Official Title of Study: A Phase 3, Randomized, Double-blind, Placebo-controlled Study to Evaluate the Efficacy and Safety of Deucravacitinib in Participants with Active Psoriatic Arthritis who are Naïve to Biologic Disease-modifying Anti-rheumatic Drugs

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CLINICAL PROTOCOL IM011054

A Phase 3, Randomized, Double-blind, Placebo-controlled Study to Evaluate the Efficacy and Safety of Deucravacitinib in Participants with Active Psoriatic Arthritis who are Naïve to Biologic Disease-modifying Anti-rheumatic Drugs

Short Title:

Efficacy and Safety of Deucravacitinib Compared with Placebo in Participants with Active Psoriatic Arthritis (PsA) who are Naïve to Biologic Disease-modifying Anti-rheumatic Drugs

Protocol Amendment 02

Incorporates Administrative Letter 01 and 05

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DOCUMENT HISTORY

Document	Date of Issue	Summary of Change
Protocol Amendment 02	06-May-2024	The IM011054 protocol is being amended to [redacted] update it with language to comply with European Union regulations.
[redacted]		
Protocol Amendment 01	20-Mar-2022	[redacted]
Original Protocol	11-Mar-2021	Not applicable

OVERALL RATIONALE FOR PROTOCOL AMENDMENT 02:

The primary purpose of this global revised protocol is to provide clarifications in the protocol to aid sites and participants in the conduct of the study.

Key modifications and clarifications are summarized as follows:

[redacted]

- Analysis of safety and exploratory efficacy data beyond week 16 will also be conducted during this Week 16 database lock on any available data.

[redacted]

[redacted] and the text was updated to comply with European Union regulations.

[redacted] Key changes are summarized below.

This protocol amendment applies to all participants.

SUMMARY OF KEY CHANGES FOR PROTOCOL AMENDMENT 02		
Section Number & Title	**Description of Change**	**Brief Rationale**
Title page	Contact information of clinical scientists and clinical trial physician-medical monitors was updated.	To report important personnel changes.
Title page	Replaced the EUDRA CT number (2020-005097-10) with the EU CTR number (2023-506256-25-00).	To comply with European Union regulations.
Table 2-1: Screening Procedural Outline (IM011054) Table 2-2: Procedural Outline: Baseline through Week 16 (IM011054) Table 2-3: Procedural Outline: Week 20 through Week 56 (IM011054) [redacted] Section 9.4.2: Vital Signs	[redacted]	

SUMMARY OF KEY CHANGES FOR PROTOCOL AMENDMENT 02		
Section Number & Title	**Description of Change**	**Brief Rationale**
[redacted]		
Section 1: Synopsis Section 5.1: Overall Design Section 8.1: Discontinuation from Study Treatment	Clarified that participants will have no further study visits if they withdraw consent in addition to those who are lost to follow-up. Clarified the exception to the requirement, participants who request to withdraw at any time from the study are required to have an ET Visit and will be asked to complete a Safety Follow-up Visit 30 days following last dose of study treatment. The only exception to this requirement is when a participant withdraws consent or is lost to follow-up for all study procedures.	For clarification that both groups of participants (lost to follow-up or withdrew consent) are not required to complete further visits.
Table 2-1: Screening Procedural Outline (IM011054)	Added the following text to the Notes for the row, AE and SAE Assessment. "All non-serious AEs must be collected from the time of initiation of study treatment until discontinuation of study. All AEs related to SARS-CoV-2 must be collected from time of consent and continuously during the study including at the Safety Follow-up Visit(s). After the initial AE/SAE report, the investigator is required to proactively follow each participant at subsequent visits/contacts. All SAEs and non-serious AEs, including SARS-CoV-2, will be followed until resolution, until the condition stabilizes, until the event is otherwise explained, or until the participant is lost to follow-up."	Clarified that non-SARS-CoV-2 adverse events (AEs)/serious adverse events (SAEs) are also being collected in addition to those for severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) AEs/SAEs. This is for consistency in other tables in the protocol that contain the same wording and were previously updated.
Table 2-2: Procedural Outline: Baseline through Week 16 (IM011054) Table 2-3: Procedural Outline: Week 20 through Week 56 (IM011054) [redacted] Section 3.3: Benefit/Risk Assessment	Updated and clarified the text [redacted] In addition, the following text was added to Section 10.3: "Week 52 analyses will be conducted after the Week 56 database lock and will include an assessment of safety and efficacy at all available time points [redacted]	Clarified that the database lock mentioned in each section refers to the newly added Week 16 database lock.

SUMMARY OF KEY CHANGES FOR PROTOCOL AMENDMENT 02		
Section Number & Title	**Description of Change**	**Brief Rationale**
Section 5.1: Overall Design Section 7.1: Treatments Administered Section 7.3: Blinding for the 16-week Treatment Period Section 7.3.1: Maintaining the Blind Section 7.3.2: Circumstances for Unblinding Section 10.3: Statistical Analyses Section 10.3-1: Efficacy Analyses Section 10.3.2: Safety Analyses [redacted]		
Table 4-1: Objectives and Endpoints	[redacted]	
Table 4-1: Objectives and Endpoints [redacted]		
Section 5.3: End of Study Definition	Modified the definitions of "Completion of the double-blinded portion of the study" and "End of trial."	Adjusted to align with the new [redacted].
Section 6.4.1: Retesting During Screening or Lead-in Period	[redacted]	
Table 7-1: Study Treatments (Week 0 to Week 52) IM011054	Added the following footnote: "Blinded up to Week 56."	To align with updates in the protocol [redacted].
Section 7.3.2: Circumstances for Unblinding	Added the following text to Section 7.3.2. [redacted]	Adjusted to align with the new [redacted].
[redacted]		

SUMMARY OF KEY CHANGES FOR PROTOCOL AMENDMENT 02		
Section Number & Title	**Description of Change**	**Brief Rationale**
[redacted]		
Section 9.2.5 Regulatory Reporting Requirements for SAEs	Replaced reference to EU "Directive 2001/20/EC" by "Regulation 536/2014".	To comply with European Union regulations.
Appendix 2: Study Governance Considerations	[redacted]	
Appendix 20: Physician's Global Assessment of Fingernails (PGA-F Scoring)		
All	Minor formatting and typographical corrections.	To correct minor errors.

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1 SYNOPSIS

Protocol Title: A Phase 3, Randomized, Double-blind, Placebo-controlled Study to Evaluate the Efficacy and Safety of Deucravacitinib in Participants with Active Psoriatic Arthritis who are Naïve to Biologic Disease-modifying Anti-rheumatic Drugs

Short Title: Efficacy and Safety of Deucravacitinib Compared with Placebo in Participants with Active Psoriatic Arthritis (PsA) who are Naïve to Biologic Disease-modifying Anti-rheumatic Drugs

Study Phase: Phase 3

Rationale:

Deucravacitinib (BMS-986165) is being evaluated as a therapeutic option for the treatment of participants with psoriatic arthritis (PsA). This Phase 3 study is a part of development program for PsA and follows the Phase 2 study (IM011084) that has met its primary and key secondary objectives. The population for this Phase 3 study (IM011054) includes participants with prior exposure to conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs), and/or apremilast, and/or nonsteroidal anti-inflammatory drugs (NSAIDs), similar to the predominant patient population studied in a Phase 2 study.

In IM011084, 203 participants were randomized to: 6 mg deucravacitinib once daily (QD) (n = 66), 12 mg deucravacitinib QD (n = 70), and placebo (n = 67). The primary objective of dose-response relationship in American College of Rheumatology 20 (ACR 20) responses after 16 weeks of treatment was met ($p < 0.001$). In the 6 mg deucravacitinib QD group 52.9% of participants and in the 12 mg deucravacitinib QD group 62.7% of participants achieved ACR 20 responses versus 31.8% of participants in the placebo group ($p = 0.0134$ and $p = 0.004$, respectively).

The Phase 3 IM011054 study is designed to confirm the efficacy and safety of 6 mg deucravacitinib QD versus placebo in a larger PsA population and with a longer duration of treatment.

[redacted]

Study Population:

Male and female participants, ≥ 18 years of age (or local age of majority), with a diagnosis of PsA for ≥ 3 months and fulfilling Classification Criteria for Psoriatic Arthritis (CASPAR) at Screening, with an active plaque psoriasis (PsO) skin lesion(s) or documented medical history of plaque PsO, active arthritis (≥ 3 swollen joints and ≥ 3 tender joints in 66/68 joint count assessments), ≥ 1 PsA-related joint erosion in X-rays of hands and/or feet, and high-sensitivity C-reactive protein (hsCRP) concentration ≥ 3 mg/L will be recruited.

All participants must have had documented inadequate response, loss of response, or intolerance to at least 1 csDMARD, and/or apremilast, and/or NSAID given for the treatment of PsA. Participants will be allowed to continue on background medications (csDMARD, and/or NSAID, and/or glucocorticoids) during the study as specified by the inclusion criteria. Participants must NOT have had prior treatment with a biologic disease-modifying anti-rheumatic drug (bDMARD)

or a Janus kinase (JAK) inhibitor for PsA and/or PsO. Participants with nonplaque PsO (eg, guttate, pustular, erythrodermic or drug-induced PsO), and/or rheumatoid arthritis and/or other arthritides will not be eligible for the study.

Men and women ≥ 18 years of age (or local age of majority) must meet the following criteria for entry into the study.

Key Inclusion Criteria:

- **Signed Written Informed Consent**
  - Participants must be willing to participate in the study and sign the informed consent form.
- **Type of Participant and Target Disease Characteristics**
  - Participant has been diagnosed to have PsA (by any criteria) of at least 3 months duration at Screening.
  - Participant meets the CASPAR criteria at Screening.
  - Participant has active plaque psoriatic skin lesion(s) or documented medical history of plaque PsO at Screening.
  - Participant has active arthritis as shown by ≥ 3 swollen joints and ≥ 3 tender joints (66/68 joint counts) at Screening and Day 1.
  - Participant has ≥ 1 PsA-related hand and/or foot joint erosion on X-ray during Screening Period that is confirmed by central reading.
  - Participant has hsCRP ≥ 3 mg/L at Screening.
  - Participant has had documented inadequate response, loss of response, or intolerance to at least 1 of the following:
    - A csDMARD at maximally tolerated dose, and/or apremilast, after a minimum of 12 weeks duration of therapy given for the treatment of PsA
    - An NSAID after a minimum of 4 weeks duration of therapy given for the treatment of PsA, or participant has intolerance to those treatments in the opinion of the investigator
  - Concurrent use of 1 csDMARD, and/or NSAID, and/or oral glucocorticoid is permitted but not required during the study.
    - If such treatment was administered, then participants must meet the following requirements:
      - If on csDMARD (methotrexate [MTX], sulfasalazine [SSZ], leflunomide [LEF], hydroxychloroquine [HCQ]), the participant must have been on it for at least 12 weeks and be on a stable dose for at least 28 days prior to Day 1.
        - If on MTX, the route of administration and dose must be stable and the dose must be ≤ 25 mg/week.
        - If on SSZ, the dose must be ≤ 3 g/day.
        - If on HCQ, the dose must be ≤ 400 mg/day.
        - If on LEF, the dose must be ≤ 20 mg/day.

Note: If currently not on MTX, SSZ, or HCQ, the participant must have not received it for at least 28 days prior to Day 1. If currently not on LEF, the participant must not have received it for at least 12 weeks prior to Day 1.

- ♦ If on an NSAID, the participant must be on a stable dose for at least 14 days prior to Day 1.
- ♦ If on oral glucocorticoids, the participant must be on a stable dose of ≤ 10 mg/day prednisone equivalent for at least 28 days prior to Day 1.

Note: If currently not on oral glucocorticoids, the participant must not have received oral glucocorticoids within 28 days prior to Day 1.

– Concurrent permitted topical therapy for plaque PsO must be stable for at least 14 days prior to Day 1.

[redacted]

Key Exclusion Criteria:

- **Target Disease Exceptions**
  - Participant has nonplaque PsO (ie, guttate, pustular, erythrodermic or drug-induced PsO) at Screening or Day 1.
  - Participant has any other autoimmune condition such as systemic lupus erythematous, mixed connective tissue disease, multiple sclerosis, or vasculitis.
  - Participant has prior history of or current inflammatory joint disease other than PsA (eg, gout, reactive arthritis, rheumatoid arthritis, ankylosing spondylitis, Lyme disease).
  - Participant has active (ie, currently symptomatic) fibromyalgia whose symptoms or therapy will significantly impact the assessment of PsA disease manifestations and activity in the opinion of the investigator.
- **Concomitant Medication and Medical History/Concurrent Diseases**
  - Participant has received an approved or investigational biologic therapy for the treatment of PsA or PsO.
  - Participant has received a JAK inhibitor for the treatment of PsA and/or PsO.

Objectives and Endpoints:

Objective	Endpoint
Primary	
To compare the efficacy of deucravacitinib to placebo in the treatment of participants with active PsA	• Proportion of participants meeting ACR 20 response at Week 16
Key Secondary	
To compare the efficacy of deucravacitinib to placebo at Week 16 as assessed by DAS28-CRP	Change from baseline in DAS28-CRP score at Week 16
To compare the efficacy of deucravacitinib to placebo as assessed by HAQ-DI score at Week 16	Change from baseline in HAQ-DI score at Week 16
To compare the efficacy of deucravacitinib to placebo as assessed by PASI 75 response at Week 16	Proportion of participants meeting PASI 75 response at Week 16, in participants with at least 3% BSA involvement AND at least sPGA 2 at baseline
To compare the efficacy of deucravacitinib to placebo as assessed by SF-36 PCS score at Week 16	Change from baseline in the SF-36 PCS score at Week 16
To compare the efficacy of deucravacitinib to placebo in enthesitis resolution at Week 16	Proportion of participants meeting enthesitis resolution (score of 0) among participants with enthesitis at baseline by LEI at Week 16
To compare the efficacy of deucravacitinib to placebo in MDA response at Week 16	Proportion of participants meeting achievement of MDA where an MDA response is achievement of 5 of 7 following outcomes at Week 16: a) Tender joint count ≤ 1 b) Swollen joint count ≤ 1 c) PASI ≤ 1 or BSA ≤ 3% d) Patient assessment of PsA pain ≤ 15 e) Patient Global Assessment of PsA disease activity ≤ 20 f) HAQ-DI ≤ 0.5 g) Tender enthesial points ≤ 1
To compare the efficacy of deucravacitinib to placebo in FACIT-Fatigue score at Week 16	Change from baseline in FACIT-Fatigue score at Week 16

Objective	Endpoint
To compare the efficacy of deucravacitinib to placebo in dactylitis resolution at Week 16	Proportion of participants meeting dactylitis resolution at Week 16 among the participants with dactylitis at baseline, where resolution is defined as a tender dactylitis count of 0 in participants with a tender dactylitis count ≥ 1 at baseline
To compare the efficacy of deucravacitinib to placebo as assessed by structural damage at Week 16	Change from baseline in PsA-modified SvdH score at Week 16

Abbreviations: ACR, American College of Rheumatology; BSA, body surface area; DAS28-CRP, Disease Activity Score 28 with C-reactive protein; FACIT, Functional Assessment of Chronic Illness Therapy; HAQ-DI, Health Assessment Questionnaire - Disability Index; LEI, Leeds Enthesitis Index; MDA, minimal disease activity; PASI, Psoriasis Area and Severity Index; PCS, Physical Component Summary; PsA, psoriatic arthritis; SF-36, Short Form-36; sPGA, static Physician's Global Assessment; SvdH, Sharp-van der Heijde.

Overall Design:

This is a Phase 3, 52-week, multi-center, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of deucravacitinib versus placebo in participants with active PsA who are naïve to biologic therapy. [redacted]

- Screening Period (28 days)
- Treatment Period (52 weeks), comprised of
  - ♦ Placebo-controlled Treatment Period (16 weeks) (Week 0 to Week 16)
    [redacted]
- Safety Follow-up Period (30 days) (following last dose of investigational product [IP] unless participant has continued in study for 30 days or more after discontinuation of IP)

Participants will undergo screening evaluations to determine eligibility within 28 days prior to administration of investigational product. Following the screening process, eligible participants will be randomized in a 1:1 ratio to 1 of the following 2 treatment groups [redacted]

1. 6 mg deucravacitinib QD
2. Placebo

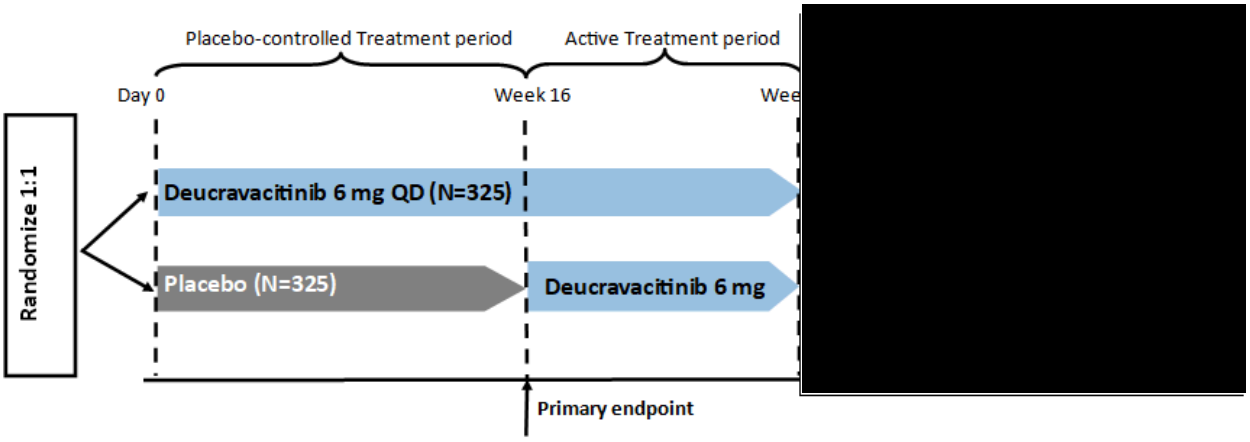
At Week 16, participants originally randomized to placebo will be reallocated in a blinded fashion (for the initially randomized treatment) to receive 6 mg deucravacitinib QD through Week 52.

Participants originally randomized to 6 mg deucravacitinib QD will continue to receive the same treatment and dose through Week 52.

[redacted]

The study design schematic is presented in Figure 1.

Figure 1: Study Design Schematic



Abbreviations: N, number; [redacted] QD, once daily.

Assessments for efficacy, safety, tolerability, quality of life, [redacted] will be performed at specified time points.

During the 52-week treatment period, participants who discontinue study treatment are required to complete an Early Termination (ET) Visit, a Safety Follow-up Visit 30 days following last dose of study treatment and should continue to be followed for protocol-specified follow-up procedures through Week 52. Only participants who are lost to follow-up or withdraw consent will have no further study visits.

[redacted]

Participants who request to withdraw at any time from the study are required to have an ET Visit and will be asked to complete a Safety Follow-up Visit 30 days following last dose of study treatment. The only exception to this requirement is when a participant withdraws consent or is lost to follow-up for all study procedures, including post-treatment study follow-up, or loses the

ability to consent freely (eg, is imprisoned or involuntarily incarcerated for the treatment of either a psychiatric or physical illness).

Number of Participants:

Approximately 650 participants will be randomized in a 1:1 ratio, in a blinded fashion, into 1 of 2 treatment arms, resulting in approximately 325 participants randomized to each treatment arm (6 mg deucravacitinib QD and placebo).

This sample size will provide > 99% power to detect a 20% treatment difference between 6 mg deucravacitinib QD and placebo at Week 16 for ACR 20 response assuming a response of 55% for 6 mg deucravacitinib QD and of 35% for placebo (2-sided alpha = 0.05, chi-square test).

The sample size of 325 participants treated with 6 mg deucravacitinib QD in this study (IM011054) was also chosen to provide, along with participants from other Phase 3 PsA studies with deucravacitinib, an adequate number of participants for the safety database for the PsA program. In addition, this sample size will also provide enough power for all key secondary endpoints (that will be tested in a testing strategy to control type I error).

The primary efficacy analysis model for the primary endpoint, ACR 20 response at Week 16 (responder/non-responder) will use a stratified Cochran-Mantel-Haenszel test stratified by the randomization stratification variables. Non-responder imputation will be used at Week 16 for participants who have a missing ACR 20 response at Week 16 or who discontinued treatment (for any reason) prior to Week 16.

Treatment Arms and Duration:

Participants will be randomized in a blinded fashion to receive deucravacitinib 6 mg QD or placebo in ratio of 1:1. While maintaining the blind, participants randomized to placebo will be reallocated at Week 16 to deucravacitinib 6 mg QD through Week 52. Participants originally randomized to deucravacitinib 6 mg QD on Day 1 will continue to receive the same treatment and dose through Week 52. [redacted]

Study Treatment:

Study Treatments (Week 0 to Week 52) IM011054		
Medication	**Potency**	**IP/Non-IP**
Deucravacitinib tablet	6 mg	IP
Placebo tablet	N/A	IP

Abbreviations: IP, investigational product; N/A, not applicable.

[redacted]

Data Monitoring Committee: Yes

An independent external Data Monitoring Committee (DMC) will be charged with monitoring accumulating data from the trial, as well as general aspects of trial conduct. The committee will meet periodically during the study to review aggregate analyses concerning efficacy and safety data from the trial. All members are selected with consideration for their respective expertise in the subject matter and/or in their experience in convening or participating in a DMC. Based on their overall benefit/risk evaluation, the DMC recommendations may include proceeding with the study per protocol, proceeding with the study with modifications, or study suspension. The scope, conduct, membership, processes, and accountabilities of the DMC are specified in the DMC Charter.

2 SCHEDULE OF ACTIVITIES

The schedule of activities are outlined in Table 2-1 (Screening procedural outline), Table 2-2 (procedural outline from baseline through Week 16), Table 2-3 (procedural outline from Week 20 through Week 56), [redacted]

Table 2-1: Screening Procedural Outline (IM011054)

Procedure	Screening Visit[a]	Notes
Eligibility Assessments		
Informed Consent	X	A participant is considered enrolled only when a protocol-specific informed consent is signed.
Inclusion/Exclusion Criteria	X	Includes CASPAR criteria (see Appendix 5), active arthritis (tender/swollen joints), and plaque PsO.
PsA History, Treatment	X	PsA history to include investigator assessment of the participant's phenotype as peripheral arthritis or peripheral plus psoriatic spondyloarthritis, including available evidence of disease (eg, clinical manifestations, imaging, etc). Type of PsA (polyarthritis, oligoarthritis, predominant distal interphalangeal joint involvement, predominant axial involvement, and arthritis mutilans). History of csDMARDs (eg, MTX) and systemic treatment of PsO and PsA. For each therapy, include length of time on treatment and reason(s) for discontinuation (eg, lack of efficacy, intolerance, AEs, loss of access to treatment) if applicable. Current use of topical treatments and therapeutic shampoos.
Other Medical History	X	See inclusion/exclusion criteria for complete eligibility criteria associated with medical history. Of note, participants need to be screened for any history of TB; any congenital or acquired immunodeficiency; any significant drug allergy such as anaphylaxis; and any cancer currently or in the previous 5 years. Investigators are encouraged to check whether participants have had preventive health measures such as cancer screening (eg, Pap smear, colonoscopy, mammograms) that are up-to-date according to local guidelines.
History of Tobacco Use	X	Include description of current tobacco use.
Other Prior and Concomitant Treatments	X	All medications for other conditions (includes prescription, over-the-counter medications, and herbal supplements).
Safety Assessments		

Table 2-1: Screening Procedural Outline (IM011054)

Procedure	Screening Visit[a]	Notes
Physical Examination	X	Complete physical examination. See Section 9.4.1.
Height and Body Weight	X	
Vital Signs	X	Includes body temperature, respiratory rate, and seated blood pressure and heart rate. See Section 9.4.2.
ECG	X	Single ECGs should be recorded. See Section 9.4.3.
Chest Imaging (eg, Chest X-ray)	X	Chest imaging is required if not performed within 6 months of Screening Visit. A copy of radiology report must be on file and reviewed by the investigator. See Section 9.4.6.
AE and SAE Assessment	X	All non-serious AEs must be collected from the time of initiation of study treatment until discontinuation of study. All AEs related to SARS-CoV-2 must be collected from time of consent and continuously during the study including at the Safety Follow-up Visit(s). After the initial AE/SAE report, the investigator is required to proactively follow each participant at subsequent visits/contacts. All SAEs and non-serious AEs, including SARS-CoV-2, will be followed until resolution, until the condition stabilizes, until the event is otherwise explained, or until the participant is lost to follow-up. SARS-CoV-2-related AEs/SAEs will be captured in specific CSP CRF pages in addition to AE/SAE pages where the event was originally reported.
Radiographic Assessment		
Radiographs of the Hands (Posteroanterior) and Feet (Anteroposterior)[a]	X	Confirmation of participant eligibility by central review prior to randomization with regard to the presence of at least 1 PsA-related hand and/or foot joint erosion. See Section 9.1.24.
Laboratory Tests		Includes blood and urine samples.
Hematology	X	CBC with differential. See Section 9.4.4.
Chemistry	X	See Section 9.4.4.
eGFR	X	See Section 9.4.5.
Urinalysis	X	See Section 9.4.4.

Table 2-1: Screening Procedural Outline (IM011054)

Procedure	Screening Visit[a]	Notes
Hemoglobin A1c	X	See Section 9.4.4.
TSH	X	See Section 9.4.4.
hsCRP	X	See Section 9.4.4.
Serology	X	Includes HCV antibody, HBsAg, HBsAb, HBcAb, and HIV antibodies. See Section 9.4.4.
TB Test	X	In accordance with QuantiFERON® TB Gold. See Section 6.2 and Section 9.4.6.
[redacted]		See Section 9.4.4.
Pregnancy Test	X	WOCBP only. See Section 9.4.4.
FSH	X	For post-menopausal women only. Serum FSH level will be determined to confirm menopausal status. See Section 9.4.4.
[redacted]		
Study Treatment		
IRT Enrollment	X	Enroll participant in the IRT system.

[a] Screening Visit window is within 28 days [redacted] prior to first investigational product treatment.

Abbreviations: AE, adverse event; CASPAR, Classification Criteria for Psoriatic Arthritis; CBC, complete blood count; CRF, case report form; csDMARD, conventional synthetic disease modifying anti-rheumatic drug; CSP, clinical safety program; ECG, electrocardiogram; eGFR, estimated glomerular filtration rate; FSH, follicle-stimulating hormone; HBcAb, hepatitis B core antibody; HBsAb, hepatitis B surface antibody; HBsAg, hepatitis B surface antigen; HCV, hepatitis C virus; HIV, human immunodeficiency virus; hsCRP, high-sensitivity C-reactive protein; [redacted] IRT, Interactive Response Technology; MTX, methotrexate; PsA, psoriatic arthritis; PsO, psoriasis; SAE, serious adverse event; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; TB, tuberculosis; TSH, thyroid-stimulating hormone; WOCBP, women of childbearing potential.

Table 2-2: Procedural Outline: Baseline through Week 16 (IM011054)

Procedure	D1	W2 D15 (± 3 d)	W4 D29 (± 3 d)	W8 D57 (± 3 d)	W12 D85 (± 3 d)	W16[a] D113 (± 3 d)	Notes
Eligibility Assessments							
Inclusion/Exclusion Criteria	X						See Section 6.1 and 6.2, respectively.
Medical History	X						
Safety Assessments[b]							
Physical Examination	X					X	See Section 9.4.1.
Targeted Physical Examination		X	X	X	X		See Section 9.4.1.
Vital Signs	X	X	X	X	X	X	Includes body temperature, respiratory rate, and seated blood pressure and heart rate. See Section 9.4.2.
Body Weight	X			X		X	
ECG	X					X	See Section 9.4.3.
AE and SAE Assessment	X	X	X	X	X	X	All non-serious AEs must be collected from the time of initiation of study treatment until discontinuation of study. All AEs related to SARS-CoV-2 must be collected from time of consent and continuously during the study including at the Safety Follow-up Visit(s). After the initial AE/SAE report, the investigator is required to proactively follow each participant at subsequent visits/contacts. All SAEs and non-serious AEs, including SARS-CoV-2, will be followed until resolution, until the condition stabilizes, until the event is otherwise explained, or until the participant is lost to follow-up. SARS-CoV-2-related AEs/SAEs will be captured in specific CSP CRF pages in addition to AE/SAE pages where the event was originally reported.
Concomitant Medication Use	X	X	X	X	X	X	See Section 7.7.

Table 2-2: Procedural Outline: Baseline through Week 16 (IM011054)

Procedure	D1	W2 D15 (± 3 d)	W4 D29 (± 3 d)	W8 D57 (± 3 d)	W12 D85 (± 3 d)	W16[a] D113 (± 3 d)	Notes
Patient-reported Outcomes							
Subject Global Assessment of Disease Activity	X	X	X	X	X	X	See Appendix 6.
Subject Global Assessment of Pain	X	X	X	X	X	X	See Appendix 7.
HAQ-DI	X	X	X	X	X	X	See Section 9.1.3 and Appendix 8.
SF-36	X		X		X	X	See Section 9.1.4 and Appendix 9.
Fatigue (FACIT Fatigue)	X	X	X	X	X	X	See Section 9.1.5 and Appendix 10.
PsAID 12	X	X	X	X	X	X	See Section 9.1.6 and Appendix 11.
DLQI	X	X	X	X	X	X	See Section 9.1.7 and Appendix 12.
EQ-5D-5L	X		X			X	See Section 9.1.8 and Appendix 13.
PROMIS Sleep Disturbance Short Form-8b	X		X		X	X	See Section 9.1.9 and Appendix 14.
WPAI	X					X	See Section 9.1.10 and Appendix 15.
BASDAI[c]	X	X	X	X	X	X	See Section 9.1.11 and Appendix 16.
Clinician-Reported Outcomes							
Physician Global Assessment of PsA	X	X	X	X	X	X	See Appendix 17.
Tender Joint Count (68 Joint Count)	X	X	X	X	X	X	See Section 9.1.2.
Swollen Joint Count (66 Joint Count)	X	X	X	X	X	X	See Section 9.1.2.

Table 2-2: Procedural Outline: Baseline through Week 16 (IM011054)

Procedure	D1	W2 D15 (± 3 d)	W4 D29 (± 3 d)	W8 D57 (± 3 d)	W12 D85 (± 3 d)	W16[a] D113 (± 3 d)	Notes
Enthesitis (LEI, SPARCC)	X		X	X	X	X	See Section 9.1.12.
Dactylitis (Count, LDI)	X		X	X	X	X	See Section 9.1.13.
PASI[d]	X		X	X	X	X	See Section 9.1.14 and Appendix 18.
sPGA	X		X	X	X	X	See Section 9.1.15 and Appendix 19.
Nail Changes (PGA-F)[e]	X		X	X	X	X	See Section 9.1.16 and Appendix 20.
Composite Measures[f]							
ACR 20/50/70	X	X	X	X	X	X	See Section 9.1.2.
PASDAS	X		X		X	X	See Section 9.1.17.
DAS28-CRP	X	X	X	X	X	X	See Section 9.1.18 and Appendix 21.
MDA/VLDA	X		X	X	X	X	See Section 9.1.19.
DAPSA	X	X	X	X	X	X	See Section 9.1.20.
mCPDAI	X		X	X	X	X	See Section 9.1.21.
PsARC	X	X	X	X	X	X	See Section 9.1.22.
ASDAS-CRP	X	X	X	X	X	X	See Section 9.1.23.

Table 2-2: Procedural Outline: Baseline through Week 16 (IM011054)

Procedure	D1	W2 D15 (± 3 d)	W4 D29 (± 3 d)	W8 D57 (± 3 d)	W12 D85 (± 3 d)	W16[a] D113 (± 3 d)	Notes
Radiographic Assessment							
Radiographs of the Hands (Posteroanterior) and Feet (Anteroposterior)						X[g]	If ET Visit occurs before W16, then X-ray should not be performed at ET Visit if ET Visit occurs before W8. If ET Visit occurs on or after W8 and participant is continuing in study, then X-ray at ET Visit should not be performed, as it will be performed at Week 16. However, X-ray should be done at any visit after Week 8 if participant withdraws consent from the study or if participant is discontinued from the study. See Section 9.1.24.
[redacted]							
Laboratory Tests							
Hematology	X	X	X	X	X	X	CBC with differential. See Section 9.4.4.
Chemistry	X	X	X	X	X	X	See Section 9.4.4.
eGFR	X	X	X	X	X	X	See Section 9.4.5.
Glucose (Fasting)[h]	X			X		X	See Section 9.4.4.
Lipid Panel (Fasting)	X			X		X	See Section 9.4.4.
Urinalysis	X					X	See Section 9.4.4.
[redacted]							See Section 9.4.4.
Hemoglobin A1c	X					X	See Section 9.4.4.
hsCRP[i]	X	X	X	X	X	X	See Section 9.4.4.

Table 2-2: Procedural Outline: Baseline through Week 16 (IM011054)

Procedure	D1	W2 D15 (± 3 d)	W4 D29 (± 3 d)	W8 D57 (± 3 d)	W12 D85 (± 3 d)	W16[a] D113 (± 3 d)	Notes
Pregnancy Test (Urine or Serum) and Counseling	X		X	X	X	X	WOCBP only. See Section 9.4.4.
HBV DNA Test	X		X	X	X	X	See Section 9.4.4. (For participants with a negative HBsAg, but a positive HBcAb and/or HBs Ab at Screening, in select countries only. See Appendix 22.)
[redacted]							
Study Treatment							
Randomize[j]	X						

Table 2-2: Procedural Outline: Baseline through Week 16 (IM011054)

Procedure	D1	W2 D15 (± 3 d)	W4 D29 (± 3 d)	W8 D57 (± 3 d)	W12 D85 (± 3 d)	W16[a] D113 (± 3 d)	Notes
Dispense Study Treatment	X	X	X	X	X	X	
Study Treatment Compliance		X	X	X	X	X	See Section 7.6.

[a] If rescue is needed at this visit, all efficacy and safety assessments must be performed prior [redacted].

[b] For unscheduled visits, see Section 9.4.9.

[c] In participants with baseline evidence of PsA spondylitis.

[d] BSA calculation will be an automated calculation.

[e] In participants with nail PsO at baseline.

[f] Composite measures will not be performed by sites and will be calculated based on assessments received.

[g] The visit window for radiographs of the hands and feet for Week 16 is ± 5 days.

[h] Glucose is part of the chemistry panel. Fasting glucose will be collected at time points indicated.

[i] Post-baseline hsCRP results will remain blinded to the site, participant, and Sponsor (up to Week 16 for the Sponsor) to preserve the blinded treatment assignments.

[j] At Week 16, participants originally randomized to placebo will be reallocated in a blinded fashion (for the initially randomized treatment) to receive 6 mg deucravacitinib QD through Week 52.

[redacted]

Abbreviations: ACR, American College of Rheumatology; AE, adverse event; ASDAS-CRP, Ankylosing Spondylitis Disease Activity Score with C-reactive protein; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BSA, body surface area; CBC, complete blood count; CRF, case report form; CSP, clinical safety program; d, day(s); D, Day; DAPSA, Disease Activity Index for Psoriatic Arthritis Score; DAS28 CRP, Disease Activity Score 28 with C-reactive protein; DLQI, Dermatology Life Quality Index; DNA, deoxyribonucleic acid; ECG, electrocardiogram; eGFR, estimated glomerular filtration rate; EQ-5D-5L, 5-level EuroQoL 5-dimension; ET, Early Termination; FACIT, Functional Assessment of Chronic Illness Therapy; HAQ DI, Health Assessment Questionnaire - Disability Index; HBcAb, hepatitis B core antibody; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; hsCRP, high-sensitivity C-reactive protein; [redacted] LDI, Leeds Dactylitis Index; LEI, Leeds Enthesitis Index; mCPDAI, modified Composite Psoriatic Disease Activity Index; MDA, minimal disease activity; PASDAS, Psoriatic Arthritis Disease Activity Score; PASI, Psoriatic Area and Severity Index; PGA-F, Physician Global Assessment Fingernails; [redacted] PROMIS, Patient-Reported Outcome Measures Information System; PsA, psoriatic arthritis; PsAID, Psoriatic Arthritis Impact of Disease; PsARC, Psoriatic Arthritis Response Criteria; PsO, psoriasis; [redacted]

[redacted] SAE, serious adverse events; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; [redacted] SPARCC, Spondyloarthritis Research Consortium of Canada; sPGA, static Physician's Global Assessment; [redacted] VLDA, very low disease activity; W, Week; WOCBP, women of childbearing potential; WPAI, Work Productivity and Activity Impairment Questionnaire.

Table 2-3: Procedural Outline: Week 20 through Week 56 (IM011054)

Procedure	W20 D141 (± 5 d)	W24 D169 (± 5 d)	W28 D197 (± 5 d)	W32 D225 (± 5 d)	W40 D281 (± 5 d)	W48 D337 (± 5 d)	W52 or ET[b] D365 (± 5 d)	Safety Follow-up W56[c] D395 (30 days after last dose)[d] (+ 5 d)	Notes
Safety Assessments[e]									
Physical Examination							X	X	See Section 9.4.1.
Targeted Physical Examination	X	X	X	X	X	X			See Section 9.4.1.
Vital Signs	X	X	X	X	X	X	X	X	Includes body temperature, respiratory rate, and seated blood pressure and heart rate. See Section 9.4.2.
Body Weight	X			X			X	X	
ECG				X			X		See Section 9.4.3.
AE and SAE Assessment	X	X	X	X	X	X	X	X	All non-serious AEs must be collected from the time of initiation of study treatment until discontinuation of study. All AEs related to SARS-CoV-2 must be collected from time of consent and continuously during the study, including at the Safety Follow-up Visit(s). After the initial AE/SAE report, the investigator is required to proactively follow each participant at subsequent visits/contacts. All SAEs and non-serious AEs, including SARS-CoV-2, will be followed until resolution, until the condition stabilizes, until

Table 2-3: Procedural Outline: Week 20 through Week 56 (IM011054)

Procedure	W20 D141 (± 5 d)	W24 D169 (± 5 d)	W28 D197 (± 5 d)	W32 D225 (± 5 d)	W40 D281 (± 5 d)	W48 D337 (± 5 d)	W52 or ET[b] D365 (± 5 d)	Safety Follow-up W56[c] D395 (30 days after last dose)[d] (+ 5 d)	Notes
									the event is otherwise explained, or until the participant is lost to follow-up. SARS-CoV-2-related AEs/SAEs will be captured in specific CSP CRF pages in addition to AE/SAE pages where the event was originally reported.
Concomitant Medication Use	X	X	X	X	X	X	X	X	See Section 7.7.
Patient-Reported Outcomes									
Subject Global Assessment of Disease Activity	X	X	X	X	X	X	X		See Appendix 6.
Subject Global Assessment of Pain	X	X	X	X	X	X	X		See Appendix 7.
HAQ-DI	X	X	X	X	X	X	X		See Section 9.1.3and Appendix 8.
SF-36	X	X		X	X		X		See Section 9.1.4 and Appendix 9.
Fatigue (FACIT Fatigue)		X		X			X		See Section 9.1.5 and Appendix 10.
PsAID 12	X	X		X			X		See Section 9.1.6 and Appendix 11.

Table 2-3: Procedural Outline: Week 20 through Week 56 (IM011054)

Procedure	W20 D141 (± 5 d)	W24 D169 (± 5 d)	W28 D197 (± 5 d)	W32 D225 (± 5 d)	W40 D281 (± 5 d)	W48 D337 (± 5 d)	W52 or ET[b] D365 (± 5 d)	Safety Follow-up W56[c] D395 (30 days after last dose)[d] (+ 5 d)	Notes
DLQI	X	X		X	X		X		See Section 9.1.7 and Appendix 12.
EQ-5D-5L		X		X	X		X		See Section 9.1.8 and Appendix 13.
PROMIS Sleep Disturbance Short Form-8b	X	X		X	X		X		See Section 9.1.9 and Appendix 14.
WPAI				X			X		See Section 9.1.10 and Appendix 15.
BASDAI[f]	X	X	X	X	X		X		See Section 9.1.11 and Appendix 16.
Clinician-reported Outcomes									
Physician Global Assessment of PsA	X	X	X	X	X	X	X		See Appendix 17.
Tender Joint Count (68 Joint Count)	X	X	X	X	X	X	X		See Section 9.1.12.
Swollen Joint Count (66 Joint Count)	X	X	X	X	X	X	X		See Section 9.1.2.
Enthesitis (LEI, SPARCC)	X	X		X	X	X	X		See Section 9.1.12.
Dactylitis (Count, LDI)	X	X		X	X	X	X		See Section 9.1.13.

Table 2-3: Procedural Outline: Week 20 through Week 56 (IM011054)

Procedure	W20 D141 (± 5 d)	W24 D169 (± 5 d)	W28 D197 (± 5 d)	W32 D225 (± 5 d)	W40 D281 (± 5 d)	W48 D337 (± 5 d)	W52 or ET[b] D365 (± 5 d)	Safety Follow-up W56[c] D395 (30 days after last dose)[d] (+ 5 d)	Notes
PASI[g]	X	X		X	X	X	X		See Section 9.1.14 and Appendix 18.
sPGA	X	X		X	X	X	X		See Section 9.1.15 and Appendix 19.
Nail Changes (PGA-F)[h]	X	X		X	X	X	X		See Section 9.1.16 and Appendix 20.
Composite Measures[i]									
ACR 20/50/70	X	X	X	X	X	X	X		See Section 9.1.2.
PASDAS	X	X		X	X		X		See Section 9.1.17.
DAS28-CRP	X	X	X	X	X	X	X		See Section 9.1.18 and Appendix 21.
MDA/VLDA	X	X		X	X	X	X		See Section 9.1.19.
DAPSA	X	X	X	X	X	X	X		See Section 9.1.20.
mCPDAI	X	X		X	X		X		See Section 9.1.21.
PsARC	X	X		X	X	X	X		See Section 9.1.22.
ASDAS-CRP	X	X	X	X	X		X		See Section 9.1.23.
Radiographic Assessment									
Radiographs of the Hands (Posteroanterior)							X		If the ET Visit occurs between W16 and W52, then X-ray should not be performed if ET

Table 2-3: Procedural Outline: Week 20 through Week 56 (IM011054)

Procedure	W20 D141 (± 5 d)	W24 D169 (± 5 d)	W28 D197 (± 5 d)	W32 D225 (± 5 d)	W40 D281 (± 5 d)	W48 D337 (± 5 d)	W52 or ET[b] D365 (± 5 d)	Safety Follow-up W56[c] D395 (30 days after last dose)[d] (+ 5 d)	Notes
and Feet (Anteroposterior)[j]									Visit occurs before W24. If X-ray is taken at the ET Visit, it must be at least 8 weeks after previous X-ray and no sooner than 8 weeks before W52. See Section 9.1.24.
[redacted]									
Laboratory Tests									
Hematology	X	X	X	X	X	X	X	X	CBC with differential. See Section 9.4.4.
Chemistry	X	X	X	X	X	X	X	X	See Section 9.4.4.
eGFR	X	X	X	X	X	X	X	X	See Section 9.4.5.
Glucose (Fasting)[k]				X			X		See Section 9.4.4.
Lipid Panel (Fasting)				X			X		See Section 9.4.4.
Urinalysis	X			X			X		See Section 9.4.4.
[redacted]									See Section 9.4.4.
Hemoglobin A1c				X			X		See Section 9.4.4.

Table 2-3: Procedural Outline: Week 20 through Week 56 (IM011054)

Procedure	W20 D141 (± 5 d)	W24 D169 (± 5 d)	W28 D197 (± 5 d)	W32 D225 (± 5 d)	W40 D281 (± 5 d)	W48 D337 (± 5 d)	W52 [redacted] or ET[b] D365 (± 5 d)	Safety Follow-up W56[c] D395 (30 days after last dose)[d] (+ 5 d)	Notes
hsCRP[l]	X	X	X	X	X	X	X		See Section 9.4.4.
Pregnancy Test (Urine or Serum) and Counseling[m]	X	X	X	X	X	X	X	X	WOCBP only. See Section 9.4.4. Telephone visit(s) will be performed to verbally obtain monthly pregnancy test results between office visits.
HBV DNA Test	X	X	X	X	Testing will occur every 4 to 8 weeks (frequency of testing is at the discretion of the investigator).				See Section 9.4.4 (requirement for select countries only. See Appendix 22). For participants with a negative HBsAg, but a positive HBcAb and/or HBs Ab at Screening.
[redacted]									

Table 2-3: Procedural Outline: Week 20 through Week 56 (IM011054)

Procedure	W20 D141 (± 5 d)	W24 D169 (± 5 d)	W28 D197 (± 5 d)	W32 D225 (± 5 d)	W40 D281 (± 5 d)	W48 D337 (± 5 d)	W52 or ET[b] D365 (± 5 d)	Safety Follow-up W56[c] D395 (30 days after last dose)[d] (+ 5 d)	Notes
[redacted]									
Study Treatment									
Dispense Study Treatment	X	X	X	X	X	X			
Study Treatment Compliance	X	X	X	X	X	X	X		See Section 7.6.
[redacted]									

b Participants who discontinue from study treatment are required to complete an ET Visit and must be evaluated for safety 30 days following the last dose of study treatment. All participants should remain in the study for follow-up until the Week 52 Visit (see Section 8.1). Participants who discontinue study treatment and request to discontinue from the study will be asked to complete an ET Visit and a Safety Follow-up Visit (or phone call if a visit is not possible) 30 days following last dose of study treatment to determine the status of any ongoing AEs/SAEs or the occurrence of any new AEs/SAEs (see Section 8.1.2).

c Participants who complete [redacted] will have a Safety Follow-up Visit 30 days following last dose of study treatment (Week 56).

[d] All participants must be evaluated for safety 30 days following last dose of IP (see Section 8.2). If the Safety Follow-up Visit occurs within window of the next planned study visit, then only assessments from the planned study visit should be performed in addition to a full physical examination and body weight.

[e] For unscheduled visits, see Section 9.4.9.

[f] In participants with baseline evidence of PsA spondylitis.

[g] BSA calculation will be an automated calculation.

[h] In participants with nail PsO at baseline.

[i] Composite measures will not be performed by sites and will be calculated based on assessments received.

[j] Visit windows are the following: Week 52 ± 5 days of the scheduled visit and ET ± 5 days of the scheduled visit (if ET Visit is after Week 8 of the Placebo-controlled Treatment Period or after Week 24 of the Active Treatment Period).

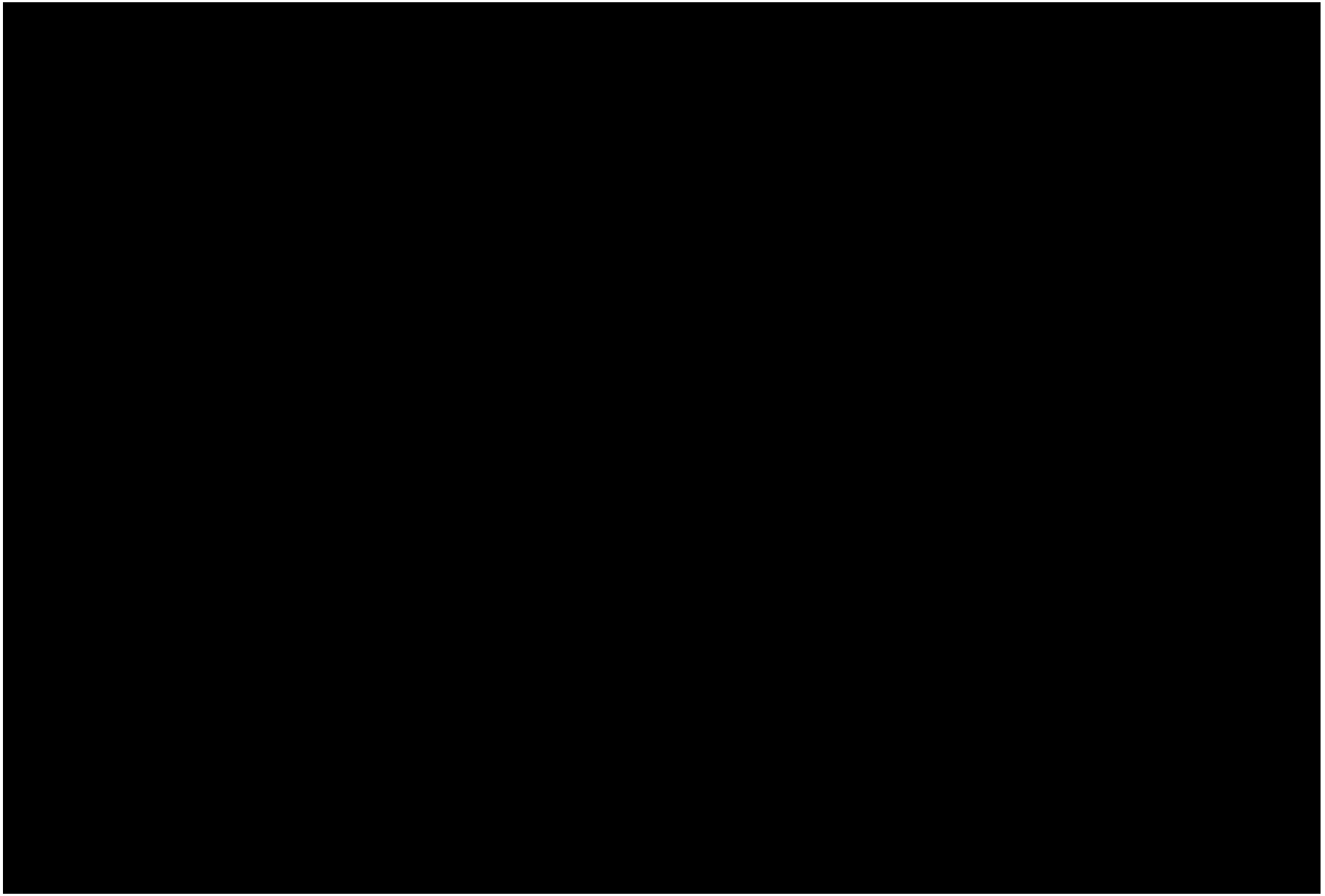
[k] Glucose is part of the chemistry panel. Fasting glucose will be collected at time points indicated.

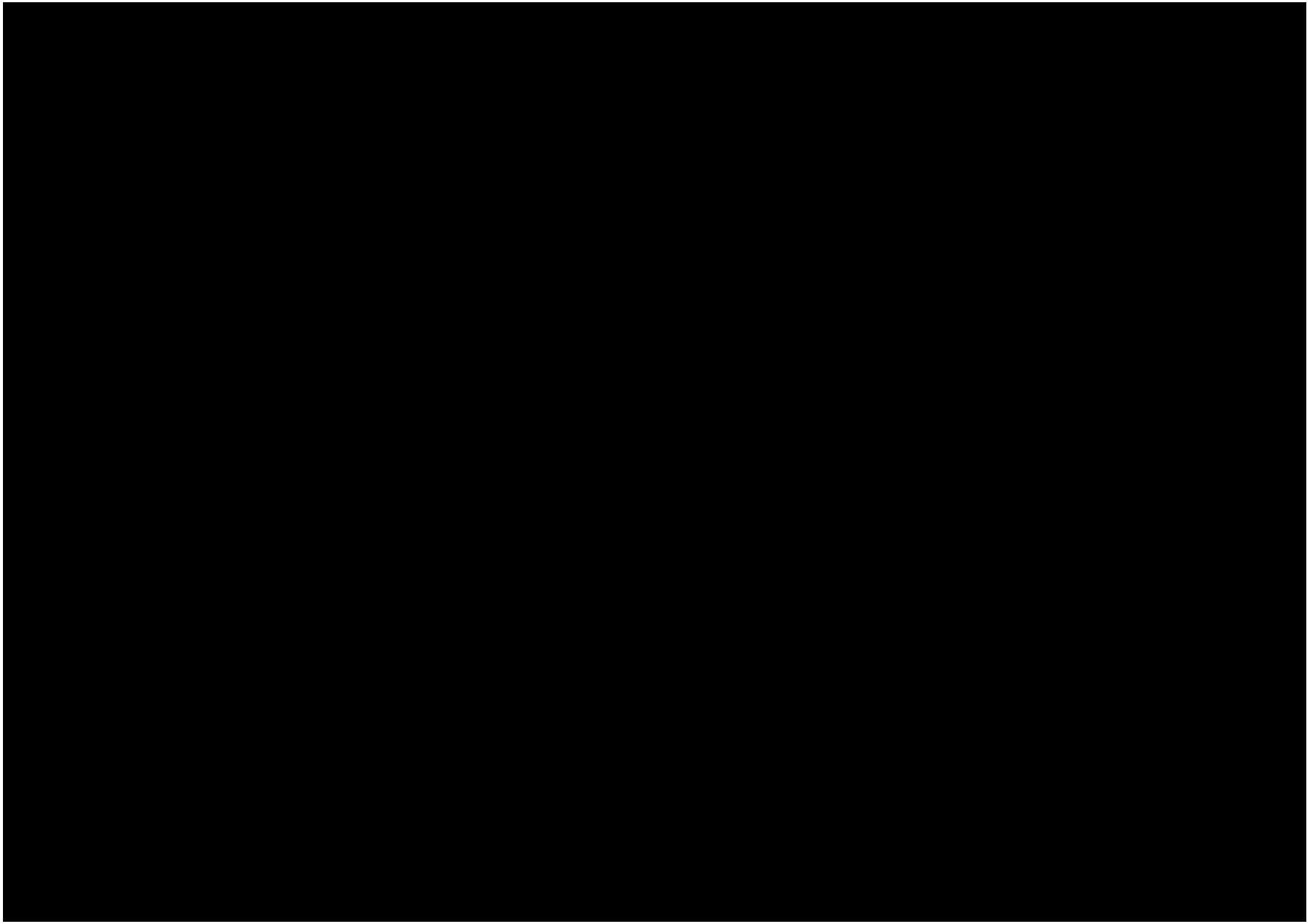
[l] Post-baseline hsCRP results will remain blinded to the site, participant, and Sponsor (up to Week 16 for Sponsor) to preserve the blinded treatment assignments.

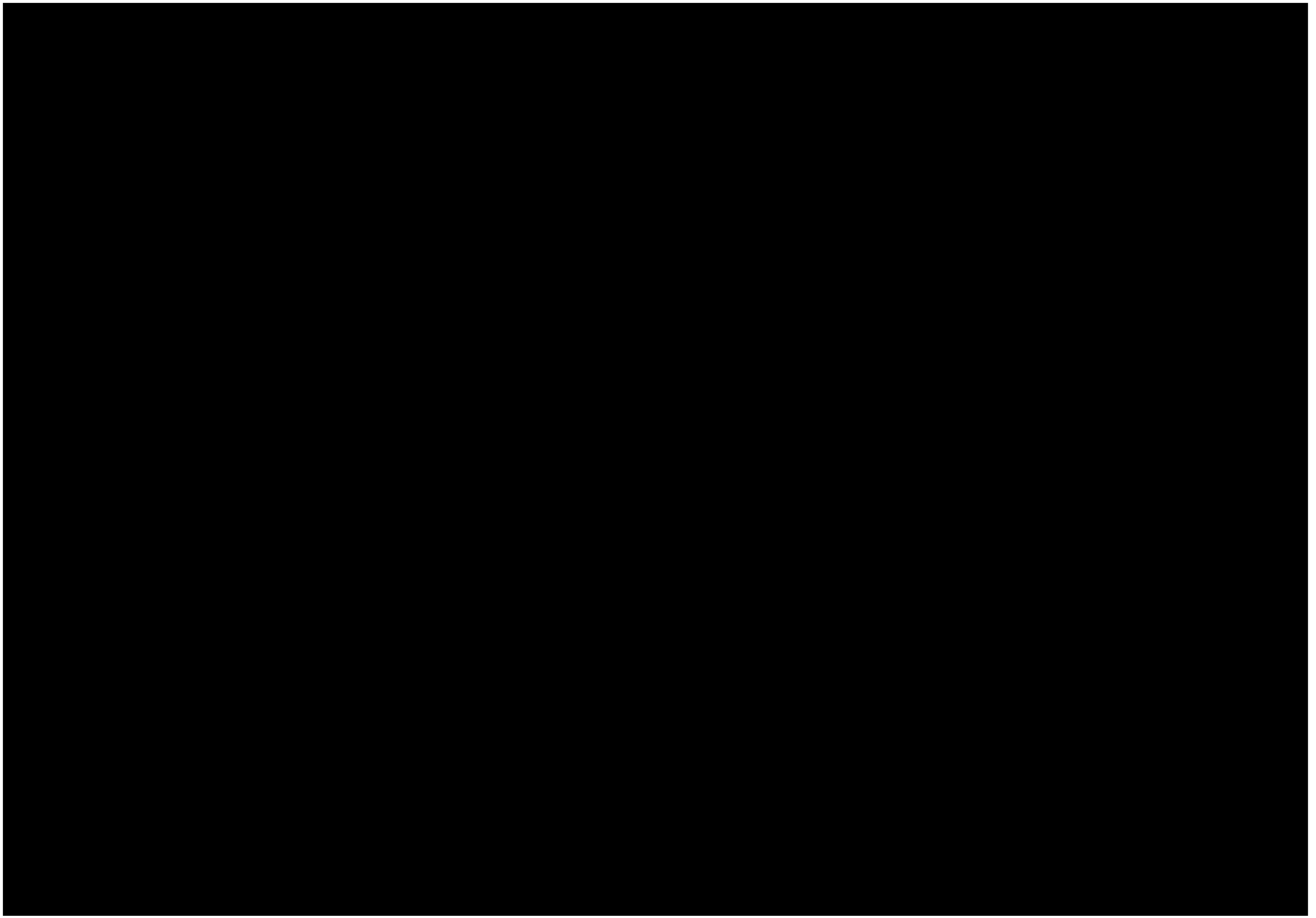
[m] At-home urine pregnancy test kits will be provided to maintain monthly pregnancy testing between Weeks 32 and 48. Site staff will record the telephone visit and result in the participant's source document.

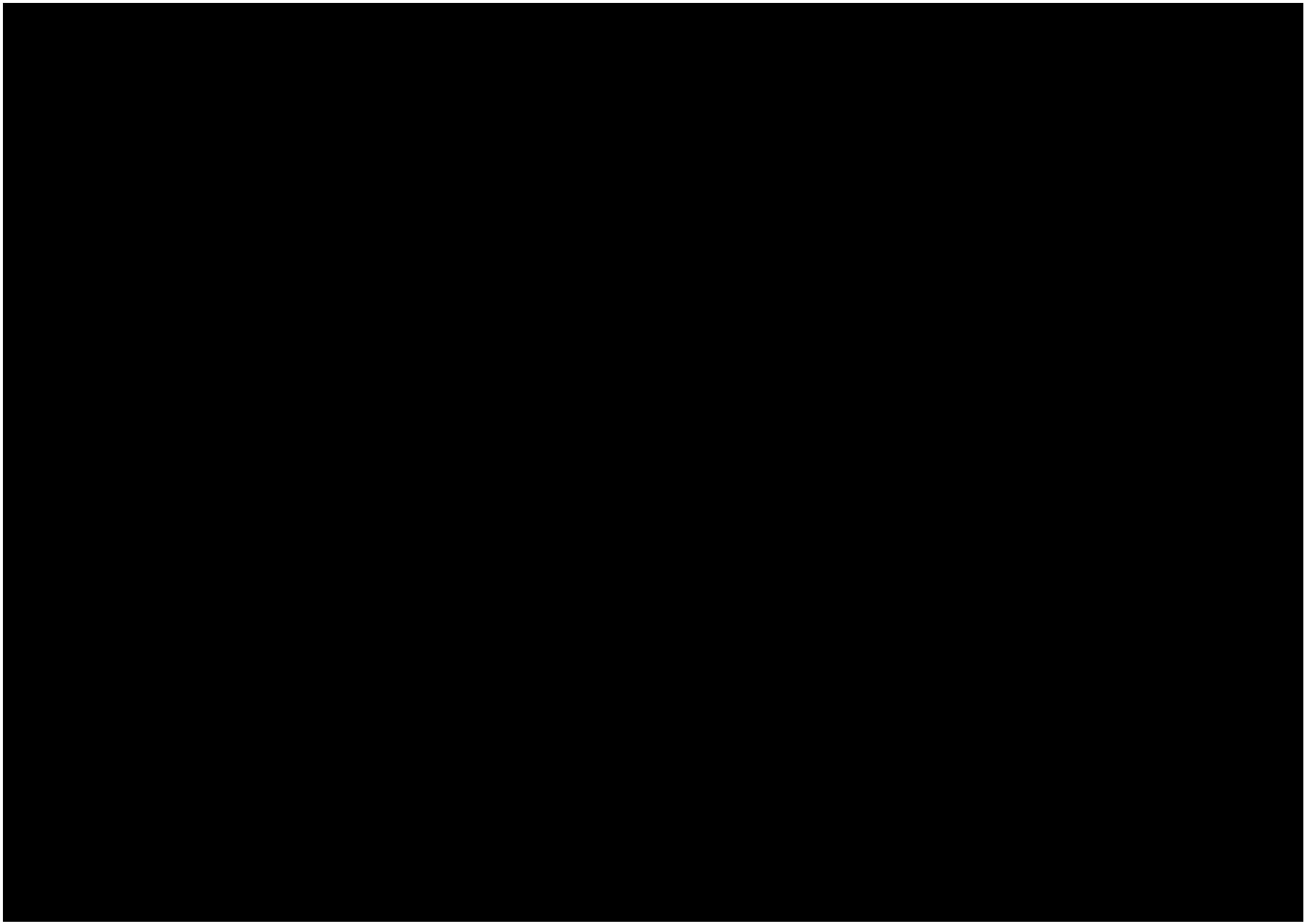
[redacted]

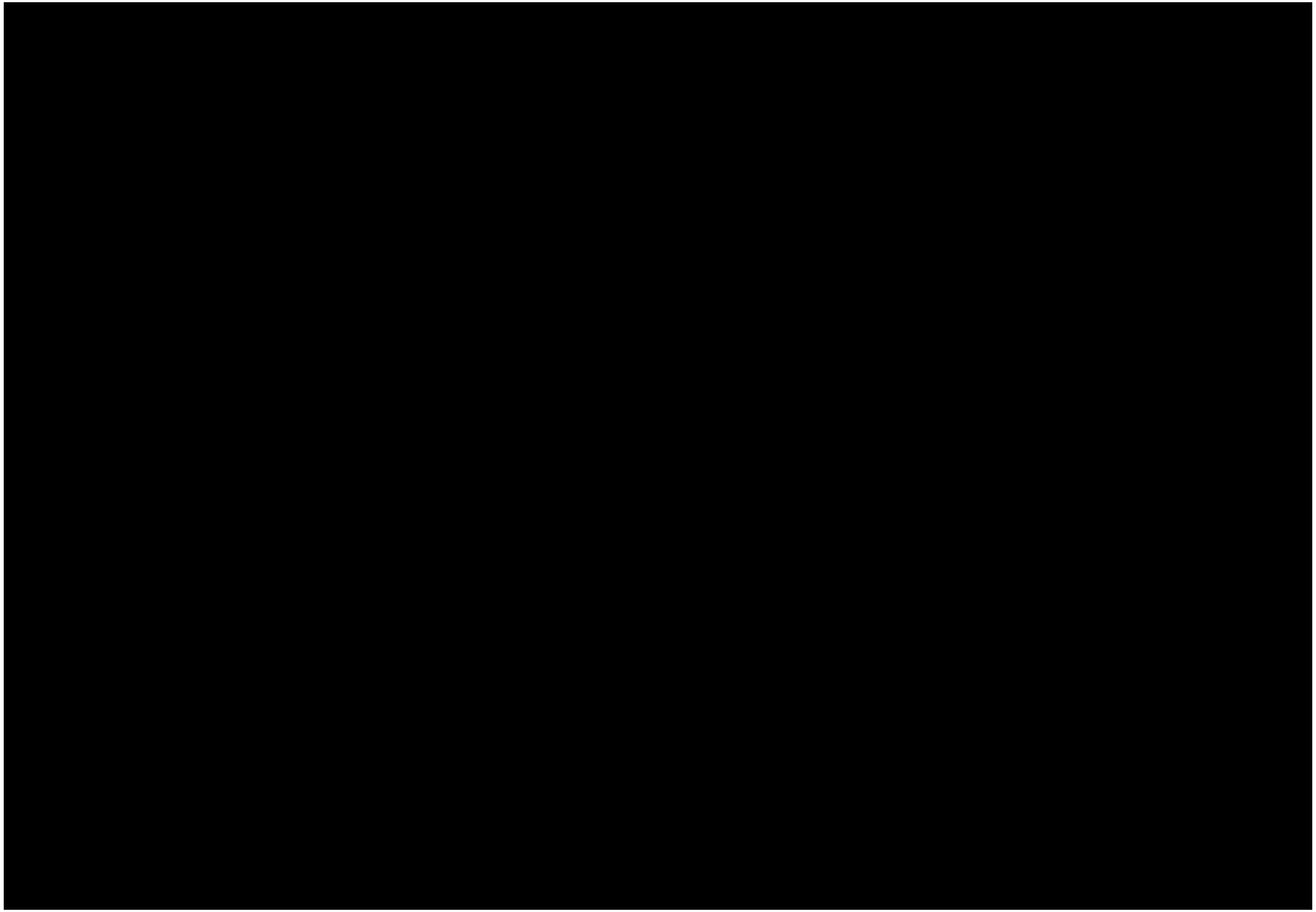
Abbreviations: ACR, American College of Rheumatology; AE, adverse event; ASDAS-CRP, Ankylosing Spondylitis Disease Activity Score with C-reactive protein; BASDAI, Bath Ankylosing Spondylitis Disease Activity Index; BSA, body surface area; CBC, complete blood count; CRF, case report form; CSP, clinical safety program; d, day(s); D, Day; DAPSA, Disease Activity Index for Psoriatic Arthritis Score; DAS28-CRP, Disease Activity Score 28 with C-reactive protein; DLQI, Dermatology Life Quality Index; DNA, deoxyribonucleic acid; ECG, electrocardiogram; eGFR, estimated glomerular filtration rate; EQ-5D-5L, 5-level EuroQol 5-dimension; ET, Early Termination; FACIT, Functional Assessment of Chronic Illness Therapy; HAQ-DI, Health Assessment Questionnaire - Disability Index; HBV, hepatitis B virus; hsCRP, high-sensitivity C-reactive protein; [redacted] IP, investigational product; LDI, Leeds Dactylitis Index; LEI, Leeds Enthesitis Index; mCPDAI, modified Composite Psoriatic Disease Activity Index; MDA, Minimal Disease Activity; [redacted] PASDAS, Psoriatic Arthritis Disease Activity Score; PASI, Psoriatic Area and Severity Index; PGA-F, Physician Global Assessment-Fingernails; [redacted] PROMIS, Patient-Reported Outcome Measures Information System; PsA, psoriatic arthritis; PsAID, Psoriatic Arthritis Impact of Disease; PsARC, Psoriatic Arthritis Response Criteria; PsO, psoriasis; [redacted] SAE, serious adverse event; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; SF-36, Short Form-36; SPARCC, Spondyloarthritis Research Consortium of Canada; sPGA, static Physician's Global Assessment; [redacted] VLDA, very low disease activity; W, Week; WPAI, Work Productivity and Activity Impairment; WOCBP, women of childbearing potential.

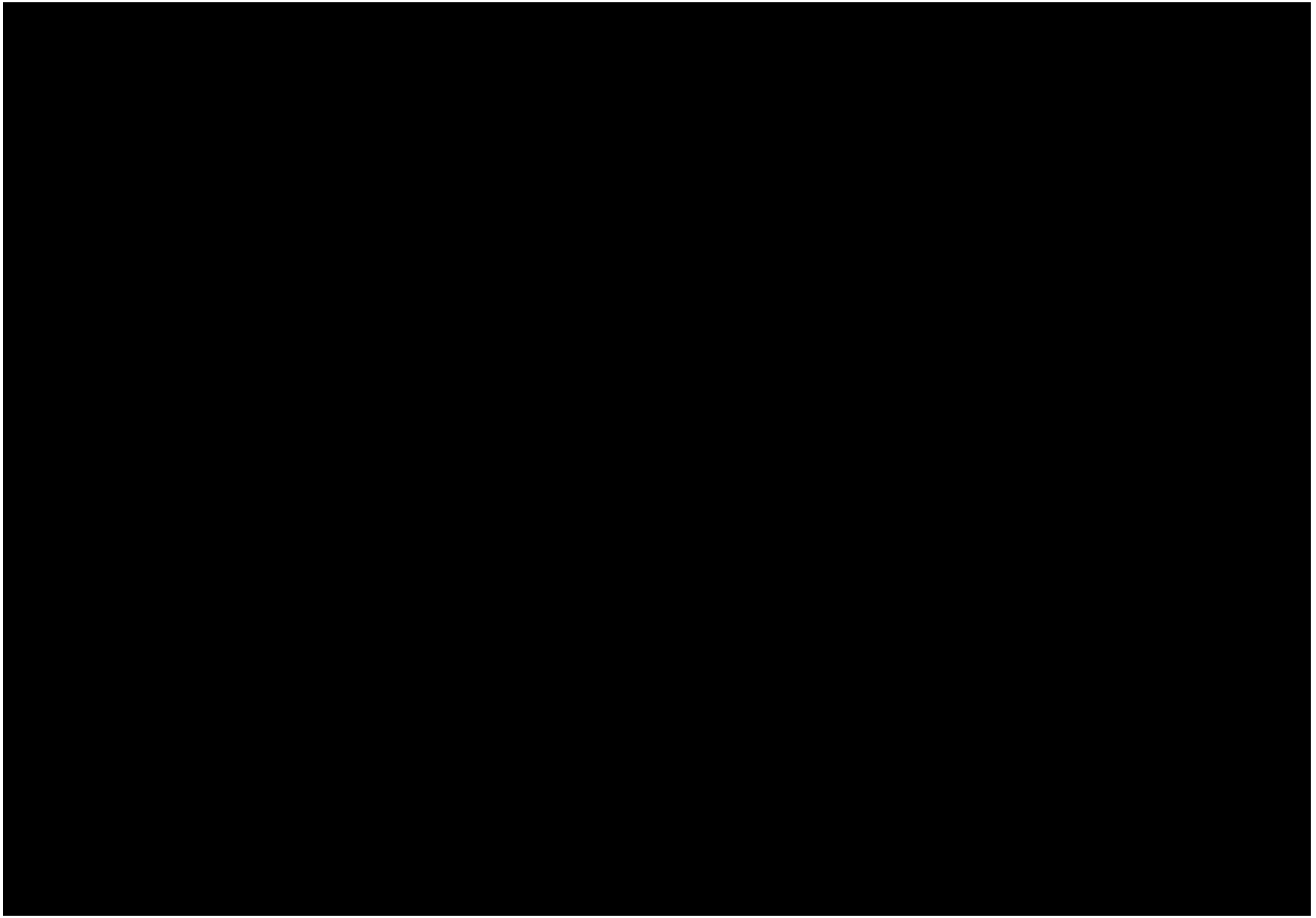


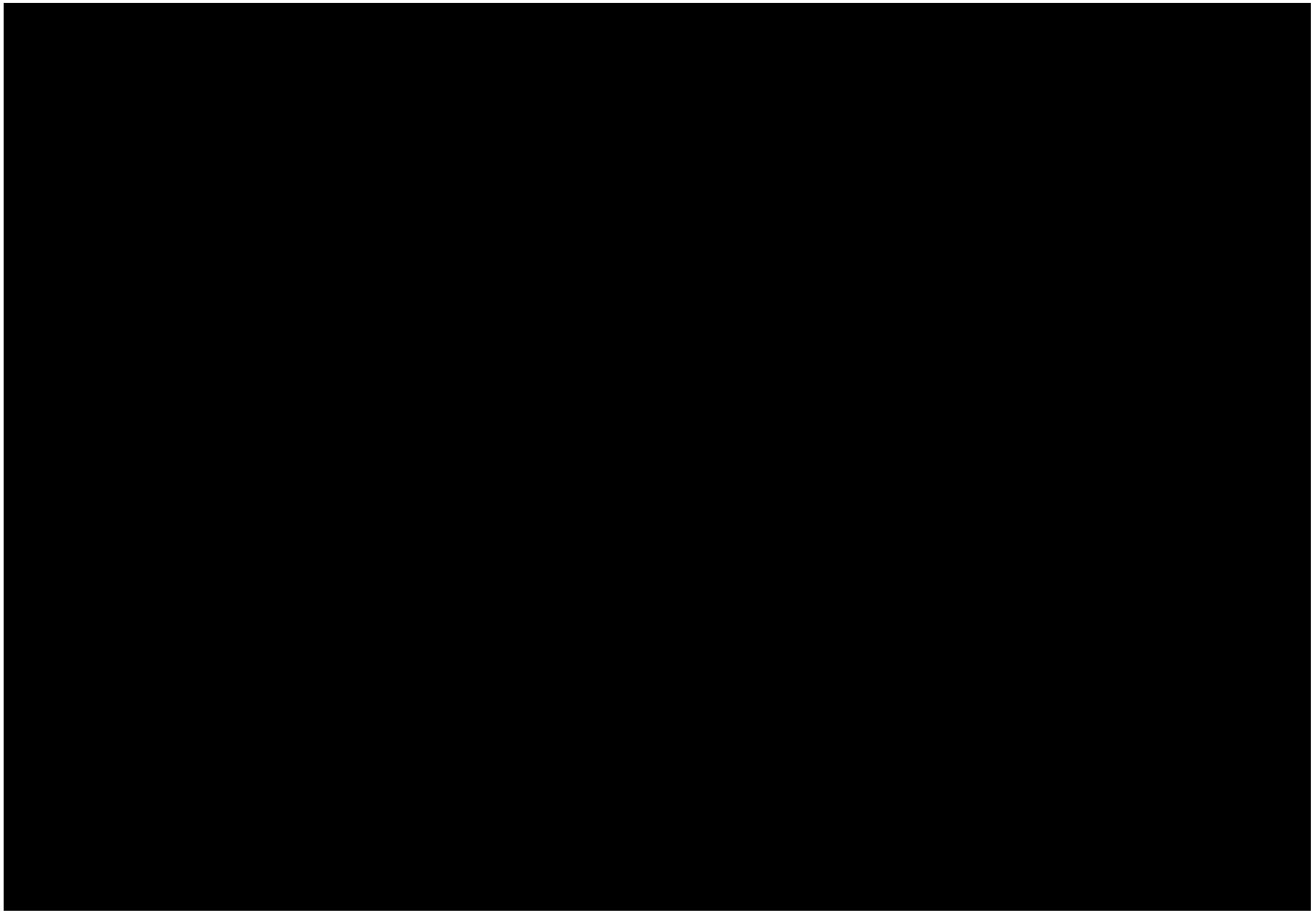


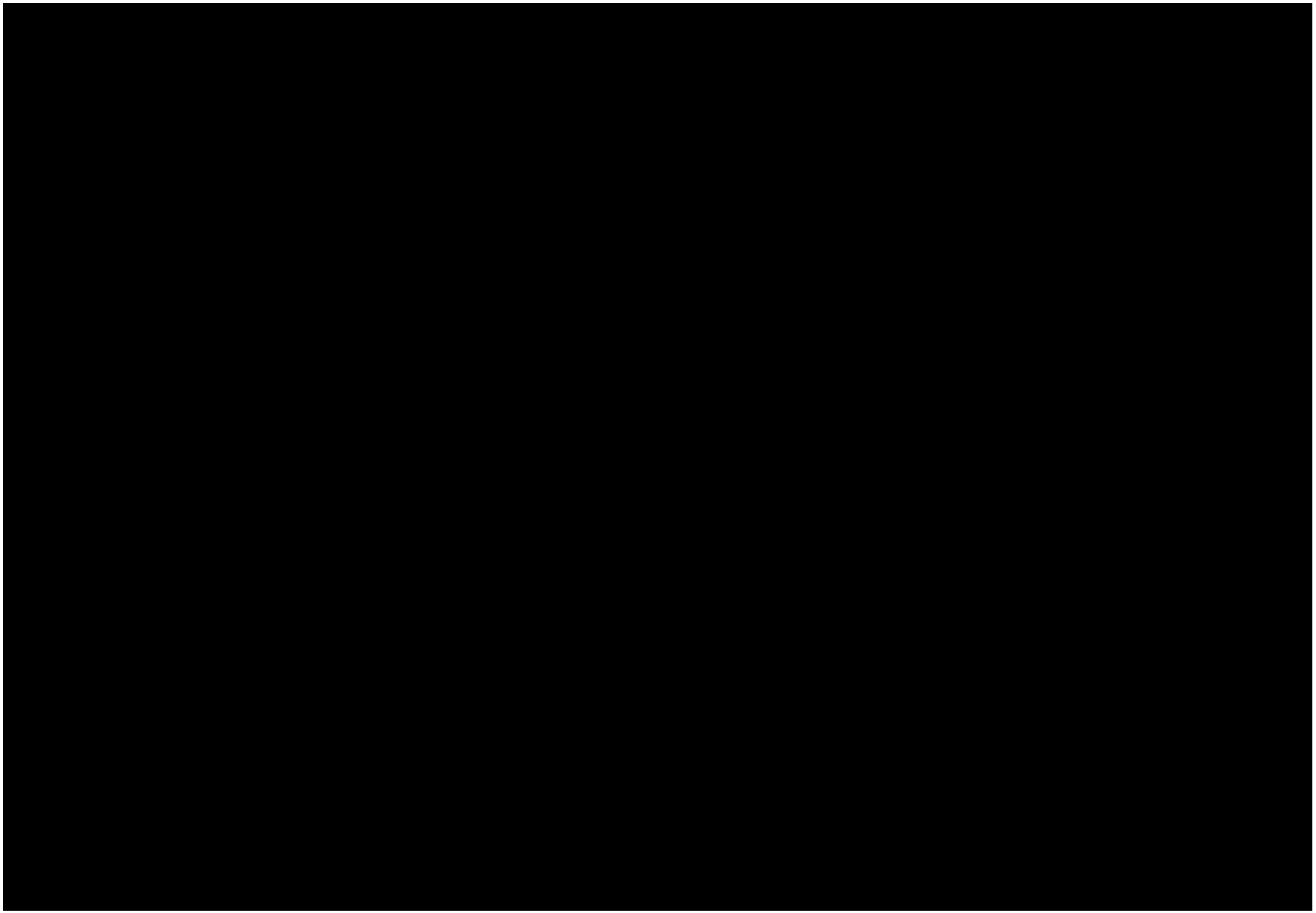












3 INTRODUCTION

Psoriatic arthritis (PsA) is a chronic inflammatory articular disease that occurs in up to 30% of patients with psoriasis (PsO). PsA has manifestations that include peripheral arthritis, axial disease, enthesitis, dactylitis, and skin and nail disease. This condition can lead to disability and reduced quality of life over time without adequate treatment.

Deucravacitinib (BMS-986165) is an oral, potent, highly selective inhibitor of the intracellular signaling kinase, tyrosine kinase 2 (TYK2). Selective inhibition of TYK2 may provide a unique mechanism to treat conditions dependent upon interleukin (IL)-23 and its downstream signaling pathways such as PsO and PsA.

3.1 Study Rationale

Deucravacitinib is being evaluated as a therapeutic option for the treatment of participants with PsA. This Phase 3 study is a part of development program for PsA and follows the Phase 2 study (IM011084) that has met its primary and key secondary objectives. The population for this Phase 3 study (IM011054) includes participants with prior exposure to conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs), and/or apremilast, and/or nonsteroidal anti-inflammatory drugs (NSAIDs), similar to the predominant patient population studied in a Phase 2 study.

In IM011084, 203 participants were randomized to: 6 mg deucravacitinib once daily (QD) (n = 66), 12 mg deucravacitinib QD (n = 70), and placebo (n = 67). The primary objective of dose-response relationship in American College of Rheumatology (ACR) 20 responses after 16 weeks of treatment was met ($p < 0.001$). In the 6 mg deucravacitinib QD group 52.9% of participants and in the 12 mg deucravacitinib QD group 62.7% of participants achieved ACR 20 responses versus 31.8% of participants in the placebo group ($p = 0.0134$ and $p = 0.004$, respectively).

All key secondary endpoints were also achieved as measured by mean change from baseline in Health Assessment Questionnaire - Disability Index (HAQ-DI) scores (-0.37 on 6 mg QD and -0.39 on 12 mg QD versus -0.11 on placebo, $p = 0.0020$ and $p = 0.0008$, respectively), Psoriatic Area and Severity Index (PASI) 75 responses (42.4 on 6 mg QD and 59.6 on 12 mg QD versus 20.4 on placebo; $p = 0.0136$ and $p < 0.0001$, respectively) and mean change from baseline in Short Form-36 (SF-36) Physical Component Summary (PCS) scores (5.6 on 6 mg QD and 5.8 on 12 mg QD versus 2.3 on placebo; $p = 0.0062$ and $p = 0.0042$, respectively). Participants in both 6 mg deucravacitinib and 12 mg deucravacitinib treatment groups achieved higher ACR 50 responses versus placebo (24.3% on 6 mg QD and 32.8% on 12 mg QD versus 10.6% on placebo; $p = 0.0326$ and $p = 0.0016$, respectively), and higher ACR 70 responses versus placebo (14.3% on 6 mg QD and 19.4% on 12 mg QD versus 1.5% on placebo; $p = 0.0044$ and $p = 0.0003$, respectively) after 16 weeks of treatment. Although efficacy was numerically higher for 12 mg QD versus 6 mg QD for some measures, meaningful dose separation in responses was not consistently observed. Deucravacitinib was generally well tolerated at both doses with adverse events (AEs) that were mostly mild to moderate in severity and were able to be managed, monitored, and resulted in few discontinuations. Based on the totality of data available to date, these data support the potential

benefit of deucravacitinib in the treatment of PsA. There are no significant safety issues to limit further clinical investigation of deucravacitinib in PsA.

The Phase 3 IM01154 study is designed to confirm the efficacy and safety of 6 mg deucravacitinib QD versus placebo in larger PsA population and with longer duration of treatment.

[redacted]

3.2 Background

PsA is a chronic, heterogeneous disorder characterized by progressive inflammatory arthritis that can occur in up to 30% of patients with PsO and may result in permanent joint damage and disability as well as health consequences beyond joint function, such as cardiovascular disease.[1,2,3]

It is estimated that the prevalence of PsA is about 2% to 4% in the Western population.[4] The incidence of PsA in the general population is reported as approximately 3.6 to 7.2 per 100,000 per year.[3] Disease onset occurs between the ages of 40 and 50 years and affects both sexes equally. It is estimated that 80% of patients with PsA have active concurrent PsO, with 10% to 15% of patients developing arthritis prior to developing PsO.[5]

PsA is one of the seronegative spondyloarthropathies and affects multiple tissues, including peripheral joints, skin and nails, axial joints (spondylitis), entheses (enthesitis), and digits (dactylitis). At initial presentation, oligoarticular disease is the most common subtype, but as the disease evolves, the polyarticular variant becomes more prevalent.[5,6,7] Approximately 25% of patients with PsA have spondylitis in addition to peripheral arthritis. Other, less common clinical patterns of PsA include distal arthritis that is characterized by an involvement of distal interphalangeal (DIP) joints and arthritis mutilans that is characterized by deforming and destructive arthritis.

Progressive joint inflammation and destruction over time is detectable radiographically in at least 40% of patients.[8] Radiographic features of PsA include (but are not limited to) osteolysis, “pencil-in-cup” deformity, and ankylosis.

The treatment options for PsA include NSAIDs; oral csDMARDs (eg, csDMARDs: methotrexate [MTX], leflunomide [LEF], sulfasalazine [SSZ]); targeted synthetic disease-modifying anti-rheumatic drugs (DMARDs) (tofacitinib); apremilast; biologic disease-modifying anti-rheumatic drugs (bDMARDs) such as tumor necrosis factor (TNF) antagonists (golimumab, adalimumab, certolizumab, etanercept, infliximab); inhibitors of co-stimulation of T-cells (abatacept); IL-12/IL-23p40 inhibitor (ustekinumab); IL-23 inhibitor (guselkumab); and IL-17A inhibitors (secukinumab, ixekizumab).[9,10,11,12]

For patients with PsA, there is a need for alternative treatment options, beyond currently available csDMARDs, to treat multiple manifestations of the disease with an acceptable safety and tolerability profile. MTX is frequently used but has limited efficacy and tolerability. Patients

experience nausea, headache, and fatigue, and there is a need for regular monitoring of laboratory tests for potential hematologic and liver toxicities.[1,13,14,15,16,17,18,19]

Targeted synthetic DMARDs, like the Janus kinase (JAK)1 and JAK3 inhibitor tofacitinib, could provide better efficacy than csDMARDs but may have potential safety issues (as per the label) that preclude very early use in patients with PsA.

TNF antagonists form the mainstay of treatment for patients with an inadequate response to csDMARDs.[15] TNF antagonists are biological drugs efficacious for both skin and joint diseases, but approximately 40% of patients treated with these agents do not reach ACR 20, and these drugs are associated with the risk of some significant safety concerns and require monitoring.[19]

A number of other biologic therapies have been developed to inhibit different targets of the IL-23 signaling pathway. Blocking antibodies of either the IL-23p40 subunit with ustekinumab or IL-17 with secukinumab and ixekizumab is highly effective but has not been shown to have meaningfully improved efficacy with regards to musculoskeletal manifestations compared with anti-TNF agents. While bDMARDs are found to be well tolerated and efficacious in some patients, they must be administered intravenously (IV) or subcutaneously.[20]

Deucravacitinib is an oral therapy, and the advantages of an oral route of administration are well known. These include improvement in patient compliance, avoidance of infusion and injection-site reactions, and quicker washout in case there is a need for study treatment discontinuation due to adverse effects.

Thus, for treatment options for PsA, there is a need for a new therapy with a novel mechanism of action and an acceptable safety profile without the need for periodic laboratory monitoring and the convenience of QD oral dosing.

Tyrosine Kinase 2

TYK2 is a nonreceptor tyrosine kinase associated with receptors for the p40 subunit-containing cytokines IL-12 and IL-23, as well as the Type I interferon (IFN) receptor, and is required for downstream activation of those signaling pathways. IL-23 is produced by keratinocytes and activated antigen-presenting cells, including Langerhans cells, macrophages and dendritic cells. IL-23 binds to its receptor IL-23R and the complex activates JAK2 and TYK2, members of the Janus family of tyrosine kinases.[21,22,23] Upon cytokine binding to the receptor, TYK2 and JAK2 transactivate to initiate signal transduction. TYK2 catalyzes the phosphorylation of the intracellular receptor domains and signal transducer and activator of transcription (STAT) proteins, resulting in the activation of STAT-dependent transcription and functional responses specific for these cytokines.

IL-23 is critical in the expansion and survival of pathogenic T-helper (TH)17 cells as well as the induction of innate lymphoid cells in autoimmunity.[24,25] TH17 cells produce key proinflammatory cytokines, including IL-17 and IL-22. IL-17 and IL-22 are effector molecules important for the pathogenesis of immune-mediated conditions, including PsA and PsO. IL-17 and IL-22 are overexpressed in psoriatic skin and in the synovial membrane in PsA.[26,27,28,29] TYK2-dependent

pathways (IL-23, IL-12, and Type I IFNs) and the cytokine networks they modulate (eg, IL-17, IL-22, IFN-γ) have been implicated in the pathophysiology of multiple immune-mediated diseases, including PsA, PsO, and Crohn's disease.

Deucravacitinib

Deucravacitinib is a potent, highly selective, oral small-molecule inhibitor of TYK2 that binds to the regulatory pseudokinase domain of TYK2. The binding of deucravacitinib to the pseudokinase domain of TYK2 stabilizes the inhibitory interactions between the pseudokinase and the catalytic domains of the enzyme, causing a blockade of receptor-mediated activation of TYK2 and its downstream functions in cells stimulated through the IL-23, IL-12, and Type I IFN pathways. The binding mode of deucravacitinib takes advantage of unique structural features of the TYK2 pseudokinase domain compared with other kinases and pseudokinases to provide high biochemical, cellular, and functional selectivity. This approach differentiates deucravacitinib from non-selective inhibitors of the JAK family of kinases that target the highly conserved adenosine triphosphate binding site within the active site of the catalytic domain.

Selective inhibition of TYK2 may provide a unique avenue to treat conditions dependent upon IL-23 and its downstream signaling pathways. A key element in this hypothesis is the selectivity of the drug. Cytokine or growth factor pathways dependent on TYK2 (IL-23, IL-12, Type I IFNs) are distinct from those dependent on the other family members JAK1/JAK3 (eg, IL-2, IL-15, IL-7); JAK2/JAK2 (eg, erythropoietin, thrombopoietin, granulocyte macrophage colony-stimulating factor); or JAK1/JAK2 (eg, IFNγ, IL-6). Non-selective inhibitors of JAK family members can result in AEs such as dyslipidemia, lymphopenia, neutropenia, and anemia.[30] Selective TYK2 inhibition is expected to result in a differentiated profile from the inhibitors of multiple JAK family kinases.

3.3 Benefit/Risk Assessment

A dosage of 6 mg deucravacitinib QD was selected to be used in this Phase 3 study to further characterize the benefit/risk of deucravacitinib in adult participants with active PsA. The dose selection is based on observed efficacy [redacted].

In the Phase 2 study (IM011084) of 203 participants with active PsA, efficacy was assessed by the dose-response relationship in ACR 20 responses after 16 weeks of treatment. The primary and key secondary objectives of the study were met. See Section 3.1.

The overall safety of deucravacitinib was acceptable in the Phase 2 study in PsA. There were no serious adverse events (SAEs) reported in active treatment arms [redacted]. There were no cases of herpes zoster or systemic opportunistic infections in active treatment arms. The incidence of participants with AEs was numerically higher in active treatment groups compared with placebo (42.4% [placebo] versus 65.7% [6 deucravacitinib QD group] and 65.7% [12 mg deucravacitinib QD group], respectively).

The most common AEs in the 6 mg deucravacitinib QD arm were headache (7.1%), nasopharyngitis, upper respiratory tract infections, bronchitis, and diarrhea (each in 5.7% of

participants). All AEs in this treatment group were mild or moderate and rarely led to discontinuation of treatment (3 participants).

The favorable benefit/risk profile of deucravacitinib in Phase 2 suggests that a wide range of PsA patients can benefit from treatment and that 6 mg deucravacitinib QD could be a useful addition to the therapeutic armamentarium across varied therapeutic settings: after NSAID failure, concurrent with or following treatment with csDMARD agents and/or following inadequate response or intolerance to bDMARD therapy.[31]

[redacted]

Safety will be monitored by the study Sponsor as well as by an independent Data Monitoring Committee (DMC). Details of DMC responsibilities and procedures will be specified in the DMC Charter. [redacted]

[redacted]

The initial treatment randomization blinding is up to Week 56/[redacted] for participants and investigators to ensure reliable efficacy and safety measures. Blinding for the study Sponsor will be through the Week 16 visit for the primary analysis.

Severe Acute Respiratory Syndrome Coronavirus 2 Pandemic-related Risk Assessment

While the global severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) pandemic has been identified as a potential risk to clinical trial participants in general, and it may particularly affect individuals with underlying chronic diseases and on immunosuppressive therapies, the overall benefit/risk for participation in this PsA study with deucravacitinib appears favorable. The individual benefit/risk considerations regarding SARS-CoV-2 infection remains the responsibility of the investigator. Testing to exclude SARS-CoV-2 infection prior to enrollment and to inform decisions about participant care during the study should follow local standard practice and requirements.

4 OBJECTIVES AND ENDPOINTS

The objectives and endpoints for IM011054 are listed in Table 4-1.

Table 4-1: Objectives and Endpoints

Objective	Endpoint
Primary	
To compare the efficacy of deucravacitinib to placebo in the treatment of participants with active PsA	Proportion of participants meeting ACR 20 response at Week 16
Key Secondary	
To compare the efficacy of deucravacitinib to placebo at Week 16 as assessed by DAS28-CRP	Change from baseline in DAS28-CRP score at Week 16
To compare the efficacy of deucravacitinib to placebo as assessed by HAQ-DI score at Week 16	Change from baseline in HAQ-DI score at Week 16
To compare the efficacy of deucravacitinib to placebo as assessed by PASI 75 response at Week 16	Proportion of participants meeting PASI 75 response at Week 16, in participants with at least 3% BSA involvement AND at least sPGA 2 at baseline
To compare the efficacy of deucravacitinib to placebo as assessed by SF-36 PCS score at Week 16	Change from baseline in the SF-36 PCS score at Week 16
To compare the efficacy of deucravacitinib to placebo in enthesitis resolution at Week 16	Proportion of participants meeting enthesitis resolution (score of 0) among participants with enthesitis at baseline by LEI at Week 16
To compare the efficacy of deucravacitinib to placebo in MDA response at Week 16	Proportion of participants meeting achievement of MDA where an MDA response is achievement of 5 of 7 following outcomes at Week 16: a) Tender joint count ≤ 1 b) Swollen joint count ≤ 1 c) PASI ≤ 1 or BSA ≤ 3% d) Patient assessment of PsA pain ≤ 15 e) Patient Global Assessment of PsA disease activity ≤ 20 f) HAQ-DI ≤ 0.5 g) Tender enthesial points ≤ 1
To compare the efficacy of deucravacitinib to placebo in FACIT-Fatigue score at Week 16	Change from baseline in FACIT-Fatigue score at Week 16

Table 4-1: Objectives and Endpoints

Objective	Endpoint
To compare the efficacy of deucravacitinib to placebo in dactylitis resolution at Week 16	Proportion of participants meeting dactylitis resolution at Week 16 among the participants with dactylitis at baseline, where resolution is defined as a tender dactylitis count of 0 in participants with a tender dactylitis count ≥ 1 at baseline
To compare the efficacy of deucravacitinib to placebo as assessed by structural damage at Week 16	Change from baseline in PsA-modified SvdH score at Week 16
Additional Secondary Objectives and Endpoints (At Each Time Point up to Week 16)	
To assess the efficacy of deucravacitinib to placebo in ACR 20, ACR 50, and ACR 70 up to Week 16	Proportion of participants meeting ACR 20, ACR 50, and ACR 70 response
To assess the efficacy of deucravacitinib (6 mg QD) to placebo as assessed by HAQ-DI score up to Week 16	• Change from baseline in HAQ-DI score • Proportion of participants who achieve a clinically meaningful improvement (≥ 0.35 improvement from baseline) in HAQ-DI score among participants with a HAQ-DI score ≥ 0.35 at baseline
To assess the efficacy of deucravacitinib (6 mg QD) to placebo as assessed by PASI response up to Week 16	Proportion of participants with achievement of PASI 75/90/100 response, in participants with at least 3% BSA and at least sPGA 2 at baseline
To assess the efficacy of deucravacitinib (6 mg QD) to placebo as measured by SF-36 PCS score up to Week 16	Change from baseline in the SF-36 PCS score
To assess the efficacy of deucravacitinib (6 mg QD) to placebo in enthesitis resolution up to Week 16	Proportion of participants meeting enthesitis resolution among participants with enthesitis at baseline by LEI and SPARCC
To assess the efficacy of deucravacitinib (6 mg QD) to placebo in MDA response up to Week 16	Proportion of participants meeting achievement of MDA where an MDA responder is based on a participant fulfilling 5 of 7 below outcomes: a) Tender joint count ≤ 1 b) Swollen Joint Count ≤ 1 c) PASI ≤ 1 or BSA ≤ 3% d) Patient assessment of PsA pain ≤ 15

Table 4-1: Objectives and Endpoints

Objective	Endpoint
	e) Patient Global Assessment of PsA disease activity ≤ 20 f) HAQ-DI ≤ 0.5 g) Tender enthesial points ≤ 1
To assess the efficacy of deucravacitinib (6 mg QD) to placebo in SF-36 MCS score up to Week 16	Change from baseline in SF-36 MCS score
To assess the efficacy of deucravacitinib (6 mg QD) to placebo in FACIT-Fatigue score up to Week 16	Change from baseline in FACIT-Fatigue score
To assess the efficacy of deucravacitinib (6 mg QD) to placebo in dactylitis resolution up to Week 16	Proportion of participants meeting dactylitis resolution among the participants with dactylitis at baseline, where resolution is defined as a tender dactylitis count of 0 in participants with a tender dactylitis count ≥ 1 at baseline
To assess the efficacy of deucravacitinib (6 mg QD) to placebo as assessed by PsAID 12 score up to Week 16	Change from baseline in PsAID 12 score
To assess the efficacy of deucravacitinib (6 mg QD) to placebo as assessed by DAPSA score up to Week 16	• Change from baseline in DAPSA score • Proportion of participants with achievement of DAPSA Low Disease Activity response • Proportion of participants with achievement of DAPSA disease remission
To assess the efficacy of deucravacitinib (6 mg QD) to placebo as measured by PGA-F up to Week 16	Proportion of participants meeting achievement of PGA-F of 0/1 in participants with a baseline PGA-F score of ≥ 3
To assess the efficacy of deucravacitinib (6 mg QD) to placebo up to Week 16 in DAS28-CRP	• Change from baseline in DAS28-CRP score • Proportion of participants with achievement of a DAS28-CRP Low Disease Activity response • Proportion of participants with achievement of a DAS28-CRP disease remission

Table 4-1: Objectives and Endpoints

Objective	Endpoint
To assess the efficacy of deucravacitinib (6 mg QD) to placebo as measured by the PASDAS up to Week 16	Change from baseline in PASDAS
To assess the efficacy of deucravacitinib (6 mg QD) in mCPDAI score up to Week 16	Change from baseline in mCPDAI score
To assess the efficacy of deucravacitinib (6 mg QD) to placebo as measured by the PsARC up to Week 16	Proportion of participants achieving PsARC, where participants must achieve improvement in 2 of 4 measures, 1 of which must be joint pain or swelling, without worsening in any measure
To assess the efficacy of deucravacitinib (6 mg QD) to placebo as measured by the BASDAI score up to Week 16	Proportion of participants meeting achievement of improvement from baseline in BASDAI score among participants with spondylitis in addition to peripheral joint involvement as their presentation of PsA
To assess inhibition of structural damage up to Week 16	• Proportion of participants meeting achievement of total PsA-modified SvdH score of ≤ 0, ≤ 0.5, and ≤ SDC at Week 16 • Proportion of participants meeting achievement of PsA-modified SvdH erosion score change of ≤ 0, ≤ 0.5, and ≤ SDC at Week 16 • Proportion of participants meeting achievement of PsA-modified SvdH JSN score change of ≤ 0, ≤ 0.5, and ≤ SDC at Week 16
	• Change in PsA-modified SvdH erosion score from baseline at Week 16 • Change in PsA-modified SvdH JSN score at Week 16
To assess the efficacy of deucravacitinib (6 mg QD) to placebo as measured by improvement in domain scales scores, PCS score, and MCS score of SF-36 up to Week 16	Change from baseline in domain scales scores, PCS score, and MCS score of SF-36

Table 4-1: Objectives and Endpoints

Objective	Endpoint
To assess the efficacy of deucravacitinib (6 mg QD) to placebo as measured by improvement in WPAI up to Week 16	Change from baseline in the subcomponents of the WPAI questionnaire
To assess the efficacy of deucravacitinib (6 mg QD) to placebo on general quality of life up to Week 16	Change from baseline in the EQ-5D-5L utility scores and its subcomponents
To assess the efficacy of 6 mg deucravacitinib QD to placebo on sleep disturbance score up to Week 16	Change from baseline in PROMIS sleep disturbance score (short form)
[redacted]	[redacted]

Table 4-1: Objectives and Endpoints

Objective	Endpoint
[redacted]	

Table 4-1: Objectives and Endpoints

Objective	Endpoint
[redacted]	

Table 4-1: Objectives and Endpoints

Objective	Endpoint
[redacted]	

Table 4-1: Objectives and Endpoints

Objective	Endpoint
[redacted]	
Safety	
To assess the safety and tolerability of deucravacitinib in participants with active PsA	Incidence of AEs, SAEs, AEs leading to discontinuation of treatment and study discontinuation, [redacted]; change in laboratory, ECG, and vital signs; and abnormalities in laboratory, ECG, and vital signs
[redacted]	

Table 4-1: Objectives and Endpoints

Objective	Endpoint
[redacted]	

Table 4-1: Objectives and Endpoints

Objective	Endpoint
[redacted]	

Abbreviations: ACR, American College of Rheumatology; AE, adverse event; BASDAI, Bath Ankylosing Spondylitis Disease Activity; BSA, body surface area; DAPSA, Disease Activity Index for Psoriatic Arthritis; DAS28-CRP, Disease Activity Score 28 with C-reactive protein; ECG, electrocardiogram; EQ-5D-5L, 5-level EuroQoL 5-dimension; FACIT, Functional Assessment of Chronic Illness Therapy; HAQ-DI, Health Assessment Questionnaire - Disability Index; IL, interleukin; JSN, joint space narrowing; LEI, Leeds Enthesitis Index; mCPDAI, modified Composite Psoriatic Disease Activity Index; MCS, Mental Component Summary; MDA, minimal disease activity; PASDAS, Psoriatic Arthritis Disease Activity Score; PASI, Psoriasis Area and Severity Index; PCS, Physical Component Summary; PGA-F, Physician Global Assessment-Fingernails; PROMIS, Patient-Reported Outcome Measures Information System; PsA, psoriatic arthritis; PsAID, Psoriatic Arthritis Impact of Disease; PsARC, Psoriatic Arthritis Response Criteria; QD, once daily; SAE, serious adverse event; SDC, smallest detectable change; SF-36, Short Form-36; SPARCC, Spondyloarthritis Research Consortium of Canada; sPGA, static Physician's Global Assessment; SvdH, Sharp-van der Heijde; TH, T-helper; WPAI, Work Productivity and Activity Impairment.

5 STUDY DESIGN

5.1 Overall Design

This is a Phase 3, 52-week, multi-center, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of deucravacitinib versus placebo in participants with active PsA

who are naïve to biologic therapy. [redacted]

Approximately 650 qualified participants will be randomized with equal allocation to receive either 6 mg deucravacitinib QD or matching placebo for an initial 16 weeks. All participants must have had a documented inadequate response, loss of response, or intolerance to at least 1 csDMARD, and/or apremilast, and/or NSAID given for the treatment of PsA. Participants will be allowed to continue on background medications (csDMARD, NSAID, and/or glucocorticoid) during the study as specified by the inclusion criteria. Participants must NOT have had prior treatment with a bDMARD or a JAK inhibitor for PsA and/or PsO.

[redacted]

- Screening Period (28 days)
- Treatment Period (52 weeks), comprised of
  - ♦ Placebo-controlled Treatment Period (16 weeks) (Week 0 to Week 16)

[redacted]

- Safety Follow-up Period (30 days) (following last dose of investigational product [IP] unless participant has continued in study for 30 days or more after discontinuation of IP)

Participants will undergo screening evaluations to determine eligibility within 28 days prior to administration of investigational product. Following the screening process, eligible participants will be randomized in a 1:1 ratio to 1 of the following 2 treatment groups:

1. 6 mg deucravacitinib QD
2. Placebo

[redacted]

At Week 16, participants originally randomized to placebo will be reallocated (in a blinded fashion for the initially randomized treatment) to receive 6 mg deucravacitinib QD through Week 52. Participants originally randomized to 6 mg deucravacitinib QD will continue to receive the same treatment and dose through Week 52.

[redacted]

[redacted]

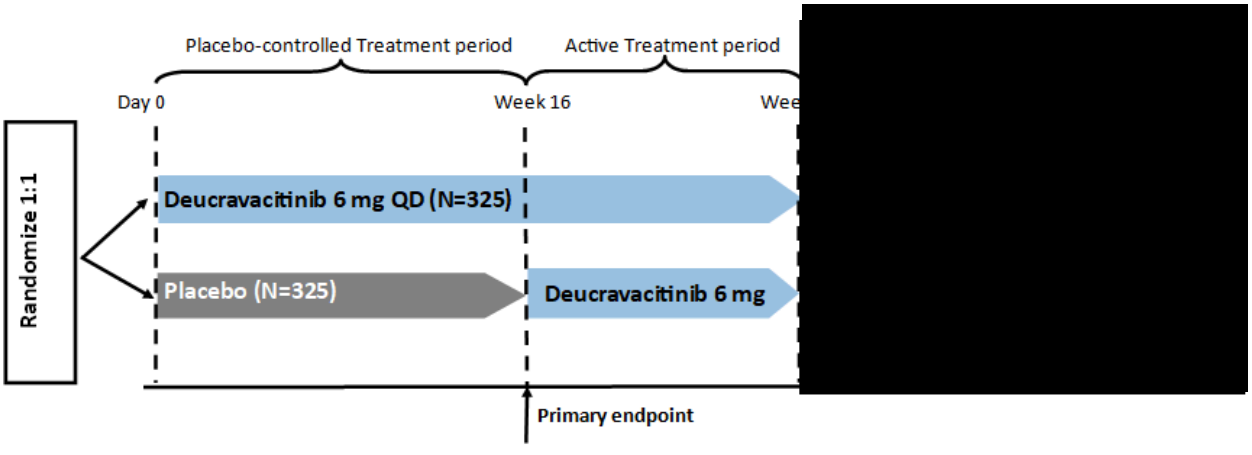
Assessments for efficacy, safety, tolerability, quality of life, [redacted] will be performed at specified time points as outlined in the Schedule of Activities (see Section 2).

[redacted]

Participants who discontinue study treatment will complete an Early Termination (ET) Visit, a Safety Follow-up Visit 30 days following the last dose of study treatment, and should complete each study visit through Week 52. Only participants who are lost to follow-up or withdraw consent will have no further study visits (see Section 8).

The study design schematic is presented in Figure 5.1-1.

Figure 5.1-1: Study Design Schematic



Abbreviations: N, number; [redacted] QD, once daily.

5.1.1 Data Monitoring Committee [redacted]

5.1.1.1 Data Monitoring Committee

An independent external DMC will be charged with monitoring accumulating data from the trial, as well as general aspects of trial conduct. The committee will meet periodically during the study to review aggregate analyses concerning efficacy and safety data from the trial. All members are selected with consideration for their respective expertise in the subject matter and/or in their experience in convening or participating in a DMC. Based on their overall benefit/risk evaluation, the DMC recommendations may include proceeding with the study per protocol, proceeding with the study with modifications, or study suspension. The scope, conduct, membership, processes, and accountabilities of the DMC are specified in the DMC Charter.

[redacted]

5.2 Number of Participants

A total sample size of approximately 650 participants will be randomized in a blinded fashion at a 1:1 ratio (approximately 325 participants each randomized to 6 mg deucravacitinib QD arm and placebo).

5.3 End of Study Definition

The start of the trial is defined as the first visit for the first participant screened. End of trial is defined as the last visit or scheduled procedure as shown in the Schedule of Activities (Section 2) for the last participant. Completion of the double-blinded portion of the study is defined as the final date on which data was or is expected to be collected up to Week 16 for all participants.

5.4 Scientific Rationale for Study Design

As described in Section 3.2, there is an unmet need for novel treatment options for PsA. Deucravacitinib 6 mg QD was shown to be safe and efficacious in Phase 2 clinical trial in PsA (IM011084) and is now proposed to be studied in a Phase 3 study.

The study is intended to confirm the safety and efficacy of 6 mg deucravacitinib QD compared with placebo in adults with active PsA.

Study Population

The target study population includes participants with active PsA who are biologic naïve and have had a documented inadequate response, loss of response, or intolerance to standard therapies (eg, DMARDs, and/or NSAIDs, and/or apremilast). This population should maximize the applicability of the results of IM011054 to the broad and heterogeneous bDMARD-naïve patients typically seen in clinical practice. Furthermore, this population is similar to that in the Phase 2 study (IM011084) and is considered appropriate to provide relevant efficacy and safety information for the intended use of deucravacitinib in PsA. Eligible participants are required to have at least 1 erosion on X-rays of hands or feet as well as pre-specified level of hsCRP ≥ 3 mg/L (upper level of normal [ULN] is 5 mg/L for central laboratory).

Study Control, Blinding

A placebo control will be used to establish the frequency and magnitude of changes in endpoints that may occur in the absence of active treatment.

Study will include a 16-week Placebo-controlled, Double-blind Treatment Period followed by an additional 36 weeks of an Active Treatment Period. At Week 16, participants originally randomized to placebo will be reallocated in a blinded fashion to receive 6 mg deucravacitinib QD through Week 52. Participants originally randomized to 6 mg deucravacitinib QD Day 1 will continue to receive the same dose through Week 52.

The duration of placebo-controlled treatment is limited to 16 weeks to avoid potential disease progression and at the same time to allow sufficient duration for detection of treatment effect in multiple domains of disease.

Blinded treatment up to Week 16 will be used to reduce potential bias during data collection and evaluation of clinical endpoints.

Study Evaluations

The primary endpoint chosen for the study of ACR 20 response has been very well established in previous studies of therapeutic agents for PsA and has been accepted by regulatory authorities globally, including European Medicines Agency Guideline on Clinical Investigation of Medicinal Products Indicated for the Treatment of Psoriatic Arthritis.[32] Similarly, key secondary endpoints are well established, validated, and clinically relevant and have been used in previous and ongoing clinical trials in PsA.[33,34,35,36] Key secondary endpoints in the study include the following: Disease Activity Score (DAS)28 C-reactive protein (CRP) score (DAS28-CRP), HAQ-DI, SF-36 Physical Component Summary (PCS), Functional Assessment of Chronic Illness Therapy (FACIT)-Fatigue, PASI 75 response, achievement of minimal disease activity (MDA), resolution of enthesitis, resolution of dactylitis, and change from baseline in Sharp-van der Heijde (SvdH) score modified for PsA. Patient-reported outcomes (PROs) selected as key secondary endpoints

are consistent with clinically relevant measurements that are accepted in the medical literature for other studies in PsA.[37,38,39,54]

5.5 Justification for Dose

The Phase 3 IM011054 study is designed to confirm the efficacy and safety of 6 mg deucravacitinib QD versus placebo in PsA. This dose was selected based on observed efficacy [redacted].

Results from the Phase 2 study (IM011084) indicated that both the 6 mg QD and 12 mg QD doses achieved higher ACR 20/50/70 responses compared with placebo. At Week 16, ACR 20/50/70 responses were met in the 6 mg QD group in 52.9%, 24.3%, and 14.3% of participants, respectively, and in the 12 mg QD group in 62.7%, 32.8%, and 19.4% of participants, respectively (refer to Section 3.1 for additional details). [redacted]

The overall safety of deucravacitinib was acceptable in the Phase 2 study in PsA. The incidence of participants with AEs was numerically higher in both active treatment groups compared with placebo (42.4%, 65.7%, and 65.7% in the placebo and 6 mg and 12 mg deucravacitinib QD groups, respectively). Participants in the 6 mg deucravacitinib versus the 12 mg deucravacitinib group had less frequent nasopharyngitis (5.7% versus 17.9%), sinusitis (none versus 7.5%), and rash (4.3% versus 6.0%). Infections were numerically lower in the placebo and 6 mg deucravacitinib treatment groups (22.7% and 28.6%, respectively) compared with the 12 mg deucravacitinib group (35.8%). The most common infections were respiratory tract related. Importantly, there were no serious or severe infections, no herpes zoster, and no systemic opportunistic infections. Infections only rarely led to discontinuation of treatment (1 participant in each active treatment group). All AEs in the 6 mg deucravacitinib QD treatment group were mild or moderate and rarely led to discontinuation of treatment (3 participants); similarly, most AEs in 12 mg deucravacitinib QD treatment group were mild or moderate (except 1 participant with severe AE of creatine kinase [CK] elevation that has resolved without treatment) and rarely led to discontinuation of treatment (4 participants). There were no SAEs reported in active treatment arms. There were no cases of herpes zoster or opportunistic infections in active treatment arms.

[redacted]

6 STUDY POPULATION

For entry into the study, the following criteria MUST be met.

6.1 Inclusion Criteria

1) Signed Written Informed Consent

a) Participants must be willing to participate in the study and sign the informed consent form (ICF).

2) Type of Participant and Target Disease Characteristics

a) Participant has been diagnosed to have PsA (by any criteria) of at least 3 months, duration at Screening.

b) Participant meets the Classification Criteria for Psoriatic Arthritis (see Appendix 5) at Screening.

c) Participant has active plaque psoriatic skin lesion(s) or documented medical history of plaque PsO at Screening.

d) Participant has active arthritis as shown by ≥ 3 swollen joints and ≥ 3 tender joints (66/68 joint counts) at Screening and Day 1.

e) Participant has ≥ 1 PsA-related hand and/or foot joint erosion on X-ray during Screening Period that is confirmed by central reading.

f) Participant has hsCRP ≥ 3 mg/L at Screening.

g) Participant has had documented inadequate response, loss of response, or intolerance to at least 1 of the following:

  i) A csDMARD (MTX, SSZ, LEF, or hydroxychloroquine [HCQ]) maximally tolerated dose, and/or apremilast, after a minimum of 12 weeks, duration of therapy given for the treatment of PsA.

  ii) An NSAID after a minimum of 4 weeks, duration of therapy given for the treatment of PsA, or participant has intolerance to those treatments in the opinion of the investigator.

h) Concurrent use of 1 csDMARD, and/or NSAID, and/or oral glucocorticoid is permitted but not required during the study.

  i) If such treatment was administered, then participants must meet the following requirements:

    (1) If on csDMARD (MTX, SSZ, LEF, hydroxychloroquine [HCQ]), the participant must have been on it for at least 12 weeks and be on a stable dose for at least 28 days prior to Day 1.

      (a) If on MTX, the route of administration and dose must be stable and the dose must be ≤ 25 mg/week.

      (b) If on SSZ, the dose must be ≤ 3 g/day.

      (c) If on HCQ, the dose must be ≤ 400 mg/day.

      (d) If on LEF, the dose must be ≤ 20 mg/day.

      Note: If currently not on MTX, SSZ, or HCQ, the participant must have not received it for at least 28 days prior to Day 1. If currently not on LEF, the participant must not have received it for at least 12 weeks prior to Day 1.

  ii) If on NSAID, the participant must be on a stable dose for at least 14 days prior to Day 1.

  iii) If on oral glucocorticoids, the participant must be on a stable dose of ≤ 10 mg/day prednisone equivalent for at least 28 days prior to Day 1.

    Note: If currently not on oral glucocorticoids, the participant must not have received oral glucocorticoids within 28 days prior to Day 1.

i) Concurrent permitted topical therapy for plaque PsO must be stable for at least 14 days prior to Day 1.

[redacted]

3) Age and Reproductive Status

Investigators shall counsel women of childbearing potential (WOCBP) participants, and male participants who are sexually active with WOCBP, on the importance of pregnancy prevention and the implications of an unexpected pregnancy.

The investigator shall evaluate the effectiveness of the contraceptive method in relationship to the first dose of study intervention.

Local laws and regulations may require the use of alternative and/or additional contraception methods.

a) Female participants:
   i) Female, age at least 18 years or local age of majority at Screening.
   ii) Women who are not of childbearing potential (as defined in Appendix 4) are exempt from contraceptive requirements.
   iii) Women participants must have documented proof that they are not of childbearing potential.
   iv) WOCBP must have a negative serum pregnancy test at Screening Visit, and a negative urine pregnancy test (minimum sensitivity 25 IU/L or equivalent units of human chorionic gonadotropin) within 24 hours prior to the start of study treatment.
      (1) If a urine test cannot be confirmed as negative (eg, an ambiguous result), a serum pregnancy test is required. In such cases, the participant must be excluded from participation if the serum pregnancy result is positive.
   v) Additional requirements for pregnancy testing during and after study intervention are located in Section 2, Schedule of Activities.
   vi) The investigator is responsible for review of medical history, menstrual history, and recent sexual activity to decrease the risk for inclusion of a woman with an early undetected pregnancy.
   vii) Women must not be pregnant, lactating, breastfeeding, or planning pregnancy during the study period.
   viii) WOCBP must agree to use highly effective (with a failure rate of < 1% per year) method(s) of contraception, preferably with low user dependency, as described in Appendix 4 of the protocol, during the study period until study completion or 30 days after discontinuation of the study treatment, whichever is longer (See Section 5.3).
   ix) WOCBP are permitted to use hormonal contraception methods (as described in Appendix 4 of the protocol).

   Note: Local laws and regulations may require use of alternative and/or additional contraception methods; additionally, alternative and/or additional contraceptives may be

required (eg, based on background DMARDs the participant may be taking, such as MTX, LEF, etc).

b) Male participants:

i) Males, age at least 18 years or local age of majority at Screening.

ii) Male participants should maintain their usual practice with regard to contraception (if any); however, no specific contraceptive measures are required.

Note: Local laws and regulations may require use of alternative and/or additional contraception methods; additionally, alternative and/or additional contraceptives may be required (eg, based on background DMARDs the participant may be taking, such as MTX, LEF, etc).

6.1.1 *Inclusion Criteria* [redacted]

1) Signed Written Informed Consent

a) Participants must be willing to participate in the study and sign the informed consent form (ICF).

2) Type of Participant and Target Disease Characteristics

a) Completion of study treatment through Week 52.

b) In the opinion of the investigator, the participant may benefit from continuation in the [redacted] Period.

3) Reproductive Status

a) WOCBP must have a negative urine pregnancy test at Initial Visit (minimum sensitivity 25 IU/L or equivalent units of human chorionic gonadotropin).

i) If a urine test cannot be confirmed as negative (eg, an ambiguous result), a serum pregnancy test is required. In such cases, the participant must be discontinued from participation if the serum pregnancy result is positive.

ii) Women must not be pregnant, lactating, breastfeeding, or planning pregnancy during the study period.

iii) WOCBP must agree to continue using highly effective (with a failure rate of < 1% per year) method(s) of contraception, preferably with low user dependency, as described in Appendix 4 of the protocol, during the study period until study completion or 30 days after discontinuation of the study treatment, whichever is longer (See Section 5.3).

(1) WOCBP are permitted to use hormonal contraception methods (as described in Appendix 4 of the protocol).

(2) Male participants should maintain their usual practice with regard to contraception (if any); however, no specific contraceptive measures are required.

Note: Local laws and regulations may require use of alternative and/or additional contraception methods; additionally, alternative and/or additional contraceptives may be required (eg, based on background DMARDs the participant may be taking, such as MTX, LEF, etc).

6.2 Exclusion Criteria

1) Target Disease Exceptions

a) Participant has nonplaque PsO (ie, guttate, pustular, erythrodermic, or drug-induced PsO) at Screening or Day 1.

b) Participant has any other autoimmune condition such as systemic lupus erythematous, mixed connective tissue disease, multiple sclerosis, or vasculitis.

c) Participant has prior history of or current inflammatory joint disease other than PsA (eg, gout, reactive arthritis, rheumatoid arthritis, ankylosing spondylitis, Lyme disease).

d) Participant has active (ie, currently symptomatic) fibromyalgia whose symptoms or therapy will significantly impact the assessment of PsA disease manifestations and activity in the opinion of the investigator.

2) Concomitant Medication and Medical History/Concurrent Diseases

a) Participant has received an approved or investigational biologic therapy for the treatment of PsA or PsO (eg, TNF-α inhibitor [eg, etanercept, adalimumab, infliximab, golimumab, certolizumab], agents that modulate lymphocyte trafficking [eg, natalizumab, efalizumab], agents that modulate B cells or T cells [eg, alemtuzumab, abatacept, alefacept, or visilizumab], monoclonal antibodies against IL-17 [eg, secukinumab, ixekizumab, brodalumab, bimekizumab], IL-12/IL-23p40 [eg, ustekinumab], or IL-23 [eg, guselkumab, risankizumab, tildrakizumab, mirikizumab]).

b) Participant has received a JAK inhibitor (eg, baricitinib, tofacitinib, upadacitinib, filgotinib) for the treatment of PsA and/or PsO.

c) Participant has received a phosphodiesterase 4 inhibitor (eg, apremilast) within 28 days prior to Day 1.

d) Participant has received intra-articular, intramuscular, or IV glucocorticoids, including adrenocorticotropic hormone, within the 28 days prior to Day 1.

e) Participant has had prior exposure to the IP (ie, deucravacitinib).

f) ***Not applicable per Protocol Amendment 01:*** Participant has received systemic non-biologic PsO medications and/or any systemic immunosuppressant therapy other than what is permitted in inclusion criteria (Section 6.1).

g) Participant has used any opioid analgesic at average daily doses of > 30 mg/day of morphine or its equivalent or use of variable doses of any opiate analgesic within 28 days prior to Day 1.

h) Participant has used medical marijuana or prescription marijuana for medicinal reasons.

i) Participant has received phototherapy (including either oral or topical psoralen ultraviolet A light therapy, ultraviolet B, or self-treatment with tanning beds, or therapeutic sunbathing) within 28 days prior to Day 1.

j) Participant has used topical medications/treatments that could affect PsO evaluation, including, but not limited to, medium- or high-potency glucocorticoids (WHO Classes I through V), anthralin, calcipotriene, topical vitamin D derivatives, retinoids, tazarotene, methoxsalen, trimethylpsoralen, picrolimus, and tacrolimus, within 14 days of Day 1.

[redacted]

[redacted]

k) Participant has used shampoos that contain glucocorticoids, coal tar, or vitamin D3 analogues within 14 days prior to Day 1.

l) Participant who has received any experimental therapy or new investigational agent, including those for SARS-CoV-2, may not participate in the study until the protocol-specific washout period is achieved (4 weeks or 5 half-lives, whichever is longer) prior to Day 1 or is currently enrolled in an investigational study.

Note: As outlined in exclusion criterion 3), if a study participant has received an investigational SARS-CoV-2 vaccine prior to Screening, enrollment should be delayed until the biologic impact of the vaccine is stabilized, as determined by discussion between the investigator and the Bristol-Myers Squibb Company (BMS) Medical Monitor.

m) Participant has had any major surgery within 8 weeks prior to Day 1, or any planned surgery for the first 52 weeks of the study.

n) Participant has donated blood > 500 mL within 28 days prior to Day 1, or intends to donate blood during the course of the study.

o) Participant has abused drugs or alcohol, as determined by the investigator, within 6 months prior to Day 1.

p) Participant has had any major illness/condition or evidence of an unstable clinical condition (eg, renal, hepatic, hematologic, gastrointestinal, endocrine, pulmonary, psychiatric, immunologic, or local active infection/infectious illness) that, in the investigator's judgment or after consultation with the Medical Monitor, will substantially increase the risk to the participant if he or she participates in the study.

q) Participant has had unstable cardiovascular disease, defined as a recent clinical deterioration (eg, unstable angina, myocardial infarction, stroke, rapid atrial fibrillation) in the last 6 months prior to Screening, or a cardiac hospitalization within the 6 months prior to Screening.

r) Participant has uncontrolled arterial hypertension characterized by a systolic blood pressure (BP) > 160 mm Hg or diastolic BP > 100 mm Hg at Day 1.

Note: Determined by 2 consecutive elevated readings. If an initial BP reading exceeds this limit, the BP may be repeated once after the participant has rested sitting for ≥ 10 minutes. If the repeat value is less than the criterion limits, the second value may be accepted.

s) Participant has Class III or IV congestive heart failure by New York Heart Association Criteria.

t) Participant has cancer, history or recurrence of cancer (including skin cancer, carcinoma of the cervix or high grade cervical intraepithelial neoplasia, irrespective of past treatment), or lymphoproliferative disease within the previous 5 years.

u) Participant has any other sound medical and/or social reason as determined by the investigator.

v) Participant has received systemic non-biologic medications and/or any systemic immunosuppressant therapy for PsO and/or PsA other than what is permitted in inclusion criteria (see Section 6.1) (including, but not limited to, azathioprine, cyclosporine,

6-thioguanine, mercaptopurine, mycophenolate mofetil, hydroxyurea, tacrolimus, retinoids, 1,25-dihydroxy vitamin D3 [oral vitamin D supplements are permitted] and analogues, psoralens, or fumaric acid derivatives) within 28 days prior to Day 1.

w) Participant has received and/or used any traditional Chinese medicines intended to treat PsA and/or PsO, within 4 weeks prior to Study Day 1.

3) Infectious/Immune-related Exclusions

a) Participant has a history or evidence of participant's active infection and/or febrile illness within 14 days prior to Day 1.

b) Participant has a history of serious bacterial, fungal, or viral infection requiring hospitalization and IV antimicrobial treatment within 60 days prior to Day 1. Additionally, in the case of prior SARS-CoV-2 infection, symptoms must have completely resolved and, based on investigator assessment in consultation with the Medical Monitor, there are no sequelae that would place the participant at a higher risk of receiving investigational treatment.

c) Participant has a history of an infected joint prosthesis or has ever received antibiotics for a suspected infection of a joint prosthesis, if that prosthesis has not been removed or replaced.

d) Participant has received live vaccine(s) within 60 days prior to Day 1 or plans to receive a live vaccine during the study or within 60 days after completing study treatment. Heat-killed or otherwise inactivated vaccines or protein or subunit vaccines (eg, influenza and pneumococcal vaccines) may be received at any time on study. Note: If a study participant has received a SARS-CoV-2 vaccine authorized under an Emergency Use Authorization or alternative authorization prior to Screening, enrollment should be delayed until the biologic impact of the vaccine is stabilized, as determined by discussion between the investigator and the BMS Medical Monitor.

e) Participant has a presence of herpes zoster lesions at Screening or Day 1 or history of serious herpes zoster or serious herpes simplex infection, which includes, but is not limited to, any episode of disseminated herpes simplex, multidermatomal herpes zoster, herpes encephalitis, ophthalmic herpes, or recurrent herpes zoster.

f) Participant has evidence of, or positive test for, hepatitis C virus (HCV) or hepatitis B virus (HBV) at Screening. (For selected countries: Hepatitis B surface antigen [HBsAg]-positive participants are excluded from the study. Participants who are HBsAg-negative but positive for hepatitis B surface antibody [HBsAb] and/or hepatitis B core antibody [HBcAb] may be eligible and must also be tested for quantitative HBV deoxyribonucleic acid [DNA]. Participants with detectable levels as specified by local guidelines at Screening are excluded; see Appendix 22.)

g) Participant is positive for human immunodeficiency virus (HIV-1 or -2) antibody at Screening. A positive test result will disqualify the participant from participation in the study. The investigator should refer any participant who tests positive for HIV to the appropriate HIV counsellor or health advisor (per the investigator's medical practice procedure) for further follow-up.

h) Participant has any history of known or suspected congenital or acquired immunodeficiency state or condition that would compromise the participant's immune status (eg, history of opportunistic infections [eg, *Pneumocystis jirovecii* pneumonia,

histoplasmosis, or coccidioidomycosis], history of splenectomy, primary immunodeficiency).

4) Any of the Following TB Criteria:

a) Participant has a history of active TB prior to Screening Visit, regardless of completion of adequate treatment.

b) Participant has signs or symptoms of active TB (eg, fever, cough, night sweats, and weight loss) during Screening as judged by the investigator.

c) Participant has any imaging of the chest (eg, chest X-ray, chest computed tomography scan) obtained during the Screening Period, or anytime within 6 months prior to Screening with documentation, showing evidence of current active or history of active pulmonary TB.

d) Participant has latent TB infection (LTBI), defined as positive IFN gamma release assay (IGRA) by QuantiFERON®-TB Gold testing at Screening in the absence of clinical manifestations.

i) Participant may be eligible if (i) there are no current signs or symptoms of active TB and (ii) participant has received adequate documented treatment for LTBI within 5 years of Screening or has initiated prophylactic treatment for LTBI per local guidelines and is rescreening now after 1 month of treatment. To continue in the study, participant must agree to complete a locally recommended course of treatment for LTBI.

ii) For participants who are not currently on prophylactic treatment for LTBI per local guidelines, including participants who have documented completed treatment for LTBI within 5 years of Screening, results of initial IGRA test that is indeterminate with no signs or symptoms of active TB must be retested for confirmation. If the second test is again indeterminate, the participant will be excluded from the study. If the retest is positive, the participant must be treated as having LTBI. If the retest is negative, the participant may be eligible provided no other exclusion criteria for TB are met.

iii) For participants who are on prophylactic treatment for LTBI per local guidelines, and there are no current signs or symptoms of active TB, retesting of an initial positive or indeterminate result is not required and participants may be eligible provided no other exclusion criteria for TB are met, and participants continue to complete treatment for LTBI per local guidelines.

e) Participant has a history of active or latent TB infection, and participant lives in, or has emigrated from, a multi-drug resistant TB high-burden country (see Appendix 23).

f) Participant has had a household contact with a person with active TB and participant did not receive appropriate and documented prophylaxis for TB.

Note: Household contact is a person who shared the same enclosed living space as the index case for 1 or more nights or for frequent or extended daytime periods during the 3 months prior to Day 1.

5) Physical and Laboratory Test Findings

a) Absolute white blood cell count < 3000/mm^3 at Screening.

b) Absolute lymphocyte count < 500/mm^3 at Screening.

c) Absolute neutrophil count < 1000/mm^3 at Screening.

d) Platelet count < 100,000/mm^3 at Screening.

e) Hemoglobin < 9 g/dL at Screening.

f) Alanine aminotransferase (ALT) and/or aspartate aminotransferase (AST) > 2× upper limit of normal (ULN) at Screening.

g) Total, unconjugated, and/or conjugated bilirubin > 1.5× ULN at Screening, except for any participant with a confirmed diagnosis of Gilbert's syndrome.

h) Estimated glomerular filtration rate (eGFR) < 45 mL/min.

i) Any other significant laboratory or procedure abnormalities that, in the opinion of the investigator, might place the participant at unacceptable risk for participation in this study.

6) Allergies and Adverse Drug Reactions

a) History of any significant drug allergy or intolerance (such as anaphylaxis).

7) Other Exclusion Criteria

a) Prisoners or participants who are involuntarily incarcerated.

b) Participants who are compulsorily detained for treatment of either a psychiatric or physical (eg, infectious disease) illness.

c) Inability to comply with restrictions and prohibited activities/treatments as listed in body of protocol.

d) Site personnel or their immediate family.

6.2.1 Exclusion Criteria [redacted]

An individual who meets any of the following criteria will be excluded from participation in the [redacted] Period of the study:

1) Medical History and Concurrent Diseases

a) Any disease or medical condition that, in the opinion of the investigator, would make the participant unsuitable for this study, would interfere with the interpretation of participant safety or study results, or is considered unsuitable by the investigator for any other reason.

2) Findings Related to Possible TB Infection

a) Evidence of active TB (see Section 9.4.6).

[redacted]

[redacted]

Eligibility criteria for this study have been carefully considered to ensure the safety of the study participants and that the results of the study can be used. It is imperative that participants fully meet all eligibility criteria.

6.3 Lifestyle Restrictions

General skin care measures (with above restrictions for topical treatments) are recommended that are standard for patients with plaque PsO. Participants should avoid excessive sun exposure and avoid risks that are known to provoke flare of PsO and/or PsA.

6.3.1 Meals and Dietary Restrictions

Study treatment may be taken without regard to meals. However, samples are to be collected in a fasted state during specified visits. Refer to Schedule of Activities (Section 2).

6.3.2 Caffeine, Alcohol, and Tobacco

No restrictions are required; however, extensive use of caffeine, alcohol, and tobacco or other nicotine-containing products should be avoided.

6.3.3 Activity

No restrictions are required; however, unusual physical exertion should be avoided during the study.

6.4 Screen Failures

Screen failures are defined as participants who consent to participate in the clinical study but who are not subsequently randomized in the study/included in the analysis population. A minimal set of screen failure information is required to ensure transparent reporting of screen failure participants, to meet the Consolidated Standards of Reporting Trials (CONSORT) publishing requirements, as applicable, and to respond to queries from regulatory authorities. Minimal information includes date of consent, demography, screen failure details, eligibility criteria, and any serious AEs.

6.4.1 Retesting During Screening or Lead-in Period

For laboratory parameters that initially do not meet eligibility requirements, [redacted] is permitted before a participant is declared a screen failure. This is an effort to find all possible well-qualified participants. Consultation with the Medical Monitor may be needed to identify whether repeat testing of any particular parameter would be clinically relevant.

The study permits the rescreening [redacted] of a participant who discontinues the study as a pretreatment failure (ie, the participant fails to meet eligibility criteria and has not been treated). The participant must be re-consented and will be assigned a new identification number, and a full Screening Visit must be performed again. A

participant can only be rescreened 1 time (ie, if the participant fails 1 rescreening attempt, no additional rescreening is allowed). Duration of existing treatments and required discontinuation periods shall be considered relative to the new Screening Visit and/or randomization.

The most current result prior to randomization is the value by which study inclusion will be assessed, as it represents the participant's most current clinical state.

Rescreening is allowed once with consultation with the Medical Monitor.

7 TREATMENT

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

Study treatment includes both investigational (medicinal) product (IP/IMP) and non-investigational (medicinal) product (Non-IP/Non-IMP) and can consist of the following: deucravacitinib and placebo.

An IP, also known as IMP in some regions, is defined a pharmaceutical form of an active substance or placebo being tested or used as a reference in a clinical study, including products already with a marketing authorization but used or assembled (formulated or packaged) differently than the authorized form, or used for an unauthorized indication, or when used to gain further information about the authorized form.

Other medications used as support or escape medication for preventative, diagnostic, or therapeutic reasons, as components of the standard of care for a given diagnosis, may be considered as non-IPs.

Study treatments for IM011054 are listed in Table 7-1 [redacted].

Table 7-1: Study Treatments (Week 0 to Week 52) IM011054

Product Description/Class and Dosage Form	Potency	IP/Non-IMP	Blinded* or Open Label	Packaging/Appearance	Storage Conditions (per label)
6 mg deucravacitinib (BMS-986165) tablet	6 mg	IP	Blinded	Bottle	Refer to the label on container and/or Pharmacy Manual
Placebo matching 6 mg deucravacitinib (BMS-986165) tablet	N/A	IP	Blinded	Bottle	Refer to the label on container and/or Pharmacy Manual

Abbreviations: IMP, investigational medicinal product; IP, investigational product; N/A, not applicable.

*Blinded up to Week 56.

7.1 Treatments Administered

The study treatment will be administered in a double-blind fashion for the initial 16-week treatment period [redacted], as described in Section 5.1. The selection and timing of dose for each participant is as follows:

Table 7.1-1: Selection and Timing of Dose for 52-week Treatment Period

Study Treatment	Unit Dose Strength(s)/Dosage Level(s)	Dosage Formulation Frequency of Administration	Route of Administration
Deucravacitinib	6 mg	QD	Oral
Placebo	N/A	QD	Oral

Abbreviations: N/A, not applicable; QD, once daily.

[redacted]

7.2 Method of Treatment Assignment

All participants will be centrally randomized using Interactive Response Technology (IRT). Before the study is initiated, each user will receive log in information and directions on how to access IRT.

Study treatment will be dispensed at the study visits as listed in Schedule of Activities (Section 2).

Those enrolled participants meeting inclusion and exclusion criteria will be eligible to be randomized.

7.3 Blinding for the 16-week Treatment Period

7.3.1 Maintaining the Blind

Blinded treatment assignments will be managed using IRT. IP supply will be controlled by IRT at each visit.

All tablets are identical in appearance and will be supplied in bottles, with each daily dose made up of the appropriate combination of active and/or placebo tablets to provide the correct treatment,

as shown in Table 7.1-1. Investigative site staff, Sponsor and designee personnel, and participants and their families will remain blinded to treatment assignments.

[redacted]

7.3.2 Circumstances for Unblinding

This is a randomized, double-blind study [redacted]. The Week 16 database lock will occur once all randomized participants have completed Week 16 visits or have discontinued early, and all expected data are collected. The Week 16 database lock will enable an assessment of the primary and secondary efficacy objectives as well as assessment of safety up to Week 52 in participants who have reached that visit. The Week 56 database lock will occur once all randomized participants have completed Week 56 or discontinued early, and all expected data are collected. The Week 56 database lock will enable a full assessment of safety at Week 52 and exploratory efficacy objectives.

[redacted]

Blinding of treatment assignment is critical to the integrity of this clinical study. However, in the event of a medical emergency or pregnancy in an individual participant in which knowledge of the IP is critical to the participant's management, the blind for that participant may be broken by the investigator. The participant's safety takes priority over any other considerations in determining if a treatment assignment should be unblinded.

Before breaking the blind of an individual participant's treatment, the investigator should determine that the unblinded information is necessary (ie, that it will alter the participant's immediate management). In many cases, particularly when the emergency is clearly not related to the IP, the problem may be properly managed by assuming that the participant is receiving active investigational product. It is highly desirable that the decision to unblind treatment assignment be discussed with the Medical Monitor, but the investigator always has ultimate authority for the decision to unblind. The actual TASK of unblinding can be delegated by the investigator to a designee assigned the task on the Delegation of Authority. The principal investigator or appointed designee should only call in for emergency unblinding AFTER the decision to unblind the participant has been documented.

For this study, the method of unblinding for emergency purposes is through the IRT system.

In cases of accidental unblinding, contact the Medical Monitor and ensure every attempt is made to preserve the blind.

Any request to unblind a participant for nonemergency purposes should be discussed with the Medical Monitor.

In case of an emergency, the investigator(s) has unrestricted access to randomization information via the IRT and is capable of breaking the blind through the IRT system without prior approval from the Sponsor. Following the unblinding the investigator shall notify the Medical Monitor and/or study director.

Additionally, the DMC will assess safety on an ongoing basis and will have access to unblinded treatment for individual participants. An analysis team, including a reporting statistician and programming support who are not involved with the conduct of the study, will provide analyses to the DMC. The procedures to be respected and the reasons for unblinding of the DMC are outlined in the DMC Charter.

7.4 Dosage Modification

There is no provision for dose modification of study treatment.

7.5 Preparation/Handling/Storage/Accountability

The IP should be stored in a secure area according to local regulations. It is the responsibility of the investigator to ensure that IP is only dispensed to study participants. The IP must be dispensed only from official study sites by authorized personnel according to local regulations.

The product storage manager should ensure that the study treatment is stored in accordance with the environmental conditions (temperature, light, and humidity) as determined by BMS. If concerns regarding the quality or appearance of the study treatment arise, the study treatment should not be dispensed and contact BMS immediately.

Study treatment not supplied by BMS will be stored in accordance with the package insert.

IP documentation (whether supplied by BMS or not) must be maintained that includes all processes required to ensure drug is accurately administered. This includes documentation of drug storage, administration and, as applicable, storage temperatures, reconstitution, and use of required processes (eg, required diluents, administration sets).

Please refer to the current version of the Investigator's Brochure and/or Pharmacy Manual for complete preparation, storage, and handling information.

Further guidance and information for final disposition of unused study treatment are provided in Appendix 2.

7.5.1 Retained Samples for Bioavailability/Bioequivalence/Biocomparability

Not applicable.

7.6 Treatment Compliance

Study treatment compliance will be periodically monitored using standard drug accountability procedures (comparing the number of tablets returned to number dispensed). Drug accountability should be reviewed by the site study staff at each visit to confirm treatment compliance. Sites should discuss discrepancies with the participant at each on-treatment study visit.

7.7 Concomitant Therapy

All previous and current systemic medications taken for PsA and PsO must be reported.

Current medications and medications taken within 4 weeks prior to IP administration for conditions other than PsA and PsO must be recorded on the case report form (CRF).

7.7.1 Permitted Treatments

- Use of NSAIDs for the treatment of PsA during the study is permitted for participants enrolled on a stable dose of NSAIDs.
- Use of csDMARD (MTX, SSZ, LEF, HCQ) for the treatment of PsA is permitted for participants enrolled in the study on a stable dose of csDMARD.
  - If on MTX, the route of administration and dose must be stable and the dose must be ≤ 25 mg/week.
  - If on SSZ, the dose must be ≤ 3 g/day.
  - If on HCQ, the dose must be ≤ 400 mg/day.
  - If on LEF, the dose must be ≤ 20 mg/day.

  Note: Use of only 1 csDMARD at a time is permitted [redacted].
- Use of oral glucocorticoids (≤ 10 mg/day prednisone equivalent) for the treatment of PsA during the study is permitted for participants enrolled on a stable dose of oral glucocorticoids; however, they must remain on a stable dose until Week 32.

[redacted]

7.7.2 SARS-CoV-2 Permitted Treatments

SARS-CoV-2 vaccines that are NOT live are permitted during the study. Details of the vaccine and date should be recorded. If a participant receives a SARS-CoV-2 vaccination during the study, key study visits (ie, Day 1, Week 16, Week 52/[redacted]), should not take place within 5 days after vaccine administration so that any acute reaction to the vaccine will not be reflected in the study assessments. The BMS Medical Monitor should be consulted with any questions.

7.7.3 Prohibited [redacted]

Prohibited [redacted] during the study are described below.

7.7.3.1 Prohibited Treatments

- Use of opioid analgesics, if the average daily dose is > 30 mg/day of morphine or its equivalent (see Section 6.2), unless it is considered necessary for the participant's welfare and/or treatment of an AE/SAE.
- Phototherapy: use of tanning booths or therapeutic sunbathing are prohibited up to Week 52.
- Any use of the following oral PsO medications: cyclosporine, retinoids, fumaric acid derivatives are prohibited up to Week 52.
- High-potency glucocorticoids (WHO Classes I through V), > 3% salicylic acid, urea, alpha or beta hydroxy acids, anthralin, calcipotriene, vitamin D derivatives (oral vitamin D supplements are permitted), retinoids, tazarotene. Any medicated shampoos that contain glucocorticoids, coal tar, > 3% salicylic acid, or vitamin D3 analogues up to Week 52.
- Live vaccination, including live SARS-CoV-2 vaccines, during the study or within 60 days after completing study treatment (Section 6.2).
- Immune-suppressing immunomodulatory agents such as tacrolimus, sirolimus, mycophenolate mofetil, JAK inhibitors, and immunosuppressant biologic agents, including, but not limited to, TNF antagonists, anti-IL-17, anti-IL-12/23, anti-IL-23, and abatacept.

[redacted]

[redacted]

[redacted]

8 DISCONTINUATION CRITERIA

8.1 Discontinuation from Study Treatment

Participants MUST discontinue IP (and non-IP at the discretion of the investigator) for any of the following reasons:

- Clinically significant worsening of disease that requires medications other than those permitted [redacted] at any time during the study.
- Use of bDMARDs, JAK inhibitors, or phosphodiesterase 4 inhibitors taken [redacted].
- Participant's request to stop study treatment.
- Any clinical AE, laboratory abnormality, or intercurrent illness which, in the opinion of the investigator, indicates that continued participation in the study is not in the best interest of the participant.
- Termination of the study by BMS.
- Loss of ability to freely provide consent through imprisonment or involuntarily incarceration for treatment of either a psychiatric or physical (eg, infectious disease) illness.
- Note: Under specific circumstances and only in countries where local regulations permit, a participant who has been imprisoned may be permitted to continue as a participant. Strict conditions apply and BMS approval is required.
- eGFR < 45 mL/min confirmed on a repeat assessment within 7 days unless the investigator, in consultation with the Medical Monitor, deems that it is in the best interest of the participant to repeat testing and further evaluate participant's eligibility to continue in the study.
- The participant develops a malignancy, with the exception of a participant who develops nonmelanoma skin cancer who may continue in the study at the discretion of the investigator.
- Pregnancy, positive pregnancy test, or participant expresses an interest in becoming pregnant (refer to Section 9.2.6).
- Participant develops active TB during the study or prematurely discontinues treatment for LTBI, or participant is noncompliant with LTBI therapy (refer to Section 9.4.6).
- Participant with positive HBsAb or positive HBcAb with undetectable HBV DNA at Screening, for whom the quantitative HBV DNA test becomes detectable anytime during treatment with the IP.
- Unblinding of a participant's treatment assignment for any reason (emergency or nonemergency).
- Inability or failure to comply with protocol requirements in the opinion of the investigator.

Discontinuation of the study treatment for abnormal liver tests should be considered by the investigator when a participant meets 1 of the conditions outlined in Section 9.2.8 or if the investigator believes that it is in the best interest of the participant.

Refer to the Schedule of Activities (Section 2) for data to be collected at the time of study treatment discontinuation and follow-up and for any further evaluations that can be completed.

In the case of pregnancy, the investigator must immediately, within 24 hours of awareness of the pregnancy, notify the BMS Medical Monitor/designee of this event. The study treatment will be permanently discontinued. See Section 9.2.6.

If study treatment is discontinued prior to the participant's completion of the study, the reason for the discontinuation must be documented in the participant's medical records and entered on the appropriate CRF page.

Participants who discontinue study treatment are required to complete an ET Visit, a Safety Follow-up Visit 30 days following last dose of study treatment, and should complete each study visit through Week 52. [redacted]

Only participants who are lost to follow-up or withdraw study consent will have no further study visits. Participants who request to withdraw at any time from the study will be asked to complete the Safety Follow-up Visit 30 days following last dose of study treatment. The only exception to this requirement is when a participant withdraws consent for all study procedures, including post-treatment study follow-up, or loses the ability to consent freely (eg, is imprisoned or involuntarily incarcerated for the treatment of either a psychiatric or physical illness).

8.1.1 Temporary Discontinuation

Temporary study treatment discontinuation is only allowed if the participant develops an AE which, in the opinion of the investigator, indicates that it is in the participant's best interest that the study treatment be placed on hold. Study treatment in this situation should be stopped until the AE is medically treated and has resolved per principal investigator's judgment. Any temporary study treatment discontinuation as well as restart must be documented on the corresponding electronic CRF (eCRF).

Temporary discontinuation of IP is allowed in the context of clinical suspicion for SARS-CoV-2 or a positive diagnostic test for SARS-CoV-2 and requires complete resolution of a SARS-CoV-2 infection, which must be confirmed by a negative diagnostic test prior to re-commencing IP. Temporary discontinuation of IP may be considered in the event of SARS-CoV-2 vaccination according to local guidelines. In order to facilitate reporting of SARS-CoV-2 events that occur during the study, all AEs and SAEs related to SARS-CoV-2 must be reported from the time of consent. In addition, AEs or SAEs will trigger additional data collection through dedicated eCRF pages, which will allow the Sponsor to further evaluate these events.

8.1.2 Post Study Treatment Study Follow-up

Participants who discontinue study treatment are required to complete an ET Visit, a Safety Follow-up Visit 30 days following last dose of study treatment and should complete each study visit through Week 52. [redacted]

8.2 Discontinuation from the Study

Participants who request to discontinue study treatment will remain in the study and should continue to be followed for protocol-specified follow-up procedures through Week 52 (see Section 2 and Section 8.1.2). The only exception to this requirement is when a participant specifically withdraws consent for all study procedures, including post-treatment study follow-up, or loses the ability to consent freely will have no further study visits.

- Participants should notify the investigator of the decision to withdraw consent from future follow-up **in writing**, whenever possible.
- The withdrawal of consent should be explained in detail in the medical records by the investigator, as to whether the withdrawal is from further treatment with study treatment only or also from study procedures and/or post treatment study follow-up, and entered on the appropriate CRF page.
- In the event that vital status (whether the participant is alive or dead) is being measured, publicly available information should be used to determine vital status only as appropriately directed in accordance with local law.
- If the participant withdraws consent for disclosure of future information, the Sponsor may retain and continue to use any data collected before such a withdrawal of consent.

Participants who request to discontinue from the study are required to complete the ET Visit and will be asked to complete a Safety Follow-up Visit 30 days following last dose of study treatment (or phone call if a visit is not possible) to determine the status of any ongoing AEs/SAEs or the occurrence of any new AEs/SAEs.

[redacted]

8.3 Lost to Follow-up

- All reasonable efforts must be made to locate participants to determine and report their ongoing status. This includes follow-up with persons authorized by the participant.
- Lost to follow-up is defined by the inability to reach the participant after a minimum of **three (3)** documented phone calls, faxes, or emails as well as lack of response by participant to 1 registered mail letter. All attempts should be documented in the participant's medical records.

- If it is determined that the participant has died, the site will use permissible local methods to obtain date and cause of death.
- If investigator's use of third-party representative to assist in the follow-up portion of the study has been included in the participant's informed consent, then the investigator may use a Sponsor-retained third-party representative to assist site staff with obtaining participant's contact information or other public vital status data necessary to complete the follow-up portion of the study.
- The site staff and representative will consult publicly available sources, such as public health registries and databases, in order to obtain updated contact information.
- If after all attempts, the participant remains lost to follow-up, then the last known alive date as determined by the investigator should be reported and documented in the participant's medical records.

9 STUDY ASSESSMENTS AND PROCEDURES

[redacted]

Study procedures and timing are summarized in the Schedule of Activities (Section 2).

- Protocol waivers or exemptions are not allowed.
- All immediate safety concerns must be discussed with the Sponsor immediately upon occurrence or awareness to determine if the participant should continue or discontinue treatment.
- Adherence to the study design requirements, including those specified in the Schedule of Activities, is essential and required for study conduct.
- All screening evaluations must be completed and reviewed to confirm that potential participants meet all eligibility criteria before randomization. The investigator will maintain a screening log to record details of all participants screened and to confirm eligibility or record reasons for screening failure, as applicable.

[redacted]

- Procedures conducted as part of the participant's routine clinical management (eg, blood count) and obtained before signing of informed consent may be utilized for Screening or baseline purposes provided the procedure meets the protocol-defined criteria and has been performed within the timeframe defined in the Schedule of Activities (Section 2).

9.1 Efficacy Assessments

9.1.1 Rater Qualifications

Clinical efficacy assessments must be performed by a qualified assessor. At minimum, there are 2 qualified assessors required to complete the clinical efficacy assessments at each site: 1) an independent Joint Assessor (who should not have access to previous efficacy assessments and safety data) to complete the tender and swollen joint count; the Joint Assessor may also complete the enthesitis and dactylitis assessment, Physician Global Assessment - Fingernails (PGA-F), and PASI and static Physician's Global Assessment (sPGA) scoring unless the site designates an alternate staff member(s) to complete these assessments; and 2) an investigator to perform the Physician Global Assessment of PsA. Every effort must be made to ensure the same assessor completes the clinical efficacy assessments for each participant at all visits at approximately the same time throughout the study, according to the Schedule of Activities (Section 2). Visits should be scheduled with the availability of the assessor taken into account.

To be an eligible Joint Assessor, individuals must receive standardized joint count training provided by BMS, be trained by an individual who completed the standardized training or complete an alternative training method approved by BMS (eg, training documentation provided for another Sponsor's study in a similar indication). Documentation should be filed in the Investigator File or the Study File. Such individuals should have appropriate medical credentials and/or should be individuals with appropriate scientific/medical background who are experienced in performing joint assessments. If the individual does not have medical credentials, documentation of their experience (preferably on a curriculum vitae) must be provided to the study site manager, and their eligibility as Joint Assessor must be confirmed by the BMS Medical Monitor before the individual's participation in the study as Joint Assessor.

The individual performing the Physician's Global Assessment of PsA must be an investigator who is competent to perform the assessment.

In order to minimize variability, the same assessor should evaluate the participant at each visit for the duration of the trial, and a back-up assessor should be identified. The assessor should be a qualified medical professional (eg, nurse, physician's assistant, or physician). Any assessor must be trained and competent in performing such assessments. It is the responsibility of the investigator to ensure that all assessors are qualified and trained to perform assessments and that all training is documented. If the assessor is not available, the pre-identified back-up assessor should perform such assessments. Participants will complete all participant-reported questionnaires, which will be considered source documents in this study.

9.1.2 American College of Rheumatology Improvement Criteria

The ACR 20, ACR 50, or ACR 70 definition of improvement is a 20%, 50%, or 70% improvement, respectively, over baseline in tender (68) and swollen (66) joint counts and a 20%, 50%, or 70% improvement, respectively, in 3 of the 5 remaining core data set measures (see Appendix 25):

- Subject Global Assessment of Disease Activity (see Appendix 6)
- Subject Global Assessment of Pain (see Appendix 7)

- HAQ-DI (see Appendix 8)
- Physician Global Assessment of PsA (see Appendix 17)
- hsCRP

9.1.3 Health Assessment Questionnaire - Disability Index

The HAQ-DI is a patient-reported outcome measure that assesses the degree of difficulty a participant has experienced during the past week in 8 domains of daily living activities: dressing and grooming, arising, eating, walking, hygiene, reach, grip, and other activities. Each activity category consists of 2 to 3 items. For each item in the questionnaire, the level of activity is scored from 0 to 3, with 0 representing "no difficulty," 1 representing "some difficulty," 2 representing "much difficulty," and 3 representing "unable to do." Any activity that requires assistance from another individual or requires the use of an assistive device adjusts to a minimum score of 2 to represent a more limited functional status (see Appendix 8).

9.1.4 Short Form-36

The SF-36 version 2 standard was designed as an indicator of health status in population surveys and health policy evaluations and for use as an outcome measure in clinical research. The instrument includes 36 items in a Likert-type format to measure the following 8 health dimensions:

- The Physical Component Summary (PCS) of the SF-36 consists of these 4 subscales:
  - physical functioning
  - role-physical
  - bodily pain, and
  - general health.
- The Mental Component Summary of the SF-36 consists of these 4 subscales:
  - vitality
  - social functioning
  - role-emotional, and
  - mental health.

Scores for each domain range from 0 to 100, with high scores indicating a better health status. An example of the SF-36 is provided in Appendix 9.

9.1.5 Fatigue (Functional Assessment of Chronic Illness Therapy - Fatigue)

FACIT-Fatigue evaluates a range of self-reported symptoms over the past week, from mild subjective feelings of tiredness to an overwhelming, debilitating, and sustained sense of exhaustion that likely decreases one's ability to execute daily activities and function normally in family or social roles. Fatigue is divided into the experience or symptoms of fatigue (frequency, duration, and intensity) and the impact of fatigue on physical, mental, and social activities.

The recall period is 7 days. Each item is rated on a 5-point Likert scale ranging from 0 = "not at all" to 4 = "very much." Sum scores for the 13 items range from 0 through 52, where higher scores indicate less fatigue. An example is provided in Appendix 10.

9.1.6 Psoriatic Arthritis Impact of Disease 12

The Psoriatic Arthritis Impact of Disease (PsAID) is a 12-item self-report that measures PsA symptoms and impact of disease. Each item is scored on a 0 to 10 numeric rating scale with a 1-week recall period. The PsAID has a total score, with a higher value indicating worse health (see Appendix 11).

9.1.7 Dermatology Life Quality Index

The Dermatology Life Quality Index (DLQI) is a participant-reported quality-of-life index which consists of 10 questions concerning symptoms and feelings, daily activities, leisure, work, school, personal relationships, and treatment during the past week.[40] Each question is scored on a scale of 0 to 3 by a tick box: 0 = "not at all," 1 = "a little," 2 = "a lot," or 3 = "very much." The scores are summed, giving a range from 0 (no impairment of life quality) to 30 (maximum impairment) (see Appendix 12).

9.1.8 5-level EuroQol 5-dimension

The 5-level EuroQol 5-dimension (EQ-5D-5L) is an instrument widely used in cost-utility analysis. Using a system of 5 health dimensions (mobility, self-care, usual activities, pain/discomfort, and anxiety/depression) and 5 levels (1 = no problems, 2 = slight problems, 3 = moderate problems, 4 = severe problems, 5 = extreme problems) for each dimension, it provides utility values for a total of 3,125 health states. The utility values are measured from the general population using the time trade-off method. An example is provided in Appendix 13.

9.1.9 Patient-Reported Outcome Measures Information System Sleep Disturbance Short Form 8b

The Patient-Reported Outcome Measures Information System Sleep Disturbance Short Form 8b assess self-reported perceptions of sleep quality, sleep depth, and restoration associated with sleep. This includes perceived difficulties and concerns with getting to sleep or staying asleep, as well as perceptions of the adequacy of and satisfaction with sleep. The items are evaluated on a 5-point Likert scale ranging from 1 = "not at all" to 5 = "very much" with a 7-day recall period. An example is provided in Appendix 14.

9.1.10 Work Productivity and Activity Impairment Questionnaire

The Work Productivity and Activity Impairment (WPAI) questionnaire will be used to measure aspects of productivity and activity impairment over the previous 7 days. The WPAI is a 6-item questionnaire that includes 2 visual analog scales: 1 for impact of disease on work and 1 for impact of disease on other daily activities. The WPAI also assesses absenteeism (work time missed), presenteeism (impairment at work/reduced on-the-job effectiveness), work productivity (overall work impairment/absenteeism plus presenteeism), and activity impairment. An example is provided in Appendix 15.

9.1.11 Bath Ankylosing Spondylitis Disease Activity Index

In participants with baseline evidence of PsA spondylitis, symptoms will be evaluated using the Bath Ankylosing Spondylitis Disease Activity Index (BASDAI; see Appendix 16), which consists of a 0 to 10 scale measuring discomfort, pain, and fatigue in response to 6 questions pertaining to the 5 major symptoms of ankylosing spondylitis:

- Fatigue (medical)
- Spinal pain
- Joint pain and swelling
- Areas of localized tenderness
- Morning stiffness duration
- Morning stiffness severity

A higher count indicates worse disease. The recall period is 1 week.

9.1.12 Enthesitis (Leeds Enthesitis Index, Spondyloarthritis Research Consortium of Canada)

The number of sites with enthesitis will be evaluated by a blinded assessor using the Spondyloarthritis Research Consortium of Canada (SPARCC) Enthesitis Index and the Leeds Enthesitis Index (LEI).

The SPARCC Enthesitis Index has a 0 to 16 score that is derived from the evaluation of 8 locations: the greater trochanter (right [R]/left [L]), quadriceps tendon insertion into the patella (R/L), patellar ligament insertion into the patella and tibial tuberosity (R/L), Achilles tendon insertion (R/L), plantar fascia insertion (R/L), medial and lateral epicondyles (R/L), and supraspinatus insertion (R/L). A higher count indicates a higher enthesitis burden based on the current evaluation. It has been validated in ankylosing spondylitis and correlates well with the Leeds Dactylitis Index (LDI).[41]

The LEI was developed specifically for PsA. An overall score of 0 to 6 is derived from the presence or absence of tenderness at 6 enthesial sites (right and left: lateral epicondyle, medial femoral condyle, and Achilles tendon insertion) at the time of evaluation. A higher count indicates a greater enthesitis burden.[42]

9.1.13 Dactylitis (Tender Count, Leeds Dactylitis Index)

The number of digits in hands and feet with dactylitis will be counted by a blinded assessor. The LDI Basic is a quantitative measurement of dactylitis in the 20 digits using a dactylometer. The circumference of the affected and contralateral digits and tenderness of the affected digits are measured to generate a total score. A higher score indicates worse dactylitis and is based on the current evaluation. Training will be provided so dactylitis will be evaluated in a consistent manner throughout the study.[43]

9.1.14 Psoriasis Area and Severity Index

The PASI is a measure of the average erythema, induration thickness, and scaling of psoriatic skin lesions (each graded on a 0 to 4 scale), weighted by the area of involvement (head, arms, trunk to groin, and legs to top of buttocks).[44] The PASI produces a numeric score that can range from 0 to 72, with higher PASI scores denoting more severe disease activity. The PASI can also be used to assess response to treatment. The PASI 50 is the proportion of participants who experience at least a 50% improvement in PASI score as compared with the baseline value. The PASI 75, PASI 90, and PASI 100 are defined similarly. BMS will host a training session prior to initiation of the study to demonstrate proper PASI scoring. All PASI assessments should be performed by a trained assessor experienced in the assessment of PsO patients (see Appendix 18).

9.1.15 Static Physician's Global Assessment

The sPGA is a 5-point scale of an average assessment of all psoriatic lesions based on erythema, scale, and induration.[45] The sPGA measure determines psoriasis severity at a single point in time (without taking into account the baseline disease condition) as clear (0), minimal (1), mild (2), moderate (3), or severe (4). sPGA assessments should be performed by a trained physician (eg, dermatologist) or appropriately trained investigator who is experienced in the assessment of PsO patients. Every effort should be made to ensure that the physician or designee who performed the sPGA evaluations for a participant at randomization performs the sPGA for that participant at all subsequent visits (see Appendix 19).

9.1.16 Physician Global Assessment-Fingernails

In this assessment, the overall condition of the fingernails is rated on a 5-point scale:

0 = clear, 1 = minimal, 2 = mild, 3 = moderate, and 4 = severe

The PGA-F will be performed only in participants with psoriatic fingernail involvement to assess severity and subsequent improvement. An example is provided in Appendix 20. The PGA-F should be performed by an appropriately trained assessor experienced in the assessment of PsO patients.

9.1.17 Psoriatic Arthritis Disease Activity Score

The Psoriatic Arthritis Disease Activity Score is a composite measure calculated from the Physician Global Assessment of PsA, the Subject Global Assessment of Disease Activity, the SF-36 PCS, the swollen joint count, the tender joint count, the LEI, the LDI (Basic), and the hsCRP.

9.1.18 Disease Activity Score 28 CRP

A DAS can be used to assess patients' PsA disease activity, to determine whether it is under control and if any treatment adjustments are required. It can also assist in establishing a target score to aim for, to help inform treatment decisions and optimize disease management. See Appendix 21.

The DAS28-CRP is a composite outcome measure that assesses:

- How many joints in the hands (including metacarpophalangeal and proximal interphalangeal joints but excluding DIPs), wrists, elbows, shoulders, and knees are swollen and/or tender out of a total of 28

- CRP in the blood to measure the degree of inflammation
- Subject Global Assessment of Disease Activity (see Appendix 6)

The results are combined to produce the DAS28-CRP score, which correlates with the extent of disease activity:

- < 2.6: Disease remission
- 2.6 to 3.2: Low disease activity
- 3.2 to 5.1: Moderate disease activity
- > 5.1: High disease activity

9.1.19 Minimal Disease Activity and Very Low Disease Activity

MDA response is where an MDA responder is defined as a participant fulfilling 5 of 7 of the following outcomes:

- Tender joint count ≤ 1
- Swollen joint count ≤ 1
- PASI ≤ 1 or body surface area (BSA) ≤ 3% (see Appendix 18)
- Subject Global Assessment of Disease Activity ≤ 20 (see Appendix 6)
- Subject Global Assessment of Pain ≤ 15 (see Appendix 7)
- HAQ-DI ≤ 0.5 (see Appendix 8)
- Tender enthesial points ≤ 1

Very low disease activity (VLDA) response is where a VLDA responder is defined as a participant fulfilling all 7 of 7 of the MDA outcomes.

9.1.20 Disease Activity Index for Psoriatic Arthritis Score

The Disease Activity Index for Psoriatic Arthritis Score is a composite measure to assess peripheral joint involvement that is based upon numerical summation of 5 variables of disease activity: tender joint count, swollen joint count, Subject Global Assessment of Disease Activity (see Appendix 6), Subject Global Assessment of Pain (see Appendix 7), and CRP.

9.1.21 Modified Composite Psoriatic Disease Activity Index

Four domains are used to calculate the modified Composite Psoriatic Disease Activity Index (mCPDAI): joints (66 swollen joint count and 68 tender joint count; Health Assessment Questionnaire), skin (PASI and DLQI), dactylitis (a simple count of each digit involved), and enthesitis (number of tendons/fascia insertion sites showing enthesitis scored from 0 to 4, based on palpation of Achilles tendon and bilateral plantar fasciae insertion). The mCPDAI is scored using a 4-point scale from 0 (no disease activity) to 3 (most severe disease activity), giving an mCPDAI score range of 0 through 12.[46]

9.1.22 Psoriatic Arthritis Response Criteria

The Psoriatic Arthritis Response Criteria (PsARC) consists of 4 measurements: tender joint count, swollen joint count, Physician Global Assessment of PsA, and Subject Global Assessment of Disease Activity.

In order to be classified as a PsARC responder, participants must achieve improvement in 2 of 4 measures, 1 of which must be joint pain or swelling, without worsening in any measure. Improvement in each of the measures is defined below:

- Decrease of ≥ 30% in tender joint counts
- Decrease of ≥ 30% in swollen joint counts
- Decrease of ≥ 20% in Physician Global Assessment of PsA
- Decrease of ≥ 20% in Subject's Global Assessment of Disease Activity

9.1.23 Ankylosing Spondylitis Disease Activity Score with CRP

The Ankylosing Spondylitis Disease Activity Score with C-reactive protein (ASDAS–CRP) is a validated disease activity index in ankylosing spondylitis that combines patient-reported assessments of back pain (BASDAI question 2), duration of morning stiffness (BASDAI question 6), peripheral joint pain and/or swelling (BASDAI question 3), general well-being, and CRP, in a weighted manner.[47] The cut-off values for disease activity states and improvement scores are defined as follows: < 1.3 inactive disease, ≥ 1.3 and < 2.1 low disease activity, ≥ 2.1 and ≤ 3.5 high disease activity, and > 3.5 very high disease activity. The minimum clinically important difference is defined as: change of at least 1.1 unit for "clinically important improvement" and change of at least 2.0 units for "major improvement."[48,49]

9.1.24 Imaging Assessment for the Study

Images will be submitted by the sites to a central imaging vendor for blinded independent central review. Prior to scanning the first participants, sites should be trained by the central imaging vendor to understand the image acquisition guidelines and submission process as outlined in the X-ray Imaging Manual provided by the central imaging vendor.

Any incidental findings of potential clinical relevance that are not directly associated with the objectives of the protocol should be evaluated and handled by the primary study investigator as per standard medical/clinical judgment.

Digital radiographic (X-ray) assessments of both hands and both feet will be performed at Screening, Week 16, [redacted] Visits as noted in the Schedule of Activities. Visit windows are the following: Screening Visit within 28 days [redacted] prior to first investigational product treatment, Week 16 ± 5 days, Week [redacted] days, Week [redacted] days, and Week [redacted] days of the scheduled visit, and ET ± 5 days of the scheduled visit (if ET Visit is after Week 8 of the Placebo-controlled Treatment Period or after Week 24 of the Active Treatment Period).

X-ray scans with technical issues identified at the investigator site or by the central imaging vendor should be repeated within 7 days of notification. Additional information is provided in a separate X-ray Imaging Manual provided by central imaging vendor.

Radiographic assessments will be performed according to the PsA-modified SvdH score. The evaluation of the X-ray scans will be performed centrally by 2 independent primary readers. An adjudication will be performed in case of significant discrepancy among the 2 readers. All readers will be blinded to clinical details and treatment. Central image evaluation methodology will be described in an Imaging Charter.

Participant eligibility must be confirmed by central review prior to randomization with regard to the presence of at least 1 PsA-related hand and/or foot joint erosion on the screening X-ray scans. The sites will be notified by the central imaging vendor on the outcome of the central eligibility assessments.

9.2 Adverse Events

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

AEs will be reported by the participant (or, when appropriate, by a caregiver, surrogate, or the participant's legally authorized representative).

The investigator and any designees are responsible for detecting, documenting, and reporting events that meet the definition of an AE or SAE and remain responsible for following up AEs that are serious, that are considered related to the study treatment or the study, or that caused the participant to discontinue before completing the study.

Contacts for SAE reporting specified in Appendix 3.

9.2.2 Time Period and Frequency for Collecting AE and SAE Information

All non-serious AEs must be collected from the time of initiation of study treatment until discontinuation of study. All SAEs and all AEs (SAEs or non-serious AEs) related to SARS-CoV-2 infection must be collected from the time of signing the consent, including those thought to be

associated with protocol-specified procedures and within 30 days of discontinuation of dosing or participant's participation in the study if the last scheduled visit occurs at a later time.

The investigator must report any SAE that occurs after these time periods and that is believed to be related to IP or protocol-specified procedures (eg, a follow-up skin biopsy).

- Medical occurrences that begin before the start of study treatment but after obtaining informed consent will be recorded on the appropriate section of the CRF module.
- All SAEs will be recorded and reported to Sponsor or designee within 24 hours, as indicated in Appendix 3.
- The investigator will submit any updated SAE data to the Sponsor or designee within 24 hours of updated information being available.

Investigators are not obligated to actively seek AEs or SAEs in former study participants. However, if the investigator learns of any SAE, including a death, at any time after a participant has been discharged from the study, and he/she considers the event reasonably related to the study treatment or study participation, the investigator must promptly notify the Sponsor.

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

9.2.3 Method of Detecting AEs and SAEs

AEs can be spontaneously reported or elicited during open-ended questioning, examination, or evaluation of a participant. Care should be taken not to introduce bias when collecting AEs and/or SAEs. Inquiry about specific AEs should be guided by clinical judgement in the context of known AEs, when appropriate for the program or protocol.

9.2.4 Follow-up of AEs and SAEs

- Non-serious AEs should be followed to resolution or stabilization, or reported as SAEs if they become serious (see Appendix 3).
- Follow-up is also required for non-serious AEs that cause interruption or discontinuation of study treatment and for those present at the end of study treatment as appropriate.
- All identified non-serious AEs must be recorded and described on the non-serious AE page of the CRF (paper or electronic). Completion of supplemental CRFs may be requested for AEs and/or laboratory abnormalities that are reported/identified during the course of the study.

After the initial AE/SAE report, the investigator is required to proactively follow each participant at subsequent visits/contacts. All SAEs and non-serious AEs of interest (as defined in Section 9.2) will be followed until resolution, until the condition stabilizes, until the event is otherwise explained, or until the participant is lost to follow-up (as defined in Section 8.3).

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

9.2.5 Regulatory Reporting Requirements for SAEs

- Prompt notification by the investigator to the Sponsor of SAEs is essential so that legal obligations and ethical responsibilities toward the safety of participants and the safety of a product under clinical investigation are met.
- An investigator who receives an investigator safety report describing SAEs or other specific safety information (eg, summary or listing of SAEs) from the Sponsor will file it along with the Investigator's Brochure and will notify the Institutional Review Board (IRB)/Independent Ethics Committee if appropriate according to local requirements.

Sponsor or designee will be reporting AEs to regulatory authorities and ethics committees according to local applicable laws, including European Regulation 536/2014 and United States of America (USA) Food and Drug Administration Code of Federal Regulations Title 21 Parts 312 and 320. A suspected, unexpected serious adverse reaction is a subset of SAEs and will be reported to the appropriate regulatory authorities and investigators following local and global guidelines and requirements.

9.2.6 Pregnancy

If, following initiation of the study treatment, it is subsequently discovered that a participant is pregnant or may have been pregnant at the time of study exposure, including during at least for the study period until study completion or 30 days after discontinuation of study treatment, whichever is longer (See Section 5.3), the investigator must immediately notify the BMS Medical Monitor/designee of this event and complete and forward a Pregnancy Surveillance Form to BMS designee within 24 hours of awareness of the event and in accordance with SAE reporting procedures described in Appendix 3.

In the event a participant becomes pregnant during the trial, the study treatment must be discontinued immediately. Protocol-required procedures for study discontinuation and follow-up must be performed on the participant.

Follow-up information regarding the course of the pregnancy, including perinatal and neonatal outcome and, where applicable, offspring information, must be reported on the Pregnancy Surveillance Form.

Any pregnancy that occurs in a female partner of a male study participant should be reported to the Sponsor or designee. In order for the Sponsor or designee to collect any pregnancy surveillance information from the female partner, the female partner must sign an ICF for disclosure of this information. Information on this pregnancy will be collected on the Pregnancy Surveillance Form.

9.2.7 Laboratory Test Result Abnormalities

The following laboratory test result abnormalities should be captured on the non-serious AE CRF page or SAE CRF electronic, as appropriate. Paper forms are only intended as a back-up option when the electronic system is not functioning.

- Any laboratory test result that is clinically significant or meets the definition of an SAE.

- Any laboratory test result abnormality that required the participant to have study treatment discontinued or interrupted.
- Any laboratory test result abnormality that required the participant to receive specific corrective therapy.

It is expected that wherever possible, the clinical rather than laboratory term would be used by the reporting investigator (eg, anemia versus low hemoglobin value).

9.2.8 Potential Drug-induced Liver Injury

Wherever possible, timely confirmation of initial liver-related laboratory abnormalities should occur prior to the reporting of a potential drug-induced liver injury (DILI) event. All occurrences of potential DILIs meeting the defined criteria must be reported as SAEs (see Section 9.2.5 and Appendix 3 for reporting details).

Potential DILI is defined as:

- Aminotransferase (AT; ALT or AST) elevation > 3 times ULN,

AND

- Total bilirubin > 2 times ULN, without initial findings of cholestasis (elevated serum alkaline phosphatase),

AND

- No other immediately apparent possible causes of AT elevation and hyperbilirubinemia, including, but not limited to, viral hepatitis, pre-existing chronic or acute liver disease, or the administration of other drug(s) known to be hepatotoxic.

9.2.9 Other Safety Considerations

Any significant worsening noted during interim or final physical examinations, electrocardiogram (ECG), X-ray filming, any other potential safety assessment required or not required by the protocol should also be recorded as a non-serious or serious AE, as appropriate, and reported accordingly.

9.3 Overdose

[redacted]

In the event of an overdose, the investigator should:

- Contact the Medical Monitor immediately.
- Closely monitor the participant for AEs/SAEs and laboratory abnormalities.

Decisions regarding dose interruptions will be made by the investigator in consultation with the Medical Monitor based on the clinical evaluation of the participant.

9.4 Safety

Planned time points for all safety assessments are listed in the Schedule of Activities (Section 2).

9.4.1 Physical Examinations

Refer to Schedule of Activities (Section 2). A complete physical examination will include general appearance, eyes, ears, nose, mouth, throat, neck, respiratory, cardiovascular, gastrointestinal/abdomen, lymphatic, musculoskeletal, skin, psychiatric, and neurologic exams. A targeted physical examination will include any organ system associated with an AE or a laboratory abnormality.

9.4.2 Vital Signs

Vital signs include body temperature, respiratory rate, and seated blood pressure and heart rate. Refer to Schedule of Activities (Section 2).

9.4.3 Electrocardiograms

Refer to Schedule of Activities (Section 2). A 12-lead ECG will be performed at the visits indicated in the Schedule of Activities. The participant must have his or her lab work done after the ECG tracing so that the ECG results remain as accurate as possible. The ECG results will be read by the primary study investigator or a designee.

9.4.4 Clinical Safety Laboratory Assessments

Investigators must document their review of each laboratory safety report.

A central/local laboratory will perform the analyses and will provide reference ranges for these tests.

Hematology	
Complete blood count: Hemoglobin Hematocrit Total leukocyte count, including differential Platelet count	
Chemistry	
Aspartate aminotransferase (AST) Alanine aminotransferase (ALT) Total bilirubin Direct bilirubin Alkaline phosphatase Lactate dehydrogenase (LDH) Creatinine Blood urea nitrogen (BUN) Uric acid Glucose[a]	Total protein Albumin Sodium Potassium Chloride Calcium Phosphorus Magnesium Creatine kinase Creatinine clearance (CLcr)- screening only
Lipid Panel (Fasting)	
Cholesterol (total) High-density lipoprotein (HDL) Low-density lipoprotein (LDL) Triglycerides	

Urinalysis
Protein Glucose Blood Leukocyte esterase Specific gravity pH Microscopic examination of the sediment if blood, protein, or leukocytes esterase are positive on the dipstick
Serology
Hepatitis C antibody confirmed by HCV-ribonucleic acid (RNA) testing if required Hepatitis B surface antigen (HBsAg) Hepatitis B surface antibody (HBsAb) Hepatitis B core antibody (HBcAb) HBV DNA as required with confirmed HBV infection; see Appendix 22 HIV antibody (screening only) [redacted] Hemoglobin A1c
Thyroid-stimulating hormone (TSH)

[a] Fasting glucose will be collected at time points indicated in the Schedule of Activities; non-fasting glucose will be collected at all other time points.

[redacted]

Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; BUN, blood urea nitrogen; CLcr, creatinine clearance; DNA, deoxyribonucleic acid; [redacted] HBcAb, hepatitis B core antibody; HBsAb, hepatitis B surface antibody; HBsAg, hepatitis B surface antigen; HBV, hepatitis B virus; HCV, hepatitis C virus; HDL, high-density lipoprotein; HIV, human immunodeficiency virus; [redacted] LDH, lactate dehydrogenase; LDL, low-density lipoprotein; [redacted] RNA, ribonucleic acid; TSH, thyroid-stimulating hormone; [redacted]

9.4.5 Estimated Glomerular Filtration Rate

Glomerular filtration rate will be estimated using the Modification of Diet in Renal Disease (MDRD) equation at Screening and during the study at select visits.

The MDRD equation is as follows:

$$eGFR = 175 \times \text{standardized serum creatinine (SCr)}^{-1.154} \times \text{age}^{-0.203} \times 1.212 \text{ (if Black) or } 0.742 \text{ (if female)}$$

Note: GFR is expressed as mL/min/1.73 m^2 of BSA and SCr is expressed in mg/dL.

Participants with an eGFR < 45 mL/min will be excluded from participation.

9.4.6 Tuberculosis Testing

9.4.6.1 Tuberculosis Screening and Chest Imaging

Chest imaging results and physical examinations are part of the process to assess a participant's eligibility, as outlined in Section 2 and as defined in exclusion criterion 4c, Section 6.2. Chest imaging (eg, chest X-ray, chest computed tomography scan) at the Screening Visit is required if not already performed and documented within 6 months of Screening Visit. A participant must not have active signs or symptoms of TB, as judged by the investigator, to be eligible for the study.

In addition to a complete physical examination and medical history to evaluate exposure to TB, all participants will have a screening test, an IGRA (eg, QuantiFERON®-TB Gold), performed centrally. If unable to obtain central laboratory results, an IGRA test could be obtained locally, after consultation with the Medical Monitor. A participant with an indeterminate IGRA test result must be re-tested for confirmation. If the second result is again indeterminate, the participant will be excluded from the study. If the second result is positive, the participant should be considered as having LTBI provided there are no signs or symptoms of active TB. If the second result is negative, the participant may be eligible provided no other exclusion criterion for TB is met.

9.4.8 Imaging Safety Assessment

Any incidental findings of potential clinical relevance that are not directly associated with the objectives of the protocol should be evaluated and handled by the primary study investigator as per standard medical/clinical judgment.

9.4.9 Unscheduled Safety Visits

The protocol does not mandate specific investigations at unscheduled visits. Unscheduled visit study procedures should be based on the clinical judgment of the investigator.

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

10 STATISTICAL CONSIDERATIONS

10.1 Sample Size Determination

A total sample size of approximately 650 participants randomized in a 1:1 ratio in a blinded fashion (approximately 325 participants each randomized to 6 mg deucravacitinib QD arm and placebo) will provide > 99% power to detect a 20% treatment difference between 6 mg deucravacitinib QD and placebo at Week 16 for ACR 20 response assuming a response of 55% for 6 mg deucravacitinib QD and of 35% for placebo (2-sided alpha = 0.05, chi-square test).

The sample size of 325 participants treated with 6 mg deucravacitinib QD in this study (IM011054) was also chosen to provide, along with participants from other Phase 3 PsA studies with

deucravacitinib, an adequate number of participants for the overall safety database for the PsA program.

In addition, this sample size will also provide enough power for all key secondary endpoints (that are tested in a testing strategy to control Type I error) as given in Table 10.3.1-1.

10.2 Populations for Analyses

For purposes of analysis, the following populations are defined:

Population	Description
Enrolled	All participants who sign informed consent
All Randomized	All randomized participants. Following the intent-to-treat principle, participants will be analyzed according to the treatment assigned at randomization. The efficacy analysis population will be the All Randomized Population.
All Treated	All participants who were randomized and took at least 1 dose of investigational product. Data in this data set will be analyzed based on randomized treatment, except in the following cases: • If a participant received the same incorrect treatment throughout the study, then the participant will be analyzed based on the treatment received. • If a participant received IP from more than 1 treatment group, and none of the administrations were consistent with the assigned randomized treatment group, then the participant will be analyzed based on the first treatment received. The safety analysis population will be the All Treated Population.

10.3 Statistical Analyses

[redacted] will describe the selection of participants to be included in the analyses and procedures for accounting for missing, unused, and spurious data. Below is a summary of planned statistical analyses of the primary and secondary endpoints.

A description of the participant population will be included in a statistical output report, including subgroups of age, gender, and race.

[redacted]

Week 52 analyses will be conducted after the Week 56 database lock and will include an assessment of safety and efficacy at all available time points [redacted].

10.3.1 Efficacy Analyses

Endpoint	Statistical Analysis Methods
Primary	The primary efficacy analysis model for the primary endpoint, ACR 20 response at Week 16 (responder/non-responder), will use a Cochran-Mantel-Haenszel test [redacted] to compare the response rates of 6 mg deucravacitinib QD to placebo. The risk difference and odds ratio and the corresponding 2-sided 95% confidence interval will be provided. Non-responder imputation will be used at Week 16 for participants who have a missing ACR 20 response at Week 16 or who discontinued treatment (for any reason) prior to Week 16. The same imputation will be used for the analysis of this outcome at other time points. The primary estimand for the primary endpoint, ACR 20 response at Week 16, will be the treatment difference between deucravacitinib 6 mg QD and placebo in ACR 20 response at Week 16 for all randomized participants. The occurrence of the intercurrent event of study treatment discontinuation (for any reason) prior to Week 16 or a missing ACR 20 response at Week 16 will be considered as a measure of nonresponse to treatment at Week 16 if the participant would have continued on the study treatment up to Week 16. Non-responder imputation will be used for the above intercurrent event. Study treatment discontinuation is the only intercurrent event that will be accounted for in the primary estimand and a composite variable strategy is applied. Two sensitivity analyses using different imputation methods will be conducted for the primary endpoint at Week 16 to examine the impact of missing data. • A multiple imputation (MI) approach • A tipping point approach A supportive analysis will be provided for the primary endpoint at Week 16, including all available efficacy measurement for all randomized participants. These available data will include efficacy measurements observed after study treatment discontinuation and efficacy measurements observed after switch to other treatments. Details will be given in the SAP.

Endpoint	Statistical Analysis Methods
Secondary	Binary Endpoints: Binary endpoints (other than ACR 20 response at Week 16) up to Week 16 will be analyzed using the same method as for the primary endpoint. Continuous Endpoints (except structural damage): Change from baseline at Week 16 will be analyzed using an analysis of covariance (ANCOVA) model. The model will include treatment, randomization stratification variables, and baseline value. The primary estimand at Week 16 will be the treatment difference between deucravacitinib 6 mg QD and placebo for changes from baseline at Week 16 for all randomized participants. In case an intercurrent event of study treatment discontinuation (for any reason) prior to Week 16 occurs, the efficacy assessments after the discontinuation of treatment will be considered missing. Missing values will be imputed with MI method assuming missing not at random (MNAR). The MNAR imputation assumes that after discontinuation of treatment, participants from the deucravacitinib 6 mg QD group (if they would have continued deucravacitinib 6 mg QD) exhibit a similar future evolution as participants from the placebo group. Study treatment discontinuation is the only intercurrent event that will be accounted for in the primary estimand and a composite variable strategy is applied. Structural Damage: Change from baseline in PsA-modified SvdH score (structural damage) at Week 16 will be analyzed using an ANCOVA model. The model will include treatment, randomization stratification variables, and baseline value. The primary estimand at Week 16 will be the treatment difference between deucravacitinib 6 mg QD and placebo for changes from baseline in PsA-modified SvdH score at Week 16 for all randomized participants based on all available data at Week 16, including those collected after study treatment discontinuation. Missing values at Week 16 will be imputed with MI method assuming MNAR. A treatment policy strategy is applied. Details will be provided in the SAP.
[redacted]	

Multiplicity

In order to control the overall Type I error rate at 5%, a testing strategy for the primary and key secondary endpoints will be implemented. The primary endpoint, ACR 20 response at Week 16, will be tested at an alpha = 0.05. If the primary endpoint is significant at alpha = 0.05, then a testing strategy for the key secondary endpoints will be applied to control for the overall Type I error of 5%. The details about the full testing strategy including any hierarchy of key secondary endpoints will be provided [redacted]. For the analysis of the key secondary endpoints, enthesitis and dactylitis, the data will be pooled for the studies IM011054 and IM011055.

The key secondary endpoints displayed in Table 10.3.1-1 will be included in a testing strategy to control for multiplicity to protect the overall 2-sided Type I error. Additional endpoints may also be included in the testing strategy (eg, ACR 50 and ACR 70) and will be detailed in the SAP. The power for those key secondary endpoints for a sample size of 325 participants each randomized to placebo and 6 mg deucravacitinib QD is given in Table 10.3.1-1.

Table 10.3.1-1: Power

Key Secondary Endpoint (Week 16)	Assumption - Treatment Effect	Power (with Nominal 2-sided Alpha = 0.05)
HAQ-DI	[redacted]	
PASI 75		
Enthesitis resolution		
Dactylitis resolution		
SF-36 PCS		
MDA		
FACIT-Fatigue		

Table 10.3.1-1: Power

Structural progression (PsA-modified SvdH)	[redacted]
DAS28-CRP	

Note: Chi-square test applied for binary variables, 2-groups t-test for continuous variables, alpha = 5% (2-sided).

Abbreviations: [redacted] DAS28-CRP, Disease Activity Score 28 with C-reactive protein; FACIT, Functional Assessment of Chronic Illness Therapy; HAQ-DI, Health Assessment Questionnaire - Disability Index; MDA, minimal disease activity; PASI, Psoriatic Area and Severity Index; [redacted] PCS, Physical Component Summary; PsA, psoriatic arthritis; [redacted] SF-36, Short Form-36; SvdH, Sharp-van der Heijde.

The treatment estimates are based on results from the deucravacitinib Phase 2 study IM011084 and on results of golimumab, guselkumab, secukinumab, ixekizumab, upadacitinib (for modified total Sharp score).[51,52,53,54,55]

Further details will be provided in the SAP.

10.3.2 Safety Analyses

All safety analyses will be performed on the All Treated analysis population.

Endpoint	Statistical Analysis Methods
Safety	Treatment-emergent AEs and SAEs, AEs leading to discontinuation of treatment, and AEs of special interest will be summarized using counts and percentages of participants experiencing the event by System Organ Class, Preferred Term, and treatment group. Vital signs, clinical laboratory test results, and ECG test results will be summarized by treatment group using descriptive statistics (n, mean, [redacted] median, minimum, and maximum) for continuous variables and frequency distributions (counts and percentages) for categorical variables. [redacted]

[redacted]

10.3.4 Interim Analyses

Not applicable.

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12 APPENDICES

APPENDIX 1 ABBREVIATIONS AND TRADEMARKS

Term	Definition
[redacted]	
ACR	American College of Rheumatology
AE	adverse event
[redacted]	
ALT	alanine aminotransferase
ANCOVA	analysis of covariance
anti-HBc	hepatitis B core antibody
anti-HBs	hepatitis B surface antibody
ASDAS-CRP	Ankylosing Spondylitis Disease Activity Score with C-reactive protein
AST	aspartate aminotransferase
AT	aminotransferase
BASDAI	Bath Ankylosing Spondylitis Disease Activity Index
[redacted]	
bDMARD	biologic disease-modifying anti-rheumatic drug
BMS	Bristol-Myers Squibb
BP	blood pressure
BSA	body surface area
BUN	blood urea nitrogen
[redacted]	
CASPAR	Classification Criteria for Psoriatic Arthritis
CBC	complete blood count
CIOMS	Council for International Organizations of Medical Sciences
CK	creatine kinase
CLcr	creatinine clearance
CONSORT	Consolidated Standards of Reporting Trials
CRF	case report form
CRP	C-reactive protein
csDMARD	conventional synthetic disease-modifying anti-rheumatic drug
CSP	clinical safety program

Term	Definition
CSR	clinical study report
CTAg	clinical trial agreement
d	days
D	Day
DAPSA	Disease Activity Index for Psoriatic Arthritis Score
DAS	Disease Activity Score
DAS28-CRP	Disease Activity Score 28 with C-reactive protein
DILI	drug-induced liver injury
DIP	distal interphalangeal
DLQI	Dermatology Life Quality Index
DMARD	disease-modifying anti-rheumatic drug
DMC	Data Monitoring Committee
DNA	deoxyribonucleic acid
ECG	electrocardiogram
eCRF	electronic case report form
EDC	electronic data capture
eGFR	estimated glomerular filtration rate
EHR	electronic health record
ELISA	enzyme-linked immunosorbent assay
EMR	electronic medical record
EQ-5D-5L	5-level EuroQoL 5-dimension
ET	Early Termination
FACIT	Functional Assessment of Chronic Illness Therapy
FSH	follicle-stimulating hormone
GCP	Good Clinical Practice
HAQ-DI	Health Assessment Questionnaire - Disability Index
HBcAb	hepatitis B core antibody
HBsAb	hepatitis B surface antibody
HBsAg	hepatitis B surface antigen
HBV	hepatitis B virus
HCQ	hydroxychloroquine

Term	Definition
HCV	hepatitis C virus
HDL	high-density lipoprotein
HIPAA	Health Insurance Portability and Accountability Act
HIV	human immunodeficiency virus
[redacted]	
HRT	hormone replacement therapy
hsCRP	high-sensitivity C-reactive protein
IB	Investigator's Brochure
ICF	informed consent form
ICH	International Council for Harmonisation
ICMJE	International Committee of Medical Journal Editors
IFN	interferon
[redacted]	
IGRA	interferon gamma release assay
IL	interleukin
IMP	investigational medicinal product
IP	investigational product
IRB	Institutional Review Board
IRT	Interactive Response Technology
IUS	intrauterine hormone-releasing system
IV	intravenous
JAK	Janus kinase
JSN	joint space narrowing
L	left
LAM	lactational amenorrhea method
LDH	lactate dehydrogenase
LDI	Leeds Dactylitis Index
LDL	low-density lipoprotein

Term	Definition
LEF	leflunomide
LEI	Leeds Enthesitis Index
LTBI	latent tuberculosis infection
mCPDAI	modified Composite Psoriatic Disease Activity Index
MCS	Mental Component Summary
MDA	minimal disease activity
MDRD	Modification of Diet in Renal Disease
MI	multiple imputation
[redacted]	
MNAR	missing not at random
MTX	methotrexate
N	number
N/A	not applicable
neg	negative
NSAID	nonsteroidal anti-inflammatory drug
[redacted]	
PASDAS	Psoriatic Arthritis Disease Activity Score
PASI	Psoriatic Area and Severity Index
[redacted]	
PCS	Physical Component Summary
[redacted]	
PGA-F	Physician Global Assessment [Fingernails
[redacted]	
POS	positive
[redacted]	
PRO	patient-reported outcome
PROMIS	Patient-Reported Outcome Measures Information System
PsA	psoriatic arthritis
PsAID	Psoriatic Arthritis Impact of Disease

Term	Definition
PsARC	Psoriatic Arthritis Response Criteria
PsO	psoriasis
QD	once daily
R	right
RNA	ribonucleic acid
SAE	serious adverse event
SAP	statistical analysis plan
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SCr	serum creatinine
[redacted]	
SDC	smallest detectable change
SF-36	Short Form-36
SOP	standard operating procedure
SPARCC	Spondyloarthritis Research Consortium of Canada
sPGA	static Physician's Global Assessment
SSZ	sulfasalazine
STAT	signal transducer and activator of transcription
SvdH	Sharp-van der Heijde
TB	tuberculosis
[redacted]	
TH	T-helper
TNF	tumor necrosis factor
TSH	thyroid-stimulating hormone
TYK2	tyrosine kinase 2
ULN	upper limit of normal
US	United States
USA	United States of America
VLDA	very low disease activity
W	Week
WHO	World Health Organization
WOCBP	women of childbearing potential

Term	Definition
WPAI	Work Productivity and Activity Impairment

APPENDIX 2 STUDY GOVERNANCE CONSIDERATIONS

The term 'Participant' is used in the protocol to refer to a person who has consented to participate in the clinical research study. The term 'Subject' used in the CRF is intended to refer to a person (Participant) who has consented to participate in the clinical research study.

REGULATORY AND ETHICAL CONSIDERATIONS

GOOD CLINICAL PRACTICE

This study will be conducted in accordance with:

- Consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines
- Applicable International Council for Harmonisation (ICH) Good Clinical Practice (GCP),
- Applicable local requirements.

The study will be conducted in compliance with the protocol. The protocol and any amendments and the participant informed consent will receive approval/favorable opinion by Institutional Review Board/Independent Ethics Committee (IRB/IEC), and regulatory authorities according to applicable local regulations prior to initiation of the study.

All potential serious breaches must be reported to the Sponsor or designee immediately. A potential serious breach is defined as a Quality Issue (eg, protocol deviation, etc) that is likely to affect, to a significant degree one or more of the following: (1) the physical, safety or mental integrity of one or more subjects/participants; (2) the scientific value of the trial (eg, reliability and robustness of generated data). Items (1) or (2) can be associated with either GCP Regulation(s) or Trial protocol(s).

Personnel involved in conducting this study will be qualified by education, training, and experience to perform their respective tasks.

This study will not use the services of study personnel where sanctions have been invoked or where there has been scientific misconduct or fraud (eg, loss of medical licensure, debarment).

INSTITUTIONAL REVIEW BOARD/INDEPENDENT ETHICS COMMITTEE

Before study initiation, the investigator must have written and dated approval/favorable opinion from the IRB/IEC for the protocol, consent form, participant recruitment materials (eg, advertisements), and any other written information to be provided to subjects/participants. The investigator or BMS should also provide the IRB/IEC with a copy of the Investigator Brochure or product labeling information to be provided to subjects/participants and any updates.

The investigator, Sponsor or designee should provide the IRB/IEC with reports, updates and other information (eg, expedited safety reports, amendments, and administrative letters) according to regulatory requirements or institution procedures.

The investigator is responsible for providing oversight of the conduct of the study at the site and adherence to requirements of the following where applicable:

- ICH guidelines
- United States (US) Code of Federal Regulations, Title 21, Part 50 (21CFR50)
- European Regulation 536/2014 for clinical studies,
- European Medical Device Regulation 2017/745 for clinical device research,
- the IRB/IEC
- all other applicable local regulations

COMPLIANCE WITH THE PROTOCOL AND PROTOCOL REVISIONS

The investigator should not implement any deviation or change to the protocol without prior review and documented approval/favorable opinion of an amendment from the IRB/IEC (and if applicable, also by local health authority) except where necessary to eliminate an immediate hazard(s) to study subjects/participants.

If a deviation or change to a protocol is implemented to eliminate an immediate hazard(s) prior to obtaining relevant approval/favorable opinion(s) the deviation or change will be submitted, as soon as possible to:

- IRB/IEC
- Regulatory Authority(ies), if applicable by local regulations (per national requirements)

Documentation of approval/favorable opinion signed by the chairperson or designee of the IRB(s)/IEC(s) and if applicable, also by local health authority must be sent to BMS.

If an amendment substantially alters the study design or increases the potential risk to the participant: (1) the consent form must be revised and submitted to the IRB(s)/IEC(s) for review and approval/favorable opinion; (2) the revised form must be used to obtain consent from subjects/participants currently enrolled in the study if they are affected by the amendment; and (3) the new form must be used to obtain consent from new subjects/participants prior to enrollment.

If the revision is done via an administrative letter, investigators must inform their IRB(s)/IEC(s).

FINANCIAL DISCLOSURE

Investigators and sub-Investigators will provide the Sponsor with sufficient, accurate financial information in accordance with local regulations to allow the Sponsor to submit complete and accurate financial certification or disclosure statements to the appropriate health authorities. Investigators are responsible for providing information on financial interests during the course of the study and for 1 year after completion of the study.

INFORMED CONSENT PROCESS

Investigators must ensure that subjects/participants are clearly and fully informed about the purpose, potential risks, and other critical issues regarding clinical studies in which they volunteer to participate.

In situations where consent cannot be given by subjects/participants, their legally acceptable representatives (as per country guidelines) are clearly and fully informed about the purpose, potential risks, and other critical issues regarding clinical studies in which the participant volunteers to participate.

Sponsor or designee will provide the investigator with an appropriate (ie, Global or Local) sample informed consent form which will include all elements required by ICH, GCP and applicable regulatory requirements. The sample informed consent form will adhere to the ethical principles that have their origin in the Declaration of Helsinki.

Investigators must:

- Provide a copy of the consent form and written information about the study in the language in which the participant is most proficient prior to clinical study participation. The language must be non-technical and easily understood.
- Allow time necessary for participant or participant's legally acceptable representative to inquire about the details of the study.
- Obtain an informed consent signed and personally dated by the participant or the participant's legally acceptable representative and by the person who conducted the informed consent discussion.
- Obtain the IRB/IEC's written approval/favorable opinion of the written informed consent form and any other information to be provided to the subjects/participants, prior to the beginning of the study, and after any revisions are completed for new information.

If informed consent is initially given by a participant's legally acceptable representative or legal guardian, and the participant subsequently becomes capable of making and communicating his or her informed consent during the study, consent must additionally be obtained from the participant.

Revise the informed consent whenever important new information becomes available that is relevant to the participant's consent. The investigator, or a person designated by the investigator, should fully inform the participant or the participant's legally acceptable representative or legal guardian, of all pertinent aspects of the study and of any new information relevant to the participant's willingness to continue participation in the study. This communication should be documented.

The confidentiality of records that could identify subjects/participants must be protected, respecting the privacy and confidentiality rules applicable to regulatory requirements, the subjects'/participants' signed ICF and, in the US, the subjects'/participants' signed HIPAA Authorization.

The consent form must also include a statement that BMS and regulatory authorities have direct access to participant records.

The rights, safety, and well-being of the study subjects/participants are the most important considerations and should prevail over interests of science and society.

[redacted]

RECRUITMENT STRATEGY

A patient engagement and recruitment program will be developed and implemented to assist sites with recruitment efforts. Tactics will support patient education and awareness and health care provider outreach. This program will also include solutions to address anticipated recruitment challenges.

[redacted]

SOURCE DOCUMENTS

The investigator is responsible for ensuring that the source data are accurate, legible, contemporaneous, original and attributable, whether the data are hand-written on paper or entered electronically. If source data are created (first entered), modified, maintained, archived, retrieved, or transmitted electronically via computerized systems (and/or any other kind of electronic devices) as part of regulated clinical trial activities, such systems must be compliant with all applicable laws and regulations governing use of electronic records and/or electronic signatures. Such systems may include, but are not limited to, electronic medical/health records (EMRs/EHRs), adverse event tracking/reporting, protocol required assessments, and/or drug accountability records).

When paper records from such systems are used in place of electronic format to perform regulated activities, such paper records should be certified copies. A certified copy consists of a copy of original information that has been verified, as indicated by a dated signature, as an exact copy having all of the same attributes and information as the original.

STUDY TREATMENT RECORDS

Records for study treatments (whether supplied by BMS, its vendors, or the site) must substantiate study treatment integrity and traceability from receipt, preparation, administration, and through

destruction or return. Records must be made available for review at the request of BMS/designee or a Health Authority.

If	Then
Supplied by BMS (or its vendors):	Records or logs must comply with applicable regulations and guidelines and should include: • amount received and placed in storage area • amount currently in storage area • label identification number or batch number • amount dispensed to and returned by each participant, including unique participant identifiers • amount transferred to another area/site for dispensing or storage • nonstudy disposition (eg, lost, wasted) • amount destroyed at study site, if applicable • amount returned to BMS • retain samples for bioavailability/bioequivalence/biocomparability, if applicable • dates and initials of person responsible for Investigational Product dispensing/accountability, as per the Delegation of Authority Form.
Sourced by site, and not supplied by BMS or its vendors (examples include IP sourced from the sites stock or commercial supply, or a specialty pharmacy)	The investigator or designee accepts responsibility for documenting traceability and study treatment integrity in accordance with requirements applicable under law and the SOPs/standards of the sourcing pharmacy.

BMS or designee will provide forms to facilitate inventory control if the investigational site does not have an established system that meets these requirements.

CASE REPORT FORMS

An investigator is required to prepare and maintain adequate and accurate case histories designed to record all observations and other data pertinent to the investigation on each individual treated or entered as a control in the investigation. Data that are derived from source documents and reported on the CRF must be consistent with the source documents or the discrepancies must be explained. Additional clinical information may be collected and analyzed in an effort to enhance understanding of product safety. CRFs may be requested for AEs and/or laboratory abnormalities that are reported or identified during the course of the study.

For sites using the Sponsor or designee electronic data capture tool, electronic CRFs will be prepared for all data collection fields except for fields specific to SAEs and pregnancy, which will

be reported on the electronic SAE form and Pregnancy Surveillance form, respectively. If electronic SAE form is not available, a paper SAE form can be used. Spaces may be left blank only in those circumstances permitted by study-specific CRF instructions provided by Sponsor or designee.

The confidentiality of records that could identify subjects/participants must be protected, respecting the privacy and confidentiality rules in accordance with the applicable regulatory requirement(s).

The investigator will maintain a signature sheet to document signatures and initials of all persons authorized to make entries and/or corrections on CRFs.

The completed CRF, SAE/pregnancy CRFs, must be promptly reviewed, signed, and dated by the investigator or qualified physician who is a subinvestigator and who is delegated this task on the Delegation of Authority Form. Subinvestigators in Japan may not be delegated the CRF approval task. For electronic CRFs, review and approval/signature is completed electronically through the BMS electronic data capture tool. The investigator must retain a copy of the CRFs including records of the changes and corrections.

Each individual electronically signing electronic CRFs must meet Sponsor or designee training requirements and must only access the BMS electronic data capture tool using the unique user account provided by Sponsor or designee. User accounts are not to be shared or reassigned to other individuals

MONITORING

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

Representatives of BMS must be allowed to visit all study site locations periodically to assess the data quality and study integrity. On site they will review study records and directly compare them with source documents, discuss the conduct of the study with the investigator, and verify that the facilities remain acceptable. Certain CRF pages and/or electronic files may serve as the source documents.

In addition, the study may be evaluated by Sponsor or designee internal auditors and government inspectors who must be allowed access to CRFs, source documents, other study files, and study facilities. BMS audit reports will be kept confidential.

The investigator must notify BMS promptly of any inspections scheduled by regulatory authorities, and promptly forward copies of inspection reports to Sponsor or designee.

RECORDS RETENTION

The investigator (or head of the study site in Japan) must retain all study records and source documents for the maximum period required by applicable regulations and guidelines, or

institution procedures, or for the period specified by BMS or designee, whichever is longer. The investigator (or head of the study site in Japan) must contact BMS prior to destroying any records associated with the study.

BMS or designee will notify the investigator (or head of the study site in Japan) when the study records are no longer needed.

If the investigator withdraws from the study (eg, relocation, retirement), the records shall be transferred to a mutually agreed upon designee (eg, another investigator, study site, IRB). Notice of such transfer will be given in writing to BMS or designee.

Records collected throughout the study will be stored in the BMS clinical data management system for a duration of the life of the product plus 25 years.

RETURN OF STUDY TREATMENT

For this study, study treatments (those supplied by BMS, a vendor or sourced by the investigator) such as partially used study treatment containers, vials, and syringes may be destroyed on site.

If..	Then
Study treatments supplied by BMS (including its vendors	Any unused study treatments supplied by BMS can only be destroyed after being inspected and reconciled by the responsible Study Monitor unless study treatments containers must be immediately destroyed as required for safety or to meet local regulations (eg, cytotoxics or biologics). If study treatments will be returned, the return will be arranged by the responsible Study Monitor.
Study treatments sourced by site, not supplied by BMS (or its vendors) (examples include study treatments sourced from the sites stock or commercial supply, or a specialty pharmacy)	It is the investigator's or designee's responsibility to dispose of all containers according to the institutional guidelines and procedures.

It is the investigator's or designee's responsibility to arrange for disposal, provided that procedures for proper disposal have been established according to applicable federal, state, local, and institutional guidelines and procedures, and provided that appropriate records of disposal are kept. The following minimal standards must be met:

- On-site disposal practices must not expose humans to risks from the drug.
- On-site disposal practices and procedures are in agreement with applicable laws and regulations, including any special requirements for controlled or hazardous substances.

- Written procedures for on-site disposal are available and followed. The procedures must be filed with the site's SOPs and a copy provided to BMS upon request.
- Records are maintained that allow for traceability of each container, including the date disposed of, quantity disposed, and identification of the person disposing the containers. The method of disposal (ie, incinerator, licensed sanitary landfill, or licensed waste disposal vendor) must be documented.
- Accountability and disposal records are complete, up-to-date, and available for the Monitor to review throughout the clinical trial period.

It is the investigator's or designee's responsibility to arrange for disposal of all empty containers.

If conditions for destruction cannot be met, the responsible Study Monitor will make arrangements for return of study treatments provided by BMS (or its vendors). Destruction of nonstudy treatments sourced by the site, not supplied by BMS, is solely the responsibility of the investigator or designee.

[redacted]

CLINICAL STUDY REPORT

A Signatory Investigator must be selected to sign the clinical study report.

For each CSR related to this protocol, the following criteria will be used to select the signatory investigator:

- External Principal Investigator designated at protocol development
- National Coordinating Investigator
- Study Steering Committee chair or their designee
- Participant recruitment (eg, among the top quartile of enrollers)
- Involvement in trial design
- Regional representation (eg, among top quartile of enrollers from a specified region or country)

SCIENTIFIC PUBLICATIONS

The data collected during this study are confidential and proprietary to Sponsor or designee. Any publications or abstracts arising from this study must adhere to the publication requirements set

forth in the clinical trial agreement (CTAg) governing [Study site or Investigator] participation in the study. These requirements include, but are not limited to, submitting proposed publications to Sponsor or designee at the earliest practicable time prior to submission or presentation and otherwise within the time period set forth in the CTAg.

Scientific Publications (such as abstracts, congress podium presentations and posters, and manuscripts) of the study results will be a collaborative effort between the study Sponsor and the external authors. No public presentation or publication of any interim results may be made by any principal investigator, sub-investigator or any other member of the study staff without the prior written consent of the Sponsor.

Authorship of publications at BMS is aligned with the criteria of the International Committee of Medical Journal Editors (ICMJE, www.icmje.org). Authorship selection is based upon significant contributions to the study (ie, ICMJE criterion #1). Authors must meet all 4 ICMJE criteria for authorship:

1) Substantial intellectual contribution to the conception or design of the work; or the acquisition of data (ie, evaluable subjects with quality data), analysis, or interpretation of data for the work (eg, problem solving, advice, evaluation, insights and conclusion); AND
2) Drafting the work or revising it critically for important intellectual content; AND
3) Final approval of the version to be published; AND
4) Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

Those who make the most significant contributions, as defined above, will be considered by BMS for authorship of the primary publication. Sub-investigators will generally not be considered for authorship in the primary publication. Geographic representation will also be considered.

Authors will be listed by order of significant contributions (highest to lowest), with the exception of the last author. Authors in first and last position have provided the most significant contributions to the work.

For secondary analyses and related publications, author list and author order may vary from primary to reflect additional contributions.

APPENDIX 3 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS: DEFINITIONS AND PROCEDURES FOR RECORDING, EVALUATING, FOLLOW UP, AND REPORTING

ADVERSE EVENTS

Adverse Event Definition:
An Adverse Event (AE) is defined as any new untoward medical occurrence or worsening of a preexisting medical condition in a clinical investigation participant administered study treatment and that does not necessarily have a causal relationship with this treatment.
An AE can therefore be any unfavorable and unintended sign (such as an abnormal laboratory finding), symptom, or disease temporally associated with the use of study treatment, whether or not considered related to the study treatment.
Events <u>Meeting</u> the AE Definition
Any abnormal laboratory test results (hematology, clinical chemistry, or urinalysis) or results from other safety assessments (eg, ECG, radiological scans, vital signs measurements), including those that worsen from baseline, considered clinically significant in the medical and scientific judgment of the investigator. Note that abnormal lab tests or other safety assessments should only be reported as AEs if the final diagnosis is not available. Once the final diagnosis is known, the reported term should be updated to be the diagnosis. Exacerbation of a chronic or intermittent pre-existing condition including either an increase in frequency and/or intensity of the condition. New conditions detected or diagnosed after study intervention administration even though it may have been present before the start of the study. Signs, symptoms, or the clinical sequelae of a suspected drug-drug interaction. Signs, symptoms, or the clinical sequelae of a suspected overdose of either study intervention or a concomitant medication. Overdose, as a verbatim term (as reported by the investigator), should not be reported as an AE/SAE unless it is an intentional overdose taken with possible suicidal/self-harming intent. Such overdoses should be reported regardless of sequelae and should specify “intentional overdose” as the verbatim term
Events <u>NOT</u> Meeting the AE Definition
Medical or surgical procedure (eg, endoscopy, appendectomy): the condition that leads to the procedure is the AE. Situations in which an untoward medical occurrence did not occur (social and/or convenience admission to a hospital).

DEFINITION OF SAE

If an event is not an AE per definition above, then it cannot be an SAE even if serious conditions are met.

SERIOUS ADVERSE EVENTS

Serious Adverse Event (SAE) is defined as any untoward medical occurrence that, at any dose:
Results in death
Is life-threatening (defined as an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe)
Requires inpatient hospitalization or causes prolongation of existing hospitalization (see NOTE below) NOTE: The following hospitalizations are not considered SAEs in BMS clinical studies: • a visit to the emergency room or other hospital department < 24 hours, that does not result in admission (unless considered an important medical or life-threatening event) • elective surgery, planned prior to signing consent • admissions as per protocol for a planned medical/surgical procedure • routine health assessment requiring admission for baseline/trending of health status (eg, routine colonoscopy) • medical/surgical admission other than to remedy ill health and planned prior to entry into the study. Appropriate documentation is required in these cases • admission encountered for another life circumstance that carries no bearing on health status and requires no medical/surgical intervention (eg, lack of housing, economic inadequacy, caregiver respite, family circumstances, administrative reason) • admission for administration of anticancer therapy in the absence of any other SAEs (applies to oncology protocols)
Results in persistent or significant disability/incapacity
Is a congenital anomaly/birth defect
Is an important medical event (defined as a medical event(s) that may not be immediately life-threatening or result in death or hospitalization but, based upon appropriate medical and scientific judgment, may jeopardize the participant or may require intervention [eg, medical, surgical] to prevent one of the other serious outcomes listed in the definition above.) Examples of such events include, but are not limited to, intensive treatment in an emergency room or at home for allergic bronchospasm; blood dyscrasias or convulsions that do not result in hospitalization.) Potential drug induced liver injury (DILI) is also considered an important medical event. (See Section 9.2.8 for the definition of potential DILI.)

Pregnancy and potential drug induced liver injury (DILI) must follow the same transmission timing and processes to BMS as used for SAEs (see Section 9.2.6 for reporting pregnancies).

Any component of a study endpoint that is considered related to study therapy should be reported as SAE (eg, death is an endpoint, if death occurred due to anaphylaxis, anaphylaxis must be reported).

EVALUATING AES AND SAES

Assessment of Causality

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

Follow-up of AEs and SAEs

If only limited information is initially available, follow-up reports are required. (Note: Follow-up SAE reports must include the same investigator term(s) initially reported.)

If an ongoing SAE changes in its intensity or relationship to study treatment or if new information becomes available, the SAE report must be updated and submitted within 24 hours to BMS (or designee) using the same procedure used for transmitting the initial SAE report.

All SAEs must be followed to resolution or stabilization.

REPORTING OF SAES TO SPONSOR OR DESIGNEE

- SAEs, whether related or not related to study treatment, and pregnancies must be reported to BMS (or designee) immediately within 24 hours of awareness of the event.
- SAEs must be recorded on the SAE Report Form.
  - The required method for SAE data reporting is through the eCRF.
  - The paper SAE Report Form is only intended as a back-up option when the electronic data capture (EDC) system is unavailable/not functioning for transmission of the eCRF to BMS (or designee).
    - In this case, the paper form is transmitted via email or confirmed facsimile (fax) transmission
    - When paper forms are used, the original paper forms are to remain on site
- Pregnancies must be recorded on a paper Pregnancy Surveillance Form and transmitted via email or confirmed facsimile (fax) transmission

SAE Email Address: Refer to Contact Information list.

SAE Facsimile Number: Refer to Contact Information list.

SAE Telephone Contact (required for SAE and pregnancy reporting): Refer to Contact Information list

APPENDIX 4 WOMEN OF CHILDBEARING POTENTIAL DEFINITIONS AND METHODS OF CONTRACEPTION

Appendix 4 provides general information and definitions related to woman of childbearing potential and methods of contraception that can be applied to most clinical trials. For information specific to this study regarding acceptable contraception requirements for female and male participants, refer to Section 6.1 of the protocol. Only the contraception methods as described in Section 6.1 are acceptable for this study.

DEFINITIONS

Woman of Childbearing Potential (WOCBP)

A woman is considered fertile following menarche and until becoming postmenopausal unless permanently sterile. Permanent sterilization methods include hysterectomy, bilateral salpingectomy, and bilateral oophorectomy.

Women in the following categories are not considered WOCBP:

- Premenarchal
- Premenopausal female with 1 of the following:
  - Documented hysterectomy
  - Documented bilateral salpingectomy
  - Documented bilateral oophorectomy

Note: Documentation can come from the site personnel's review of the participant's medical records, medical examination, or medical history interview.

- Postmenopausal female
  - A postmenopausal state is defined as 12 months of amenorrhea in a woman over age 45 years in the absence of other biological or physiological causes. In addition, females under the age of 55 years must have a serum follicle-stimulating hormone (FSH) level > 40 mIU/mL to confirm menopause.

Note: Females treated with hormone replacement therapy (HRT) are likely to have artificially suppressed FSH levels and may require a washout period in order to obtain a physiologic FSH level. The duration of the washout period is a function of the type of HRT used. Suggested guidelines for the duration of the washout periods for HRT types are presented below. Investigators should use their judgement in checking serum FSH levels.

- 1-week minimum for vaginal hormonal products (rings, creams, gels)
- 4-week minimum for transdermal products
- 8-week minimum for oral products

Other parenteral products may require washout periods as long as 6 months. If the serum FSH level is > 40 mIU/mL at any time during the washout period, the woman can be considered postmenopausal.

End of Relevant Systemic Exposure

End of relevant systemic exposure is the timepoint where the Investigational Medicinal Product (IMP) or any active major metabolites have decreased to a concentration that is no longer considered to be relevant for human teratogenicity or fetotoxicity. This should be evaluated in context of safety margins from the no-observed-adverse-effect level or the time required for 5 half-lives of the IMP to pass.

METHODS OF CONTRACEPTION

Local laws and regulations may require use of alternative and/or additional contraception methods.

Highly Effective Contraceptive Methods That Are <u>User Dependent</u> *Failure rate of < 1% per year when used consistently and correctly.*[a]
• Combined (estrogen- and progestogen-containing) hormonal contraception associated with inhibition of ovulation and/or implantation. (This method of contraception can only be used by WOCBP participants in studies where hormonal contraception is permitted by the study protocol.)[b] – Oral (birth control pills) – Intravaginal (rings) – Transdermal • Combined (estrogen-and progestogen-containing) hormonal contraception must begin at least 30 days prior to initiation of study therapy.
• Progestogen-only hormonal contraception associated with inhibition of ovulation. (This method of contraception can only be used by WOCBP participants in studies where hormonal contraception is permitted by the study protocol.)[b] – Oral – Injectable • Progestogen-only hormonal contraception must begin at least 30 days prior to initiation of study therapy.
Highly Effective Methods That Are User Independent
• Implantable progestogen-only hormonal contraception associated with inhibition of ovulation and/or implantation. (This method of contraception can only be used by WOCBP participants in studies where hormonal contraception is permitted by the study protocol.)[b] • Intrauterine device. • Intrauterine hormone-releasing system (IUS). (This method of contraception can only be used by WOCBP participants in studies where hormonal contraception is permitted by the study protocol.)[b,c]

• Bilateral tubal occlusion.
• Vasectomized partner Having a vasectomized partner is a highly effective contraception method provided that the partner is the sole male sexual partner of the WOCBP and the absence of sperm has been confirmed. If not, an additional highly effective method of contraception should be used. A vasectomy is a highly effective contraception method provided that the participant is the sole male sexual partner of the WOCBP and the absence of sperm has been confirmed. If not, an additional highly effective method of contraception should be used.
• Sexual abstinence. *Sexual abstinence is considered a highly effective method only if defined as refraining from heterosexual intercourse during the entire period of risk associated with the study treatment. The reliability of sexual abstinence needs to be evaluated in relation to the duration of the study and the preferred and usual lifestyle of the participant.* • Continuous abstinence must begin at least 30 days prior to initiation of study therapy. • It is not necessary to use any other method of contraception when complete abstinence is elected. • WOCBP participants who choose complete abstinence must continue to have pregnancy tests, as specified in Section 2. • Acceptable alternate methods of highly effective contraception must be discussed in the event that the WOCBP participant chooses to forego complete abstinence. • Periodic abstinence (including, but not limited to, calendar, symptothermal, postovulation methods), withdrawal (coitus interruptus), spermicides only, and lactational amenorrhea method (LAM) are not acceptable methods of contraception for this study.
NOTES: [a] Typical use failure rates may differ from failure rates when contraceptive methods are used consistently and correctly. Use should be consistent with local regulations regarding the use of contraceptive methods for participants in clinical studies. [b] Hormonal contraception may be susceptible to interaction with the study treatment, which may reduce the efficacy of the contraceptive method. Hormonal contraception is permissible only when there is sufficient evidence that the IMP and other investigational products will not alter hormonal exposures such that contraception would be ineffective or result in increased exposures that could be potentially hazardous. In this case, alternative methods of contraception should be utilized. For information specific to this study regarding permissibility of hormonal contraception, refer to Sections 6.1 INCLUSION CRITERIA and 7.7.2 PROHIBITED [redacted] of the protocol. [c] IUSs are acceptable methods of contraception in the absence of definitive drug interaction studies when hormone exposures from intrauterine devices do not alter contraception effectiveness. For information specific to this study regarding permissibility of hormonal contraception, refer to Sections 6.1 INCLUSION CRITERIA and 7.7.2 PROHIBITED [redacted] of the protocol.

Less Than Highly Effective Contraceptive Methods That Are User Dependent *Failure rate of > 1% per year when used consistently and correctly.*
• Male or female condom with or without spermicide. Male and female condoms cannot be used simultaneously. • Diaphragm with spermicide. • Cervical cap with spermicide. • Vaginal sponge with spermicide. • Progestogen-only oral hormonal contraception, where inhibition of ovulation is not the primary mechanism of action. (This method of contraception cannot be used by WOCBP participants in studies where hormonal contraception is prohibited.)
Unacceptable Methods of Contraception
• Periodic abstinence (calendar, symptothermal, postovulation methods). • Withdrawal (coitus interruptus). • Spermicide only. • LAM.

COLLECTION OF PREGNANCY INFORMATION

Guidance for collection of pregnancy information and outcome of pregnancy on the Pregnancy Surveillance Form is provided in Section 9.2.6 and Appendix 3, the appendix for Adverse Events and Serious Adverse Events: Definitions and Procedures for Recording, Evaluating, Follow-up, and Reporting.

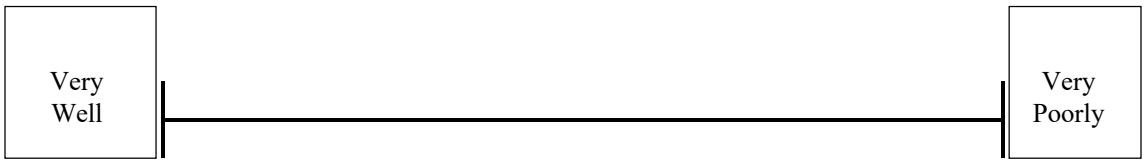
APPENDIX 5 CLASSIFICATION CRITERIA FOR PSORIATIC ARTHRITIS (CASPAR) CRITERIA

CASPAR CRITERIA (Specificity 0.987, Sensitivity 0.914)	
Inflammatory articular disease (joint, spine, or entheseal)	
With 3 or more points from the following	
1. Current psoriasis (scores 2 points)	*Psoriatic skin or scalp disease present today as judged by a rheumatologist*
2. Personal history of psoriasis (if current psoriasis not present)	*A history of psoriasis that may be obtained from patient, family doctor, dermatologist, or rheumatologist*
3. Family history of psoriasis (if personal history of psoriasis or current psoriasis not present)	*A history of psoriasis in a first or second degree relative according to patient report*
4. Psoriatic nail dystrophy	*Typical psoriatic nail dystrophy including onycholysis, pitting, and hyperkeratosis observed on current physical examination*
5. A negative test for rheumatoid factor	*By any method except latex but preferably by ELISA or nephlemetry, according to the local laboratory reference range*
6. Current dactylitis	*Swelling of an entire digit*
7. History of dactylitis (if current dactylitis is not present)	*A history of dactylitis recorded by a rheumatologist*
8. Radiological evidence of juxta-articular new bone formation	*Ill-defined ossification near joint margins (but excluding osteophyte formation) on plain X-rays of hand or foot*

Reference:
Taylor W, Gladman D, Helliwell P, et al. Classification criteria for psoriatic arthritis: development of new criteria from a large international study. Arthritis Rheum 2006;54:2665-73.

APPENDIX 6 SUBJECT ASSESSMENT OF DISEASE ACTIVITY (PSORIATIC ARTHRITIS) VISUAL ASSESSMENT SCALE

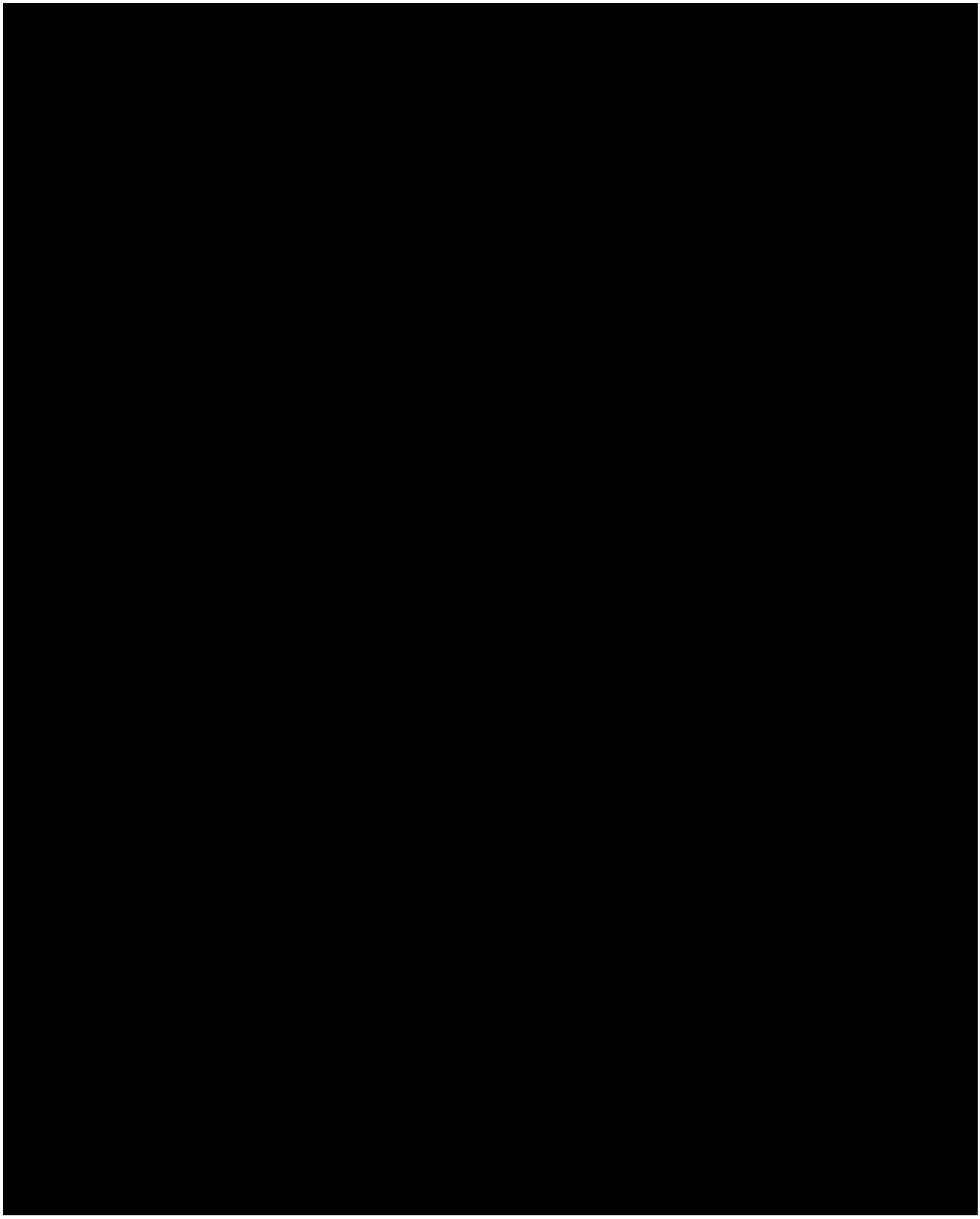
In all the ways in which your psoriatic arthritis as a whole, affects you, how would you rate the way you felt over the past week?



APPENDIX 7 SUBJECT ASSESSMENT OF PAIN SCALE (PSORIATIC ARTHRITIS)

How much pain have you had because of your psoriatic arthritis over the past week? Place a mark on the line below to indicate how severe your pain has been:

APPENDIX 8 AMERICAN COLLEGE OF RHEUMATOLOGY SUBJECT ASSESSMENT OF PHYSICAL FUNCTION SCALE: HEALTH ASSESSMENT QUESTIONNAIRE (HAQ)



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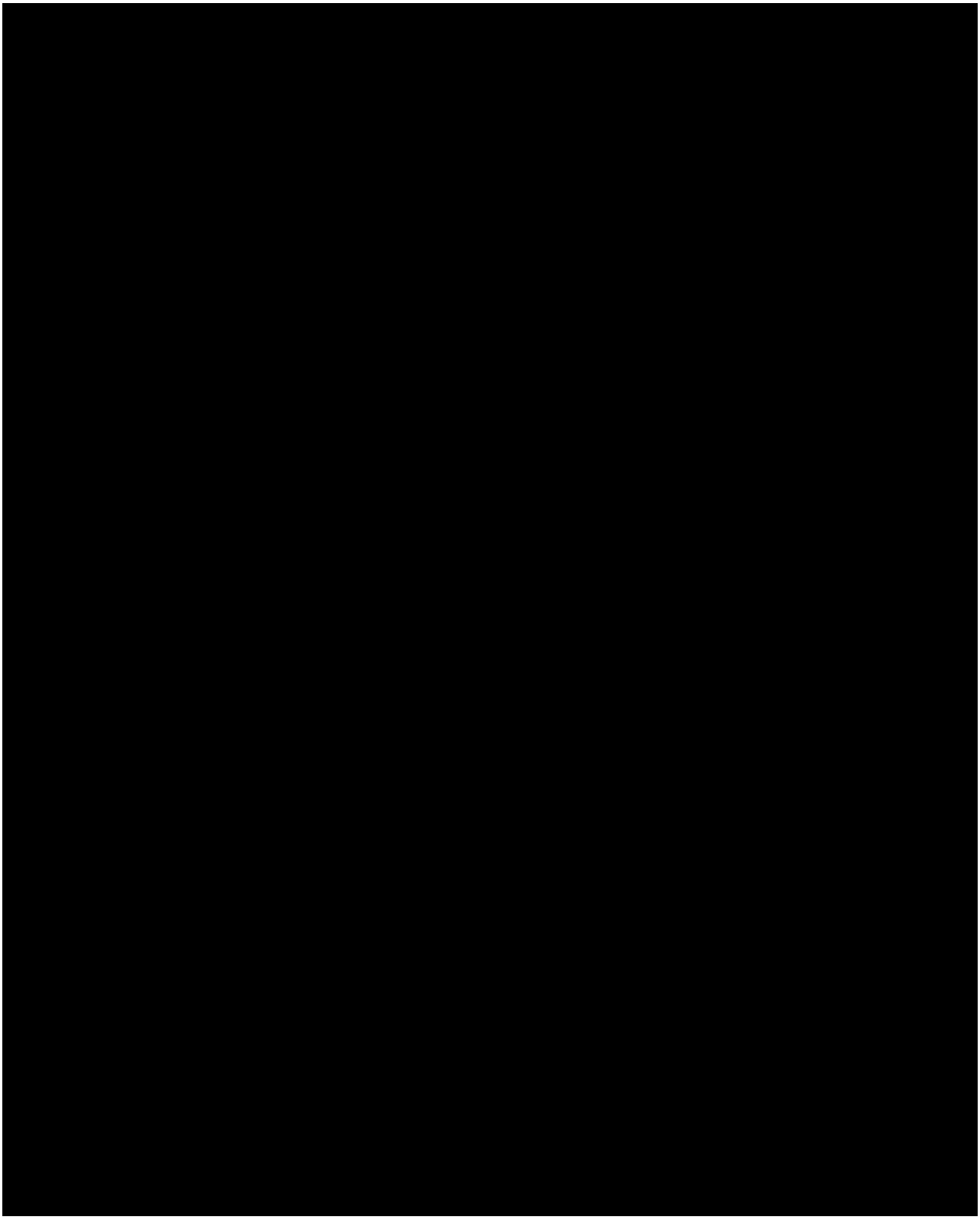
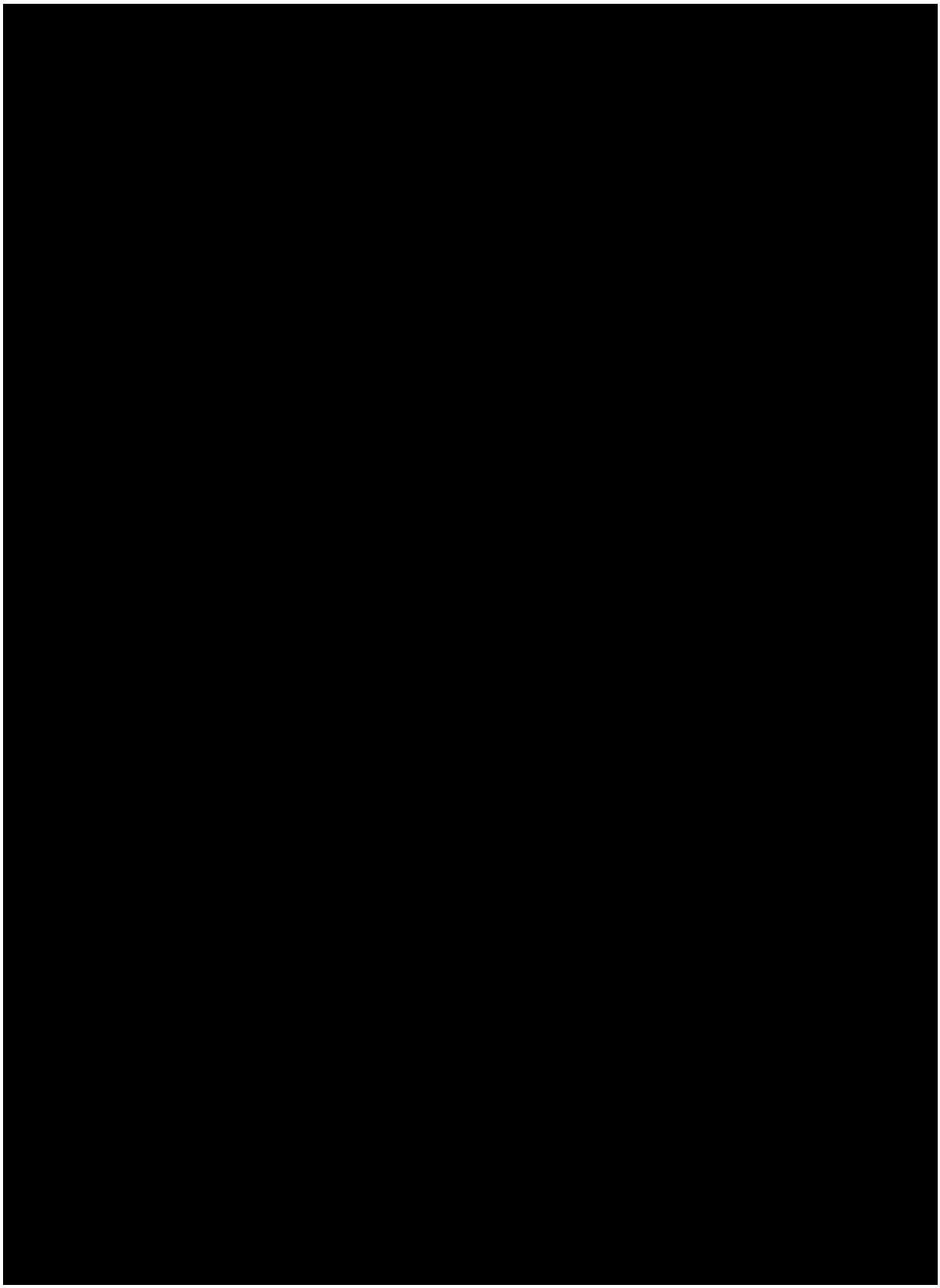
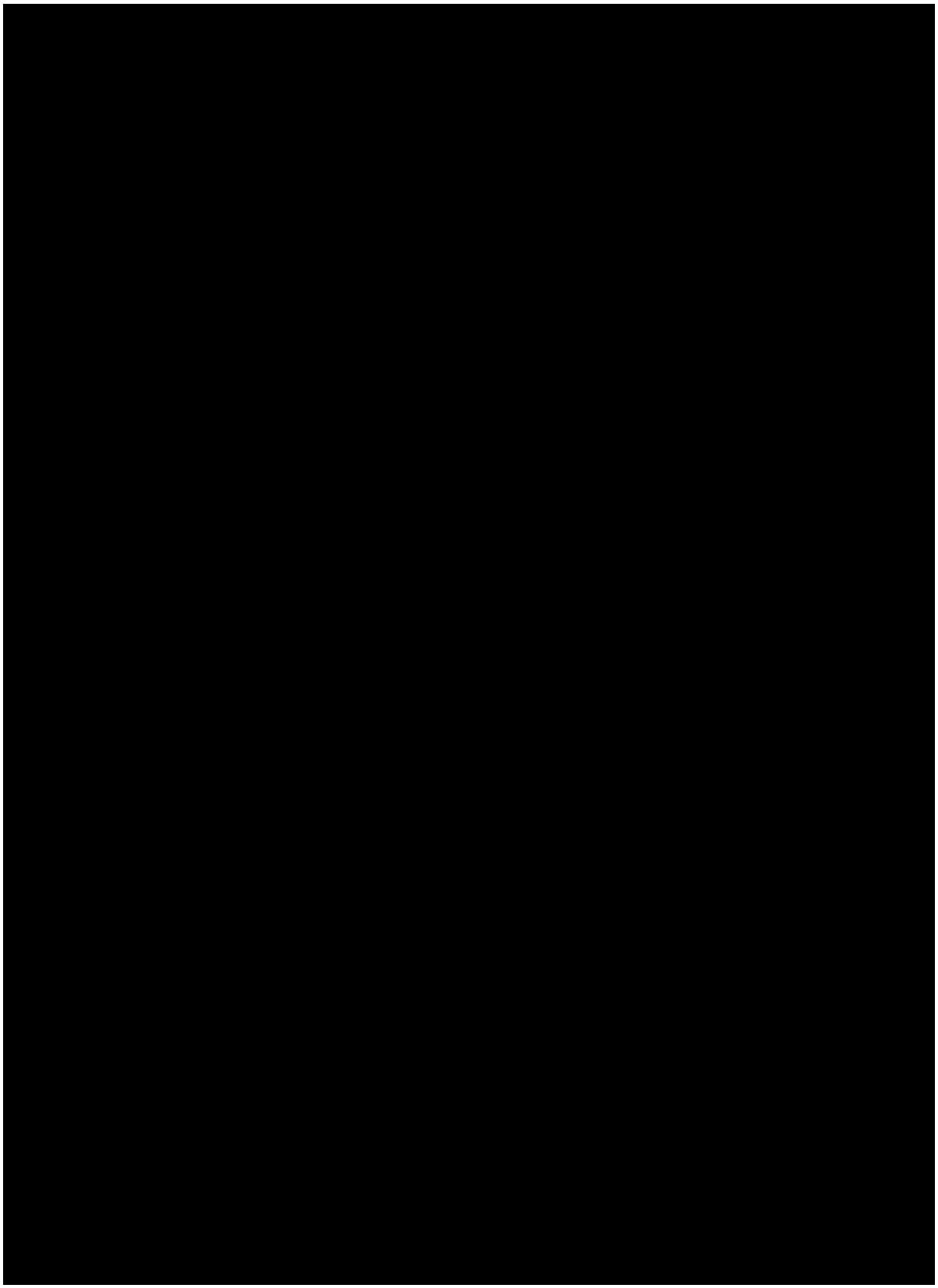
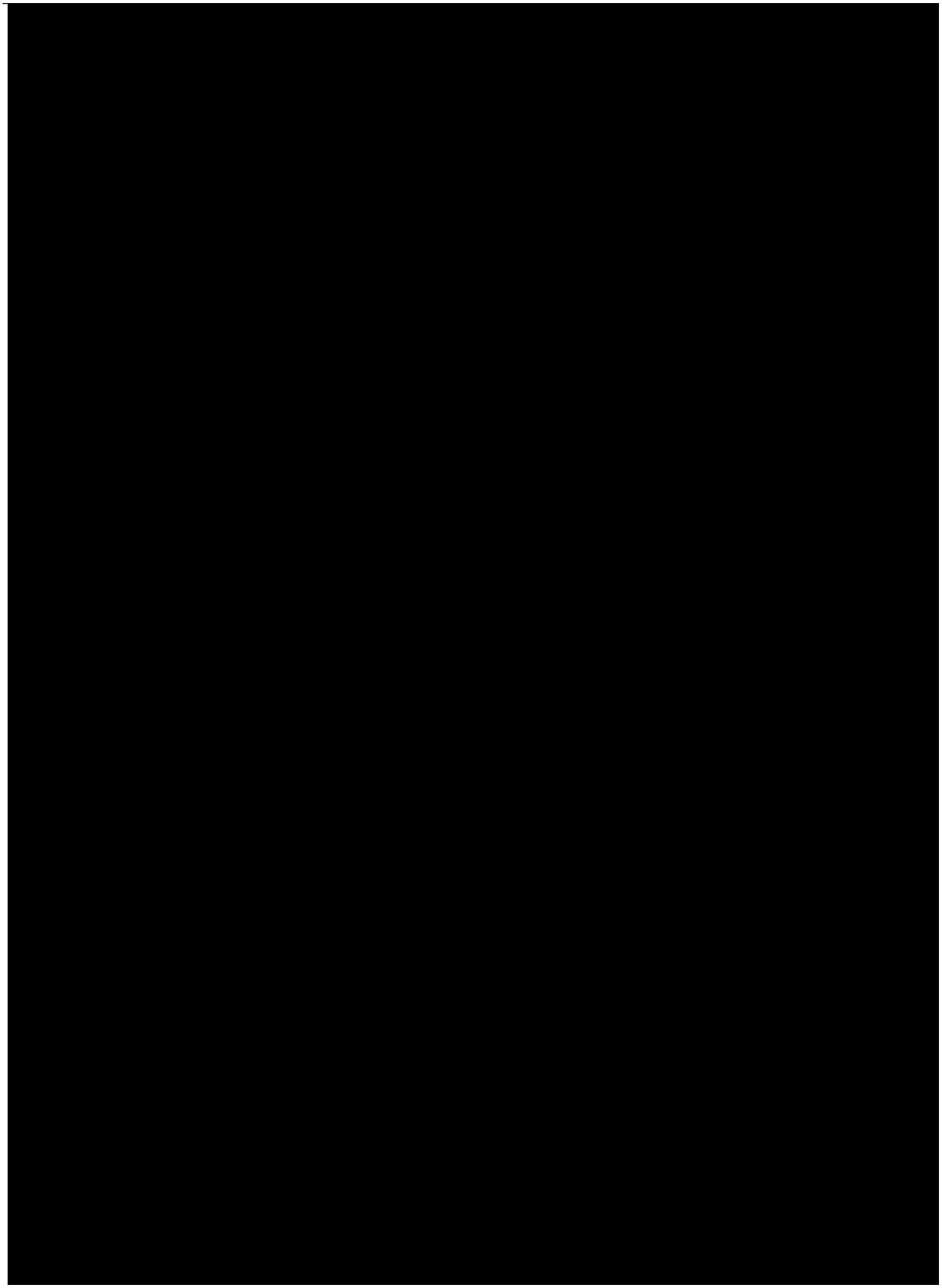
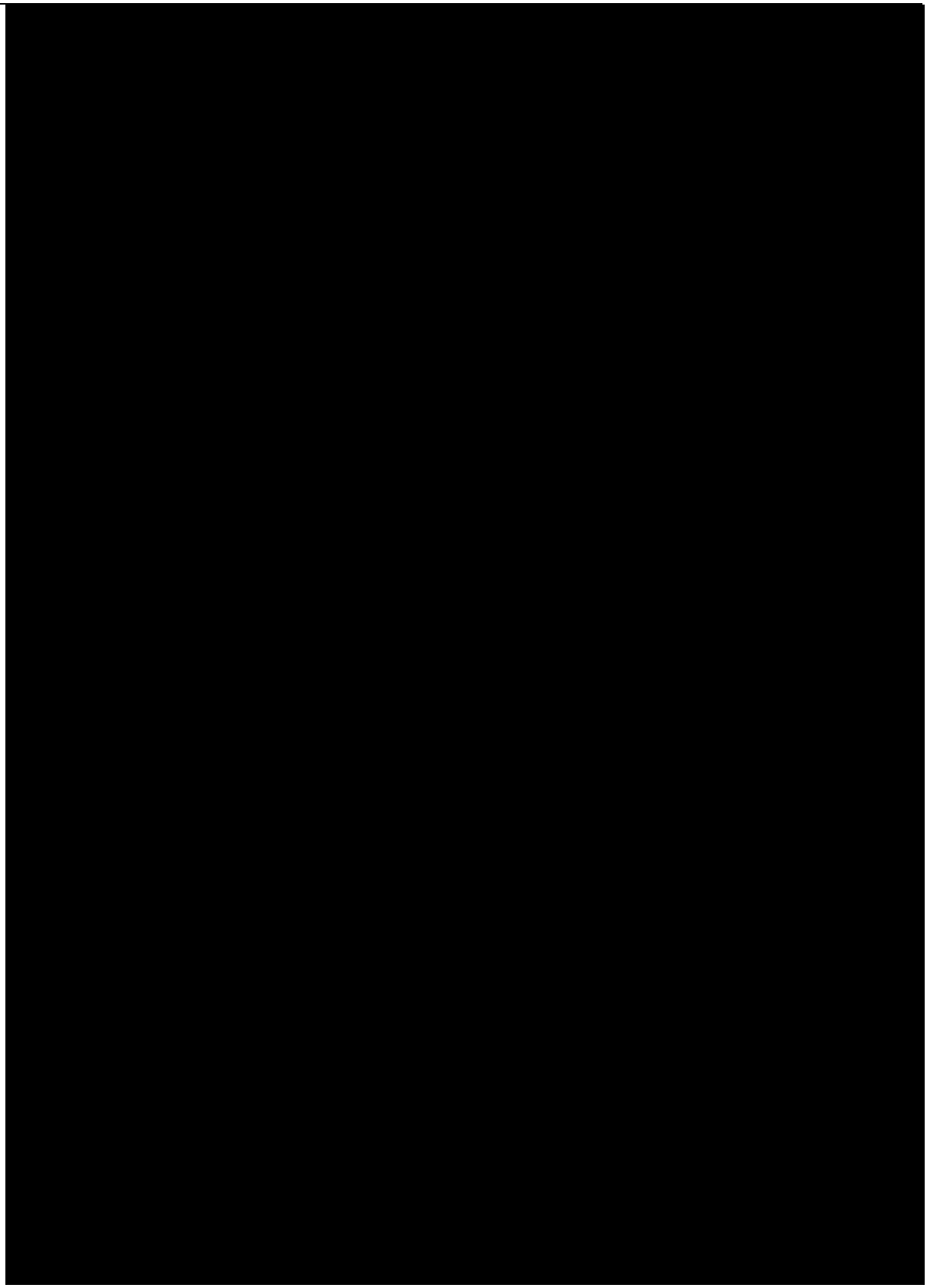


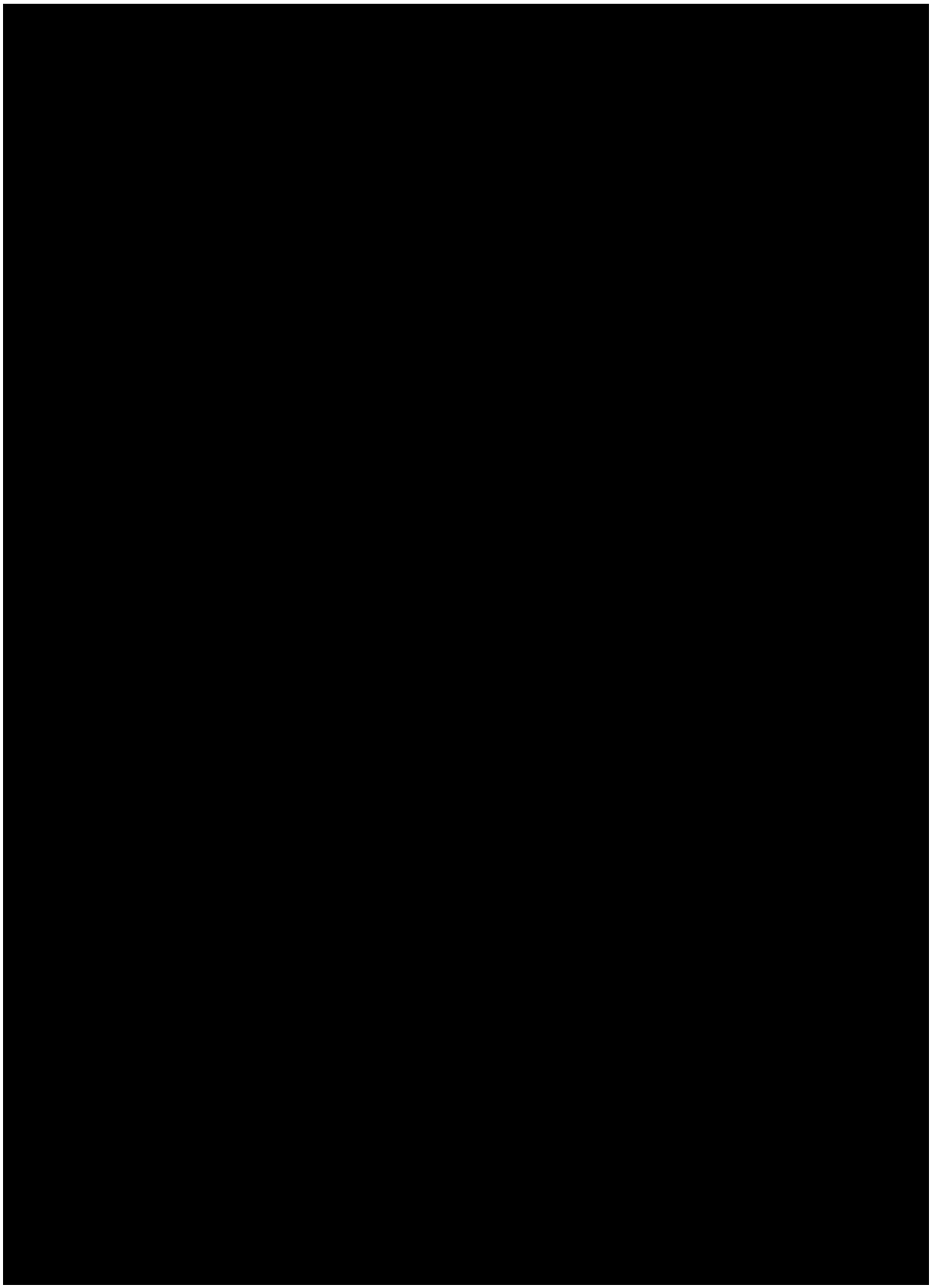
APPENDIX 9 SHORT FORM HEALTH SURVEY-36 ITEM (SF-36)

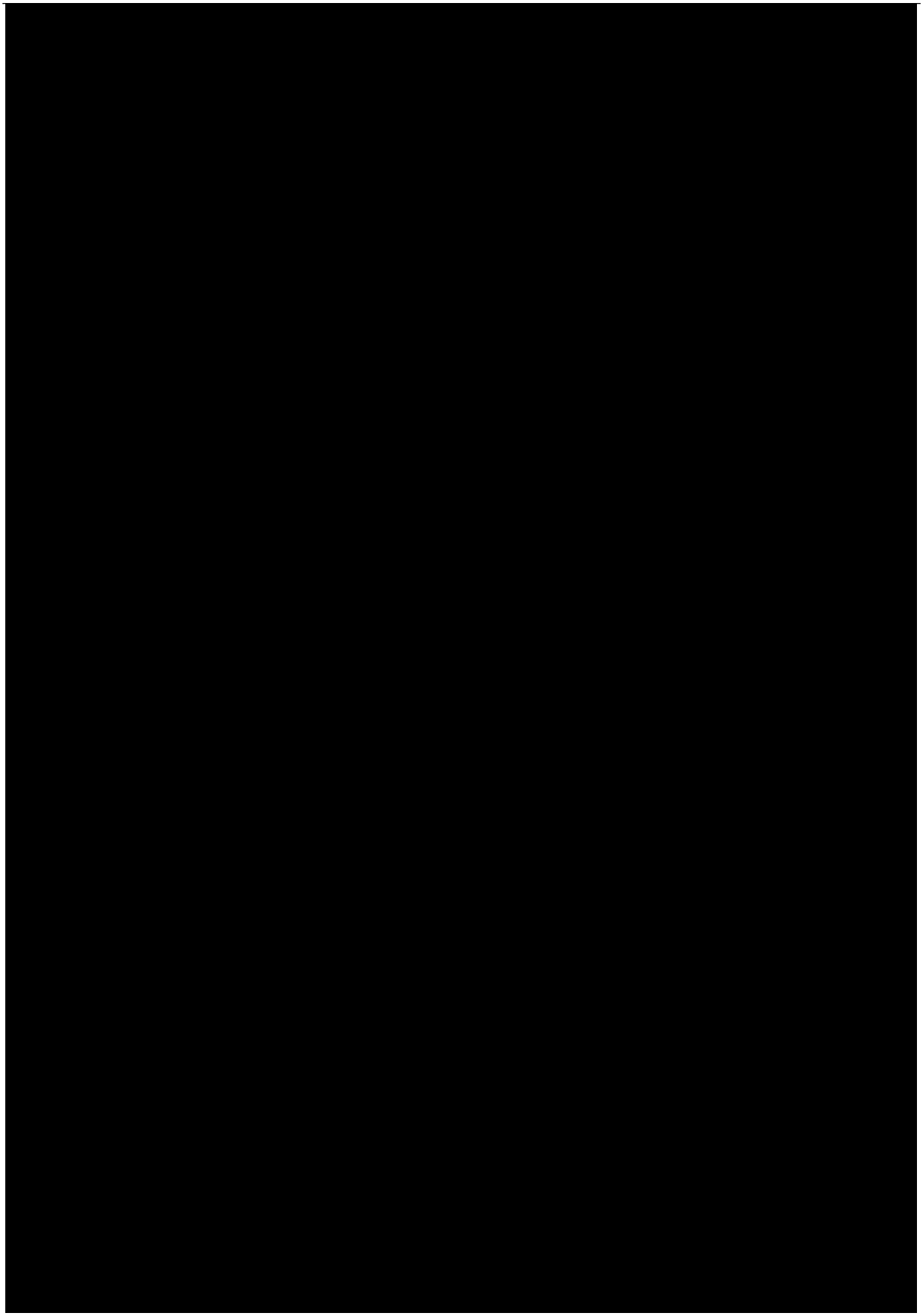


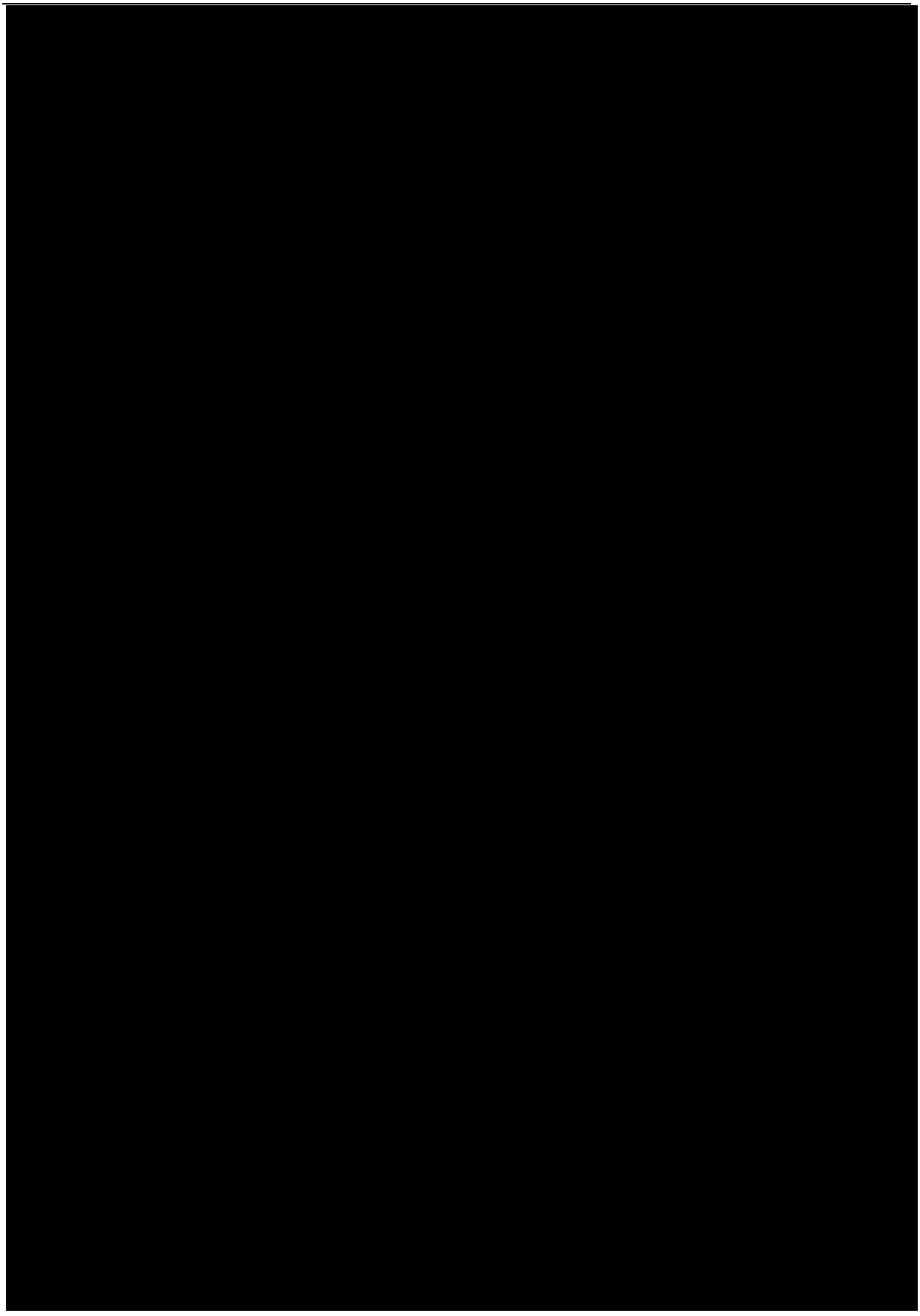


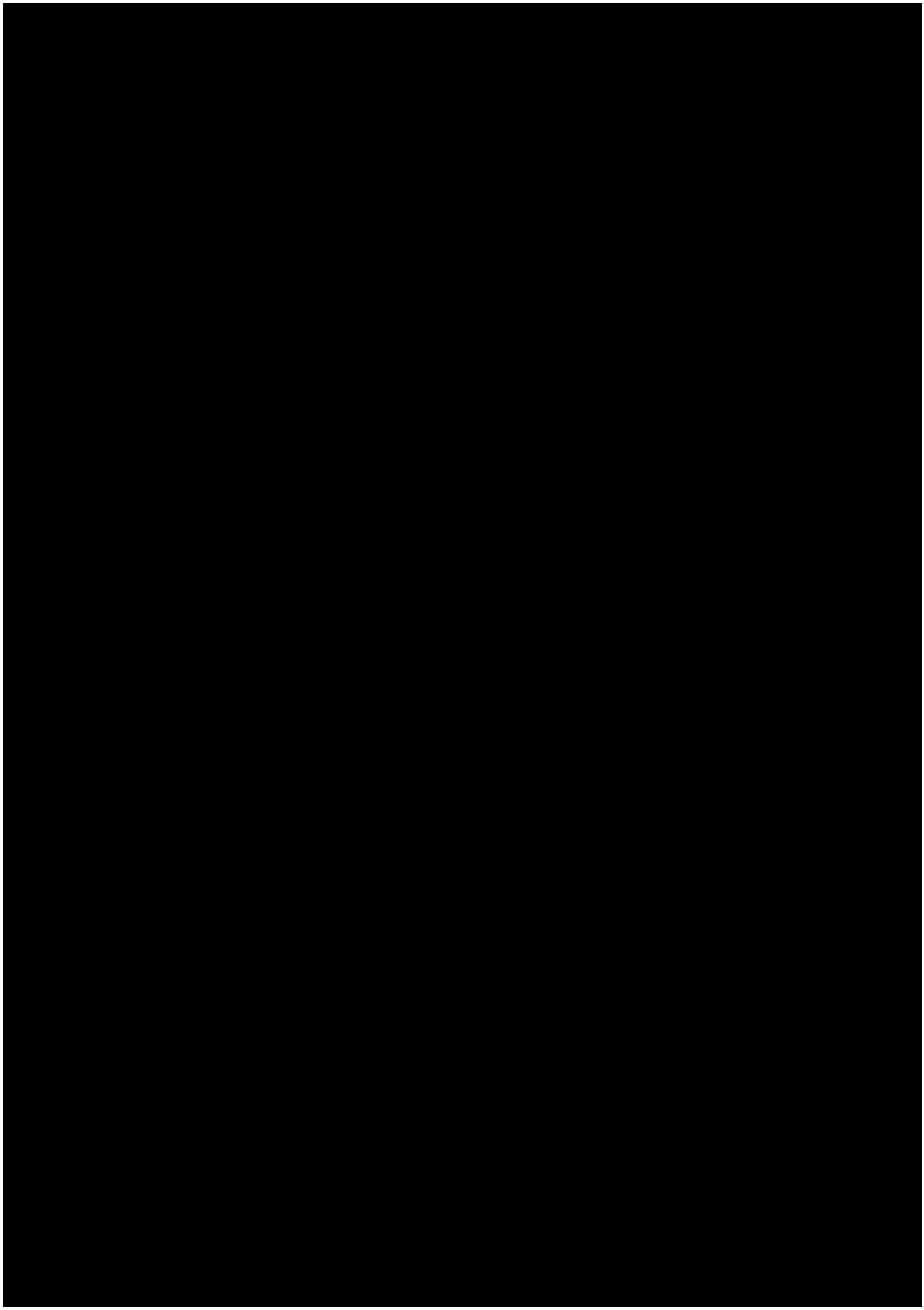


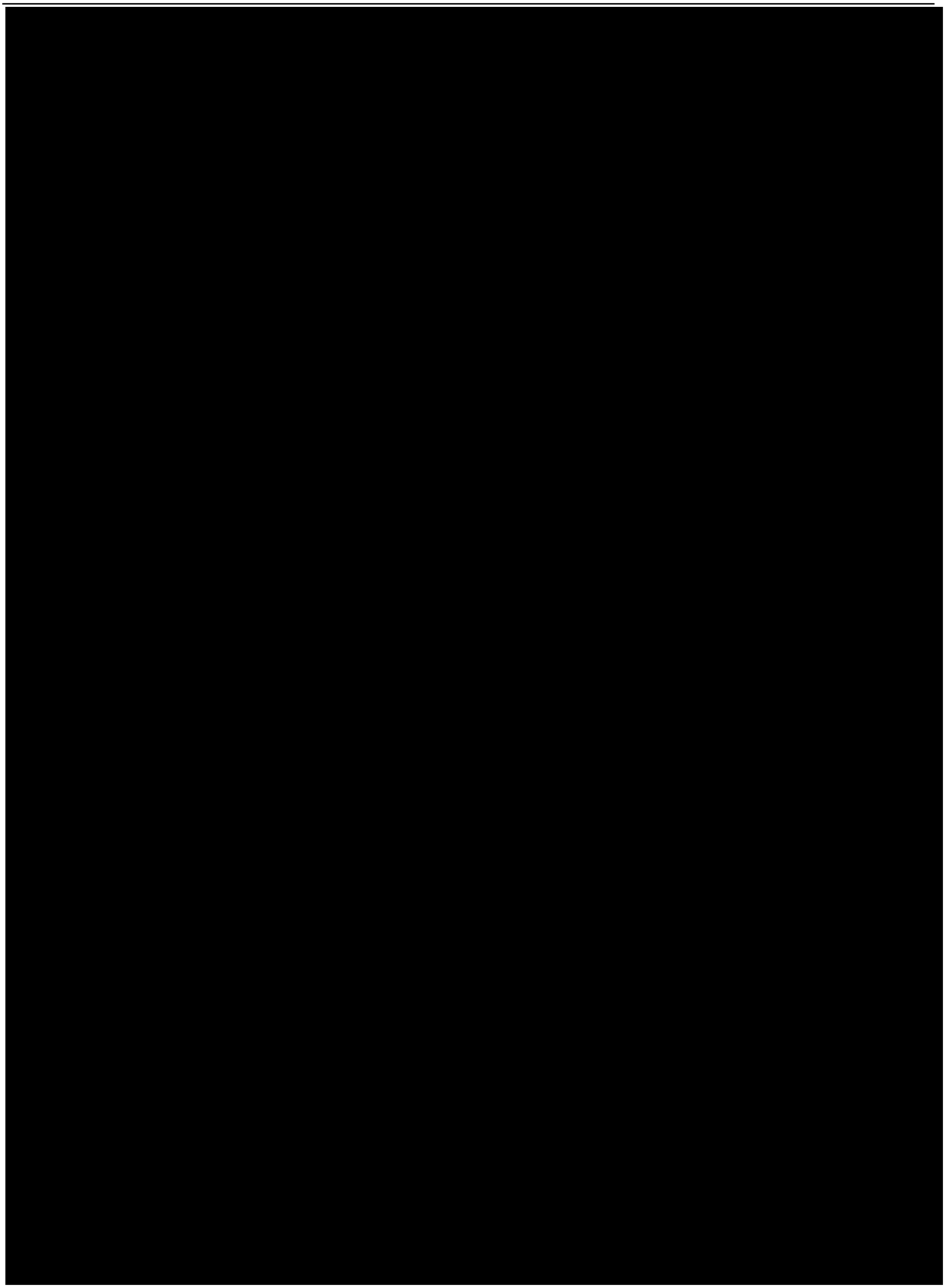


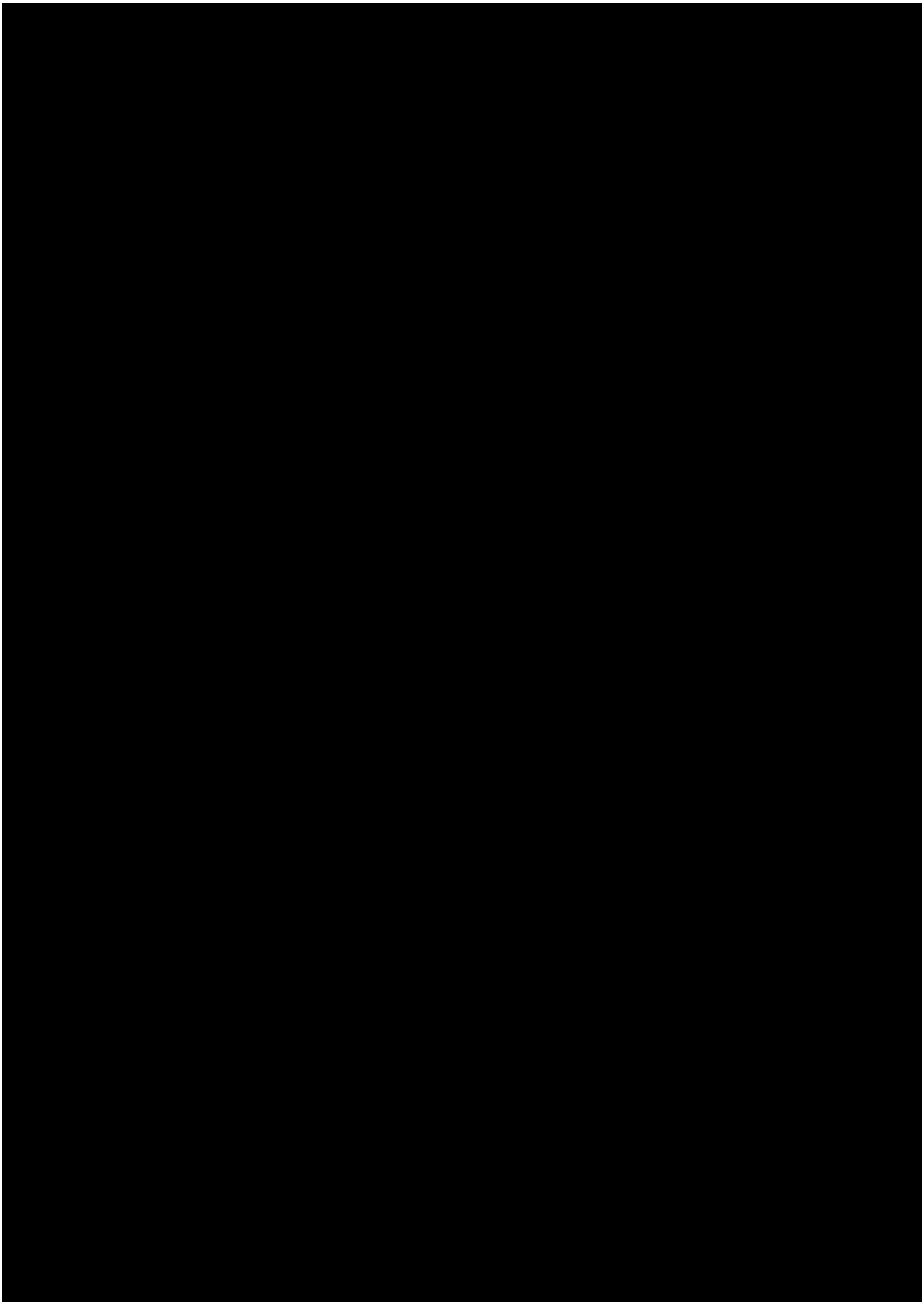


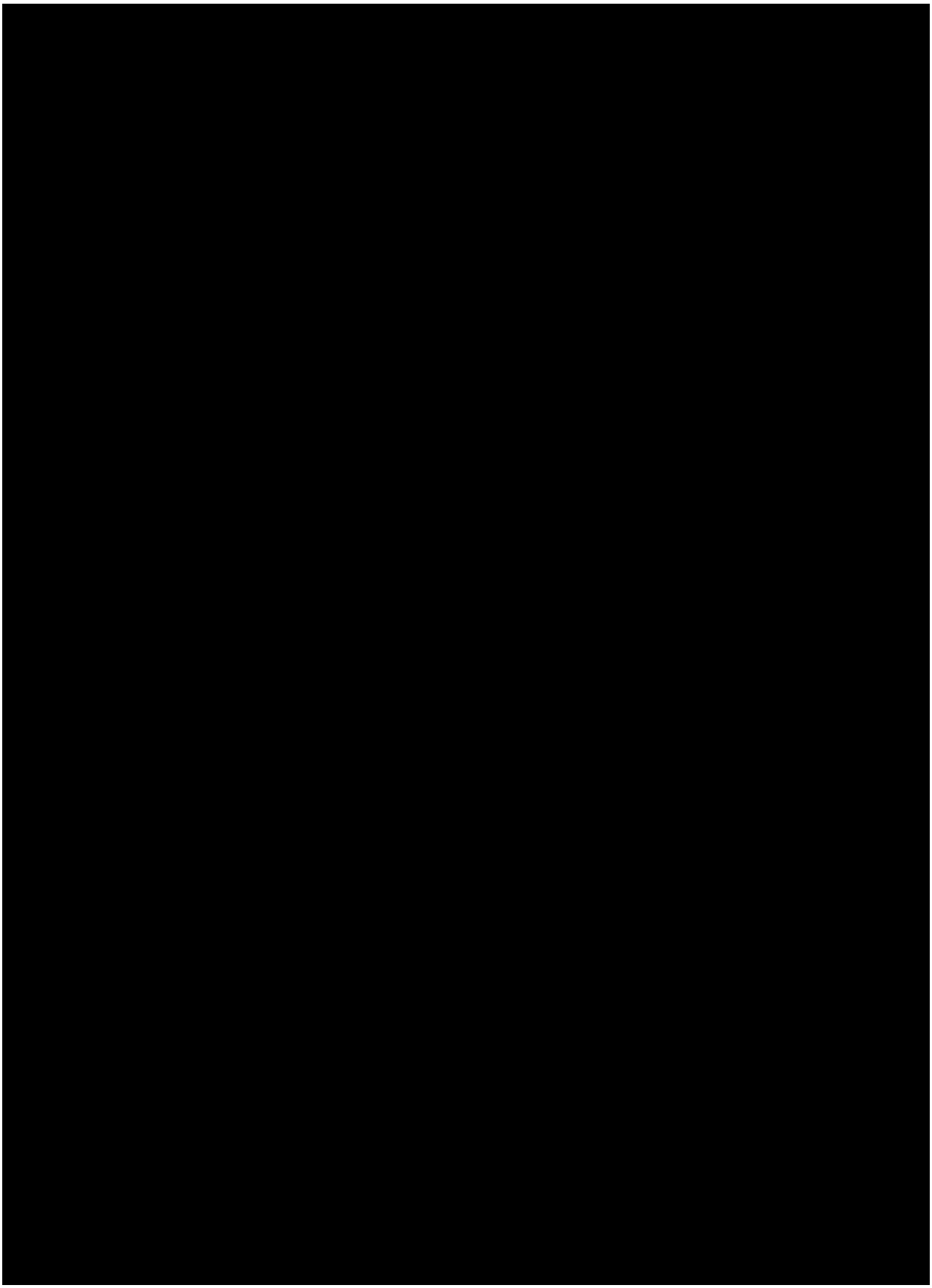




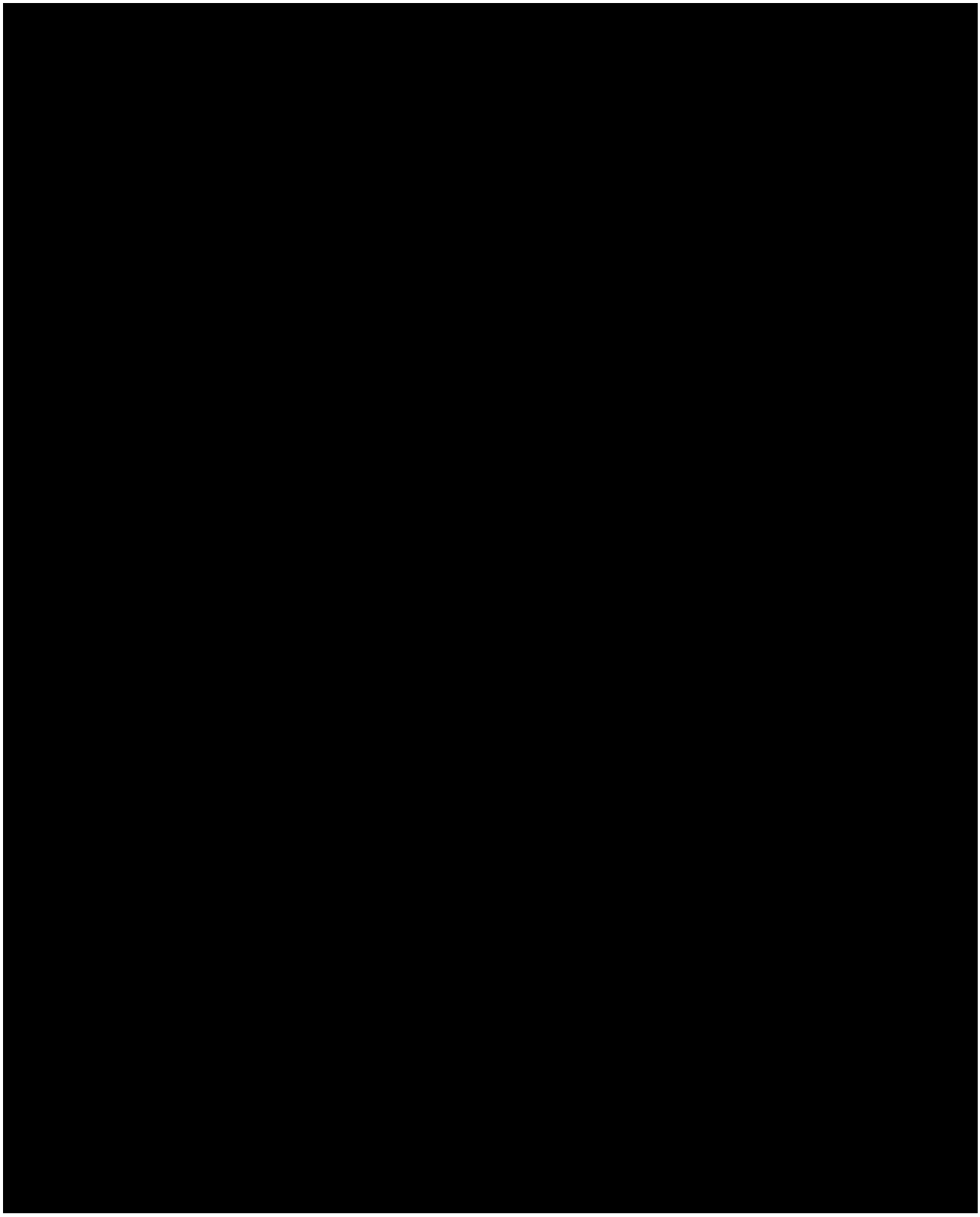




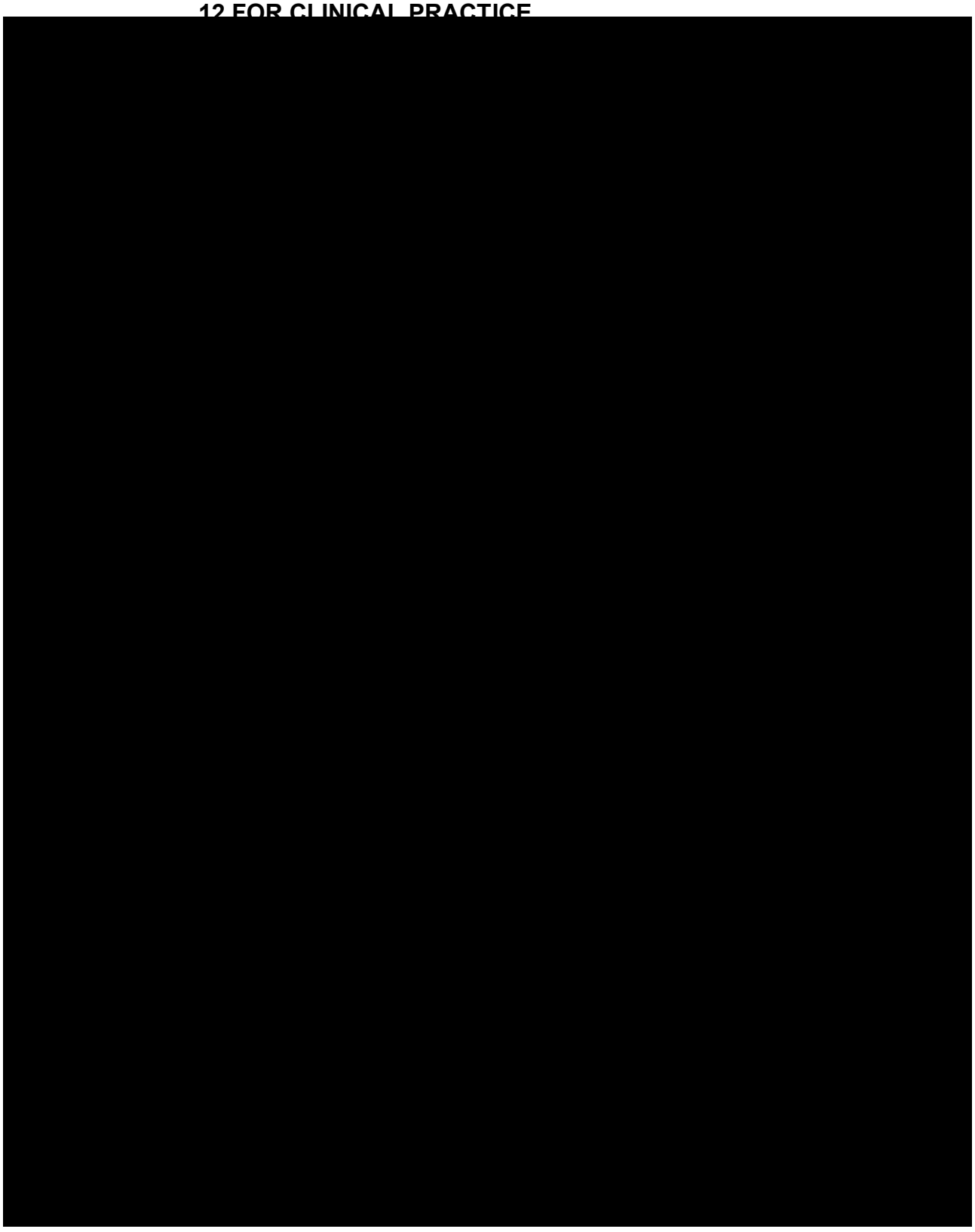




APPENDIX 10 FUNCTIONAL ASSESSMENT OF CHRONIC ILLNESS THERAPY FATIGUE



APPENDIX 11 THE EULAR PSORIATIC ARTHRITIS IMPACT OF DISEASE: PSAID 12 FOR CLINICAL PRACTICE



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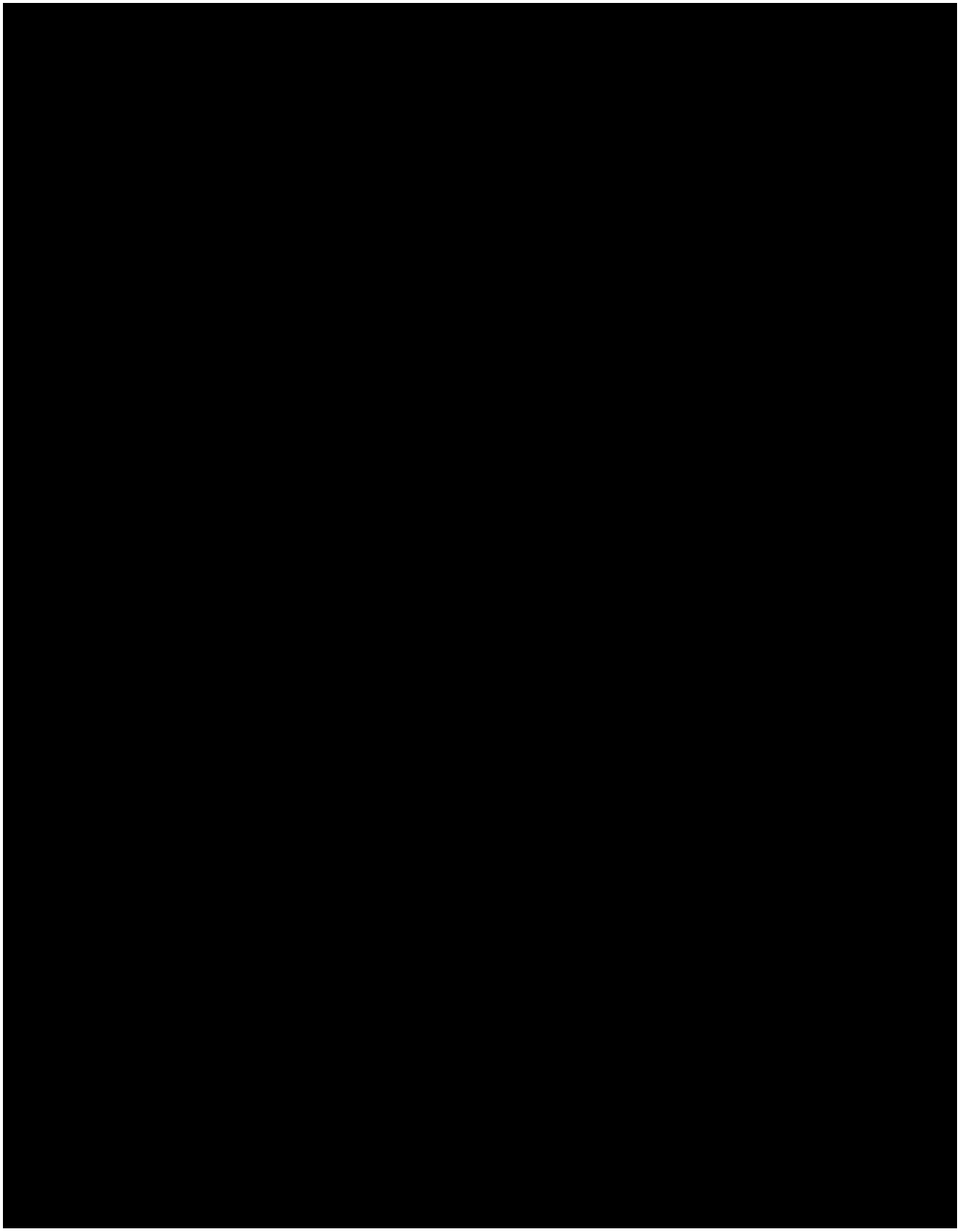
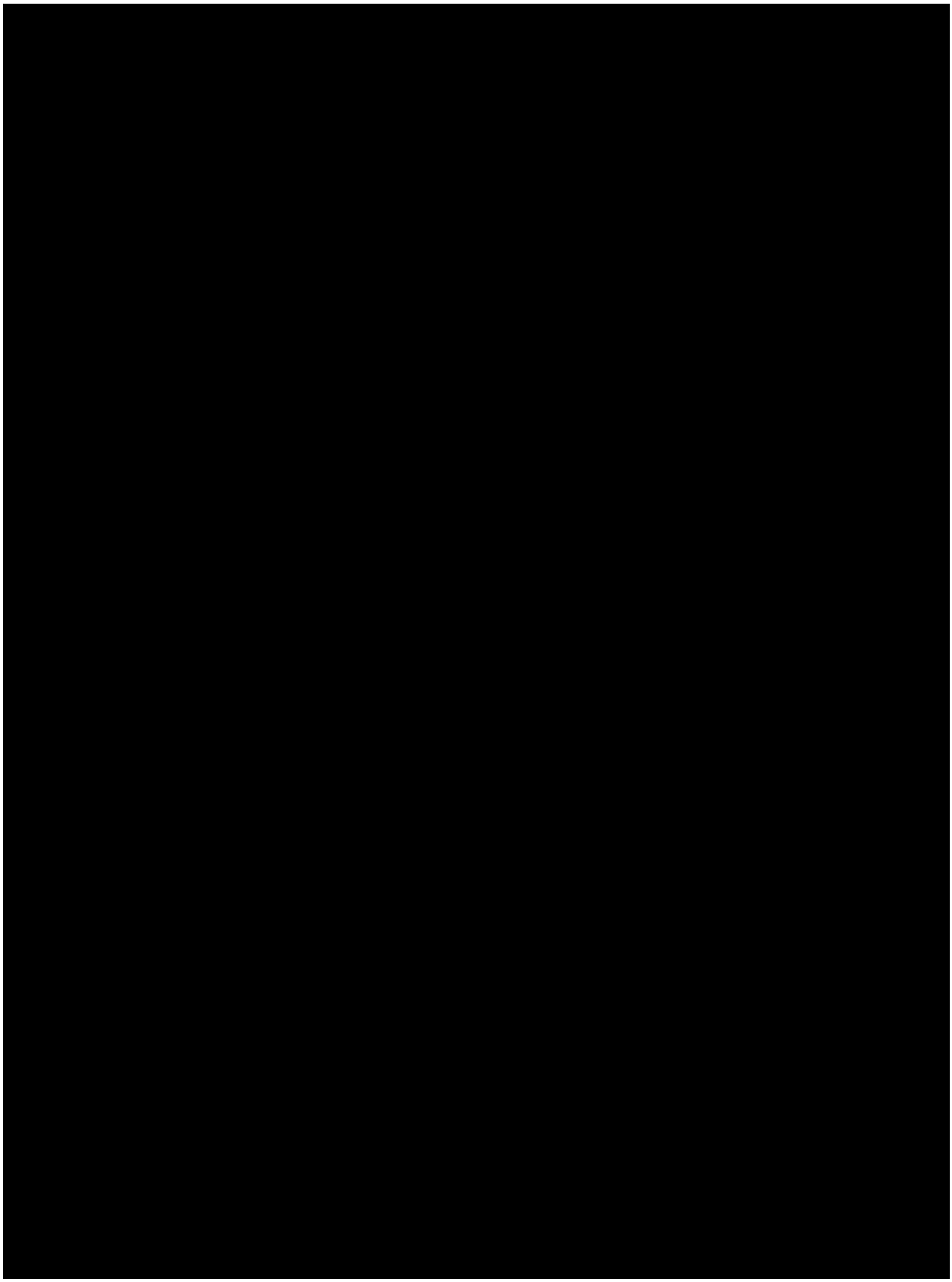
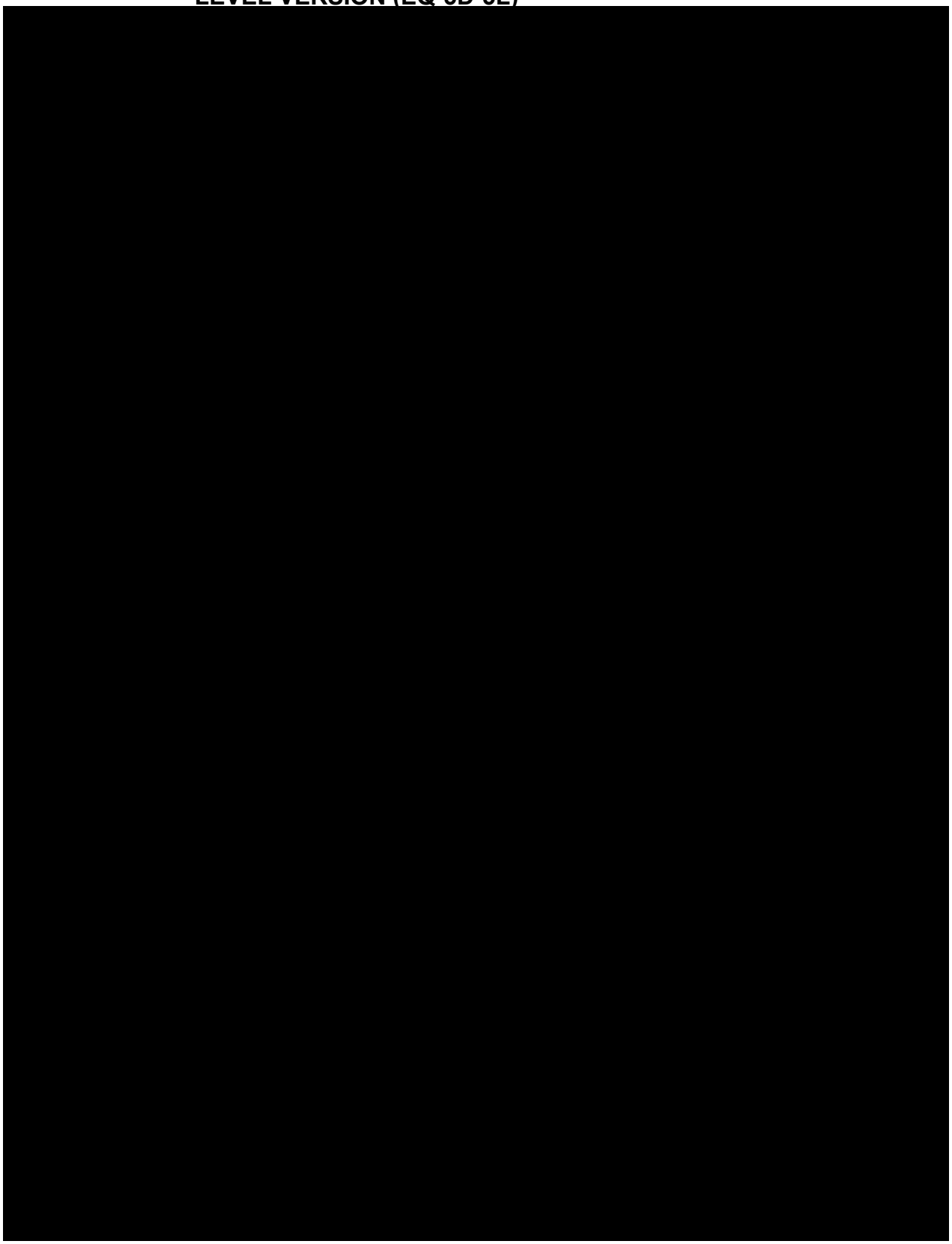
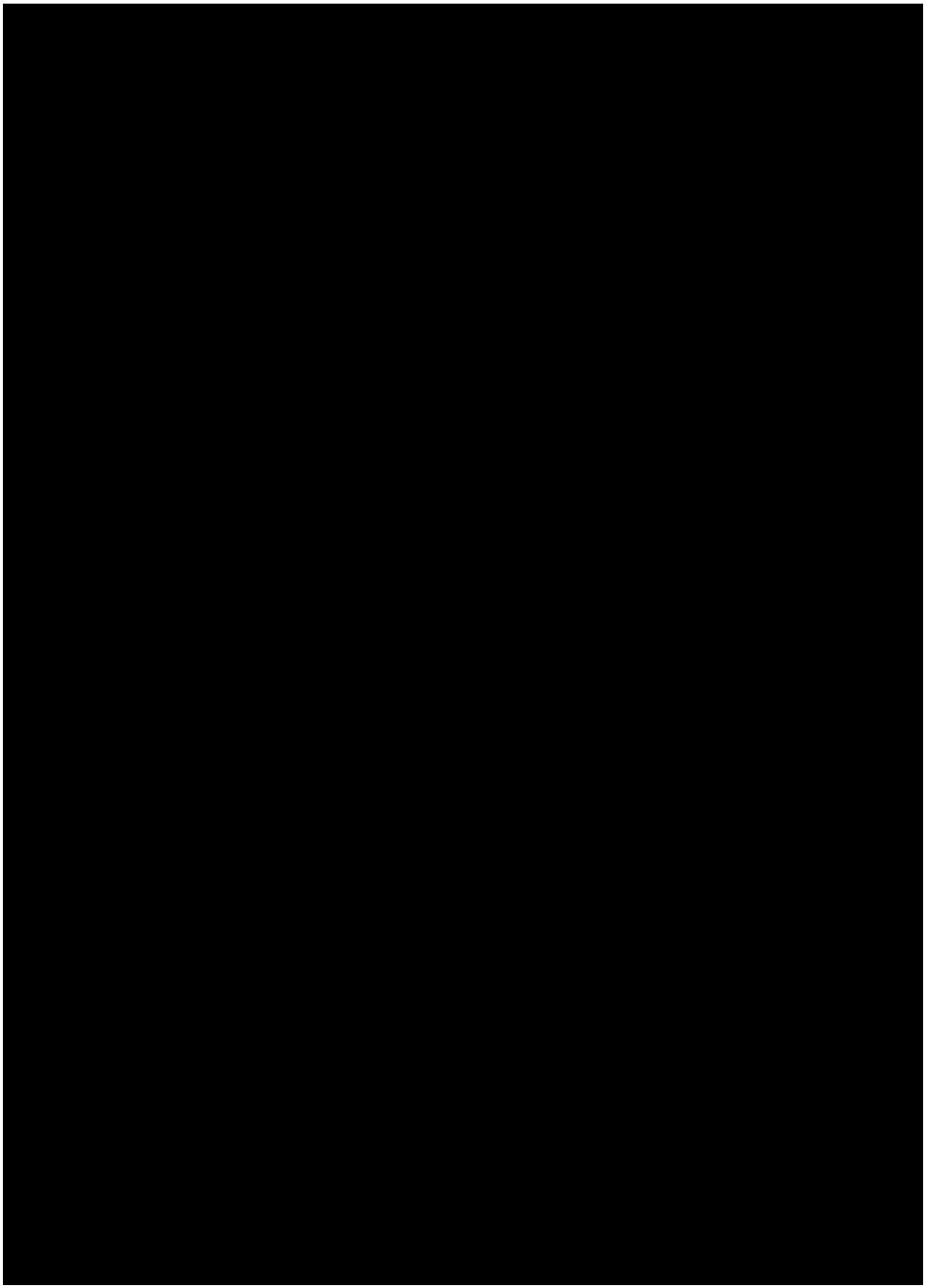
APPENDIX 12 DERMATOLOGY LIFE QUALITY INDEX (DLQI)

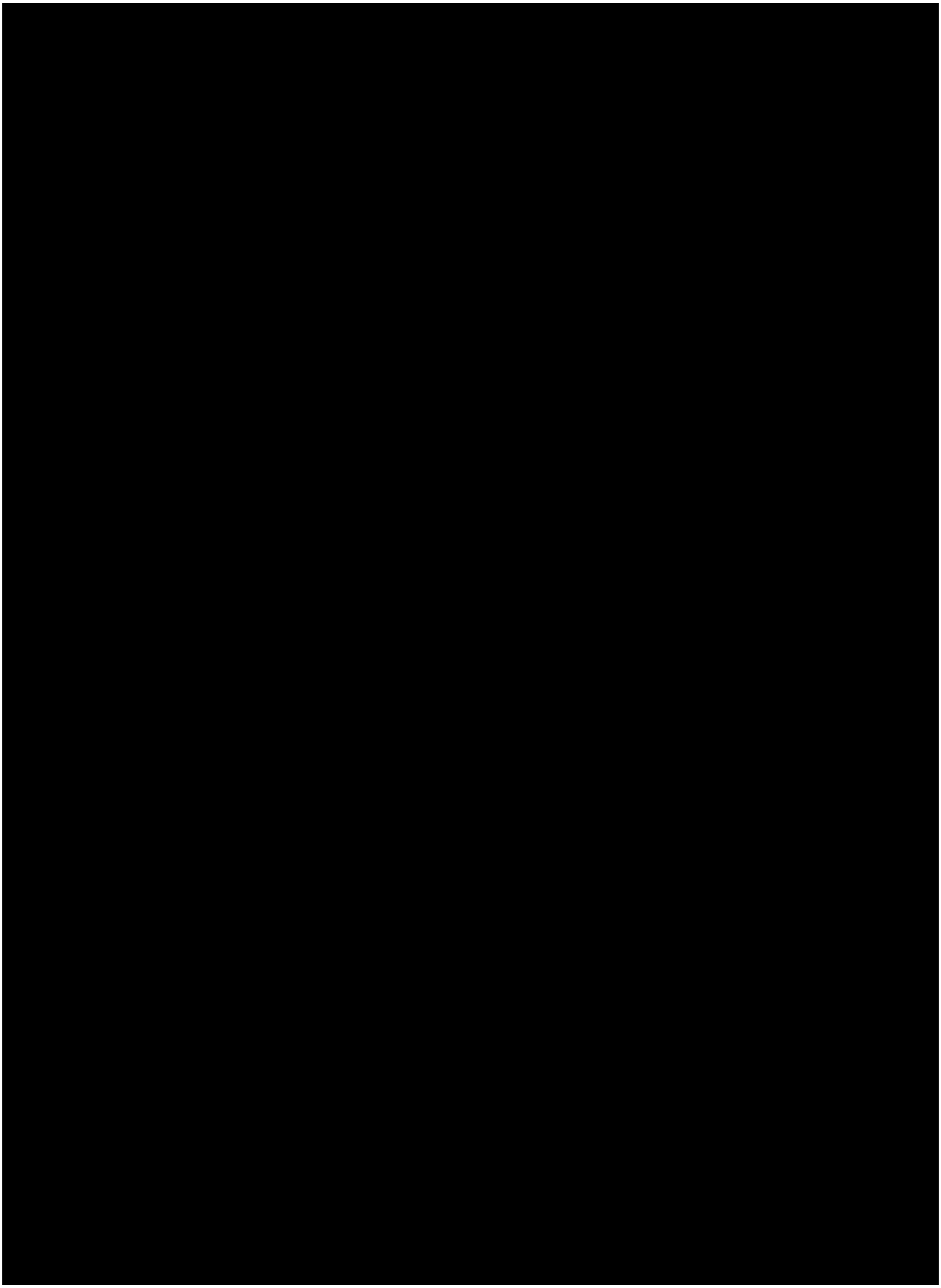




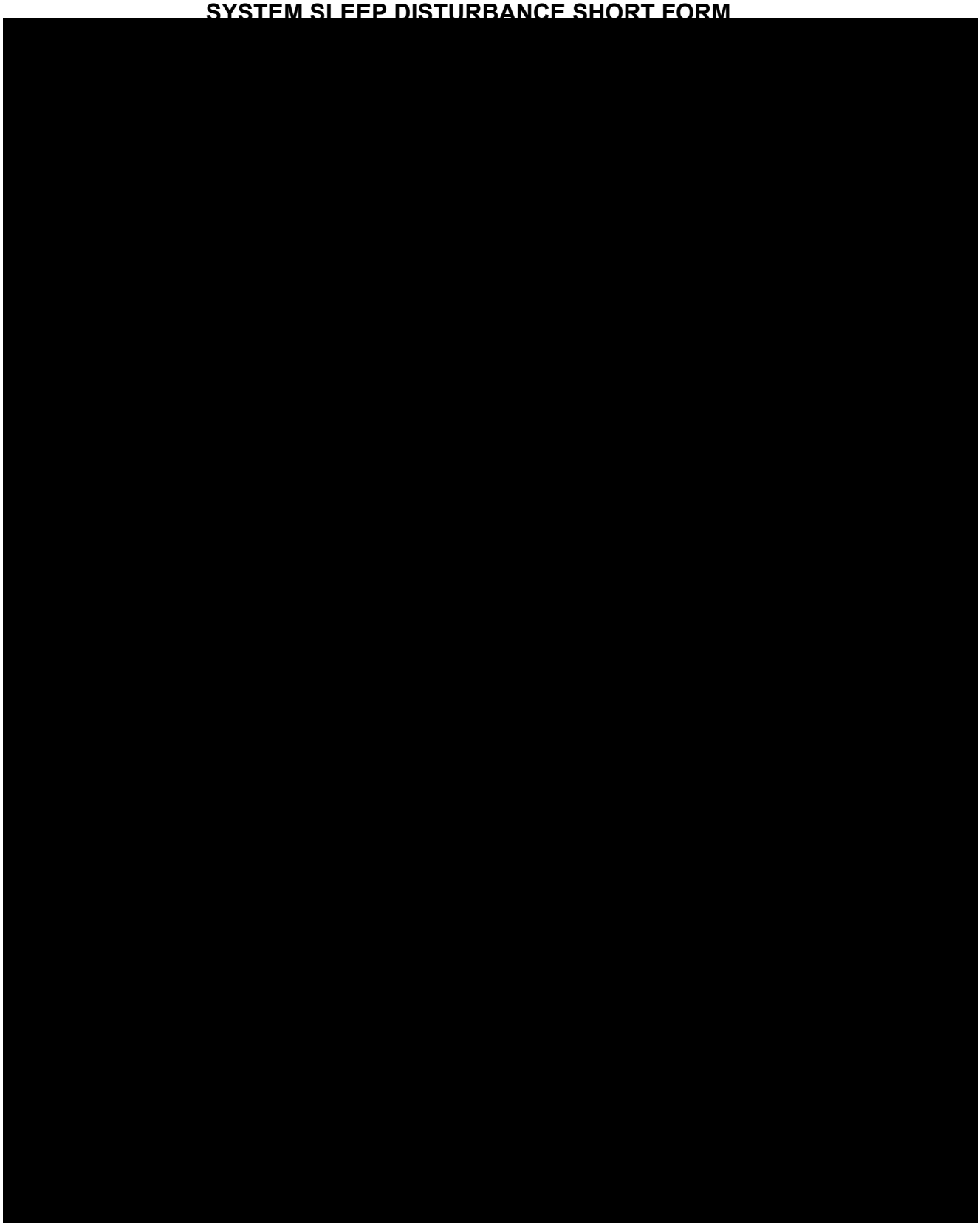
APPENDIX 13 EURO QUALITY OF LIFE FIVE DIMENSIONS QUESTIONNAIRE: 5-LEVEL VERSION (EQ-5D-5L)



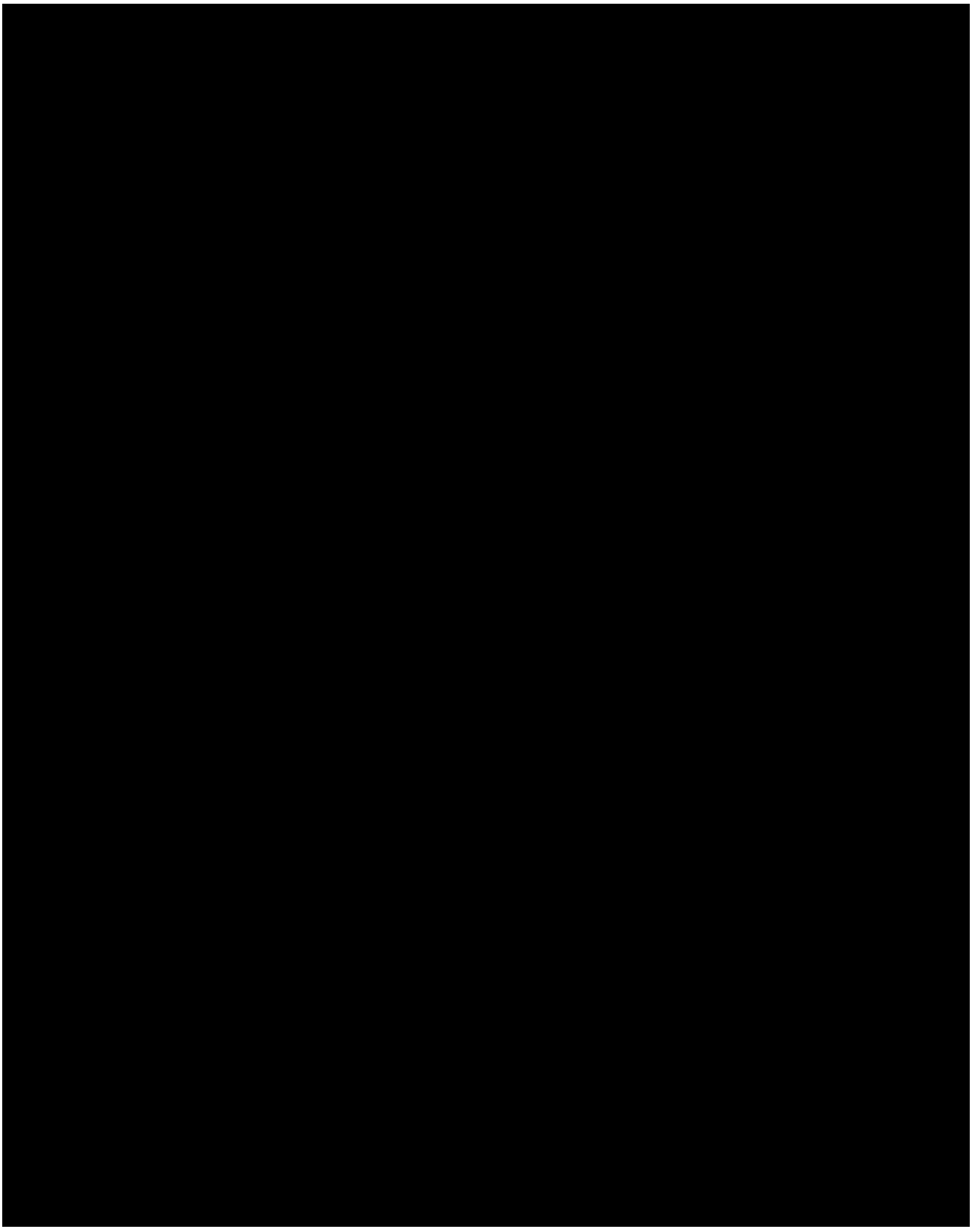


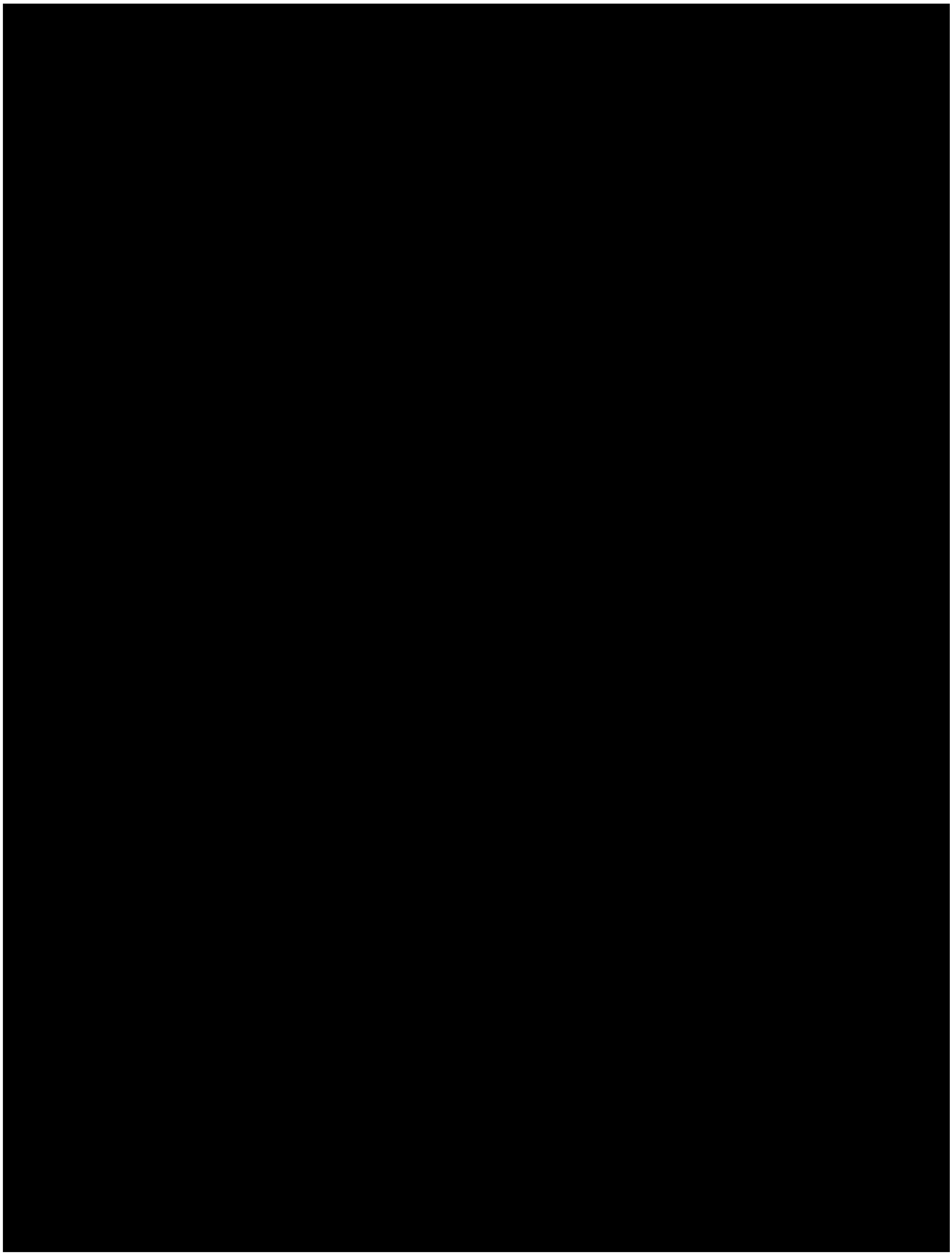


APPENDIX 14 PATIENT-REPORTED OUTCOME MEASURES INFORMATION SYSTEM SLEEP DISTURBANCE SHORT FORM

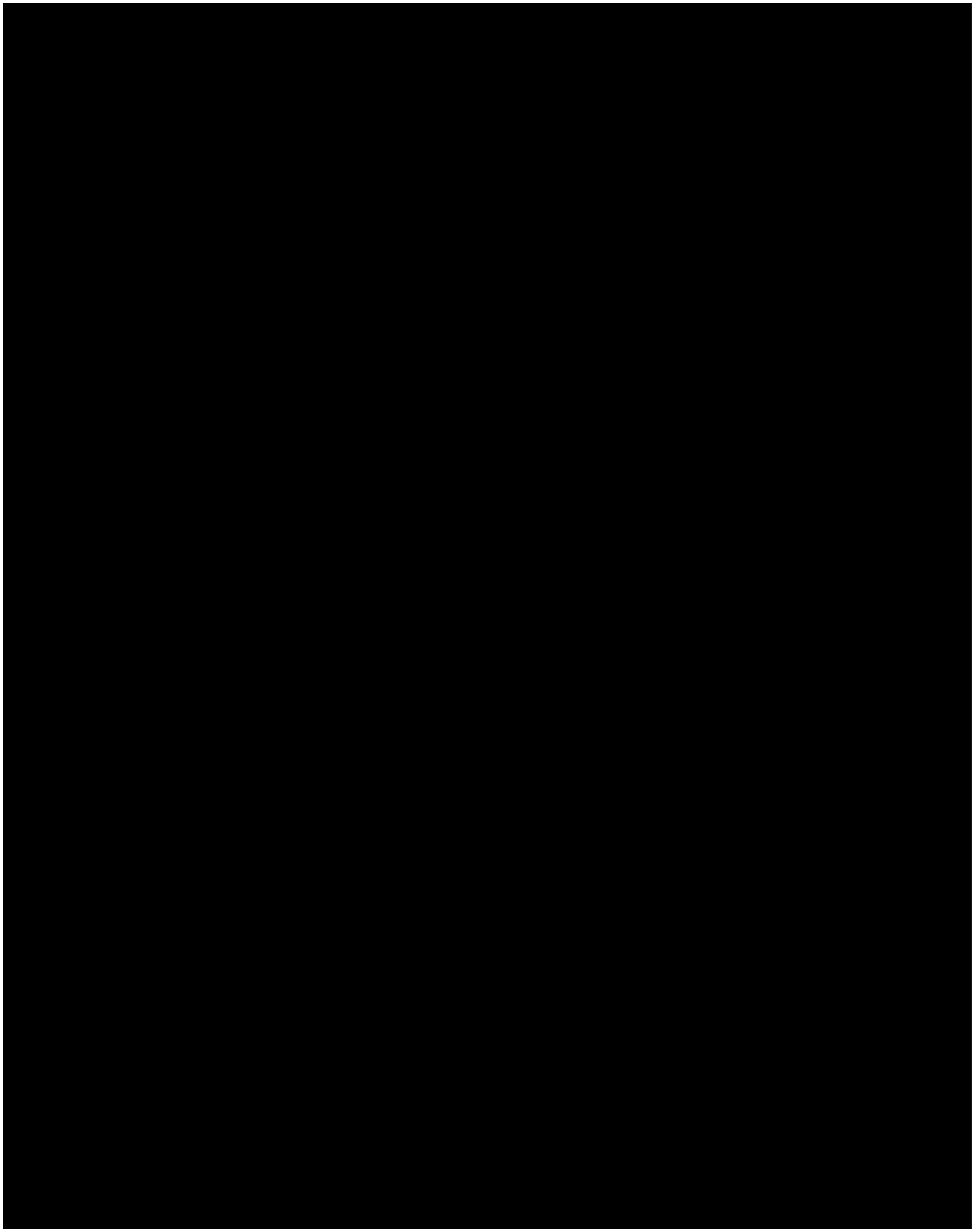


APPENDIX 15 WORK PRODUCTIVITY AND ACTIVITY IMPAIRMENT QUESTIONNAIRE: PSORIATIC ARTHRITIS (WPAI:PSA)





APPENDIX 16 THE BATH ANKYLOSING SPONDYLITIS DISEASE ACTIVITY INDEX (BASDAI)



APPENDIX 17 PHYSICIAN'S GLOBAL ASSESSMENT OF PSORIATIC ARTHRITIS

How would you rate global skin and musculoskeletal disease in this patient?

APPENDIX 18 PSORIASIS AREA AND SEVERITY INDEX (PASI)

[redacted]

APPENDIX 19 STATIC PHYSICIAN'S GLOBAL ASSESSMENT OF PSORIASIS (SPGA)

The static Physician's Global Assessment (sPGA) is used to determine the participant's psoriasis lesions overall at a given time point. Overall lesions will be graded for erythema, induration, and scaling based on the scales below. The average of the 3 scales, which is rounded to the nearest whole number, is the final sPGA score.

Characteristics	Score	Rating Score
Erythema (E) (averaged over the whole body)		0 = No evidence of erythema, but post inflammatory hyper/hypopigmentation changes may be present 1 = Faint erythema 2 = Light red coloration 3 = Moderate red coloration 4 = Bright red coloration
Induration (I) (averaged over the whole body)		0 = No evidence of plaque elevation 1 = Minimal plaque elevation, barely palpable, = 0.25 mm 2 = Mild plaque elevation, slight but definite elevation, indistinct edge, = 0.5 mm 3 = Moderate plaque elevation, elevated with distinct edges, = 0.75 mm 4 = Severe plaque elevation, hard/sharp borders, ≥1 mm
Scaling (S) (averaged over the whole body)		0 = No evidence of scaling 1 = Minimal; occasional fine scaling 2 = Mild; fine scale dominates 3 = Moderate; coarse scale predominates 4 = Severe; thick scale predominates

E + I + S = / 3 = (Total Average)

sPGA based upon above total average

0 = Clear, except for residual discoloration
1 = Almost clear -majority of lesions have individual scores for E + I + S / 3 that averages 1
2 = Mild -majority of lesions have individual scores for E + I + S / 3 that averages 2
3 = Moderate -majority of lesions have individual scores for E + I + S / 3 that averages 3
4 = Severe -majority of lesions have individual scores for E + I + S / 3 that averages 4

Note: Scores should be rounded to the nearest whole number. If total ≤1.49, score = 1; if total ≥1.50, score = 2.

APPENDIX 20 PHYSICIAN'S GLOBAL ASSESSMENT OF FINGERNAILS (PGA-F SCORING)

Instructions:

- Subject's fingernails need to be globally assessed separately for nail bed signs and nail matrix signs of disease, following the criteria specified below. A global score between '0' (clear) and '4' (severe) should be separately assigned for nail bed involvement and nail matrix involvement. A subject's overall global score is the worse of the nail bed score and nail matrix score. For example, if a subject has a nail bed score of '2' and a nail matrix score of '4,' this subject's overall score is '4.'
- If a subject has signs of nail bed (or nail matrix) disease intermediate between two grades, then the subject's nail bed (or nail matrix score) should be assigned the higher of the two grades. For example, if a subject's nail bed hyperkeratosis is considered to be worse than 'mild' but less than 'moderate', and all other nail bed signs are mild or less, the subject's nail bed score should be considered 'moderate.'
- Please record your patient's degree of Nail Bed Signs by selecting the appropriate descriptor in the Nail Bed Signs column below.
  -AND-
  Please record your patient's degree of Nail Matrix Signs by selecting the appropriate descriptor in the Nail Matrix Signs column below.

	Nail Bed Signs	Nail Matrix Signs[a,b]
Clear (0)	☐ Onycholysis: consistent with a normal nail AND Hyperkeratosis: none, AND Splinter hemorrhages: consistent with non-psoriatic splinter hemorrhages, AND No evidence of nail bed erythema	☐ No non-psoriatic nail plate irregularities including pitting, crumbling, Beau's lines, senile onychorrhexis, and non-psoriatic leukonychia.
Minimal (1)	☐ Onycholysis: < 10% involvement on all nails, OR Hyperkeratosis: present with barely detectable elevation of nail plate, OR Faint nail bed erythema, AND Splinter hemorrhages: consistent with non-psoriatic splinter hemorrhages	☐ No more than 5 pits or psoriatic leukonychia on any nail, AND No crumbling
Mild (2)	☐ Onycholysis: > 10% involvement on five or more nails, OR Hyperkeratosis: present with mild elevation of nail plate, OR Splinter hemorrhages: present on four or less nails, OR Mild nail bed erythema	☐ Five or more nails with mild pitting (e.g., > 10 pits) or psoriatic leukonychia, AND No crumbling

	Nail Bed Signs	Nail Matrix Signs[a,b]
Moderate (3)	☐ Onycholysis: > 30% involvement on at least one nail, OR Hyperkeratosis: present with at least moderate elevation of nail plate, OR Splinter hemorrhage: scattered and present on five or more nails, OR Moderate nail bed erythema	☐ Five or more nails with moderate pitting (e.g., > 25 pits/nail) or psoriatic leukonychia, AND ≤ 25% crumbling on all nails
Severe (4)	☐ Onycholysis: > 50% involvement on at least one nail, OR Hyperkeratosis: present with severe elevation of nail plate, OR Splinter hemorrhages: numerous and present on five or more nails, OR Severe nail bed erythema	☐ Five or more nails with severe pitting (e.g., > 50 pits/nail) or psoriatic leukonychia, OR > 25% crumbling on any nail

Evidence of psoriatic leukonychia should be counted toward the presence of pits. Confluent pits causing marked indentation of the nail plate should be considered crumbling.
Extent of crumbling defined by % of nail plate surface area missing or abnormal due to crumbling.

APPENDIX 21 DISEASE ACTIVITY SCORE 28 WITH C-REACTIVE PROTEIN

DAS28 CRP form

Patient name ..... Date of Birth ____ - ____ - ____

Observer name ..... Date ____ - ____ - ____

		Left		**Right**	
		Swollen	Tender	Swollen	Tender
Shoulder					
Elbow					
Wrist					
MCP	1				
	2				
	3				
	4				
	5				
PIP	1				
	2				
	3				
	4				
	5				
Knee					
Subtotal					
Total		Swollen		Tender	

How active was your arthritis during the past week?
(Please mark the degree of activity on the scale below by placing a vertical line |)

Not active at all ——————————————— **Extremely active**

Swollen Joint Count (0-28)	
Tender Joint Count (0-28)	
CRP	
VAS disease activity (0-100mm)	

DAS28-CRP = 0.56*√(TJC28) + 0.28*√(SJC28) + 0.36*ln(CRP+1) + 0.014*VAS + 0.96

For free calculator visit www.das28.nl

Interpretation of the results:
High disease activity >5.1, low disease activity ≤3.2, remission ≤2.6

DAS-28 © Pet Van Riel, 1995.
DAS-28_CRP_AU1.2_eng.GBori

APPENDIX 22 INTERPRETATION OF HEPATITIS B SEROLOGIC TEST RESULTS

HEPATITIS C VIRUS

Testing for hepatitis C virus (HCV) is a 2-step process: (i) anti-HCV antibody and (ii) HCV ribonucleic acid (RNA).

Participants with a negative anti-HCV antibody may be eligible for the study.

Participants with a positive or indeterminate anti-HCV antibody require additional HCV RNA testing to determine eligibility. Participants with negative or undetectable HCV RNA may be eligible for the study. Participants with positive or detectable HCV RNA have HCV infection, are excluded from the study, and should be referred for appropriate assessment and consideration for treatment.

Participants who were previously treated with an approved treatment regimen for HCV infection may be eligible to participate in the study provided they achieve a Week 24 sustained virologic response; that is, negative or undetectable HCV RNA 24 weeks after completion of a full course of an approved treatment regimen for HCV infection. Such participants must be discussed with the Medical Monitor prior to screening.

HEPATITS B SEROLOGIC TEST RESULTS

As study treatment in this study is expected to demonstrate immunosuppressive effects, it is imperative to carefully evaluate and exclude participants with potentially active hepatitis B infection. For this reason, in order to fully evaluate a participant's eligibility for enrollment, the exclusion criterion (see Section 6.2) requires interpretation of data from 3 standard tests for hepatitis B (ie, measurement of hepatitis B surface antigen [HBsAg], hepatitis B core antibody [HBcAb], and hepatitis B surface antibody [HBsAb]).

Participants' eligibility for enrollment should be assessed as described below. Participants who are:

Hepatitis B serological test negative (neg) for all results may be included in the study

HBsAg (neg), HBcAb (neg), and HBsAb positive (POS) may be included in the study (immunized due to hepatitis B vaccination)

HBsAg (neg), HBcAb (POS), and HBsAb (POS) are to be excluded from the study (immune due to natural infection exposure)

HBsAg (POS) are excluded from the study (acute or chronic infection)

HBcAb (POS) are excluded from the study (acute or chronic infection)

HBsAg (neg), HBcAb (POS), and HBsAb (neg) are to be excluded from the study (interpretation unclear)

Please refer to the below "Interpretation of Hepatitis B Serologic Test Results" provided by the Department of Health and Human Services, Centers for Disease Control and Prevention.

Interpretation of Hepatitis B Serologic Test Results

Hepatitis B serologic testing involves measurement of several hepatitis B virus (HBV)-specific antigens and antibodies. Different serologic "markers" or combinations of markers are used to identify different phases of HBV infection and to determine whether a patient has acute or chronic HBV infection, is immune to HBV as a result of prior infection or vaccination, or is susceptible to infection.

HBsAg **anti-HBc** **anti-HBs**	negative negative negative	Susceptible
HBsAg **anti-HBc** **anti-HBs**	negative positive positive	Immune due to natural infection
HBsAg **anti-HBc** **anti-HBs**	negative negative positive	Immune due to hepatitis B vaccination
HBsAg **anti-HBc** **IgM anti-HBc** **anti-HBs**	positive positive positive negative	Acutely infected
HBsAg **anti-HBc** **IgM anti-HBc** **anti-HBs**	positive positive negative negative	Chronically infected
HBsAg **anti-HBc** **anti-HBs**	negative positive negative	Interpretation unclear; four possibilities: 1. Resolved infection (most common) 2. False-positive anti-HBc, thus susceptible 3. "Low level" chronic infection 4. Resolving acute infection

Adapted from: A Comprehensive Immunization Strategy to Eliminate Transmission of Hepatitis B Virus Infection in the United States: Recommendations of the Advisory Committee on Immunization Practices. Part I: Immunization of Infants, Children, and Adolescents. MMWR 2005;54(No. RR-16).

DEPARTMENT OF HEALTH & HUMAN SERVICES
Centers for Disease Control and Prevention
Division of Viral Hepatitis

www.cdc.gov/hepatitis

- **Hepatitis B surface antigen (HBsAg):** A protein on the surface of hepatitis B virus; it can be detected in high levels in serum during acute or chronic hepatitis B virus infection. The presence of HBsAg indicates that the person is infectious. The body normally produces antibodies to HBsAg as part of the normal immune response to infection. HBsAg is the antigen used to make hepatitis B vaccine.
- **Hepatitis B surface antibody (anti-HBs):** The presence of anti-HBs is generally interpreted as indicating recovery and immunity from hepatitis B virus infection. Anti-HBs also develops in a person who has been successfully vaccinated against hepatitis B.
- **Total hepatitis B core antibody (anti-HBc):** Appears at the onset of symptoms in acute hepatitis B and persists for life. The presence of anti-HBc indicates previous or ongoing infection with hepatitis B virus in an undefined time frame.
- **IgM antibody to hepatitis B core antigen (IgM anti-HBc):** Positivity indicates recent infection with hepatitis B virus (≤6 mos). Its presence indicates acute infection.

FOR JAPAN AND SELECTED COUNTRIES

Participants with a positive HBcAb and/or HBsAb and a negative HBsAg may be eligible for the study. HBV deoxyribonucleic acid (DNA) testing will be performed in participants with a negative HBsAg, but a positive HBcAb and/or HBsAb at screening. Participants with detectable HBV DNA levels, which are defined as per the local guidelines at screening, are excluded. Participants in this subgroup (with a negative HBsAg, but a positive HBcAb and/or HBsAb) will be allowed to be randomized if HBV DNA levels, which are defined as per the local guidelines, are undetectable on this assay during screening. These participants will have follow-up HBV DNA testing and review of liver chemistries throughout their participation in the study.

During the study, participants in this subgroup will have HBV DNA tested every 4 weeks, up to and including the Week 32 visit and every 4 to 8 weeks thereafter at the discretion of the investigator. [redacted]

If participants in this subgroup have detectable HBV DNA levels, which are defined as per the local guidelines at any time, they must permanently discontinue study treatment; the investigator should consider referring them for appropriate specialty care and follow-up. Participants should continue in the study as described in Section 8.1.

APPENDIX 23 MULTI-DRUG RESISTANT TUBERCULOSIS HIGH-BURDEN COUNTRIES

- Angola
- Bangladesh
- Brazil
- China
- Democratic Peoples Republic of Korea
- Democratic Republic of Congo
- Ethiopia
- India
- Indonesia
- Kenya
- Mozambique
- Myanmar
- Nigeria
- Pakistan
- Philippines
- Russian Federation
- South Africa
- Thailand
- Tanzania, United Republic of
- Viet Nam
- Cambodia
- Central African Republic
- Congo
- Lesotho
- Liberia
- Namibia
- Papua New Guinea
- Sierra Leone
- Zambia
- Zimbabwe

World Health Organization. Stop TB Partnership; high burden countries. UNOPS 2021 [accessed 2021 Feb 23]. Available from: http://www.stoptb.org/countries/tbdata.asp.

APPENDIX 24 COMMONLY USED CORTICOSTEROID EQUIVALENTS

Medication	Dose Equivalent
Prednisone	20 mg
Cortisone	100 mg
Hydrocortisone	80 mg
Prednisolone	20 mg
Methylprednisolone	16 mg
Triamcinolone	16 mg
Budesonide	4 mg
Dexamethasone	3 mg
Betamethasone	2.4 mg
Deflazacort	26 mg

APPENDIX 25 AMERICAN COLLEGE OF RHEUMATOLOGY CORE DATASET AND RESPONSE DEFINITIONS

• **American College of Rheumatology (ACR) Core Data Set Component**	• **Validated Measurement Tool**
• Tender joint count	• Standardized 68 joint count
• Swollen joint count	• Standardized 66 joint count
• Subject global assessment of pain	• A 0-100 mm visual analog scale
• Subject global assessment of disease	• A 0-100 mm visual analog scale
• Physician global assessment of psoriatic arthritis	• A 0-100 mm visual analog scale
• Subject assessment of physical function	• Health Assessment
• Acute phase reactant value	• ESR (Westergren) and C-

The ACR 20, ACR 50, or ACR 70 definition of improvement is a 20%, 50%, or 70% improvement, respectively, over baseline in tender and swollen joint counts (#1 and #2) and a 20%, 50%, or 70% improvement, respectively, in 3 of the 5 remaining core data set measures (components #3 to #7).

APPENDIX 26 PROTOCOL AMENDMENT SUMMARY OF CHANGE HISTORY

Overall Rationale for Protocol Amendment 01, 20-Mar-2022

[redacted]

SUMMARY OF KEY CHANGES FOR PROTOCOL AMENDMENT 01		
Section Number & Title	**Description of Change**	**Brief Rationale**
Title Page	Updated contact information.	Updated due to administrative changes.
Section 1: Synopsis	Updated section with applicable changes made as described below throughout the body.	Updated for consistency across the protocol.
Table 2-1: Screening Procedural Outline (IM011054)	• Added body weight to height row. • Updated adverse event (AE) and serious adverse event (SAE) assessment note.	• Added for creatinine clearance calculation. • To clarify collection, reporting, and follow-up of all AEs and SAEs, and severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2)-related AEs and SAEs.
Table 2-2: Procedural Outline: Baseline through Week 16 (IM011054)	• Updated AE and SAE assessment note. • Added footnote "b" to refer to Section 9.4.9 for unscheduled visits.	• To clarify collection, reporting, and follow-up of all AEs and SAEs, and severe acute respiratory syndrome coronavirus 2 (SARS CoV 2)-related AEs and SAEs. • To note that unscheduled visit study procedures should be based on the clinical judgment of the investigator.
Table 2-3: Procedural Outline: Week 20 through Week 56 (IM011054)	• Added that Week 56 Visit is 30 days after last dose. • Added to the Pregnancy Test notes that telephone visits will be	• To clarify when visit will be performed. • At-home pregnancy test kits will be

SUMMARY OF KEY CHANGES FOR PROTOCOL AMENDMENT 01		
Section Number & Title	**Description of Change**	**Brief Rationale**
	performed to obtain monthly pregnancy test results. • Updated AE and SAE assessment note. [redacted]	provided to maintain monthly pregnancy testing between visits. • To clarify collection, reporting, and follow-up of all AEs and SAEs, and severe acute respiratory syndrome coronavirus 2 (SARS CoV 2)-related AEs and SAEs. [redacted]
	• Updated footnote "b" to say that participants who discontinue from study treatment and request to discontinue from the study will be asked to complete an Early Termination (ET) Visit and a Safety Follow-up Visit 30 days following last dose of study treatment. • Updated footnote "c" regarding participants who complete [redacted] will have a Safety Follow-up Visit 30 days following the last dose. • Added footnote "d" that all participants must be evaluated for safety 30 days following last dose of IP.	• A participant will be asked to complete an ET Visit and a Safety Follow-up Visit 30 days following last dose. • A participant who completes [redacted] will have a Safety Follow-up Visit 30 days following the last dose of study treatment. • All participants must be evaluated for safety 30 days following last

SUMMARY OF KEY CHANGES FOR PROTOCOL AMENDMENT 01		
Section Number & Title	**Description of Change**	**Brief Rationale**
	• Added footnote "e" to refer to Section 9.4.9 for unscheduled visits. • Added footnote "m" to state that at-home urine pregnancy test kits will be provided. • Added to footnote "n" that states for participants who discontinue study treatment and continue in the study until Week 52, [redacted].	dose of study treatment. • To note that unscheduled visit study procedures should be based on the clinical judgment of the investigator. • At-home pregnancy test kits will be provided to maintain monthly pregnancy testing between visits. [redacted]
[redacted]		
Section 3.1: Study Rationale Section 3.3: Benefit/Risk Assessment Table 4-1: Objectives and Endpoints	[redacted]	
Section 5.1: Overall Design Figure 5.1-1: Study Design Schematic	• Updated length of study. [redacted] • Added text regarding [redacted] discontinuation of study treatment. [redacted]	[redacted]

SUMMARY OF KEY CHANGES FOR PROTOCOL AMENDMENT 01		
Section Number & Title	**Description of Change**	**Brief Rationale**
Section 5.3: End of Study Definition	[redacted]	
Section 6.1: Inclusion Criteria	• Updated criterion 2) g) i) with names of conventional synthetic disease-modifying anti-rheumatic drugs (csDMARDs). • Updated criterion 3) a) viii) to include study completion or 30 days after discontinuation of the study treatment, whichever is longer.	• Criterion revised to clarify that failure or intolerance to one of the csDMARDs (methotrexate, sulfasalazine, leflunomide, hydroxychloroquine) listed will qualify a participant for the study. • Criterion revised to clarify time period for contraceptive requirements for participants completing all expected study visits on treatment versus participants who discontinue study treatment early but remain in the study for follow-up.
Section 6.1.1: Inclusion Criteria [redacted] Section 6.2.1: Exclusion Criteria [redacted]	Added sections for inclusion/exclusion criteria for participants entering the [redacted] Period.	Updated to include [redacted] Period.
Section 6.2: Exclusion Criteria	• Added that criterion 2) f) is no longer applicable. • Added new criterion 2) v) with added details clarifying that	Updated to provide examples of commonly prescribed medications that are excluded.

SUMMARY OF KEY CHANGES FOR PROTOCOL AMENDMENT 01		
Section Number & Title	**Description of Change**	**Brief Rationale**
	participants will be excluded if they have received systemic non-biologic medications and/or any immunosuppressant therapy for psoriasis (PsO) and/or psoriatic arthritis (PsA) other than what is permitted in the inclusion criteria within 28 days prior to Day 1. • Added new criterion 2) w) regarding use of traditional Chinese medicines.	
[redacted]		
Section 7.3: Blinding for the 52-week Treatment Period Section 7.3.2: Circumstances for Unblinding	[redacted]	

SUMMARY OF KEY CHANGES FOR PROTOCOL AMENDMENT 01		
Section Number & Title	**Description of Change**	**Brief Rationale**
Section 7.7.1: Permitted Treatments	[redacted]	
Section 7.7.2: SARS-CoV-2 Permitted Treatments	[redacted]	[redacted] therefore, the SARS-CoV-2 vaccination guidelines are aligned with key visits.
Section 7.7.3.1: Prohibited Treatments	• Updated that phototherapy, oral PsO medications, high-potency glucocorticoids, and use of strong CYP450 inducers are prohibited up to Week 52. • Clarified that oral vitamin D supplements are permitted.	Updated to clarify what is permitted for study participants and when.
[redacted]		

SUMMARY OF KEY CHANGES FOR PROTOCOL AMENDMENT 01		
Section Number & Title	**Description of Change**	**Brief Rationale**
[redacted]		
Section 8.1: Discontinuation from Study Treatment	Modified text regarding estimated glomerular filtration rate.	Criterion revised to provide Investigators and Medical Monitor the discretion to make a more informed decision and use clinical judgment to determine whether or not it is in the best interest of the participant to continue in the study while providing close oversight of the safety.
Section 8.1: Discontinuation from Study Treatment Section 8.1.2: Post Study Treatment Study Follow-up Section 8.2: Discontinuation from the Study	Updated information on participants who discontinue from study treatment during the Treatment Period [redacted].	[redacted]
Section 9.1.24: Imaging Assessment for the Study	[redacted]	

SUMMARY OF KEY CHANGES FOR PROTOCOL AMENDMENT 01		
Section Number & Title	**Description of Change**	**Brief Rationale**
		[redacted]
Section 9.2.2: Time Period and Frequency for Collecting AE and SAE Information	• Added language regarding collection of nonserious AEs. • Updated when SAEs and all AEs related to SARS-CoV-2 infection must be collected.	• Added to clarify time period nonserious AEs must be collected. • Updated to clarify they should be collected from the time of signing consent and within 30 days of discontinuation of dosing or participants' participation in the study if the last scheduled visit occurs at a later time.
Section 9.2.6: Pregnancy	Updated duration the investigator is required to notify the BMS Medical Monitor/designee of pregnancy.	To align with TYK2 program-wide safety guidance on the collection of pregnancy information.
Section 9.4.4: Clinical Safety Laboratory Assessments	Added instruction to refer to Appendix 4 for detailed information on the definitions of women of childbearing potential (WOCBP) and post-menopausal female.	Added to clarify follicle-stimulating hormone analysis and definitions of WOCBP and post-menopausal female.
[redacted]		
Section 9.4.9: Unscheduled Safety Visits	Added section for unscheduled safety visits.	To clarify that the protocol does not mandate specific investigations at unscheduled visits, and that study procedures at unscheduled visits should be based on the clinical judgment of the investigator.

SUMMARY OF KEY CHANGES FOR PROTOCOL AMENDMENT 01		
Section Number & Title	**Description of Change**	**Brief Rationale**
[redacted]		
[redacted]		
Section 10.3: Statistical Analyses	[redacted]	The planned submission activities rely only on safety and efficacy data collected through Week 52. Data that report the long-term safety profile and maintenance of efficacy after up to 3 years of exposure to active treatment [redacted].

SUMMARY OF KEY CHANGES FOR PROTOCOL AMENDMENT 01		
Section Number & Title	**Description of Change**	**Brief Rationale**
Appendix 2: Study Governance Considerations	[redacted]	
Appendix 6: Subject Assessment of Disease Activity (Psoriatic Arthritis) Visual Assessment Scale Appendix 7: Subject Assessment of Pain Scale (Psoriatic Arthritis) Appendix 8: American College of Rheumatology Subject Assessment of Physical Function Scale: Health Assessment Questionnaire (HAQ) Appendix 9: Short Form Health Survey-36 Item (SF-36) Appendix 10: Functional Assessment of Chronic Illness Therapy Fatigue Appendix 12: Dermatology Life Quality Index (DLQI) Appendix 15: Work Productivity and Activity Impairment Questionnaire: Psoriatic Arthritis (WPAI:PSA)	Updated participant-reported outcomes appendices.	Appendices have been modified to reflect the exact participant-facing text that the participant will see on the electronic Clinical Outcomes Assessment device.
Appendix 22: Interpretation of	[redacted]	

SUMMARY OF KEY CHANGES FOR PROTOCOL AMENDMENT 01		
Section Number & Title	**Description of Change**	**Brief Rationale**
Hepatitis B Serologic Test Results	[redacted]	
All	Minor formatting and typographical corrections.	Minor, therefore have not been summarized.