Protocol C0251013

A PHASE 2, DOUBLE-BLIND, RANDOMIZED, PLACEBO-CONTROLLED, MULTICENTER STUDY TO EVALUATE THE CLINICAL EFFECT, PHARMACODYNAMIC, PHARMACOKINETIC AND SAFETY PROFILE OF PF-06823859 IN ADULT PARTICIPANTS WITH ACTIVE CLE OR SLE WITH CUTANEOUS MANIFESTATIONS

Statistical Analysis Plan
(SAP)

Version: **3**

Date: November 25, 2025

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1. VERSION HISTORY

Table 1. Summary of Changes

Version Date	Associated Protocol Amendment	Rationale	Specific Changes
Version 1 June 23, 2023	Original Mar 29, 2023	*NA*	*NA*
Version 2 July 30, 2025	Amendment 2 Oct 26, 2023	Early termination of the study based on business decision	For the primary endpoint of change from baseline of type 1 IFN GS score at Week 12, treatment comparison with formal hypothesis testing will be conducted based on primary analysis set only. For all the other efficacy endpoints (continuous or binary), only descriptive analysis will be generated. For all efficacy endpoints, results will be summarized based on study treatment received instead of randomized. There will not be subset analysis for the subpopulation of participants entering the study with a diagnosis of SLE as there is only one participant of SLE The 3-tier approach for safety analysis will not be conducted. Editorial changes for better clarity are made throughout the document.
Version 3 Nov 25, 2025	Amendment 2 Oct 26, 2023	Replace PF-06823859 with its generic name Dazukibart for planned analysis as generic name is preferred in	Section 5.2: In the tables, listings and figures, the generic name of PF-06823859 known as Dazukibart will be used as its treatment label.

Table 1. Summary of Changes

Version Date	Associated Protocol Amendment	Rationale	Specific Changes
		reporting of study results	
Version 3 Nov 25, 2025	Amendment 2 Oct 26, 2023	Revise planned analysis by randomized treatment group (2G) and treatment sequence (3G) to enhance clarity in data summarization and review ability considering the small number of participants.	Section 5 & 6: update planned analysis by randomized treatment group (2G) and treatment sequence (3G). Section 9.1: update definition of visit window for Week 16
Version 3 Nov 25, 2025	Amendment 2 Oct 26, 2023	Add a data listing for joint assessment as the data are collected for SLE participants	Section 6.4: specify the data listing for joint assessment for the one participant with SLE
Version 3 Nov 25, 2025	Amendment 2 Oct 26, 2023	Specify categories of medications to be summarized for prior and concomitant medication	Section 6.5: list the categories of medications to be summarized for prior and concomitant medication
Version 3 Nov 25, 2025	Amendment 2 Oct 26, 2023	Remove time to analysis for immunogenicity assessment due to small number of participants	Section 6.6.6: remove the analysis for time to first ADA and NAb post baseline.
Version 3 Nov 25, 2025	Amendment 2 Oct 26, 2023	Describe planned analysis for immune-based treatment emergent adverse events	Section 6.6.6: specify the determination of immune-based treatment emergent adverse events and a data listing to be produced with occurrence of the events.

Table 1. Summary of Changes

Version Date	Associated Protocol Amendment	Rationale	Specific Changes
Version 3 Nov 25, 2025	Amendment 2 Oct 26, 2023	PK parameters will not be calculated as non-compartmental analysis will not be performed for the study.	Section 6.7: remove data summary for PK parameters
Version 3 Nov 25, 2025	Amendment 2 Oct 26, 2023	Specify planned analysis for biomarker results	Section 6.8: specify the biomarkers to be summarized and presented in data listings only.
Version 3 Nov 25, 2025	Amendment 2 Oct 26, 2023	Enhance clarity of the document	Editorial changes for better clarity are made throughout the document.

2. INTRODUCTION

This statistical analysis plan (SAP) provides the detailed methodology for summary and statistical analyses of the data collected in Study C0251013.

2.1. Modifications to the Analysis Plan Described in the Protocol

The study was decided to be early terminated in June 2025 based on a business decision and not due to any safety concerns of PF-06823859 (dazukibart) or requests from regulatory authorities.

At the time of study termination, only 8 (16.7%) of the planned 48 participants enrolled in the study with one participant of SLE. The planned statistical analyses based on collected data of the study are modified as follows:

- For the primary endpoint of change from baseline of type 1 IFN GS score at Week 12, treatment comparison with formal hypothesis testing will be conducted based on primary analysis set (PAS) only defined in Table 3.
- For all the other efficacy endpoints (continuous or binary), only descriptive analysis will be generated.
- For all efficacy endpoints, results will be summarized based on study treatment received instead of randomized.

- There will not be subset analysis for the subpopulation of participants entering the study with a diagnosis of SLE as there is only one participant of SLE.
- The 3-tier approach for safety analysis will not be conducted.

2.2. Study Objectives, Endpoints, and Estimands

The definition of an estimand includes the following five components.

1. The treatment condition of interest and the alternative treatment condition to which comparison will be made.
2. The population, that is, the participants targeted by the scientific question.
3. The variable (or endpoint) to be obtained for each participant that is required to address the scientific question.
4. The specification of the intercurrent events of interest and how to account for these intercurrent events to reflect the scientific question of interest. The identification of the intercurrent events is completed before the data unblinding.
5. The population-level summary for the variable that provides, as required, a basis for a comparison between treatment conditions.

The study design is discussed in Section 2.3. The active and placebo treatments will be administered in eligible participants with permitted background treatments.

For both efficacy and safety analyses, participants are to be analyzed according to the treatment that they received (see Section 4 for the discussion of the corresponding datasets).

The population targeted by scientific question is the population of study participants defined by the inclusion and exclusion criteria. In addition to these criteria that define subject's inclusion into the study an additional requirement is added for some analyses (see Section 4). For example, subjects who were randomized but were not exposed to at least 1 dose of the study intervention are excluded from the populations of interest and analyses sets.

Table 2. Objectives, Endpoints, Estimands and Descriptive Statistics

Type	**Objective**	**Endpoint**	**Key Estimand, [Supportive Estimand] and Descriptive Statistics**
	Primary	**Primary**	**Primary**
Biomarker	To evaluate the effect of PF-06823859 on the	Change from baseline in type 1 IFN GS score in	The estimand will be the mean difference between the

Table 2. Objectives, Endpoints, Estimands and Descriptive Statistics

Type	Objective	Endpoint	Key Estimand, [Supportive Estimand] and Descriptive Statistics
(Section 3.1)	type 1 IFN GS score at Week 12 in participants with CLE or SLE with cutaneous manifestations	lesional skin at Week 12	PF-06823859 treatment and placebo groups at Week 12 in participants as defined by the inclusion and exclusion criteria in the primary analysis set. A hypothetical strategy will be used for the estimand.
	Key Secondary	**Key Secondary**	**Key Secondary**
Efficacy (Section 3.2)	To evaluate the effect of PF-06823859 on the CLASI-A score at Week 12 in participants with CLE or SLE with cutaneous manifestations	Percent change from baseline in CLASI-A score at Week 12	A descriptive analysis of the endpoint will be used for the estimand.
	Other Secondary	**Other Secondary**	**Other Secondary**
Efficacy (Section 3.2)	To evaluate the effect of PF-06823859 on the additional measures of CLASI-A score at Week 12 and over time in participants with CLE or SLE with cutaneous manifestations	Percent change from baseline in CLASI-A (over time). The percent change at Week 12 is categorized as the key secondary endpoint Change from baseline in	A descriptive analysis of each endpoint will be used for the estimand.

Table 2. Objectives, Endpoints, Estimands and Descriptive Statistics

Type	Objective	Endpoint	Key Estimand, [Supportive Estimand] and Descriptive Statistics
		CLASI-A (over time) Achieving ≥50 % points reduction in CLASI-A (over time) Achieving 4 points reduction in CLASI-A (over time) Achieving 7 points reduction in CLASI-A (over time)	
Efficacy (Section 3.3)	To evaluate the effect of PF-06823859 on the PhGA in participants with CLE or SLE with cutaneous manifestations	Change from baseline in PhGA (over time)	A descriptive analysis of the endpoint will be used for the estimand.
Safety (Section 3.5)	To evaluate the safety and tolerability of PF-06823859 in participants with CLE or SLE with cutaneous manifestations	Incidence and severity of laboratory, vital signs, 12-lead ECG abnormalities, AEs, SAEs, and withdrawals due to AEs over time	A descriptive analysis of each endpoint will be used for the estimand.
	Exploratory	**Exploratory**	**Exploratory**
Biomarker (Section 3.7)	To evaluate changes in molecular biomarkers from skin, blood, and saliva in response to	Change over time in molecular biomarkers. The biomarkers of interest include total	A descriptive analysis of each endpoint will be used for the estimand.

Table 2. Objectives, Endpoints, Estimands and Descriptive Statistics

Type	Objective	Endpoint	Key Estimand, [Supportive Estimand] and Descriptive Statistics
	PF-06823859 and change following treatment in participants with CLE or SLE with cutaneous manifestations To evaluate the effect of PF-06823859 on the type 1 IFN GS score in lesional skin at week 32 in participants with CLE or SLE with cutaneous manifestations	CCI Change from baseline in type 1 IFN GS score in lesional skin at Week 32 as available)	A descriptive analysis of each endpoint will be used for the estimand.
Pharmacokinetics (Section 3.6)	To characterize the PK of PF-06823859 in participants with CLE and SLE with cutaneous manifestations	PF-06823859 concentrations	A descriptive analysis of the endpoint will be used for the estimand.
Immunogenicity (Section 3.5.6)	To characterize the immunogenicity of PF-06823859 in participants with CLE and SLE with cutaneous manifestation during the study	Incidence of development of ADAs/NAb through the end of study visit	A descriptive analysis of the endpoint will be used for the estimand.
Efficacy (Section 3.3)	To evaluate the effect of PF-06823859 on SLE manifestations	Change from baseline in SLEDAI-2K score over time in the subpopulation	A data listing will be provided with only 1 participant of SLE

Table 2. Objectives, Endpoints, Estimands and Descriptive Statistics

Type	Objective	Endpoint	Key Estimand, [Supportive Estimand] and Descriptive Statistics
	of disease (SLEDAI-2K score) in the subset of participants with SLE	of participants entering the study with a diagnosis of SLE	

2.2.1. Primary Efficacy Estimand

For the primary endpoint of change from baseline in type 1 IFN gene signature (GS) score in lesional skin at Week 12, the estimated mean and least square mean from analysis of covariance (ANCOVA) and their respective 90% confidence intervals will be calculated for each treatment group. The estimand for the primary endpoint is as follows:

- **Treatment**: Treatment refers to study intervention plus background therapy received prior to inter-current events. For treatment comparison, the treatment groups will be labeled as PF-06823859 and Placebo.
- **Population**: Participants with either SLE with cutaneous manifestations or CLE having skin lesions classified as chronic cutaneous and/or subacute cutaneous lupus as defined by the inclusion and exclusion criteria
- **Variable**: Change from baseline to Week 12 in type 1 IFN GS score in lesional skin.
- **Intercurrent events**: Missing two consecutive doses of treatment or exposure to a new or protocol prohibited medication for the treatment of CLE or SLE. A hypothetical strategy approach to intercurrent events will exclude Week 12 observations collected after an intercurrent event.
- **Population-level summary**: Difference of variable means between active (PF-06823859) and placebo treatment groups.

2.2.2. Secondary Efficacy Estimands

A descriptive analysis of each endpoint will be used for the estimand.

2.2.3. Additional Efficacy Estimands and Safety Estimand

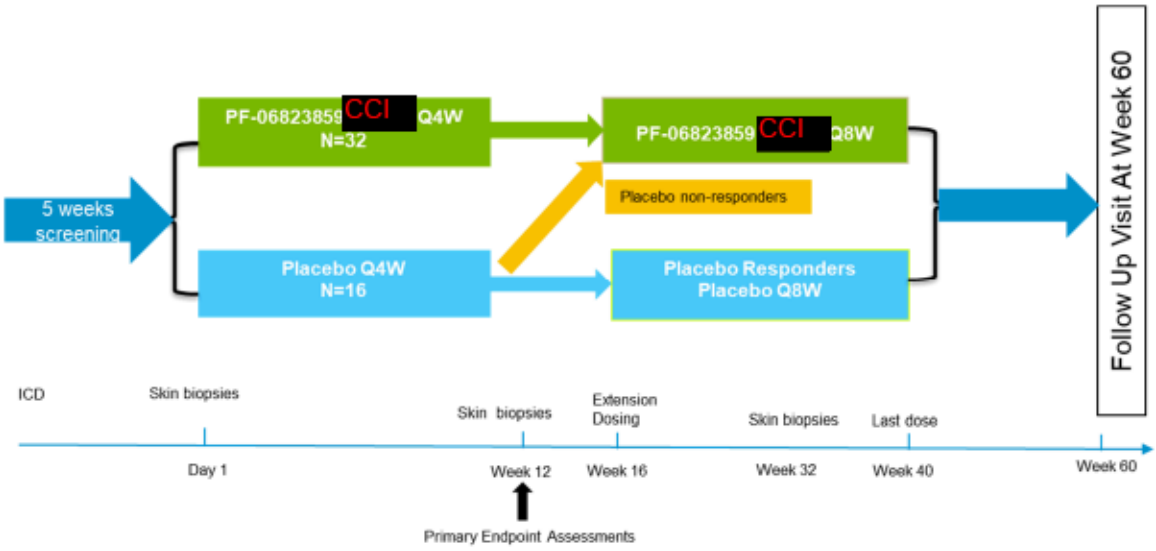
A descriptive analysis of each endpoint will be used for the estimand.

2.3. Study Design

This is a Phase 2, double-blind, randomized, placebo-controlled, multicenter study to evaluate the clinical effect, PD, PK, and safety profile of PF-06823859 in adult participants with active CLE or SLE with cutaneous manifestations. Approximately 48 participants will be enrolled in the study.

The study duration will be approximately 65 weeks. This includes up to a 5-week screening period, a 12-week Q4W treatment period, a 36-week Q8W treatment period, and a 12-week follow-up period. After up to a 5-week screening period, eligible participants will be randomized in a 2:1 ratio to receive either PF-06823859 CCI or placebo Q4W dosing on Day 1, Week 4 and Week 8 in addition to protocol permitted SOC treatment. Following assessments for the primary endpoint at Week 12, participants who are receiving active PF-06823859 or who are placebo non-responders (responder is defined by ≥4-point reduction from the baseline in CLASI-A score) will receive PF-06823859 CCI Q8W beginning at Week 16, while placebo responders will continue to be treated by the placebo treatment. The last dose of study intervention will be administered at Week 40 followed by last full study assessments at Week 48. The follow up visit will be conducted at Week 60. Two interim analyses (IA) may be performed. A brief discussion of the interim analyses is presented in the Section 7. The schema of the study design is shown in Figure 1.

Figure 1. Study Design



The study was decided to be early terminated in June 2025 based on a business decision and not due to any safety concerns with PF-06823859 or requests from regulatory authorities. There were 8 participants enrolled in the study including one participant of SLE.

3. ENDPOINTS AND BASELINE VARIABLES: DEFINITIONS AND CONVENTIONS

The evaluation of the treatment efficacy is based on the measurements of type 1 IFN gene signature (GS) score, Cutaneous Lupus Erythematosus Disease Area and Severity Index Activity Score (CLASI-A), Physician Global Assessment Score (PhGA), and Systemic

Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K) score for subjects with the SLE. For each of these scores the high value of the score is associated with the worse disease activity and effective treatment is expected to produce a noticeable decrease of the mean value of the score.

- A value of the gene signature score $GS_{ij}(t)$ of subject i in the treatment group j at time t is calculated as the average value of gene-specific gene values of $log_2\left(CPM_{ijk}(t)\right)$ for k=1,…, K pre-specified genes

$$GS_{ij}(t) = \frac{1}{K}\sum_{k=1}^{K} log_2\left(CPM_{ijk}(t)\right)$$

Here the $CPM_{ijk}(t)$ is the count per million of the mRNA mapped to the gene k. The detailed description of the procedure of measuring the CPM values for an individual gene and list of genes will be included into the calculation of the gene signature score that is described in the additional document (RNA-sequencing Bioanalytical Plan for C0251013).

Chang from baseline GS is calculated as GS(t) – GS(0), where GS(t) is the gene signature score at week 12 and GS(0) is the gene signature score at baseline. Percent change from baseline (GS) is calculated as 100*(2^(GS(t) – GS(0)) - 1).

The Cutaneous Lupus Erythematosus Disease Area and Severity Index (CLASI) scores are defined by Albrecht et al (2005). The scores include the activity (CLASI-A) and damage (CLASI-D) scores. (CLASI-A) measures erythema and scaling or hypertrophy in thirteen skin regions; scores range from 0 to 70.

The Physician Global Assessment (PhGA) Score is assigned by physician as the number within the 0-10 (cm) range on visual assessment scale and provides a global characterization of disease.

The Systemic Lupus Erythematosus Disease Activity Index 2000 (SLEDAI-2K**)** is the is a global index that evaluates the SLE disease activity. scores range from 0 to 105, based on the presence or absence of twenty-four symptoms. The description of the score is presented by Gladman et al (2020).

3.1. Primary Efficacy Endpoint

The primary efficacy endpoint is defined as a change from baseline in type 1 IFN gene signature (GS) score in lesional skin at Week 12.

3.2. Secondary Efficacy Endpoints

The secondary efficacy endpoints are based on the measurements of Cutaneous Lupus Erythematosus Disease Area and Severity Index Activity Score (CLASI-A) and Physician Global Assessment Score (PhGA). The key secondary efficacy point is the percent change from baseline in CLASI-A score at Week 12.

The continuous secondary efficacy endpoints based on CLASI-A include percent change from baseline in CLASI-A (over time in addition to Week 12) and change from baseline in CLASI-A over time. The binary secondary efficacy endpoints based on CLASI-A include achieving ≥ 50%, 4 or 7 points reduction in CLASI-A (explored over time).

The additional continuous secondary efficacy endpoint is the change from baseline in PhGA over time.

3.3. Other Efficacy Endpoint

Change from baseline over time in SLEDAI-2K will be calculated and listed for the one participant of SLE.

Joint assessment was performed for SLE. As there is only one participant of SLE, results from joint assessment on this participant will be presented in a data listing.

Percent change from baseline in GS will be calculated as shown above.

3.4. Baseline Variables

Demographics, medical history, and prior medications will be collected at screening visit. Baseline value of other outcomes is defined as pre-dose value collected on Day 1. Data from the screening period will be used if Day 1 data are missing. If multiple data points are available, the closest observation on or prior to Day 1 will be used.

3.5. Safety Endpoints

3.5.1. Adverse Events

An AE is considered a treatment emergent adverse event (TEAE) if the event starts during or after the first dosing and within 20 weeks of the last dosing day of the study treatment.

Per the protocol, the investigator will make an assessment of intensity for each AE and SAE reported during the study using NCI-CTCAE.

3.5.2. Laboratory Data

The laboratory tests will be performed at time points identified in the Schedule of Activities. Unscheduled clinical labs may be obtained at any time during the study to assess any perceived safety concerns at the investigator's discretion or Sponsor's request.

3.5.3. Vital Signs

Vital signs (blood pressure, pulse, pulse oximeter) will be measured as indicated in the Schedule of Activities of the protocol.

3.5.4. Electrocardiograms

Standard 12-lead ECGs will be collected at times specified in the Schedule of Activities of the protocol.

3.5.5. Physical Examination

Physical examinations will be performed at times specified in the Schedule of Activities of the protocol.

3.5.6. Immunogenicity Assessments

Immunogenicity assessments should be done at times specified in the Schedule of Activities of the protocol. Samples determined to be positive for ADA will be further characterized for NAb.

3.6. Pharmacokinetic Endpoints

Pharmacokinetic sampling will be collected at times specified in the Schedule of Activities of the protocol

3.7. Pharmacodynamic, Pharmacogenomic or Biomarker Endpoint

Pharmacodynamic, pharmacogenomic or biomarker sampling will be collected at times specified in the Schedule of Activities of the protocol.

4. ANALYSIS SETS (POPULATIONS FOR ANALYSIS)

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

Table 3. Analysis Sets

Analysis Set/ Population	Description	Applicable Analyses
Primary Analysis Set (PAS)	Participants will be analyzed according to the study treatment they actually received. Excludes participants with missing two consecutive doses of treatment or exposure to a new or protocol prohibited medication for the treatment of CLE or SLE by Week 12*.	Primary endpoint
Full Analysis Set (FAS)	Includes data collected during the study. Observations for participants randomly assigned to study intervention who take at least 1 dose of study intervention. Participants will be analyzed according	Secondary and exploratory efficacy endpoints.

Table 3. Analysis Sets

Analysis Set/ Population	Description	Applicable Analyses
	to the study treatment they actually received.	
Safety analysis set (SAS)	Observations for participants randomly assigned to study intervention who take at least 1 dose of study intervention. Participants will be analyzed according to the study treatment they received.	Safety analyses
PK concentration set (PK)	All participants randomly assigned to study intervention and who take at least 1 dose of PF-06823859 and have at least 1 measurable concentration.	Analysis of PF-06823859 concentrations
PD data set (PD)	Observations for participants randomly assigned to study intervention and who take at least 1 dose of study intervention and have at least 1 of PD parameters of interest. Participants will be analyzed according to the study treatment they received.	Analyses of laboratory data

*Prohibited medications include a protocol prohibited dose of corticosteroids, immunosuppressants, colchicine, retinoids, dapsone, or biologics.

5. GENERAL METHODOLOGY AND CONVENTIONS

Final analyses will occur after database lock after Last Participant Last Visit (LPLV).

5.1. Hypotheses and Decision Rules

The null hypothesis for the primary endpoint is that the efficacy in the active (PF-06823859) treatment arm is not superior to the efficacy of placebo treatment. The null hypothesis needs to be rejected at the one-sided significance level of 0.05 for the declaration of the superior efficacy of the active treatment arm.

5.2. General Methods

In the tables, listings and figures, the generic name of PF-06823859 known as Dazukibart will be used as its treatment label. The cross-over of the non-responders in the placebo treatment group (at the Week 12 visit) to the active treatment group occurs at the Week 16 visit. Summary tables at baseline, by study visits and without study visits will be displayed as follows.

- Summary tables at baseline: 2 sets of tables
  - Set 1 (2G) per initially received study treatment: Dazukibart [CCI], Placebo
  - Set 2 (3G) per treatment sequence: Dazukibart [CCI] in Q4W and Q8W, Placebo in Q4W and Q8W, Placebo in Q4W and Dazukibart [CCI] in Q8W

  The above 2 sets of tables will also be used for summarizing number and participants of participants in each analysis set defined in Section 4.

- Summary tables by study visits: 2 sets of tables
  - Set 1 (2G): visits include baseline and each post baseline visit up to and include Week 16 (on or prior to Week 16 dosing date)
  - Set 2 (3G): visits include baseline and each post baseline visit, including results from follow-up

- Summary tables without study visits (excluding tables with baseline results only): 1 set by treatment sequence (3G) as the follows

Placebo in Q4W and Q8W			Placebo in Q4W and Dazukibart [CCI] in Q8W		Dazukibart [CCI] in Q4W and Q8W		
Q4W	Q8W	Total	Q4W	Q8W	Q4W	Q8W	Total

Q4W: includes results during Q4W treatment period and prior to Week 16 study treatment dosing.
Q8W: includes results during Q8W treatment period and post Week 16 study treatment dosing, including results from follow-up

5.2.1. Analyses for Continuous Efficacy Endpoints

For the primary endpoint of change from baseline in type 1 IFN gene signature (GS) score in lesional skin at Week 12, the estimated mean and least square mean from ANCOVA and their respective 90% confidence intervals will be calculated for each treatment group. Treatment comparison will be conducted based on the estimand described in Section 2.2.1 using ANCOVA with baseline GS score as the covariate. For treatment comparison, the estimated least square mean difference, its 90% confidence interval and p-value will be calculated.

The data for all continuous endpoints will be summarized by treatment group and by time point in tables containing descriptive statistics (N [which is the number of participants evaluable for the endpoint at the time point], arithmetic mean or geometric mean, standard deviation, coefficient of variation [CV], minimum, median and maximum) for actual and change from baseline (or percent change from baseline) values for those endpoints measured at baseline. For change or percent change from baseline, 90% confidence interval of the estimated mean value will also be calculated. In case when N=1 (i.e., only one participant is available/evaluable for summary), standard deviation and 90% confidence interval will be reported as "NA" (not applicable).

5.2.2. Analyses for Binary Efficacy Endpoints

The data for all response-type endpoints will be summarized by treatment group and by time point in tables showing descriptive statistics: N, n (i.e., number of responders), response rate (%) and 90% confidence interval of the response rate based on the exact (Clopper-Pearson) method.

5.2.3. Analyses for Categorical Endpoints

Not applicable

5.2.4. Analyses for Time-to-Event Endpoints

Not applicable.

5.3. Methods to Manage Missing Data

No imputation of missing data will be implemented.

6. ANALYSES AND SUMMARIES

6.1. Primary Efficacy Endpoint(s)

The primary (efficacy) endpoint is the change from baseline in type 1 IFN GS score in lesional skin at Week 12. The planned analyses will use the GS dataset from third GS data transfer (RNA-sequencing bioanalytical plan, section 3.4.2). For the primary endpoint, the estimated mean and least square mean from analysis of covariance (ANCOVA) and their respective 90% confidence intervals will be calculated for each treatment group. Treatment comparison will be conducted based on the estimand described in Section 2.2.1 using ANCOVA with baseline GS score as the covariate. For treatment comparison, the estimated least square mean difference, its 90% confidence interval and p-value will be calculated.

6.2. Key Secondary Efficacy Endpoint

The key secondary endpoint is the percent change from baseline in CLASI-A score at Week 12. A descriptive analysis will be conducted.

6.3. Secondary Efficacy Endpoint(s)

The secondary efficacy endpoints are listed in the Section 3.2. A descriptive analysis will be conducted for each endpoint.

6.4. Other Endpoint(s)

Descriptive analyses will be implemented for the change from baseline for the other biomarker and efficacy outcomes of interest as shown in the Table 2. Change from baseline over time in SLEDAI-2K will be calculated and listed for the one participant of SLE.

In addition, joint assessment is performed for SLE. As there is only one participant of SLE, results of joint assessment on this participant will be presented in a data listing. In the listing, number of swollen joints, number of tender joints, and number of both swollen and tender joints will be presented.

The percent change from baseline in GS will be calculated using the formula described in Section 3, and its 90% confidence interval will be calculated using the formula below:

- Lower limit of confidence interval of percent change from baseline in GS=100*(2^(lower limit of change from baseline in GS) - 1)
- Upper limit of confidence interval of percent change from baseline in GS=100*(2^(upper limit of change from baseline in GS) - 1)

6.5. Baseline and Other Summaries and Analyses

6.5.1. Baseline Summaries

Baseline characteristics will include but may not be limited to the ones listed below and will be summarized descriptively by treatment group for 2G and 3G analyses as described in Section 5.2. For summary tables by 2G, a total column will also be displayed.

Standard summaries for baseline distributions will be created for the following characteristics of participants.

- Demographics: age, gender, race, and ethnic group

- Baseline characteristics of disease: CLASI-A score, proportions of subjects with CLASI-A score > 10, proportions of subjects with different types of CLE (e.g., subacute, and chronic types), proportions of subjects with SLE, SLEDAI-2K (for the participants with SLE).

- Medications ongoing during screening period and continued into the study: proportions of participants received

  - antimalarials
  - systemic immunosuppressants
  - topical immunosuppressants
  - biologics
  - systemic corticosteroids
  - topical corticosteroids
  - >=2 of the above agents

6.5.2. Study Conduct and Participant Disposition

Participants disposition and discontinuation will be summarized by treatment sequence as described in Section 5.2 for summary tables without study visits (excluding tables with baseline results only) according to Pfizer standards.

6.5.3. Study Treatment Exposure

A summary of number of doses received, dose missed, and exposure to study treatment (last dose date – first dose date +1) and number of days on study (study completion/discontinuation date – first dose date +1) will be tabulated by treatment sequence as described in Section 5.2 for summary tables without study visits (excluding tables with baseline results only).

6.5.4. Concomitant Medications and Nondrug Treatments

Prior medications are the ones started prior to Day 1. Concomitant treatments are those treatments that are taken on Day 1 or after. If a drug is started prior to Day 1 and is continued during the study, it will also be considered a concomitant medication. Prior medications, concomitant treatments, concomitant treatments for CLE/SLE, and nondrug treatment will be summarized by treatment sequence as described in Section 5.2 for summary tables without study visits (excluding tables with baseline results only)according to Pfizer standards.

For concomitant treatments, a summary table will also be provided with proportion of participants taking the following medications by treatment sequence as described in Section 5.2 for summary tables without study visits (excluding tables with baseline results only).

- antimalarials
- systemic immunosuppressants
- topical immunosuppressants
- biologics
- systemic corticosteroids
- topical corticosteroids

6.6. Safety Summaries and Analyses

All safety analyses will be performed on the safety population. The safety data will be summarized as described in Section 5.2 in accordance with Pfizer Standards.

6.6.1. Adverse Events

Standard adverse events (AE) summaries will be created for treatment-emergent all causality and treatment-emergent study treatment-related AEs. A treatment-emergent AE (TEAE) is an event that starts during or after the first dosing and ends within 20 weeks of last study treatment day. The relationship to study treatment is assessed by the investigator. Treatment-emergent AEs (all causality, study treatment-related, serious adverse events, discontinuation due to AEs) will be summarized by treatment sequence as described in Section 5.2 for summary tables without study visits (excluding tables with baseline results only). If an

TEAE occurred during Q4W and continued into Q8W, it will be counted under Q4W. A data listing of TEAE occurred during Q4W and continued into Q8W will be created.

A separate listing of the events that start prior to the date of the first dose will be created.

6.6.2. Laboratory Data

Laboratory data will be listed and summarized as described in Section 5.2 in accordance with the Pfizer standards. Summaries of incidence of clinically significant abnormalities will include frequency and percentages. Laboratory data criteria for safety monitoring and discontinuation of study intervention can be found in Appendix 10 of the protocol. A data listing will be provided for participants meeting retest and discontinuation criteria.

6.6.3. Vital Signs

Vital signs will be summarized at baseline and all post-baseline visits as described for summary tables by study visits in Section 5.2. The data will be listed and summarized in accordance with the Pfizer standards. Summaries of incidence of clinically significant abnormalities (e.g., pulse rate <40, >100 bpm; systolic blood pressure increase from baseline ≥30 or decrease ≤30 mmHg; diastolic blood pressure increase from baseline ≥20 or decrease ≤20 mmHg) will include frequency and percentages and displayed as described for summary tables without study visits (excluding tables with baseline results only) in Section 5.2.

6.6.4. Electrocardiograms

The ECG values at Screening will serve as each participant's baseline values. Data from local ECG readings will be used for statistical analyses.

Changes from baseline for the ECG parameters, HR, QTcF, PR interval, and QRS complex will be summarized over time as described for summary tables by study visits in Section 5.2. The number (%) of participants with uncorrected QT values above 500 ms will be tabulated by treatment sequence as described for summary tables without study visits (excluding tables with baseline results only) in Section 5.2.

The number (%) of participants with maximum post dose QTcF values and maximum increases from baseline in the following categories will be tabulated by treatment sequence as described for summary tables without study visits (excluding tables with baseline results only) in Section 5.2.

Table 4. Safety QTcF Assessment

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

6.6.5. Physical Examination

Physical examinations will be summarized at baseline and all-available post-baseline visits as described for summary tables by study visits in Section 5.2.

6.6.6. Immunogenicity Assessments

The ADA and NAbs for dazukibart will be summarized for the treatment group of dazukibart by study visits till Week 16, for treatment sequence of Dazukibart CCI in Q4W and Q8W by study visits, and for treatment sequence of Placebo in Q4W and Dazukibart CCI in Q8W at baseline and by study visit post Week 16 dosing.

Table may be produced summarizing the total number of samples analyzed for ADAs, NAbs, positive ADA at baseline, positive ADA Post Dose, positive NAb at Baseline and positive NAb Post Dose.

- The incidence, cumulative incidence (numbers and percentage) of participants deemed Post Dose positive for ADA and NAb will be summarized over time. A separate tabulation will be made for the numbers and percentages of participants with treatment induced and treatment boosted ADAs and NAbs.
- Number and percent of participants with positive ADA and NAbs number for each of the treatment groups (sequences) over time.
- Standard descriptive statistics for the ADA titers.
- Listing of individual level ADA and NAb responses

A data listing will be provided for medically evaluated potential immune-related treatment emergent adverse events if any. Immune-based events will include clinically evaluated infusion related reaction, AEs under the Anaphylactic Reaction Standardized MedDRA Query (SMQ), Angioedema SMQ, and Hypersensitivity SMQ and clinically-evaluated potential cases of anaphylaxis based on the Sampson's Criteria.

Data permitting, the following analyses will be explored:

- Impact of ADA and NAb status on PF-06823859 concentrations
- Impact of ADA and NAb status on biomarker concentration
- Combined plot of PK, PD (total IFNb), ADA and NAb response over time
- Impact of ADA and NAb status on CLASI-A

6.7. Pharmacokinetic Analyses

Plasma PF-06823859 concentration data will be listed and summarized at each nominal time point for the treatment sequence of Dazukibart CCI in Q4W and Q8W, and Placebo in

Q4W and PF-0682385 in Q8W. The summary statistics will include number (%) of participants with PF-06823859 concentration above the lower limit of quantification (LLQ), mean, standard deviation, coefficient of variation (CV), geometric mean, median, minimum, and maximum. The summaries will be generated for all of the visits where the concentration is measured. Deviations from the nominal time will be given in a separate listing. Listings of the concentrations of PF-06823859 for the individual participants will also be produced.

The following figures for PF-06823859 concentration will be produced.

- Median concentrations time plots (on both linear and semi-log scales) against nominal time post-dose.
- Mean (SE) concentrations time plots (on both linear and semi-log scales) against nominal time post-dose.
- Individual concentration time plots by participant (on both linear and semi-log scales) against actual time post-dose (there will be separate plots for each participant per scale).

6.8. Pharmacodynamic, Pharmacogenomic or Biomarker Analyses

Absolute values, change from baseline and percent change from baseline in the values of selected biomarkers CCI [redacted] CCI [redacted], and autoantibody seropositivity status/titers in serum/plasma) will be summarized at all scheduled time points as described for summary tables by study visits in Section 5.2. The following plots may also be produced.

- Median biomarker concentrations time plots (on both linear and semi-log scales) against nominal time post-dose.
- Mean (SE) biomarker concentrations time plots (on both linear and semi-log scales) against nominal time post-dose.
- Individual biomarker concentration time plots by participant (on both linear and semi-log scales) against actual time post-dose (there will be separate plots for each participant per scale).

Individual listing of biomarker concentrations will be presented CCI [redacted] CCI [redacted]

Pharmacogenomic or biomarker data from Banked Biospecimens may be collected during or after the trial. Potential relationship between pre-treatment IFN status (IFN profiling at Screening) and treatment responses may be explored and reported separately. The analyses of those results are out of scope for this SAP and may be reported separately.

7. INTERIM ANALYSES

No interim analysis will be conducted.

8. REFERENCES

1. Albrecht J, Taylor L, Berlin JA, et al. The CLASI (Cutaneous LE Disease Area and Severity Index): an outcome instrument for cutaneous lupus erythematosus. (2005). J Invest Dermatol, 125(5): 889-894.

2. Gladman DD, Ibañez D, Urowitz MB. Systemic lupus erythematosus disease activity index 2000 (2002). J Rheumatol. 29(2):288-91.

9. APPENDICES

9.1. Definition and Use of Visit Windows in Reporting

Visit windows will be used for efficacy variables, and for any safety data that display/summarize by study visit. For other endpoints (e.g., vital signs, physical examinations), visit windows will be applied for summary statistics by study visits if required.

A visit window will be assigned to an observation based on the table below. Baseline is defined as pre-dose on Day 1. Data from the screening period may be used if Day 1 data are missing. If multiple data points are available, the closest observation on or prior to Day 1 will be used. If more than one observation falls within the same visit window, the observation that is closest to the target day will be retained; if there are 2 observations with equal distance to the target day, then the later one will be retained. For endpoints with scheduled visits not included in the table below, the visit windows will be specified in the statistical analysis programming plan.

Definition of Visit Windows

Visit Label	Target Day	Definition [Day window]
Screening		Prior to Day 1
Baseline	1	Day 1
Week 4	29	Days 2 to 42
Week 8	57	Days 43 to 70
Week 12	85	Days 71 to 98
Week 16	113	Days 99 to Week 16 study treatment dosing date for analysis by the 2 randomized study treatment groups Days 99 to 126 for analysis by the 3 treatment sequences
Week 20	141	Days 127 to 154
Week 24	169	Days 155 to 182

Definition of Visit Windows

Visit Label	Target Day	Definition [Day window]
Week 28	197	Days 183 to 210
Week 32	225	Days 211 to 238
Week 36	253	Days 239 to 266
Week 40	281	Days 267 to 294
Week 44	309	Days 295 to 322
Week 48	337	Days 323 to 364
Week 56	393	Days 365 to 406
Week 60	421	Days 407 to -

CCI

[redacted]

9.3. List of Abbreviations

Abbreviation	Term
AE	Adverse event
ADA	Anti-drug antibody
ANCOVA	Analysis of covariance
CLASI-A	Cutaneous Lupus Erythematosus Disease Area and Severity Index Activity Score
CLE	Cutaneous Lupus Erythematosus
CV	Coefficient of variation
GS	Gene signature
ECG	Electrocardiogram
HR	Heart rate
IFN	Interferon
IS	Immunosuppressant
LPLV	Last Participant Last Visit
CCI	
NAb	Neutralizing antibody
PD	Pharmacodynamic(s)
PhGA	Physician global assessment
PK	Pharmacokinetic(s)
PR interval	The time from the beginning of the P wave (atrial depolarization) to the beginning of the QRS complex (ventricular depolarization) from ECG
Q4W	Every 4 weeks
Q8W	Every 8 weeks
QRS	Q-wave, R-wave, and S-wave from ECG
QT interval	The total time from the beginning of ventricular depolarization to the end of ventricular repolarization from ECG
QTc	Corrected QT
QTcF	Corrected QT (Fridericia method)
SAE	Serious adverse event
SAP	Statistical analysis plan
SLE	Systemic Lupus Erythematosus
SLEDAI-2K	Systemic Lupus Erythematosus Disease Activity Index 2000
TEAE	Treatment emergent AE effect
2G	Two groups classification of treatment groups
3G	Three groups (sequences) classification of treatment groups