Official Title: **A Phase 2, Randomized, Double-Blind, Placebo-Controlled, Dose Ranging Study of the Efficacy and Safety of INCB054707 Followed by an Extension Period in Participants With Vitiligo**

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Clinical Study Protocol

INCB 54707-205

A Phase 2, Randomized, Double-Blind, Placebo-Controlled, Dose-Ranging Study of the Efficacy and Safety of INCB054707 Followed by an Extension Period in Participants With Vitiligo

Product:	**INCB054707**
IND Number:	[redacted]
Phase of Study:	**2**
Sponsor:	**Incyte Corporation** **1801 Augustine Cut-Off** **Wilmington, Delaware, USA 19803**
Original Protocol:	**16 NOV 2020**
Amendment 1:	**19 AUG 2021**
Amendment 2:	**09 FEB 2022**
Amendment 3:	**19 MAY 2022**
Amendment 4:	**12 JUL 2022**

INVESTIGATOR'S AGREEMENT

I have read the INCB 54707-205 Protocol Amendment 4 (dated 12 JUL 2022) and agree to conduct the study as outlined. I agree to maintain the confidentiality of all information received or developed in connection with this Protocol.

_____

(Printed Name of Investigator)

_____ _____

(Signature of Investigator) (Date)

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LIST OF ABBREVIATIONS

Abbreviations and Special Terms	Definition
AE	adverse event
ALP	alkaline phosphatase
ALT	alanine transaminase
ANC	absolute neutrophil count
anti-HBc	antibody to hepatitis B core antigen
AST	aspartate transaminase
BSA	body surface area
CFR	Code of Federal Regulations
[redacted]	
COVID-19	coronavirus disease 2019
CSR	Clinical Study Report
CTCAE	Common Terminology Criteria for Adverse Events
CYP	cytochrome P450
[redacted]	
DNA	deoxyribonucleic acid
DSMB	Data Safety Monitoring Board
ECG	electrocardiogram
eCRF	electronic case report form
EDC	electronic data capture
[redacted]	
EOS	end of study
EOT	end of treatment
EOT1	end of treatment during the placebo-controlled period
EOT2	end of treatment during the extension period
[redacted]	[redacted]
[redacted]	[redacted]
F-BSA	facial body surface area
FDA	Food and Drug Administration
[redacted]	[redacted]
FSH	follicle-stimulating hormone

Abbreviations and Special Terms	Definition
[redacted]	
F-VASI	Facial Vitiligo Area Scoring Index
[redacted]	
GCP	Good Clinical Practice
GDPR	General Data Protection Regulation
GGT	gamma-glutamyl transferase
[redacted]	
HBcAb	hepatitis B core antibody
HBsAb	hepatitis B surface antibody
HBsAg	hepatitis B surface antigen
HBV	hepatitis B virus
HCV	hepatitis C virus
HCVAb	hepatitis C virus antibody
HDL	high-density lipoprotein
HIPAA	Health Insurance Portability and Accountability Act
HIV	human immunodeficiency virus
HS	hidradenitis suppurativa
hsCRP	high-sensitivity C-reactive protein
IB	Investigator's Brochure
ICF	informed consent form
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
IEC	independent ethics committee
IFN	interferon
INR	international normalized ratio
IRB	institutional review board
IRT	interactive response technology
ITT	intent-to-treat
JAK	Janus kinase
LDL	low-density lipoprotein
MedDRA	Medical Dictionary for Regulatory Activities
MMRM	mixed-effect model for repeated measures
OTC	over-the-counter
[redacted]	
PDE-4	phosphodiesterase-4

Abbreviations and Special Terms	Definition
[redacted]	
PPD	purified protein derivative
PT	prothrombin time
QALY	quality-adjusted life year
QD	once daily
QFT-GIT	QuantiFERON®-TB Gold In-Tube test
RDW	red blood cell distribution width
RNA	ribonucleic acid
RSI	Reference Safety Information
SAE	serious adverse event
SAP	Statistical Analysis Plan
[redacted]	
SoA	schedule(s) of activities
SOP	standard operating procedure
STAT	signal transducer and activator of transcription
[redacted]	
T_4	thyroxine
TB	tuberculosis
T-BSA	total body surface area
TEAE	treatment-emergent adverse event
[redacted]	
TSH	thyroid-stimulating hormone
[redacted]	
T-VASI	Total Body Vitiligo Area Scoring Index
T-VASI50[redacted]	≥ 50%[redacted] improvement in total body Vitiligo Area Scoring Index
TYK	tyrosine kinase
ULN	upper limit of normal
UV	ultraviolet
VASI	Vitiligo Area Scoring Index
[redacted]	
WBC	white blood cell

Abbreviations and Special Terms	Definition
[redacted]	
WOCBP	women of childbearing potential
WONCBP	women of nonchildbearing potential

1. PROTOCOL SUMMARY

Protocol Title: A Phase 2, Randomized, Double-Blind, Placebo-Controlled, Dose-Ranging Study of the Efficacy and Safety of INCB054707 Followed by an Extension Period in Participants With Vitiligo

Protocol Number: INCB 54707-205

Objectives and Endpoints:

Table 1 presents the primary and key secondary objectives and endpoints.

Table 1: Primary and Secondary Objectives and Endpoints

Objectives	Endpoints
Primary	
To determine the efficacy of INCB054707.	Percent change from baseline in Total Vitiligo Area Scoring Index (T-VASI) at Week 24.
Key Secondary	
To further determine the efficacy of INCB054707.	Proportion of participants achieving T-VASI50 at Week 24. T-VASI50 is defined as 50% or greater reduction in the Total Vitiligo Area Scoring Index.

Overall Design:

Table 2 presents the key study design elements. Further study details are presented after the table.

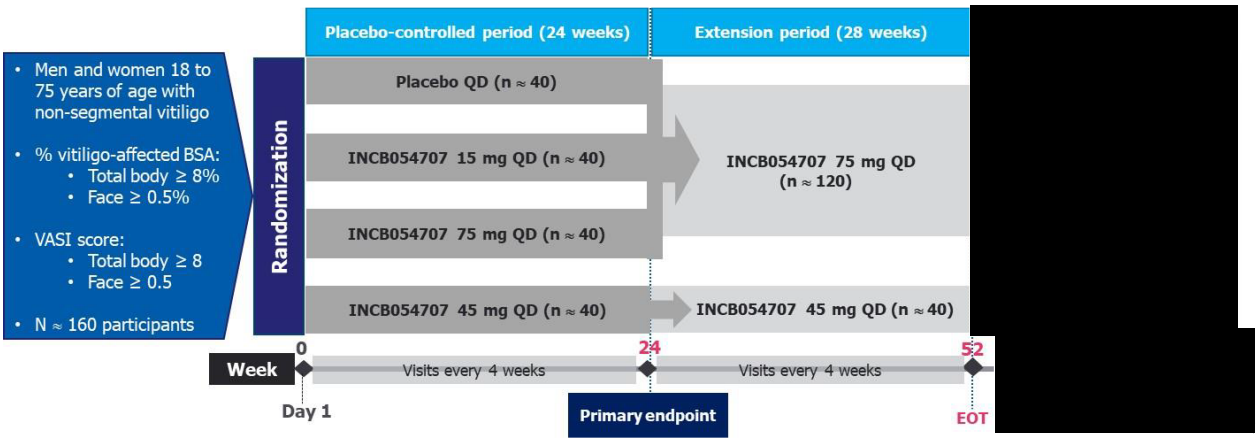
Table 2: Key Study Design Elements

Study Phase	Phase 2
Clinical Indication	Treatment of adult patients with vitiligo.
Population	Men or women aged 18 to 75 years with nonsegmental vitiligo who have depigmented areas including T-BSA ≥ 8%, T-VASI ≥ 8, F-BSA ≥ 0.5%, and F-VASI ≥ 0.5.
Number of Participants	Approximately 160 participants will be randomized 1:1:1:1 to receive 1 of 3 doses of INCB054707 or placebo. The 28-week double-blind extension period will include all participants who successfully complete the placebo-controlled period.
Study Design	This is a Phase 2, randomized, double-blind, placebo-controlled, dose-ranging, multicenter study to evaluate the efficacy and safety of INCB054707 (15, 45, and 75 mg QD) over a 24-week treatment period, followed by a 28-week double-blind extension period (45 mg and 75 mg QD) and a 24-week follow-up period. Participants will be stratified based on total BSA involvement (8%-20% and > 20%).
Estimated Duration of Study Participation	Screening: Up to 32 days Placebo-controlled period (double-blind): 24 weeks Extension period (double-blind): 28 weeks Safety follow-up: 4 weeks after last dose of study drug [redacted] Total: Up to approximately 80 weeks (19 months)
DSMB	Yes (external)
Coordinating Principal Investigator	[redacted], MD

Treatment Groups and Duration:

The study design is shown in Figure 1. The SoA for the placebo-controlled and extension periods are detailed in Table 3 and Table 4, respectively.

Figure 1: Study Design Schema



Participants will be screened for up to 32 days prior to the first dose of INCB054707 on Day 1. Stratification will be based on total BSA involvement, with 2 strata: 8% to 20% and > 20%.

Approximately 160 participants will take oral INCB054707 (15 mg, 45 mg, or 75 mg) or placebo QD in a blinded manner for 24 weeks. Following completion of the Week 24 visit, participants will enter the 28-week double-blind extension period with 45 mg QD (for participants who received 45 mg during the placebo-controlled period) or 75 mg (for participants who received placebo, 15 mg, or 75 mg during the placebo-controlled period), with a safety follow-up visit scheduled 4 weeks after the last dose of study drug, [redacted]

Efficacy will be assessed via changes in the [redacted], T-VASI [redacted] photography, [redacted]

Participants will be assessed for safety and tolerability by monitoring the frequency and severity of AEs and performing physical examinations, ECGs, vital signs measurements, and clinical laboratory assessments at various timepoints during the study.

[redacted]

The COVID-19 global pandemic may present challenges to the normal conduct of this study, requiring the outline of potential mitigation strategies described in Appendix E.

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

Table 3: Schedule of Activities (Placebo-Controlled Period)

Visit Day (Range)	Screening	Treatment (Placebo-Controlled Period)									Notes
	Days −32 to −1	Baseline (Day 1)	Wk 2 (± 3 d) (Remote Visit)	Wk 4 (± 3 d)	Wk 6 (± 3 d) (Remote Visit)	Wk 8 (± 3 d)	Wk 12 (± 3 d)	Wk 16 (± 3 d)	Wk 20 (± 3 d)	Wk 24 (± 3 d) (EOT1)	Remote visits may be performed in-clinic at the discretion of the investigator.
Administrative procedures											
Informed consent	X										Section 8.1.1
Inclusion/exclusion criteria	X	X									Section 5.1 and Section 5.2
Demographic data, general medical history, and vitiligo medical and treatment history	X										Section 8.1.5
Prior/concomitant medications	X	X	X	X	X	X	X	X	X	X	Section 6.6 and Section 8.1.5
Contact IRT	X	X		X		X	X	X	X	X	Section 8.1.3
Randomization		X									Section 6.3 and Section 8.1.3
Distribute reminder cards and diaries	X	X		X		X	X	X	X	X	Section 8.1.4
Dispense study drug		X		X		X	X	X	X	X	Section 6.2
Collect study drug and review diary cards				X		X	X	X	X	X	Section 8.1.4
Assess study drug compliance				X		X	X	X	X	X	Section 6.4
Safety assessments											
AE assessments	X	X	X	X	X	X	X	X	X	X	Section 8.3.1
Comprehensive physical examination	X	X								X	Section 8.3.2
Height	X										Section 8.3.2
Weight	X	X								X	Section 8.3.2
Targeted physical examination				X		X	X	X	X		Section 8.3.2
Vital signs	X	X		X		X	X	X	X	X	Section 8.3.3
12-lead ECG	X									X	Section 8.3.4
Efficacy assessments											
[redacted]											

Table 3: Schedule of Activities (Placebo-Controlled Period) (Continued)

Visit Day (Range)	Screening Days −32 to −1	Treatment (Placebo-Controlled Period) Baseline (Day 1)	Wk 2 (± 3 d) (Remote Visit)	Wk 4 (± 3 d)	Wk 6 (± 3 d) (Remote Visit)	Wk 8 (± 3 d)	Wk 12 (± 3 d)	Wk 16 (± 3 d)	Wk 20 (± 3 d)	Wk 24 (± 3 d) (EOT1)	Notes Remote visits may be performed in-clinic at the discretion of the investigator.
Efficacy assessments (continued)											
[redacted]											
T-VASI	X	X		X		X	X	X	X	X	Section 8.2.2
[redacted]											
Photography of the face	X	X					X			X	If photo quality at screening is not adequate, the photography may be repeated at Day 1. The baseline photo is defined as the most adequate one either taken at screening or Day 1. (Section 8.2.6)
Photography of nonfacial targeted areas	X	X					X			X	The genitalia area should not be photographed. If photo quality at screening is not adequate, the photography may be repeated at Day 1. The baseline photo is defined as the most adequate one either taken at screening or Day 1. (Section 8.2.6)
[redacted]											

Table 3: Schedule of Activities (Placebo-Controlled Period) (Continued)

Visit Day (Range)	Screening Days −32 to −1	Treatment (Placebo-Controlled Period) Baseline (Day 1)	Wk 2 (± 3 d) (Remote Visit)	Wk 4 (± 3 d)	Wk 6 (± 3 d) (Remote Visit)	Wk 8 (± 3 d)	Wk 12 (± 3 d)	Wk 16 (± 3 d)	Wk 20 (± 3 d)	Wk 24 (± 3 d) (EOT1)	Notes Remote visits may be performed in-clinic at the discretion of the investigator.
[redacted]											
Laboratory assessments											
Serum FSH (WONCBP only)	X										Section 8.3.5.1 and Table 13
Serum pregnancy test (WOCBP)	X									X	Section 8.3.5.1 and Table 13
Urine pregnancy test (WOCBP)		X		X		X	X	X	X		Section 8.3.5.1 and Table 13
TB screening	X										Chest x-ray may be required for some participants. Section 8.3.5.3 and Table 13
HIV testing	X										Section 8.3.5.2 and Table 13
Hepatitis testing	X										Section 8.3.5.2 and Table 13
Urinalysis	X						X			X	Table 13
Hematology and blood chemistry assessments	X	X	X	X	X	X	X	X	X	X	Table 13; at-home blood collection for remote visits
Coagulation	X										Reflexive testing during the study per Appendix D (also Table 13).
Lipid panel		X					X			X	Table 13
Thyroid function markers	X						X			X	Table 13
Inflammation marker		X					X			X	Table 13
[redacted]											

Table 4: Schedule of Activities (Extension Period)

Visit Day (Range)	Treatment (Extension Period)									Safety Follow-Up	[redacted]	Notes
	Wk 26 (± 3 d) (Remote Visit)	Wk 28 (± 3 d)	Wk 30 (± 3 d) (Remote Visit)	Wk 32 (± 3 d)	Wk 36 (± 3 d)	Wk 40 (± 3 d)	Wk 44 (± 3 d)	Wk 48 (± 3 d)	Wk 52 (± 3 d) (EOT2)	Wk 56 (4 wks post last dose + 7 d) (EOS)		Remote visits may be performed in-clinic at the discretion of the investigator.
Administrative procedures												
Concomitant medications	X	X	X	X	X	X	X	X	X	X		Section 6.6 and Section 8.1.5
Contact IRT		X		X	X	X	X	X	X			Section 8.1.3
Distribute reminder cards and diaries		X		X	X	X	X	X	X			Section 8.1.4
Dispense study drug		X		X	X	X	X	X				Section 6.2
Collect study drug and review diary cards		X		X	X	X	X	X	X			Section 8.1.4
Assess study drug compliance		X		X	X	X	X	X	X			Section 6.4
Safety assessments												
AE assessments	X	X	X	X	X	X	X	X	X	X		Section 8.3.1
Comprehensive physical examination									X			Section 8.3.2
Weight									X			Section 8.3.2
Targeted physical examination		X		X	X	X	X	X		X		Section 8.3.2
Vital signs		X		X	X	X	X	X	X	X		Section 8.3.3
12-lead ECG									X			Section 8.3.4

Table 4: Schedule of Activities (Extension Period) (Continued)

	Treatment (Extension Period)									Safety Follow-Up			Notes
Visit Day (Range)	**Wk 26 (± 3 d) (Remote Visit)**	**Wk 28 (± 3 d)**	**Wk 30 (± 3 d) (Remote Visit)**	**Wk 32 (± 3 d)**	**Wk 36 (± 3 d)**	**Wk 40 (± 3 d)**	**Wk 44 (± 3 d)**	**Wk 48 (± 3 d)**	**Wk 52 (± 3 d) (EOT2)**	**Wk 56 (4 wks post last dose + 7 d) (EOS)**			Remote visits may be performed in-clinic at the discretion of the investigator.
Efficacy assessments													
[redacted]													
T-VASI		X		X	X	X	X	X	X	X	X	X	Section 8.2.2
[redacted]													
Photography of the face					X				X				Section 8.2.6
Photography of nonfacial targeted areas					X				X				Section 8.2.6
[redacted]													

Table 4: Schedule of Activities (Extension Period) (Continued)

Visit Day (Range)	Treatment (Extension Period)									Safety Follow-Up	[redacted]	Notes
	Wk 26 (± 3 d) (Remote Visit)	Wk 28 (± 3 d)	Wk 30 (± 3 d) (Remote Visit)	Wk 32 (± 3 d)	Wk 36 (± 3 d)	Wk 40 (± 3 d)	Wk 44 (± 3 d)	Wk 48 (± 3 d)	Wk 52 (± 3 d) (EOT2)	Wk 56 (4 wks post last dose + 7 d) (EOS)		Remote visits may be performed in-clinic at the discretion of the investigator.
Laboratory assessments												
Serum pregnancy test (WOCBP)									X	X		Section 8.3.5.1 and Table 13
Urine pregnancy test (WOCBP)		X		X	X	X	X	X				Section 8.3.5.1 and Table 13
Urinalysis					X			X	X			Table 13
Hematology and blood chemistry assessments	X	X	X	X	X	X	X	X	X	X		Table 13; at-home blood collection for remote visits.
Coagulation		X										Reflexive testing during the study per Appendix D (also Table 13).
Lipid panel					X				X			Table 13
Thyroid function markers					X		X		X	X		Table 13
Inflammation marker					X				X			Table 13
[redacted]												

[a] Only for participants who consent to additional follow-up visits.

2. INTRODUCTION

INCB054707 is an oral JAK inhibitor with selectivity for JAK1 that is currently under development for the treatment of patients with HS. Proinflammatory cytokines are strongly implicated in the pathogenesis of several dermatologic diseases, such as HS, atopic dermatitis, plaque psoriasis, alopecia areata, and vitiligo. [redacted]

2.1. Background

Vitiligo is an autoimmune disease characterized by depigmented patches of skin due to destruction of melanocytes and is estimated to affect 0.5% to 2% of the population worldwide (Krüger and Schallreuter 2012). Prevalence is similar between men and women, and there is no known difference in presentation based on skin type or race. Nearly 70% to 80% of patients develop vitiligo before 30 years of age, with almost 50% presenting before 20 years of age and 25% presenting before 10 years of age (Bergqvist and Ezzedine 2020). Generalized (nonsegmental) vitiligo is the most common type, accounting for up to 90% of cases (Taïeb and Picardo 2009). Other autoimmune diseases such as thyroid disorders, type 1 diabetes mellitus, pernicious anemia, and Addison disease are often associated with vitiligo, and its natural course is generally unpredictable but often progressive.

The pathogenesis of vitiligo appears to involve intrinsic defects within melanocytes and autoimmunity that targets these cells. Melanocytes from patients with vitiligo are more vulnerable to intrinsic and/or extrinsic factors that induce a cellular stress response than those from healthy individuals (Rodrigues et al 2017, Speeckaert and van Geel 2017). Melanocyte stress response activates innate immunity, which may represent the initiating vitiligo event. The oxidative stress, cell damage, and cytokines secreted from innate immune cells trigger release of chemotaxis factors, such as CXCL9 and CXCL10, by keratinocytes and recruit cytotoxic CD8+ T cells to the skin. Activated CD8+ T cells release proinflammatory IFN-γ, which triggers more CXCL9 and CXCL10 release from keratinocytes through JAK1- and JAK2-mediated signaling, leading to recruitment of more melanocyte-specific CD8+ cells that destroy melanocytes and result in skin depigmentation (Frisoli and Harris 2017). Because IFN-γ signaling requires the JAK-STAT pathway, inhibition of JAK signaling may be an effective strategy for the treatment of patients with vitiligo.

No drugs are currently approved for the treatment of patients with vitiligo. In general, first-line treatment consists of off-label use of topical corticosteroids and calcineurin inhibitors. Second-line treatment consists of phototherapy (narrow-band UVB and psoralen plus UVA) and systemic corticosteroids (Bergqvist and Ezzedine 2020). Less common therapies include surgical grafting techniques and depigmenting treatments. The response to these therapies varies, can be time-intensive, can be slow, and often produces disappointing results if repigmentation is cosmetically unacceptable (Narayan et al 2020).

The chronic nature of vitiligo and lack of effective therapy can have a negative psychosocial impact on patients, with effects on quality of life similar to those of other dermatologic diseases, such as psoriasis and atopic dermatitis (Cupertino et al 2017). Involvement of cosmetically sensitive areas, such as the face and hands, can have a major impact on self-esteem and eventually link to the psychological burden and quality of life; individuals with more than 25% of BSA involvement may have difficulties performing daily tasks, such as gardening, shopping, or clothing selection, and difficulty with socialization, such as participating in sports activities and initiating and maintaining romantic relationships (Silverberg and Silverberg 2013). In some societies, affected individuals even face discrimination due to poor understanding and lack of acceptance of the disease (Yazdani Abyaneh et al 2014). Approximately 75% of patients with vitiligo feel their appearance is moderately to severely intolerable, and 41% of patients feel that there is little they can do to improve their condition, with feelings of hopelessness increasing with time (Salzer and Schallreuter 1995). Not surprisingly, 66% of patients report being distressed by their disease, and 92% have experienced stigmatization (Krüger and Schallreuter 2014). Feelings of embarrassment and fear of rejection can cause patients with vitiligo to withdraw and lead to social isolation in both personal and professional relationships. A majority of patients with vitiligo have reported feelings of anxiety and embarrassment when meeting strangers or beginning a new sexual relationship (Porter et al 1990). Additionally, clinical depression or depressive symptoms are associated with vitiligo. Based on various meta-analyses, patients with vitiligo are approximately 5 times more likely to have depression than healthy controls, with vitiligo being considered one of the most psychologically devastating diseases in dermatology (Lai et al 2017, Osinubi et al 2018).

[redacted] The largest published vitiligo study to date reported treatment of 157 participants (with at least 0.5% F-BSA and at least 3% nonfacial BSA with depigmented areas) with topical administration of ruxolitinib (a JAK1/2 inhibitor) cream for up to 52 weeks. At Week 24, 50% of the participants treated with ruxolitinib 1.5% cream QD achieved F-VASI50 compared with 3% applying vehicle; additionally, 32% of the participants achieved T-VASI50 at Week 24 compared with 0% applying vehicle (Rosmarin et al 2020).

[redacted]

2.2. Study Rationale

Vitiligo is an autoimmune disease characterized by depigmented patches of skin due to a loss of melanocytes. The chronic nature of the disease, the lack of a uniform and effective therapy, and the unpredictable course of the disease have a profound psychosocial impact on patients, affecting their quality of life. [redacted]

2.2.1. Scientific Rationale for Study Design

INCB054707 is an oral small-molecule JAK1 inhibitor and has been evaluated in 36 participants with HS in 2 clinical studies with oral doses of up to 90 mg for 8 weeks. During the treatment period, INCB054707-treated participants demonstrated improvement, characterized as decreased number of abscesses and inflammatory nodules, decreased HS-associated pain, and improved quality of life. Observed AEs were mild to moderate in intensity and mostly unrelated to study medication, with no associated SAEs or withdrawals. Immunological commonalities exist between HS and vitiligo, in which lesions have increased expression of lymphocyte-recruiting chemokines, including CXCL10 (Vossen et al 2019), and elevated IFN-γ levels (Banerjee et al 2017). Treatment of patients with vitiligo for 24 weeks with the topical JAK1/2 inhibitor ruxolitinib cream demonstrated that inhibition of the JAK-STAT pathway leads to repigmentation (Rosmarin et al 2020). [redacted]

In the proposed study, the clinical safety and efficacy of 3 doses of INCB054707 (15, 45, and 75 mg) compared with placebo will be evaluated in male and female adult participants with extensive vitiligo (T-BSA ≥ 8%, T-VASI ≥ 8, F-BSA ≥ 0.5%, and T-VASI ≥ 0.5) for 24 weeks, which is consistent with the duration of other systemic therapies and with narrow-band UVB phototherapy (Hamzavi et al 2004). Efficacy will be assessed via changes in the [redacted] affected by vitiligo lesions, [redacted] and T-VASI, [redacted] and photography. [redacted]

With the goal of obtaining long-term efficacy and safety data for the compound (up to 52 weeks in total), after the 24-week placebo-controlled period, all participants will enter into a double-blind extension period for 28 weeks and will receive either 45 mg or 75 mg QD, followed by a 4-week safety follow-up period [redacted] to monitor safety and potential change in pigmentation after discontinuation or completion of treatment with INCB054707.

It is expected that the outcome of this study will be instrumental in informing dose selection to be evaluated in a potential Phase 3 study in the future.

[redacted]

[redacted]

2.3. Benefit/Risk Assessment

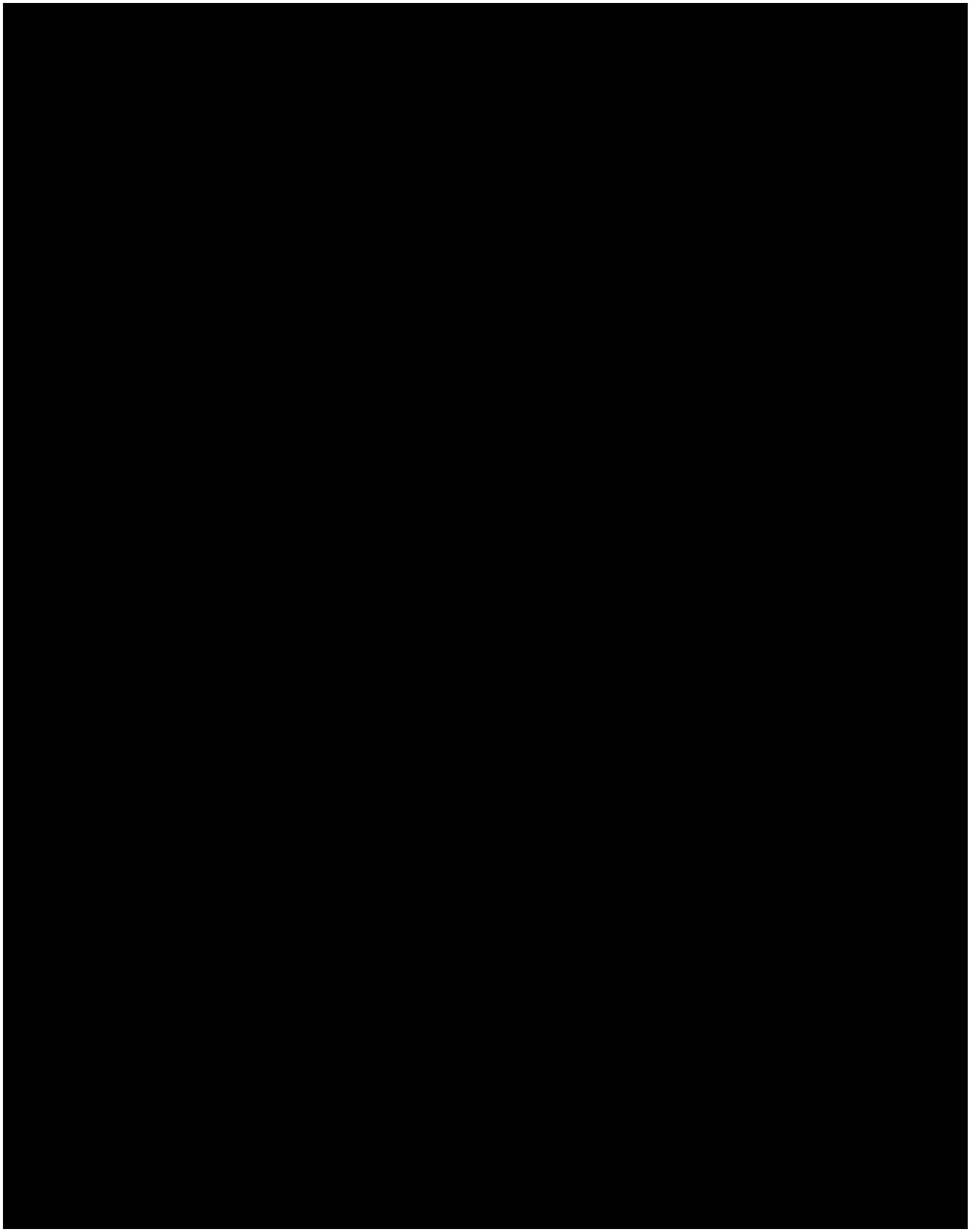
More detailed information about the known and expected benefits and risks and reasonably expected AEs of INCB054707 may be found in the IB.

2.3.1. Clinical Studies

Single doses of INCB054707 up to 405 mg and multiple doses of INCB054707 up to 120 mg QD for up to 10 days have been evaluated in 2 placebo-controlled studies in healthy participants. The most common TEAEs were mild to moderate headache in 31% of participants who received INCB054707 in the multiple-dose study; the events were not dose-dependent and resolved spontaneously following discontinuation of INCB054707. Furthermore, decreases in platelet counts were observed among participants treated with INCB054707 at doses ≥ 60 mg QD. The magnitude of the decrease was larger for participants treated with 120 mg QD compared with those who received 60 mg QD, suggesting a dose-related trend. Of note, for the participants with a treatment-emergent decrease in platelet counts, the platelet counts remained within the normal range.

In 2 clinical studies in participants with HS, INCB 54707-202 (15 mg only) and INCB 54707-203 (placebo and 30, 60, and 90 mg), QD doses of study drug were administered for up to 8 weeks. Transient and asymptomatic thrombocytopenia was observed in 4 of 8 participants who received INCB054707 90 mg QD after 4 weeks of exposure, which led to dose interruption for a maximum of 2 weeks, and resolved without medical intervention. All participants returned to their normal dosing schedule after dose interruption and completed the study without clinical sequelae or re-emergence of thrombocytopenia. Platelet count decreases have been transient and stabilize over time, as observed in studies with other JAK1 inhibitors for treatment of other dermatologic indications, such as abrocitinib in atopic dermatitis (Gooderham et al 2019) and itacitinib in plaque psoriasis (Bissonnette et al 2016). Thrombocytopenia TEAEs were asymptomatic and judged as treatment-related. Hemoglobin levels remained within normal limits and were mostly unchanged during the study, while neutrophil counts showed a mild dose-dependent decrease within normal limits. Across the 2 studies, the most common TEAE was fatigue, observed in 6 of the 36 participants (17%). Mild-to-moderate headache was observed in 11% (4 of 36) of the participants exposed to INCB054707 and in 22% (2 of 9) of the participants exposed to placebo. No serious or fatal TEAEs were reported in the studies; more details are provided in the IB.

Based on the available nonclinical and clinical data, the potential risks to participants are summarized in Table 5.



2.3.2. Benefit Assessment

Based on the expected mode of action of INCB054707, participants randomly assigned to 1 of the 3 active treatment groups may experience clinically meaningful improvements in their vitiligo lesions during the placebo-controlled (24 weeks) period, and all participants will be offered drug therapy with 45 mg or 75 mg during the extension period (28 weeks).

Vitiligo is characterized by a progressive loss of functional melanocytes and associated with auditory abnormalities, including SNHL, with a prevalence ranging from 4.0% to 68.8% when compared with healthy controls (de Jong et al 2017). During embryogenesis, precursor melanocyte cells (melanoblasts) migrate to the dermis and also to the base of the cochlea, which is responsible for hearing high frequencies. It appears that inner ear melanocytes are very important for cochlear hair cell function and normal hearing (Rahimi et al 2019). [redacted]

Participants will also contribute to the process of developing a novel anti-inflammatory agent expected to induce repigmentation in vitiligo, a disease with high unmet need and that is severely debilitating to participants' psychosocial well-being.

2.3.3. Benefit-Risk Conclusion

Currently, there are no approved drug therapies for vitiligo, and treatments are empirical and directed by the available clinical guidelines. There are limited data on the effectiveness and long-term safety of current therapies, including topical or oral corticosteroids and calcineurin inhibitors. Given the psychosocial burden and stigma caused by vitiligo, patients continue to need effective and safe treatments for their disease.

Considering the safety measures initiated to minimize risk to participants in this study, the potential risks identified in association with INCB054707 are justifiable and appropriately balanced by the anticipated efficacy benefits expected to be afforded to participants.

3. OBJECTIVES AND ENDPOINTS

Table 6 presents the objectives and endpoints.

Table 6: Objectives and Endpoints

Objectives	Endpoints
Primary	
To determine the efficacy of INCB054707.	• Percent change from baseline in Total Vitiligo Area Scoring Index (T-VASI) at Week 24.
Key Secondary	
To further determine the efficacy of INCB054707.	• Proportion of participants achieving T-VASI50 at Week 24. T-VASI50 is defined as 50% or greater reduction in the Total Vitiligo Area Scoring Index.
Secondary	
To evaluate the safety and tolerability of INCB054707.	• Frequency and severity of AEs, including the results of physical examinations, vital signs, evaluation of clinical laboratory studies, and ECGs.
[redacted]	

Table 6: Objectives and Endpoints (Continued)

Objectives	Endpoints
[redacted]	

Table 6: Objectives and Endpoints (Continued)

Objectives	Endpoints
[redacted]	

Table 6: Objectives and Endpoints (Continued)

4. STUDY DESIGN

4.1. Overall Design

This is a Phase 2, multicenter, randomized, parallel-group, placebo-controlled, double-blind, dose-ranging study to evaluate the efficacy and safety of INCB054707 (15, 45, and 75 mg QD) over a 24-week treatment period followed by a 28-week double-blind extension period (INCB054707 45 mg and 75 mg QD), a 4-week safety follow-up period [redacted]. The study will enroll approximately 160 men and women aged 18 to 75 years with nonsegmental vitiligo. Figure 1 presents the study design schema, and Table 3 and Table 4 present the SoA for the placebo-controlled and extension periods, respectively.

Participants will be screened for up to 32 days before the first dose of study drug. Key entry criteria for participants are diagnosis of nonsegmental vitiligo, with depigmented areas including T-BSA ≥ 8%, T-VASI ≥ 8, F-BSA ≥ 0.5%, and F-VASI ≥ 0.5. Screening will include assessments described in Table 3.

Participants who meet all the study entry criteria and none of the exclusion criteria will return to the study site on Day 1 of dosing and be randomized in a 1:1:1:1 ratio to 1 of 4 treatment groups (placebo or INCB054707 15, 45, or 75 mg QD). Participant randomization will be stratified based on total BSA involvement, with 2 strata: 8% to 20% and > 20%.

Approximately 160 participants will take oral study drug (placebo, 15 mg, 45 mg, or 75 mg) QD in a blinded manner for 24 weeks. Participants who complete the Week 24 visit will enter the 28-week double-blind extension period with 45 mg QD (for participants who received 45 mg during the placebo-controlled period) or 75 mg (for participants who received placebo, 15 mg, or 75 mg during the placebo-controlled period), with a 4-week safety follow-up period after the last dose of study drug [redacted].

The external DSMB will review safety data throughout the study and may provide recommendations regarding changes in the study conduct (see Section 5.6).

Participants will be assessed for safety and tolerability by monitoring the frequency and severity of AEs and performing physical examinations, ECGs, vital signs measurements, and clinical laboratory assessments at various timepoints during the study.

[redacted]

The COVID-19 global pandemic may present challenges to the normal conduct of this study, requiring the outline of potential mitigation strategies described in Appendix E.

4.2. Overall Study Duration

The study begins when the first participant signs the study ICF. The end of the study is defined as the date of the last visit of the last participant in the study or the last scheduled procedure shown in the SoA (see Table 3 and Table 4) for the last participant in the study globally.

It is estimated that an individual will participate for approximately 19 months, including up to 32 days for screening, continuous treatment for 52 weeks (including placebo-controlled and extension periods, as long as participants are receiving benefit and have not met any criteria for study withdrawal), [redacted]

A participant is considered to have completed the study if he/she has completed both the placebo-controlled and the extension periods of the study, including the Week 56 safety follow-up (EOS) visit (see Table 3 and Table 4). A study is considered completed when the last participant's last visit has occurred.

4.3. Study Termination

The investigator retains the right to terminate study participation at any time, according to the terms specified in the study contract. The investigator is to notify the IRB/IEC of the study's completion or early termination in writing, send a copy of the notification to the sponsor or sponsor's designee, and retain 1 copy for the site study regulatory file.

The sponsor may terminate the study electively if, for example, required by regulatory decision or upon advice of the DSMB (see Section 5.6). If the study is terminated prematurely, the sponsor will notify the investigators, the IRBs and IECs, and the regulatory bodies of the decision and reason for termination of the study.

5. STUDY POPULATION

Deviations from eligibility criteria are not allowed because they can potentially jeopardize the scientific integrity of the study, regulatory acceptability, and/or participant safety. Therefore, adherence to the criteria as specified in the Protocol is essential. Prospective approval of Protocol deviations to recruitment and enrollment criteria, also known as Protocol waivers or exemptions, are not permitted.

5.1. Inclusion Criteria

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

1. Ability to comprehend and willingness to sign an ICF.
2. Men and women aged 18 to 75 years at the time of consent.
3. Clinical diagnosis of nonsegmental vitiligo, with depigmented areas including:
   a. T-BSA $\geq$ 8%, and
   b. T-VASI $\geq$ 8, and
   c. F-BSA $\geq$ 0.5%, and
   d. F-VASI $\geq$ 0.5.
4. Removed during Protocol Amendment 1.
5. Agreement to discontinue all agents and procedures used to treat vitiligo from screening through the final safety follow-up visit.

6. Agreement to use contraception, as follows (see Appendix A):
    a. Male participants and female participants of childbearing potential must agree to take appropriate precautions to avoid pregnancy (with at least 99% certainty) from screening through 90 days after the last dose of study drug.
    b. Male participants must refrain from donating sperm during this period. Female participants must refrain from donating oocytes during this period.
    c. Permitted methods that are at least 99% effective in preventing pregnancy should be communicated to the participant and his/her understanding confirmed.

    Note: This criterion does not apply to women of nonchildbearing potential (ie, surgically sterile with a hysterectomy and/or bilateral oophorectomy OR postmenopausal, defined as amenorrhea at least 12 months before screening, confirmed by FSH levels at screening).

5.2. Exclusion Criteria

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

1. Inability or unwillingness of the participant to sign the ICF.
2. Other forms of vitiligo (eg, segmental) or other skin depigmentation disorders (eg, piebaldism, pityriasis alba, leprosy, postinflammatory hypopigmentation, progressive macule hypomelanosis, nevus anemicus, chemical leukoderma, and tinea versicolor).
3. Uncontrolled thyroid function at screening as determined by the investigator.

    Note: If the participant has a history of thyroid disease and is on treatment, the participant must be on a stable thyroid regimen for at least 3 months prior to Day 1.
4. Use of laser or light-based treatment (phototherapy), including tanning beds, within 8 weeks prior to Day 1.
5. Use of dihydroxyacetone (generally present in self-tanning products) within 4 weeks prior to Day 1.
6. Current or past use of the depigmenting agent monobenzyl ether of hydroquinone, including Benoquin® (monobenzone).
7. History of melanocyte-keratinocyte transplantation procedure (MKTP) or other surgical treatment for vitiligo.
8. Spontaneous and significant repigmentation within 6 months prior to screening (eg, repigmentation without any treatment, and significant in amount as determined by the investigator).
9. Women who are pregnant, considering pregnancy, or breastfeeding.

10. Concurrent conditions or history of other diseases, as follows:
    a. Thrombocytopenia, coagulopathy, platelet dysfunction, or history of thrombotic events.
    b. Any clinically significant medical condition other than vitiligo, as determined by the investigator, that is not adequately controlled with appropriate treatment **OR** may interfere with the course, severity, or assessments of this study.
    c. Any other active skin disease or condition that may interfere with the course, severity, or assessments of this study.
    d. Any bacterial, fungal, or viral infection that, based on the investigator's clinical assessment, makes the participant an unsuitable candidate for the study.
    e. Current herpes zoster infection, a history of disseminated herpes simplex, or a history of herpes zoster.
    f. History of malignancy, including melanoma, lymphoma, and leukemia within 5 years before Day 1, other than a successfully treated nonmetastatic cutaneous squamous cell carcinoma, basal cell carcinoma, or localized carcinoma in situ of the cervix.
    g. Albinism.
11. History of treatment failure for vitiligo, or any other inflammatory condition, with any systemic or topical JAK or TYK2 inhibitor (eg, ruxolitinib, tofacitinib, baricitinib, filgotinib, lestaurtinib, pacritinib, abrocitinib, brepocitinib).
12. Current use of anticoagulants or medications known to cause thrombocytopenia.
13. Receipt of medications or investigational drugs within the following interval before Day 1 (first administration of study drug):
    a. < 12 weeks or 5 half-lives (if known), whichever is longer, for any topical or systemic JAK or TYK2 inhibitor.
    b. < 12 weeks or 5 half-lives (if known), whichever is longer, for any investigational or experimental treatments.
    c. < 12 weeks or 5 half-lives (if known), whichever is longer, for systemic immunosuppressive or immunomodulating biologic drugs (eg, adalimumab, etanercept, infliximab, golimumab, certolizumab, ustekinumab, secukinumab, brodalumab, ixekizumab, risankizumab, guselkumab, bimekizumab, iscalimab, bermekimab, rituximab, anakinra).
    d. < 6 weeks for live vaccine, or planning to receive live vaccine during the course of the study or within 6 weeks after the last dose of study drug.
    e. < 4 weeks for systemic immunosuppressive or immunomodulating small-molecule drugs (eg, oral or injectable corticosteroids, methotrexate, cyclosporine, dapsone, azathioprine).
       Note 1: Use of corticosteroid inhalers and intranasal sprays is allowed.
       Note 2: Use of oral corticosteroids for nondermatologic conditions (eg, asthma exacerbation, bronchitis) is allowed for no longer than 7 days, if deemed acceptable by the investigator and the sponsor.
       Note 3: Use of topical corticosteroids for dermatologic disease other than vitiligo (eg, atopic dermatitis or psoriasis) is allowed for areas not being treated for vitiligo. The total BSA involvement for other dermatologic diseases, outside of the areas treated for vitiligo, must not exceed 10%.

f. < 3 weeks for any oral or topical PDE-4 inhibitor (eg, apremilast, crisaborole).
g. < 2 weeks for any topical drug applied onto vitiligo lesions.
h. < 2 weeks for any OTC therapies used for vitiligo treatment.
i. < 2 weeks or 5 half-lives (if known), whichever is longer, for strong and moderate systemic CYP3A4 inhibitors and strong systemic CYP3A4 inducers. Examples include but are not limited to the following (see Appendix B for details): erythromycin, rifampicin/rifampin, ciprofloxacin, some azole antifungals (eg, ketoconazole, fluconazole), nefazodone, St John's wort, diltiazem, mibefradil, verapamil, grapefruit/grapefruit juice, and Seville oranges.
j. < 1 week for antiplatelet drugs.
Note: Low-dose acetylsalicylic acid (≤ 100 mg QD) is permitted for the purpose of cardiovascular prophylaxis at the discretion of the investigator.

14. Laboratory values at screening defined in Table 7.

Table 7: Exclusionary Laboratory Values

Laboratory Parameter		**Exclusion Criterion**
Hematology		
a	Platelets	< 150×10^9/L
b	Hemoglobin	< 10 g/L
c	ANC	< 1.5×10^9/L
d	WBC	≤ 3.0×10^9/L
Hepatic		
e	ALT	≥ 2 × ULN
f	AST	≥ 2 × ULN
g	Total bilirubin	≥ 1.5 × ULN (Note: unless clinical diagnosis of Gilbert's syndrome)
h	Alkaline phosphatase	≥ 2× ULN
Renal		
j	Serum creatinine	> 1.25 × ULN
Coagulation		
l	PT	> ULN
m	INR	> ULN

15. Evidence of HBV or HCV infection or risk of reactivation. Participants cannot be positive for hepatitis B surface antigen, anti–hepatitis B core antibody, or HCV antibody; participants also cannot be positive for HBV DNA or HCV RNA in case these reflexive assessments are required to be performed.

Note: Participants with no prior history of HBV infection who have been vaccinated against HBV and who have a positive antibody (hepatitis B surface antibody) against HBsAg as the only evidence of prior exposure may participate in the study.

16. Known HIV infection.
17. Evidence of active or latent or inadequately treated infection with *Mycobacterium tuberculosis* (ie, TB) as defined by the following:
    a. A positive QFT-GIT or positive Mantoux/PPD tuberculin skin test performed at or within the 12 weeks prior to Day 1 is exclusionary; a negative test is required for eligibility unless other criteria as described here are applicable. It is recommended that participants with a history of Bacille Calmette-Guérin vaccination be tested with the QFT-GIT, because the Mantoux/PPD tuberculin skin test may be positive due to vaccination. A QFT-GIT or Mantoux/PPD tuberculin skin test is not required if the participant has previously received a documented adequate course of therapy for either latent or active TB infection.
    b. A history of either untreated or inadequately treated latent or active TB infection.
    c. If a participant has previously received an adequate course of therapy for either latent TB infection (9 months of isoniazid in a locale where rates of primary multidrug TB resistance are < 5% or an acceptable alternative regimen) or active TB infection (an acceptable multidrug regimen), neither a QFT-GIT nor a Mantoux/PPD tuberculin skin test is needed, but a chest x-ray(s) or other appropriate diagnostic image, performed within 3 months of Day 1, is required. To be considered eligible for the study, the x-ray(s) must be negative for active TB infection as determined by a qualified radiologist. Documentation of adequate treatment for TB and negative chest x-ray(s) results must be obtained prior to Day 1.
    d. A participant who is currently being treated for active TB infection is to be excluded.
18. Known hypersensitivity or severe reaction to INCB054707 or excipients of INCB054707 (refer to IB).
19. Inability or unlikeliness of the participant to comply with the dose schedule and study evaluations, in the opinion of the investigator.
20. Any condition that would, in the investigator's judgment, interfere with full participation in the study, including administration of study drug and attending required study visits; pose a significant risk to the participant; or interfere with interpretation of study data.

5.3. Lifestyle Considerations

Participants are not allowed to use tanning beds within 8 weeks prior to Day 1 and during the study.

Participants are not allowed to use dihydroxyacetone (generally present in self-tanning products) within 4 weeks prior to Day 1 and during the study.

Participants are allowed to use of bland emollients, camouflage makeups, or sunscreen agents.

5.3.1. Meals and Dietary Restrictions

Participants must abstain from consumption of grapefruit or grapefruit juice (pomelos, exotic citrus fruits, grapefruit hybrids, or fruit juices) and of Seville oranges from 14 days before the start of study drug until after the final dose of study drug.

Participants must abstain from consumption of dietary supplements containing St John's wort (*Hypericum perforatum*) from 14 days before the start of study drug until after the final dose of study drug.

5.4. Screen Failures

Screen failures are defined as participants who consent to participate in the clinical study but are not subsequently randomly assigned to study drug.

Tests with results that fail eligibility requirements may be repeated once during screening if the investigator believes the result to be in error. Additionally, a participant who fails screening may repeat the screening process 1 time if the investigator believes that there has been a change in eligibility status. Participants who rescreen must reconsent and be assigned a new participant number.

5.5. Replacement of Participants

No participants will be replaced at any time during this study. However the COVID-19 global pandemic may present challenges to the normal conduct of this study, requiring the outline of potential mitigation strategies described in Appendix E.

5.6. Data Safety Monitoring Board

This study will use an external DSMB to monitor safety. There will be 1 planned DSMB review following randomization of the initial 40 participants in the study and their respective completion of visit at Week 24, with at least 2 additional reviews at a time to be determined after the first assessment. The DSMB members will be blinded to participants' treatment assignment for the initial safety review; however, the DSMB members may request unblinding at any time. Participants and investigators will remain blinded to each participant's treatment assignment during both the placebo-controlled and extension periods of the study. The sponsor will remain blinded through completion of the placebo-controlled period. The sponsor will be unblinded after the primary database lock, when all participants have completed the placebo-controlled, double-blind treatment period (Week 24 analysis).

The voting members of the committee are external to the sponsor. The members of the DSMB will not be involved with the study in any other way (eg, they cannot be study investigators) and will have no competing interests that could affect their roles with respect to the study.

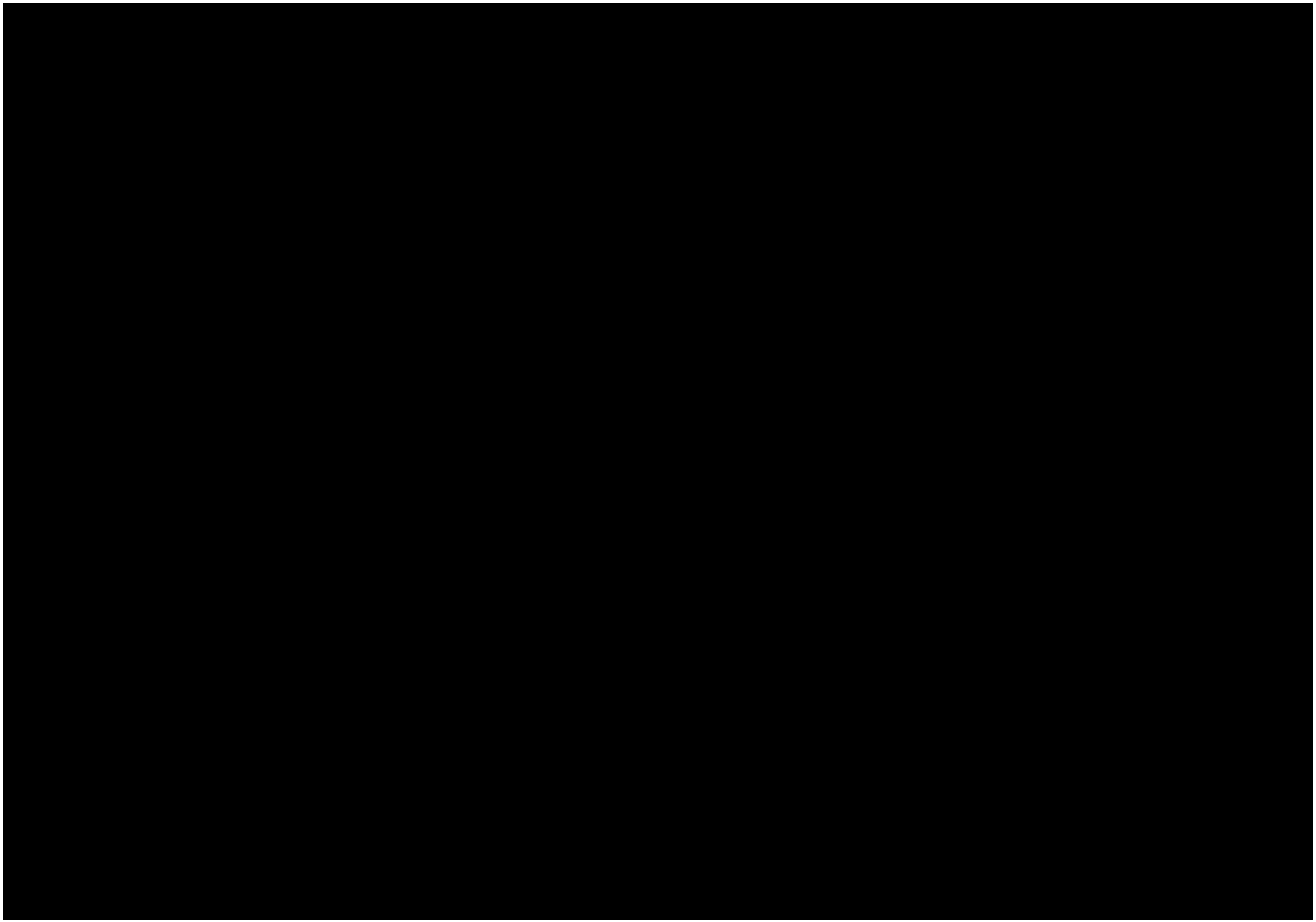
The DSMB will make recommendations to the sponsor regarding steps to ensure both participant safety and the continued ethical integrity of the study. Specific details regarding composition, responsibilities, and governance, including the roles and responsibilities of the various members of the clinical study team, and requirements for the proper documentation of DSMB reports, minutes, and recommendations will be described in the DSMB charter that is reviewed and approved by all DSMB members.

6. STUDY TREATMENT

6.1. Study Treatments Administered

Information regarding study drug and administration is provided in Table 8. Participants will record study drug administration in a daily diary. Further information regarding study drug administration is provided in Appendix C.

The COVID-19 global pandemic may present challenges to the normal conduct of this study, requiring the outline of potential mitigation strategies described in Appendix E.



6.2. Preparation, Handling, and Accountability

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

Only participants enrolled in the study may receive study treatment, and only authorized site staff may supply or administer study treatment. All study treatment must be stored in a secure, environmentally controlled, and monitored (manual or automated) area in accordance with the labeled storage conditions with access limited to the investigator, and authorized site staff.

The investigator (or designee) is responsible for study treatment accountability, reconciliation, and record maintenance (ie, receipt, reconciliation, and final disposition records). Inventory and accountability records must be maintained and readily available for inspection by the study monitor and are open to inspection at any time by any applicable regulatory authorities. The investigator or designee must maintain records that document:

- Delivery of study drug to the study site.
- Inventory of study drug at the site.
- Participant use of the study drug, including tablet counts from each supply dispensed.
- Return of study drug to the investigator or designee by participants.

The investigational product must be used only in accordance with the Protocol (see Appendix C). The investigator will also maintain records adequately documenting that the participants were provided the specified study drug. These records should include dates, quantities, and any available batch or serial numbers or unique code numbers assigned to the investigational product and study participants.

Completed accountability records will be archived by the site. The investigator or designee will be expected to collect and retain all used, unused, and partially used containers of study drug until verified by the study monitor (unless otherwise agreed to by the sponsor). At the conclusion of the study, the investigator or designee will oversee shipment of any remaining study drug back to the sponsor or its designee for destruction according to institutional SOPs. If local procedures mandate on-site destruction of the investigational supply, the site should (where local procedures allow) maintain the investigational supply until the study monitor inspects the accountability records in order to evaluate compliance and accuracy of accountability by the investigative site. At sites where the study drug is destroyed before monitor inspection, the monitors rely on documentation of destruction per the site SOP.

Further guidance and information for the final disposition of unused study treatments are provided in the Pharmacy Manual.

The COVID-19 global pandemic may present challenges to the normal conduct of this study, requiring the outline of potential mitigation strategies described in Appendix E.

6.3. Measures to Minimize Bias: Randomization and Blinding

All participants will be centrally assigned to study treatment using an IRT system (see Section 8.1.3). Participant randomization will be stratified based on total BSA involvement (8%-20% and > 20%). Once a randomization number has been assigned, it must not be reassigned. Full details will be provided in the IRT Study Reference Manual.

Study drug will be dispensed at study visits summarized in the SoA (see Table 3 and Table 4).

Returned study drug should not be redispensed to participants.

Participants and investigators will remain blinded to each participant's treatment assignment during both the placebo-controlled and extension periods of the study. The sponsor will remain blinded through completion of the placebo-controlled period. The sponsor will be unblinded after the primary database lock, when all participants have completed the placebo-controlled, double-blind treatment period (Week 24 analysis). Emergency unblinding will occur if an AE requires the investigator to be made aware of the participant's treatment assignment (see emergency unblinding procedures in Section 9.6 and refer to the IRT Manual).

6.4. Study Treatment Compliance

Compliance with all study-related treatments should be emphasized to the participant by the site personnel, and appropriate steps should be taken to optimize compliance during the study.

Compliance with study drug will be monitored by the study site based on the drug accountability and reported in the eCRF. Participants will be instructed to bring all unused study drug with them to study visits in order for site personnel to conduct tablet counts to assess study drug accountability.

Participant' compliance must be within 80% to 120%, assessed at each study visit. If outside of this range, it will be considered a protocol deviation. Participants consistently noncompliant with the study drug may be withdrawn from the study. The decision on withdrawal will be made by the investigator after consultation with the sponsor, and relevant correspondence will be archived in the site study file.

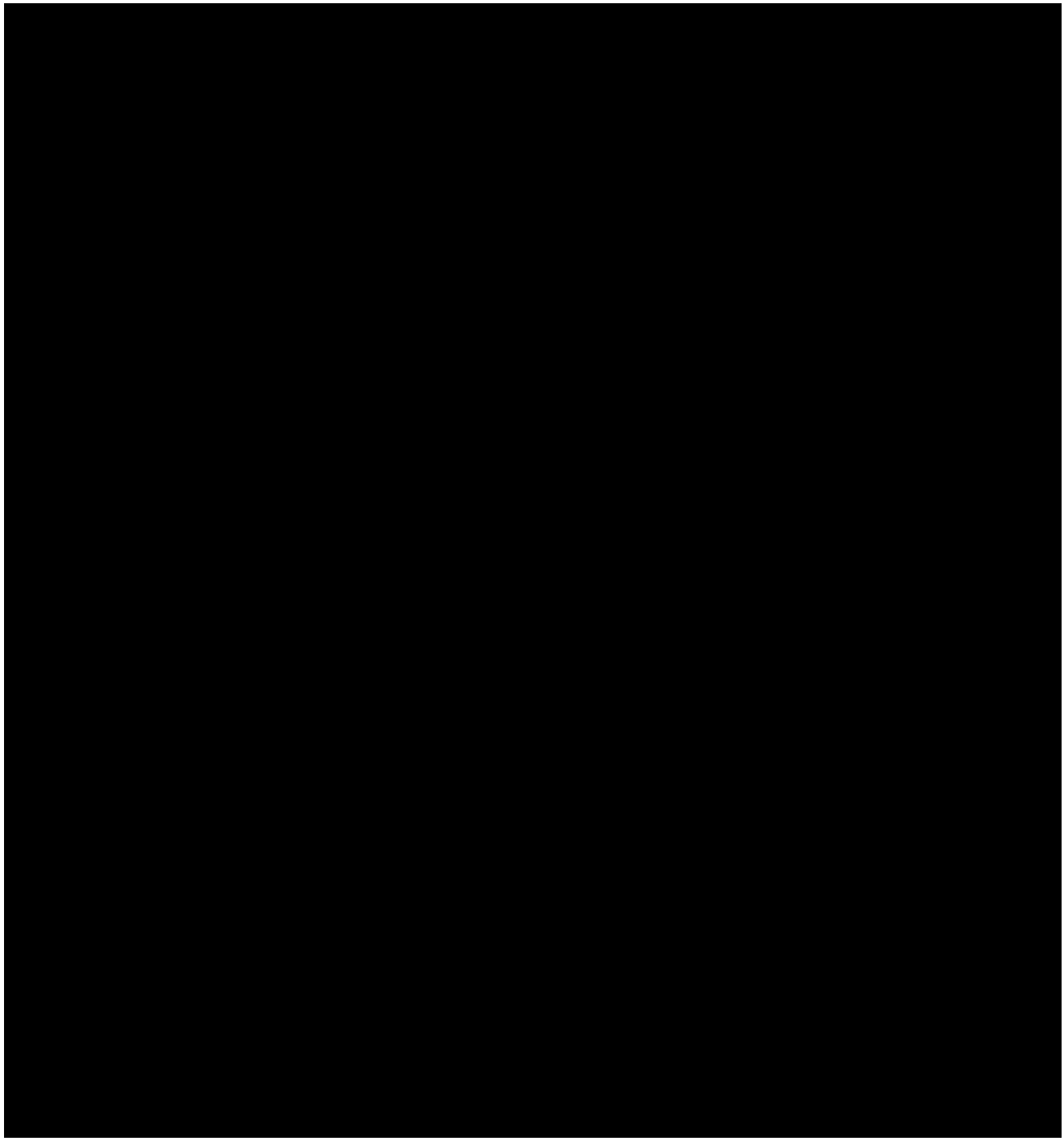
6.5. Dose Modifications

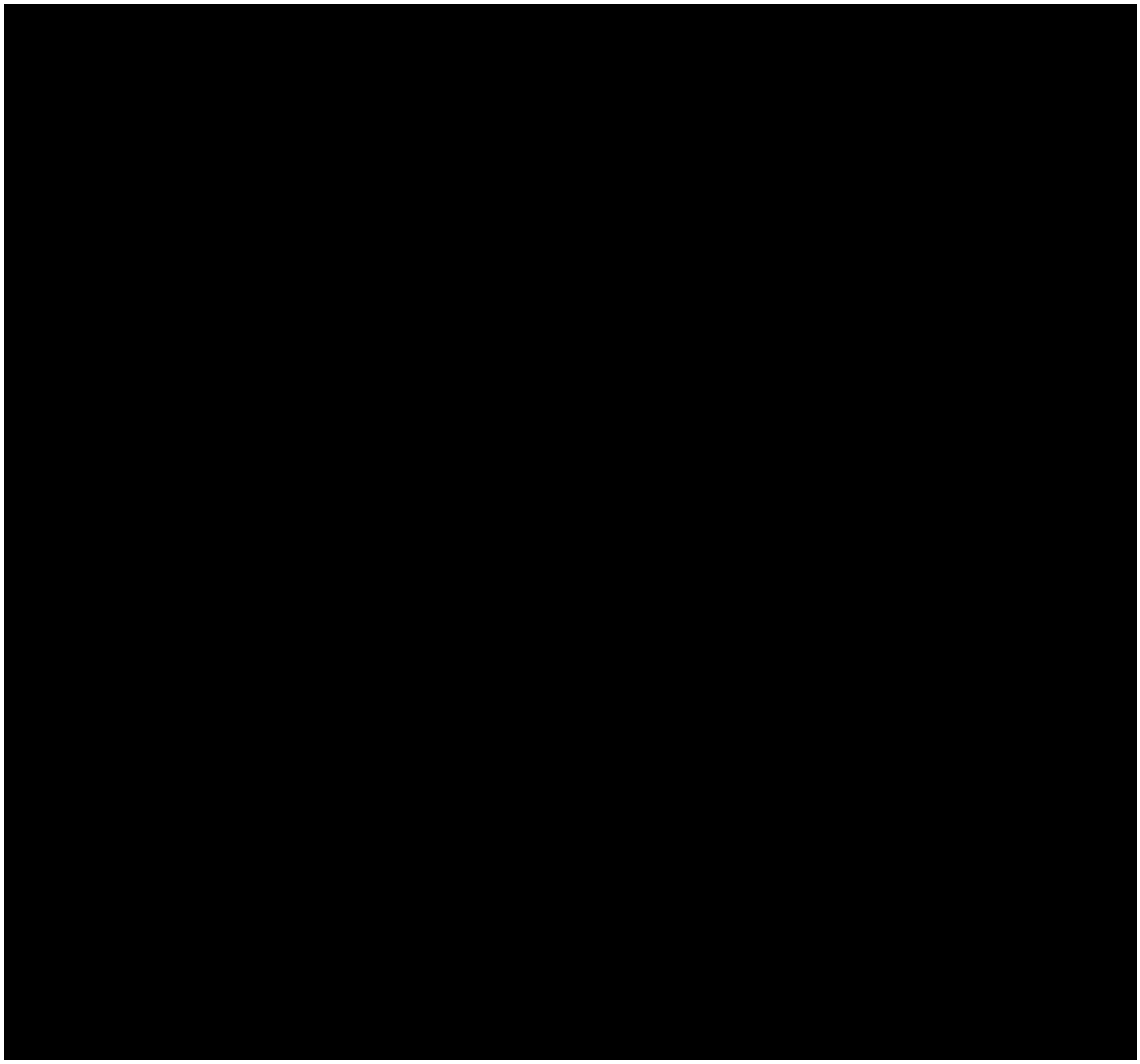
No dose modifications will be allowed during the study. In some circumstances, it may be necessary to temporarily interrupt treatment with study drug as a result of AEs or laboratory abnormalities that have an unclear relationship to the study drug. Further details are described in Section 6.5.1.

6.5.1. Criteria and Procedures for Dose Interruptions and Adjustments of Study Drug

Instructions for dose interruption or discontinuation of INCB054707 are outlined in Table 9 and Table 10; in addition to these guidance steps, safety concerns should be discussed with the sponsor (or representative) immediately upon occurrence or awareness.

The COVID-19 global pandemic may present challenges to the normal conduct of this study (including AE and laboratory assessments), requiring the outline of potential mitigation strategies described in Appendix E.





[redacted]

6.5.2. Criteria for Permanent Discontinuation of Study Drug

The occurrence of unacceptable toxicity not caused by the underlying disease will require that the study drug be permanently discontinued. Unacceptable toxicity is defined as follows:

- The occurrence of an AE that is related to study drug that, in the judgment of the investigator or the sponsor's medical monitor, compromises the participant's ability to continue study-specific procedures or is considered to not be in the participant's best interest.

Table 9 and Table 10 provide specifics on further reasons for permanent discontinuation of study drug.

See Section 7.1 for discontinuation procedures.

6.6. Concomitant Medications and Procedures

All concomitant medications and treatments (including OTC or prescription medicines, vitamins, vaccines, and/or herbal supplements) must be recorded in the eCRF. Any prior medication received up to 12 weeks before Day 1, and 28 (+ 7) days after the last dose of study drug (or up to the EOS visit, whichever occurs last), will be recorded in the eCRF. Any addition, deletion, or change in the dose of these medications will also be recorded.

[redacted]. Only medications or treatments with a potential therapeutic impact on vitiligo, per discretion of the investigator or designee, will be prohibited [redacted].

Concomitant treatments/procedures that are required to manage a participant's medical condition during the study will also be recorded in the eCRF. The medical monitor should be contacted if

there are any questions regarding concomitant or prior therapy, restricted or prohibited medications, or procedures. If visits at Week 2, Week 6, Week 26, and Week 30 are scheduled as remote, concomitant medications will also be assessed remotely, via a phone call conducted by the study site; otherwise information will be captured during in-clinic visit (see Table 3 and Table 4).

6.6.1. Permitted Medications and Procedures

The following are permitted during the study with application guidance. Investigators and site staff are expected to use their best clinical judgement with these recommendations and adhere to the guidelines as closely as possible. Please consult the sponsor if there are specific questions.

- Participants may use bland emollients, camouflage makeups, and sunscreen agents.

  Note: Emollients, camouflage makeups, or sunscreen agents may need to be removed prior to study assessment of the vitiligo lesions.

- Concomitant oral vitamins, herbal supplements, and other skin products should be approved by the investigator and ideally should remain stable during the study.

6.6.2. Restricted Medications and Procedures

The following are restricted during the study under specified conditions:

- Use of topical treatment for dermatologic disease other than vitiligo (eg, atopic dermatitis or psoriasis) is allowed for areas not being treated for vitiligo.

  [redacted]

- Use of oral corticosteroids for no longer than 7 days, if deemed acceptable by the investigator and the sponsor, is allowed for nondermatologic conditions (eg, asthma exacerbation, bronchitis).

  Note: Use of corticosteroid inhalers and intranasal sprays is allowed.

6.6.3. Prohibited Medications and Procedures

The following medications are prohibited for all participants in the study:

- Any topical or systemic JAK or TYK2 inhibitor other than INCB054707 (eg, ruxolitinib, tofacitinib, baricitinib, filgotinib, lestaurtinib, pacritinib, abrocitinib, brepocitinib).
- Any other investigational or experimental treatments, including those for vitiligo.
- Systemic immunosuppressive or immunomodulating biologic drugs (eg, adalimumab, etanercept, infliximab, golimumab, certolizumab, ustekinumab, secukinumab, brodalumab, ixekizumab, risankizumab, guselkumab, bimekizumab, iscalimab, bermekimab, rituximab, anakinra).
- Systemic immunosuppressive or immunomodulating small-molecule drugs (eg, oral or injectable corticosteroids, methotrexate, cyclosporine, dapsone, azathioprine).

- Systemic or topical PDE-4 inhibitors (eg, apremilast, crisaborole).
- Other topical agents for vitiligo, including corticosteroids, vitamin D derivatives, and calcineurin inhibitors.
- Conventional therapies with a potential therapeutic impact on vitiligo, per discretion of the investigator or designee.
- Any phototherapy, including tanning beds.
- Laser or surgical treatments for vitiligo.
- Any topical drug applied onto vitiligo lesions.
- Any OTC therapies used for vitiligo treatment.
- Dihydroxyacetone (generally present in self-tanning products).
- Treatment known to affect the course of vitiligo, such as skin bleaching treatments (eg, hydroquinone) or depigmenting agents (eg, monobenzone).
- Anticoagulants, antiplatelet drugs, or medications known to cause thrombocytopenia.
- Acetylsalicylic acid (aspirin).

  Note: Low-dose acetylsalicylic acid (≤ 100 mg QD) is permitted for the purpose of cardiovascular prophylaxis at the discretion of the investigator.
- Live vaccines (during the study and within 6 weeks after the last dose of study drug).
- Strong and moderate systemic CYP3A4 inhibitors and strong systemic CYP3A4 inducers within 2 weeks or 5 half-lives (if known). Examples include but are not limited to the following (see Appendix B for details): erythromycin, rifampicin/rifampin, ciprofloxacin, some azole antifungals (eg, ketoconazole, fluconazole), nefazodone, St. John's wort, diltiazem, mibefradil, verapamil, grapefruit/grapefruit juice, and Seville oranges.

6.7. Treatment After the End of the Study

Upon completion of the 52 weeks of treatment, participants will not be provided additional treatment within this study.

7. DISCONTINUATION OF STUDY TREATMENT AND PARTICIPANT WITHDRAWAL

7.1. Discontinuation of Study Treatment

7.1.1. Reasons for Discontinuation

Participants **must** be discontinued from study treatment for the following reasons:

- The participant becomes pregnant.
- Consent is withdrawn.
  Note: Consent withdrawn means that the participant has explicitly indicated that he/she does not want to be followed any longer; in this case, no further data, except data in the public domain, may be solicited from or collected on the participant. Participants may choose to discontinue study treatment and remain in the study.
- Further participation would be injurious to the participant's health or well-being, in the investigator's medical judgment.
- Any AE of unacceptable severity as noted in Section 6.5.
- Participant meets discontinuation criteria as described in Section 6.5.
- The study is terminated by the sponsor.
- The study is terminated by the local health authority, IRB, or IEC.

A participant **may** be discontinued from study treatment as follows:

- If, during the course of the study, a participant is found not to have met eligibility criteria, the medical monitor, in collaboration with the investigator, will determine whether the participant should be withdrawn from study treatment.
- If a participant is noncompliant with study procedures or study drug administration in the investigator's or sponsor's opinion, the sponsor should be consulted for instruction on handling the participant.

7.1.2. Discontinuation Procedures

In the event that the decision is made to permanently discontinue the study treatment, the EOT visit (EOT1 during the placebo-controlled period; EOT2 during the extension period) should be conducted. Reasonable efforts should be made to have the participant return for a safety follow-up visit 4 weeks after last dose (EOS) [redacted]. These visits are described in Table 3 and Table 4.

The last date of the last dose of study drug and the reason for discontinuation of study drug will be recorded in the eCRF.

If a participant is discontinued from study treatment:

- The study monitor or sponsor must be notified.
- The reason(s) for discontinuation must be documented in the participant's medical record and the primary reason for discontinuation must be included in the eCRF.
- The EOT visit should be performed and date recorded.
- The status of the participant should be updated to EOT in the IRT.
- Participants must be followed for safety until the time of the follow-up visit or until study drug–related toxicities resolve, return to baseline, or are deemed irreversible, whichever is longest.

If the participant discontinues study treatment and actively withdraws consent for collection of follow-up data (safety follow-up or disease assessment), then no additional data collection should occur; however, participants will have the option of withdrawing consent for study treatment but continuing in the follow-up period of the study for safety/efficacy assessments.

7.2. Participant Withdrawal From the Study

A participant may withdraw from the study at any time at his/her own request or may be withdrawn at any time at the discretion of the investigator for safety, behavioral, compliance, or administrative reasons. When a participant is withdrawn from the study, the EOT visit procedures should be performed; if possible, the safety follow-up visit should also be conducted within 28 (+ 7) days of the last dose of study drug [redacted].

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

7.3. Lost to Follow-Up

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

The following actions must be taken if a participant fails to return to the clinic for a required study visit:

- The site must attempt to contact the participant and reschedule the missed visit as soon as possible and counsel the participant on the importance of maintaining the assigned visit schedule and ascertain whether or not the participant wishes to and/or should continue in the study.
- Before a participant is deemed lost to follow-up, the investigator or designee must make every effort to regain contact with the participant (where possible, 3 telephone calls and, if necessary, a certified letter to the participant's last known mailing address or local equivalent methods). These contact attempts should be documented in the participant's medical record.

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

8. STUDY ASSESSMENTS AND PROCEDURES

8.1. Administrative and General Procedures

8.1.1. Informed Consent Process

- The investigator or his/her representative will explain the nature of the study to the participant or his/her legally authorized representative and answer all questions regarding the study.
  - Informed consent must be obtained before any study-related procedures are conducted, unless otherwise specified by the Protocol.
  - Informed consent must be obtained using the IRB/IEC-approved version in a language that is native and understandable to the participant. A template will be provided by the sponsor or its designee. The sponsor or its designee must review and acknowledge the site-specific changes to the ICF template. The ICF must include a statement that the sponsor or its designee and regulatory authorities have direct access to participant records.
  - The ICF must contain all required elements and describe the nature, scope, and possible consequences of the study in a form understandable to the study participant.
- Participants must be informed that their participation is voluntary. Participants or their legally authorized representative will be required to sign a statement of informed consent that meets the applicable requirements and regulations for the countries in which the study is being conducted as well as the IRB/IEC or study center.
- The participant must be informed that his/her personal study-related data will be used by the sponsor in accordance with local data protection laws. The level of disclosure must also be explained to the participant.
- The participant must be informed that his/her medical records may be examined by Clinical Quality Assurance auditors or other authorized personnel appointed by the sponsor, by appropriate IRB/IEC members, and by inspectors from regulatory authorities.
- The medical record must include a statement that written informed consent was obtained before the participant was enrolled in the study and the date the written consent was obtained. The authorized person obtaining the informed consent must also sign the ICF.
- Participants must provide consent to the most current version of the ICF during their participation in the study.

- A copy of the ICF(s) must be provided to the participant or the participant's legally authorized representative.
- Participants who are rescreened are required to sign a new ICF.

8.1.2. Screening Procedures

Screening is the interval between signing the ICF and the day the participant is randomized in the study (Day 1). Screening may not exceed 32 days. Assessments that are required to demonstrate eligibility may be performed over the course of 1 or more days during the screening process.

Results from the screening visit evaluations will be reviewed to confirm eligibility before randomization or the administration of study drug. Tests with results that fail eligibility requirements may be repeated once during screening if the investigator believes the results to be in error. For screening assessments that are repeated, the most recent available result before randomization will be used to determine eligibility.

See Sections 5.4 and 5.5 for information regarding screen failures and replacement of participants, respectively.

8.1.3. Interactive Response Technology Procedure

Each participant will be identified in the study by a participant ID number, which is a combination of the site ID and participant number. Site staff should contact the IRT to obtain the participant ID number during screening. Upon determining that the participant is eligible for randomization, the IRT will be contacted to randomize the participant and obtain the treatment assignment. Additionally, the IRT will be contacted at each regular study visit to dispense medication to the participant and to update the study drug supply. Additional details are provided in the IRT Manual.

8.1.4. Distribution of Reminder Cards and Diaries

Participants will be provided with a reminder card at each visit. The reminder card will indicate the date/time of the next visit and will also remind the participant that they should not take their morning dose of study drug on the day of the visits at Week 4, Week 12, Week 24, and Week 36, because they will take it after blood draws for [redacted] have been completed.

Participants will be instructed on the use of the diary. [redacted] Daily study drug administration will be recorded in the diary and verified by the study investigator/designee at study visits as shown in Table 3 and Table 4.

8.1.5. Demography and Medical History

8.1.5.1. Demographics and General Medical History

Demographic data and general medical history will be collected at screening by the investigator or qualified designee and will include year of birth/age, race, ethnicity, Fitzpatrick scale score, nicotine use, medical and surgical history, and current illnesses. Medical history will include

relevant medical or surgical treatment that is considered to be clinically significant by the investigator.

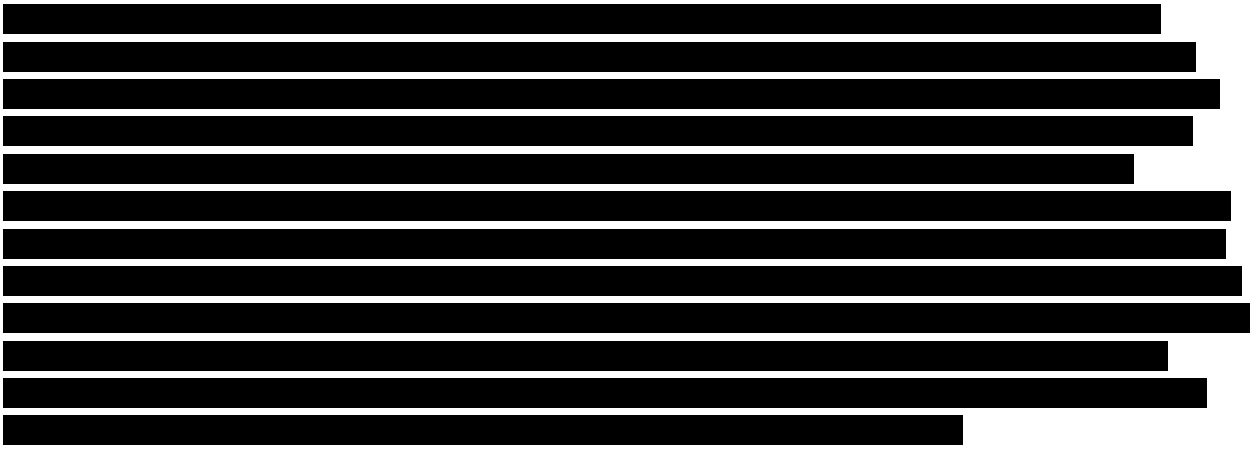
8.1.5.2. Disease Characteristics and Treatment History

A vitiligo medical and treatment history, including date of diagnosis, relevant disease characteristics, and prior treatments, including systemic treatments, phototherapy, and surgical procedures, will be collected at screening. A medical or surgical history of other conditions related to vitiligo or relevant to the conduct of this clinical trial will also be collected at screening.

8.2. Efficacy Assessments

8.2.2. Vitiligo Area Scoring Index

Areas affected by depigmentation due to vitiligo will be assessed using the VASI as shown in the SoA (see Table 3 and Table 4). It is based on a composite estimate of the overall area of vitiligo patches at baseline and the degree of macular repigmentation within these patches over time.



[redacted]

The T-VASI is calculated using a formula that includes contributions from all body regions (possible range: 0-100) as follows:

$$VASI = \Sigma \text{ [Hand Units]} \times \text{[Residual Depigmentation] All Body Sites}$$

The body is divided into the following 6 separate and mutually exclusive sites: (1) head/neck, (2) hands, (3) upper extremities (excluding hands), (4) trunk, (5) lower extremities (excluding feet), and (6) feet. The percentage of vitiligo involvement is estimated in hand units (%BSA) by the same investigator during the entire course of the study. Hand unit is based on the participant's hand size. The investigator uses his/her hand to mimic the participant's hand size to evaluate %BSA vitiligo involvement. The degree of depigmentation for each body site is determined and estimated to the nearest of the following percentages: 0, 10%, 25%, 50%, [redacted]. The T-VASI is then derived by multiplying the values assessed for the vitiligo involvement by the percentage of affected skin for each body site and summing the values of all body sites together (Hamzavi et al 2004).

[redacted]

[redacted]

8.2.6. Photography

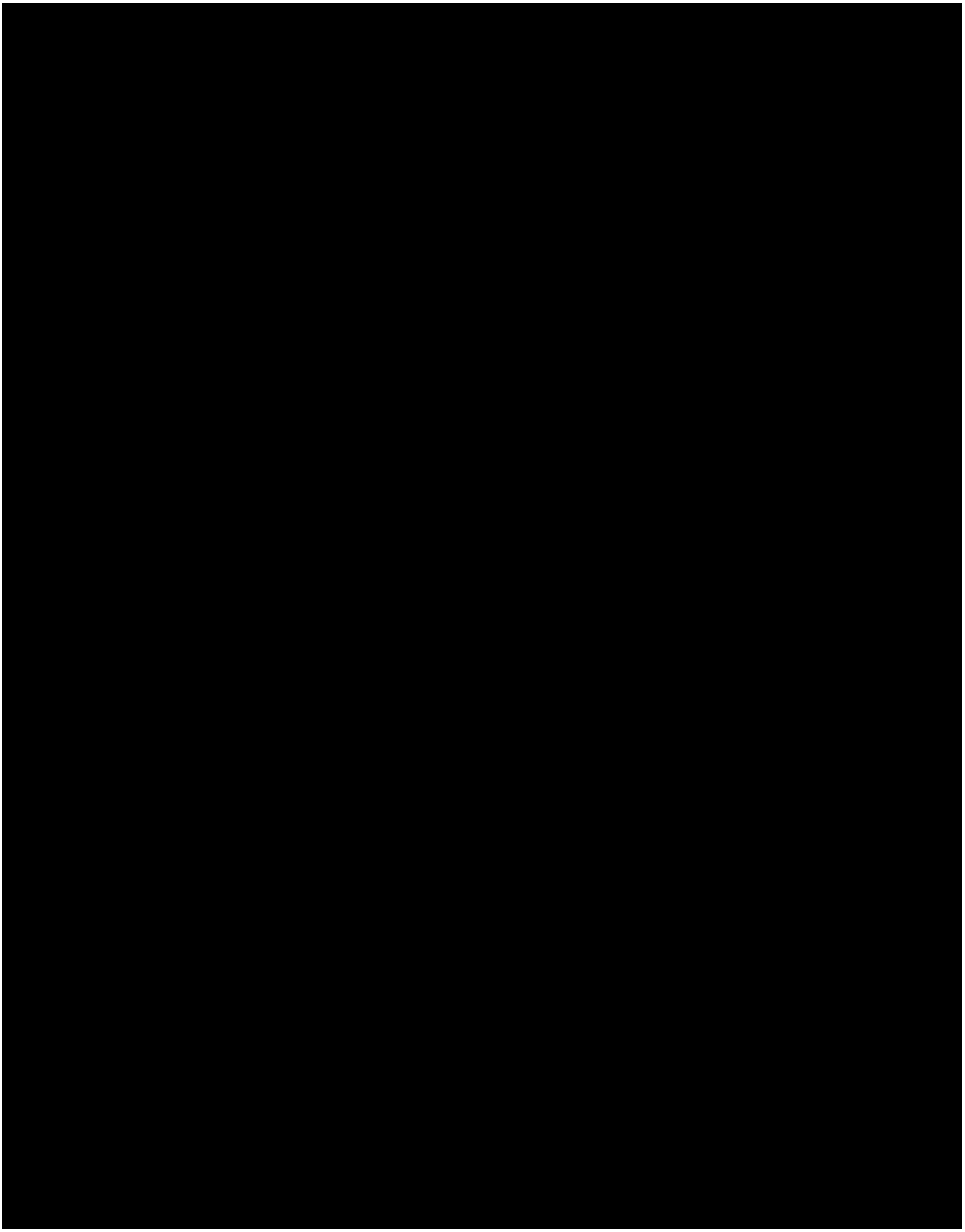
Photography of the face and/or body areas affected with vitiligo will be obtained at visits listed in Table 3 and Table 4.

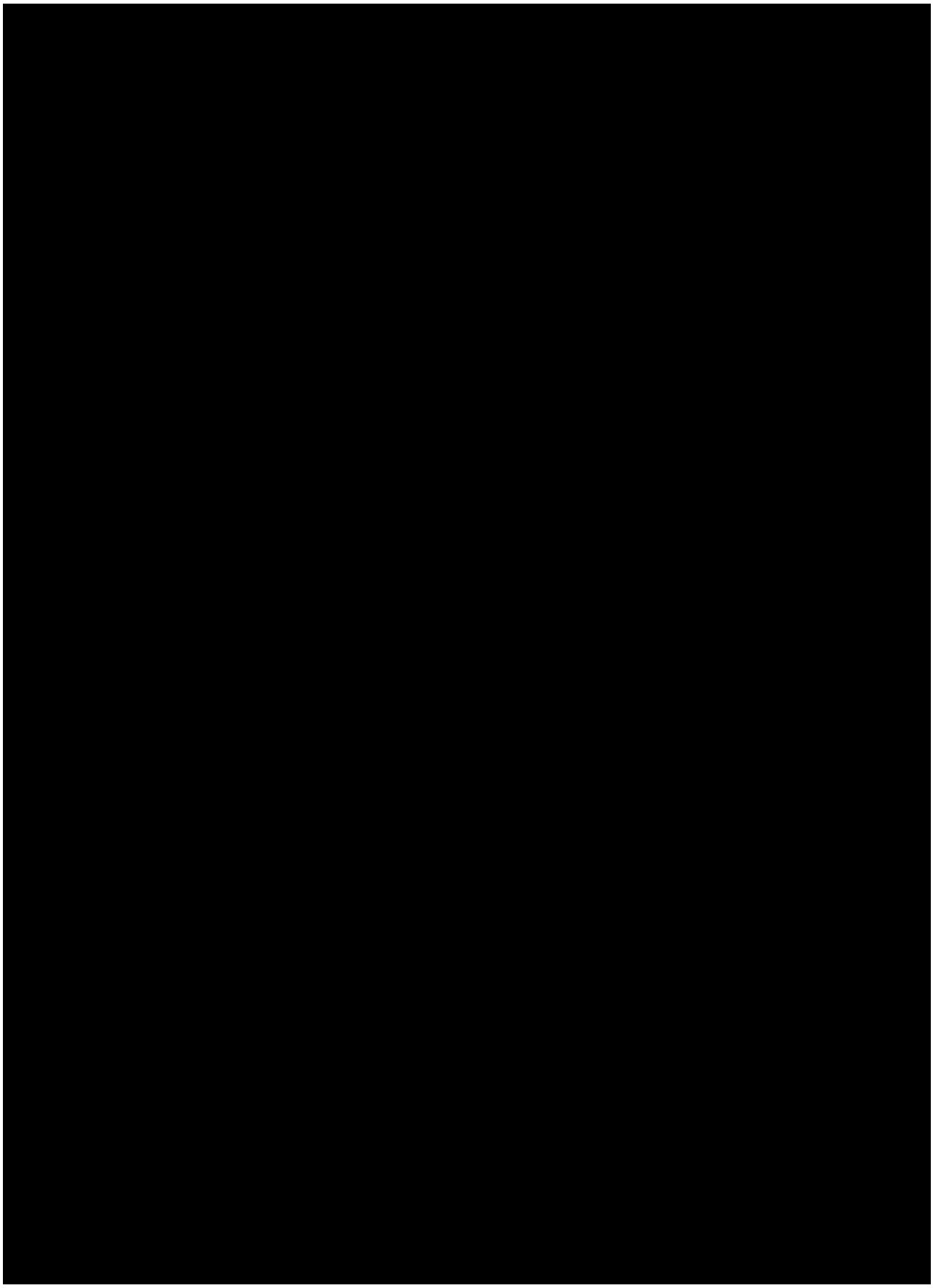
All sites will use 2-dimensional photography to photograph facial and nonfacial (targeted) depigmented areas.

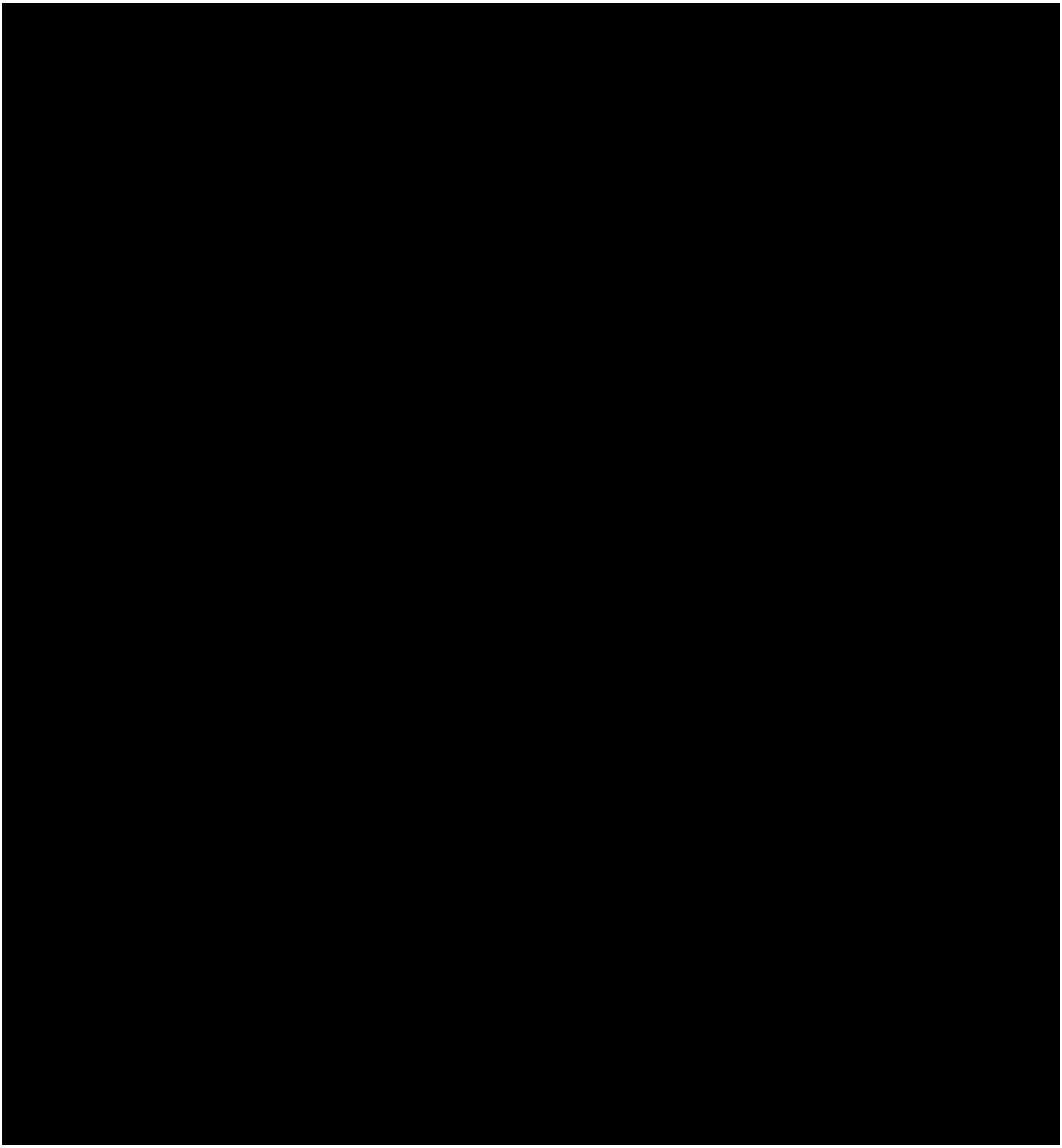
8.2.6.1. Definition of Targeted Nonfacial Vitiligo Depigmented Areas

At the baseline visit, depigmented nonfacial areas that are representative of the participant's overall disease will be selected as targeted nonfacial vitiligo depigmented areas. These areas will be assessed, measured, and documented in the participant's medical record at each subsequent visit during the study (see Table 3 and Table 4). A note should be made in the medical record, and the baseline photographs can be marked with the location of the targeted depigmented area. The genitalia area should not be photographed.

Photographic procedures will be standardized, and a full description of the methodology will be provided to the sites in a photography manual.







8.3. Safety Assessments

Planned timepoints for all safety assessments are provided in the SoA (see Table 3 and Table 4). See Section 6.5 for guidelines regarding the management of relevant laboratory or other safety assessment abnormalities.

The COVID-19 global pandemic may present challenges to the normal conduct of this study, requiring the outline of potential mitigation strategies described in Appendix E.

8.3.1. Adverse Events

Adverse events will be monitored from the time the participant signs the ICF until at least 28 (+ 7) days after the last dose of study drug [redacted]. Adverse events that begin or worsen after informed consent should be recorded on the Adverse Events Form in the eCRF regardless of the assumption of a causal relationship with the study drug. Conditions that were already present at the time of informed consent should be recorded on the Medical History Form in the eCRF. Adverse events (including laboratory abnormalities that constitute AEs) should be described using a diagnosis whenever possible rather than by individual underlying signs and symptoms.

Adverse events will be reported by the participant (or, when appropriate, by a caregiver, surrogate, or the participant's legally authorized representative). The investigator and any qualified designees are responsible for detecting, documenting, and recording events that meet the definition of an AE or SAE and remain responsible for following up on AEs that are serious, considered related to the study drug/procedures, or caused the participant to discontinue the study drug. Care will be taken not to introduce bias when detecting AEs and/or SAEs. Open-ended and nonleading verbal questioning of the participant, such as "How are you feeling?", is the preferred method to inquire about AE occurrences. Adverse events may also be detected when they are volunteered by the participant during the screening process or between visits or through physical examinations, laboratory tests, or other assessments. The definition, reporting, and recording requirements for AEs are described in Section 9.

All SAEs will be reported to the sponsor or designee within 24 hours. The investigator will submit any updated SAE data to the sponsor within 24 hours of it being available.

After the initial AE/SAE report, the investigator is required to proactively follow each participant at subsequent visits/contacts. All SAEs will be followed until resolution, stabilization, the event is otherwise explained, or the participant is lost to follow-up (as defined in Section 7.3).

If visits at Week 2, Week 6, Week 26, and Week 30 are scheduled as remote, adverse events will also be assessed remotely, via a phone call conducted by the study site; otherwise information will be captured during in-clinic visit (see Table 3 and Table 4).

8.3.2. Physical Examinations

Physical examinations will be conducted at the timepoints listed in Table 3 and Table 4.

A comprehensive physical examination will include height (at screening only) and body weight and assessment of the following organ or body systems: skin; head, eyes, ears, nose, and throat; thyroid; lungs; cardiovascular system; abdomen (liver, spleen); extremities; and lymph nodes. A brief neurologic examination will also be performed.

A targeted physical examination should be conducted as indicated by symptoms reported by the participant, AEs, or other findings. Abnormalities that are considered clinically significant in the judgment of the investigator (or designee) are to be reported as AEs.

Physical examinations must be performed by a medically qualified individual such as a licensed physician, a physician' assistant, or an advanced registered nurse practitioner, as local law permits.

8.3.3. Vital Signs

Vital signs measurements (to be taken before blood collection for laboratory tests) include blood pressure, pulse, respiratory rate, and body temperature and will be obtained as outlined in the SoA (see Table 3 and Table 4). If vital signs cannot be taken before blood collection for laboratory tests, there must be a minimum of 30 minutes from the completion of the blood collection procedures to the beginning of the vital signs collection. Blood pressure and pulse will be taken with the participant in the recumbent, semirecumbent, or sitting position after 5 minutes of rest. Abnormal vital sign results identified at any time after the first dose of study drug constitute an AE if they are considered clinically significant in the judgment of the investigator.

8.3.4. Electrocardiograms

Single 12-lead ECGs will be obtained as outlined in the SoA (see Table 3 and Table 4) using an ECG machine that automatically calculates the heart rate and measures PR, QRS, QT, and QTcF intervals; if necessary, calculation of such parameters is also acceptable if the ECG machine does not perform it automatically. All 12-lead ECGs will be performed with the participant in a recumbent or semirecumbent position after 5 minutes of rest. Prolonged QTcF values of $\geq$ 450 milliseconds are to be confirmed by performing 2 additional ECGs (within the next 5 minutes) and averaging the results to determine the averaged value.

Additional 12-lead ECGs may be performed at other visits as deemed clinically necessary. Electrocardiograms will be interpreted by the investigator at the site or designee, and the results will be used for immediate management of the participant's care. The decision to include or exclude a participant or withdraw a participant from the study based on an ECG flagged as "Abnormal, Clinically Significant" is the responsibility of the investigator, in consultation with the sponsor's medical monitor, as appropriate. Any abnormalities that are considered clinically significant in the judgment of the investigator are to be reported as AEs. ECGs should be performed in line with local standards and results reported in the eCRF.

8.3.5. Laboratory Assessments

See Table 13 for the list of clinical laboratory tests to be performed and Table 3 and Table 4 for the laboratory assessment visit schedule. A central laboratory will perform all clinical laboratory assessments for safety (ie, blood chemistries, hematology assessments, coagulation tests, endocrine function, and urinalysis), [redacted]. Additional testing may be required by the investigator or sponsor based on emerging safety data. All Protocol-required laboratory assessments must be conducted in accordance with the Laboratory Manual and Table 3 and Table 4.

If visits at Week 2, Week 6, Week 26, and Week 30 are scheduled as remote, blood collection will be conducted remotely (eg, participant's home or workplace); otherwise blood will be collected during in-clinic visit (see Table 3 and Table 4). At-home sampling for additional laboratory assessments may also be conducted; see Appendix E for COVID-19–related guidance.

Information regarding collection, processing, and shipping of samples for laboratory assessment is provided in the Laboratory Manual.

Clinically significant abnormal laboratory findings are those that are not associated with the underlying disease, unless judged by the investigator to be more severe than expected for the participant's condition. All laboratory tests with values considered clinically significantly abnormal during participation in the study (including any unscheduled testing within the 24-week follow-up period) should be repeated until the values return to normal or baseline or are no longer considered clinically significant by the investigator or medical monitor.

If screening laboratory assessments are performed more than 32 days before Day 1, then the tests must be repeated and eligibility confirmed before study drug administration on Day 1.

Laboratory sample collection on Day 1 must be performed before study drug administration.

See Section 9.1 for information regarding laboratory abnormalities that should be recorded as an AE in the eCRF.

Table 13: Required Laboratory Analytes

<table>
<tr><th>Blood Chemistries</th><th>Hematology</th><th>Urinalysis</th><th>Serology / Infection</th><th>Pregnancy Testing</th></tr>
<tr>
<td rowspan="4">• Albumin
• Alkaline phosphatase
• ALT
• AST
• Bicarbonate or CO_2
• Blood urea nitrogen or urea
• Calcium
• Chloride
• Creatine kinase
• Creatinine
• Glucose
• GGT
• Lactate dehydrogenase
• Phosphate
• Potassium
• Sodium
• Total bilirubin
• Direct bilirubin (if total bilirubin is elevated above 1.5 × ULN)
• Total protein</td>
<td rowspan="4">Complete blood count, including:
• Hemoglobin
• Mean corpuscular volume
• Hematocrit
• Platelet count
• Mean platelet volume
• In samples with abnormalities in platelet count or size distribution (as indicated by an automated analyzer), a blood film should be examined.
• Red blood cell count
• Red blood cell distribution width (RDW)
• WBC count
Differential count (% and absolute values), including:
• Basophils
• Eosinophils
• Lymphocytes
• Monocytes
• Neutrophils</td>
<td>• Color and appearance
• pH and specific gravity
• Bilirubin
• Glucose
• Ketones
• Leukocyte esterase
• Nitrite
• Occult blood
• Protein
• Microscopic evaluation (in case of abnormal urinalysis results)</td>
<td>• HBsAg*
• HBsAb
• HBcAb*
• HCVAb*
• HIV
• QuantiFERON-TB Gold test

*Observation: If either HBsAg or HBcAb is positive, a reflexive HBV DNA must be obtained. If HCVAb is positive, a reflexive HCV RNA must be obtained.</td>
<td>Pregnancy testing will be performed only for female participants. Further instructions are provided in Section 8.3.5.1.
• Serum FSH: for confirmation of nonchildbearing status for WONCBP (screening only)
• Serum pregnancy test (WOCBP): to be performed at visits indicated in Table 3 and Table 4.
• Urine pregnancy test (WOCBP): to be performed at visits indicated in Table 3 and Table 4.
Pregnancy tests (serum or urine) should be repeated if required by local regulations.</td>
</tr>
<tr>
<th>Lipid Panel</th>
<th>Coagulation</th>
<th>Thyroid Function Markers</th>
</tr>
<tr>
<td>• Total cholesterol
• Triglycerides
• LDL
• HDL

Observation: Fasting is not required.</td>
<td rowspan="2">• PT
• INR</td>
<td>• TSH
• Free T_4
Inflammation Marker
• hsCRP</td>
</tr>
</table>

Note: Additional tests may be required, as agreed upon by the investigator and sponsor, based on emerging safety data or to rule out a diagnosis.
Note: Alternative tests (ie, CO_2 or CO_2 Combining Power or HCO_3) are also allowed as per regional standard of care.

8.3.5.1. Pregnancy Testing

A serum FSH test will be required for all WONCBP during screening (before the first dose of study drug) for confirmation of nonchildbearing status. Women of nonchildbearing potential are defined as surgically sterile with a hysterectomy and/or bilateral oophorectomy OR postmenopausal, defined as amenorrhea ≥ 12 months prior to screening.

A serum pregnancy test will be required for all WOCBP during screening (before the first dose of study drug) and at the visits indicated in Table 3 and Table 4. Urine pregnancy tests will be performed locally as outlined in Table 3 and Table 4, as medically indicated (eg, in case of loss of menstrual cycle, when pregnancy is suspected), or per country-specific requirement (note that country-required urine pregnancy testing will be outlined and communicated to investigational sites under separate cover). If a urine pregnancy test is positive, the results should be confirmed with a serum pregnancy test.

If the serum pregnancy test is negative after a urine test was positive, the investigator will assess the potential benefit/risk to the participant and determine whether it is in the participant's best interest to resume study drug and continue participation in the study.

If a pregnancy is confirmed by a serum pregnancy test, the participant should be immediately discontinued (see Section 7.1). Additionally, Section 9.7 should be followed for reporting requirements.

8.3.5.2. Serology

Hepatitis B and C and HIV screening assessments will be performed at the screening visit to rule out infection; required analytes are shown in Table 13. Generally, hepatitis and HIV tests should be performed early in the screening process due to the length of time needed to obtain the results. Additional tests may be performed if clinically indicated.

Eligibility criteria for participants with a history of HCV infection should generally require participants to have completed curative antiviral treatment and require HCV viral quantitative RNA below the limit of quantification 12 weeks after the end of HCV therapy. A patient who is HCVAb positive but HCV RNA negative due to prior treatment or natural resolution should be eligible.

Reactivation of HBV can occur in chronic carriers of HBV infection (HBsAg-positive, undetectable or low HBV DNA, and normal ALT) who are not on HBV therapy or in individuals who have serologic evidence of a resolved prior HBV infection (ie, HBsAg-negative and anti-HBc–positive). While HBsAg-negative, anti-HBc–positive patients are at lower risk of HBV reactivation compared with HBsAg-positive patients, risk of HBV reactivation should be considered in all participants.

Participants with no prior history of HBV infection who have been vaccinated against HBV and who have a positive antibody against HBV surface antigen as the only evidence of prior exposure may participate in the study.

8.3.5.3. Tuberculosis Screening

At the time of screening, all participants will undergo TB screening. Depending on the TB status of the participant, different assessments may be performed.

The QFT-GIT is the preferred testing method. If the QFT-GIT cannot be performed, or if the results cannot be determined by the reference laboratory to be either positive or negative (eg, indeterminate), then participants may be screened using the PPD tuberculin skin test (Mantoux method; see Note 1) with approval of the medical monitor (or designee). The QFT-GIT is an indirect test for *Mycobacterium tuberculosis* infection (including disease) and is intended for use in conjunction with risk assessment, radiography (see Note 2), and other medical and diagnostic evaluations.

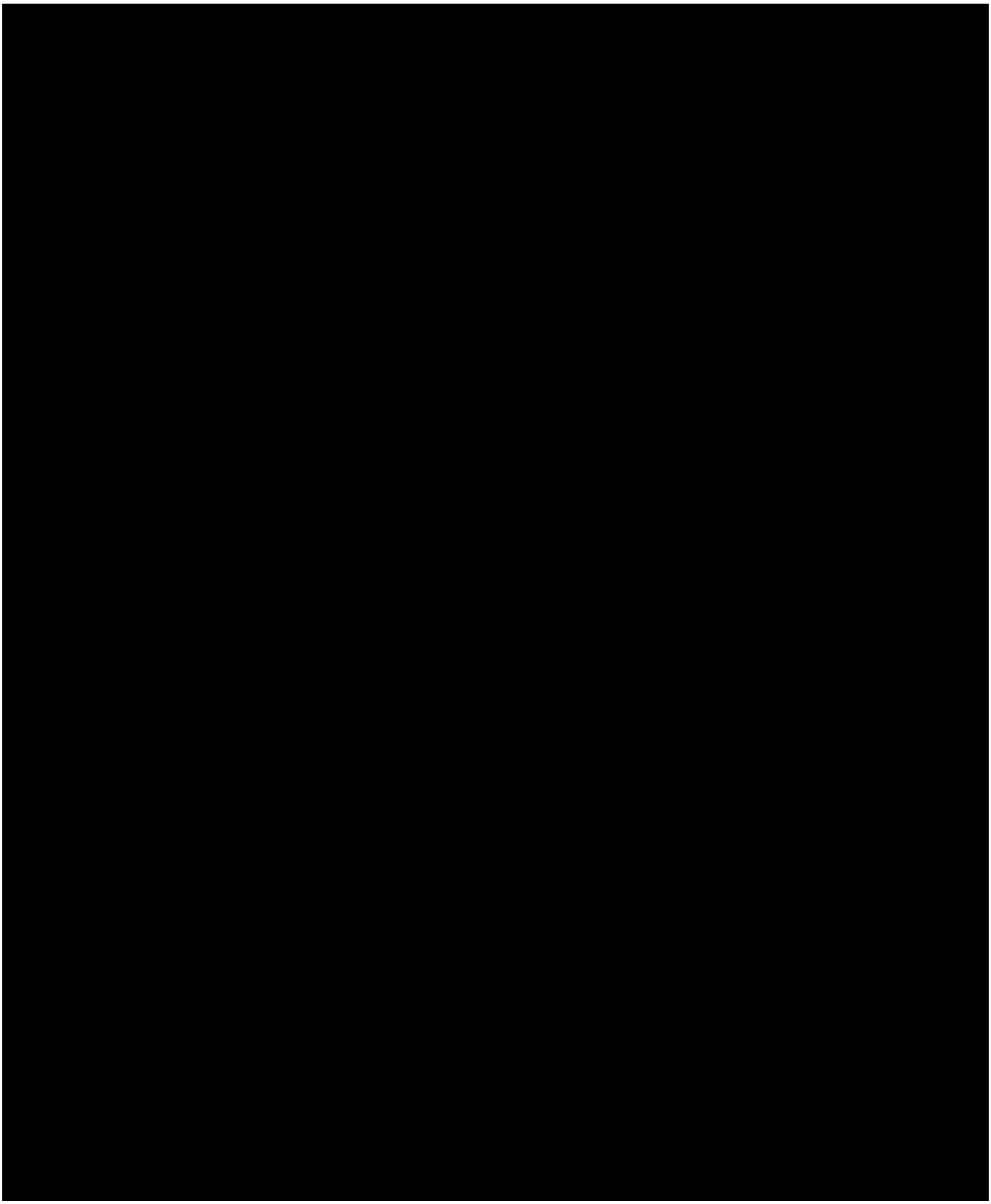
It is recommended that participants with a history of Bacille Calmette-Guérin vaccination be tested with the QFT-GIT, because the Mantoux/PPD tuberculin skin test may be positive due to vaccination.

A QFT-GIT or Mantoux/PPD tuberculin skin test is not required if the participant has previously received a documented adequate course of therapy for either latent TB infection (eg, 9 months of isoniazid in a locale where rates of primary multidrug TB resistance are < 5% or an acceptable alternative regimen) or active TB infection (an acceptable multidrug regimen). In such cases, a chest x-ray(s) or other appropriate diagnostic image, performed within 3 months of Day 1, is required (see Note 2). To be considered eligible for the study, the x-ray(s) must be negative for active TB infection as determined by a qualified radiologist (see Note 2). Documentation of adequate treatment for TB and negative chest x-ray(s) results must be obtained prior to Day 1.

Note 1: If the QFT-GIT cannot be performed, or if the results cannot be determined to be positive or negative (eg, indeterminate), then participants may be screened using the PPD tuberculin test (Mantoux method), with the approval of the medical monitor (or designee).

Participants must have the PPD test administered and evaluated by a health care professional 48 to 72 hours later in order to be eligible for the study, unless performed and documented within the past 3 months. The test should be performed according to local standards with induration of < 5 mm required for inclusion.

Note 2: At the discretion of the investigator or medical monitor (or designee), participants may be required to have a chest x-ray (posterior-anterior and lateral views) or other appropriate diagnostic image (ie, computed tomography or magnetic resonance imaging) taken at screening, or previously taken within 3 months prior to Study Day 1, and read by a qualified radiologist to potentially distinguish between latent and active TB. Documentation of adequate treatment for TB and negative chest x-ray(s) results must be obtained prior to Day 1.



8.6. Unscheduled Visits

Unscheduled visits may occur at any time at the investigator's (or designee's) discretion and appropriate clinical and laboratory tests may be performed as clinically indicated.

If there is a potential clinically significant abnormality in hematology or chemistry assessments (particularly in platelet count) during the study, an unscheduled visit within the following week should occur to repeat laboratory assessments (further details are provided in Table 9 and Table 10). The investigator must inform and consult the sponsor (or designee) regarding any hematologic abnormality.

8.7. End of Treatment and/or Early Termination

When the participant permanently discontinues study drug, whether the participant is terminating the study early or the participant has completed the study, the EOT visit should be conducted. If the EOT visit coincides with a regular study visit, the EOT evaluations will supersede those of that scheduled visit, and the data should be entered in the EOT visit in the eCRF. The participant should be encouraged to return for the follow-up visits (EOS,).

8.8. Follow-Up

Adverse events and SAEs must be reported up until at least 28 (+ 7) days after the last dose of study drug , and ongoing AEs and SAEs must be followed up until toxicities resolve, return to baseline, or are deemed irreversible, whichever is longer. Reasonable efforts should be made to have the participant return for the follow-up visit and report any AEs that may

occur during this period. In exceptional cases when the participant cannot return to the site for the safety follow-up visit, the participant should be contacted by telephone for assessment of AEs and SAEs and the site should properly document the contact.

8.8.1. Safety Follow-Up

The safety follow-up period is the interval between the EOT visit and the scheduled follow-up visit (EOS), which should occur 28 (+ 7 days) after the EOT visit (or after the last dose of study drug if the EOT visit was not performed).

[redacted]

9. ADVERSE EVENTS: DEFINITIONS AND PROCEDURES FOR RECORDING, EVALUATING, FOLLOW-UP, AND REPORTING

9.1. Definition of Adverse Event

Adverse Event Definition
• An AE is any untoward medical occurrence associated with the use of a drug in humans, whether or not it is considered drug-related. • An AE can therefore be any unfavorable or unintended sign (including an abnormal laboratory finding), symptom, or disease (new or exacerbated) temporally associated with the use of study drug.
Additional Guidance for Events Meeting the Adverse Event Definition
• Any safety assessments (eg, ECG, vital signs measurements), including those that worsen from baseline, considered clinically significant in the medical and scientific judgment of the investigator (ie, not related to progression of underlying disease) are to be reported as an AE. • Abnormal laboratory test results are to be reported as an AE if they are considered clinically meaningful, induce clinical signs or symptoms, require concomitant therapy, or require changes in study drug. Whenever possible, a diagnosis (eg, anemia, thrombocytopenia) should be recorded in the eCRF rather than the abnormal laboratory test result (eg, low hemoglobin, platelet count decreased). • Exacerbation of a chronic or intermittent pre-existing condition/disease, including either an increase in the frequency and/or intensity of the condition, is to be reported as an AE. • New conditions detected or diagnosed after the start of study drug administration are to be reported as an AE. • Signs, symptoms, or the clinical sequelae of a suspected drug-drug interaction are to be reported as an AE. • Signs and/or symptoms from dosing errors of a study drug (eg, overdose) or a concomitant medication are to be reported as an AE. • "Lack of efficacy," "disease progression," or "failure of expected pharmacological action" will not be reported as an AE or SAE. Such instances will be captured in the efficacy assessments. • A condition that leads to a medical or surgical procedure (eg, endoscopy, appendectomy) will be reported as an AE if it occurs after obtaining informed consent. If the condition is present before entering the study, then it should be captured as medical history. • Pre-existing diseases or conditions with expected fluctuations in signs or symptoms should be reported as an AE only if the investigator judges the fluctuation to have worsened more than expected during study participation.

9.2. Definition of Serious Adverse Event

If an event is not an AE per the definition above, then it cannot be an SAE even if serious conditions are met (eg, hospitalization for signs/symptoms of the disease under study, death due to progression of disease).

A serious adverse event is defined as any untoward medical occurrence that, at any dose:
a. Results in death
b. Is life-threatening The term "life-threatening" in the definition of "serious" refers to an adverse drug experience that places the participant, in the opinion of the initial reporter, at immediate risk of death from the adverse experience as it occurs. This does not include an adverse drug experience that, had it occurred in a more severe form, might have caused death.
c. Requires inpatient hospitalization or prolongation of existing hospitalization In general, hospitalization signifies that the participant has been detained (involving at least an overnight stay) at the hospital or emergency ward for observation and/or treatment that would not have been appropriate in the physician's office or outpatient setting. Complications that occur during hospitalization are AEs. If a complication prolongs hospitalization or fulfills any other serious criteria, the event is serious. When in doubt as to whether hospitalization occurred or was necessary, the AE should be considered serious. Hospitalization for elective treatment or planned surgery (eg, stent replacement, hip surgery) is not considered an SAE. Hospitalization for medical interventions in which no unfavorable medical occurrence occurred (ie, elective procedures or routine medical visits) is not considered an SAE.
d. Results in persistent or significant disability/incapacity • The term "disability" means a substantial disruption of a person's ability to conduct normal life functions. This definition is not intended to include experiences of relatively minor medical significance, such as uncomplicated headache, nausea, vomiting, diarrhea, influenza, and accidental trauma (eg, sprained ankle), that may interfere with or prevent everyday life functions but do not constitute a substantial disruption.
e. Is a congenital anomaly/birth defect
f. Is an important medical event An important medical event is an event that may not result in death, be immediately life-threatening, or require hospitalization but may be considered serious when, based on appropriate medical judgment, the event may jeopardize the participant and may require medical or surgical intervention to prevent one of the outcomes listed in the above definition. Examples of such events include new invasive or malignant cancers, intensive treatment in an emergency department or at home for allergic bronchospasm, blood dyscrasias, or convulsions that do not result in hospitalization, development of drug dependency or drug abuse, or suspected transmission of an infectious agent via a medicinal product. Secondary malignancies should always be considered SAEs.

9.3. Recording and Follow-Up of Adverse Events and/or Serious Adverse Events

Adverse Event and Serious Adverse Event Recording

- An AE/SAE that begins or worsens after informed consent is signed should be recorded on the Adverse Event Form in the eCRF. Conditions that were present at the time informed consent was given should be recorded on the Medical History Form in the eCRF.
- When an AE/SAE occurs, it is the responsibility of the investigator to review all documentation (eg, hospital progress notes, laboratory reports, and diagnostic reports) related to the event.
- The investigator (or delegate) will then record all relevant AE/SAE information in the eCRF.
- It is **not** acceptable for the investigator to send photocopies of the participant's medical records in lieu of completing the Adverse Event Form in the eCRF.
- There may be rare instances when copies of medical records for certain cases are requested. In this case, all participant identifiers, with the exception of the participant number, will be redacted by the site staff on the copies of the medical records before submission. These records can be submitted to Incyte Pharmacovigilance by email/fax per the contact information listed in the Study Reference Manual or as per SAE completing guidelines.
- The investigator will attempt to establish a diagnosis of the event based on signs, symptoms, and/or other clinical information. Whenever possible, the diagnosis (not the individual signs/symptoms) will be documented as the AE/SAE. When a clear diagnosis cannot be identified, each sign or symptom should be reported as a separate AE/SAE.

To the extent possible, each AE/SAE should be evaluated to determine the following:

- The severity grade (CTCAE v5.0 Grade 1 to 5). See below for further instructions on the assessment of intensity.
- Whether there is at least a reasonable possibility that the AE is related to the study drug: suspected (yes) or not suspected (no). See below for further instructions on the assessment of causality.
- The start and end dates, unless unresolved at the final safety follow-up visit [redacted].
- The action taken with regard to study drug as a result of the AE/SAE(s).
- The event outcome (eg, not recovered/not resolved, recovered/resolved, recovering/resolving, recovered/resolved with sequelae, fatal, unknown).
- The seriousness, as per the SAE definition provided in Section 9.2.
- The action taken with regard to the event. Note: If an AE is treated with a concomitant medication or nondrug therapy, this action should be recorded on the Adverse Event Form and the treatment should be specified on the appropriate eCRF (eg, Prior/Concomitant Medications).

Assessment of Intensity

The severity of AEs will be assessed using CTCAE v5.0 Grades 1 through 5. If an event is not classified by CTCAE, the severity of the AE will be graded according to the scale below to estimate the grade of severity.

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

- **Grade 1:** Mild; asymptomatic or mild symptoms; clinical or diagnostic observations only; treatment not indicated.
- **Grade 2:** Moderate; minimal, local, or noninvasive treatment indicated; limiting age-appropriate activities of daily living.
- **Grade 3:** Severe or medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care activities of daily living.
- **Grade 4:** Life-threatening consequences; urgent treatment indicated.
- **Grade 5:** Fatal.

Assessment of Causality

- The investigator is obligated to assess the relationship between study drug and each occurrence of each AE/SAE.
- A "reasonable possibility" of a relationship conveys that there are medical facts, evidence, and/or arguments to suggest a causal relationship, rather than that a relationship cannot be ruled out.
- The investigator will use clinical judgment to determine the possibility of a relationship.
- The investigator will also consult the RSI in the IB or Product Information for study drug, or marketed products, respectively, in making his/her assessment.
- Alternative causes, such as underlying or concurrent disease(s), concomitant therapy, and other risk factors, as well as the temporal relationship of the event to study drug administration, will be considered and investigated.
- 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.
- With regard to assessing causality of SAEs:
  - There may be situations in which an SAE has occurred and the investigator has minimal information to include in the initial report. However, the causality assessment is one of the criteria used when determining regulatory reporting requirements. **Therefore, it is very important that the investigator always make an assessment of causality based on the available information for every event before the initial transmission of the SAE.**
  - The investigator may change his/her opinion of causality in light of follow-up information and submit the updated causality assessment.

Follow-Up of Adverse Events and Serious Adverse Events
• The investigator is obligated to perform or arrange for the conduct of supplemental measurements and/or evaluations as medically indicated or as requested by the sponsor to elucidate the nature and/or causality of the AE or SAE as fully as possible. This may include additional laboratory tests or investigations, histopathological examinations, or consultation with other health care professionals. • Once an AE is detected, it should be followed in the AE eCRFs until it has resolved or until it is judged to be permanent; assessment should be made at each visit (or more frequently if necessary) of any changes in severity, the suspected relationship to the study drug, the interventions required to treat the event, and the outcome. • When the severity of an AE changes over time for a reporting period (eg, between visits), each change in severity will be reported as a separate AE. • If a participant dies during participation in the study or during a recognized follow-up period, the investigator will provide the sponsor with a copy of any postmortem findings, including histopathology. • Updated SAE information will be recorded in the originally completed eCRF and reported to Incyte Pharmacovigilance (either via email/fax if paper SAE form is used or in the SAE EDC CRF) until resolution, stabilization, the event is otherwise explained, or the participant is lost to follow-up. • Any updated SAE data (including SAEs being downgraded to nonserious) will be submitted to the sponsor (or designee) within 24 hours of receipt of the information.

See Appendix D for the management of potential Hy's Law cases.

9.4. Reporting of Serious Adverse Events

Regardless of suspected causality (eg, relationship to study drug or study procedures), all SAEs occurring after the participant has signed the ICF through the last study visit (or up until the end of the safety follow-up period, whichever occurs later) must be reported to the sponsor (or designee) immediately, without undue delay but not later than within **24 hours** of obtaining knowledge of its occurrence unless otherwise specified by the Protocol. The investigator will submit any updated SAE data to the sponsor (or designee) immediately, without undue delay but not later than within 24 hours of it being available.

Investigators are not obligated to actively seek SAE information after conclusion of study participation. If the investigator learns of any SAE, including death, at any time after a participant has been discharged from the study, and he/she considers the event to be reasonably related to the study drug or study participation, then the investigator must notify the sponsor (or designee) within 24 hours of becoming aware of the event.

After the initial AE/SAE report, the investigator is required to proactively follow each participant at subsequent visits/contacts. All SAEs will be followed until resolution, stabilization, the event is otherwise explained, or the participant is lost to follow-up (as defined in Section 7.3).

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

If the SAE is not documented in the RSI of the IB for the study drug (new occurrence) and is thought to be related to the study drug, the sponsor or its designee may urgently require further

information from the investigator for expedited reporting to health authorities. The sponsor or its designee may need to issue an Investigator Notification to inform all investigators involved in any study with the same drug that this SAE has been reported. Suspected unexpected serious adverse reactions will be collected and reported to the competent authorities and relevant ethics committees in accordance with Directive 2001/20/EC or as per national regulatory requirements in participating countries.

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

Investigator safety reports must be prepared for suspected unexpected serious adverse reactions according to local regulatory requirements and sponsor policy and forwarded to investigators as necessary.

An investigator who receives an investigator safety report describing an SAE or other specific safety information (eg, summary or listing of SAEs) from the sponsor will review and then file it along with the IB and will notify the IRB/IEC, if appropriate, according to local requirements.

Serious Adverse Event Reporting

- Information about all SAEs is collected and recorded on the Adverse Event Form in the eCRF.
- The investigator must report within 24 hours of learning of its occurrence any SAE via the EDC system (primary method) or by completing the Serious Adverse Event Report Form in English (only if the EDC system is not available. The contact information for Incyte Pharmacovigilance by email/fax is listed in the Study Reference Manual or as per the Incyte Reference Guide for Completing the Serious Adverse Event Report Form).
- In circumstances where the EDC system is not accessible for reporting SAE information (initial and/or follow-up SAE information) to the sponsor within 24 hours, refer to the Incyte Reference Guide for Completing the Serious Adverse Report Form. Once the EDC system is functional, the SAE report should be retrospectively added to the EDC system and follow-up should be completed through the EDC. The original copy of the Serious Adverse Event Report Form and the email or facsimile confirmation sheet must be kept at the study site (refer to the Incyte Reference Guide for Completing the Serious Adverse Report Form or Study Reference Manual for details and for the email address or fax number).
- Follow-up information is also recorded in the eCRF and transmitted to Incyte Pharmacovigilance via the EDC system. The follow-up report should include information that was not provided previously, such as the outcome of the event, treatment provided, action taken with study drug because of the SAE (eg, dose reduced, interrupted, or discontinued), or participant disposition (eg, continued or withdrew from study participation). Each recurrence, complication, or progression of the original event should be reported as follow-up to that event, regardless of when it occurs.

9.5. Events of Clinical Interest

Not applicable.

9.5.1. Adverse Events of Special Interest

Not applicable.

9.6. Emergency Unblinding of Treatment Assignment

In case of a medical emergency, for a participant's safety management, the procedure for emergency unblinding is provided to the investigator in the IRT Manual. If a participant's treatment assignment is unblinded, the sponsor or its designee should be notified immediately by telephone for awareness.

If an investigator, the site personnel performing assessments, or a participant is unblinded, then the participant must discontinue study drug unless there are ethical reasons to have the participant remain on the study treatment. In these cases, the investigator must obtain specific approval from the sponsor's (or its designee's) medical monitor for the participant to continue in the study.

9.7. Pregnancy

Pregnancy, in and of itself, is not regarded as an AE unless there is suspicion that the study drug may have interfered with the effectiveness of a contraceptive medication or method. When a pregnancy has been confirmed in a participant during maternal or paternal exposure to study drug, the following procedures should be followed in order to ensure safety:

- The study drug must be discontinued immediately (female participants only).
- The investigator must complete and submit the Incyte Clinical Trial Pregnancy Form to the sponsor or its designee within **24 hours** of learning of the pregnancy.

Data on fetal outcome are collected for regulatory reporting and drug safety evaluation. Follow-up should be conducted for each pregnancy to determine outcome, including spontaneous or voluntary termination, details of the birth, and the presence or absence of any birth defects, congenital abnormalities, or maternal and/or newborn complications, by following until the first well-baby visit. Pregnancy should be recorded on a Clinical Trial Pregnancy Form and reported by the investigator to the sponsor or its designee. Pregnancy follow-up information should be recorded on the same form and should include an assessment of the possible causal relationship to the sponsor's study drug to any pregnancy outcome, as well as follow-up to the first well-baby visit or the duration specified in local regulations, whichever is later. Refer to the Incyte Reference Guide for Completing the Clinical Trial Pregnancy Form or Study Reference Manual.

Any SAE occurring during pregnancy of a study participant must be recorded on the Serious Adverse Event Report Form and submitted to the sponsor or its designee.

Abnormal pregnancy outcomes (eg, spontaneous abortion, fetal death, stillbirth, congenital anomalies, or ectopic pregnancy) are considered SAEs (if occurring in the study participant) and must be reported as described in Section 9.4. If an abnormal pregnancy outcome is reported in a study participant's partner, the event should be reported to the sponsor on the Clinical Trial Pregnancy Form.

9.8. Warnings and Precautions

Special warnings or precautions for the study drug, derived from safety information collected by the sponsor or its designee, are presented in the IB. Additional safety information collected between IB updates will be communicated in the form of Investigator Notifications. Any important new safety information should be discussed with the participant during the study as necessary. If new significant risks are identified, they will be added to the ICF.

9.9. Product Complaints

The sponsor collects product complaints on study drugs and drug delivery systems used in clinical studies in order to ensure the safety of study participants, monitor quality, and facilitate process and product improvements.

All product complaints associated with material packaged, labeled, and released by the sponsor or its designee will be reported to the sponsor. All product complaints associated with other study material will be reported directly to the respective manufacturer.

The investigator or his/her designee is responsible for reporting a complete description of the product complaint via email or other written communication to the sponsor contact or respective manufacturer as noted in the packaging information. Any AE associated with a product complaint should be recorded as described in Section 9.3.

If the investigator is asked to return the product for investigation, he/she will return a copy of the product complaint communication with the product.

9.10. Treatment of Overdose

There has been no clinical experience with overdose of INCB054707. Treatment of overdose should consist of general supportive measures.

10. STATISTICS

10.1. Sample Size Determination

[redacted]

10.2. Populations for Analysis

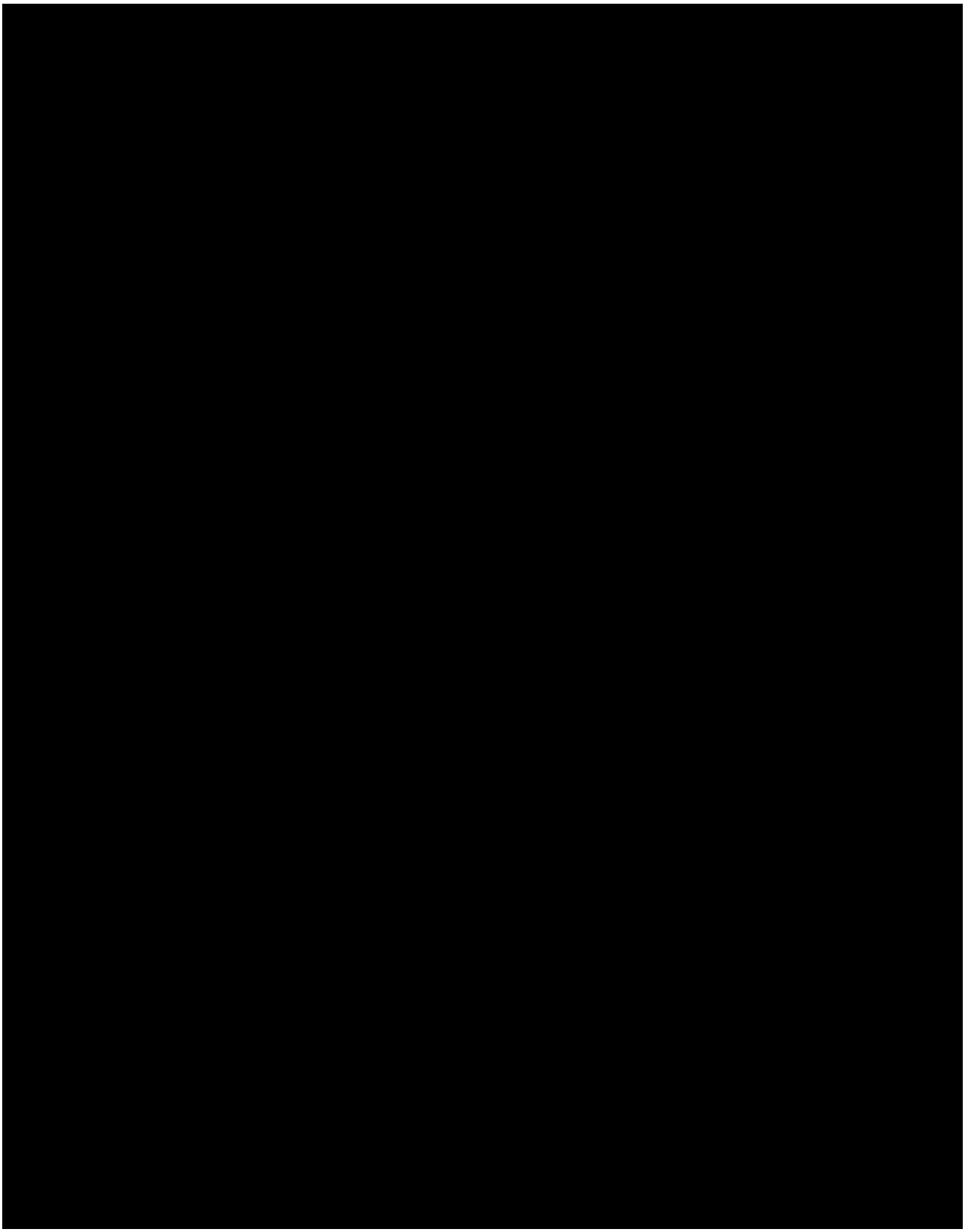
The populations for analysis are provided in Table 16.

Table 16: Populations for Analysis

Population	Description
ITT	The ITT population includes all randomized participants. Treatment groups for this population will be defined according to the treatment assignment at randomization.
Safety	The safety population includes all participants who received at least 1 dose of study drug, Treatment groups for this population will be determined according to the actual treatment the participant received on Day 1.
[redacted]	

10.3. Level of Significance

[redacted]



10.4.1. Primary Analysis

[redacted]

10.4.2. Secondary Analysis

[redacted]

10.4.3. Safety Analyses

Safety analyses will be conducted for the safety population. A TEAE is any AE either reported for the first time or worsening of a pre-existing event after the first dose of study drug until the end of the safety follow-up period. Analysis of AEs will be limited to TEAEs, but data listings will include all AEs regardless of their timing to study drug administration. Adverse events will be tabulated by the MedDRA preferred term and system organ class. Severity of AEs will be based on the National Cancer Institute CTCAE v5.0 using Grades 1 through 5.

The subset of AEs considered by the investigator to have a relationship to study drug will be considered to be treatment-related AEs. If the investigator does not specify the relationship of the AE to study drug, then the AE will be considered treatment-related. The incidence of AEs and treatment-related AEs will be tabulated.

The clinical laboratory data will be analyzed using summary statistics; no formal treatment group comparisons are planned. Laboratory test values outside the normal range will be assessed for severity based on the normal ranges for the clinical reference laboratory. The incidence of abnormal laboratory values and shift tables relative to baseline will be tabulated. Descriptive statistics and mean change from baseline will be determined for vital signs (blood pressure, pulse, respiratory rate, and body temperature) at each assessment time. Descriptive statistics and mean change from baseline will be determined for each ECG parameter at each assessment time.

10.5. Interim Analysis

No formal interim analysis is planned in this study. However, preplanned analyses of safety (blinded data) will be provided to an external DSMB (see Section 5.6) as specified in the DSMB charter. The process by which the DSMB will review data and make recommendations and decisions will be documented in the DSMB charter. The SAP will describe the planned analyses in greater detail.

11. SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

11.1. Investigator Responsibilities

- The Protocol, Protocol amendments, ICF, IB, and other relevant documents (eg, advertisements) must be submitted to an IRB/IEC by the investigator and reviewed and approved by the IRB/IEC before the study is initiated.
- The investigator is responsible for ensuring that the safety reports provided by the sponsor are reviewed and processed in accordance with regulatory requirements, the policies and procedures established by the IRB/IEC, and institutional requirements.
- Any amendments to the Protocol will require approval from both Health Authorities and IRB/IEC before implementation of changes made to the study design, except for changes necessary to eliminate an immediate hazard to study participants.
- The investigator will be responsible for the following:
  - Providing written summaries of the status of the study to the IRB/IEC annually or more frequently in accordance with the requirements, policies, and procedures established by the IRB/IEC.
  - Notifying the IRB/IEC of SAEs or other significant safety findings as required by IRB/IEC procedures.
  - Providing oversight of the conduct of the study at the site and adherence to GCP, IRB/IEC requirements, institutional requirements, and applicable laws and country-specific regulations.
- Adhering to the Protocol as described in this document and agreeing that changes to the Protocol procedures, with the exception of medical emergencies, must be discussed and approved, first, by the sponsor or its designee and, second, by the IRB/IEC. Each investigator is responsible for enrolling participants who have met the specified eligibility criteria.
- Retaining records in accordance with all local, national, and regulatory laws but for a minimum period of at least 2 years after the last marketing application approval in an ICH region and until there are no pending or contemplated marketing applications in an ICH region, or if not approved, 2 years after the termination of the test article for investigation to ensure the availability of study documentation should it become necessary for the sponsor or a regulatory authority to review.
  - The investigator must not destroy any records associated with the study without receiving approval from the sponsor. The investigator must notify the sponsor or its designee in the event of accidental loss or destruction of any study records. If the investigator leaves the institution where the study was conducted, the sponsor or its designee must be contacted to arrange alternative record storage options.
  - All eCRF data entered by the site (including audit trail), as well as computer hardware and software (for accessing the data), will be maintained or made available at the site in compliance with applicable record retention regulations. The sponsor will retain the original eCRF data and audit trail.

11.1.1. Identification of the Coordinating Principal Investigator

A coordinating principal investigator will be appointed by the sponsor before the end of the study. As part of his/her responsibilities, the coordinating principal investigator will review the final CSR. Agreement with the final CSR will be documented by the dated signature of the coordinating principal investigator.

11.2. Data Management

Data management will be performed in a validated EDC system. The investigator will be provided with access to an EDC system so that an eCRF can be completed for each participant.

The site will be provided with eCRF completion guidelines for instructions on data entry in the eCRF. The study monitor will reference the Monitoring Plan in order to ensure that each issue identified is appropriately documented, reported, and resolved in a timely manner in accordance with the plan's requirements. Other data outside the EDC system required in the study conduct of the Protocol such as documents or results transmitted to the sponsor via a central laboratory or specialized technical vendors and, as designated by the sponsor, will have their own data flow management plans, study charters, [redacted] as applicable.

The sponsor (or designee) will be responsible for:

- Managing the integrity of the data and the quality of the conduct of the study, such as ensuring that study monitors perform ongoing source data verification to confirm that data entered into the eCRF by authorized site personnel are accurate, complete, and verifiable from source documents; that the safety and rights of participants are being protected; and that the study is being conducted in accordance with the currently approved Protocol and any other study agreements, ICH GCP, and all applicable regulatory requirements.
- Managing and reconciling the data generated, and/or collected, including documents and results such as laboratory or imaging data analyzed centrally by a designated vendor of the sponsor.

The investigator will be responsible for:

- Recording, or ensuring the recording of, all relevant data relating to the study in the eCRF.
- Delivering, or ensuring the delivery of, all other results, documents, data, know-how, or formulas relating to the study to the sponsor or designee electronically and/or centrally (eg, laboratory data, imaging data, [redacted] photographs, diary data), or as otherwise specified in the Protocol.
- Maintaining adequate and accurate source documents and trial records that include all pertinent observations on each of the site's trial participants. Source data should be attributable, legible, contemporaneous, original, accurate, and complete. Changes to source data should be traceable, should not obscure the original entry, and should be explained if necessary (eg, via an audit trail). Source data are in general all information in original records and certified copies of original records of clinical findings, observations, or other activities in a clinical trial necessary for the reconstruction and evaluation of the trial. Source data are contained in source documents (original records or certified copies).

- Verifying that data entries are accurate and correct by physically or electronically signing the eCRF.
- Maintaining accurate documentation (source data) that supports the information entered in the eCRF, or sent to a central vendor designated by the sponsor, or as described in other study and data flow manuals.
  - Source documents provide evidence for the existence of the participant and substantiate the integrity of the data collected. Source documents are filed and available at the investigator's site. Examples of source documents are original documents, data, and records (eg, hospital records, electronic hospital records, clinical and office charts, laboratory notes, memoranda, participants' diaries or evaluation checklists, pharmacy dispensing records, recorded data from automated instruments, copies or transcriptions certified after verification as being accurate copies, microfiches, photographic negatives, microfilm or magnetic media, x-rays, participants' files, and e-records/records kept at the pharmacy, at the laboratories, and at medico-technical departments involved in the clinical trial).
  - Data entered in the eCRF that are transcribed from source documents must be consistent with the source documents or the discrepancies must be explained. The investigator may need to request previous medical records or transfer records, depending on the study. Current applicable medical records must be available.
- Sending participants' data, either as unique samples, or copies, or photographs, to be evaluated centrally or analyzed centrally, or both, by a qualified vendor designated by the sponsor.
- Permitting study-related monitoring, sponsor audits, IRB/IEC review, and regulatory inspections by providing direct access to source data and other relevant clinical study documents.
  - Monitoring: Qualified representatives of the sponsor or its designee, study monitors, will monitor the study according to a predetermined plan. The investigator must allow the study monitors to review any study materials and participant records at each monitoring visit.
  - Auditing: Qualified representatives of the sponsor or its designee may audit the clinical study site and study data to evaluate compliance with the Protocol, applicable local clinical study regulations, and overall study conduct. The investigator must allow the auditors to review original source records and study documentation for all participants.
  - Regulatory inspection: Regulatory authorities may conduct an inspection of the study and the site at any time during the development of an investigational product. The investigator and staff are expected to cooperate with the inspectors and allow access to all source documents supporting the eCRFs and other study-related documents. The investigator must immediately notify the sponsor when contacted by any regulatory authority for the purposes of conducting an inspection.

11.3. Data Privacy and Confidentiality of Study Records

The investigator and the sponsor or its designee must adhere to applicable data protection laws and regulations. The investigator and the sponsor or its designee are responsible for ensuring that sensitive personal information is handled in accordance with local data protection laws (including but not limited to HIPAA and GDPR) as applicable. Appropriate consent for collection, use and disclosure and/or transfer (if applicable) of personal information must be obtained in accordance with local data protection laws.

Participant names will not be supplied to the sponsor or its designee. Only the participant number will be recorded in the eCRF; if the participant's name appears on any other document (eg, laboratory report), it must be obliterated on the copy of the document to be supplied to the sponsor or its designee. Study findings stored on a computer will be stored in accordance with appropriate technical and organizational measures as required by local data protection laws.

Records and documents, including signed ICFs, pertaining to the conduct of this study must be retained by the investigator for 30 years after study completion unless local regulations require otherwise. No records may be destroyed during the retention period without the written approval of the sponsor. No records may be transferred to another location or party without written notification to the sponsor.

11.4. Financial Disclosure

Before study initiation, all clinical investigators participating in clinical studies subject to FDA Regulation Title 21 CFR Part 54 – Financial Disclosure by Clinical Investigators (ie, "covered studies") are required to submit a completed Clinical Investigator Financial Disclosure form that sufficiently details any financial interests and arrangements that apply. For the purpose of this regulation, "clinical investigator" is defined as any investigator or subinvestigator who is directly involved in the treatment or evaluation of research participants, including the spouse and each dependent child of the clinical investigator or subinvestigator. These requirements apply to both US and foreign clinical investigators conducting covered clinical studies.

Any new clinical investigators added to the covered clinical study during its conduct must also submit a completed Investigator Financial Disclosure Form. During a covered clinical study, any changes to the financial information previously reported by a clinical investigator must be reported to the sponsor or its designee. At the conclusion of the covered clinical study, the clinical investigators will be reminded of their obligations. In the event that the clinical investigator is not reminded, they nevertheless will remain obligated to report to the sponsor or its designee any changes to the financial information previously reported, as well as any changes in their financial information for a period of 1 year after completion of the covered clinical study.

11.5. Publication Policy

By signing the study Protocol, the investigator and his/her institution agree that the results of the study may be used by the sponsor, Incyte Corporation (Incyte), for the purposes of national and international registration, publication, and information for medical and pharmaceutical professionals. Study results will be published in accordance with applicable local and national regulations. If necessary, the authorities will be notified of the investigator's name, address, qualifications, and extent of involvement. The terms regarding the publication of study results

are contained in the agreement signed with the sponsor or its designee. A signed agreement will be retained by the sponsor or its designee.

The results of this study may be published or presented at scientific meetings. If this is foreseen, the investigator agrees to submit all manuscripts or abstracts to the sponsor before submission. This allows the sponsor to protect proprietary information and to provide comments.

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

Authorship will be determined in line with International Committee of Medical Journal Editors authorship requirements.

11.6. Study and Site Closure

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

The investigator may initiate study-site closure at any time, provided there is reasonable cause and sufficient notice is given in advance of the intended termination.

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

- Failure of the investigator to comply with the Protocol, the requirements of the IRB/IEC or local health authorities, the sponsor's procedures, or GCP guidelines.
- Inadequate recruitment of participants by the investigator.
- Discontinuation of further study treatment development.

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APPENDIX A. INFORMATION REGARDING EFFECTIVENESS OF CONTRACEPTIVE METHODS AND DEFINITIONS

Definitions

Woman of Childbearing Potential (WOCBP)

A woman is considered fertile following menarche and until becoming postmenopausal unless permanently sterile (see below).

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 no menses for 12 months without an alternative medical cause.
    - A high follicle-stimulating hormone (FSH) level in the postmenopausal range may be used to confirm a postmenopausal state in women not using hormonal contraception or hormonal replacement therapy (HRT). However, in the absence of 12 months of amenorrhea, confirmation with 2 FSH measurements in the postmenopausal range is required.
  - Female participants on HRT and whose menopausal status is in doubt will be required to use one of the nonhormonal highly effective contraception methods if they wish to continue their HRT during the study. Otherwise, they must discontinue HRT to allow confirmation of postmenopausal status before study enrollment.

For male participants of reproductive potential[a]

The following methods during the protocol-defined timeframe in Section 5.1 are highly effective:

- Use a male condom plus partner use of an additional contraceptive method when having penile-vaginal intercourse with a woman of childbearing potential who is not currently pregnant.
- Vasectomy with medical assessment of the surgical success (verified by site personnel's review of the participant's medical records)
- Sexual abstinence[b]
  - Be abstinent from penile-vaginal intercourse as their usual and preferred lifestyle (abstinent on a long-term and persistent basis) and agree to remain abstinent.

The following are **not** acceptable methods of contraception:

- Periodic abstinence (calendar, symptothermal, postovulation methods), withdrawal (coitus interruptus), spermicides only, and lactational amenorrhea method.
- Male condom with cap, diaphragm, or sponge with spermicide.
- Male and female condom cannot be used together.

Note: Men with a pregnant or breastfeeding partner must agree to remain abstinent from penile-vaginal intercourse or use a male condom during each episode of penile penetration.

For female participants who are WOCBP

The following methods during the protocol-defined timeframe in Section 5.1 that can achieve a failure rate of less than 1% per year when used consistently and correctly are considered highly effective birth control methods:

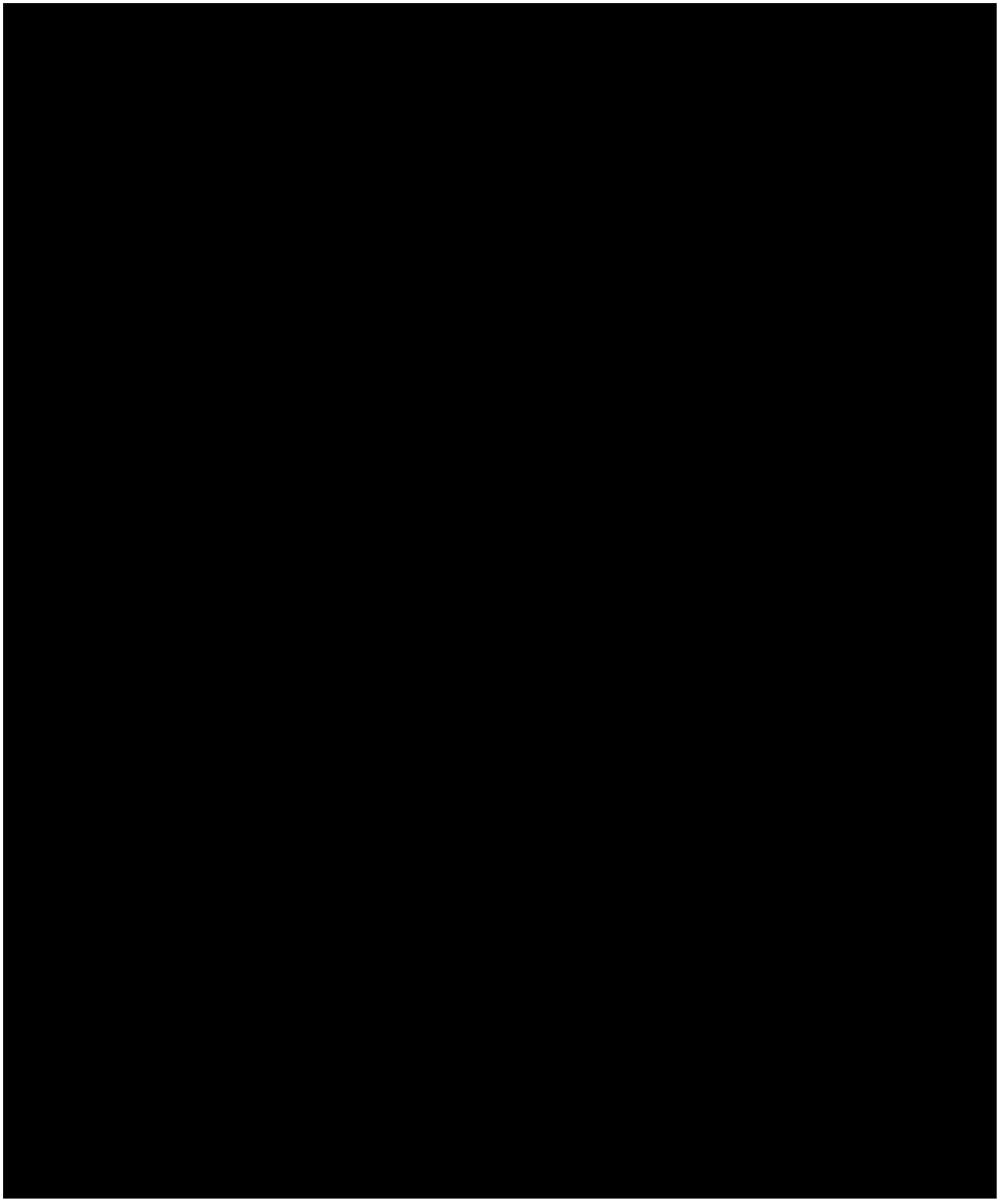
- Combined (estrogen and progestogen containing) hormonal contraception associated with inhibition of ovulation[c]
  - Oral
  - Intravaginal
  - Transdermal
- Progestogen-only hormonal contraception associated with inhibition of ovulation[c]
  - Oral
  - Injectable
  - Implantable[d]
- Intrauterine device[d]
- Intrauterine hormone-releasing system[d]
- Bilateral tubal occlusion[d]
- Vasectomized partner[d,e]
- Sexual abstinence[b]

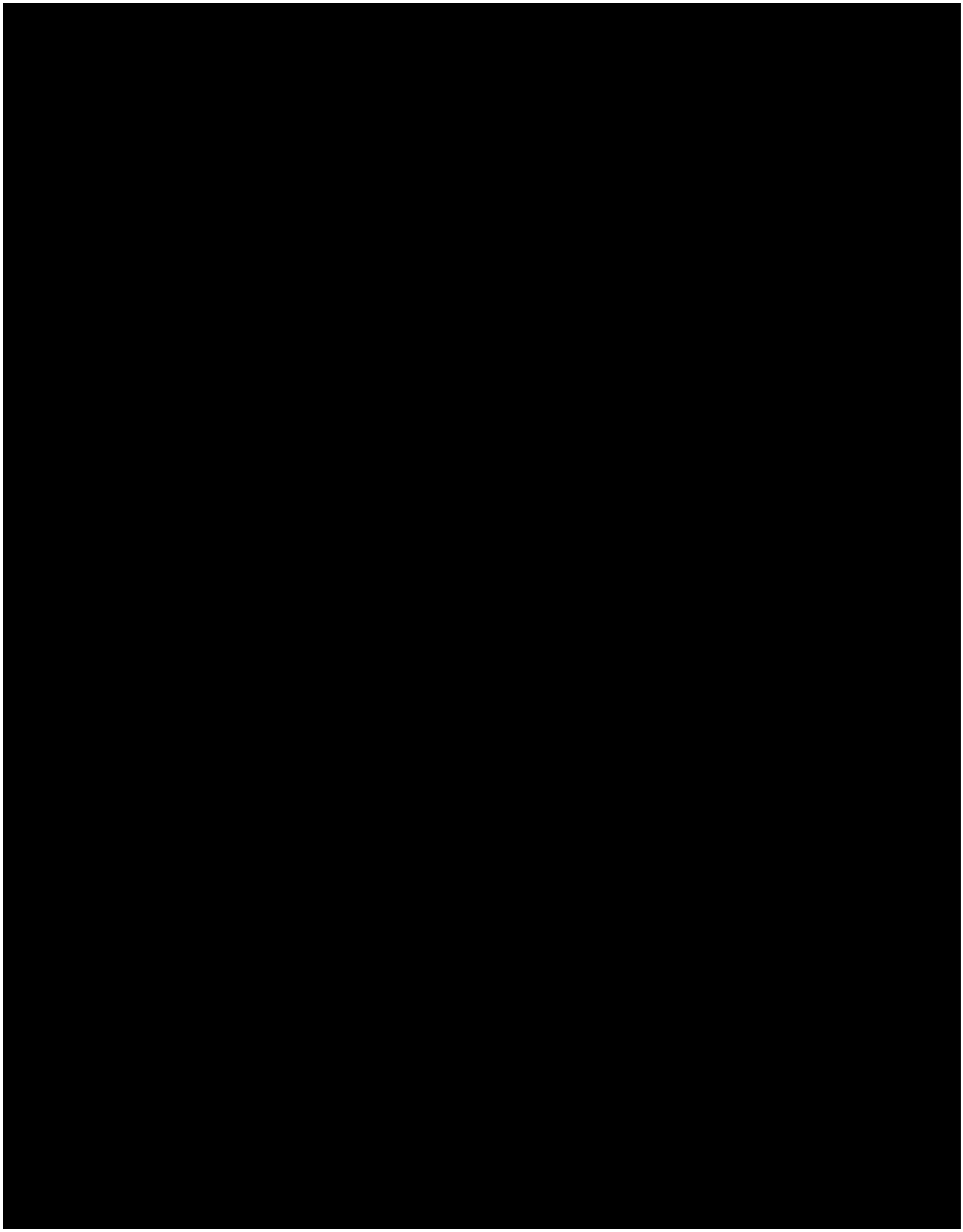
[a] If the male participant has a partner with childbearing potential, the partner should also use contraceptives.
[b] In the context of this guidance, sexual abstinence is considered a highly effective method only if defined as refraining from heterosexual intercourse during the entire period of risk associated with the study treatments. The reliability of sexual abstinence needs to be evaluated in relation to the duration of the clinical study and the preferred and usual lifestyle of the participant.
[c] Hormonal contraception may be susceptible to interaction with the investigational medicinal product, which may reduce the efficacy of the contraception method.
[d] Contraception methods that in the context of this guidance are considered to have low user dependency.
[,e] Vasectomized partner is a highly effective method of avoiding pregnancy provided that partner is the sole sexual partner of the woman of childbearing potential study participant and that the vasectomized partner has received medical assessment of the surgical success.
Source: Clinical Trials Facilitation and Coordination Group 2014.

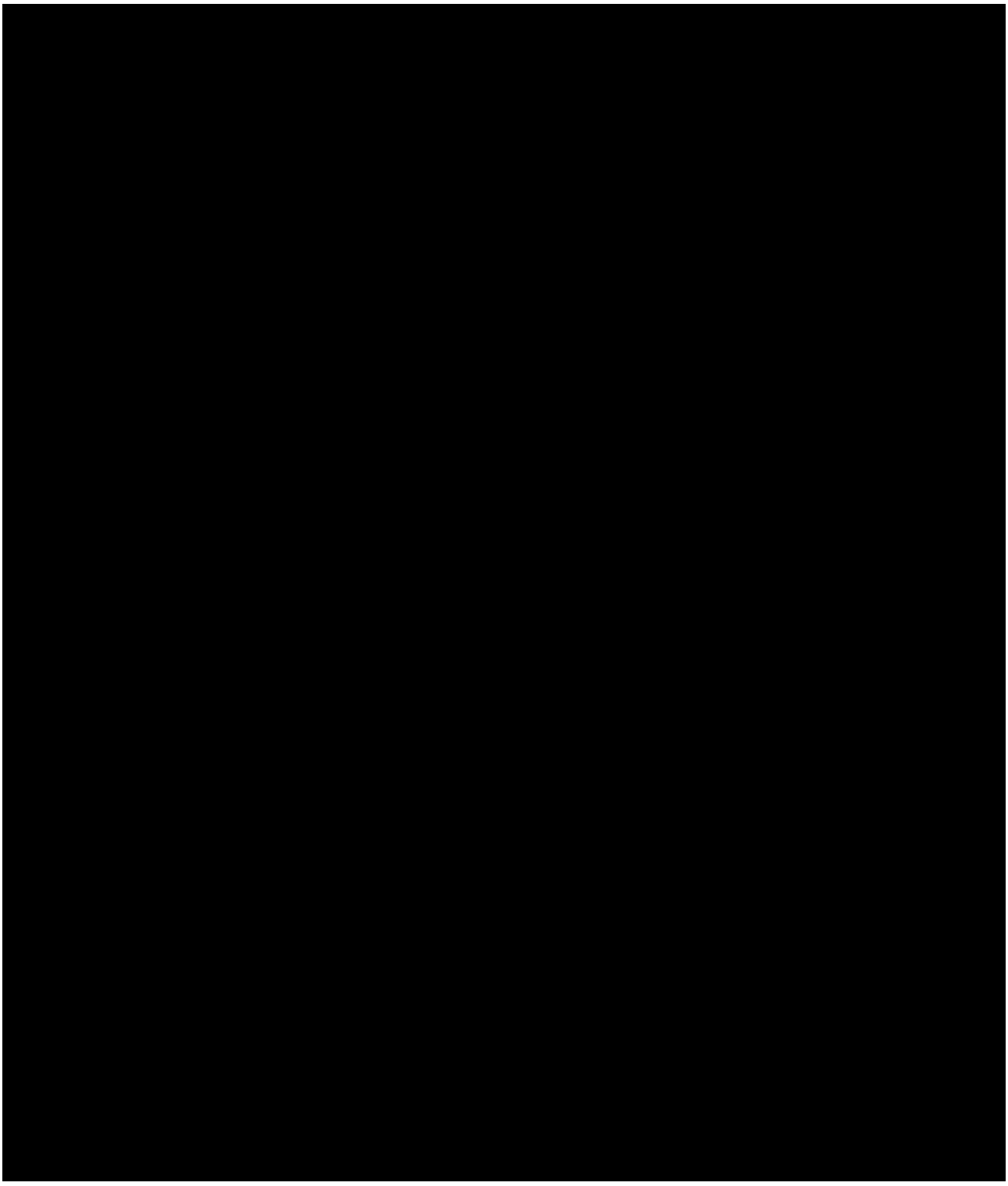
APPENDIX B. LIST OF STRONG/MODERATE SYSTEMIC CYP3A4 INHIBITORS AND STRONG SYSTEMIC CYP3A4 INDUCERS

Strong and Moderate Systemic CYP3A4 Inhibitors	Strong Systemic CYP3A4 Inducers
• Erythromycin • Troleandomycin, Clarithromycin, Telithromycin • Ciprofloxacin • Ketoconazole, Fluconazole, Itraconazole, Voriconazole, Posaconazole • Nefazodone • Diltiazem • Mibefradil • Verapamil • Aprepitant, Casopitant • Grapefruit/grapefruit juice • Seville oranges • Indinavir, Atazanavir, Nelfinavir, Ritonavir, Saquinavir, Boceprevir, Danoprevir, Elvitegravir, Lopinavir, Paritaprevir, Saquinavir, Telaprevir, Tipranavir, Ombitasvir, Cobicistat • Idelalisib • Conivaptan • Crizotinib • Cyclosporine • Dronedarone • Fluvoxamine • Imatinib • Tofisopam	• Rifampicin/rifampin • St John's wort • Phenytoin • Apalutamide • Carbamazepine • Bosentan • Efavirenz • Etravirine • Enzalutamide • Mitotane • Phenobarbital • Primidone

Note: Updated lists of CYP3A4 inhibitors/inducers can be found at Food and Drug Administration. Drug Development and Drug Interactions: Table of Substrates, Inhibitors and Inducers. Available at: https://www.fda.gov/drugs/drug-interactions-labeling/drug-development-and-drug-interactions-table-substrates-inhibitors-and-inducers.







APPENDIX E. COVID-19 PANDEMIC MITIGATION STRATEGIES AND INSTRUCTIONS

The COVID-19 global pandemic is an evolving situation and presents numerous challenges to the ongoing conduct of clinical trials. The sponsor has issued the following Protocol considerations to ensure participant safety is maintained and adequate benefit/risk analyses are applied relative to the completion of study procedures and maintaining the investigational product supply chain.

Recognizing the flexibility required to manage the impact of the pandemic on this clinical trial, additional details will be added as needed to respective study manuals and project plan documents and communicated to the investigative sites as needed.

Number of Study Participants

The evolving situation of the pandemic may result in a substantial number of participants' early dropout from the study, which could affect the data integrity of the trial. Because of this risk and in order to mitigate it, the sponsor may decide to recruit additional participants in the study, beyond the expected number.

Study Visits

Remote Site Visit Guidelines:

In addition to the remote visits already specified in the Protocol, the evolving situation of the pandemic may require further travel restrictions and isolation requirements, or the investigator's benefit/risk assessment may determine it to be unsafe for participants to attend study visits at the investigational site. In such cases, the site staff may elect to pursue the following:

- In order to minimize participant risk, study visits may be conducted via telemedicine modalities (phone or video calls). At a minimum, a review of AEs, concomitant medications, and study drug compliance must be completed. Periodic on-site visits should be conducted whenever feasible, in addition to the mandatory on-site visits outlined below.
- No efficacy assessments can be performed via telemedicine (video call, phone call, or via photography).
- Laboratory sampling: in order to support investigator oversight of participant safety and disease management, off-site laboratory sampling (in accordance with the SoA, see Table 3 and Table 4) may be allowed in 1 of 2 ways:
  - Use of home nursing services
  - Instruct the participant to undergo some laboratory tests at a local (nearby) hospital laboratory or facility closer to the participant's residence rather than at the investigational site. In this case, the study physician will provide the participant with the list of parameters to be checked. These tests should be performed at certified laboratories and copies of results provided to the site.

Mandatory On-Site Visits:

The visits outlined below **must be performed in person** in order to capture the investigator's efficacy assessments [redacted], even if the date that the participant eventually comes into the clinic deviates from the visit window.

No efficacy assessments can be performed via telemedicine (video call, phone call, or photography).

The visit window deviation must be documented, and the sponsor's representative must be informed of when it is believed that the participant can come into the clinic. Further instructions will be provided if needed.

During the placebo-controlled period, the following visits must be performed in person:

- Screening
- Day 1 (Baseline)
- Week 12 visit
- Week 24 visit

During the extension period, the following visits must be performed in person:

- Week 36 visit
- Week 52 visit

Investigational Medicinal Product Dispensation and Distribution

In order to ensure the continuity of providing their participants' clinical supplies within the constraints imparted by the pandemic, the site staff can decide to supply study drug via shipment to participants.

If the participant cannot attend a visit at the study site, adequate supplies of study drug determined by the investigator can be shipped to the participant by the investigator or appropriately delegated staff (eg, the study pharmacy staff) using a third-party service if duly authorized by the participant.

The study site may use their own preferred courier, provided the courier adheres to certain standards (eg, use of personal protection equipment, maintenance of temperature-controlled transit environment), or one centrally contracted by the sponsor.

Clinical Trial Monitoring

Study monitoring visits may be postponed due to documented COVID-19–related reasons; however, the site monitor will continue to employ off-site monitoring practices such as routine communication methods (eg, phone calls, e-mails, video visits) with the sites to get information on trial progress, subject status, and information on issue resolution. The study monitor may remotely review data entered into the EDC for accuracy and completeness. If allowed by local regulations, remote source data verification may be implemented with agreement of the principal investigator and institution, as applicable.

If the study site monitor cannot be on-site to perform the final drug accountability for reconciliation purposes and the operation cannot be postponed, it may be performed by a pharmacist from the hospital pharmacy or by the study coordinator/data manager with suitable training. The study drug can be returned to the sponsor by the hospital pharmacy directly or destroyed in accordance with local practices, if applicable, and with sponsor approval.

Other Considerations

If necessary, direct contracts can be established with third-party local physicians to conduct activities related to the clinical management of participants for whom the investigator is responsible and maintains oversight. In such situations, the investigator is required to provide the local physician with a delegation letter listing all delegated activities. The sponsor, through the study investigator or institution, will reimburse the local physician for the tests/procedures conducted outside of the standard of care.

- In case of need, participants may refer to the local health care provider. Participants will be requested to obtain certified copies of the source data at the local health facility with the outcome of the contact and provide those to the investigator for appropriate oversight. The investigator/delegate will be requested to enter any relevant information into the EDC.
- Should COVID-19–related restrictions be localized and have an effect on a limited number of sites, the affected sites may utilize direct contracting of third parties to support continuous study conduct (eg, home nursing services, couriers, etc).

Reimbursement of Extraordinary Expenses

The sponsor will arrange to reimburse participants for any extraordinary expenses, keeping appropriate documentation as evidence (eg, travel expenses for the local laboratory visit[s], the costs of local [nearby] laboratory tests).

APPENDIX F. PROTOCOL AMENDMENT SUMMARY OF CHANGES

Document	Date
Amendment 1	19 AUG 2021
Amendment 2	09 FEB 2022
Amendment 3	19 MAY 2022
Amendment 4	12 JUL 2022

Amendment 4 (12 JUL 2022)

Overall Rationale for the Amendment:

The primary purpose of the amendment is to extend the follow up period for the study from 4 to 24 weeks.

1. **Section 1, Protocol Summary (Table 2: Key Study Design Elements; Figure 1: Study Design Schema; Table 4: Schedule of Activities [Extension Period]); Section 2.2.1, Scientific Rationale for Study Design; Section 3, Objectives and Endpoints (Table 6: Objectives and Endpoints); Section 4.1, Overall Design; Section 4.2, Overall Study Duration; Section 6.6, Concomitant Medications and Procedures; Section 7.1.2, Discontinuation Procedures; Section 7.2, Participant Withdrawal From the Study; Section 8.3.1, Adverse Events; Section 8.3.5, Laboratory Assessments; Section 8.7, End of Treatment and/or Early Termination; Section 8.8, Follow-Up; Section 9.3, Recording and Follow-Up of Adverse Events and/or Serious Adverse Events; Section 9.4, Reporting of Serious Adverse Events.**

   Description of change: [redacted]

   Rationale for change: The follow-up period was extended to assess the change in pigmentation after completion of treatment with INCB054707.

2. **Incorporation of administrative changes.** Other minor, administrative changes have been incorporated throughout the Protocol and are noted in the redline version of the amendment.

Amendment 3 (19 MAY 2022)

Overall Rationale for the Amendment:

The primary purpose of the amendment is to clarify the unblinding procedures for the sponsor.

1. **Section 5.6, Data Safety Monitoring Board; Section 6.3, Measures to Minimize Bias: Randomization and Blinding**

   Description of change: Revised the unblinding procedures for determining that the sponsor will be unblinded after the primary database lock, when all participants have completed the placebo-controlled, double-blind treatment period (Week 24 analysis).

   Rationale for change: To clarify and describe the correct unblinding procedures after study primary endpoint completion and database lock (placebo-controlled period, Week 24 analysis).

Amendment 2 (09 FEB 2022)

Overall Rationale for the Amendment:

The primary purpose of the amendment is to provide clarification on the management of creatine kinase elevations.

1. **Section 6.5.1, Criteria and Procedures for Dose Interruptions and Adjustments of Study Drug (Table 9: Guidelines for Interrupting, Restarting, and Discontinuing of Study Drug)**

   Description of change: Added guidance to describe management of creatine kinase elevations.

   Rationale for change: To clarify how creatine kinase elevations should be managed by investigators.

2. **Incorporation of administrative changes.** Other minor, administrative changes have been incorporated throughout the Protocol and are noted in the redline version of the amendment.

Amendment 1 (19 AUG 2021)

Overall Rationale for the Amendment:

The primary purpose of the amendment is to remove the inclusion criterion requiring previous vitiligo treatment and to permit in-clinic visits for the scheduled remote visits. Additional changes are summarized below.

1. **Section 1, Protocol Summary (Table 2: Key Study Design Elements)**

   Description of change: Added the name for the coordinating principal investigator.

   Rationale for change: To update the coordinating principal investigator field in the table.

2. **Section 1, Protocol Summary [Table 3: Schedule of Activities (Placebo-Controlled Period); Table 4: Schedule of Activities (Extension Period)]; Section 6.6, Concomitant Medications and Procedures; Section 8.3.1, Adverse Events; Section 8.3.5, Laboratory Assessments**

   Description of change: Added clarification that in-clinic visits are permitted for the scheduled remote visits at Week 2, Week 6, Week 26, and Week 30.

   Rationale for change: To allow principal investigators the choice of remote or in-clinic visits based on the most adequate option for each participant.

3. **Section 5.1, Inclusion Criteria**

   Description of change: Removed Inclusion Criterion 4, "History of prior vitiligo treatment with a total duration of at least 3 months."

   Rationale for change: To align the inclusion criteria with the participant population, currently limited in terms of available treatments. There are no approved therapies for vitiligo, and the currently prescribed therapies may not offer considerable benefit.

4. **Section 5.2, Exclusion Criteria (Table 7: Exclusionary Laboratory Values)**

   Description of change: Removed "Conjugated (direct) bilirubin" and ≥ 1.2 × ULN from Exclusion Criterion 15g.

   Rationale for change: To clarify that Exclusion Criterion 15g is only applicable to total bilirubin.

5. **Section 6.5.1, Criteria and Procedures for Dose Interruptions and Adjustments of Study Drug (Table 9: Guidelines for Interrupting, Restarting, and Discontinuing of Study Drug)**

   Description of change: Added clarification for the number of times the study drug can be interrupted/restarted due to ALT and/or AST > 3.0 x ULN.

   Rationale for change: To clarify that the study drug can only be interrupted/restarted up to 2 times.

6. **Section 8.3.5, Laboratory Assessments (Table 13: Required Laboratory Analytes)**

   Description of change: Creatine kinase will be included as one of the tests under the blood chemistries column.

   Rationale for change: The inclusion of creatine kinase follows a request from the external DSMB members. The recommendation was based on their expertise on other Janus kinase inhibitors.

7. **Incorporation of administrative changes.** Other minor, administrative changes have been incorporated throughout the Protocol and are noted in the redline version of the amendment.

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Approval	[redacted] Approver [redacted] 12-Jul-2022 18:36:49 GMT+0000
Approval	[redacted] Approver [redacted] 12-Jul-2022 18:41:54 GMT+0000
Approval	[redacted] Approver [redacted] 12-Jul-2022 19:03:13 GMT+0000
Approval	[redacted] Approver [redacted] 12-Jul-2022 19:04:47 GMT+0000
Approval	[redacted] Document Preparer [redacted] 12-Jul-2022 19:06:10 GMT+0000

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