# CLINICAL STUDY REPORT SYNOPSIS

**Sponsor:** Pfizer Inc

**Investigational Product:** PF-06826647

**Clinical Study Report Synopsis:** Protocol C2501004

**Protocol Title:** A Phase 2, Randomized, Double Blind, Placebo-Controlled, Study to Evaluate the Safety and Efficacy of PF-06826647 in Participants With Moderate to Severe Plaque Psoriasis

**Investigators:** Refer to Appendix 16.1.4.1 for a list of investigators involved in this study.

**Study Center(s):** This study was conducted at 36 centers (7 in Canada, 6 in Japan, 6 in Poland, and 17 in United States). Refer to Appendix 16.1.4.1 for a list of sites involved in this study.

**Publications Based on the Study:** None

**Study Initiation Date:** 27 June 2019

**Study Completion Date:** 26 November 2020 (primary completion date: 21 May 2020).

**Report Date:** 16 April 2021

**Previous Report Date(s):** Not Applicable

**Phase of Development:** Phase 2b

**Study Objectives and Endpoints:** The study objectives and endpoints are provided in Table S1 and Table S2 for the Investigational Treatment Period (up to Week 16) and the Extension Treatment Period (Week 16 to Week 40), respectively. The terms “participant” and “subject” are used interchangeably in this Synopsis.

## CLINICAL STUDY REPORT SYNOPSIS

### Table S1. Study Objectives and Endpoints for Investigational Treatment Period

| Type | Objective | Endpoint |
|---|---|---|
| **Primary** | | |
| Efficacy | To compare the efficacy of multiple dose levels of PF-06826647 versus placebo on the proportion of participants with moderate to severe plaque psoriasis achieving PASI 90. | • Proportion of participants achieving PASI 90 (90% or greater improvement from baseline) at Week 16. |
| **Secondary** | | |
| Efficacy | To compare the efficacy of multiple dose levels of PF-06826647 versus placebo on the proportion of participants with moderate to severe plaque psoriasis achieving PASI 75. | Key secondary endpoint:<br>• Proportion of participants achieving PASI 75 (75% or greater improvement from baseline) at time points specified in the SoA. |
| Efficacy | To compare the efficacy of multiple dose levels of PF-06826647 versus placebo on PGA score in participants with moderate to severe plaque psoriasis. | • Proportion of participants with PGA score clear (0) or almost clear (1) and ≥2 points improvement from baseline at time points specified in the SoA.<br>• Proportion of participants with PGA score clear (0) or almost clear (1) at time points specified in the SoA. |
| Efficacy | To compare the efficacy of multiple dose levels of PF-06826647 versus placebo on the proportion of participants with moderate to severe plaque psoriasis achieving PASI 50 and PASI 100. | • Proportion of participants achieving PASI 50 (50% or greater improvement from baseline), PASI 100 (100% from baseline) at time points specified in the SoA. |
| Efficacy | To compare the efficacy of multiple dose levels of PF-06826647 versus placebo on PASI scores in participants with moderate to severe plaque psoriasis. | • Change from baseline and percent change from baseline in PASI scores at time points specified in the SoA. |
| PRO | To compare the effect of multiple dose levels of PF-06826647 versus placebo in PP-NRS score in participants with moderate to severe plaque psoriasis. | • Change from baseline in PP-NRS score at time points specified in the SoA. |
| PRO | To compare the effect of multiple dose levels PF-06826647 versus placebo on measures of disease and symptom severity in participants with moderate to severe plaque psoriasis. | • Proportion of participants with PSI overall score ≤8 with 0 or 1 for every individual domain at time points specified in the SoA. |

## CLINICAL STUDY REPORT SYNOPSIS

### Table S1. Study Objectives and Endpoints for Investigational Treatment Period

| Type | Objective | Endpoint |
|---|---|---|
| Safety | To assess the safety and tolerability of PF-06826647 in participants with moderate to severe plaque psoriasis. | • Incidence and severity of AEs, SAEs and withdrawals due to AEs.<br>• Change from baseline in clinical laboratory values (chemistry, hematology and lipids).<br>• Incidence of clinically significant changes in ECG (heart rate, QT, QTc, PR and QRS intervals).<br>• Change from baseline in vital signs (blood pressure, pulse rate and temperature measurements). |
| PRO | To compare the efficacy of multiple dose levels PF-06826647 versus placebo on measures of disease and symptom severity in participants with moderate to severe plaque psoriasis. | • Change from baseline PSI at time points specified in the SoA. |
| **Exploratory** | | |
| Efficacy | To compare efficacy of multiple dose levels of PF-06826647 versus placebo in L-PASI and psoriatic BSA in participants with moderate to severe plaque psoriasis. | • Change from baseline in L-PASI score at time points specified in the SoA.<br>• Absolute and change from baseline in psoriatic BSA at time points specified in SoA. |
| PRO | To compare the effect of multiple dose levels of PF-06826647 versus placebo on selected PRO in participants with moderate to severe plaque psoriasis. | • Change from baseline in Night-time Itch scale at time points specified in the SoA.<br>• Change from baseline in dermatology-specific QoL as measured by the DLQI at time points specified in the SoA.<br>• Proportion of participants who achieved DLQI response of ≥4 improvement from baseline at time points specified in the SoA.<br>• Change from baseline in the generic QoL as measured by the SF-36v2 standard survey at time points specified in the SoA.<br>• Change from baseline in PtGA of Psoriasis at time points specified in the SoA.<br>• Proportion of participants who achieved PtGA response of clear (0) or almost clear (1) at time points specified in the SoA |
| PK | To evaluate PK of PF-06826647 in participants with moderate to severe plaque psoriasis. | • PF-06826647 concentrations at time points specified in the SoA. |
| PD | To compare the effect of multiple dose levels of PF-06826647 versus placebo on biomarkers in participants with moderate to severe plaque psoriasis. | • Change from baseline over time of lymphocyte subsets (TBNK) in peripheral blood.<br>• Change from baseline in hsCRP levels at time points specified in the SoA. |

# CLINICAL STUDY REPORT SYNOPSIS

## Table S1. Study Objectives and Endpoints for Investigational Treatment Period

| Type | Objective | Endpoint |
|---|---|---|
| Banked biospecimen | To enable exploratory research through collection of banked biospecimens, unless prohibited by local regulations or ethics committee decision. | • Potential results from exploratory analysis of banked biospecimens (these results may or may not be generated in the context of the present study). |

Abbreviations: AE = adverse event; BSA = Body Surface Area; DLQI = Dermatology Life Quality Index; ECG = electrocardiogram; hsCRP = high sensitivity C-reactive protein; L-PASI = linear method Psoriasis Area and Severity Index; PASI = Psoriasis Area and Severity Index; PASI 50 = at least 50% reduction from baseline in the PASI total score; PASI 75 = at least 75% reduction from baseline in the PASI total score; PASI 90 = at least 90% reduction from baseline in the PASI total score; PASI 100 = at least 100% reduction from baseline in the PASI total score; PD = pharmacodynamic(s); PGA = Physician's Global Assessment; PK = pharmacokinetic(s); PP-NRS = Peak-Pruritus Numerical Rating Scale; PRO = patient reported outcome; PSI = Psoriasis Symptom Inventory; PtGA = Patient Global Assessment; QoL = quality of life; QTc = QT interval corrected; SAE =serious adverse event; SF-36v2 = Short Form-36 Health survey Version 2; SoA = Schedule of Activities; TBNK = T cells, B cells and Natural Killer cells.

## Table S2. Study Objectives and Endpoints for Extension Treatment Period

| Type | Objective | Endpoint |
|---|---|---|
| **Primary** | | |
| Safety | To assess the safety and tolerability of PF-06826647 in participants with moderate to severe plaque psoriasis. | • Incidence and severity of AEs, SAEs and withdrawals due to AEs.<br>• Change from baseline in clinical laboratory values (chemistry, hematology and lipids).<br>• Incidence of clinically significant changes in ECG (heart rate, QT, QTc, PR and QRS intervals).<br>• Change from baseline in vital signs (blood pressure, pulse rate and temperature measurements). |

## CLINICAL STUDY REPORT SYNOPSIS

### Table S2. Study Objectives and Endpoints for Extension Treatment Period

| Type | Objective | Endpoint |
|---|---|---|
| **Exploratory** | | |
| Efficacy/PRO | To compare long-term efficacy and durability of multiple dose levels of PF-06826647 in participants with moderate to severe plaque psoriasis. | • Proportion of participants achieving PASI 50/75/90/100.<br>• Proportion of participants with PGA score clear (0) or almost clear (1) and ≥2 points improvement from baseline at time points specified in the SoA.<br>• Proportion of participants with PGA score clear (0) or almost clear (1) at time points specified in the SoA.<br>• The proportion of participants who achieved a PSI score of 0 (not at all) or 1 (mild) on every item at time points specified in the SoA.<br>• Change from baseline in PP-NRS score at time points specified in the SoA.<br>• Change from baseline and percent change from baseline in PASI scores at time points specified in the SoA.<br>• Change from baseline in L-PASI score at time points specified in the SoA.<br>• Absolute and change from baseline in psoriatic BSA at time points specified in SoA. |
| PK | To characterize PK of PF-06826647 dosing regimens in participants with moderate to severe plaque psoriasis. | • PF-06826647 concentrations and parameters (data permitting) obtained from blood samples at time points specified in the SoA. |

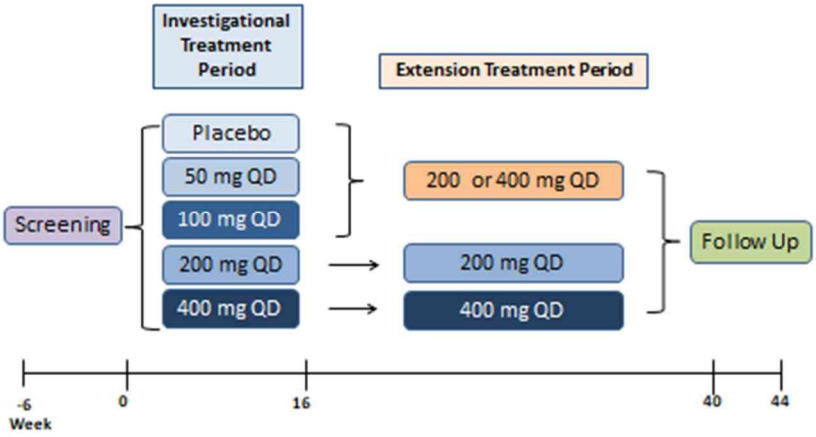
Abbreviations: AE = adverse event; BSA = Body Surface Area; ECG = electrocardiogram; L-PASI = linear method Psoriasis Area and Severity Index; PASI = Psoriasis Area and Severity Index; PASI 50 = at least 50% reduction from baseline in the PASI total score; PASI 75 = at least 75% reduction from baseline in the PASI total score; PASI 90 = at least 90% reduction from baseline in the PASI total score; PASI 100 = at least 100% reduction from baseline in the PASI total score; PGA = Physician's Global Assessment; PK = pharmacokinetic(s); PP-NRS = Peak-Pruritus Numerical Rating Scale; PRO = patient reported outcome; PSI = Psoriasis Symptom Inventory; QTc = QT interval corrected; SAE =serious adverse event.

## CLINICAL STUDY REPORT SYNOPSIS

## METHODS

**Study Design:** This was a Phase 2b, randomized, double-blind, placebo-controlled, parallel-group, and multicenter study in participants with moderate to severe plaque psoriasis. Placebo and 4 PF-06826647 daily oral dose levels (50 mg, 100 mg, 200 mg or 400 mg) were used in the study. The study schema is provided in Figure S1. Approximately 160 participants (40 participants in each of the following arms: placebo, 200 mg, and 400 mg; and 20 participants in each of the following arms: 50 mg and 100 mg) were randomly assigned to a treatment group in order to ensure a minimum of 128 evaluable participants completing Week 16 (assuming a 20% dropout rate).

**Figure S1. Study Schema**




Abbreviation: QD = once daily.

**Diagnosis and Main Criteria for Inclusion:** Male or female participants between the ages of 18 (or the minimum country-specific age of consent if >18) and 75 years, inclusive, at screening, and with body weight >40 kg, who had a diagnosis of plaque psoriasis (psoriasis vulgaris) for at least 6 months prior to baseline/Day 1, and had a Psoriasis Area and Severity Index (PASI) score ≥12, a Physician's Global Assessment (PGA) score of 3 (moderate) or 4 (severe) and a psoriatic Body Surface Area (BSA) ≥10% of total BSA at baseline/Day 1, were eligible for participating in the study.

**Study Treatment:** Blinded PF-06826647 and matching placebo were provided as tablets for oral administration (Table S3). PF-06826647 was provided in dosage strengths of 100 mg and 25 mg tablets. PF-06826647 and matching placebo were supplied in blister cards and labeled according to local regulatory requirements.

PF-06826647 and the placebo were administered once daily (QD) during the Investigational Treatment Period and the Extension Treatment Period. Participants swallowed the investigational product whole with ambient temperature water to a total volume of approximately 240 mL, and did not manipulate or chew the investigational product prior to

## CLINICAL STUDY REPORT SYNOPSIS

swallowing. It was recommended to be taken with food. Participants administered the investigational product as outpatients, except on study visit days. On study visit days, participants took their dose of study drug when instructed to do so by the investigator or designated study site staff while at the study site.

### Table S3. Investigational Product Description

| Investigational Product Description | Vendor Lot Number | Pfizer Lot Number | Strength/Potency | Dosage Form |
|---|---|---|---|---|
| Placebo oval tablet (2:1, MCC:lactose) | B16156 | 16-005224 | 0 mg | Tablet |
| PF-06826647 25 mg round white to off-white tablet (250 mg/g SDD) | N/A | 17-000496 | 25 mg | Tablet |
| PF-06826647 100 mg oval white to off-white tablet (250 mg/g SDD) | N/A | 18-000477 | 100 mg | Tablet |
| PF-06826647 100 mg oval white to off-white tablet (250 mg/g SDD) | N/A | 18-000478 | 100 mg | Tablet |
| Placebo 8 mm tablet (2:1, MCC:lactose) | N/A | 18-001357 | 0 mg | Tablet |
| PF-06826647 100 mg oval white to off-white tablet (250 mg/g SDD) | 19-DP-00025 | 19-001288 | 100 mg | Tablet |
| PF-06826647 100 mg oval white to off-white tablet (250 mg/g SDD) | 19-DP-00026 | 19-001289 | 100 mg | Tablet |
| PF-06826647 100 mg oval white to off-white tablet (250 mg/g SDD) | 19-DP-00027 | 19-001290 | 100 mg | Tablet |
| PF-06826647 100 mg oval white to off-white tablet (250 mg/g SDD) | 19-DP-00048 | 19-002536 | 100 mg | Tablet |
| PF-06826647 100 mg oval white to off-white tablet (250 mg/g SDD) | 19-DP-00049 | 19-002537 | 100 mg | Tablet |
| PF-06826647 100 mg oval white to off-white tablet (250 mg/g SDD) | 19-DP-00058 | 19-002809 | 100 mg | Tablet |
| PF-06826647 25 mg round white to off-white tablet (250 mg/g SDD) | 19-DP-00007 | 19-000554 | 25 mg | Tablet |
| PF-06826647 100 mg oval white to off-white tablet (250 mg/g SDD) | 19-DP-00008 | 19-000555 | 100 mg | Tablet |
| PF-06826647 100 mg oval white to off-white tablet (250 mg/g SDD) | 19-DP-00009 | 19-000556 | 100 mg | Tablet |
| PF-06826647 100 mg oval white to off-white tablet (250 mg/g SDD) | 19-DP-00010 | 19-000557 | 100 mg | Tablet |
| PF-06826647 100 mg oval white to off-white tablet (250 mg/g SDD) | 19-DP-00056 | 19-002807 | 100 mg | Tablet |
| PF-06826647 100 mg oval white to off-white tablet (250 mg/g SDD) | 19-DP-00057 | 19-002808 | 100 mg | Tablet |

Abbreviation: N/A = not applicable.

### Efficacy Evaluations:

- The PASI quantifies the severity of a participant's psoriasis based on both lesion severity and the percentage of body surface area affected. The PASI score can vary in increments of 0.1 unit from 0.0 to 72.0, with higher scores representing increasing severity of psoriasis. A second method of linear method Psoriasis Area and Severity Index (L-PASI) was also applied to PASI calculation.

## CLINICAL STUDY REPORT SYNOPSIS

- The PGA of psoriasis was scored on a 5-point scale, reflecting a global consideration of the erythema, induration and scaling across all psoriatic lesions. Average erythema, induration and scaling were rated separately over the whole body according to a 5-point severity scale (from 0 to 4), with appropriate morphologic descriptors. The severity rating scores were summed, and the average was taken and rounded to the nearest whole number score to determine the PGA. The 5-point scale for PGA: 0, "clear"; 1, "almost clear"; 2, "mild"; 3, "moderate"; 4 "severe".

- Assessment of BSA involved in psoriasis was performed separately for 4 areas of the body: head and neck, upper limbs, trunk (including axillae and groin) and lower limbs (including buttocks). The percentage surface area affected by psoriasis was estimated by means of the "handprint method", which represents approximately 1% of the total BSA. Based on the same body region weighting employed in the PASI calculation, the number of handprints of psoriatic skin in a body region was used to determine the extent (%) to which a body region had psoriatic involvement.

Patient-Reported Outcomes (PROs):

- Peak-Pruritus Numerical Rating Scale (PP-NRS): an 11-category numeric rating scale from 0 to 10 to assess the intensity pruritus. Participants were asked to assess their itch over the past 24 hours, anchored by the terms "no itch" (0) and "worst itch imaginable" (10) at the ends.

- Psoriasis Symptom Inventory (PSI): a self-administered 8 item questionnaire to measure the severity of psoriasis symptoms over the past 24 hours and the past 7 days. Participants were asked to respond to each item using a 5-point Likert response scale (0: not at all, 1: mild, 2: moderate, 3: severe and 4: very severe).

- Night-Time Itch scale: a single-item, 0 to 10 horizontal numeric rating scale to assess the severity of itch due to psoriasis. Participants were asked to assess their itch at the worst moment during the most recent night's sleep on a Numeric Rating Scale (NRS) anchored by the terms "no itch" (0) and "worst itch imaginable" (10) at the ends. Participants were also asked the frequency of itch on a 5-point Likert scale.

- Dermatology Life Quality Index (DLQI): a general dermatology questionnaire consisting of 10 items that assess participant health-related quality of life (daily activities, personal relationships, symptoms and feelings, leisure, work and school, and treatment) over the last week.

- Short Form-36 Health survey Version 2 (SF-36v2): a validated 36-item generic health status measure. Lower scores indicate worse physical and mental health status.

- Patient Global Assessment (PtGA) of Psoriasis: a single-item, 5-point scale to evaluate the overall cutaneous disease at that point in time. The same category labels used for the

## CLINICAL STUDY REPORT SYNOPSIS

PtGA of Psoriasis, ie, “severe”, “moderate”, “mild”, “almost clear”, and “clear (no psoriasis)”.

**Pharmacokinetic and Pharmacodynamic Evaluations:**

Pharmacokinetic(s): Blood samples were collected pre-dose at each visit and also at 0.5, 1, 2 and 4 hours post-dose at Week 8 and Week 40, for measurement of plasma concentrations of PF-06826647. Plasma samples were analyzed for concentrations of PF-06826647 using a validated high-performance liquid chromatography coupled with tandem mass spectrometry (HPLC-MS/MS) analytical method in compliance with applicable standard operating procedures (SOPs).

Pharmacodynamic(s): Blood samples were collected and analyzed by fluorescent activated cell sorting (FACS) for the assessment of percent and absolute lymphocyte subsets (T cells, B cells and Natural Killer cells [TBNK]). Blood samples were collected to provide serum for measurement of high sensitivity C-reactive protein (hsCRP). Samples were analyzed using fit-for-purpose or validated analytical methods in compliance with Pfizer SOPs.

**Safety Evaluations:** Safety evaluations included adverse event (AE) monitoring, safety laboratory tests, vital signs (heart rate, blood pressure and temperature),12-lead electrocardiograms (ECGs), physical examinations and Columbia Suicide Severity Rating Scale (C-SSRS).

**Statistical Methods:** The full analysis set (FAS) population was defined as all randomized participants who received at least 1 dose of investigational product. The safety analysis set was defined as all participants who received at least 1 dose of investigational product. The PK analysis set was defined as all participants who received at least 1 dose of PF-06826647 and in whom at least 1 concentration value was reported. The efficacy and PRO endpoints were analyzed using the FAS. The safety endpoints were analyzed using the safety analysis set. PK endpoints were analyzed using the PK analysis set.

Efficacy and PRO: Analysis was done pairwise between each of the PF-06826647 treated groups and the placebo group. An analysis with point estimates of the difference, the associated 90% confidence intervals (CIs) and p-values were also reported.

- Hypotheses and Decision Rules: Statistical inference was made on the primary endpoint. The global null hypothesis was that there was no difference between any arm of PF-06826647 and placebo arm. The alternative hypothesis was that one of the PF-06826647 arms being tested was superior to the placebo arm at Week 16. The study was to be considered positive if the null hypothesis was rejected. The familywise error rate was controlled in strong sense at the 1-sided 0.05 level for these tests with a Hochberg step-up procedure.

- Analyses for Binary Endpoints: Landmark (cross-sectional) analyses of key binary endpoints calculated and tested for risk differences using the method of (Chan and Zhang

## CLINICAL STUDY REPORT SYNOPSIS

1999). Covariates were not included in the primary analyses. Risk differences and 90% CIs were presented. All key binary endpoints that were measured repeatedly over time were analyzed using generalized linear mixed effect model (GLMM) with treatment group (defined as factor variable), visit, treatment group by visit interaction and subjects as the random effect. An unstructured covariance matrix was used to fit such model.

- Analyses for Continuous Endpoints: Landmark (cross-sectional) analysis of key continuous endpoints used analysis of covariance (ANCOVA). Least squares (LS) means at the mean overall baseline score were presented along with 90% CIs. Mixed model repeated measures (MMRM) models were used. The fixed effects of treatment, visit (Weeks 1 2, 4, 6, 8, 12 and 16), and treatment by visit interaction were included. At each visit, estimates of LS mean values and the LS mean differences between the PF-06826647 treated groups and placebo group were derived from the model. The corresponding p-values and 90% CIs were also derived from the model.

- Exploratory endpoints, including PROs, were analyzed with respect to an estimand, and were also analyzed descriptively. All endpoints for the Extension Treatment Period were analyzed with descriptive statistics and graphical displays when appropriate.

PK: PK concentrations were summarized and presented with descriptive statistics. Summary statistics (N, geometric mean, geometric coefficient of variation [CV], median, arithmetic mean, CV, minimum, maximum) of concentrations of PF-06826647 at nominal time of collection were calculated for each dose groups.

Safety: The safety data were summarized descriptively through appropriate data tabulations, descriptive statistics, categorical summaries, and graphical presentations.

## RESULTS

For Results sections, the treatment groups will be referred to as follows in the text.

- Placebo QD → PF-06826647 200 mg QD group: placebo to 200 mg QD group.
- Placebo QD → PF-06826647 400 mg QD group: placebo to 400 mg QD group.
- PF-06826647 50 mg QD → PF-06826647 200 mg QD group: 50 to 200 mg QD group.
- PF-06826647 50 mg QD → PF-06826647 400 mg QD group: 50 to 400 mg QD group.
- PF-06826647 100 mg QD → PF-06826647 200 mg QD group: 100 to 200 mg QD group.
- PF-06826647 100 mg QD → PF-06826647 400 mg QD group: 100 to 400 mg QD group.
- PF-06826647 200 mg QD → PF-06826647 200 mg QD group: 200 to 200 mg QD group.
- PF-06826647 400 mg QD → PF-06826647 400 mg QD group: 400 to 400 mg QD group.

## CLINICAL STUDY REPORT SYNOPSIS

**Subject Disposition and Demography:** A total of 179 participants were randomized, and 178 participants were treated. All 178 treated participants were included in the full analysis set and safety analysis set.

A total of 178 participants entered and 153 (86%) participants completed the Investigational Treatment Period. A total of 153 participants entered and 130 (85%) participants completed the Extension Treatment Period (Table S4). The discontinuation rate overall was approximately 14% and 15% for the Investigational Treatment Period and the Extension Treatment Period, respectively. The most frequent reason for early termination was withdrawal by subject (11 [6.2%] during the Investigational Treatment Period and 7 [3.9%] during the Extension Treatment Period).

Demographic characteristics were similar across treatment groups. The majority of the treated participants were male (68.5%) and White (88.8%). The median age was 45.0 years (range: 18-72 years). The mean weight was 86.7 kg (standard deviation [SD]: 20.37), and the mean body mass index (BMI) was 28.9 $kg/m^2$ (SD: 5.91). The disease characteristics at baseline was comparable for participants in all treatment groups.

## CLINICAL STUDY REPORT SYNOPSIS

### Table S4. Disposition Events Summary - Safety Analysis Set (Protocol C2501004)

| Number (%) of Subjects | Placebo QD -> PF-06826647 200 mg QD (N=23) n (%) | Placebo QD -> PF-06826647 400 mg QD (N=22) n (%) | PF-06826647 50 mg QD -> PF-06826647 200 mg QD (N=11) n (%) | PF-06826647 50 mg QD -> PF-06826647 400 mg QD (N=11) n (%) | PF-06826647 100 mg QD -> PF-06826647 200 mg QD (N=12) n (%) | PF-06826647 100 mg QD -> PF-06826647 400 mg QD (N=11) n (%) | PF-06826647 200 mg QD -> PF-06826647 200 mg QD (N=45) n (%) | PF-06826647 400 mg QD -> PF-06826647 400 mg QD (N=43) n (%) | Total (N=178) n (%) |
|---|---|---|---|---|---|---|---|---|---|
| Disposition phase: Screening | | | | | | | | | |
| Subjects Entered: | 23 (100.0) | 22 (100.0) | 11 (100.0) | 11 (100.0) | 12 (100.0) | 11 (100.0) | 45 (100.0) | 43 (100.0) | 178 (100.0) |
| Discontinued | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Reason for discontinuation | | | | | | | | | |
| Adverse Event | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Lack of Efficacy | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Lost to Follow-Up | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Pregnancy | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Protocol Deviation | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Withdrawal By Subject | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Other | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Completed | 23 (100.0) | 22 (100.0) | 11 (100.0) | 11 (100.0) | 12 (100.0) | 11 (100.0) | 45 (100.0) | 43 (100.0) | 178 (100.0) |
| Ongoing | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Disposition phase: Investigational Treatment Period | | | | | | | | | |
| Subjects Entered: | 23 (100.0) | 22 (100.0) | 11 (100.0) | 11 (100.0) | 12 (100.0) | 11 (100.0) | 45 (100.0) | 43 (100.0) | 178 (100.0) |
| Discontinued | 4 (17.4) | 3 (13.6) | 1 (9.1) | 2 (18.2) | 0 | 2 (18.2) | 8 (17.8) | 5 (11.6) | 25 (14.0) |

## CLINICAL STUDY REPORT SYNOPSIS

### Table S4. Disposition Events Summary - Safety Analysis Set (Protocol C2501004)

| Number (%) of Subjects | Placebo QD -> PF-06826647 200 mg QD (N=23) n (%) | Placebo QD -> PF-06826647 400 mg QD (N=22) n (%) | PF-06826647 50 mg QD -> PF-06826647 200 mg QD (N=11) n (%) | PF-06826647 50 mg QD -> PF-06826647 400 mg QD (N=11) n (%) | PF-06826647 100 mg QD -> PF-06826647 200 mg QD (N=12) n (%) | PF-06826647 100 mg QD -> PF-06826647 400 mg QD (N=11) n (%) | PF-06826647 200 mg QD -> PF-06826647 200 mg QD (N=45) n (%) | PF-06826647 400 mg QD -> PF-06826647 400 mg QD (N=43) n (%) | Total (N=178) n (%) |
|---|---|---|---|---|---|---|---|---|---|
| Reason for discontinuation | | | | | | | | | |
| Adverse Event | 1 (4.3) | 0 | 0 | 0 | 0 | 0 | 4 (8.9) | 3 (7.0) | 8 (4.5) |
| Lack of Efficacy | 1 (4.3) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 (0.6) |
| Lost to Follow-Up | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.2) | 0 | 1 (0.6) |
| Pregnancy | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Protocol Deviation | 0 | 0 | 0 | 1 (9.1) | 0 | 0 | 0 | 0 | 1 (0.6) |
| Withdrawal By Subject | 2 (8.7) | 3 (13.6) | 1 (9.1) | 1 (9.1) | 0 | 1 (9.1) | 3 (6.7) | 0 | 11 (6.2) |
| Other | 0 | 0 | 0 | 0 | 0 | 1 (9.1) | 0 | 2 (4.7) | 3 (1.7) |
| Completed | 19 (82.6) | 19 (86.4) | 10 (90.9) | 9 (81.8) | 12 (100.0) | 9 (81.8) | 37 (82.2) | 38 (88.4) | 153 (86.0) |
| Ongoing | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Disposition phase: Extention Treatment Period | | | | | | | | | |
| Subjects Entered: | 19 (82.6) | 19 (86.4) | 10 (90.9) | 9 (81.8) | 12 (100.0) | 9 (81.8) | 37 (82.2) | 38 (88.4) | 153 (86.0) |
| Discontinued | 3 (13.0) | 5 (22.7) | 0 | 1 (9.1) | 3 (25.0) | 1 (9.1) | 4 (8.9) | 6 (14.0) | 23 (12.9) |
| Reason for discontinuation | | | | | | | | | |
| Adverse Event | 0 | 1 (4.5) | 0 | 1 (9.1) | 0 | 0 | 3 (6.7) | 3 (7.0) | 8 (4.5) |
| Lack of Efficacy | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Lost to Follow-Up | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Pregnancy | 0 | 0 | 0 | 0 | 1 (8.3) | 0 | 0 | 0 | 1 (0.6) |
| Protocol Deviation | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

## CLINICAL STUDY REPORT SYNOPSIS

### Table S4. Disposition Events Summary - Safety Analysis Set (Protocol C2501004)

| Number (%) of Subjects | Placebo QD -> PF-06826647 200 mg QD (N=23) n (%) | Placebo QD -> PF-06826647 400 mg QD (N=22) n (%) | PF-06826647 50 mg QD -> PF-06826647 200 mg QD (N=11) n (%) | PF-06826647 50 mg QD -> PF-06826647 400 mg QD (N=11) n (%) | PF-06826647 100 mg QD -> PF-06826647 200 mg QD (N=12) n (%) | PF-06826647 100 mg QD -> PF-06826647 400 mg QD (N=11) n (%) | PF-06826647 200 mg QD -> PF-06826647 200 mg QD (N=45) n (%) | PF-06826647 400 mg QD -> PF-06826647 400 mg QD (N=43) n (%) | Total (N=178) n (%) |
|---|---|---|---|---|---|---|---|---|---|
| Withdrawal By Subject | 2 (8.7) | 1 (4.5) | 0 | 0 | 1 (8.3) | 1 (9.1) | 1 (2.2) | 1 (2.3) | 7 (3.9) |
| Other | 1 (4.3) | 3 (13.6) | 0 | 0 | 1 (8.3) | 0 | 0 | 2 (4.7) | 7 (3.9) |
| Completed | 16 (69.6) | 14 (63.6) | 10 (90.9) | 8 (72.7) | 9 (75.0) | 8 (72.7) | 33 (73.3) | 32 (74.4) | 130 (73.0) |
| Ongoing | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Disposition phase: Follow-Up | | | | | | | | | |
| Subjects Entered: | 16 (69.6) | 16 (72.7) | 10 (90.9) | 8 (72.7) | 9 (75.0) | 8 (72.7) | 33 (73.3) | 33 (76.7) | 133 (74.7) |
| Discontinued | 0 | 1 (4.5) | 0 | 0 | 0 | 0 | 0 | 1 (2.3) | 2 (1.1) |
| Reason for discontinuation | | | | | | | | | |
| Adverse Event | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 (2.3) | 1 (0.6) |
| Lack of Efficacy | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Lost to Follow-Up | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Pregnancy | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Protocol Deviation | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Withdrawal By Subject | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| Other | 0 | 1 (4.5) | 0 | 0 | 0 | 0 | 0 | 0 | 1 (0.6) |
| Completed | 16 (69.6) | 15 (68.2) | 10 (90.9) | 8 (72.7) | 9 (75.0) | 8 (72.7) | 33 (73.3) | 32 (74.4) | 131 (73.6) |
| Ongoing | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |

## CLINICAL STUDY REPORT SYNOPSIS

### Table S4. Disposition Events Summary - Safety Analysis Set (Protocol C2501004)

| | Placebo QD -> PF-06826647 200 mg QD (N=23) | Placebo QD -> PF-06826647 400 mg QD (N=22) | PF-06826647 50 mg QD -> PF-06826647 200 mg QD (N=11) | PF-06826647 50 mg QD -> PF-06826647 400 mg QD (N=11) | PF-06826647 100 mg QD -> PF-06826647 200 mg QD (N=12) | PF-06826647 100 mg QD -> PF-06826647 400 mg QD (N=11) | PF-06826647 200 mg QD -> PF-06826647 200 mg QD (N=45) | PF-06826647 400 mg QD -> PF-06826647 400 mg QD (N=43) | Total (N=178) |
|---|---|---|---|---|---|---|---|---|---|
| **Number (%) of Subjects** | **n (%)** | **n (%)** | **n (%)** | **n (%)** | **n (%)** | **n (%)** | **n (%)** | **n (%)** | **n (%)** |

PFIZER [redacted] SDTM Creation: 23DEC2020 (00:59) Source Data: adds Table Generation: 11JAN2021 (05:07)
Output File: ./nda1_cdisc/C2501004_CSR/adds_s001_i
Table 14.1.1.2.1 PF-06826647 is for Pfizer internal use.

## CLINICAL STUDY REPORT SYNOPSIS

**Efficacy Results:**

Primary Efficacy Endpoint: All the active treatment groups had greater proportions of participants achieving PASI 90 response at Week 16 compared with the placebo group (Table S5). There were statistically significant differences from the placebo QD group in the proportion of participants achieving PASI 90 response at Week 16 for the 400 mg QD group and the 200 mg QD group.

**Table S5. Statistical Summary of Subjects Achieving PASI90 Response at Week 16 - Chan and Zhang, NRI - FAS (Protocol C2501004)**

| | | | | | Difference from Placebo QD | | | |
|---|---|---|---|---|---|---|---|---|
| **Analysis Visit** | **Treatment Group** | **N2** | **n (%)** | **90% CI[a]** | **Risk Difference** | **90% CI[b]** | **One-sided P-value** | **Hochberg P-value** |
| Week 16 | Placebo QD (N=45) | 42 | 2 ( 4.8) | ( 1.27, 13.53) | | | | |
| | PF-06826647 50 mg QD (N=22) | 22 | 3 ( 13.6) | ( 5.12, 31.13) | 8.87 | (-4.50, 26.26) | 0.1587 | 0.2621 |
| | PF-06826647 100 mg QD (N=23) | 21 | 2 ( 9.5) | ( 2.56, 24.50) | 4.76 | (-7.07, 21.48) | 0.2621 | 0.2621 |
| | PF-06826647 200 mg QD (N=45) | 45 | 17 ( 37.8) | (25.96, 50.95) | 33.02 | (18.01, 47.11) | 0.0001 | 0.0004 |
| | PF-06826647 400 mg QD (N=43) | 41 | 21 ( 51.2) | (37.44, 64.86) | 46.46 | (30.62, 60.56) | <.0001 | <.0001 |

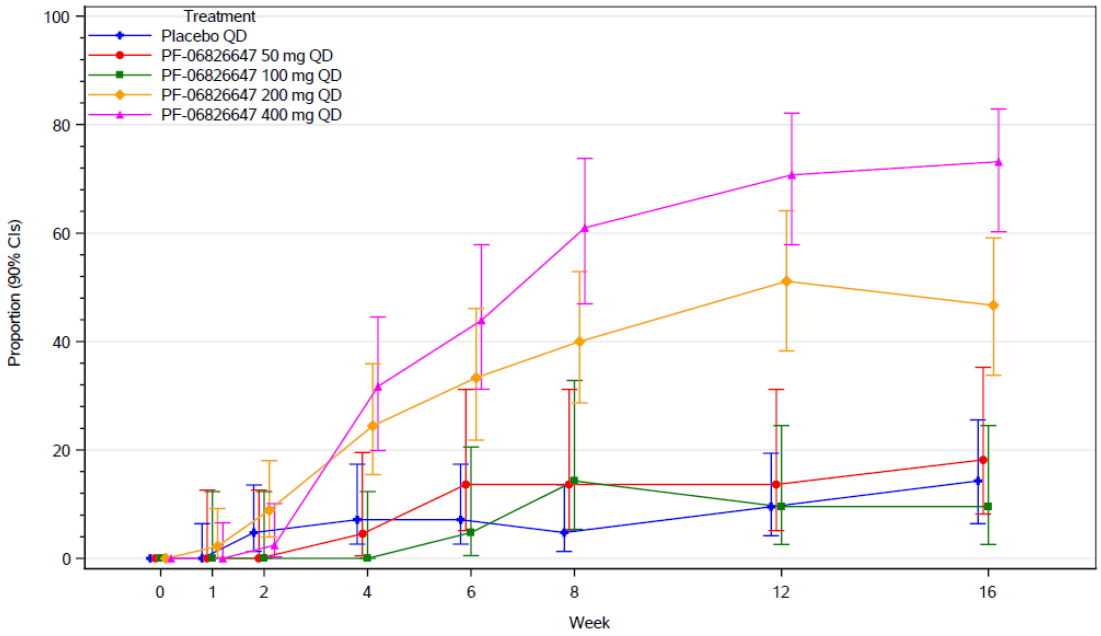
PASI90: >=90% reduction from baseline in the PASI total score; NRI: imputed missing value to non-responder.
All data for a subject after the initiation of prohibited medications was set to non-responder. No NRI was done on missing data collected via remote visit.
a. calculated using Blyth-Still-Casella (Casella (1986)) method.
b. calculated using Chan and Zhang (1999) method.
N=number of subjects in FAS population; N2=number of subjects after non-responder imputation applied (the subjects discontinued due to COVID-19 were removed); n (%)=number of subjects achieving PASI90 response (percentage based on N2).
90% CI and Risk Difference were represented as percent in the report.
Baseline was defined as the last available measurement prior to randomization on Day 1, if a Day 1 measurement was not available, the value from the Screening visit could be used.
PFIZER [redacted] SDTM Creation: 18DEC2020 (06:35) Source Data: adps Table Generation: 12JAN2021 (21:12)
Output File: ./nda1_cdisc/C2501004_CSR/adps_s401_2_i
Table 14.2.1.4.1.1 PF-06826647 is for Pfizer internal use.

Key Secondary Efficacy Endpoint: Greater proportions of participants achieving PASI 75 responses compared with the placebo QD group were observed from Week 6 to Week 16 for all active treatment groups except for the 100 mg QD group at Weeks 6, 12 and 16 (Figure S2). There were significant differences from the placebo QD group in the proportion of participants achieving PASI 75 responses for the 400 mg QD group and the 200 mg QD group from Week 4 to Week 16, with the greatest difference in the 400 mg QD group

## CLINICAL STUDY REPORT SYNOPSIS

observed at Week 12 (90% CI: 44.52%, 74.44%; one-sided p-value < 0.0001) and in the 200 mg QD group observed at Week 12 (90% CI: 25.56%, 55.93%; one-sided p-value < 0.0001).

**Figure S2. Proportion (90% CIs) of Subjects Achieving PASI 75 Response Up to Week 16 - Blyth-Still-Casella, NRI - FAS**




PASI75: >=75% reduction from baseline in the PASI total score; NRI: imputed missing value to non-responder.
All data for a subject after the initiation of prohibited medications was set to non-responder.
No NRI was done on missing data collected via remote visit.
90% CI of Proportion was calculated using Blyth-Still-Casella (Casella (1986)) method.
Week 0 represented baseline. Baseline was defined as the last available measurement prior to randomization on Day 1, if a Day 1 measurement was not available, the value from the Screening visit could be used.
The subjects discontinued due to COVID-19 were removed from this analysis.
PFIZER [redacted] SDTM Creation: 18DEC2020 (06:35) Source Data: adps Table Generation: 12JAN2021 (21:12)
Output File: ./ndal_cdisc/C2501004_CSR/adps_f401_i

Other Efficacy Endpoints:

*Proportion of Participants with PGA Score Clear (0) or Almost Clear (1) (and ≥2 Points Improvement From baseline), Up to Week 16:* There were significant differences from the placebo QD group in the proportion of participants achieving PGA responses of clear or almost clear and ≥2 points improvement from baseline for the 200 mg QD group and the 400 mg QD group from Week 4 to Week 16, with the greatest difference in the 400 mg QD group observed at Week 12 (90% CI: 46.94%, 76.61%; one-sided p-value<0.0001), and in the 200 mg QD group observed at Week 6 and Week 12 (with same 90% CI: 14.32%, 47.52%; one-sided p-value=0.0006). Identical results were shown for the proportion of participants with PGA score clear or almost clear up to Week 16.

*Change and Percent Change From Baseline in PASI Scores, Up to Week 16*: Greater LS mean percent decreases from baseline in PASI score were observed for all active treatment

## CLINICAL STUDY REPORT SYNOPSIS

groups from Week 6 to Week 16 compared with the placebo QD group. There were significant differences from the placebo QD group in the LS mean percent change from baseline in PASI score for the 400 mg QD group and 200 mg QD group from Week 1 to Week 16, with the greatest difference in the 400 mg QD group observed at Week 16 (90% CI: -65.44%, -40.63%; one-sided p-value<0.0001) and in the 200 mg QD group observed at Week 16 (90% CI: -53.02%, -28.46%; one-sided p-value<0.0001). Similar results were observed for the LS mean decreases from baseline in PASI score up to Week 16.

*Categorical Summary of PASI Responses*: Greater proportions of participants achieving PASI 90, PASI 50 and PASI 100 responses compared with the placebo QD group were observed from Week 6 to Week 16 for all active treatment groups except for the 100 mg QD group. For PASI 50, PASI 75 and PASI 90, generally there were gradual increases in the proportion of participants achieving these responses over time from Week 18 for all the treatment groups, which then stabilized up to Week 40. There were general increases in the proportion of participants achieving PASI 100 responses from Week 18 to Week 40.

*Change From Baseline in L-PASI Score:* Greater mean decreases from baseline in L-PASI score were observed for all active treatment groups up to Week 16 compared with the placebo QD group except for the 50 mg QD group (at Weeks 4, 8 and 12) and the 100 mg QD group (at Weeks 2 and 4). A mean decrease from baseline in L-PASI score was observed in all the treatment groups from Week 18 to Week 40, and remained stable throughout the Extension Treatment Period.

*Change and Percent Change From Baseline in PASI Scores, Week 16 to Week 40:* A mean decrease from baseline in PASI score was observed in all the treatment groups from Week 18 to Week 40, and remained stable throughout the Extension Treatment Period. The mean percent decrease from baseline increased from Week 18 to Week 24 for all the treatment groups, and had a tendency to converge to a similar level across the treatment groups.

*Absolute and Change From Baseline in Psoriatic BSA*: Greater LS mean decreases from baseline in psoriatic BSA were observed for the 400 mg QD group and the 200 mg QD group up to Week 16 compared with the placebo QD group. A similar trend was observed for the mean change from baseline in psoriatic BSA up to Week 16. A mean decrease from baseline in psoriatic BSA was observed in all the treatment groups from Week 18 to Week 40, and remained stable throughout the Extension Treatment Period.

*Categorical Summary of PGA Scores, Week 16 to Week 40*: Generally, a high proportion of participants achieving PGA responses of clear or almost clear was maintained for all the treatment groups from Week 18 to Week 40. Identical results were observed for the proportion of participants achieving PGA responses of clear or almost clear and ≥2 points improvement from baseline.

## CLINICAL STUDY REPORT SYNOPSIS

PRO Summary:

- There were significant differences from the placebo QD group in the LS mean change from baseline in PP-NRS score for the 400 mg QD group from Day 12 to Day 16 and from Week 4 to Week 16, and for the 200 mg QD group from Day 5 to Day 16 and from Week 4 to Week 16. A similar trend was observed for the mean change from baseline in PP-NRS scores up to Week 16. A mean decrease from baseline in PP-NRS score was observed in all the treatment groups from Week 24 to Week 40, and remained stable during the period.

- Significant differences from the placebo QD group in the proportion of participants achieving a PSI score of 0 or 1 on every item were observed for the 400 mg QD group on Days 6, 11, 12, from Day 14 to Day 16 and from Week 4 to Week 16, and for the 200 mg QD group on Day 6, from Day 12 to Day 15 and from Week 4 to Week 16. The high proportion of participants achieving a PSI score of 0 or 1 on every item was maintained for all the treatment groups from Week 24 to Week 40.

- There were significant differences from the placebo QD group in the LS mean change from baseline in PSI score for the 400 mg QD group on Day 6, from Day 8 to Day 16 and from Week 4 to Week 16, and for the 200 mg QD group from Day 4 to Day 16 and from Week 4 to Week 16. A similar trend was observed for the mean change from baseline in PSI score up to Week 16.

- Greater mean decreases from baseline in Night-Time Itch Scale were observed for all active treatment groups up to Week 16 compared with the placebo QD group except for the 100 mg QD group (up to Day 16, and at Week 4), the 50 mg QD group (on Days 2 and 5) and the 400 mg QD group (on Days 2 and 3).

- There were significant differences from the placebo QD group in the LS mean change from baseline in DLQI for the 400 mg QD group and the 200 mg QD group from Week 4 to Week 16. A similar trend was observed for the mean change from baseline in DLQI up to Week 16.

- A higher proportion of participants achieving DLQI response of ≥4 improvement from baseline was observed for all the active treatment groups compared with the placebo QD group from Week 4 to Week 16. Significant differences from the placebo QD group in the proportion of participants achieving this DLQI response were observed for the 400 mg QD group and the 200 mg QD group from Week 4 to Week 16.

- A numerically greater LS mean increase from baseline was observed in all the 10 domains of SF-36v2 in the 400 mg QD group and the 200 mg QD group at Week 4 and Week 16 compared with the placebo QD group, except for physical functioning at Week 16 and mental health at Week 4 in the 200 mg QD group.

## CLINICAL STUDY REPORT SYNOPSIS

- A greater mean decrease from baseline in PtGA was observed for all the active treatment groups up to Week 16 compared with the placebo QD group. The greatest difference from the placebo QD group was observed in the 400 mg QD group, followed by the 200 mg QD group.

- Significant differences from the placebo QD group in the proportion of participants achieving PtGA response of clear or almost clear were observed for the 400 mg QD group from Week 2 to Week 16, and for the 200 mg QD group from Week 4 to Week 16. Significant difference from the placebo QD group was also observed for the 50 mg QD group at Week 12.

**Pharmacokinetic and Pharmacodynamic Results:**

Pharmacokinetic Results

- The median pre-dose plasma concentration appears to achieve steady state by Week 1. The median pre-dose concentrations across visits at steady state at 50 mg QD and 100 mg QD were similar. The increase in mean pre-dose plasma concentrations across visits at 400 mg QD compared with the 200 mg QD did not appear to be dose-proportional. The post-dose mean and median concentrations of PF-06826647 at Week 8 generally increased less than proportionally with dose, with a high degree of overlap in observed post-dose concentrations between 50 mg QD and 100 mg QD, and between 200 mg QD and 400 mg QD. The geometric percent coefficients of variation (%CVs) of pre-dose concentrations across all visits up to Week 16 and all PF-06826647 treatment groups at steady state ranged between 164% and 692%.

- The median pre-dose concentrations across visits after Week 16 and up to Week 40 generally overlapped among all treatments. Similarly, there was a high degree of overlap in observed post-dose concentrations across treatment groups. The geometric %CVs of pre-dose concentration across all visits between Week 16 and Week 40 and all treatment groups ranged between 109% and 1469%.

Pharmacodynamic Results

- The mean decrease from baseline in hsCRP in the 200 mg QD group was generally numerically greater than the placebo QD group up to Week 16. The mean decrease from baseline in hsCRP in the 100 mg QD group was generally numerically lower than the placebo QD group up to Week 16. CIs in all active treatment groups overlapped with CIs in the placebo QD group.

- There was a greater mean decrease from baseline in natural killer (NK) cell absolute counts in the 200 mg QD and 400 mg QD group compared with the placebo QD group up to Week 4 and then the value was maintained up to Week 16. There were generally greater mean increases from baseline in B cell absolute counts in all the active treatment groups up to Week 16 compared with the placebo QD group. The mean change from

## CLINICAL STUDY REPORT SYNOPSIS

baseline in T cells and helper T cells in the 200 mg QD group was generally numerically higher than the placebo QD group up to Week 16, though the data showed wide variability and CIs for all active treatment groups generally overlapped with CIs for the placebo QD group. No obvious differences from the placebo group in the mean change from baseline in cytotoxic T cells were observed in all the active treatment groups up to Week 16.

**Safety Results:**

Adverse Event:

*Up to Week 16*: All AEs described in this Synopsis were treatment-emergent unless otherwise specified. The proportion of participants with AEs up to Week 16 was comparable across all the treatment groups, but numerically higher in the active treatment groups (59.1% to 69.6%) than that in the placebo group (51.1%). Two (1.1%) participants were reported with serious adverse events (SAEs). A total of 9 (5.1%) participants discontinued from the study due to AEs. No deaths were reported. The most frequently reported all-causality AEs by system organ class (SOC) were Infections and Infestations (62 [34.8%] participants) and Investigations (31 [17.4%] participants). The majority of the participants in each treatment group experienced mild or moderate AEs. The most frequently reported all-causality AEs regardless of SOC were nasopharyngitis (29 [16.3%] participants), upper respiratory tract infection (14 [7.9%] participants) and blood pressure increased (12 [6.7%] participants).

*Week 16 to Week 40*: The proportion of participants with AEs from Week 16 to Week 40 was comparable across all the treatment groups (44.4% to 77.8%). Four (2.6%) participants were reported with SAEs. A total of 9 (5.9%) participants discontinued from the study due to AEs. No deaths were reported. The most frequently reported all-causality AEs by SOC were Infections and Infestations (36 [23.7%] participants) and Investigations (36 [23.7%] participants). The majority of the participants in each treatment group experienced mild or moderate AEs. The most frequently reported all-causality AEs regardless of SOC was blood creatine phosphokinase increased (12 [7.9%] participants).

Laboratory Values:

For participants with confirmed (through re-testing within 48 hours) laboratory abnormalities meeting the pre-specified criteria, the study drug was permanently discontinued:

- There was a confirmed case of 2 sequential hemoglobin <10.0 g/dL for 1 participant in the 200 to 200 mg QD group, which led to the discontinuation of study drug.

- There was a confirmed case of 2 sequential alanine aminotransferase (ALT) >3×upper limit of normal (ULN) for 1 participant in the placebo QD group, which led to the discontinuation of study drug.

## CLINICAL STUDY REPORT SYNOPSIS

**Hemoglobin**: Abnormally low levels of hemoglobin (<0.8×lower limit of normal [LLN]) were reported for participants receiving either PF-06826647 400 mg QD or 200 mg QD (5 participants up to Week 16 and 2 participants from Week 16 to Week 40). A numerically greater mean decrease from baseline in hemoglobin was observed for all active treatment groups compared with the placebo QD group from Week 2 to Week 16 and these decreases were generally dose-related. The mean decrease from baseline in hemoglobin was maintained over time for all the treatment groups from Week 16 to Week 40.

**Reticulocyte**: Abnormally low (<0.5×LLN) and high (>1.5×ULN) levels of reticulocytes were reported for participants receiving PF-06826647 400 mg QD (2 participants with abnormally low levels and 2 participants with abnormally high levels up to Week 16, and 2 participants with abnormally low levels and 2 participants with abnormally high levels from Week 16 to Week 40). There appeared to be a dose-dependent decline in reticulocytes in the active treatment groups within the first 2 weeks of treatment followed by a return towards baseline after Week 2. The mean decrease from baseline in reticulocyte count was similar across the treatment groups from Week 16 to Week 40 and was maintained over time for all the treatment groups.

**Platelet:** Abnormally low platelet counts (<0.5×LLN) were reported for participants receiving PF-06826647 400 mg QD (1 participant up to Week 16 and 1 participant from Week 16 to Week 40). A numerically greater mean increase from baseline in platelet counts was observed for all the active treatment groups compared with the placebo QD group up to Week 16, with the greatest difference from the placebo QD group in the 400 mg QD group or 200 mg QD group. The mean increase from baseline in platelet count was maintained over time for all the treatment groups from Week 16 to Week 40.

Clinically significant laboratory abnormalities were reported as AEs by the investigator. The most frequently reported laboratory abnormality AEs (treatment-related) during the Investigational Treatment Period by Medical Dictionary for Regulatory Activities (MedDRA) SOC were: Investigations in 14 (7.9%) participants and Blood and Lymphatic System Disorders in 6 (3.4%) participants. The most frequently reported laboratory abnormality AEs (treatment-related) during the Extension Treatment Period by MedDRA SOC were: Investigations in 13 (8.6%) participants and Blood and Lymphatic System Disorders in 14 (9.2%) participants.

Other Safety Evaluations:

Clinically significant findings in vital signs data were reported as AEs by the investigator (all the AEs were reported in participants in the active treatment groups unless otherwise specified): the AE of hypertension was reported for 7 participants up to Week 16, and for 9 participants from Week 16 to Week 40; the AE of blood pressure increased was reported for 12 participants up to Week 16 (1 participant was in the placebo QD group), and for 8 participants from Week 16 to Week 40; the AE of sinus tachycardia was reported for 1 participant from Week 16 to Week 40; the AE of blood pressure diastolic increased was

## CLINICAL STUDY REPORT SYNOPSIS

reported for 1 participant from Week 16 to Week 40; the AE of pyrexia was reported for 1 participant from Week 16 to Week 40.

Clinically significant findings in ECG data were reported as AEs by the investigator (all the AEs were reported in participants in the active treatment groups unless otherwise specified): the AE of electrocardiogram PR prolongation was reported for 1 participant up to Week 16 (the participant was in the placebo QD group); the AE of palpitations was reported for 1 participant up to Week 16; the AE of electrocardiogram QT prolonged was reported for 1 participant from Week 16 to Week 40; the AE of atrial fibrillation was reported for 2 participants from Week 16 to Week 40; the AE of atrioventricular block first degree for 1 participant from Week 16 to Week 40.

No clinically significant physical examination findings were reported. No suicidal behavior or ideation, or no onset of post-baseline suicidality was reported.

**Conclusions:**

- PF-06826647 400 mg QD and 200 mg QD were both statistically superior to placebo for the proportion of participants achieving PASI 90 at Week 16. For both PF-06826647 400 mg QD and 200 mg QD groups, there were significant differences from placebo in the proportion of participants achieving PASI 90 responses from Week 4 to Week 16.

- PF-06826647 400 mg QD and 200 mg QD both showed significant efficacy over placebo based on proportion of participants achieving PASI 75 and PGA response of clear or almost clear; there was significant improvement compared with placebo based on the proportion of participants achieving the responses from Week 4 to Week 16.

- The observed efficacy responses were generally better in the PF-06826647 400 mg QD and 200 mg QD groups compared with placebo for all secondary efficacy endpoints and PRO results up to Week 16.

- Generally, efficacy continued to improve for the PF-06826647 400 mg QD and 200 mg QD groups compared with the placebo up to Week 16, and this efficacy was maintained throughout the 24-week Extension Treatment Period.

- For all the treatment groups including those transitioned from placebo, 50 mg QD and 100 mg QD to 200 or 400 mg QD, the efficacy continued to improve from Week 16 to Week 40, and had a tendency to converge to a similar level across the treatment groups.

- PF-06826647 was generally safe and well tolerated when administered in daily oral doses of 50 mg, 100 mg, 200 mg and 400 mg for 16 weeks, and this continued following daily doses of 200 mg and 400 mg for an additional 24 weeks, in participants with moderate to severe psoriasis.

## CLINICAL STUDY REPORT SYNOPSIS

- There were no notable differences in the rate of AEs, SAEs and discontinuations due to AEs between the active treatment groups and the placebo group up to Week 16.

- The majority of AEs were mild or moderate.

- For active treatment groups during the Investigational Treatment Period, there was a general trend of greater mean decrease from baseline in hemoglobin over time, with the greatest decreases from baseline in the 400 mg QD group or 200 mg QD group. The mean changes from baseline values across all treatment groups in the Extension Treatment Period were maintained.

- For active treatment groups during the Investigational Treatment Period, there appeared to be a dose-dependent decline in reticulocytes in the active treatment groups within the first 2 weeks of treatment followed by a return towards baseline after Week 2. The mean changes from baseline values across all treatment groups in the Extension Treatment Period were maintained.

- For active treatment groups during the Investigational Treatment Period, a numerically greater mean increase from baseline in platelet count was observed for all the active treatment groups compared with the placebo QD group up to Week 16, with the greatest difference from the placebo QD group in the 400 mg QD group or 200 mg QD group. The mean changes from baseline values across all treatment groups in the Extension Treatment Period were maintained.

- The median pre-dose plasma concentration appeared to achieve steady state by Week 1. The median pre-dose concentrations across visits at steady state at 50 mg QD and 100 mg QD were similar. The median pre-dose concentrations across visits at 200 mg QD were higher than 400 mg QD; however, the mean pre-dose concentrations across visits at steady state at 400 mg QD were generally higher than those at 200 mg QD but the increase in mean pre-dose plasma concentration did not appear to be dose-proportional.

- Inter-participant variability of pre-dose concentration across all visits and all treatment groups, as assessed by %CV, was high for both the Investigational Treatment Period and the Extension Treatment Period.