CLINICAL STUDY REPORT SYNOPSIS

Sponsor: Pfizer Inc.

Investigational Product: Brepocitinib (PF-06700841)

Clinical Study Report Synopsis: Protocol B7931030

Protocol Title: A Phase 2b, Randomized, Double-Blind, Placebo-Controlled Study of PF-06700841 to Evaluate the Efficacy at 16 Weeks and to Evaluate the Safety and Efficacy up to 1 Year in Subjects With Active Psoriatic Arthritis

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

Study Centers: This study was conducted at 47 centers (2 in Australia, 6 in Bulgaria, 5 in Czech Republic, 3 in Estonia, 2 in Hungary, 2 in Lithuania, 10 in Poland, 8 in Russian Federation, 3 in Serbia, 3 in Slovakia and 3 in Spain). 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: 13 June 2019

Study Completion Date: 15 January 2021

Report Date: 20 May 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. The terms “participant”, “patient” and “subject” are used interchangeably in this Synopsis.

Table S1. Study Objectives and Endpoints

Type	Objective	Endpoint
Primary		
Efficacy	To evaluate the efficacy of PF-06700841 compared to placebo in participants with active PsA.	• The proportion of participants achieving an ACR20 response at Week 16.
Secondary		
Efficacy	To evaluate the efficacy of PF-06700841 compared to placebo in participants with active PsA who were TNFα inhibitor naïve.	• The proportion of participants achieving an ACR20 response at Week 16 in the subgroup of participants who were TNFα inhibitor naïve.

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Table S1. Study Objectives and Endpoints

Type	Objective	Endpoint
	To evaluate the improvement in signs and symptoms related PsA Core Domain Set in PF-06700841 treated participants.	Assessed at all treatment timepoints: • The proportion of participants achieving an ACR20 response at all treatment timepoints (other than Week 16), and proportion of participants achieving an ACR50 and ACR70 response; • Change from baseline in the ACR response criteria components (Tender/painful joint count, Swollen joint count, Patient's Assessment of Arthritis Pain, Patient's Global Assessment of Arthritis, Physician's Global Assessment of Arthritis, HAQ-DI and hsCRP; • The proportion of participants achieving a Psoriasis Area and Severity Index 75/90/100 (PASI75/90/100) response; • Change from baseline in the enthesitis score (using the SPARCC Enthesitis Index and Leeds Enthesitis Index); • Change from baseline in the Dactylitis Severity Score; • Change from baseline in the NAPSI Score.
	To evaluate the improvement in patient reported outcome measures related PsA Core Domain Set in PF-06700841 treated participants.	Assessed at all treatment timepoints: • Change from baseline in the PGJS-VAS; • Change from baseline in the FACIT-Fatigue; Assessed at all treatment timepoints except Week 2: • Change from baseline in the SF-36 Version 2, Acute.
	To evaluate the improvement in additional composite outcome measures in PF-06700841 treated participants.	Assessed at all treatment timepoints except Week 2: • The proportion of participants achieving MDA and VLDA response; • Change from baseline in the DAREA/DAPSA; • The proportion of participants achieving the PsARC; • Change from baseline in the PASDAS.
Safety	To evaluate the safety and tolerability of PF-06700841.	• Incidence of AEs, SAEs and SIEs, withdrawals due to AEs and SAEs, and laboratory abnormalities, changes in vital signs, and ECG findings throughout the study.
Key Tertiary/Exploratory		
Efficacy	To evaluate the improvement in additional patient reported outcome measures related PsA Core Domain Set in PF-06700841 treated participants.	Assessed at all treatment timepoints: • Change from baseline in the BASDAI; • Change from baseline in the PsAID-12; • Change from baseline in the ISI; • Change from baseline in the DLQI.
	To evaluate other measures of clinical response.	Assessed at all treatment timepoints: • Change from baseline in the PASI and PASI component scores; • Change from baseline in the DAS28-3(CRP); • The proportion of participants with dactylitis (Presence

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Table S1. Study Objectives and Endpoints

Type	Objective	Endpoint
		of dactylitis); • The proportion of participants with enthesitis (Presence of enthesitis); • Change from baseline in the PGA-PsO response; • Change from baseline in the PsAJAI.
PK	To characterize pharmacokinetics of PF-06700841 in participants with active PsA.	• Plasma concentration of PF-06700841 from blood sample at 0 (pre-dose), 0.5, 1, 2 and 4 hours post-dose at Week 2 visit, and also at Week 4, 8, 12, 16, 20, 36 and 52 (at any time during the visit).

Abbreviations: PsA = Psoriatic Arthritis, ACR = American College of Rheumatology; TNF = tumor necrosis factor; HAQ-DI = Health Assessment Questionnaire disability index; hsCRP = high sensitivity C-reactive protein; PASI = Psoriasis Area and Severity Index; SPARCC = Spondyloarthritis Research Consortium of Canada; NAPSI = Nail Psoriasis Severity Index, PGJS-VAS = Patient's Global Joint and Skin Assessment-Visual Analog Scale; FACIT-Fatigue = Functional Assessment of Chronic Illness Therapy-Fatigue; SF-36 = Short Form-36 health survey; MDA = Minimal Disease Activity; VLDA = Very Low Disease Activity; DAREA/DAPSA = Disease Activity Index for Reactive Arthritis/PsA; PsARC = Psoriatic Arthritis Response Criteria; PASDAS = Psoriatic Arthritis Disease Activity Score; AE = adverse event; SAE = serious adverse event; SIE = serious infectious event; ECG = electrocardiogram; BASDAI = Bath Ankylosing Spondylitis Disease Assessment Index; PsAID-12 = Psoriatic Arthritis Impact of Disease 12-item; ISI = Itch Severity Item; DLQI = Dermatology Life Quality Index; DAS28 = Disease Activity Score-28; PGA-PsO = Physician's Global Assessment of Psoriasis; PsAJAI = Psoriatic Arthritis Joint Activity Index; PK = pharmacokinetics.

METHODS

Study Design: This was a Phase 2b, randomized, double-blind, placebo-controlled, dose-ranging, parallel treatment group, efficacy and safety study designed to characterize the dose response of PF-06700841 in participants with active Psoriatic Arthritis (PsA).

The study consisted of a screening period of up to 5 weeks, a double-blind treatment period of 52 weeks, including a placebo-controlled phase from Day 1 to Week 16, an extended active treatment phase from Week 17 through Week 52, and a safety follow-up period of 4 weeks from last dose of study drug to last study visit (Figure S1).

Approximately 196 participants were planned to be randomized in a 4:4:1:1:2:2 ratio to one of the 6 parallel treatment sequences as listed in Table S2. Some participants (up to 30% of study population) may have been previously treated with no more than one TNFi (tumor necrosis factor inhibitor). Randomization was stratified by prior TNFi exposure. Starting after the Week 16 visit, participants receiving the 60 mg once daily (QD) dose or the 30 mg QD dose continued on their initial dose; while all other participants, including those from the 10 mg QD dose arm and placebo arm, were reassigned to receive either the 60 mg QD dose or 30 mg QD dose until Week 52, as predetermined at randomization.

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Figure S1. Schematic of Study Design

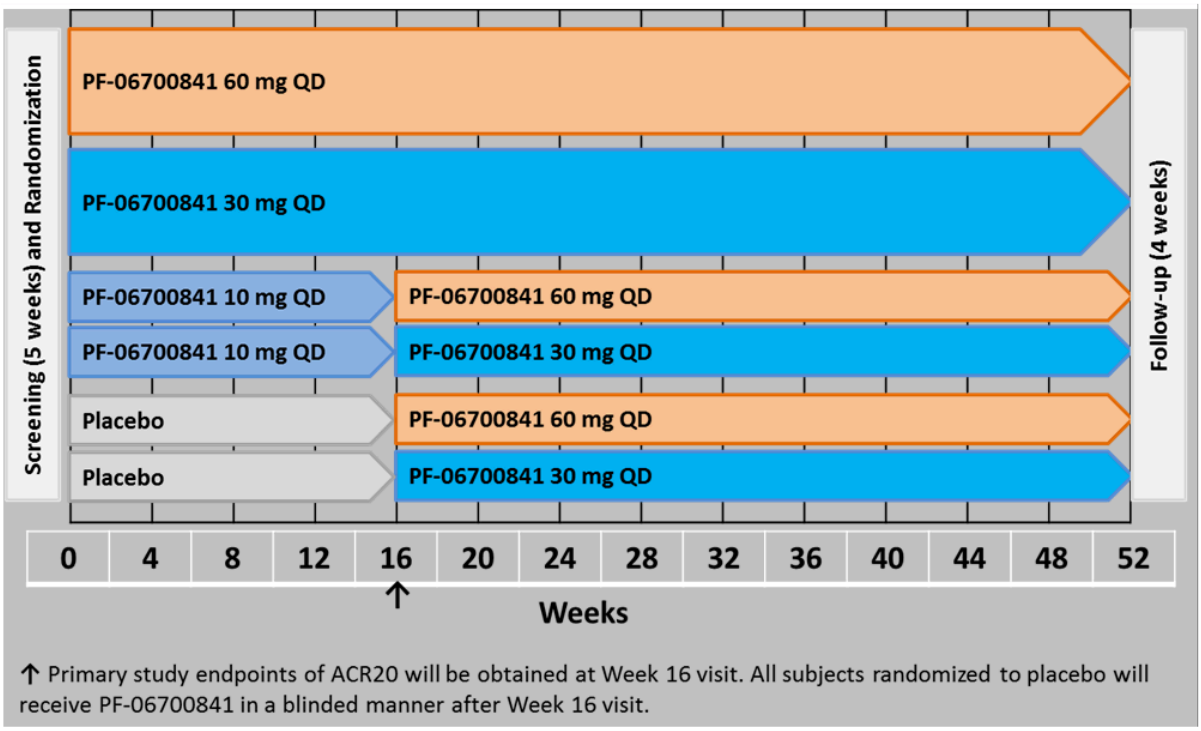

Table S2. Treatment Sequence

Treatment Sequence	Treatment	Number of Participants
A	PF-06700841 60 mg QD	56
B	PF-06700841 30 mg QD	56
C[1]	PF-06700841 10 mg QD first & advance to 60 mg QD after the Week 16 visit	14
D[2]	PF-06700841 10 mg QD first & advance to 30 mg QD after the Week 16 visit	14
E[1]	Placebo QD first & advance to PF-06700841 60 mg QD after the Week 16 visit	28
F[2]	Placebo QD first & advance to PF-06700841 30 mg QD after the Week 16 visit	28

1. Starting after the Week 16 visit, participants randomized to treatment sequences C or E received PF-06700841 60 mg QD in a blinded fashion for the remainder of the study.
2. Starting after the Week 16 visit, participants randomized to treatment sequences D or F received PF-06700841 30 mg QD in a blinded fashion for the remainder of the study.

Diagnosis and Main Criteria for Inclusion: The study population consisted of active PsA participants at least 18 years of age, Rheumatoid factor (RF) and cyclic citrullinated peptide (CCP) antibodies negative, fulfilling the ClASsification criteria for Psoriatic ARthritis (CASPAR) criteria, and having active disease despite previous or current nonsteroidal anti-

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inflammatory drug (NSAID), or corticosteroids, or disease-modifying antirheumatic drug (DMARD) and/or TNF inhibitors therapy.

Study Treatment: Participants received the blinded PF-06700841 oral tablets 5 mg or 25 mg or their matching placebos (Table S3) as QD dosing according to their assigned treatment regimen throughout the study treatment period (from Study Day 1 through Week 52).

Table S3. Investigational Product Description

Investigational Product Description	Vendor Lot Number	Pfizer Lot Number	Strength/Potency	Dosage Form Capsule
Placebo 10mm Tablet (2:1, MCC: Lactose)	N/A	16-004787	0 mg	Tablet
PF-06700841-15 5 mg Round White to Off-White Tablet	N/A	18-000453	5 mg	Tablet
PF-06700841-15 25 mg Round White to Off-White Tablet	N/A	18-000455	25 mg	Tablet
Placebo 10mm Tablet (2:1, MCC:Lactose)	668P-1810-E401	18-000767	0 mg	Tablet
PF-06700841-15 5 mg Round White to Off-White Tablet	N/A	19-000338	5 mg	Tablet
PF-06700841-15 25 mg Round White to Off-White Tablet	N/A	19-000340	25 mg	Tablet
PF-06700841-15 5 mg Round White to Off-White Tablet	N/A	19-002282	5 mg	Tablet
PF-06700841-15 5 mg Round White to Off-White Tablet	N/A	19-002283	5 mg	Tablet

Abbreviation: N/A = not applicable.

Efficacy Evaluations:

Composite efficacy endpoints:

- American College of Rheumatology (ACR) response criteria: the ACR20 was calculated as a ≥20% improvement in tender and swollen joint counts and ≥20% improvement in 3 of the 5 remaining ACR-core set measures: patient and physician global assessments, pain, disability, and an acute-phase reactant. Similarly, ACR50, 70 and 90 were calculated with the respective percent improvement.

  The specific components of the ACR Assessments used in this study included tender/painful joint Count (TJC68), swollen joint count (SJC66), Patient's Assessment of Arthritis Pain (Visual Analog Scale [VAS]), Patient's Global Assessment of Arthritis (VAS), Physician's Global Assessment of Arthritis (VAS), C-Reactive Protein (CRP) and Health Assessment Questionnaire (HAQ) Disability Index (DI).

- Other composite efficacy endpoints included Minimal Disease Activity (MDA) and Very Low Disease Activity (VLDA) Score, Psoriatic Arthritis Disease Activity Score (PASDAS), Disease Activity Index for Reactive Arthritis/Psoriatic Arthritis

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(DAREA/DAPSA), Psoriatic Arthritis Response Criteria (PsARC), Disease Activity Score 28-3-CRP (DAS28-3-CRP) and Psoriatic Arthritis Joint Activity Index (PsAJAI)

Clinical dermatology assessments:

- PASI: The PASI score: PASI assessment was performed for PsA participant with Baseline psoriasis affecting ≥3% BSA to quantify the severity of a participant's psoriasis based on both lesion severity and the percentage of body surface area affected.

- Other clinical dermatology assessments included the evaluation of Plaque Psoriasis, Body surface area (BSA), Nail Psoriasis Severity Score (NAPSI) and Physician's Global Assessment of Psoriasis (PGA-PsO).

Additional clinical rheumatology assessments: Physician's Global Assessment of Psoriatic Arthritis, Dactylitis Assessment and Enthesitis Assessment (evaluated by the Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis Index and LEI).

Additional Patient Reported Outcomes (PROs): Patient's Global Joint and Skin Assessment-Visual Analog Scale (PGJS-VAS), Functional Assessment of Chronic Illness Therapy-Fatigue (FACIT-Fatigue), Short-Form-36 Health Survey (SF-36), Bath Ankylosing Spondylitis Disease Assessment Index (BASDAI), Psoriatic Arthritis Impact of Disease 12-item (PsAID-12), Itch Severity Item (ISI) and Dermatology Life Quality Index (DLQI).

Pharmacokinetic Evaluations: Blood samples were collected at 0 (pre-dose), 0.5, 1, 2 and 4 hours post-dose at Week 2 visit, and also at Week 4, 8, 12, 16, 20, 36 and 52 (at any time during the visit), for measurement of plasma concentrations of PF-06700841.

Safety Evaluations: Safety evaluations included monitoring of adverse events (AEs), serious adverse events (SAEs), serious infectious events (SIEs), withdrawals due to AEs and SAEs, laboratory abnormalities, changes in vital signs(pulse rate, blood pressure and temperature), electrocardiogram (ECG) findings, and events for adjudication/review committee submission.

Statistical Methods:

The population for analysis defined for the study are detailed in Table S4.

Table S4. Description of the Analysis Sets

Population	Description
Evaluable Population	All participants who were randomized to the study and received at least one dose of the randomized study treatment. The Evaluable Population is the primary efficacy analysis population. Participants were analyzed according to the randomized treatment group.
Safety Analysis Population	All participants who received at least 1 dose of the randomized study treatment. Participants were analyzed according to study treatment they actually received. A

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Table S4. Description of the Analysis Sets

Population	Description
	randomized but not treated participant was excluded from the safety analyses.
PK Concentration Population	All participants who received at least one dose of PF-06700841 and in whom at least 1 concentration value of was reported.

Analysis of Efficacy Endpoints:

In general, the data for all continuous efficacy endpoints were summarized by timepoint and treatment sequence group (or combined treatment sequence when appropriate) in tables containing descriptive statistics for baseline and change (or percent change) from baseline.

For all binary efficacy endpoint, data were summarized by treatment group and by visit in tabular and/or graphic format with descriptive statistics, including N (number of participants evaluable for the endpoint in the corresponding treatment group/visit), n (number of responders), response rates (%), standard errors of the response rate, and 95% confidence intervals (CIs). Treatment differences between each dose group of PF-06700841 and placebo were summarized by point estimates and two-sided 90% CIs.

Longitudinal continuous efficacy endpoints were analyzed in a repeated measure model; binary efficacy endpoints were summarized using normal approximation method, and Cochran-Mantel-Haenszel method adjusting for prior TNFi exposure when appropriate. For all of these endpoints, descriptive statistics were provided by study visit and treatment sequence, or combined when appropriate.

Particularly, secondary efficacy endpoints were tested hierarchically in Evaluable Population at the significance level of 10% (2-sided) in the order of PASI75→ACR50→PASI90→PASI100→HAQ-DI, for the treatment groups that were statistically significant different from placebo for the primary efficacy endpoint.

For analyses through the initial 16-week placebo-controlled period, participants were analyzed according to 4 treatment groups (placebo, PF-06700841 10 mg, 30 mg and 60 mg treatment group). Participants who received treatment sequence E and F were combined into a single placebo group and participants who received treatment sequence C and D were combined into a single PF-06700841 10 mg group (Table S2).

For analyses through the Follow-up Visit (Week 56), participants were analyzed according to the 6 randomized treatment groups included the placebo→PF-06700841 30 mg treatment group, placebo→PF-06700841 60 mg treatment group, PF-06700841 10 mg→30 mg treatment group, PF-06700841 10 mg→60 mg treatment group, PF-06700841 30 mg treatment group and PF-06700841 60 mg treatment group.

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Participants were also combined to 2 dose groups as the combined→PF-06700841 30 mg treatment group and the combined→PF-06700841 60 mg treatment group for the analysis of efficacy endpoints and certain safety endpoints at Week 52.

PK: PK concentrations were summarized and presented with descriptive statistics. Summary statistics of concentrations of PF-06700841 at nominal time of collection were calculated for each treatment group.

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

RESULTS

Participant Disposition and Demography: A total of 285 participants were screened from 47 sites in 11 countries, among whom 219 participants were randomized.

Of the 218 treated study participants, 203 (93.1%) participants completed the Week 16 visit, which were generally balanced among different treatment groups. Fifteen (6.9%) participants discontinued from the study before Week 16 due to withdrawal by participant (3.2%), AE (2.8%) and lack of efficacy (0.9%). A total of 168 participants (77.1%) completed the Week 52 visit: 78 in the combined→PF-06700841 60 mg treatment group and 90 in the combined→PF-06700841 30 mg treatment group. The most common reasons for discontinuation (> 2%) were AE (8.3%), withdrawal by participant (3.2%), and other (2.3%). A total of 197 participants (90.4%) completed the follow-up visit.

The 218 treated study participants consisted of 102 (46.8%) males and 116 (53.2%) females. The median age of participants was 48 years (ranged from 21 to 73 years). All the participants were White (Caucasian) except for 1 participant in the PF-06700841 60 mg treatment group who was Asian. Approximately 83% of participants were enrolled from four countries: Poland (80 participants, 36.7%), Czech Republic and Russia (37 participants each, 17.0%) and Bulgaria (27 participants, 12.4%). The median (range) weight and BMI were 82.0 (50 to 150) kg and 27.940 (18.16 to 48.47) kg/m^2, respectively.

A total of 153 participants had ongoing methotrexate treatment at baseline. Eighteen (18, 8.3%) participants had prior TNFi exposure. The median PsA disease duration was 3.850 years (ranged from 0.09 to 37.75 years), and 208 participants (95.4%) had ≥5 joints involved. The mean (SD) tender/painful and swollen joint counts for the overall population were 16.6 (10.21) and 9.8 (6.22). There were 111 participants (50.9%) with hsCRP >2.87 mg/L (ULN). The mean (SD) PASDAS and DAREA/DAPSA scores for the overall population were 5.621 (1.0106) and 38.180 (16.7904), respectively.

There were 141 participants (64.7%) who had baseline BSA ≥3% and PASI >0. A total of 63 participants (28.9%) had evidence of ongoing dactylitis with baseline Dactylitis Severity Score (DSS) >0, There were 132 participants (60.6%) who had baseline SPARCC enthesitis

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score >0 and 110 participants (50.5%) who had baseline LEI Score >0. All treated participants of the study were Rheumatoid Factor and anti-CCP negative.

Efficacy Results:

Primary Efficacy Endpoint: As early as Week 4, statistical separation from placebo was observed for the PF-06700841 30 mg and 60 mg treatment groups (2-sided p-value < 0.1). From Week 8 to Week 16, a dose-dependent increase of ACR20 response rate was observed. At Week 16, statistical significance was achieved in both PF-06700841 30 mg and 60 mg comparisons with placebo for the ACR20 response rate (Table S5).

Table S5. Normal Approximation to ACR20 Response Rates at Week 16 - Evaluable Population - Primary Analysis (Protocol B7931030)

							Difference from Placebo					
					95% Confidence Interval				90% Confidence Interval			
Analysis Visit	Treatment	N	n	Response Rate (%)	Standard Error (%)	Lower (%)	Upper (%)	Difference (%)	Standard Error (%)	Lower (%)	Upper (%)	2-sided P-value	2-sided Adjusted P-value
Week 16	Placebo	67	29	43.28	6.05	31.42	55.15						
	PF-06700841 10 mg QD	31	20	64.52	8.59	47.67	81.36	21.23	10.51	3.94	38.52	0.0434	0.1172
	PF-06700841 30 mg QD	60	40	66.67	6.09	54.74	78.59	23.38	8.58	9.26	37.50	0.0064	0.0197
	PF-06700841 60 mg QD	59	44	74.58	5.67	63.47	85.69	31.29	8.29	17.65	44.93	0.0002	0.0006

N: number of subjects evaluable at each visit. n: number of responders. Response rates were based on N.
95% CIs, Two-sided 90% CIs and Two-sided p-value were based on the normal approximation for binomial proportions.
Missing response not due to COVID-19 was imputed as non-response.
Two-sided adjusted p-value was based on Dunnett's method.
PFIZER CONFIDENTIAL SDTM Creation: 20FEB2021 (09:40) Source Data: adac Table Generation: 21FEB2021 (20:58)
Output File: ./nda1_cdisc/B7931030/adac_acr20_s001
Table 14.2.1.1.1.1 PF-06700841 is for Pfizer internal use.

Hierarchical Testing Results: The secondary endpoints were tested hierarchically in the order of PASI75→ACR50→PASI90→PASI100→HAQ-DI under the significance level of 2-sided p-value < 0.1 at Week 16. As the PF-06700841 10 mg group was not tested as significant in

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the primary endpoint, formal testing on secondary endpoints was only performed for the other 2 dose groups (30 mg and 60 mg) of PF-06700841 compared with placebo (Table S6).

Table S6. Hierarchical Testing Results (Week 16)

Secondary Endpoint	Treatment Comparisons (Y/N, p-value)		
	PF-06700841 10 mg versus Placebo	PF-06700841 30 mg versus Placebo	PF-06700841 60 mg versus Placebo
PASI75	NA*	Y (0.0008)	Y (<0.0001)
ACR50	NA*	Y (<0.0001)	Y (<0.0001)
PASI90	NA*	Y (0.0204)	Y (<0.0001)
PASI100	NA*	N (0.4473)	Y (0.0036)
HAQ-DI	NA*	NA*	Y (<0.0001)

* Not formally tested due to non-significant testing result in the previous endpoint in the pre-defined hierarchical testing sequence (ACR20→PASI75→ACR50→PASI90→PASI100→HAQ-DI).

For ACR50, PASI75 and PASI90 response rates at Week 16, statistical significance was achieved in both PF-06700841 30 mg and 60 mg comparisons with placebo. For PASI100 and HAQ-DI response rates at Week 16, statistical significance was achieved in PF-06700841 60 mg comparison with placebo.

Other Secondary Efficacy Endpoints:

Proportion of Participants Achieving an ACR20/50/70 Response at All Treatment Timepoints: The TNFi naive subpopulation (91.7% of the overall population) in all active treatment groups showed significantly higher ACR20 response rate at Week 16 compared to the placebo group. Significant differences from placebo in ACR50/70 responses were observed in both PF-06700841 30 mg and 60 mg treatment groups at Week 16

The mean ACR20 responses were generally stable between Week 20 and Week 52, with a small decline between Weeks 44 and 52. The mean ACR50 response rates plateaued around Week 36 for most PF-06700841 treatment groups and remained stable through Week 52. The mean ACR70 responses demonstrated maximal effects by Week 36-44 across all treatment groups, including participants receiving the placebo or PF-06700841 10 mg dose.

At Week 52, similar ACR20/70 response rates were observed in the combined→PF-06700841 30 mg treatment group (ACR20: 67.59%; ACR70: 41.67%) and combined→PF-06700841 60 mg treatment group (ACR20: 60.91%; ACR70: 36.36%). The ACR50 response rate in combined→PF-06700841 30 mg treatment group (54.63%) was numerically higher than that of combined→PF-06700841 60 mg treatment group (44.55%).

ACR Response Criteria Components Change Over Time: At Week 16, PF-06700841 10 mg treatment group showed significant improvement (2-sided p-value < 0.01) in ACR response criteria components of patient's global assessment of arthritis and physician's global assessment of arthritis; PF-06700841 30 mg treatment group showed significant improvement in ACR response criteria components of patient's assessment of arthritis pain,

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patient's global assessment of arthritis, physician's global assessment of arthritis and hsCRP; PF-06700841 60 mg treatment group showed significant improvement in all ACR response criteria components (tender/painful joint count, swollen joint count, patient's assessment of arthritis pain, patient's global assessment of arthritis, physician's global assessment of arthritis, HAO-DI and hsCRP [2-sided p-value: 0.0155]). The improvements in the ACR response criteria components of patient's global assessment of arthritis and physician's global assessment of arthritis were significant across all these 3 doses. In general, ACR response criteria components continued to improve through Week 52.

Proportion of Participants Achieving an PASI75/90/100 Response at All Treatment Timepoints: The separations from placebo in PASI75/90 responses were observed in the PF-06700841 30 mg and 60 mg treatment groups early at Week 4 or Week 8 (2-sided p-value < 0.1). The separations from placebo in PASI100 responses were observed in the PF-06700841 60 mg treatment group early at Week 8

The mean PASI75 responses plateaued for the PF-06700841 60 mg treatment group around Week 20, and generally increased for all other treatment groups through Week 36-44 followed by a plateau through Week 52. The mean PASI90 responses for most treatment groups continued to increase through Week 36-44, followed by a plateau through Week 52. The mean PASI100 response generally increased through Week 20-28 and then plateaued through Week 52 except for the placebo→PF-06700841 30 mg treatment group which continued to increase through Week 52.

At Week 52, similar PASI75/100 responses were observed in combined→PF-06700841 30 mg treatment group (PASI75: 64.18%; PASI100: 38.81%) and combined→PF-06700841 60 mg treatment group (PASI75: 60.81%; PASI100: 36.49%). Numerically higher PASI90 response was observed in combined→PF-06700841 30 mg treatment group (53.73%) when compared with combined→PF-06700841 60 mg treatment group at Week 52 (45.95%).

Proportion of Participants Achieving MDA Response: Significant differences versus placebo in MDA response rate were observed in both PF-06700841 30 mg and 60 mg treatment groups at Week 16 (2-sided p-value < 0.01) as well as in the PF 06700841 10 mg treatment group (2-sided p-value: 0.0268). The proportions of participants achieving MDA at Week 16 were 2.99%, 19.35%, 35.00% and 35.59% for the placebo, PF-06700841 10 mg, 30 mg and 60 mg treatment groups, respectively. In general, MDA responses increased across all treatment groups between Week 16 and Week 36, with response generally stabilized between Week 36-52. A decrease between Week 36 and Week 52 was observed for the PF-06700841 10 mg→30 mg treatment group and PF-06700841 10 mg→60 mg treatment group. At Week 52, similar MDA response rates were observed in combined→PF-06700841 30 mg treatment group and combined→PF-06700841 60 mg treatment group (46.30% and 42.73%, respectively).

Proportion of Participants Achieving VLDA Response: Significant difference versus placebo in VLDA response rate was not observed in any PF-06700841 treatment group at Week 16.

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VLDA response rates in all treatment groups continued to increase through Week 52. At Week 52, similar VLDA response rates were observed between combined→PF-06700841 30 mg treatment group and combined→PF-06700841 60 mg treatment group (17.59% and 18.18%, respectively).

Enthesitis Score Change Over Time Measured by SPARCC (in Participants with Baseline SPARCC Enthesitis Index Score>0): The mean SPARCC enthesitis index scores at baseline were balanced across all treatment groups (ranged from 3.4 to 4.0). At Week 16, significant improvement in enthesitis scores measured by SPARCC was not observed in any PF-06700841 treatment group when compared with the placebo. Mean SPARCC enthesitis index in all treatment groups continued to decrease through Week 52. At Week 52, both combined→PF-06700841 30 mg treatment group and combined→PF-06700841 60 mg treatment group demonstrated similar decrease from baseline in SPARCC enthesitis index (mean [standard deviation]: -2.6 [2.33] and -3.1 [2.48], respectively).

Enthesitis Score Change Over Time Measured by LEI (in Participants with Baseline LEI Score>0): The mean LEI scores at baseline were balanced across all treatment groups (ranged from 2.0 to 2.2). At Week 16, significant improvement in enthesitis scores measured by LEI was not observed in any PF-06700841 treatment group when compared with the placebo. Mean LEI score in all treatment groups continued to decrease through Week 52. At Week 52, both combined→PF-06700841 30 mg treatment group and combined→PF-06700841 60 mg treatment group showed similar change from baseline in LEI (mean [standard deviation]: -1.6 [1.41] and -1.8 [1.28], respectively).

Dactylitis Severity Score (DSS) Change Over Time (in Participants with Baseline DSS>0): At baseline, a numerically higher mean DSS (6.8) was observed in the placebo group when compared with other treatment groups (ranged from 4.3 to 5.4). At Week 16, significant improvements in DSS were not observed in any PF-06700841 treatment group when compared with the placebo. The mean DSS in all treatment groups continued to improve through Week 52. At Week 52, dactylitis (DSS >0) was present in 1 participant in the combined→PF-06700841 60 mg treatment group, and no participants in the combined→PF-06700841 30 mg treatment group. The mean changes from baseline (standard deviation) in DSS were -5.1 (5.12) and -5.1 (4.41) for the combined→PF-06700841 30 mg treatment group and the combined→PF-06700841 60 mg treatment group, respectively.

NAPSI Change Over Time (in Participants with Baseline NAPSI>0): A numerically higher mean baseline NAPSI score was observed in PF-06700841 60 mg treatment group (5.7) when compared with other treatment groups (ranged from 3.9 to 4.3). At Week 16, significant improvement in NAPSI was observed in PF-06700841 60 mg treatment groups when compared with the placebo (2-sided p-value <0.01). The mean NAPSI for all treatment groups improved through Week 52. At Week 52, the median changes from baseline (range) in NAPSI in the combined→PF-06700841 30 mg treatment group and combined→PF-06700841 60 mg treatment group were -2.0 (-10, 4) and -3.0 (-10, 0), respectively.

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Patient's Global Joint and Skin Assessment (PGJS)-VAS Change Over Time: PGJS-VAS was assessed in 3 categories: psoriasis and arthritis (global, PGA), arthritis only (PJA) and psoriasis only (PSA). For all the above categories (PGA, PJA and PSA), significant difference from placebo was observed in all PF-06700841 treatment groups at Week 16 (2-sided p-value < 0.01). The mean PGA, PJA and PSA rating in all treatment groups continued to decrease through Week 52. At Week 52, similar mean change from baseline in PGA, PJA and PSA rating were observed between combined→PF-06700841 30 mg treatment group (-34.5, -36.2 and -35.6 for PGA, PJA and PSA, respectively) and combined→PF-06700841 60 mg treatment group (-35.4, -36.9 and -40.6 for PGA, PJA and PSA, respectively).

FACIT-Fatigue Change Over Time: The mean baseline FACIT-Fatigue total scores were similar across all treatment groups (ranged from 28.1 to 31.7). At Week 16, significant improvement in FACIT-Fatigue was observed in PF-06700841 30 mg treatment group when compared with the placebo (2-sided p-value: 0.0143). The mean FACIT-Fatigue total scores in all treatment groups continued to improve through Week 52. At Week 52, the median change from baseline (range) in FACIT-Fatigue for combined→PF-06700841 30 mg treatment group and combined→PF-06700841 60 mg treatment group was similar (9.5 [-8, 39] and 8.0 [-7, 27], respectively).

SF-36 Change Over Time: The SF-36 scores are summarized as physical and mental component scores (PCS and MCS).

For SF-36 PCS, the mean values at baseline were generally balanced across all treatment groups (ranged from 34.74 to 38.87). The significant differences versus placebo were observed in PF-06700841 30 mg and 60 mg treatment groups at Week 16 (2-sided p-value: <0.0001 and = 0.0001, respectively). The mean SF-36 PCS in all treatment groups continued to improve through Week 52. At Week 52, the median changes from baseline (range) in the rating of SF-36 PCS were 8.82 (-8.7, 31.7) and 5.88 (-24.5, 26.0) in the combined→PF-06700841 30 mg treatment group and combined→PF-06700841 60 mg treatment group, respectively.

For SF-36 MCS, the mean values at baseline were generally balanced across all treatment groups (ranged from 41.72 to 43.73). Significant difference versus placebo was not observed in PF-06700841 treatment groups at Week 16. The mean SF-36 MCS in all treatment groups continued to improve through Week 52. At Week 52, the median changes from baseline (range) in the rating of SF-36 MCS were 4.21 (-23.3, 35.1) and 3.95 (-22.1, 25.9) in the combined→PF-06700841 30 mg treatment group and combined→PF-06700841 60 mg treatment group, respectively.

PASDAS Change Over Time: The mean PASDAS scores at baseline were balanced across all treatment groups (ranged from 5.403 to 5.721). At Week 16, the least squares (LS) mean of change from baseline in PASDAS was -0.90, -1.86, -2.20 and -2.35 for the placebo, PF-06700841 10 mg, 30 mg and 60 mg treatment groups, respectively. All PF-06700841

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treatment groups showed a dose-dependent and clinically significant improvement in PASDAS response rate (2-sided p-value: 0.0002, <0.0001 and <0.0001 in the PF-06700841 10 mg, 30 mg and 60 mg treatment groups, respectively). The mean PASDAS continued to decrease in all treatment groups through Week 52. At Week 52, both combined→PF-06700841 30 mg treatment group and combined→PF-06700841 60 mg treatment group demonstrated similar changes from baseline in PASDAS (median [range]: -2.93 [-8.0, -0.1] and -3.06 [-5.7, 0.5], respectively).

DAREA/DAPSA Change Over Time: At baseline, a balanced mean DAREA/DAPSA across all treatment groups was observed (ranged from 37.188 to 39.888). At Week 16, significant differences versus placebo in change from baseline in DAREA/DAPSA were observed in all PF-06700841 treatment groups (2-sided p-value < 0.001). The mean DAREA/DAPSA continued to decrease in all treatment groups through Week 52. At Week 52, the median changes from baseline (range) in DAREA/DAPSA for combined→PF-06700841 30 mg treatment group and combined→PF-06700841 60 mg treatment group were -24.16 (-84.1, 1.0) and -28.36 (-63.7, 6.7), respectively.

Proportion of Participants Achieving the PsARC: The mean PsARC response rate at baseline was numerically lower in the placebo group (23.88%) when compared with other treatment groups (ranged from 45.16% to 55.00%). At Week 16, both PF-06700841 30 mg and 60 mg treatment groups showed significant improvement of PsARC response rate when compared with the placebo. PsARC response rates for all treatment groups continued to increase through Week 36, followed by a decline between Weeks 36 and 52. At Week 52, PsARC response rates were 68.52% [95% CI: 59.76%, 77.28%] and 60.00% [95% CI: 50.85%, 69.15%] in the combined→PF-06700841 30 mg treatment group and combined→PF-06700841 60 mg treatment group, respectively.

Summary of Exploratory Efficacy Results:

The exploratory endpoints assessed during the study included the proportions of participants with dactylitis and with enthesitis (measured by both SPARCC and LEI) as well as the changes in PsAID-12, DLQI, BASDAI, ISI, BSA, DAS28-3-CRP, PsAJAI, PGA-PsO, PASI and PASI component scores.

At Week 16, significant improvement was not observed in PF-06700841 30 mg comparison with placebo for dactylitis or enthesitis presence rate; significant improvement was observed in PF-06700841 60 mg comparisons with placebo for dactylitis presence rate. The dactylitis presence rates in all treatment groups were mostly resolved between Week 36 and Week 52 while enthesitis presence rates (measured by either SPARCC or LEI) continued to decrease through Week 52.

At Week 16, significant improvements in PsAID-12, DLQI, BASDAI, ISI, PASI/PASI component scores, PGA-PsO DAS28-3-CRP and PsAJAI were observed in both PF-06700841 30 mg and 60 mg treatment groups. At Week 52, the combined→PF-06700841

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30 mg and combined→PF-06700841 60 mg treatment groups demonstrated similar changes from baseline in these endpoints.

Pharmacokinetic Results:

A dose dependent increase of PF-06700841 plasma concentration was observed across PF-06700841 10 mg to 60 mg QD doses with the maximum mean plasma concentration observed at 1-hour post-dose at Week 2 when serial PK samples were collected up to 4 hours post-dose. The mean plasma concentrations observed in this study were in line with PK data observed in healthy volunteers, alopecia areata and psoriasis patients following the same doses.

After Week 16, for participants who switched PF-06700841 doses (in the placebo→PF-06700841 30 mg treatment group, placebo→PF-06700841 60 mg treatment group, PF-06700841 10 mg→30 mg treatment group and PF-06700841 10 mg→60 mg treatment group), the expected PF-06700841 plasma concentrations at the respective doses were observed at Weeks 20, 36 and 52.

Safety Results:

AEs, SAEs and SIEs:

All AEs described in this Synopsis were treatment-emergent unless otherwise specified.

Up to Week 16: A total of 119 participants reported 257 AEs during the placebo-controlled period, 65 of the AEs were characterized by the investigator as treatment-related. The majority of AEs were mild or moderate in severity. The percentages of participants with all-causality (treatment-related) AEs were 47.8% (13.4%) in the placebo group, 45.2% (19.4%) in the PF-06700841 10 mg treatment group, 55.0% (20.0%) in the PF-06700841 30 mg treatment group and 66.7% (25.0%) in the PF-06700841 60 mg treatment group. The top 4 SOCs containing the highest percentage of participants experiencing all-causality AEs were: INFECTIONS AND INFESTATIONS (30.7%), followed by INVESTIGATIONS (14.2%) and GASTROINTESTINAL DISORDERS (11.0%) and NERVOUS SYSTEM DISORDERS (8.3%). Six (6) all-causality SAE cases (6 events) were reported in 5 participants (2.3%). Two (2) participants experienced SAEs due to serious infections including Otitis media acute and Appendicitis respectively.

During the whole study (inclusive of the 16-week placebo-controlled period): A total of 469 AEs were reported during the study, of which 108 were characterized by the investigator as treatment-related. The percentages of participants with all-causality AEs were similar across all 6 treatment groups (ranged from 62.5% to 76.7%), and between Combined→PF-06700841 30 mg treatment group (74.1%) and Combined→PF-06700841 60 mg treatment group (72.7%). The majority of AEs were mild or moderate in severity over the whole study. Overall, The top 5 SOCs containing the highest percentage of participants experiencing all-causality AEs were: INFECTIONS AND INFESTATIONS (45.0%),

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followed by INVESTIGATIONS (23.9%) and GASTROINTESTINAL DISORDERS (16.1%), NERVOUS SYSTEM DISORDERS (11.9%), and MUSCULOSKELETAL AND CONNECTIVE TISSUE DISORDERS (11.0%).

Herpes zoster (One Varicella event [SAE] included) was reported in 4 participants and Herpes simplex was reported in 1 participant. Additionally, Herpes virus infection was reported in 2 participants and Oral herpes was reported in 6 participants. All these events (except for the SAE of Varicella) were mild or moderate in severity and did not appear to be dose-related. There were 2 adjudicated opportunistic infection events during the study (Herpes zoster and Varicella). Both events were considered not related to the study drug

A total of 15 all-causality SAE cases were reported in 12 participants (5.5%) during the study, of which 3 SAE cases were considered treatment-related. Between Week 16 and Week 52, there were 4 participants who developed serious infections including Pneumonia viral, Pneumonia, Varicella (which resulted in permanent withdrawal from the study treatment) and COVID-19 pneumonia (which resulted in permanent withdrawal from the study treatment).

There were no deaths or pregnancies reported during the study. There were no major adverse cardiovascular events or venous thromboembolic events reported during the study.

Laboratory Values:

Up to Week 16, there were 47 (70.1%) participants in the placebo group who reported laboratory abnormalities, compared with 25 (80.6%), 47 (79.7%) and 50 (83.3%) participants in the PF-06700841 10 mg, 30 mg and 60 mg treatment groups, respectively. Up to Week 52, the number of laboratory abnormalities was generally similar across all treatment groups. There were no cases of Hy's Law reported during the study.

During the 16-week placebo-controlled period, a dose-dependent decrease was observed in mean hemoglobin values, and dose-dependent increases were observed in mean alanine minotransferase (ALT) and aspartate aminotransferase (AST) values. These changes in hemoglobin, ALT, AST were continuously observed throughout the study. The dose-dependent increases in ALT and AST were not associated with evidence of drug-induced liver injury or Hy's Law, and were consistent with changes observed in the Janus Kinase (JAK) inhibitor class. The decrease in hemoglobin level was most pronounced at the highest dose of PF-06700841 but was not associated with the incidence of hemoglobin related AEs (i.e., Anaemia) reported during the study.

Other Safety Evaluations: In general, there were no clinically significant findings observed on ECG parameters or vital signs.

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Conclusions:

PF-06700841 is efficacious in active PsA as demonstrated by the clinical effect observed in the primary endpoint (ACR20) and multiple secondary endpoints that include joint (ACR20/50/70, MDA) and skin metrics (PASI75/90/100). At Week 16, PF-06700841 30 mg and 60 mg treatment groups showed significant improvement in ACR20/50/70, PASI75/90 and MDA when compared with the placebo group.

Clinical effect of PF-06700841 (both 30 mg and 60 mg doses) were also observed at Week 16 across both clinical rheumatology (Physician's Global Assessment of Arthritis) and dermatology domains (PASI component scores and PGA-PsO), as well as PROs (Patient's Assessment of Arthritis Pain, Patient's Global Assessment of Arthritis, PGJS-VAS, SF-36 physical components scores, PsAID-12, DLQI, BASDAI and ISI) and additional composite efficacy endpoints (PASDAS, DAREA/DAPSA, PsARC, DAS28-3-CRP and PsAJAI).

The dose dependent trend in efficacy endpoints was apparent during the placebo controlled period (up to Week 16), most notably in the skin endpoints, but was not apparent up to Week 52 where the numerically higher responses for multiple efficacy endpoints were observed in the combined→PF-06700841 30 mg treatment group. The lower efficacy in PF-06700841 60 mg dose at Week 52 may be related to participant discontinuations from various safety events after Week 16.

PF-06700841 demonstrated an acceptable safety and tolerability profile in participants with active PsA based on the analysis of AEs, SAEs, SIEs and AEs leading to permanent discontinuation reported during the study. The safety profile of PF-06700841 is consistent with what has been observed for other JAK inhibitors, including dose dependent effects on hematology (decrease in hemoglobin), liver function tests (increases in AST and ALT), increases in creatine kinase (CK), Herpes zoster infections and other serious infection events.