			X			X			X			X	X		X		X	X
Patient Reported Outcomes																			
PtGA[f]	D			X			X			X			X	X		X		X	X
HAQ-DI[f]	D			X			X			X			X	X		X		X	X
SF-36 v2 Acute[f]	D			X			X			X			X			X		X	X

Protocol Activity	**Treatment Period**														**Follow-up[s]**				
Visit identifier (Study Visit)	1 Baseline	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18 EOS	Participant withdrawal or Early Termination [a]
Study Day/Week	Week 24 C0251002 DAY 1	Week 4	Week 8	Week 12	Week 16	Week 20	Week 24	Week 28	Week 32	Week 36	Week 40	Week 44	Week 48	Week 52	Week 56	Week 60	Week 64	Week 68	N/A
EQ-5D-5L & EQ-VAS[f]	X			X			X			X			X			X		X	X
Medical Assessments																			
Vital Signs (BP, HR, Pulse and temperature)[g]	D	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Weight[h]	D						X						X					X	X
Height[h]	D																		
Complete physical examination[i]	D					X					X							X	X
Targeted physical examination[i]		X	X	X	X		X	X	X	X		X	X	X	X	X	X		
ECG	D			X			X			X			X			X		X	X
Contraception check[j]	D	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Laboratory Safety Assessments																			
Safety Labs/Urine	X			X			X			X			X	X		X		X	X
eGFR	X						X						X					X	X
Serum cystatin C	X						X						X					X	X
Urine β-hCG (conducted at site)[k]	D	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Immunogenicity (ADA, NAb) serum	X[l]			X[l]			X[l]			X[l]			X[l]	X				X	X
Pharmacokinetic (PK)/serum[m]	X			X			X			X			X	X				X	X
IVIG sample collection[n]	X			X			X			X			X						

Protocol Activity	**Treatment Period**														**Follow-up**[s]				
Visit identifier (Study Visit)	1 Baseline	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18 EOS	Participant withdrawal or Early Termination [a]
Study Day/Week	Week 24 C0251002 DAY 1	Week 4	Week 8	Week 12	Week 16	Week 20	Week 24	Week 28	Week 32	Week 36	Week 40	Week 44	Week 48	Week 52	Week 56	Week 60	Week 64	Week 68	N/A
Retained Research Samples																			
Prep B1.5 plasma, B2.5 serum, R1 whole blood	D			X			X			X			X			X		X	
Biomarkers[o]																			
Blood for muscle biomarkers	D			X			X			X			X	X		X		X	X
Total IFNβ	X			X			X			X			X	X				X	X
hsCRP	X			X			X			X			X	X		X		X	X
Study Intervention																			
Study intervention administration[q]	X[p]	X	X	X	X	X	X	X	X	X	X	X	X						
Infusion Site Reaction	X	X	X	X	X	X	X	X	X	X	X	X	X						
Ongoing Medications[r]																			
Ongoing AEs[s,c]																			
Concomitant Medications and Treatment(s)	D	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	X	X
Adverse event monitoring	D	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	→	X	X

Note: D=Done in week 24 visit (C0251002); "X" at week 24 indicates procedure/sample needs to be completed under study C0251008 * (+7 days for baseline): Baseline date should be the same date as the last visit from the previous study. In rare circumstances, up to 7 days may occur between the last visit in the feeder study and the baseline date of this study. Sponsor approval is required.

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. Inclusion and exclusion criteria need to be reviewed to ensure participant is eligible for the study. No CRF will be completed, however source documentation is required to reflect that participant is eligible for study participation.

c. Medical History for this study is any ongoing adverse events from the previous study. Please record only ongoing adverse events from the previous study onto the medical history page, so that these can be monitored. Any AEs occurring after receiving study drug administration will be considered an AE for this study.

d. The C-SSRS will be used to assess suicidal ideation and behavior during the conduct of the study. At any visits, if there are "yes" answers on items 4, 5 or on any suicidal 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. Please see Section 8.2.10.1.

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, 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, SF-36 (v2 acute), EQ-5D-5L & EQ-VAS.

g. Vital Signs include blood pressure, heart rate (pulse), 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 5-10 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.

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, please record in source documentation. 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 and recorded in source documentation.

j. Contraception check should be completed and documented in source at each visit.

k. Urine pregnancy test must be performed at baseline for all WOCBP prior to dosing with study intervention and at all subsequent visits.

l. ADA, NAb, and INFβ will be collected prior to investigational drug administration according to the SoA.

m. At dosing visits, PK samples will be collected pre and post dose, preferably after vital signs data and within approximately 30 minutes prior to dosing. PK will also be collected at the end of the study infusion in the opposite arm of the infusion at all PK collection visits according to the SoA.

n. All participants who are on IVIG concomitantly will have a pre-dose blood sample collected. See Section 8.4.3.

o. Biomarkers will be collected prior to study drug administration according to the SoA.

p. All Day 1 and Week 24 from previous study (eg, C0251002) procedures should be completed prior to investigational treatment administration.

q. Once the infusion has been administered over 60 minutes, all participants will be monitored for an additional 60 minutes to ensure no infusion site reactions.

r. All ongoing medications from the previous study should be re-written in the new concomitant medication page for this study.

s. 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 5 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.

2. INTRODUCTION

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]

2.1. Study Rationale

The purpose of the study is to evaluate the long-term safety, and tolerability of PF-06823859 in adult participants with DM who are eligible for enrollment from a qualifying study.

2.2. Background

DM has no known cure and there were no previously approved treatments prior to 2021 when IVIG, Octagam® 10% became the first approved treatment for adults with DM. However, complications of IVIG therapy have been well documented).[3] 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, 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 also well documented. Other novel approaches have emerged as potential treatment, including tacrolimus (broadly immunosuppressive drug developed for transplant use), and rituximab, following positive outcomes in some case studies. However, additional randomized controlled trials with these treatments are needed to guide clinical practice.[4] Consequently, DM remains a disease with very high unmet medical need, and development of safe and effective therapies is warranted.

PF-06823859 is a potent, selective, humanized IgG1 neutralizing antibody directed against the human soluble cytokine IFNβ, a member of the type I IFN family of cytokines. PF-06823859 is a novel compound in development for the treatment of DM with added potential for therapeutic benefit in SLE.

2.2.1. Clinical Overview

2.2.1.1.1. Safety (FIH C0251001)

A 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 adult Participants[5] completed in August 2017. This study consisted of 8 dosing cohorts. There were 5 single dose cohorts 30 mg IV, 100 mg IV, 300 mg IV, 900 mg IV, and 2000 mg IV. The other 3 cohorts were multiple dose cohorts consisting of

100 mg x 3 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).

A total of 62 participants completed the study; 48 participants were randomized to receive PF-06823859 and 14 participants were randomized to receive placebo. Results from this study suggest that PF-06823859 is generally well tolerated and safe when given up to 2000 mg as single dose and up to 600 mg administered IV every 2 weeks or every 4 weeks. The most common treatment-related TEAEs were somnolence, upper respiratory tract infection and headache. These adverse events were generally mild and resolved without further intervention. No serious AE or death occurred during the study.

One participant experienced an ISR after each of the 100 mg SC doses 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 2.2.1.1.3; Immunogenicity Results).

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

There were no clinically significant changes in vital signs or laboratory abnormalities.

2.2.1.1.2. PK Summary for C0251001

Following single IV infusion dosing of PF-06823859, exposure based on AUC_{inf} and C_{max} exhibited approximately dose-proportional increase with increasing doses across the dose ranges from 30 mg to 2000 mg. Geometric mean CL was slow with values ranging from 0.006 to 0.007 L/hr across all doses, and small V_{ss} values (geometric mean values ranging from 4.8 L to 6.0 L) indicative of distribution primarily in the plasma volume. Mean $t_{½}$ values were similar across the doses ranging from 23 to 29 days.

Following multiple SC doses of 100 mg and 300 mg administered Q2W for a total of 3 doses, peak serum concentrations were achieved with a median T_{max} of 96 hours post dose on Day 1, and 48 hours post dose on Day 15 and Day 29. No marked departures from dose proportionality were observed for AUCτ and C_{max} for the 2 dose regimens. R_{ac} for serum AUCτ and C_{max} were <2.5 fold and mean $t_{1/2}$ values ranging from 25 to 35 days. CL/F was similar across the 2 dose regimens with geometric mean estimates at 0.016 L/h, while the geometric mean V_z/F estimates were approximately similar ranging from 13.9 to 18.9 L.

Estimated bioavailability values based on geometric mean AUC_τ for the 100 mg and 300 mg SC doses on Day 1 were 43% and 44%, respectively, relative to the corresponding IV doses in the SAD period.

Following multiple IV doses of 600 mg administered Q2W for a total of 3 doses; geometric mean AUC_τ values were slightly higher on Days 15 and 29 compared to that observed on Day 1 with similar C_{max} values observed across all dosing days. Serum AUC_τ for the 600 mg IV (Q4W) × 2 doses treatment group was slightly higher compared to AUC_τ from the 600 mg IV (Q2W) × 3 doses treatment group on Day 1 and Day 29. Multiple IV dose PK results were generally consistent with single dose IV PK data. R_{ac} for serum AUC_τ and C_{max} were <1.9 fold and mean $t_{½}$ of 27 and 28 days was observed following 600 mg IV Q2W and 600 mg IV Q4W dosing, respectively.

2.2.1.1.3. Immunogenicity Results for C0251001

A tiered approach for screening, characterization and ADA titer assessment of serum samples was adopted to characterize immunogenicity.

During the SAD period, there were 3 out of 26 subjects who were confirmed positive for treatment induced ADA and none of them were confirmed positive for NAb. During the MAD period, there were 2 out of 22 subjects who were confirmed positive for treatment induced ADA and 1 of the 2 subjects was confirmed positive for NAb; and 1 out of 22 subjects was confirmed positive for treatment boosted ADA.

The low immunogenicity incidence rates, especially for the NAb, did not provide sufficient information to adequately determine the impact of ADA/NAb on the PK and safety; there were no immunologically related clinical responses of concern observed during the study.

2.2.1.1.4. Efficacy and Safety (Phase 2 C0251002 Study, Stage 1)

C0251002 is an ongoing multi-center, double blind randomized placebo-controlled Phase 2 study to evaluate the efficacy, safety, tolerability and PK of PF-06823859 in adult patients with active DM. Stage 1 of the study was designed to evaluate the effects of 600 mg PF-06823859 and placebo administered IV at baseline, Week 4 and Week 8 in participants with skin-predominant DM. The data summarized below are a high level summary based upon a snapshot date of 27 February 2020. In that the database of this study is not yet final, this should be considered preliminary evidence.

The primary endpoint of Stage 1 of the study was the change from baseline in the CDASI-A score at Week 12. A clinically and statistically significant difference in CDASI-A score over time was observed between the active and placebo treatment arms. The least squares mean difference estimate of CFB in the CDASI-A in the active treatment versus the placebo group (primary endpoint) was -14.82 (90% CI -20.26, -9.37, p=0.0001).

A 13-gene Type 1 IFN gene signature was used to assess pharmacodynamic activity in skin biopsies. The % change from baseline levels of the gene signature at Week 12 on lesional skin was markedly lower (83.6%) for the PF-06823859 group compared to the placebo group (11.8%), showing- pharmacodynamic activity (one sided p=0.00016).

PF-06823859 at a dose of 600 mg IV was generally safe and well tolerated, with a comparable safety profile between the PF-06823859 and placebo groups. No deaths occurred in Stage 1 of the Phase 2 study. There were 3 SAEs and 2 permanent discontinuations due to TEAEs, all of which were considered unrelated to treatment by both investigator and Sponsor. Most TEAEs were mild or moderate in severity and occurred at a similar frequency in the active treatment and placebo groups. Based on the preliminary estimates of effect from the Stage 1 data of Study C0251002, PF-06823859 demonstrates a favorable benefit-risk profile in the potential treatment of DM.

2.3. Benefit/Risk Assessment

DM is a rare disease with higher prevalence in females than males. Therefore, the trial objectives cannot be met without inclusion of WOCBP. Nonclinical data to date has not identified any risk to reproductive organs in sexually mature cynomolgus monkeys, the pharmacologically relevant species. Given that an ePPND study is ongoing, this protocol that allows enrollment of WOCBP has stringent requirements to mitigate unintended exposures (pregnancy testing and use of contraceptives).

Based on non-clinical in vitro data, PF-06832859 did not activate the classical complement pathway, induce the release of proinflammatory cytokines or complement-dependent cytotoxicity, or suppress a recall immune response to a T-cell-dependent antigens. In nonclinical toxicity studies in cynomolgus monkeys, the only pharmacologically relevant species, no adverse effects were noted after once weekly IV or SC administration of PF-06823859 for up to 6-months in duration to sexually mature or juvenile male and female monkeys. PF-06823859 was administered to cynomolgus monkeys by the IV and/or SC routes once weekly in the repeat-dose pivotal GLP-compliant toxicity study for a 14-week dosing phase followed by an 8-week recovery (dose-free) phase. In that study, the only PF-06823859-related effects were non-adverse changes in selected clinical pathology parameters which had resolved by the end of the 9-week recovery phase. In the 6-month chronic toxicity study, once-weekly IV administration of PF-06823859 at doses of 20, 100, and 300 mg/kg/week resulted in likely an immune-mediated hypersensitivity response in 1 animal at 100 and 1 animal at 300 mg/kg/week, and non-adverse changes in clinical chemistry parameters. There were no macroscopic or microscopic effects in male or female reproductive organ systems and no hemodynamic effects (ie, ECG or HR) on the cardiovascular system were noted.

More detailed information about the known and expected benefits and risks and reasonably expected AEs of PF-06823859 may be found in the current Investigator's Brochure, which is the SRSD for this study.

2.3.1. Risk Assessment

Potential Risk of Clinical Significance	Summary of Data/Rationale for Risk	Mitigation Strategy
Study Intervention(s) PF-06823859		
Increased susceptibility to viral infections	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). Participants may have increased risk of SARS-CoV-2 exposure by undergoing a study procedure at a study facility.	Serious and non-serious adverse event monitoring will occur on an ongoing/continuous manner as indicated in the Safety Review Plan. Alternative measures including use of telehealth, home health, etc will be utilized in the study in the case of a public emergency to minimize potential exposure of trial participants to SARS-CoV-2 (see Appendix 9; Section 10.9.
Interaction with other medicinal products and other forms of interaction	In vitro or in vivo PK drug interaction studies have not been conducted with PF-06823859. Although several cytokines such as IL-6 and TNF-α have been shown to modulate expression of CYP enzymes and transporters, cytokine mediated drug interactions observed in the clinic to date have been modest with these agents, resulting in a less than 2-fold change in the exposure of a co-administered small molecule drugs. Overall, the DDI risk is expected to be low.	Participants will abstain from prohibited concomitant treatments as described in the Appendix 10.8.

2.3.2. Benefit Assessment

Based on the clinical data from the FIH study (C0251001), the preliminary efficacy and safety data from the ongoing Phase 2 study (C0251002) in participants with DM, 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 participants with DM.

2.3.3. Overall Benefit/Risk Conclusion

Taking into account the measures to minimize risk to study participants, the potential risks identified in association with PF-06823859 are justified by the anticipated benefits that may be afforded to participants with moderate to severe DM.

3. OBJECTIVES, ENDPOINTS, AND ESTIMANDS

Objectives	Endpoints	Estimands
Primary:	**Primary:**	**Primary:**
• To evaluate the long-term safety and tolerability of PF-06823859.	• Incidence of AEs, laboratory abnormalities, changes in vital signs, and ECG findings.	• There are no defined estimands for safety and tolerability endpoints; these will be analyzed using Pfizer data standards, as applicable.
Secondary:	**Secondary:**	**Secondary:**
• To evaluate the long-term efficacy of PF-06823859 in adult participants with moderate to severe DM.	• Change from baseline in CDASI activity score at Week 52.	• E1: This estimand uses a hypothetical estimand strategy (ICH E9 addendum) estimating the mean effect of PF-06823859 in the absence of intercurrent events (study withdrawal). This is the mean change from baseline to Week 52 CDASI activity score for all randomized and dosed participants with non-missing baseline score in the (a) Skin Analysis Set and (b) Muscle Analysis Set (see details in Section 9.1.1).
	• Absolute values and change from baseline of CDASI activity and CDASI damage scores at all scheduled timepoints.	• These additional CDASI endpoints will be analyzed using E1 at all scheduled timepoints.
	• TIS score at Week 52 and at intermediate scheduled timepoints for participants who	• E2: This estimand uses a hypothetical estimand strategy (ICH E9 addendum) estimating the mean effect of PF-06823859 in the absence of intercurrent events (study

	entered from Stage 3 of Protocol C0251002. • Change from baseline in the CSMs of the TIS including PhGA, PtGA, MMT-8, HAQ-DI, muscle enzymes, and MDAAT at Week 52 and at intermediate scheduled timepoints.	withdrawal). This is the mean TIS at Week 52 for all randomized and dosed participants included with non-missing baseline score in the Muscle Analysis Set (see details in Section 9.1.1). • The endpoints for the CSM of the TIS will be analyzed using E2 at Week 52 and all intermediate scheduled timepoints.
Tertiary/Exploratory:	**Tertiary/Exploratory:**	**Tertiary/Exploratory:**
• To characterize pharmacokinetics (PK) of PF-06823859. • To characterize pharmacodynamics (PD) effects of PF 06823859. • To evaluate immunogenicity of PF-06823859. • To evaluate the effect of PF-0682359 on suicidality assessment over time in participants with active DM. • To evaluate the effect of PF-0682359 on SF-36 (v2 acute) and EQ-5D-5L PROs.	• Plasma concentrations of PF-06823859. • Absolute values and change from baseline in the values of selected biomarkers at all scheduled time points. • Incidence of ADA and NAb. • Absolute values and change from baseline values of Columbia-Suicide Severity Rating Scale (C-SSRS) at all scheduled time points. • Absolute values and change from baseline in the values of PROs including SF-36 (v2 acute) and EQ-5D-5L at all scheduled timepoints.	• Not applicable.

4. STUDY DESIGN

4.1. Overall Design

This is a Phase 2b, OLE study to evaluate the long-term safety and tolerability of PF-06823859 in adult participants with moderate to severe DM who completed the treatment period of a qualifying study (including Protocol C0251002) and have agreement from their study doctor to continue active treatment. Eligible participants will not have had any significant protocol deviations (eg, not following the protocol, taking prohibited medications, not using appropriate contraception) or have not completed all study treatment in the qualifying study. Approximately 30 participants who complete the Week 24 visit during the treatment period in Study C0251002 or equivalent in another qualifying study, may be

enrolled in Protocol C0251008. The treatment duration of OLE study participation will be up to 48 weeks (treatment period is up through and including Week 52), with a 16 week follow up period. See Section 1.2 for the study schematic.

Qualified participants will be randomized to receive open-label PF-06823859 600 mg IV every 4 weeks for up to 48 weeks, however the treatment period is up to Week 52. All participants will be followed for another 16 weeks in the Follow-up Period. Participants who are discontinued from study intervention will also enter the follow-up period.

4.2. Scientific Rationale for Study Design

Based on the mechanism of action of PF-06823859 and preliminary results from the Phase 2 C0251002 clinical study in adults with DM (see Section 2.2.1.1.4), this OLE study is being conducted to provide additional data on the long-term safety and tolerability of IV PF-06823859 in adult participants with active DM.

4.2.1. Diversity of Study Population

The diversity of this study population is dependent upon the qualifying studies and those participants that become eligible for this OLE study.

4.2.2. Choice of Contraception/Barrier Requirements

Potential reproductive and/or developmental toxicities are currently not known for PF-06823859; therefore, use of a highly effective method of contraception is required. Please see Appendix 4 for definitions of highly effective birth control measures and user dependent vs. low user dependent examples of contraceptives.

4.2.3. Collection of Retained Research Samples

Retained Research Samples will be collected and stored for further analyses which may, for example, provide greater understanding of the study intervention.

4.3. Justification for Dose

A 600 mg IV dose administered Q4W was chosen as a suitable dose for this study based on preliminary efficacy and gene suppression data from Stage 1 of Study C0251002 (see Section 2.2.1.1.4).

Results from Stage 1 in Study C0251002 showed a difference in CDASI-A over time between the active and placebo treatment arms that was clinically and statistically significant. The observed mean CFB in CDASI-A at Week 12 (standard deviation) were -19.62 (9.14) and -3.44 (5.27) for the PF-06823859 600 mg IV and placebo groups, respectively. The least squares mean difference estimate of CFB in the CDASI-A in the active versus the placebo group (primary endpoint) was -14.82 (90% CI -20.26, -9.37), showing statistical significance (p=0.0001). Sensitivity analysis using a ANCOVA model for CFB in the CDASI-A at Week 12 with baseline CDASI-A and treatment as variables in the model gave an estimated mean difference of CFB in the CDASI-A for PF-06823859 600 mg compared to placebo at Week 12 of -15.39 (CI -20.24, -10.54), showing similar level of efficacy (p<0.0001)

consistent with the primary analysis. The separation of treatment effect for PF-06823859 compared with placebo, as measured by the CFB in CDASI-A, was observed as early as Week 4 and persisted through Week 24 (for available interim data). These results clearly suggest that the 600 mg IV dose administered Q4W was highly efficacious in DM participants.

Additionally, the 600 mg IV Q4W was previously tested in healthy participants from Study C0251001 as well as DM participants in Study C0251002 and was considered safe. In the GLP-compliant 6-month chronic toxicity study in cynomolgus monkeys, there were no test article-related adverse effects up to highest dose tested, 300 mg/kg/dose (IV). At the proposed clinical dose of 600 mg IV Q4W, exposure margins (ie, safety margins) after the third dose relative to the highest dose in the chronic toxicity study are approximately 54x for C_{av} and 40x for C_{max}. The proposed dose of 600 mg IV Q4W will maximize the potential for efficacy, especially since target engagement of PF-06823859 in skin and muscle is unclear. IV was chosen as the route of administration to support the large volume of the dose that will be required to obtain the targeted gene signature suppression as well as for participant adherence. The frequency of administration was chosen as 4 weeks to achieve targeted gene signature suppression but also to reduce study burden on the participant.

The proposed dose of 600 mg IV Q4W was determined to be suitable in Study C0251008 to confirm pharmacology and to test durability of clinical efficacy, with sufficient safety margins relative to the toxicology exposure limits.

Additional information for this compound may be found in the SRSD, which for this study is the IB.

4.4. End of Study Definition

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.

A participant is considered to have completed the study if he/she has completed all periods of the study, including Visit 18, EOS visit, Week 68 as shown on the SoA.

5. STUDY POPULATION

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.

Prospective approval of protocol deviations to recruitment and enrollment criteria, also known as protocol waivers or exemptions, is not permitted.

5.1. Inclusion Criteria

Participants are eligible to be included in the study only if all of the following criteria apply:

Age and Sex:

1. Participants aged ≥18 and ≤80 with moderate to severe DM, that have completed the treatment period of the qualifying study.

Type of Participant and Disease Characteristics:

2. Participants who are willing and able to comply with all scheduled visits, treatment plan, laboratory tests, lifestyle considerations, and other study procedures.

3. Refer to Appendix 4 for reproductive criteria for male (Section 10.4.1) and female (Section 10.4.2) participants.

Informed Consent:

4. Capable of giving signed informed consent as described in Appendix 1, which includes compliance with the requirements and restrictions listed in the ICD and in this protocol.

5.2. Exclusion Criteria

Participants are excluded from the study if any of the following criteria apply:

Medical Conditions:

1. Other medical or psychiatric condition including recent (within the past year) or active suicidal ideation/behavior or laboratory abnormality that may increase the risk of study participation or, in the investigator's judgment, make the participant inappropriate for the study.

Prior/Concomitant Therapy:

2. Current use of any prohibited concomitant medication(s) listed in Appendix 8.

3. Hematologic abnormalities defined as:

   - ANC ≤1000/mm^3;
   - Platelets ≤25,000/mm^3;
   - Hemoglobin ≤8g/dL.

4. Hepatic dysfunction defined as:

    - Total bilirubin ≥2x ULN (≥3x ULN for Gilbert's disease);
    - AST ≥2.5 x ULN;
    - ALT ≥2.5 x ULN;
        - 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.

5. Baseline standard 12-lead ECG that demonstrates clinically relevant abnormalities that may affect participant safety or interpretation of study results (eg, QTcF interval >450 msec, complete LBBB, signs of an acute or indeterminate age myocardial infarction, ST-T interval changes suggestive of myocardial ischemia, second or third degree AV block, or serious bradyarrhythmias or tachyarrhythmias). If the baseline uncorrected QT interval is >450 msec, this interval should be rate corrected using the Fridericia method and the resulting QTcF should be used for decision making and reporting. If QTcF exceeds 450 msec, or QRS exceeds 120 msec, the ECG should be repeated 2 more times and the average of the 3 QTcF or QRS values should be used to determine the participant's eligibility. Computer interpreted ECGs should be overread by a physician experienced in reading ECGs before excluding a participant.

6. Participants who met discontinuation criteria at any point during the participating qualifying studies.

7. Participants with an ongoing safety event in the qualifying studies which, in the opinion of the investigator or sponsor, is an ongoing safety concern OR the participant has met safety monitoring criteria in the qualifying study that has not resolved.

8. Participants with significant protocol deviations (eg, not following the protocol, not using appropriate contraception) or have had a serious adverse event related to study drug in the previous qualifying studies.

Other Exclusions:

9. Investigator site staff or Pfizer employees directly involved in the conduct of the study, site staff otherwise supervised by the investigator, and their respective family members.

5.3. Lifestyle Considerations

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 this section.

5.3.1. 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 Section 10.4).

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 4 Section 10.4.4) 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 2 of the selected methods of contraception, preferably 1 highly effective method of low user dependency, or a high user dependency method with a barrier method) 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.

5.3.2. Surgery

During the study, no elective surgery should occur without first consulting with the sponsor. Preferably, elective surgery should 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 study intervention prior to the surgical procedure. In general, planned surgical procedures should not be performed unless the study intervention 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.

5.4. Screen Failures

Since this is an open-label long-term continuation study for participants who have completed other qualifying studies, eg, Protocol C0251002, screen failures are not applicable.

6. STUDY INTERVENTION(S) AND CONCOMITANT THERAPY

Study intervention is defined as any investigational intervention(s), marketed product(s), placebo, medical device(s), or study procedure(s) intended to be administered to a study participant according to the study protocol.

For the purposes of this protocol, study intervention refers to PF-06823859.

6.1. Study Intervention(s) Administered

For this study, the study intervention will be administered intravenously over approximately one hour. Study intervention will be administered every 4 weeks, each participant receiving 13 doses of study intervention over the duration of the trial.

Study Interventions(s)	
Intervention Name	PF-06823859
ARM Name (group of patients receiving a specific treatment (or no treatment)	PF-06823859
Type	Drug
Dose Formulation	Solution for injection
Unit Dose Strength(s)	100 mg/mL
Dosage Level(s)	600 mg Q4W
Route of Administration	IV
Use	Experimental
IMP or NIMP	IMP
Sourcing	Provided centrally by the sponsor or locally by the trial site, subsidiary, or designee. See IP manual for more information.
Packaging and Labeling	Open-label study intervention will be provided in a 6 mL glass vial sealed with a stopper and aluminum flip off cap. Each vial contains 1.35 mL PF-06823859. The vials will be packaged into cartons containing 6 vials per carton. Each vial and carton will be labeled as required per country requirement.

6.1.1. Administration

Open-label IV PF-06823859 will be administered at the investigative site or clinic over the course of approximately 60 minutes as an IV infusion, using a calibrated infusion pump. Once the infusion has completed, all participants will be monitored for an additional 60 minutes post study intervention administration to ensure no infusion site reactions.

6.1.1.1. Infusion Discontinuation

- If a participant experiences symptoms typical of an allergic reaction, the study intervention administration should be discontinued immediately and permanently and the event should be captured as an AE.

- If a participant experiences symptoms typical of infusion reactions (eg, lightheadedness, nausea, chills, fever), the study intervention 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 intervention 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.

6.1.1.2. Pre-Medication Use on the Day of IVIG Administration

For participants who enroll in the study who are receiving 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 of prednisone per day for participants in the severe skin disease cohort and 20 mg or equivalent of prednisone per day for participants in the moderate muscle disease cohort as per protocol Section 6.8.3.

There is no need to change the IVIG dosing schedule or adjust the IVIG dosing schedule related to study intervention administration.

6.2. Preparation, Handling, Storage, and Accountability

1. The investigator or designee must confirm appropriate temperature conditions have been maintained during transit for all study interventions received and any discrepancies are reported and resolved before use of the study intervention.

2. Only participants enrolled in the study may receive study intervention and only authorized site staff may supply or administer study intervention. All study interventions must be stored in a secure, environmentally controlled, and monitored (manual or automated recording) area in accordance with the labeled storage conditions with access limited to the investigator and authorized site staff. At a minimum, daily minimum and maximum temperatures for all site storage locations must be documented and available upon request. Data for nonworking days must indicate the minimum and maximum temperatures since previously documented for all site storage locations upon return to business.

3. Any excursions from the study intervention label storage conditions should be reported to Pfizer upon discovery along with any actions taken. The site should actively pursue options for returning the study intervention to the storage conditions described in the labeling, as soon as possible. Once an excursion is identified, the study intervention must be quarantined and not used until Pfizer provides permission to use the study intervention. Specific details regarding the definition of an excursion

and information the site should report for each excursion will be provided to the site in the IP manual.

4. Any storage conditions stated in the SRSD will be superseded by the storage conditions stated on the label.

5. Study interventions should be stored in their original containers.

6. The investigator, institution, or the head of the medical institution (where applicable) is responsible for study intervention accountability, reconciliation, and record maintenance (ie, receipt, reconciliation, and final disposition records), such as the IPAL or sponsor-approved equivalent. All study interventions will be accounted for using a study intervention accountability form/record.

7. Further guidance and information for the final disposition of unused study interventions are provided in the IP manual. All destruction must be adequately documented. 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.

Upon identification of a product complaint, notify the sponsor within 1 business day of discovery as described in the IP manual.

6.2.1. Preparation and Dispensing

A qualified staff member will dispense the study intervention using the IRT system via unique container numbers in the single-use vials provided, in quantities appropriate according to the dose assignment.

See the IP manual for instructions on how to prepare the study intervention for administration. Study intervention 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. A second staff member will verify the dispensing.

PF-06823859 be prepared by qualified site personnel according to the IP manual. The study intervention will be administered in an open-label fashion to the participants.

6.2.2. Study Intervention Accountability

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

6.2.2.1. Destruction of Study Intervention Supplies

The sponsor or designee will provide guidance on the destruction of unused study intervention (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 study intervention.

6.3. Measures to Minimize Bias: Randomization and Blinding

6.3.1. Allocation to Study Intervention

Study intervention will be administered at the study visits summarized in the SoA.

This is an open-label study. The site will contact the IRT prior to the start of study intervention administration for each participant. The site will record the vial numbers assigned on the applicable CRF, if required.

The investigator's knowledge of the treatment should not influence the decision to enroll a particular participant or affect the order in which participants are enrolled.

6.4. Study Intervention Compliance

Participants will receive study intervention directly from the investigator or designee, under medical supervision. The date and time of each dose administered in the clinic will be recorded in the source documents and recorded in the CRF. The dose of study intervention and study participant identification will be confirmed at the time of dosing by a member of the study site staff other than the person administering the study intervention.

The site will complete the required dosage Preparation Record located in the IP manual. The use of the Preparation Record is preferred, but it does not preclude the use of an existing appropriate clinical site documentation system. The existing clinical site's documentation system should capture all pertinent/required information on the preparation and administration of the dose. This may be used in place of the Preparation Record after approval from the sponsor and/or designee.

6.5. Dose Modification

Dose modification is not permitted in this study.

6.6. Continued Access to Study Intervention After the End of the Study

No intervention will be provided to study participants at the end of their study participation.

6.7. Treatment of Overdose

For this study, any dose of PF-06823859 greater than 600 mg within a 24-hour time period will be considered an overdose.

There is no experience with overdose of PF-06823859. There is no specific antidote for overdose with PF-06823859. Treatment at the discretion of the investigator should be symptomatic and supportive. In case of an overdose, it is recommended that the subject be monitored for signs and symptoms of adverse reactions. Participants who develop adverse reactions should receive appropriate treatment.

In the event of an overdose, the investigator/treating physician should:

1. Contact the medical monitor within 24 hours.

2. Closely monitor the participant for any AEs/SAEs and laboratory abnormalities for at least 5 half-lives or 28 calendar days after the overdose of PF-06823859 (whichever is longer). Closely monitor the participant for any AEs/SAEs.

3. Document the quantity of the excess dose as well as the duration of the overdose in the CRF.

4. Overdose is reportable to Pfizer Safety only when associated with an SAE.

5. Obtain a blood sample for PK analysis within 1-2 days from the date of the last dose of study intervention if requested by the medical monitor (determined on a case-by-case basis).

Decisions regarding dose interruptions or modifications will be made by the investigator in consultation with the medical monitor based on the clinical evaluation of the participant.

6.8. Concomitant Therapy

Hormonal contraceptives that meet the requirements of this study are allowed to be used in participants who are WOCBP (see Appendix 4).

For a list of prohibited and permitted concomitant medications refer to Appendix 8 (Section 10.8).

All ongoing medications from the previous study should be re-written in the new concomitant medication page for this study.

Participants must continue to avoid use of medications that have been washed out prior to enrollment in their prior qualifying study (eg, C0251002 Protocol). The indication for use, total daily dose, route of administration, and start and stop dates for all ongoing medications (including prescription medications and treatments, vaccinations, nonprescription medications, nondrug treatments and dietary supplements) will be pulled from the qualifying study and documented as prior 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. Medications after the first dose of study intervention has been administered in this OLE study will be documented as concomitant medications. 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).

6.8.1. Prohibited Concomitant Medications

Please see Appendix 8, Section 10.8.

6.8.2. Permitted Concomitant Medications

NSAIDs and aspirin are allowed; however, they may potentially affect efficacy parameters (eg, the skeletal disease activity VAS, arthritis assessment and gastrointestinal disease activity VAS for the MDAAT and thus should be used judiciously. Participants taking NSAIDS/analgesics should not take a dose of these medications within 12 hours prior to such assessments at those visits.

Acetaminophen is primarily an analgesic and lacks the anti-inflammatory properties of NSAIDS. The use of acetaminophen is recommended when possible to treat non-DM related conditions, in the absence of a pre-existing hepatic function deficiency.

6.8.3. Corticosteroids

Please refer to Appendix 11, Section 10.11.

The decision for increasing or tapering steroids is entirely up to the study investigator, and any change in the steroid dose should be recorded on the concomitant medication page.

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.

Oral corticosteroids taken by the participants during the study will be captured on a separate CRF. The CRF page will capture the name of the corticosteroid taken, indication for use, total daily dose, route of administration, and start date and stop dates of administration.

6.8.3.1. Guidance for Investigators

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

See Appendix 11 (Section 10.11) for further guidelines for corticosteroid use.

6.8.4. Rescue Medicine

If the participant requires the addition of higher DMARD doses or an additional DMARD for a flare or persistent increase in dermatomyositis activity, then the participant should be discontinued from the treatment period but complete the follow-up visits. High dose oral corticosteroids (>100 mg/day prednisone, or equivalent) or pulse IV doses, or any IV or IM steroid injection would exclude the participant for further treatment in the study.

See Appendix 11 (Section 10.11) for further guidelines for rescue medication.

7. DISCONTINUATION OF STUDY INTERVENTION AND PARTICIPANT DISCONTINUATION/WITHDRAWAL

7.1. Discontinuation of Study Intervention

It may be necessary for a participant to permanently discontinue study intervention. Reasons for permanent discontinuation of study intervention include the following:

- Serious infections defined as any infection;
- Other serious or severe AEs;
- Laboratory abnormalities deemed clinically significant by the investigator that can adversely affect the participant;
- Use of prohibited medications.

Full details for reasons for permanent discontinuation of study intervention as well as monitoring criteria are included in Section 10.10 (Appendix 10).

Note that discontinuation of study intervention does not represent withdrawal from the study. If study intervention is permanently discontinued, the participant will remain in the study to be evaluated for safety. See the SoA for data to be collected at the time of discontinuation of study intervention and follow-up for any further evaluations that need to be completed.

In the event of discontinuation of study intervention, it must be documented on the appropriate CRF/in the medical records whether the participant is discontinuing further receipt of study intervention or also from study procedures, posttreatment study follow-up, and/or future collection of additional information.

7.2. Participant Discontinuation/Withdrawal From the Study

A participant may withdraw from the study at any time at his/her own request. Reasons for discontinuation from the study include the following:

- Refused further study procedures;
- Lost to follow-up;
- Death;
- Study terminated by sponsor;
- Consent: Withdrawal of consent (see Section 7.2.1).

At the time of discontinuing from the study, if possible, an early discontinuation visit should be conducted. See the SoA for assessments to be collected at the time of study discontinuation and follow-up and for any further evaluations that need to be completed.

The participant will be permanently discontinued from the study intervention and the study at that time.

If a participant withdraws from the study, he/she may request destruction of any remaining samples taken and not tested, and the investigator must document any such requests in the site study records and notify the sponsor accordingly.

If the participant withdraws from the study and also withdraws consent (see Section 7.2.1 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.

7.2.1. Withdrawal of Consent

Participants who request to discontinue receipt of study intervention 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 study intervention or also from study procedures and/or posttreatment 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.

7.3. Lost to Follow-Up

A participant will be considered lost to follow-up if he or she repeatedly fails to return for scheduled visits and is unable to be contacted by the study site.

The following actions must be taken if a participant fails to attend a required study visit:

- The site must attempt to contact the participant and reschedule the missed visit as soon as possible. Counsel the participant on the importance of maintaining the assigned visit schedule, and ascertain whether the participant wishes to and/or should continue in the study;

- Before a participant is deemed lost to follow-up, the investigator or designee must make every effort to regain contact with the participant (where possible, 3 telephone calls and, if necessary, a certified letter to the participant's last known mailing address or local equivalent methods). These contact attempts should be documented in the participant's medical record;

- Should the participant continue to be unreachable, he/she will be considered to have withdrawn from the study.

8. STUDY ASSESSMENTS AND PROCEDURES

The investigator (or an appropriate delegate at the investigator site) must obtain a signed and dated ICD before performing any study-specific procedures.

Study procedures and their timing are summarized in the SoA. Protocol waivers or exemptions are not allowed.

Safety issues should be discussed with the sponsor immediately upon occurrence or awareness to determine whether the participant should continue or discontinue study intervention.

Adherence to the study design requirements, including those specified in the SoA, is essential and required for study conduct.

All baseline evaluations must be completed and reviewed to confirm that potential participants meet all eligibility criteria. The investigator will maintain a screening log to record details of all participants screened and to confirm eligibility or record reasons for screening failure, as applicable.

Procedures conducted as part of the participant's routine clinical management (eg, blood count) and obtained before signing of the ICD may be utilized for baseline purposes provided the procedures met the protocol-specified criteria and were performed within the time frame defined in the SoA.

Every effort should be made to ensure that protocol-required tests and procedures are completed as described. However, it is anticipated that from time to time there may be circumstances outside the control of the investigator that may make it unfeasible to perform the test. In these cases, the investigator must 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 the missed test and any corrective and preventive actions that he or she has taken to ensure that required processes are adhered to as soon as possible. The study team must 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.

The actual collection times of blood sampling may change. Additional blood samples may be taken for safety assessments at times specified by Pfizer or at the discretion of the investigator, provided the total volume taken during the study does not exceed 550 mL during any period of 56 consecutive days.

8.1. Efficacy Assessments

8.1.1. CDASI

The secondary endpoints for this study assess changes in the modified CDASI[6] activity score as well as the individual components.

8.1.2. Total Improvement Score (TIS)

There are 6 core set measures that comprise the total improvement score. These components are:

- PhGA, VAS (see Section 8.1.2.1);
- PtGA (see Section 8.1.3.4);
- MMT-8 score (see Section 8.1.2.2);
- HAQ- DI score (see Section 8.1.3.3);
- MDAAT Global Extramuscular Disease Activity (Section 8.1.2.3 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.

8.1.2.1. Physician Global Assessment (PhGA) Visual Analogue Scale (VAS)

The PhGA, VAS is an assessment of the participant's general health status rather than the disease activity in a specific organ. 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 clinical medical assessments.

8.1.2.2. MMT-8

This partially validated tool assesses muscle strength using 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.

8.1.2.3. MDAAT

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.

8.1.3. 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 PROs used in this study.

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

The SF-36 v2 acute is a 36 item generic health status measure.[5,7,8] 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 PCS and 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. (Section 1.3).

8.1.3.2. EuroQoL 5 Dimensions 5 Levels (EQ 5D 5L) and EQ-VAS

The EQ 5D 5L is a validated, standardized, generic instrument that is the most widely used preference based HRQoL questionnaire in cost effectiveness and HTA.[9,10,11] It is a well established instrument to measure health states and utilities in various disease areas. The EQ-5D 5L contains 5 items that cover mobility, self-care, usual activities, pain/discomfort,

and anxiety/depression, with five response levels of severity ranging from no problems to unable to/extreme problems. The measure also includes a VAS, which records the respondent's overall current health. The vertical EQ VAS, labelled with 'The best health you can imagine' and 'The worst health you can imagine', provides a quantitative measure of the patient's perception of their overall health. The EQ-5D-5L and EQ-VAS will be collected as indicated in the Schedule of Activities (Section 1.3).

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

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.[12]

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 (Section 1.3).

8.1.3.4. Patient's Global Assessment (PtGA)

The 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 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.[13,14] The PtGA will be collected as indicated in the Schedule of Activities (Section 1.3).

8.1.4. Rater Qualifications

For specific rating assessments, only qualified raters will be allowed to evaluate and/or rate participants in this study. The minimum qualifications a rater must meet for each study rating assessment will be outlined in the training materials provided to each participating site. The level of experience with the target population (or equivalent), specific scale experience (or equivalent), and certification required (if applicable) will be listed and used to determine whether a rater is approved for a given assessment. The rater must become certified to perform selected study assessments before he or she can participate in the conduct of the study. For specifically defined assessments, rater training and standardization exercises may be conducted, and written documentation will be provided by the site for each rater's certification. In return, each site will be provided written documentation outlining each rater's certification for specific study assessments. Recertification may be required at periodic intervals during the study. The raters who administer specific study assessments will

be documented in a centralized location and all site staff who administer ratings will be verified in the site study documentation during the conduct of the study.

8.1.4.1. CDASI

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 physician complete the PhGA, VAS for consistency.

8.1.4.2. MMT-8

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.

8.1.4.3. MDAAT

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.

8.2. Safety Assessments

Planned time points for all safety assessments are provided in the SoA. Unscheduled clinical laboratory measurements may be obtained at any time during the study to assess any perceived safety issues.

8.2.1. Medical History

A participant's complete medical history will be transferred from the qualifying study (eg, C0251002). In addition, all ongoing adverse events from the previous qualifying study will be recorded on the medical history page in the new study and monitored until resolved. Any new adverse events will be recorded after the administration of study intervention.

8.2.2. Physical Examinations

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

Investigators should pay special attention to clinical signs related to previous serious illnesses.

Complete and targeted physical examinations are performed at various time points, see Schedules of Activities (Section 1.3).

Physical examination findings collected during the study will be considered source data and will not be required to be reported, unless otherwise noted. Any untoward physical examination findings that are identified during the active collection period and meet the definition of an AE or SAE (Appendix 3) must be reported according to the processes in Sections 8.3.1 to 8.3.3.

8.2.3. 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 baseline only. Weight will continue to be assessed and recorded at various time points, see Schedules of Activities (Section 1.3).

8.2.4. Vital Signs

Vital signs (blood pressure, heart rate [pulse], and temperature) will be measured after approximately 5 minutes of rest as indicated in the Schedules of Activities (Section 1.3). 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.

8.2.5. Electrocardiograms

Standard 12-leads utilizing limb leads (with a 10 second rhythm strip) should be collected at times specified in the SoA section of this protocol using an ECG machine that automatically calculates the heart rate and measures PR, QT, and QTc intervals and QRS complex. Alternative lead placement methodology using torso leads (eg, Mason-Likar) should not be used given the potential risk of discrepancies with ECGs acquired using standard limb lead placement. All scheduled ECGs should be performed after the participant has rested quietly for at least 5 minutes in a supine position.

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.

If a postdose QTcF interval remains ≥60 msec from the baseline **and** is >450 msec; or b) an absolute QT value is ≥500 msec for any scheduled ECG for greater than 4 hours (or sooner, at the discretion of the investigator); or c) QTcF intervals get progressively longer, the participant should undergo continuous ECG monitoring. A cardiologist should be consulted if QTcF intervals do not return to less than the criteria listed above after 8 hours of monitoring (or sooner, at the discretion of the investigator).

ECG data will be read locally. The final ECG report should be maintained in the participant's source documentation and be the final interpretation of the ECG recording. Any clinically significant changes from the baseline/Day 1 ECG may potentially be AEs (Appendix 7) and should be 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. It is important that leads be placed in the same positions each time in order to achieve precise ECG recordings. If a machine-read QTc value is prolonged, as defined above, repeat measurements may not be necessary if a qualified medical provider's interpretation determines that the QTcF values are in the acceptable range.

ECG values of potential clinical concern are listed in Appendix 7.

8.2.6. Infusion Site Reaction Assessment

Infusion site reactions will be assessed according to the Schedules of Activities (Section 1.3). 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.

8.2.7. 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.

8.2.8. Clinical Safety Laboratory Assessments

See Appendix 2 for the list of clinical safety laboratory tests to be performed and the SoA for the timing and frequency. All protocol-required laboratory assessments, as defined in Appendix 2, must be conducted in accordance with the laboratory manual and the SoA. Unscheduled clinical laboratory measurements may be obtained at any time during the study to assess any perceived safety issues.

The investigator must review the laboratory report, document this review, and record any clinically relevant changes occurring during the study in the AE section of the CRF. Clinically significant abnormal laboratory findings are those which are not associated with the underlying disease, unless judged by the investigator to be more severe than expected for the participant's condition.

All laboratory tests with values considered clinically significantly abnormal during participation in the study or within 5 terminal half-lives after the last dose of study intervention should be repeated until the values return to normal or baseline or are no longer considered clinically significant by the investigator or medical monitor.

If such values do not return to normal/baseline within a period of time judged reasonable by the investigator, the etiology should be identified, and the sponsor notified.

See Appendix 6 for suggested actions and follow-up assessments in the event of potential drug-induced liver injury.

8.2.9. Pregnancy Testing

Pregnancy tests will be urine tests, but must have a sensitivity of at least 25 mIU/mL. Pregnancy tests will be performed in WOCBP at the times listed in the SoA. Following a negative pregnancy test result at screening, appropriate contraception must be commenced, and a second negative pregnancy test result will be required at the baseline visit prior the participant's receiving the study intervention. Pregnancy tests will also be done whenever 1 menstrual cycle is missed during the active treatment period (or when potential pregnancy

is otherwise suspected) and at the end of the study. Pregnancy tests may also be repeated if requested by IRBs/ECs or if required by local regulations. If a urine test cannot be confirmed as negative (eg, an ambiguous result), a serum pregnancy test is required. In such cases, the participant must be excluded if the serum pregnancy result is positive.

8.2.10. Assessment of Suicidal Ideation and Behavior

8.2.10.1. Columbia -Suicide Severity Rating Scale (C-SSRS)

Due to the increased rate of depression in the participants diagnosed with DM, the C-SSRS will be used to assess suicidal ideation and behavior during the conduct of the study. The C-SSRS is a patient-reported questionnaire administered by the investigator or site staff that have been trained to administer the test. The C-SSRS is a validated tool to evaluate suicidal ideation and behavior.[15]

At any visit, if the participant answers “yes” on items 4, 5 or on any suicidal 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, the participant should be sent to a local emergency room for psychiatric assessment.

8.3. Adverse Events, Serious Adverse Events, and Other Safety Reporting

The definitions of an AE and an SAE can be found in Appendix 3.

AEs may arise from symptoms or other complaints reported to the investigator by the participant (or, when appropriate, by a caregiver, surrogate, or the participant's legally authorized representative), or they may arise from clinical findings of the Investigator or other healthcare providers (clinical signs, test results, etc.).

The investigator and any qualified designees are responsible for detecting, documenting, and recording events that meet the definition of an AE or SAE and remain responsible to pursue and obtain adequate information both to determine the outcome and to assess whether the event meets the criteria for classification as an SAE or caused the participant to discontinue the study intervention (see Section 7.1).

During the active collection period as described in Section 8.3.1, each participant will be questioned about the occurrence of AEs in a nonleading manner.

In addition, the investigator may be requested by Pfizer Safety to obtain specific follow-up information in an expedited fashion.

8.3.1. Time Period and Frequency for Collecting AE and 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 study intervention), through and including a minimum of 5 months after the last administration of the study intervention.

Since this is an extension study, once the ICD is signed, any newly developed adverse events recorded prior to study drug dosing should be recorded in the participant's medical history. Once the participant receives study drug, all and any adverse events will be reviewed and recorded on the adverse event page.

Follow-up by the investigator continues throughout and after the active collection period and until the AE or SAE or its sequelae resolve or stabilize at a level acceptable to the investigator.

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

If the participant withdraws from the study and also withdraws consent for the collection of future information, the active collection period ends when consent is withdrawn.

If a participant permanently discontinues or temporarily discontinues study intervention because of an AE or SAE, the AE or SAE must be recorded on the CRF and the SAE reported using the CT SAE Report Form.

Investigators are not obligated to actively seek information on AEs or SAEs after the participant has concluded study participation. However, if the investigator learns of any SAE, including a death, at any time after a participant has completed the study, and he/she considers the event to be reasonably related to the study intervention, the investigator must promptly report the SAE to Pfizer using the CT SAE Report Form.

8.3.1.1. Reporting SAEs to Pfizer Safety

All SAEs occurring in a participant during the active collection period as described in Section 8.3.1 are reported to Pfizer Safety on the CT SAE Report Form immediately upon awareness and under no circumstance should this exceed 24 hours, as indicated in Appendix 3. The investigator will submit any updated SAE data to the sponsor within 24 hours of it being available.

8.3.1.2. Recording Nonserious AEs and SAEs on the CRF

All nonserious AEs and SAEs occurring in a participant during the active collection period, which begins after obtaining informed consent as described in Section 8.3.1, will be recorded on the AE section of the CRF.

The investigator is to record on the CRF all directly observed and all spontaneously reported AEs and SAEs reported by the participant.

8.3.2. Method of Detecting AEs and SAEs

The method of recording, evaluating, and assessing causality of AEs and SAEs and the procedures for completing and transmitting SAE reports are provided in Appendix 3.

Care will be taken not to introduce bias when detecting AEs and/or SAEs. Open-ended and nonleading verbal questioning of the participant is the preferred method to inquire about AE occurrences.

8.3.3. Follow-Up of AEs and SAEs

After the initial AE or SAE report, the investigator is required to proactively follow each participant at subsequent visits/contacts. For each event, the investigator must pursue and obtain adequate information until resolution, stabilization, the event is otherwise explained, or the participant is lost to follow-up (as defined in Section 7.3).

In general, follow-up information 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.

Further information on follow-up procedures is given in Appendix 3.

8.3.4. Regulatory Reporting Requirements for SAEs

Prompt notification by the investigator to the sponsor of an SAE is essential so that legal obligations and ethical responsibilities toward the safety of participants and the safety of a study intervention under clinical investigation are met.

The sponsor has a legal responsibility to notify both the local regulatory authority and other regulatory agencies about the safety of a study intervention under clinical investigation. The sponsor will comply with country-specific regulatory requirements relating to safety reporting to the regulatory authority, IRBs/ECs, and investigators.

Investigator safety reports must be prepared for SUSARs according to local regulatory requirements and sponsor policy and forwarded to investigators as necessary.

An investigator who receives SUSARs or other specific safety information (eg, summary or listing of SAEs) from the sponsor will review and then file it along with the SRSD(s) for the study and will notify the IRB/EC, if appropriate according to local requirements.

8.3.5. Environmental Exposure, Exposure During Pregnancy or Breastfeeding, and Occupational Exposure

Environmental exposure occurs when a person not enrolled in the study as a participant receives unplanned direct contact with or exposure to the study intervention. Such exposure may or may not lead to the occurrence of an AE or SAE. Persons at risk for environmental exposure include healthcare providers, family members, and others who may be exposed. An environmental exposure may include exposure during pregnancy, exposure during breastfeeding, and occupational exposure.

Any such exposure to the study intervention under study are reportable to Pfizer Safety within 24 hours of investigator awareness.

8.3.5.1. Exposure During Pregnancy

An EDP occurs if:

- A female participant is found to be pregnant while receiving or after discontinuing study intervention.
- A male participant who is receiving or has discontinued study intervention exposes a female partner prior to or around the time of conception.
- A female is found to be pregnant while being exposed or having been exposed to study intervention due to environmental exposure. Below are examples of environmental EDP:
    - A female family member or healthcare provider reports that she is pregnant after having been exposed to the study intervention by accidental needle stick during drug preparation.
    - A male family member or healthcare provider who has been exposed to the study intervention by accidental needle stick during drug preparation then exposes his female partner prior to or around the time of conception.

The investigator must report EDP to Pfizer Safety within 24 hours of the investigator's awareness, irrespective of whether an SAE has occurred. The initial information submitted should include the anticipated date of delivery (see below for information related to termination of pregnancy).

- If EDP occurs in a participant or a participant's partner, 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. Details of the pregnancy will be collected after the start of study intervention and until at least 5 terminal half-lives after the last dose. This time would be approximately 20 weeks or 5 months after the last dose of study intervention.

- If EDP occurs in the setting of environmental exposure, the investigator must report information to Pfizer Safety using the CT SAE Report Form and EDP Supplemental Form. Since the exposure information does not pertain to the 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.

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 preprocedure test findings are conclusive for a congenital anomaly and the findings are reported).

Abnormal pregnancy outcomes are considered SAEs. 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 including 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 study intervention.

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.

8.3.5.2. Exposure During Breastfeeding

An exposure during breastfeeding occurs if:

- A female participant is found to be breastfeeding while receiving or after discontinuing study intervention.

- A female is found to be breastfeeding while being exposed or having been exposed to study intervention (ie, environmental exposure). An example of environmental exposure during breastfeeding is a female family member or healthcare provider who reports that she is breastfeeding after having been exposed to the study intervention by accidental needle stick during drug preparation.

The investigator must report exposure during breastfeeding to Pfizer Safety within 24 hours of the investigator's awareness, irrespective of whether an SAE has occurred. The information must be reported using the CT SAE Report Form. When exposure during breastfeeding occurs in the setting of environmental exposure, the exposure information does not pertain to the participant enrolled in the study, so 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.

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, the SAE is reported together with the exposure during breastfeeding.

8.3.5.3. Occupational Exposure

The investigator must report any instance of occupational exposure 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 about the occupational exposure 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 must be maintained in the investigator site file.

8.3.6. Cardiovascular and Death Events

All CV and death events should be reported according to the instructions in Section 8.3.1 to Section 8.3.3.

8.3.7. Disease-Related Events and/or Disease-Related Outcomes Not Qualifying as AEs or SAEs

Not Applicable.

8.3.8. Adverse Events of Special Interest

Not Applicable.

8.3.8.1. Lack of Efficacy

The investigator must report signs, symptoms, and/or clinical sequelae resulting from lack of efficacy. Lack of efficacy or failure of expected pharmacological action is reportable to Pfizer Safety **only if associated with an SAE**.

8.3.9. Medical Device Deficiencies

Not Applicable.

8.3.10. Medication Errors

Medication errors may result from the administration or consumption of the study intervention by the wrong participant, or at the wrong time, or at the wrong dosage strength.

Exposures to the study intervention 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

Medication errors include:

- Medication errors involving participant exposure to the study intervention;
- Potential medication errors or uses outside of what is foreseen in the protocol that do or do not involve the study 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 within 24 hours.

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 nonserious, are recorded on the 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.**

8.4. Pharmacokinetics

8.4.1. Serum for Analysis of PF-06823859

Blood samples will be collected for measurement of serum concentrations of PF-06823859 at times specified in the Schedule of Activities. Instructions for the collection and handling of biological samples will be provided in the laboratory manual or by the sponsor. The actual date and time (24 hour clock time) of each sample will be recorded. PK should be taken from the opposite arm that the drug was administered. If a participant is suspected to

be experiencing an immune-related event, the unscheduled blood samples should be collected for concentration of PF-06823859 within 3 days of the event and sampling time and date should be documented. A PK collection will also be collected at the early withdrawal visit if necessary.

The actual times may change, but the number of samples will remain the same. All efforts will be made to obtain the samples at the exact nominal time relative to dosing.

Samples will be used to evaluate the PK of PF-06823859. Each serum sample will be prepared as described in the lab manual. Samples collected for analyses of PF-06823859 serum concentration may also be used to evaluate safety or efficacy aspects related to concerns arising during or after the study, for metabolite identification and/or evaluation of the bioanalytical method, or for other internal exploratory purposes and not reported in the CSR.

Genetic analyses will not be performed on these serum samples unless consent for this was included in the informed consent. Participant confidentiality will be maintained.

Samples collected for measurement of serum concentrations of study intervention will be analyzed using a validated analytical method in compliance with applicable SOPs.

The PK samples must be processed and shipped as indicated in the instructions provided to the investigator site to maintain sample integrity. Any deviations from the PK sample handling procedure (eg, sample collection and processing steps, interim storage or shipping conditions), including any actions taken, must be documented and reported to the sponsor. On a case-by-case basis, the sponsor may make a determination as to whether sample integrity has been compromised. Any changes in the timing or addition of time points for any planned study assessments must be documented and approved by the relevant study team member and then archived in the sponsor and site study files, but will not constitute a protocol deviation. The IRB/EC will be informed of any safety issues that require alteration of the safety monitoring scheme or amendment of the ICD.

As part of understanding the pharmacokinetics of the study intervention, samples may be used for metabolite identification and/or evaluation of the bioanalytical method. These data will be used for internal exploratory purposes and will not be included in the clinical study report.

8.4.2. 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. Refer to the central laboratory manual for further information.

8.4.3. IVIG Analysis

In this study, IVIG is permitted as a concomitant treatment and participants enrolled who are treated with IVIG concomitantly will have blood samples collected prior to study intervention administration. These samples will be collected to measure IVIG concentrations in the event that there are changes in the participant's pharmacokinetic profile. These samples may be analyzed and reported separately.

If unscheduled labs are determined to be necessary, participants who are continuing to receive IVIG will also need an IVIG sample collection and a corresponding PK specimen (see Section 8.4.3).

8.5. Genetics

8.5.1. Specified Genetics

Genetics (specified analyses) are not evaluated in this study.

8.6. Biomarkers

8.6.1. PD Biomarkers

The PD samples must be processed and shipped as indicated to maintain sample integrity. Any deviations from the PD processing steps, including any actions taken, must be documented and reported to the sponsor. On a case-by-case basis, the sponsor may make a determination as to whether sample integrity has been compromised.

All efforts will be made to obtain the PD samples at the exact nominal time relative to dosing. Please consult the laboratory manual(s) for final instructions on sample collection, storage, and shipping requirements. These laboratory manual(s) supersede the instructions listed in the applicable protocol sections. Samples that are handled according to the respective manual guidance are considered "per protocol".

Samples will be analyzed using fit for purpose or validated analytical methods in compliance with Pfizer standard operating procedures.

As part of understanding the pharmacodynamics of the study intervention and the disease under study, samples may be used for evaluation of the bioanalytical method. These data will be used for internal (ie, Pfizer) exploratory purposes and may not be included in the clinical study report.

8.6.1.1. 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 (Section 1.3).

8.6.1.2. Total IFNβ

Blood samples to provide serum for the analysis of total IFNβ will be collected into appropriately labeled tubes according to the times outlined in the Scheduled of Activities (Section 1.3).

8.6.1.3. Biospecimen for Blood Muscle Biomarkers

Blood samples to provide serum for the analysis of muscle biomarkers will be collected into appropriately labeled tubes according to the times outlined in the Schedule of Activities (Section 1.3).

8.6.2. Retained Research Samples for Biomarkers

These Retained Research Samples will be collected in this study:

- 6 mL whole blood (Prep B1.5 plasma);
- 6 mL whole blood (Prep B2.5 serum);
- 2.5 mL whole blood (Prep R1 optimized for RNA).

Retained Research Samples will be collected as local regulations and IRB/ECs allow according to the SoA.

Retained Research Samples may be used for research related to the study intervention(s): and DM. Genes and other analytes (eg, proteins, RNA, nondrug metabolites) may be studied using the retained samples.

See Appendix 5 (Section 10.5) for information regarding genetic research. Details on processes for collection and shipment of these samples can be found in the lab manual.

8.7. Immunogenicity Assessments

8.7.1. Serum for Analysis of Anti-PF-06823859

8.7.1.1. Antibodies (ADA) and Neutralizing Anti-PF-06823859 Antibodies (NAb)

Blood samples for the detection of ADA and NAb will be collected at the times specified in Schedule of Activities. Instructions for the collection and handling of biological samples will be provided in the laboratory manual or by the sponsor. The actual date and time (24-hour clock time) of each sample will be recorded.

Any changes in the timing or addition of time points for any planned study assessments must be documented and approved by the relevant study team member and then archived in the sponsor and site study files, but will not constitute a protocol deviation. The IRB/EC will be informed of any safety issues that require alteration of the safety monitoring scheme or amendment of the ICD.

Further details regarding the collection, processing, storage and shipping of the blood samples will be provided in the lab manual.

8.7.2. Immunogenicity Analyses

The immunogenicity samples must be processed and shipped as indicated to maintain sample integrity. Any deviations from the immunogenicity processing steps, including any actions taken, must be documented and reported to the sponsor. On a case by case basis, the sponsor may make a determination as to whether sample integrity has been compromised. Any sample deemed outside of established stability, or of questionable integrity, will be considered a protocol deviation.

Samples will be analyzed using validated analytical methods in compliance with Pfizer standard operating procedures. Samples tested as ADA positive, (not just confirmed positive, but also with a titer positive result) will be further tested for NAb using validated NAb assays. Participants with positive results at the conclusion of the study may be requested to return for additional follow-up for up to approximately 5 months after the last scheduled follow-up visit. An additional PK and ADA sample will be collected, and the information recorded as an unscheduled visit.

Samples collected for determination of ADA and NAb may also be used for additional characterization of the immune response and/or evaluation of the bioanalytical method, or for other internal exploratory purposes. These data will be used for internal exploratory purposes and not reported in the CSR.

Samples collected for detecting ADA and NAb will be retained in accordance to local regulations and if not used within this timeframe, will be destroyed. Additional exploratory testing of samples may be performed to further characterize the ADA response and /or evaluation of the bioanalytical method. These data will be used for internal exploratory purposes and will not be included in the clinical report.

8.7.3. Shipment of Immunogenicity (ADA/NAb) Samples

The shipment address and assay lab contact information will be provided to the investigator site prior to initiation of the study.

8.8. Health Economics

Health economics/medical resource utilization and health economics parameters are not evaluated in this study.

9. STATISTICAL CONSIDERATIONS

Detailed methodology for summary and statistical analyses of the data collected in this study is outlined here and further detailed in a 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.

9.1. Statistical Hypotheses

No statistical hypothesis testing is planned for this study.

9.1.1. Estimands

9.1.1.1. Primary Estimands

There are no defined estimands for the incidence of AEs, laboratory abnormalities, changes in vital signs, and ECG findings. These endpoints will be analyzed using Pfizer data standards as applicable. All participants who receive at least 1 dose of IP will be included in the safety analyses. All safety data will be summarized descriptively through appropriate data tabulations, descriptive statistics, categorical summaries, and graphical presentations.

9.1.1.2. Secondary Estimands

Two estimands are defined for this study. **Estimand 1** (E1) will support specified CDASI assessments at specified timepoints for participants in the Skin Analysis Set and Muscle Analysis Set separately (Section 9.2). **Estimand 2** (E2) will support TIS and CSM assessments at specified timepoints for participants in the Muscle Analysis Set.

E1 will be the population average effect of PF-06823859 on CFB in CDASI activity score at Week 52 for all randomized and dosed participants with non-missing baseline in a specified analysis set (Skin or Muscle Analysis Set) in the absence of dropout. Measurements taken after a participant withdraws from treatment will be censored and treated as missing data. The population-based estimate for the effect of PF-06823859 will be the mean CFB in CDASI-activity score at Week 52.

E1 will also be applied to each combination of the following endpoints, timepoints, and analysis sets:

- Endpoints: Change from baseline and absolute values of CDASI activity score and CDASI damage score;
- Timepoints: Week 52 and all scheduled intermediate timepoints;
- Analysis sets: Skin Analysis Set and Muscle Analysis Set.

E2 will be the population average estimate for the effect of PF-06823859 on TIS at Week 52 for all randomized and dosed participants with non-missing baseline in the Stage 3 Muscle Analysis Set in the absence of dropouts. Measurements taken after a participant withdraws from treatment will be censored and treated as missing data. The population-based estimate for the effect of PF-06823859 will be the mean TIS at Week 52.

E2 will also be applied to each combination of the following endpoints and timepoints in the Stage 3 Analysis Set:

- Endpoints: TIS and change from baseline in each of the CSM of the TIS.

- Timepoints: Week 52 and all scheduled intermediate timepoints.

9.1.2. Multiplicity Adjustment

Multiplicity adjustment is not applicable. No formal hypothesis testing is planned in this study.

9.2. Analysis Sets

For purposes of analysis, the following analysis sets are defined:

Participant Analysis Set	Description
Randomized	"Randomized" means a participant's, agreement to participate in a clinical study following completion of the informed consent process. A participant will be considered enrolled if the informed consent is not withdrawn prior to participating in any study activity.
Full Analysis Set (FAS)	All participants enrolled who take at least 1 dose of study intervention.
Safety Analysis Set	All participants enrolled who take at least 1 dose of study intervention. This includes all such participants regardless of which parent study or stage the participant entered from.
Skin Safety Analysis Set	All participants with skin predominant DM who take at least 1 dose of study intervention including participants entering from Amended Stage 2 of the C0251002 protocol.
Muscle Safety Analysis Set	Al participants with muscle predominant DM who take at least 1 dose of study intervention including participants entering from Stage 3 of the C0251002 protocol.

Defined Analysis Set (Efficacy)	Description
Skin Analysis Set	All participants with skin predominant DM in the FAS including participants who were enrolled in Amended Stage 2 of the C0251002 study.
Muscle Analysis Set	All participants with muscle predominant DM in the FAS including participants who were enrolled in Stage 3 of the C0251002 study.
Pooled Skin Analysis Set	All participants in the FAS with a CDASI activity score of 14 or greater at baseline of study C0251002. This analysis set includes all subjects from Amended Stage 2 of the C0251002

	study and potentially some subjects from Stage 3 of the C0251002 study who also have skin disease.

9.3. Statistical Analyses

The SAP will be developed and finalized before any analyses are performed and will describe the analyses and procedures for accounting for missing, unused, and spurious data. This section is a summary of the planned statistical analyses of the primary and secondary endpoints.

9.3.1. General Considerations

This is an extension study to assess the safety and tolerability of the long-term therapy of PF-06823859 in participants with DM. All efficacy endpoints are secondary endpoints. The primary analysis population for safety evaluations will be the safety analysis set (see Section 9.2). All efficacy evaluations will be completed separately for those originating from the skin-predominant DM cohort including the C0251002 protocol second stage (Amended Stage 2) or the muscle-predominant DM cohort including the C0251002 third stage (Stage 3) of the C0251002 protocol. The respective analysis sets for these efficacy evaluations are the Skin Analysis Set and Muscle Analysis Set. Baseline will be Day 1 of the C0251008 study; sensitivity analyses that redefine Baseline as Day 1 of the parent study may also be performed and will be defined in the SAP.

9.3.2. Primary Endpoint(s) Analysis

The primary objective is to assess the long-term safety and tolerability of PF-06823859 in participants with DM. 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.

9.3.3. Secondary Endpoint(s)/Estimand(s) Analysis

All efficacy endpoints are continuous variables and will be summarized with descriptive statistics at each time point (n, proportion, mean, standard deviation, median, etc.). For each efficacy endpoint, the estimates for the effect of PF-06823859 will be obtained by fitting a LANCOVA model from baseline to Week 52. Each LANCOVA model will include week as a fixed effect and baseline value as a covariate, as appropriate. An unstructured variance-covariance matrix will be allowed. Estimates and 90% CI will be reported. No p-values will be computed for the analysis. See Section 9.1.1.2 for a description of the secondary estimands.

In the longitudinal modeling (LANCOVA) of repeated measures of continuous outcomes (both efficacy measures and covariates) it is assumed that missing data are generated by the "missing at random" mechanism and, therefore imputation of the missing data is not necessary.

A sensitivity analysis will be based on the ANCOVA. The ANCOVA-based estimation of the effect of PF-06823859 will use the observations collected at baseline and Week 52 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.

Another sensitivity analysis for E1 will be performed that uses the pooled skin disease analysis set for assessment of the CDASI activity score. Other sensitivity analyses may be performed and will be described in the SAP.

Additional longitudinal efficacy and safety analyses that define baseline as Day 1 of the parent study may be performed and will be described in the SAP.

9.3.4. Tertiary/Exploratory Endpoint(s)

The values of PROs at each visit will be summarized by descriptive statistics.

Additional exploratory endpoints will be described in the SAP.

9.3.5. Other Safety Analyses

9.3.5.1. 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 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.

9.3.5.2. Electrocardiogram Analyses

Changes from baseline for the ECG parameters QT interval, heart rate, QTc interval, PR interval, and QRS complex 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 postdose QTc values and maximum increases from baseline in the following categories will be tabulated by treatment:

Safety QTc Assessment

Degree of Prolongation	Mild (msec)	Moderate (msec)	Severe (msec)
Absolute value	>450-480	>480-500	>500
Increase from baseline		30-60	>60

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

9.3.6. Other Analyse(s)

9.3.6.1. Pharmacokinetic Analysis

The PK concentration population for PF-06823859 is defined as all enrolled participants who received at least one dose of PF-06823859 and in whom at least one concentration value is reported.

PK concentrations will be summarized and presented with summary statistics and, if appropriate, noncompartmental PK parameter estimates may be provided.

A population PK/PD model may be developed to characterize the PK and PD following PF-06823859 administration as well as to understand the covariates that describe inter-subject variability in PK and PD. Any population PKPD model developed will not be part of the CSR and may be reported separately.

Data permitting, the relationship between exposure and clinical responses (efficacy and safety) in DM participants may be explored. Exposure-response analyses conducted will not be part of the CSR and may be reported separately.

Pharmacogenomic or biomarker data from Retained Research Samples may be collected during or after the trial and retained for future analyses; the results of such analyses are not planned to be included in the CSR.

9.4. Interim Analyses

No formal interim analysis will be conducted for this study. As this is an open-label study, the sponsor may conduct unblinded reviews of the data during the course of the study for the purpose of safety assessments, facilitating PK/PD modeling, and/or supporting clinical development.

9.5. Sample Size Determination

The sample size will be determined by the number of patients who enroll from Protocol C0251002 and any other future qualifying studies. It is anticipated that up to approximately 30 participants from Amended Stage 2 and Stage 3 of Protocol C0251002 will be enrolled to receive open-label study intervention.

10. SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1. Appendix 1: Regulatory, Ethical, and Study Oversight Considerations

10.1.1. Regulatory and Ethical Considerations

This study will be conducted in accordance with the protocol and with the following:

- Consensus ethical principles derived from international guidelines, including the Declaration of Helsinki and CIOMS International Ethical Guidelines;
- Applicable ICH GCP guidelines;
- Applicable laws and regulations, including applicable privacy laws.

The protocol, protocol amendments, ICD, SRSD(s), and other relevant documents (eg, advertisements) must be reviewed and approved by the sponsor, submitted to an IRB/EC by the investigator, and reviewed and approved by the IRB/EC before the study is initiated.

Any amendments to the protocol will require IRB/EC approval before implementation of changes made to the study design, except for changes necessary to eliminate an immediate hazard to study participants.

Protocols and any substantial amendments to the protocol will require health authority approval prior to initiation except for changes necessary to eliminate an immediate hazard to study participants.

The investigator will be responsible for the following:

- Providing written summaries of the status of the study to the IRB/EC annually or more frequently in accordance with the requirements, policies, and procedures established by the IRB/EC;
- Notifying the IRB/EC of SAEs or other significant safety findings as required by IRB/EC procedures;
- Providing oversight of the conduct of the study at the site and adherence to requirements of 21 CFR, ICH GCP guidelines, the IRB/EC, European regulation 536/2014 for clinical studies (if applicable), European Medical Device Regulation 2017/745 for clinical device research (if applicable), and all other applicable local regulations.

10.1.1.1. 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 study intervention, 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 the ICH GCP guidelines that the investigator becomes aware of.

10.1.2. Financial Disclosure

Investigators and sub investigators will provide the sponsor with sufficient, accurate financial information as requested to allow the sponsor to submit complete and accurate financial certification or disclosure statements to the appropriate regulatory authorities. Investigators are responsible for providing information on financial interests during the course of the study and for 1 year after completion of the study.

10.1.3. Informed Consent Process

The investigator or his/her representative will explain the nature of the study, including the risks and benefits, to the participant and answer all questions regarding the study. The participant should be given sufficient time and opportunity to ask questions and to decide whether or not to participate in the trial.

Participants must be informed that their participation is voluntary. Participants will be required to sign a statement of informed consent that meets the requirements of 21 CFR 50, local regulations, ICH guidelines, privacy and data protection requirements, where applicable, and the IRB/EC or study center.

The investigator must ensure that each study participant is fully informed about the nature and objectives of the study, the sharing of data related to the study, and possible risks associated with participation, including the risks associated with the processing of the participant's personal data.

The participant must be informed that his/her personal study-related data will be used by the sponsor in accordance with local data protection law. The level of disclosure must also be explained to the participant.

The participant must be informed that his/her medical records may be examined by Clinical Quality Assurance auditors or other authorized personnel appointed by the sponsor, by appropriate IRB/EC members, and by inspectors from regulatory authorities.

The investigator further must ensure that each study participant is fully informed about his or her right to access and correct his or her personal data and to withdraw consent for the processing of his or her personal data.

The medical record must include a statement that written informed consent was obtained before the participant was enrolled in the study and the date on which the written consent was obtained. The authorized person obtaining the informed consent must also sign the ICD.

Participants must be reconsented to the most current version of the ICD(s) during their participation in the study.

A copy of the ICD(s) must be provided to the participant.

10.1.4. Data Protection

All parties will comply with all applicable laws, including laws regarding the implementation of organizational and technical measures to ensure protection of participant data.

Participants' personal data will be stored at the study site in encrypted electronic form and will be password-protected to ensure that only authorized study staff have access. The study site will implement appropriate technical and organizational measures to ensure that the personal data can be recovered in the event of disaster. In the event of a potential personal data breach, the study site will be responsible for determining whether a personal data breach has in fact occurred and, if so, providing breach notifications as required by law.

To protect the rights and freedoms of participants with regard to the processing of personal data, participants will be assigned a single, participant-specific numerical code. Any participant records or data sets that are transferred to the sponsor will contain the numerical code; participant names will not be transferred. All other identifiable data transferred to the sponsor will be identified by this single, participant-specific code. The study 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 and medical record ID. In case of data transfer, the sponsor will protect the confidentiality of participants' personal data consistent with the clinical study agreement and applicable privacy laws.

10.1.5. Committees Structure

10.1.5.1. Data Monitoring Committee

This study will not use a DMC.

10.1.6. Dissemination of Clinical Study Data

Pfizer fulfills its commitment to publicly disclose clinical study results through posting the results of studies on www.clinicaltrials.gov (ClinicalTrials.gov), the EudraCT, and/or www.pfizer.com, and other public registries in accordance with applicable local laws/regulations. In addition, Pfizer reports study results outside of the requirements of local laws/regulations pursuant to its SOPs.

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 results on www.clinicaltrials.gov for Pfizer-sponsored interventional studies (conducted in patients) that evaluate the safety and/or efficacy of a product, regardless of the geographical location in which the study is conducted. These results are submitted for posting in accordance with the format and timelines set forth by US law.

EudraCT

Pfizer posts clinical trial results on EudraCT for Pfizer-sponsored interventional studies in accordance with the format and timelines set forth by EU requirements.

www.pfizer.com

Pfizer posts public disclosure synopses (CSR synopses in which any data that could be used to identify individual participants have been removed) on www.pfizer.com for Pfizer-sponsored interventional studies at the same time the corresponding study results are posted to www.clinicaltrials.gov.

Documents within marketing authorization packages/submissions

Pfizer complies with the European Union Policy 0070, the proactive publication of clinical data to the EMA website. Clinical data, under Phase 1 of this policy, includes clinical overviews, clinical summaries, CSRs, and appendices containing the protocol and protocol amendments, sample CRFs, and statistical methods. Clinical data, under Phase 2 of this policy, includes the publishing of individual participant data. Policy 0070 applies to new marketing authorization applications submitted via the centralized procedure since 01 January 2015 and applications for line extensions and for new indications submitted via the centralized procedure since 01 July 2015.

Data sharing

Pfizer provides researchers secure access to patient-level data or full CSRs for the purposes of "bona-fide scientific research" that contributes to the scientific understanding of the disease, target, or compound class. Pfizer will make data from these trials available 24 months after study completion. Patient-level data will be anonymized in accordance with applicable privacy laws and regulations. CSRs will have personally identifiable information redacted.

Data requests are considered from qualified researchers with the appropriate competencies to perform the proposed analyses. Research teams must include a biostatistician. Data will not be provided to applicants with significant conflicts of interest, including individuals requesting access for commercial/competitive or legal purposes.

10.1.7. Data Quality Assurance

All participant data relating to the study will be recorded on printed or electronic CRF unless transmitted to the sponsor or designee electronically (eg, laboratory data). The investigator is responsible for verifying that data entries are accurate and correct by physically or electronically signing the CRF.

Guidance on completion of CRFs will be provided in the CRF Completion Requirements document.

The investigator must ensure that the CRFs are securely stored at the study site in encrypted electronic form and are password protected to prevent access by unauthorized third parties.

The investigator must permit study-related monitoring, audits, IRB/EC review, and regulatory agency inspections and provide direct access to source data documents. This verification may also occur after study completion. 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.

Monitoring details describing strategy, including definition of study critical data items and processes (eg, risk-based initiatives in operations and quality such as risk management and mitigation strategies and analytical risk-based monitoring), methods, responsibilities, and requirements, including handling of noncompliance issues and monitoring techniques (central, virtual, or on-site monitoring), are provided in the data management plan and monitoring plan maintained and utilized by the sponsor or designee.

The sponsor or designee is responsible for the data management of this study, including quality checking of the data.

Records and documents, including signed ICDs, pertaining to the conduct of this study must be retained by the investigator for 15 years after study completion unless local regulations or institutional policies require a longer retention period. No records may be destroyed during the retention period without the written approval of the sponsor. No records may be transferred to another location or party without written notification to the sponsor. The investigator must ensure that the records continue to be stored securely for as long as they are maintained.

When participant data are to be deleted, the investigator will ensure that all copies of such data are promptly and irrevocably deleted from all systems.

The investigator(s) will notify the sponsor or its agents immediately of any regulatory retain notification in relation to the study. Furthermore, the investigator will cooperate with the sponsor or its agents to prepare the investigator site for the inspection and will allow the sponsor 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 the sponsor or its agent. Before response submission to

the regulatory authorities, the investigator will provide the sponsor or its agents with an opportunity to review and comment on responses to any such findings.

10.1.8. Source Documents

Source documents provide evidence for the existence of the participant and substantiate the integrity of the data collected. Source documents are filed at the investigator site.

Data reported on the CRF or entered in the eCRF that are from source documents must be consistent with the source documents or the discrepancies must be explained. The investigator may need to request previous medical records or transfer records, depending on the study. Also, current medical records must be available.

In this study, the CRF will serve as the source document. A document must be available at the investigative site that identifies those data that will be recorded on the CRF and for which the CRF will be the source document.

Definition of what constitutes source data and its origin can be found in the clinical monitoring plan, which is maintained by the sponsor.

Description of the use of the computerized system is documented in the Data Management Plan, which is maintained by the sponsor.

The investigator must maintain accurate documentation (source data) that supports the information entered in the CRF.

Study monitors will perform ongoing source data verification to confirm that data entered into the CRF by authorized site personnel are accurate, complete, and verifiable from source documents; that the safety and rights of participants are being protected; and that the study is being conducted in accordance with the currently approved protocol and any other study agreements, ICH GCP guidelines, and all applicable regulatory requirements.

10.1.9. Study and Site Start and Closure

The study start date is the date on which the clinical study will be open for recruitment of participants.

The first act of recruitment is the date of the first participant's first visit and will be the study start date.

The sponsor designee reserves the right to close the study site or terminate the study at any time for any reason at the sole discretion of the sponsor. Study sites will be closed upon study completion. A study site is considered closed when all required documents and study supplies have been collected and a study-site closure visit has been performed.

The investigator may initiate study-site closure at any time upon notification to the sponsor if requested to do so by the responsible IRB/EC or if such termination is required to protect the health of study participants.

Reasons for the early closure of a study site by the sponsor may include but are not limited to:

- Failure of the investigator to comply with the protocol, the requirements of the IRB/EC or local health authorities, the sponsor's procedures, or the ICH GCP guidelines;
- Inadequate recruitment of participants by the investigator;
- Discontinuation of further study intervention development.

If the study is prematurely terminated or suspended, the sponsor shall promptly inform the investigators, the ECs/IRBs, the regulatory authorities, and any CRO(s) used in the study of the reason for termination or suspension, as specified by the applicable regulatory requirements. The investigator shall promptly inform the participant and should assure appropriate participant therapy and/or follow-up.

If the sponsor decides to terminate the study for a reason unrelated to the safety of PF-06823859, participants may continue to receive PF-06823859(s) per the investigator's judgement and protocol-specified safety assessments will continue to be performed for these participants until the end of study as defined in Section 4.4. The following non-safety-related study procedures and assessments may be stopped upon written notification from the sponsor:

- CDASI;
- TIS;
- MMT-8;
- MDAAT Global extramuscular disease activity;
- PROs (SF-36 v2 acute, EQ-5D-5L, HAQ-DI, and PtGA);
- PhGA,VAS.

Study termination is also provided for in the clinical study agreement. If there is any conflict between the contract and this protocol, the contract will control as to termination rights.

10.1.10. Publication Policy

The results of this study may be published or presented at scientific meetings by the investigator after publication of the overall study results or 1 year after the end of the study (or study termination), whichever comes first.

The investigator agrees to refer to the primary publication in any subsequent publications, such as secondary manuscripts, and submits all manuscripts or abstracts to the sponsor 30 days before submission. This allows the sponsor to protect proprietary information and to provide comments, and the investigator will, on request, remove any previously undisclosed confidential information before disclosure, except for any study- or Pfizer intervention-related information necessary for the appropriate scientific presentation or understanding of the study results.

For all publications relating to the study, the investigator will comply with recognized ethical standards concerning publications and authorship, including those established by the International Committee of Medical Journal Editors.

The sponsor will comply with the requirements for publication of the overall study results covering all investigator sites. In accordance with standard editorial and ethical practice, the sponsor will support publication of multicenter studies only in their entirety and not as individual site data. In this case, a coordinating investigator will be designated by mutual agreement.

Authorship of publications for the overall study results will be determined by mutual agreement and in line with International Committee of Medical Journal Editors authorship requirements.

If publication is addressed in the clinical study agreement, the publication policy set out in this section will not apply.

10.1.11. 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 the supporting study portal.

To facilitate access to appropriately qualified medical personnel for study-related medical questions or problems, participants are provided with an Emergency Contact Card (ECC) at the time of informed consent. The ECC contains, at a minimum, (a) protocol and study intervention identifiers, (b) participant's study identification number, (c) site emergency phone number active 24 hours/day, 7 days per week, and (d) Pfizer Call Center number.

The ECC is intended to augment, not replace, the established communication pathways between the investigator, site staff, and study team. The ECC is to be used by healthcare professionals not involved in the research study only, as a means of reaching the investigator or site staff related to the care of a participant. The Pfizer Call Center number should only be used when the investigator and site staff cannot be reached. The Pfizer Call Center number is

not intended for use by the participant directly; if a participant calls that number directly, he or she will be directed back to the investigator site.

10.2. Appendix 2: Clinical Laboratory Tests

The following safety laboratory tests will be performed at times defined in the SoA section of this protocol. Additional laboratory results may be reported on these samples as a result of the method of analysis or the type of analyzer used by the clinical laboratory, or as derived from calculated values. These additional tests would not require additional collection of blood. Unscheduled clinical laboratory measurements may be obtained at any time during the study to assess any perceived safety issues.

Any unscheduled visits or unscheduled labs may be performed at the Investigator's discretion if a participant experiences a flare or an adverse event. For participants receiving concomitant IVIG, see Section 8.4.3 for unscheduled specified analyses.

Table 3. Laboratory Tests

Hematology	Chemistry	Urinalysis	Other
Hemoglobin Hematocrit RBC count Platelet count WBC count with differential Total neutrophils (%, Abs) Eosinophils (%, Abs) Basophils (%, Abs) Lymphocytes (%, Abs) Monocytes (%, Abs) PT/PTT hsCRP	BUN and Creatinine Serum cystatin C CK Glucose (fasting & non fasting) Sodium Potassium Chloride Calcium Total CO_2 (Bicarbonate) AST, ALT LDH Aldolase CK-MB (Only if CK is elevated) Total Indirect and Direct Bilirubin Alkaline phosphatase Uric acid Albumin Total protein	pH Glucose (qual) Protein (qual) Blood (qual) Ketones Nitrites Leukocyte esterase Microscopy[a] Spot Urine (Upr:Ucr) eGFR[b]	β-hcG [c] Retained Research Sample Prep R1 Retained Research Sample Prep B1.5 Retained Research Sample B2.5 PK collections IVIG collections for participants taking IVIG concomitantly. Immunogenicity, ADA.NAb, total IFNβ , Blood for muscle biomarkers

a. Only if urine dipstick at the central lab is positive for blood or protein.

b. eGFR Serum cystatin C and urinalysis will be collected every 6 months. See the SoA.

c. Urine pregnancy tests must be performed for all WOCBP as defined in the SoA.

The investigator must review the laboratory report, document this review, and record any clinically relevant changes occurring during the study in the AE section of the CRF.

The investigator must review the laboratory report, document this review, and record any clinically relevant changes occurring during the study in the AE section of the CRF.

10.3. Appendix 3: Adverse Events: Definitions and Procedures for Recording, Evaluating, Follow-Up, and Reporting

10.3.1. Definition of AE

AE Definition
• An AE is any untoward medical occurrence in a patient or clinical study participant, temporally associated with the use of study intervention, whether or not considered related to the study intervention. • Note: An AE can therefore be any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of study intervention.

Events <u>Meeting</u> the AE Definition

• Any abnormal laboratory test results (hematology, clinical chemistry, or urinalysis) or other safety assessments (eg, ECG, radiological scans, vital sign measurements), including those that worsen from baseline, considered clinically significant in the medical and scientific judgment of the investigator. Any abnormal laboratory test results that meet any of the conditions below must be recorded as an AE:
 	
  • Is associated with accompanying symptoms.
 	
  • Requires additional diagnostic testing or medical/surgical intervention.
 	
  • 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.
 	
• Exacerbation of a chronic or intermittent preexisting condition, including either an increase in frequency and/or intensity of the condition.
 	
• New condition detected or diagnosed after study intervention administration, even though it may have been present before the start of the study.
 	
• Signs, symptoms, or the clinical sequelae of a suspected drug-drug interaction.
 	
• Signs, symptoms, or the clinical sequelae of a suspected overdose of either study intervention or a concomitant medication. Overdose per se will not be reported as an AE or SAE unless it is an intentional overdose taken with possible suicidal/self-harming intent. Such overdoses should be reported regardless of sequelae.

Events NOT Meeting the AE Definition
• Any clinically significant abnormal laboratory findings or other abnormal safety assessments that are associated with the underlying disease, unless judged by the investigator to be more severe than expected for the participant's condition. • The disease/disorder being studied or expected progression, signs, or symptoms of the disease/disorder being studied, unless more severe than expected for the participant's condition. • Medical or surgical procedure (eg, endoscopy, appendectomy): the condition that leads to the procedure is the AE. • Situations in which an untoward medical occurrence did not occur (social and/or convenience admission to a hospital). • Anticipated day-to-day fluctuations of preexisting disease(s) or condition(s) present or detected at the start of the study that do not worsen.

10.3.2. Definition of an SAE

An SAE is defined as any untoward medical occurrence that, at any dose, meets one or more of the criteria listed below:
a. Results in death
b. Is life-threatening The term "life-threatening" in the definition of "serious" refers to an event in which the participant was at risk of death at the time of the event. It does not refer to an event that hypothetically might have caused death if it were more severe.
c. Requires inpatient hospitalization or prolongation of existing hospitalization In general, hospitalization signifies that the participant has been admitted (usually involving at least an overnight stay) at the hospital or emergency ward for observation and/or treatment that would not have been appropriate in the physician's office or outpatient setting. Complications that occur during hospitalization are AEs. If a complication prolongs hospitalization or fulfills any other serious criteria, the event is serious. When in doubt as to whether "hospitalization" occurred or was necessary, the AE should be considered serious.

Hospitalization for elective treatment of a preexisting condition that did not worsen from baseline is not considered an AE.

d. Results in persistent or significant disability/incapacity

- The term disability means a substantial disruption of a person's ability to conduct normal life functions.
- This definition is not intended to include experiences of relatively minor medical significance, such as uncomplicated headache, nausea, vomiting, diarrhea, influenza, and accidental trauma (eg, sprained ankle), that may interfere with or prevent everyday life functions but do not constitute a substantial disruption.

e. Is a congenital anomaly/birth defect

f. Is a suspected transmission via a Pfizer product of an infectious agent, pathogenic or non-pathogenic, is considered serious.

The event may be suspected from clinical symptoms or laboratory findings indicating an infection in a participant exposed to a Pfizer product. The terms "suspected transmission" and "transmission" are considered synonymous. These cases are considered unexpected and handled as serious expedited cases by pharmacovigilance personnel. Such cases are also considered for reporting as product defects, if appropriate.

g. Other situations:

- Medical or scientific judgment should be exercised by the investigator in deciding whether SAE reporting is appropriate in other situations, such as significant medical events that may jeopardize the participant or may require medical or surgical intervention to prevent one of the other outcomes listed in the above definition. These events should usually be considered serious.
- Examples of such events include invasive or malignant cancers, 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.

10.3.3. Recording/Reporting and Follow-Up of AEs and/or SAEs During the Active Colletion Period

AE and SAE Recording/Reporting

The table below summarizes the requirements for recording AEs on the CRF and for reporting SAEs on the CT SAE Report Form to Pfizer Safety throughout the active collection period. These requirements are delineated for 3 types of events: (1) SAEs; (2) nonserious AEs; and (3) exposure to the study intervention under study during pregnancy or breastfeeding, and occupational exposure.

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.

Safety Event	**Recorded on the CRF**	**Reported on the CT SAE Report Form to Pfizer Safety Within 24 Hours of Awareness**
SAE	All	All
Nonserious AE	All	None
Exposure to the study intervention under study during pregnancy or breastfeeding.	All AEs or SAEs associated with exposure during pregnancy or breastfeeding **Note:** Instances of EDP or not associated with an AE or SAE are not captured in the CRF.	All instances of EDP are reported (whether or not there is an associated SAE)* All instances of EDB are reported (whether or not there is an associated SAE).**
Environmental or occupational exposure to the product under study to a non-participant (not involving EDP or EDB).	None. Exposure to a study non-participant is not collected on the CRF.	The exposure (whether or not there is an associated AE or SAE) must be reported.***

* **EDP** (with or without an associated AE or SAE): any pregnancy information is reported to Pfizer Safety using CT SAE Report Form and EDP Supplemental Form; if the EDP is associated with an SAE, then the SAE is reported to Pfizer Safety using the CT SAE Report Form.

** **EDB** is reported to Pfizer Safety using the CT SAE Report Form which would also include details of any SAE that might be associated with the EDB.

*** **Environmental or Occupational exposure:** AEs or SAEs associated with occupational exposure are reported to Pfizer Safety using the CT SAE Report Form.

- When an AE or SAE occurs, it is the responsibility of the investigator to review all documentation (eg, hospital progress notes, laboratory reports, and diagnostic reports) related to the event.
- The investigator will then record all relevant AE or SAE information in the CRF.
- It is not acceptable for the investigator to send photocopies of the participant's medical records to Pfizer Safety in lieu of completion of the CT SAE Report Form/AE or SAE CRF page.
- There may be instances when copies of medical records for certain cases are requested by Pfizer Safety. In this case, all participant identifiers, with the exception of the participant number, will be redacted on the copies of the medical records before submission to Pfizer Safety.
- The investigator will attempt to establish a diagnosis of the event based on signs, symptoms, and/or other clinical information. Whenever possible, the diagnosis (not the individual signs/symptoms) will be documented as the AE or SAE.

Assessment of Intensity

The investigator will make an assessment of intensity for each AE and SAE reported during the study and assign it to 1 of the following categories:

- Mild: Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated.
- Moderate: Minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL. Instrumental ADL refers to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.
- Severe: Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling, limiting self care ADL. Self care ADL refers to bathing, dressing and undressing, feeding self, using the toilet, taking medications, and not bedridden.

An event is defined as "serious" when it meets at least 1 of the predefined outcomes as described in the definition of an SAE, NOT when it is rated as severe.

Assessment of Causality

- The investigator is obligated to assess the relationship between study intervention and each occurrence of each AE or SAE. The investigator will use clinical judgment to determine the relationship.
- A "reasonable possibility" of a relationship conveys that there are facts, evidence, and/or arguments to suggest a causal relationship, rather than a relationship cannot be ruled out.
- Alternative causes, such as underlying disease(s), concomitant therapy, and other risk factors, as well as the temporal relationship of the event to study intervention administration, will be considered and investigated.
- The investigator will also consult the IB and/or product information, for marketed products, in his/her assessment.
- For each AE or SAE, the investigator **must** document in the medical notes that he/she has reviewed the AE or SAE and has provided an assessment of causality.
- There may be situations in which an SAE has occurred and the investigator has minimal information to include in the initial report to the sponsor. However, **it is very important that the investigator always make an assessment of causality for every event before the initial transmission of the SAE data to the sponsor.**
- The investigator may change his/her opinion of causality in light of follow-up information and send an SAE follow-up report with the updated causality assessment.
- The causality assessment is one of the criteria used when determining regulatory reporting requirements.
- If the investigator does not know whether or not the study intervention caused the event, then the event will be handled as "related to study intervention" for reporting purposes, as defined by the sponsor. 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.

Follow-Up of AEs and SAEs
• The investigator is obligated to perform or arrange for the conduct of supplemental measurements and/or evaluations, as medically indicated or as requested by the sponsor, to elucidate the nature and/or causality of the AE or SAE as fully as possible. This may include additional laboratory tests or investigations, histopathological examinations, or consultation with other healthcare providers. • If a participant dies during participation in the study or during a recognized follow-up period, the investigator will provide Pfizer Safety with a copy of any postmortem findings, including histopathology. • New or updated information will be recorded in the originally submitted documents. • The investigator will submit any updated SAE data to the sponsor within 24 hours of receipt of the information.

10.3.4. Reporting of SAEs

SAE Reporting to Pfizer Safety via an Electronic Data Collection Tool
• The primary mechanism for reporting an SAE to Pfizer Safety will be the electronic data collection tool. • If the electronic system is unavailable, then the site will use the paper SAE data collection tool (see next section) to report the event within 24 hours. • The site will enter the SAE data into the electronic system as soon as the data become available. • After the study is completed at a given site, the electronic data collection tool will be taken off-line to prevent the entry of new data or changes to existing data. • If a site receives a report of a new SAE from a study participant or receives updated data on a previously reported SAE after the electronic data collection tool has been taken off-line, then the site can report this information on a paper SAE form (see next section) or to Pfizer Safety by telephone.

SAE Reporting to Pfizer Safety via CT SAE Report Form
• Facsimile transmission of the CT SAE Report Form is the preferred method to transmit this information to Pfizer Safety. • In circumstances when the facsimile is not working, notification by telephone is acceptable with a copy of the CT SAE Report Form sent by overnight mail or courier service. • Initial notification via telephone does not replace the need for the investigator to complete and sign the CT SAE Report Form pages within the designated reporting time frames.

10.4. Appendix 4: Contraceptive and Barrier Guidance

10.4.1. 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 terminal half-lives after the last dose of study intervention, (approximately 150 days) which corresponds to the time needed to eliminate reproductive safety risk of the study intervention(s):

- 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 Section 10.4.4).

10.4.2. Female Participant Reproductive Inclusion Criteria

A female participant is eligible to participate if she is not pregnant or breastfeeding, and at least 1 of the following conditions applies:

- Is not a WOCBP (see definitions below in Section 10.4.3).

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 150 days after the last dose of study intervention, which corresponds to the time needed to eliminate any reproductive safety risk of the study intervention(s). 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 150 days after the last dose of study intervention, which corresponds to the time needed to eliminate any reproductive safety risk of the study intervention(s). 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.

10.4.3. Woman of Childbearing Potential

A woman is considered fertile following menarche and until becoming postmenopausal 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.

10.4.4. 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).

10.5. Appendix 5: Genetics

Use/Analysis of DNA

- Genetic variation may impact a participant's response to study intervention, susceptibility to, and severity and progression of disease. Therefore, where local regulations and IRBs/ECs allow, a blood sample will be collected for DNA analysis.

- The scope of the genetic research may be narrow (eg, 1 or more candidate genes) or broad (eg, the entire genome), as appropriate to the scientific question under investigation.

- The samples may be analyzed as part of a multistudy assessment of genetic factors involved in the response to PF-06823859 or study interventions of this class to understand treatments for the disease(s) under study or the disease(s) themselves.

- The results of genetic analyses may be reported in CSR or in a separate study summary, or may be used for internal decision making without being included in a study report.

- The sponsor will store the DNA samples in a secure storage space with adequate measures to protect confidentiality.

- The samples will be retained as indicated:

    - Retained samples will be stored indefinitely or for another period as per local requirements.

- Participants may withdraw their consent for the storage and/or use of their Retained Research Samples at any time by making a request to the investigator; in this case, any remaining material will be destroyed. Data already generated from the samples will be retained to protect the integrity of existing analyses.

- Samples for genetic research will be labeled with a code. The key between the code and the participant's personally identifying information (eg, name, address) will be held securely at the study site.

10.6. Appendix 6: Liver Safety: Suggested Actions and Follow-Up Assessments

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 DILI. Participants who experience a transaminase elevation above 3 × ULN should be monitored more frequently to determine if they are “adaptors” or are “susceptible.”

In the majority of DILI cases, elevations in AST and/or ALT precede 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 laboratory 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 for suspected Hy's law cases, additional laboratory tests should include albumin, CK, direct and indirect bilirubin, GGT, PT/INR, total bile acids, and alkaline phosphatase. 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/paracetamol (either by itself or as a coformulated product in prescription or over-the-counter medications), recreational drug, or 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, liver imaging (eg, biliary tract), and collection of serum samples for acetaminophen/paracetamol drug and/or protein adduct levels 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 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.

10.7. Appendix 7: ECG Findings of Potential Clinical Concern

ECG Findings That <u>May</u> Qualify as AEs
• Marked sinus bradycardia (rate <40 bpm) lasting minutes. • New PR interval prolongation >280 msec. • New prolongation of QTcF to >480 msec (absolute) or by ≥60 msec from baseline. • New-onset atrial flutter or fibrillation, with controlled ventricular response rate: ie, rate <120 bpm. • New-onset type I second-degree (Wenckebach) AV block of >30 seconds' duration. • Frequent PVCs, triplets, or short intervals (<30 seconds) of consecutive ventricular complexes.
ECG Findings That <u>May</u> Qualify as SAEs

• QTcF prolongation >500 msec.
• New ST-T changes suggestive of myocardial ischemia.
• New-onset left bundle branch block (QRS >120 msec).
• New-onset right bundle branch block (QRS >120 msec).
• Symptomatic bradycardia.
• Asystole:
  • In awake, symptom-free patients in sinus rhythm, with documented periods of asystole ≥3.0 seconds or any escape rate <40 bpm, or with an escape rhythm that is below the AV node;
  • In awake, symptom-free patients with atrial fibrillation and bradycardia with 1 or more pauses of at least 5 seconds or longer;
  • Atrial flutter or fibrillation, with rapid ventricular response rate: rapid = rate >120 bpm.
• Sustained supraventricular tachycardia (rate >120 bpm) ("sustained" = short duration with relevant symptoms or lasting >1 minute).

- Ventricular rhythms >30 seconds' duration, including idioventricular rhythm (heart rate <40 bpm), accelerated idioventricular rhythm (HR 40 bpm to <100 bpm), and monomorphic/polymorphic ventricular tachycardia (HR >100 bpm (such as torsades de pointes)).
- Type II second-degree (Mobitz II) AV block.
- Complete (third-degree) heart block.

ECG Findings That Qualify as SAEs

- Change in pattern suggestive of new myocardial infarction.
- Sustained ventricular tachyarrhythmias (>30 seconds' duration).
- Second- or third-degree AV block requiring pacemaker placement.
- Asystolic pauses requiring pacemaker placement.
- Atrial flutter or fibrillation with rapid ventricular response requiring cardioversion.
- Ventricular fibrillation/flutter.
- At the discretion of the investigator, any arrhythmia classified as an adverse experience.

The enumerated list of major events of potential clinical concern are recommended as "alerts" or notifications from the core ECG laboratory to the investigator and Pfizer study team, and not to be considered as all inclusive of what to be reported as AEs/SAEs.

10.8. Appendix 8: Permitted and Prohibited Concomitant Medications

The prohibited concomitant medications listed below (Table 4) should not be taken during the C0251008 study.

The Pfizer study team is to be notified of any prohibited medications taken during the study. After consulting with the sponsor, the investigator will make a judgement on the ongoing participation of any participant with prohibited medication use during the study.

This list of drugs prohibited for potential DDI concerns with the IMP may be revised during the course of the study with written notification from the sponsor, to include or exclude specific drugs or drug categories for various reasons (eg, emerging DDI results for the IMP, availability of new information in literature on the DDI potential of other drugs).

This is not an all-inclusive list. Site staff should consult with the sponsor or designee with any questions regarding potential DDI.

Table 4. List of Prohibited and Permitted Concomitant Medications

Medications		C0251008 Treatment Period Day 1-Week 52	C0251008 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 52, 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.	Permitted

Medications	C0251008 Treatment Period Day 1-Week 52	C0251008 Follow-up Period
	• No new antimalarial drugs or increase in dose is allowed during the treatment period.	
Thalidomide, tacrolimus, calcineurin inhibitor or mizoribine	Prohibited • Any form of tacrolimus or topical calcineurin inhibitors are not allowed during the treatment period.	Permitted
Immunosuppressive topical	Permitted • Immunosuppressive topical for the scalp.	Permitted
Immunosuppressive eye drops	Permitted	Permitted
Investigational or marketed biologics (eg, abatacept, tocilizumab, TNF inhibitors)	Prohibited	Prohibited
Cyclophosphamide or chlorambucil	Prohibited	Permitted
Cyclosporine	permitted	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 the permitted steroid dosing in the protocol for skin and muscle cohorts.	Permitted	Permitted

Investigators should consult the relevant product label for any other medication used during the study for information regarding medication that is prohibited for concomitant use.

10.9. Appendix 9: 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).

10.9.1. 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 must be performed during a telehealth visit:

- Review and record any AEs and SAEs since the last contact. Refer to Section 8.3.
- Review and record any new concomitant medications or changes in concomitant medications since the last contact.
- Review and record contraceptive method and results of pregnancy testing. Confirm that the participant is adhering to the contraception method(s) required in the protocol. Refer to Appendix 4 and Section 1.3 of this appendix regarding pregnancy tests.

Study participants must be reminded to promptly notify site staff about any change in their health status.

10.9.2. Alternative Facilities for Safety Assessments

10.9.2.1. 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 3 of the protocol; not all laboratory collections may be possible.

- Hematology;
- Chemistry;

- Urinalysis;
- Pregnancy testing (if applicable);
- PK (if applicable).

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.

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 mIU/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.

10.9.2.2. Electrocardiograms

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.

10.9.3. Home Health Visits

A home health care service may 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.

10.9.4. Adverse Events and Serious Adverse Events

If a participant has COVID-19 during the study, this should be reported as an AE or serious 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.

10.10. Appendix 10: Guidelines for Participant Safety Monitoring and Discontinuation

These guidelines for participant safety monitoring and discontinuation are to be applied to all participants in Study C0251008.

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. For participants on permitted concomitant IVIG, see Section 8.4.3 for specified analyses to be performed at unscheduled visits.

10.10.1. 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 with INR, 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 (See Appendix 6 for suggested actions and follow-up assessments in the event of potential drug-induced liver injury);

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

10.10.2. 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:

- Potential Cases of Decreased eGFR

    - If an individual participant demonstrates CONCOMITANT SCr-based AND serum Cystatin C-based eGFR decline of ≥30% compared to the participant's baseline eGFR, then the participant should not be further dosed and adequate, immediate, supportive measures including immediate evaluation by a nephrologist (preferably within 24 hours) with appropriate management and treatment as clinically indicated. Results should be repeated as indicated by the

nephrologist or weekly at a minimum until the eGFR returns to baseline ±15%, or the renal parameters are deemed to be stable by the nephrologist and/or the investigator.

- If the participant cannot be seen by a nephrologist within 24 hours (as described above), then the participant should be sent to a local emergency room for evaluation and treatment as clinically indicated.

- Follow-up evaluations should include laboratory tests, detailed history, and physical assessment. In addition to repeating SCr and serum cystatin C, laboratory tests should also include: serum BUN, serum CK, serum electrolytes (including at a minimum potassium, sodium, phosphate/phosphorus, calcium), in addition to urine dipstick, urine microscopic examination, and urinary indices. All cases confirmed on repeat testing as meeting the laboratory criteria for acute kidney injury, with no other cause(s) of laboratory abnormalities identified should be considered as potential cases of drug-induced kidney injury irrespective of availability of all the results of the investigations performed to determine etiology of the abnormal SCr.

- All relevant test results will be forwarded to Sponsor Medical Monitor for review immediately upon receipt by the PI.

- 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 Section 6.8.1 and Appendix 8 (Section 10.8) for prohibited medication listing.
- A participant who meets either bulleted criterion based on repeat ECG readings will be withdrawn from the study intervention.
    - QTcF >500 msec.
    - Change from baseline: QTcF >60 msec and QTcF >450 msec.

      If a clinically significant finding is identified (including, but not limited to, changes from baseline in QTcF after enrollment), the investigator or qualified designee will determine if the participant can continue in the study and if any change in participant management is needed. This review of the ECG printed at the time of collection must be documented. Any new clinically relevant finding should be reported as an AE. See Appendix 7 (Section 10.7) for further details regarding ECG findings of potential clinical concern.
- Lack of efficacy will be the discretion of the investigator (see rescue medication guidance, Section 6.8.4).

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 study intervention 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 terminal half-lives. 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.

10.11. Appendix 11: Corticosteroid Suggested Taper and Rescue Guidance

10.11.1. Corticosteroid Suggested Taper

The following protocol recommended corticosteroid taper is provided as a guide only. Corticosteroid tapering is ultimately based upon investigator discretion.

The protocol recommended corticosteroid taper is suggested to be started after Week 4 of the C0251008 study. It is also suggested that no corticosteroid tapering occurs between Week 44 and Week 52 due to final assessments being completed. All doses are in prednisone equivalent.

Recommended Oral Prednisone Taper (all doses are approximate as these are examples only):

- **Prednisone dose of 15-20 mg:**
    - Decrease by 2.5 mg every 4 weeks. If starting dose is 19 or 18 mg, then first decrease will be to 17.5 mg a day. If starting dose is 16 or 17 mg, then first decrease will be to 15 mg a day.
- **Prednisone dose of 10-15 mg**
    - Decrease by 2.5 mg every 4 weeks. If starting dose is 13 or 14 mg, then first decrease will be to 12.5 mg. if starting dose is 11 or 12 mg, then first decrease will be to 10 mg.
- **Prednisone dose of 5-10 mg:**
    - Decrease by 1 mg every 2 weeks. If starting dose is 7.5 mg, then first decrease will be to 7 mg.
- **Prednisone dose of 5 mg or less:**
    - No taper is recommended, but prednisone dose can be tapered as per the investigator.

10.11.2. Corticosteroid Rescue Guidance

10.11.2.1. Oral or Intramuscular Corticosteroid Rescue Recommended Guidance for Dermatomyositis Related Reasons

Systemic corticosteroids may be increased as clinically required; however, are suggested to remain within the following stipulations as a guidance.

Recommended Oral or Intramuscular corticosteroid rescue therapy:

- Two of the following options, or the same option used twice are allowed at any time, except between Week 44 and Week 52 due to final assessments being completed.

- Each event of corticosteroid rescue is recommended to be recorded on the concomitant medication pages (All doses are approximate as these are examples only):

    1. Increase in oral corticosteroid dose up to the participant's baseline dose (dose at Day 1). Consideration can then be given to following the protocol driven corticosteroid recommended taper.

    2. Increase in oral corticosteroid dose up to 20 mg of prednisone equivalent per day. Consideration can then be given to following the protocol driven corticosteroid recommended taper.

    3. Oral corticosteroid taper of 20 mg prednisone equivalent per day of over 1 month can be given on top of the baseline corticosteroid dose.

       Recommended taper on top of the baseline dose as follows: 20 mg prednisone equivalent per day for 1 week, then 15 mg per day for 1 week, then 10 mg per day for 1 week, then 5 mg per day for 1 week, then back to baseline corticosteroid dose. Consideration can then be given to following the protocol driven corticosteroid recommended taper.

    4. An intramuscular injection of approximately 40 mg Depo-Medrol (methylprednisolone acetate suspension [50 mg prednisone equivalent]) as an example. Consideration can then be given to following the protocol driven corticosteroid recommended taper.

10.11.2.2. Corticosteroid Rescue Guidance for Non-Dermatomyositis Reasons

Non-DM reasons may include, for example, poison ivy, or asthma exacerbation.

For example, prednisone equivalent dose of 60 mg or less for 10 days or less. However, this is recommended to be avoided between Week 44 and Week 52 due to final assessments being completed. If corticosteroids for non-dermatomyositis reasons are needed within 4 weeks of the final trial visit, then efficacy assessments will be conducted at the first follow-up visit, such that it is as approximate to 4 weeks after the corticosteroid rescue.

10.11.2.3. Intra-Articular Corticosteroids

A participant who receives an intra-articular steroid injection will be allowed to continue in the treatment period of the trial. However, it is preferable to have an intra-articular corticosteroid injection >30 days before the clinical efficacy assessment visit.

A participant who receives an intra-articular corticosteroid injection within 30 days of when efficacy assessments are performed will need to complete the efficacy assessments.

10.11.2.4. Immunosuppressives/immunomodulatory Agent Rescue Medications.

A participant who requires an increase or additional non-steroid immunosuppressive/immunomodulatory agent, including prohibited medications, will be withdrawn from the treatment period and enter the follow-up period of the trial.

However, if there is a requirement for a decrease in a non-steroid immunosuppressive/immunomodulatory agent for a safety or a tolerability issue, then this may be allowed after a discussion with the medical monitor and should be documented.

10.11.2.5. NSAIDs and Analgesics

The dose and the frequency of NSAIDs, acetaminophen, aspirin and other analgesic or pruritis medication is recommended to remain stable throughout the clinical trial.

Addition of a new or an increase in the dose of NSAIDs, aspirin or pruritis medications are allowed, but their use is recommended to be minimized as much as possible and documented, because they may potentially affect efficacy parameters (eg, the skeletal disease activity VAS, arthritis assessment and gastrointestinal disease activity VAS for the MDAAT and thus is recommended to be used judiciously.

Participants taking additional frequency/dose of NSAIDS/analgesics, including topical NSAIDS (that were not being used at screening/baseline), are recommended to not take the additional dose of these medications within 24 hours prior to clinical assessment visits.

Acetaminophen is primarily an analgesic and lacks the anti-inflammatory properties of other NSAIDS. The use of acetaminophen is recommended, when possible, to treat non-dermatomyositis related conditions, in the absence of a pre-existing hepatic function deficiency.

10.12. Appendix 12: Abbreviations

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

Abbreviation	Term
ADA	anti-drug antibody
ADL	activities of daily living
AE	adverse event
ALT	alanine aminotransferase
ANCOVA	analysis of covariance
anti-IFNAR1	interferon-alpha/beta receptor alpha
anti-IFNα	anti-interferon alpha
AST	aspartate aminotransferase
AUC	area under the curve
AV	atriaventricular
AZA	Azathioprine
β	beta
β-hCG	beta-human chorionic gonadotropin
BP	blood pressure
BUN	Blood Urea Nitrogen
C-CASA	Columbia Classification Algorithm of Suicide Assessment
C_{max}	maximum (or peak) serum concentration
CDASI	Cutaneous Dermatomyositis Disease Area and Severity Index
CFR	Code of Federal Regulations
CI	confidence interval
CIOMS	Council for International Organizations of Medical Sciences
CK	Creatinine Kinase
CL	Chloride
CL/F	Clearance of drug from plasma
CK-MB	Creatinine Kinase MB enzyme
COVID-19	Corona Virus Disease 2019
CRF	case report form
CRO	Clinical Research Organization
CSM	core set measure
CSR	clinical study report
C-SSRS	Columbia-Suicide Severity Rating Scale
CT	clinical trial
CV	cardiovascular
CYP	cytochrome P450 enzymes
DDI	drug-drug interaction
DILI	drug-induced liver injury
DLQI	Dermatology and Life Quality Index
DM	dermatomyositis

Abbreviation	Term
DMARDs	disease-modifying antirheumatic drugs
DMC	Data monitoring committee
DNA	deoxyribonucleic acid
EC	ethics committee
ECC	Emergency contact card
ECG	electrocardiogram
EDB	Exposure during breastfeeding
EDP	exposure during pregnancy
eGFR	Estimated glomerular filtration rate
EMA	European medicines agency
EOS	end of study
ePPND	enhanced pre and postnatal development
EQ-5D-5L & EQ-VAS	European Quality of Life, 5 Dimension, 5 Level Scale and Visual Analogue Scale
EU	European Union
ET	early termination
EudraCT	European Union Drug Regulating Authorities Clinical Trials Database
FAS	Full analysis set
FDA	Food and Drug Administration
FIH	first in human
FSH	follicle-stimulating hormone
GCP	Good Clinical Practice
GGT	gamma-glutamyl transferase
GLP	good laboratory practice
HAQ-DI	Health Assessment Questionnaire and Disease Index
HEENT	head, eyes, ears, nose and throat
HR	heart rate
HRT	Hormone replacement therapy
hsCRP	high-sensitivity C-reactive protein
HTA	Health technology assessment
IA	Interim Analyses
IB	Investigator's Brochure
ICD	informed consent document
ICH	International Conference on Harmonisation
ID	identification
IFN β	interferon beta
IFNAR	interferon-α/β receptor
Ig	immunoglobulin
IgG1	immunoglobulin G1
IL-6	interleukin 6
IM	intramuscular

Abbreviation	Term
IMACS	International Myositis Assessment & Clinical Studies
IMP	investigational medicinal product
IND	investigational new drug application
INF	interferon
INR	international normalized ratio
IP	investigational product
IPAL	Investigational product accountability log
IRB	institutional review board
IRT	interactive response technology
ISR	injection site reaction
IV	intravenous
IVIG	intravenous immunoglobulin
JAK	Janus kinase
LANCOVA	longitudinal analysis of covariance
LDH	lactate dehydrogenase
LFT	liver function test
LSLV	last subject last visit
MAD	multiple ascending dose
MCS	multiple chemical sensitivity
MDAAT	Myositis Disease Activity Assessment Tool
MDI	Muscle Disease Index
MMF	Mycophenolate mofetil
MMT-8	Manual Muscle Testing-8 designated muscle groups
6-MP	Mercaptopurine
MTX	Methotrexate
N/A	not applicable
NAb	neutralizing anti-body
NIMP	Non investigational medicinal products
NSAID	Non-steroidal anti-inflammatory drugs
PCS	physical component scores
PD	Pharmacodynamics
PE	physical examination
PhGA	physician global assessment
PI	principal investigator
PK	pharmacokinetics
PR interval	period, in milliseconds, that extends from beginning of P wave until beginning of QRS complex
PRO	patient reported outcome
PT	prothrombin time
PtGA	Patient global assessment
PTT	partial thromboplastin time
PVC	Premature ventricular contractions

Abbreviation	Term
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
QTcF	QT interval calculated by Fridericia's formula
Q4W	every 4 weeks
R_{ac}	Accumulation ratio
RBC	Red blood cell
RNA	ribonucleic acid
SAD	single ascending dose
SAE	serious adverse event
SAP	statistical analysis plan
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SC	subcutaneous
SCr	Serum Creatinine
SF-36	The Short Form (36) Health Survey
SoA	schedule of assessments
SLE	systemic lupus erythematous
SOC	system organ class
SOP	standard operating procedure
SRSD	single reference safety document
SUSARs	Suspected Unexpected Serious Adverse Reaction
T_{max}	time drug is present at maximum concentration in serum
TBili	total bilirubin
TEAE	treatment-emergent adverse event
TIS	Total Improvement Score
TNF	tumor necrosis factor
$T_{1/2}$	half-life
ULN	upper limit of normal
Upr:Ucr	Urine protein: Urine creatinine
US	United States
VAS	visual analog scale
V_{ss}	volume at steady state
V_z/F	volume of distribution at pseudo-distribution equilibrium/fraction absorbed
WBC	white blood cell
WOCBP	women of child bearing potential

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