Study Title:	An open-label, Phase 2 study to assess the safety and efficacy of EQ101 in adult subjects with moderate to severe alopecia areata
Protocol Number:	EQ101-104-01
Investigational Product(s):	EQ101
Sponsor:	Equillium AUS Pty Ltd
Development Phase:	Phase 2
NCT Number:	NCT05589610
Document Version Date:	23 Sep 2022

[redacted]

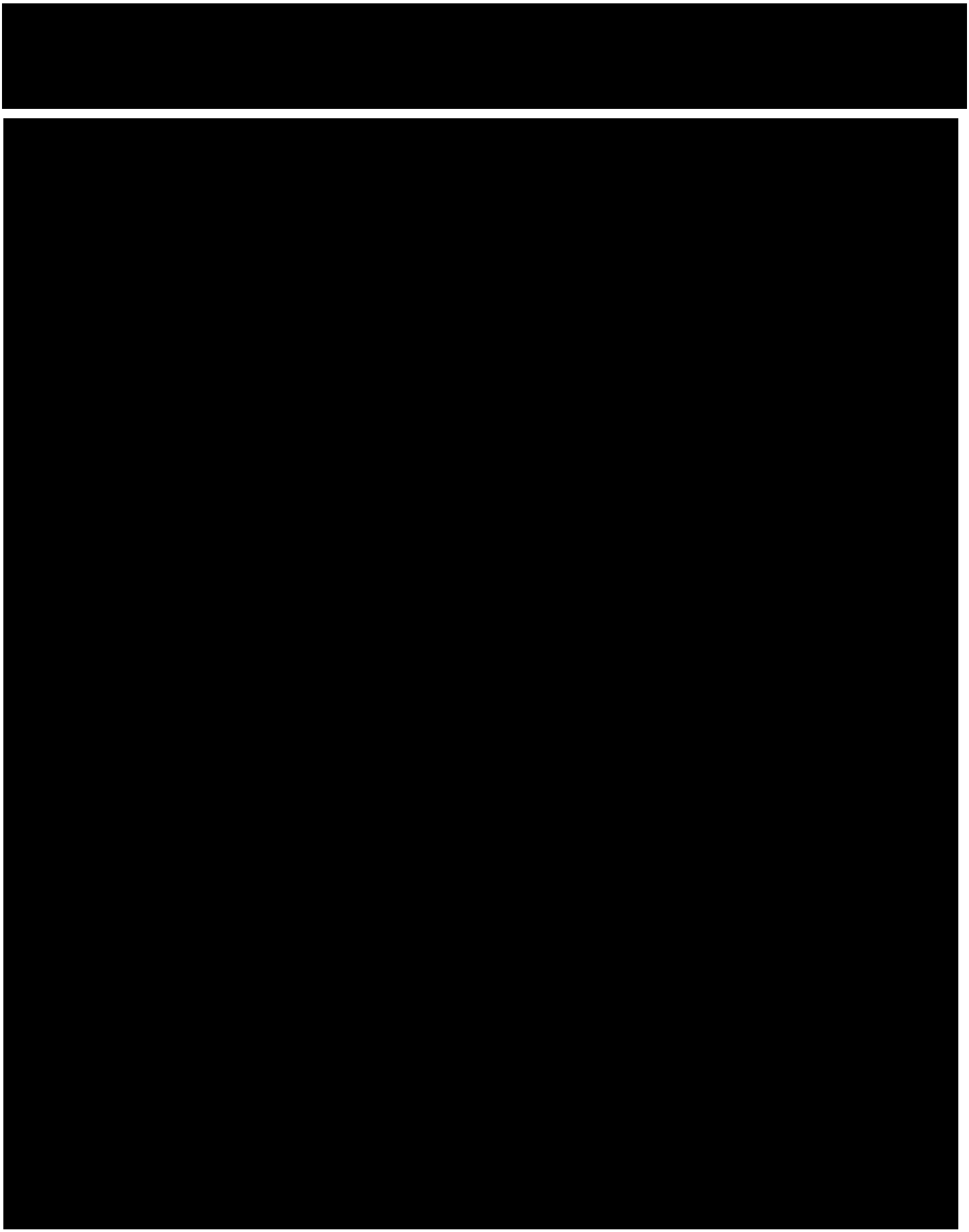
CLINICAL STUDY PROTOCOL

EQ101-104-01

Protocol Title:	An open-label, Phase 2 study to assess the safety and efficacy of EQ101 in adult subjects with moderate to severe alopecia areata
Investigational Product:	EQ101
Indication Studied:	Alopecia Areata
Phase of Development:	2
Sponsor:	Equillium AUS Pty Ltd [redacted]

[redacted]

Confidentiality Statement



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PROTOCOL SYNOPSIS

NAME OF SPONSOR	Equillium AUS Pty Ltd
NAME OF DRUG PRODUCT:	EQ101
NAME OF ACTIVE INGREDIENT:	EQ101
PROTOCOL NUMBER:	EQ101-104-01
PHASE OF DEVELOPMENT:	2
PROTOCOL TITLE: An open-label Phase 2 study to assess the safety and efficacy of EQ101 in adult subjects with moderate to severe alopecia areata	
STUDY SITES: This will be a multicenter study in Australia.	

BACKGROUND AND RATIONALE FOR THE STUDY:

Equillium is developing EQ101 (previously known as BNZ-1) for the treatment of alopecia areata (AA). This is the first study of EQ101 in AA and is a Phase 2 proof-of-concept (PoC) study. AA is a common, inflammatory, nonscarring, autoimmune-mediated hair loss with limited treatment options. The lifetime incidence of AA is estimated at about 2% globally [redacted] The cause(s) of AA remain incompletely understood, but it is believed to involve both genetic factors and a triggering event (e.g., stress, infection, trauma). The pathogenesis involves interferon-gamma (IFN-γ)-mediated loss of anagen hair follicle immune privilege and upregulation of inflammatory cytokine signalling, resulting in hair fibre breakage, premature catagen onset, and autoimmune-mediated hair loss.

The immune pathways required for autoreactive T-cell activation in AA have been recently proposed to involve 3 members of the gamma chain (γc) cytokine family (interleukin [IL]-2, IL-9, and IL-15), which have been shown to be upregulated in animal models of AA and in human biopsies of AA lesions. EQ101 is a selective antagonist of IL-2, IL-9, and IL-15 (i.e., disease-driving cytokines), and consequently provides a novel, potential therapeutic approach for the treatment of AA.

STUDY OBJECTIVES:

Primary Objective

- To evaluate the safety and tolerability of EQ101 in adult subjects with moderate to severe AA over a 24-week treatment period

Secondary Objectives

- To evaluate the efficacy of EQ101 in adult subjects with moderate to severe AA over a 24-week treatment period.
- To characterise the pharmacokinetics (PK) of EQ101 in adult subjects with moderate to severe AA.

[redacted]

[redacted]

[redacted]

METHODOLOGY:

The purpose of this study is to assess the safety, PK, [redacted] of EQ101 as well as measure the efficacy of EQ101 at Week 24 compared to Baseline in adult subjects with moderate to severe AA. The study consists of 3 phases: a screening phase of up to 5 weeks, a treatment phase of 24 weeks, and a follow-up phase of 4 weeks. Study drug will be administered via intravenous (IV) push weekly.

NUMBER OF PLANNED SUBJECTS:

Approximately 30 subjects will be enrolled.

STUDY ELIGIBILITY CRITERIA:

Inclusion Criteria

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

1. Male or female adults aged 18 – 60 years, inclusive
2. Subjects have AA, meeting all of the following criteria:
   a. Clinical diagnosis of AA with no other aetiology of hair loss (e.g., telogen effluvium, androgenetic alopecia, etc.).
   b. At least 35% scalp hair loss, as defined by a Severity of Alopecia Tool (SALT) score ≥ 35 at Screening and Baseline. (No more than approximately 25% of the study population will be comprised of subjects with 35% to < 50% scalp hair loss; also, no more than approximately 25% of the study population will be comprised of subjects with alopecia totalis [AT] and/or alopecia universalis [AU])
   c. Current episode of hair loss lasting at least 6 months and not exceeding 7 years at the time of Screening.
   d. No appreciable change (i.e., ≥ 10-point improvement in SALT) in terminal hair regrowth within 6 months of the baseline visit
3. Provide written informed consent
4. Are willing and able to comply with scheduled visits, treatment plan, laboratory tests, and other study procedures
5. Female subjects must:
   a. Be of non-childbearing potential (i.e., surgically sterilised [hysterectomy, bilateral salpingectomy, bilateral oophorectomy]) at least 6 weeks before the screening visit or postmenopausal (where postmenopausal is defined as no menses for 12 months without an alternative medical cause and a follicle-stimulating hormone (FSH) level > 40 IU/L at the screening visit), OR

[redacted]

b. If of childbearing potential, must have a negative pregnancy test at Screening (blood test) and before the first study drug administration (Day 1 urine test). Subject must agree not to attempt to become pregnant, must not donate ova, and must use a highly effective contraceptive method [redacted] from signing the consent form, until at least 60 days after the last dose of study drug, and
c. Must not be breastfeeding.

6. Male subjects must agree not to donate sperm and if engaging in sexual intercourse with a female partner who could become pregnant, must agree to use a condom in addition to having the female partner use a highly effective contraceptive method [redacted] between signing consent, during the study, and at least 150 days after the last dose of study drug.

Exclusion Criteria

Subjects are excluded from the study if <u>any</u> of the following criteria apply:

1. Known history of, or currently experiencing male pattern androgenetic alopecia (Hamilton Norwood $\geq$ 3 vertex) or female pattern hair loss (Sinclair stage $\geq$ 3).
2. Currently experiencing any other types of alopecia (including, but not limited to traction or scarring alopecia, telogen effluvium, or diffuse type of AA).
3. History of scalp hair transplantation.
4. Other scalp disease that may impact AA assessment or require topical treatment (including, but not limited to scalp psoriasis, seborrheic dermatitis, actinic keratosis).
5. Unwilling to maintain a consistent hair style, including shampoo and hair products (including hair dye, process, and timing to hair appointments), and to refrain from weaves or extensions throughout the course of the study, or shaving of scalp hair for 12 days preceding a SALT assessment.
6. Use of adhesive or difficult to remove hairpiece or wigs during the study (except banded perimeter wigs).
7. Have undergone significant trauma or major surgery within 8 weeks prior to the baseline visit or considered in imminent need for surgery or with elective surgery scheduled to occur during the study.
8. Donation of blood in excess of 500 mL within 8 weeks prior to the baseline visit.
9. Participation in other clinical studies involving investigational drug(s) within 4 weeks or within 5 half-lives (if known), whichever is longer, prior to the Baseline visit and/or during study participation.
10. History of alcohol, medication, or illicit drug abuse within 1 year prior to the baseline visit.
11. Use of any live or live attenuated vaccinations within 90 days prior to the baseline visit except for vaccines for influenza. It is noted that messenger ribonucleic acid (mRNA) or adeno-associated virus (AAV)-based coronavirus 2019 (COVID-19) vaccinations are permitted at any stage throughout the study.

[redacted]

12. Treatment with an oral Janus kinase (JAK) inhibitor within 6 months prior to the baseline visit.
13. Have previously been treated with an oral JAK inhibitor for AA for at least 12 weeks without achieving at least a 25% improvement in SALT score.
14. Have been treated with any cell-depleting agents including but not limited to rituximab within 6 months of the baseline visit, or 5 half-lives (if known), or until lymphocyte count returns to normal, whichever is longer.
15. Have been treated with any biologics (e.g., adalimumab, atlizumab, canakinumab, certolizumab, fontolizumab, golimumab, infliximab, mepolizumab, secukinumab, tocilizumab, ustekinumab, etanercept, ixekizumab, tildrakizumab, dupilumab, tralokinumab) within 12 weeks or 5 half-lives of the baseline visit, whichever is longer.
16. Have been treated with any oral immune suppressants (e.g., cyclosporine A, azathioprine, methotrexate, sulfasalazine, systemic corticosteroids, mycophenolate mofetil) within 8 weeks of the baseline visit.
17. Have received intralesional injections of corticosteroid or platelet-rich plasma (PRP) in the scalp within 6 weeks of the baseline visit.
18. Have used phototherapy [e.g., ultraviolet B (UVB), psoralen ultraviolet A (PUVA)], contact sensitisers, contact irritants, or cryotherapy within 4 weeks of the baseline visit.
19. Have used topical treatments applied to the scalp, eyebrows, or eyelashes (e.g., corticosteroid cream; JAK inhibitors; medicated shampoo; minoxidil (Rogaine) or herbal hair care that could affect AA) within 4 weeks of the baseline visit.
20. Have current or recent history of clinically significant severe, progressive, or uncontrolled renal (including, but not limited to active renal disease or recent kidney stones), hepatic, haematological, gastrointestinal, metabolic, endocrine, pulmonary, cardiovascular, psychiatric, immunologic/rheumatologic or neurologic disease; or have any other severe acute or chronic medical or psychiatric condition or laboratory abnormality that may increase the risk associated with study participation or study drug administration, or interfere with the interpretation of study results in the judgement of the Investigator or Sponsor, would make the subject inappropriate for entry into this study.
21. Have a known immunodeficiency disorder or a first-degree relative with a hereditary immunodeficiency.
22. History of solid organ or haematological transplantation.
23. History of a lymphoproliferative disease or malignancy, other than adequately treated non-melanoma skin cancer or cervical carcinoma with no evidence of recurrence.
24. Have active acute or chronic infection including:

    COVID-19 infection, infection requiring treatment with systemic antibiotics, antivirals, antiparasitics, antiprotozoals, or antifungals within 14 days before the baseline visit. Or a major episode of infection that required hospitalisation or treatment with IV

antibiotics within 60 days before the baseline visit. Or serologic evidence of HBsAg, HCV or HIV, including during screening.

25. Abnormalities in clinical laboratory tests at Screening, as confirmed by a single repeat, if deemed necessary:
    a. Absolute neutrophil count (ANC) < 1.0×10^9/L.
    b. Liver function tests (LFTs including alanine aminotransferase [ALT] and aspartate aminotransferase [AST]) > 3 x upper limit of normal (ULN).
    c. Total bilirubin > 1.5 times ULN (unless isolated Gilbert's syndrome)
    d. Serum creatinine > 1.5 ULN.

STUDY DRUG:

Study drug is defined as EQ101

INVESTIGATIONAL PRODUCT, DOSE, AND MODE OF ADMINISTRATION:

EQ101, 2 mg/kg IV push, once weekly (QW) dosing, for a total of 24 doses

CONTROL PRODUCT, DOSE, AND MODE OF ADMINISTRATION:

There will be no control product

ADDITIONAL STUDY MEDICATIONS: None

DURATION OF TREATMENT:

Subjects will receive up to 24 doses of study drug. The total duration of study participation for each subject (from Screening through the follow-up visit) will be up to 33 weeks (232 days).

STUDY ASSESSMENTS:

Safety Assessments

- Adverse events (AEs)
- Serious adverse events (SAEs)
- Physical examinations
- Vital signs
- 12-lead electrocardiogram (ECG)
- Clinical safety laboratory tests
- Antidrug Antibody (ADA) and Neutralising ADA assessments

Efficacy Assessments

- SALT score
- Clinician-Reported outcome (ClinRO) Measure for Eyebrow Hair Loss
- ClinRO Measure for Eyelash Hair Loss

- ClinRO Measure for Body Hair Loss
- Scalp Hair Assessment patient-reported outcome (PRO)
- PRO Measure for Eyebrows
- PRO Measure for Eyelashes
- PRO Measure for Body Hair

PK Assessments

- Blood samples will be collected for measurement of plasma concentrations of EQ101 and antidrug antibodies to EQ101

STUDY ENDPOINTS:

Primary Endpoints

- incidence, severity, and relationship of treatment-emergent adverse events (TEAEs), SAEs, TEAEs leading to discontinuation of study treatment;
- changes in vital sign measurements;
- changes in ECG parameters; and
- changes in clinical laboratory results.

Primary Efficacy Endpoint

- percent change from Baseline in SALT score at Week 24.

Secondary Efficacy Endpoints

- percent change from Baseline in SALT score at Weeks 4, 8, 12, 16, and 20;
- change from Baseline in SALT score at Weeks 4, 8, 12, 16, 20, and 24;
- percentages of subjects with a SALT ≤ 20 and those with a SALT ≤ 10 at Weeks 4, 8, 12, 16, 20, and 24;

[redacted]

- percentages of subjects achieving 50% Improvement of SALT ($SALT_{50}$) and those achieving 75% improvement of SALT ($SALT_{75}$) at Weeks 4, 8, 12, 16, 20, and 24;
- times to SALT score improvement of 50% ($SALT_{50}$) and SALT score improvement of 75% ($SALT_{75}$);
- percentage of subjects with Scalp Hair Assessment PRO of 0 or 1 with a ≥ 2-point improvement from Baseline among subjects with a score of ≥ 3 at Baseline at Weeks 4, 8, 12, 16, 20, and 24;
- percentage of subjects achieving clinician-reported outcome (ClinRO) Measure for eyebrow (EB) Hair Loss 0 or 1 with ≥ 2-point improvement from Baseline among subjects with ClinRO Measure for EB Hair Loss ≥2 at Baseline at Weeks 4, 8, 12, 16, 20, and 24;
- percentage of subjects achieving ClinRO Measure for eyelash (EL) Hair Loss 0 or 1 with ≥ 2-point improvement from Baseline among subjects with ClinRO Measure for EL Hair Loss ≥2 at Baseline at Weeks 4, 8, 12, 16, 20, and 24;
- percentage of subjects achieving ClinRO Measure for Body Hair Loss 0 or 1 with ≥ 2-point improvement from Baseline among subjects with ClinRO Measure for Body Hair Loss ≥ 2 at Baseline and Week 24;
- percentage of subjects achieving PRO measure for EB 0 or 1 with ≥ 2-point improvement from Baseline among subjects with PRO measure for EB ≥2 at Baseline at Weeks 4, 8, 12, 16, 20, and 24;
- percentage of subjects achieving PRO measure for EL 0 or 1 with ≥ 2-point improvement from Baseline among subjects with PRO measure EL ≥ 2 at Baseline at Weeks 4, 8, 12, 16, 20, and 24;
- percentage of subjects achieving PRO measure for Body Hair 0 or 1 with ≥ 2-point improvement from Baseline among subjects with PRO measure Body Hair ≥ 2 at Baseline and Week 24.

PK Endpoints

- plasma concentrations of EQ101 at Days 1, 8, 15, 22, 29, 57, 85, 113, 141, 169, 197 (Baseline/Week 0 and Weeks 1, 2, 3, 4, 8, 12, 16, 20, 24, 28), and
- incidence of ADA at Days 1, 29, 85, 141, 169, and 197 (Baseline/Week 0 and Weeks 4, 12, 20, 24, 28)

[redacted]

[redacted]

STATISTICAL METHODS:

General Considerations

Data will be summarised using descriptive statistics (n, mean, median, standard deviation [SD], minimum, maximum) for continuous variables and frequencies and percentages for discrete variables. Time to event variables will be summarised using the Kaplan-Meier method. All data summaries and listings will be produced using the SAS® software Version 9.4 or higher. A separate statistical analysis plan (SAP) will be prepared describing more details.

Determination of Sample Size

The objectives of the study are to evaluate the safety and efficacy of EQ101 and to characterise the PK[redacted] of EQ101 over a 24-week treatment period in adult subjects with moderate to severe AA. Though not formally powered for efficacy, the sample size of approximately 30 subjects is considered sufficient to meet these objectives.

Analysis Populations

Safety Population: Consists of all subjects who receive at least one dose of study drug.

PK Analysis Population: Subjects in the safety population who have at least one measurable post-EQ101 exposure concentration.

[redacted]

Safety Analyses

AEs will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) for the purposes of summarisation. TEAEs, AEs that start during or after the first dose of study drug or AEs with an onset prior to the first dose of study drug that worsen after study drug administration, will be summarised by system organ class (SOC) and preferred term (PT). Treatment-emergent serious AEs (TESAEs), TEAEs leading to treatment discontinuation, and TEAEs with an outcome of death will be summarised similarly. In addition, TEAEs will be further summarised by worst severity grade and relationship to study drug; AEs of special interest (AESI) will be summarised by SOC, PT, and worst severity grade.

Clinical laboratory data will be summarised descriptively including observed values at collection timepoints and change from Baseline. All laboratory parameters that can be graded using Common Terminology Criteria for Adverse Events (CTCAE) v5.0 will be graded. Other safety measures including vital signs and physical examination findings will be listed and summarised as appropriate.

Efficacy Analyses

Efficacy measures will be collected for all subjects. Efficacy measures include the SALT score [redacted], ClinRO measures for eyebrow, eyelash and body hair loss evaluated by the

[redacted]

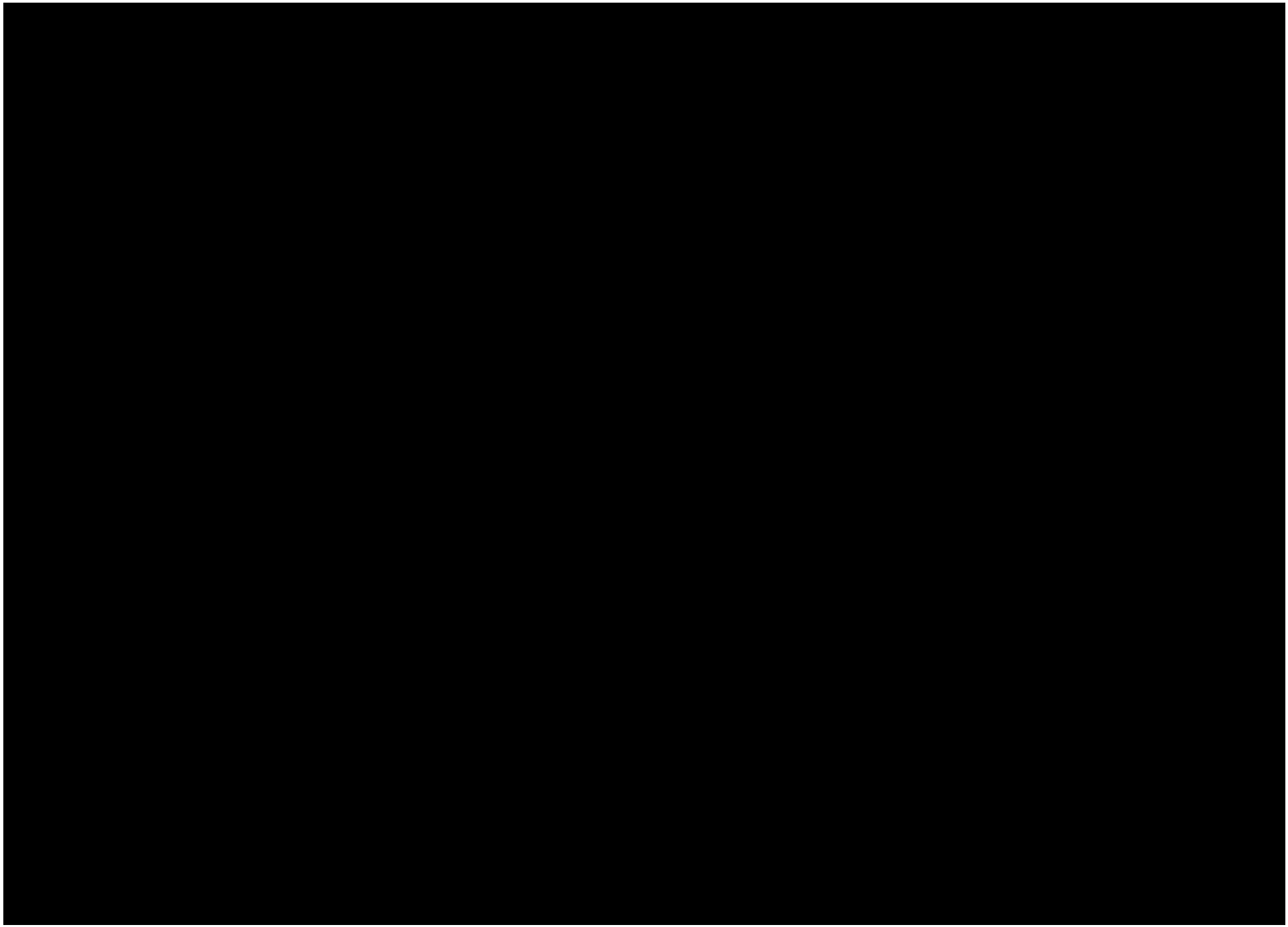
Investigator and Patient-Reported Outcome (PRO) measures. The Scalp PRO tool and ClinRO/PRO measures for eyebrow and eyelash hair loss are validated outcome measures [redacted] Efficacy endpoints will be summarised in the safety population using methods described in the General Considerations section.

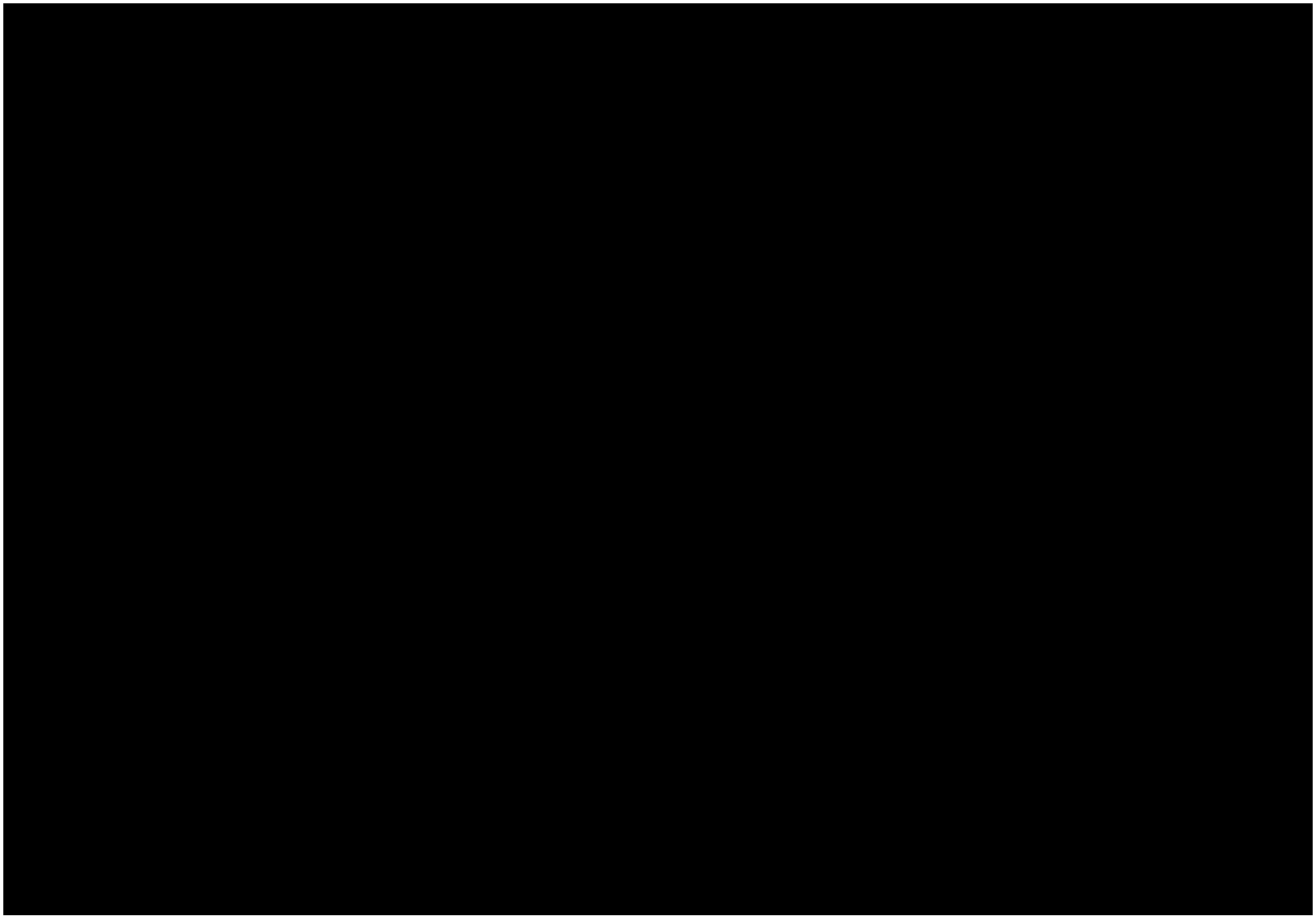
PK Analyses

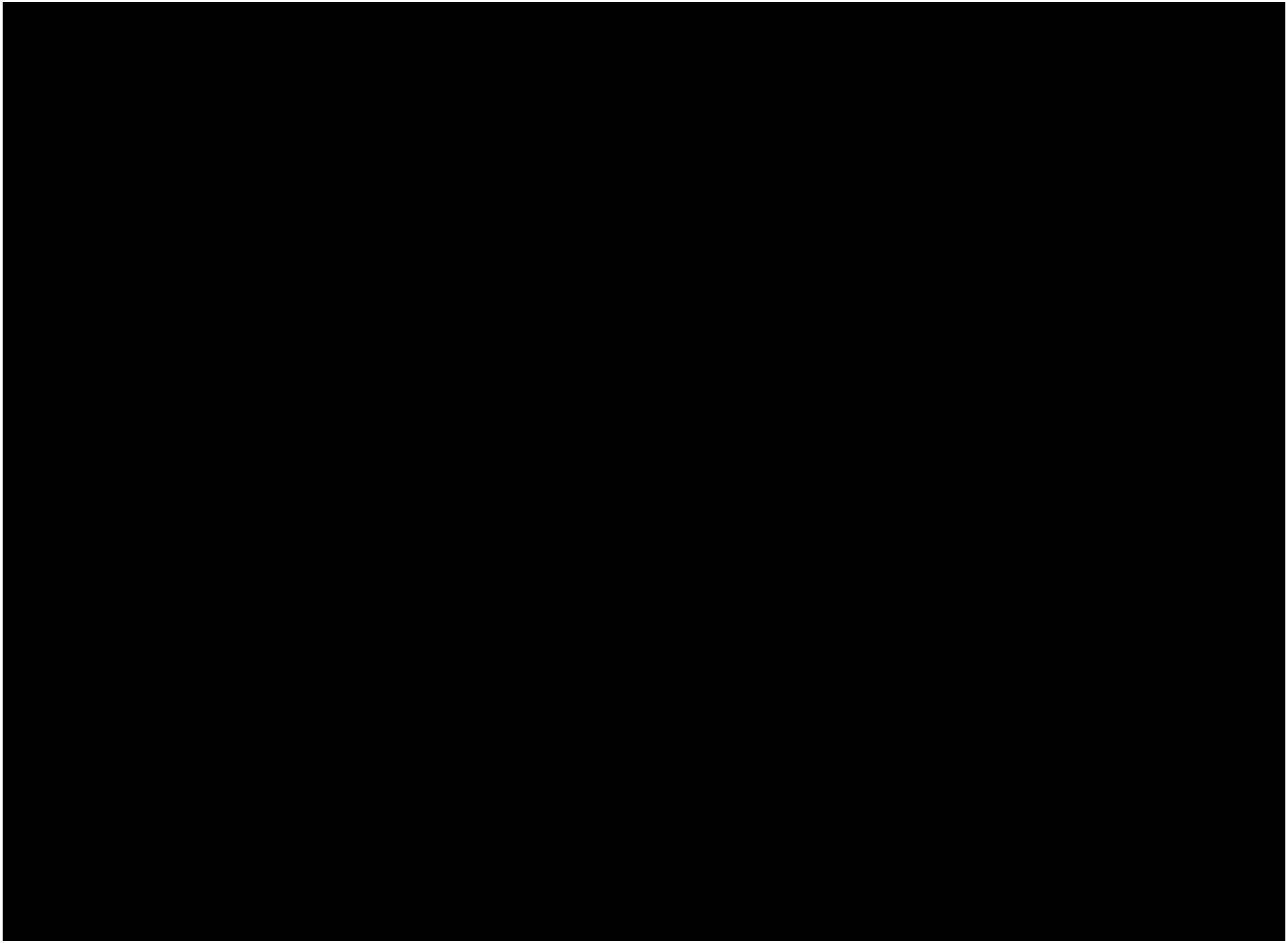
Plasma concentrations of EQ101 will be reported as listings for individual subjects and also as statistical summaries grouped by the scheduled timepoint. The statistical summary will include mean, SD, coefficient of variation (CV%), maximum, minimum, median, geometric mean, and geometric CV%.

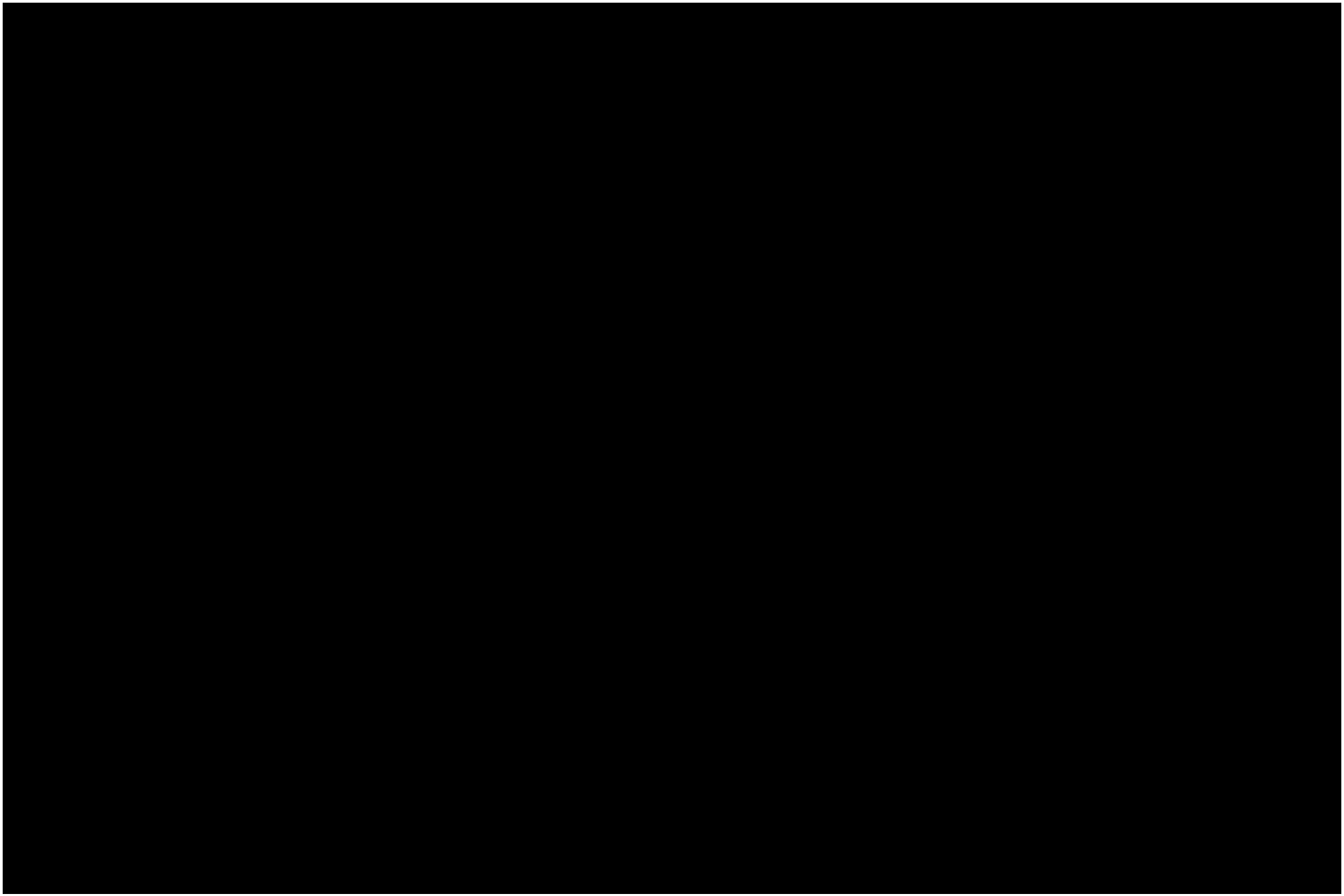
Plasma concentrations of EQ101 from this study may be included in a population PK analysis that will be documented in a separate Population PK Report

[redacted]









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LIST OF ABBREVIATIONS AND DOCUMENT CONVENTIONS

List of Abbreviations

Abbreviation	Definition
γc	Gamma chain
AA	Alopecia areata
AAV	Adeno-associated virus
ADA	Antidrug antibody
AE	Adverse event
AESI	Adverse event of special interest
Akt	Protein kinase B
ALT	Alanine aminotransferase
ANC	Absolute neutrophil count
AST	Aspartate aminotransferase
AT	Alopecia totalis (complete loss of scalp hair)
AU	Alopecia universalis (complete loss of scalp and body hair)
CD4/CD8	Cluster of differentiation 4 or 8
ClinRO	Clinician-Reported Outcome
COVID-19	Coronavirus disease 2019, an infectious disease caused by the SARS-CoV-2 virus
CTCAE	Common Terminology Criteria for Adverse Events
CTCL	Cutaneous T-cell lymphoma
CVs	Curricula vitae
CV%	Coefficient of variation
DLT	Dose-limiting toxicity
EB	Eyebrow
ECG	Electrocardiogram
eCRF	Electronic case report form
EIU	Exposure in utero
EL	Eyelash
EOS	End of study
EOT	End of treatment
EQ101	Compound formerly known as "BNZ-1"
ERK	Extracellular signal-regulated kinases
ET	Early termination
FSH	Follicle-stimulating hormone

Abbreviation	Definition
GCP	Good Clinical Practice
GMP	Good Manufacturing Practice
Hgb A1c	Glycated haemoglobin
HIV	Human immunodeficiency virus
HV	Healthy volunteer
IB	Investigator's Brochure
ICF	Informed consent form
ICH	International Council for Harmonisation
IEC	Independent Ethics Committee
IFN-γ	Interferon-gamma
IL	Interleukin
IRB	Institutional Review Board
ISF	Investigator Site File
IV	Intravenous(ly)
JAK	Janus kinase
LFT	Liver function tests
LGLL	Large granular lymphocytic leukaemia
MAD	Multiple-ascending dose
MAPK	Mitogen-activated protein kinase
MedDRA	Medical Dictionary for Regulatory Activities
mRNA	Messenger ribonucleic acid
MTD	Maximum tolerated dose
mTOR	Mammalian target of rapamycin
N	Number of subjects in the category
NAB	Neutralising antibody
NCI	National Cancer Institute
NK	Natural killer
NKG2D	Natural killer group 2 member D
NOAEL	No observed adverse effect level
PBMC	Peripheral blood mononuclear cell
PCR	Polymerase chain reaction
PD	Pharmacodynamic(s)
PEG	Polyethylene glycol
PI	Principal Investigator

Abbreviation	Definition
PI3K	Phosphoinositide 3-kinase
PICF	Participant informed consent form
PK	Pharmacokinetic(s)
PoC	Proof-of-Concept
PRO	Patient-reported outcome
PRP	Platelet-rich plasma
PT	Preferred Term
PUVA	Psoralen ultraviolet A
QW	Every week
Q2W	Every 2 weeks
RAT	Rapid antigen test
rCTCL	Refractory cutaneous T-cell lymphoma
SAD	Single-ascending dose
SAE	Serious adverse event
SALT	Severity of Alopecia Tool
$SALT_{50}/SALT_{75}$	Improvement of SALT by 50% or 75% from Baseline
SAP	Statistical Analysis Plan
SD	Standard deviation
SOC	System Organ Class
SoE	Schedule of Events
STAT	Signal transducer and activator of transcription
SUSAR	Sudden unexpected serious adverse reaction
TEAE	Treatment-emergent adverse event
TESAE	Treatment-emergent serious adverse event
TGF	Transforming growth factor
Th2	T helper cells
T_{regs}	Regulatory T cells
TSH	Thyroid-stimulating hormone
ULN	Upper limit of normal
US	United States
UVB	ultraviolet B
WOCBP	Women of childbearing potential

Note: Abbreviations used only in tables or figures are not included.

1. INTRODUCTION

1.1. Background for Alopecia Areata

Alopecia areata (AA) is a common, inflammatory, nonscarring, autoimmune-mediated hair loss which can affect any hair-bearing area of the body. The lifetime incidence of alopecia AA is estimated at about 2% globally [redacted] It affects men and women of all racial and ethnic groups. AA has a higher prevalence in children and adolescents with 40% of cases occurring prior to the age of 20 years and 80% before the age of 40 [redacted] AA is associated with other immune-mediated or autoimmune disorders such as thyroiditis, vitiligo, and atopic diseases.

Approximately 50% of patients present acutely with 1 or more circular patches of scalp hair loss and recover within 1 year without treatment; however, many patients subsequently relapse [redacted] Approximately 50% of patients have chronic relapsing, remitting disease persisting more than 12 months and approximately 10% to 35% ultimately experience complete loss of scalp hair (alopecia totalis [AT]) or complete loss of scalp and body hair (alopecia universalis [AU]) [redacted]

AA has a significant psychosocial burden, can have a significant negative impact on health-related quality of life, and has been associated with depression and anxiety [redacted] There are currently limited treatment options and few countries have approved drugs for the treatment of AA. Thus, there is a great need for efficacious treatment options for extensive or persistent disease.

Although the aetiology and pathogenesis of AA is not fully understood, the current paradigm is that a triggering event (e.g., stress, infection, trauma) induces a loss of immune privilege in the hair follicle that is characterised by an upregulation of inflammatory cytokines leading to activation of natural killer (NK) and autoreactive cluster of differentiation (CD)8+ T cells [redacted] The inflammatory cells attack the anagen hair bulb region, resulting in hair loss; however, stem cells in the bulge area are spared which allows for future hair regrowth [redacted] The immune pathways required for autoreactive T-cell activation and maintenance in AA have been proposed to involve 3 members of the gamma chain (γc) cytokine family (interleukin [IL]-2, IL-9, and IL-15), which have been shown to be upregulated in animal models of AA and in human biopsies of AA lesions [redacted] IL-2 stimulates proliferation and differentiation of T cells while IL--15 induces the proliferation and survival of NK cells, NK T cells, and CD8+ T cells, including antigen-specific memory CD8+ T cells [redacted] IL-9 is a cytokine that is produced by a subset of activated CD4+ T cells and induces the activation of epithelial cells, B cells, eosinophils, and mast cells, stimulates cell proliferation and inhibits apoptosis [redacted] Blockade of either IL-2 or IL-15 in a mouse model of AA prevents the development of disease by inhibiting activity of cytotoxic CD8+ T cells, demonstrating that these 2 cytokines are key drivers of disease pathology [redacted] Within AA patients, elevated serum levels of IL-15 are correlated with disease severity while IL-9 signatures were upregulated within lesional skin [redacted]).

IL-2, IL-9, and IL-15 are members of the CD132/γc family of cytokines, which signal through a cytokine-specific receptor complexed with the common γc receptor; IL-4, IL-7, and IL-21 also share this receptor ([redacted] IL-2 and IL-15 are glycoprotein members of the 4 α-helix bundle-containing cytokines and signal through trimeric receptor complexes that utilise the γc and the β chain (CD122; IL-2/IL-15 receptor). Cytokine binding to the β/γc complex results in heterodimerisation of their cytoplasmic domains leading to activation of 3 different major

signalling pathways that promote cellular survival and proliferation: the phosphoinositide 3-kinase-protein kinase B (PI3K-Akt) pathway, the mitogen-activated protein kinase (MAPK)/extracellular signal-regulated kinases (ERK) pathway, and the Janus family tyrosine kinases (JAK)-signal transducer and activator of transcription (STAT) pathway [redacted] Consequently, blocking all signalling pathways arising from IL-2, IL-9, and IL-15 is necessary to inhibit the functional effects of these cytokines.

1.2. EQ101

1.2.1. Background

EQ101 (previously known as BNZ-1) is a novel, synthetic peptide inhibitor of IL-2, IL-9, and IL-15 [redacted] EQ101 was designed to simultaneously and selectively inhibit IL-2, IL-9, and IL-15 from binding to the common γc signalling receptor, while not affecting IL-4, IL-7, or IL-21 (which also utilise this shared receptor). By blocking the cytokine signalling receptor, EQ101 competitively inhibits activation of all 3 pathways (JAK/STAT, PI3K/Akt, and MAPK/ERK pathways) that mediate the cellular effects of IL-2, IL-9, and IL-15, leading to decreased proliferation of NK cells and cytotoxic T cells. This is advantageous over pathway-specific inhibitors (such as the JAK inhibitors) which non-specifically block signalling from all cytokines.

[redacted]

[redacted]

1.3. Study Rationale

AA is a common, inflammatory, nonscarring, autoimmune-mediated hair loss with limited treatment options. The immune pathways required for autoreactive T-cell activation in AA have been recently proposed to involve 3 members of the γc cytokine family (IL-2, IL-9, and IL-15), which have been shown to be upregulated in animal models of AA and in human biopsies of AA lesions [redacted] These studies showed that cytotoxic CD8+ natural killer group 2 member D (NKG2D +T cells were both necessary and sufficient for the disease induction in mouse models of AA, with IL-2 increasing the number of T cells and IL-15 increasing the expression of NKG2D and the production of IFN-γ by follicular epithelial cells that aberrantly transforms these T cells into cytotoxic T cells that attack the hair follicle. IL-15 released by dendritic cells and/or the follicular epithelial cells is believed to be the initiating event that promotes production of IFN-γ, which leads to the initial loss of immune privilege of the hair follicle and production of IL-2 that leads to T-cell proliferation. Global transcriptional profiling of mouse and human AA skin revealed gene expression signatures indicative of cytotoxic T-cell infiltration and upregulation of IL-2 and IL-15 that have been shown to promote the activation and survival of IFN-γ–producing CD8+NKG2D+ effector T cells. In addition, the pathologic activation by IL-9 of mast cells that produce and secrete T helper type 2 (Th2) cytokines (IL-5/IL-6/IL-13) and transforming growth factor-β (TGF-β), and facilitate antigen presentation of the hair follicle to the cytotoxic T cells have been implicated in AA [redacted]

Several studies have been conducted with JAK inhibitors in AA. Initially, Investigator-initiated studies using tofacitinib [redacted] and ruxolitinib [redacted] produced moderate response rates in small numbers of patients that had been otherwise refractory to available conventional therapies. More recently, several adequate and well controlled

industry-sponsored studies confirmed efficacy of JAK inhibitors in the treatment of AA using baricitinib [redacted], ritlecitinib [redacted] and deuruxolitinib [redacted] The moderate efficacy of JAK inhibitors may be partially explained by their poor PK profiles that leads to inadequate blockade of JAK signalling between doses and the additional signalling pathways associated with the γc cytokines that are not inhibited by the JAK inhibitors (PI3K/Akt/mTOR [mammalian target of rapamycin] and MAPK/ERK pathways), which leads to an incomplete blockade of pathologic cytokine signalling. Furthermore, the safety profile of these JAK inhibitors, due to their wide-ranging inhibitory effects on nondisease-related cytokine signalling may limit their utility and acceptance by physicians and subjects.

Therefore, a more selective and complete blockade of IL-2, IL-9, and IL-15 (i.e., disease-driving cytokines) using EQ101 provides a novel, potential therapeutic approach for the treatment of AA.

1.4. Rationale for Study Design, Doses, and Control Groups

This proof-of-concept (PoC) Phase 2, multicenter, single-arm, open-label study will be the first investigation of the safety and efficacy of EQ101 in subjects with AA. The objectives of this study are to evaluate the safety, tolerability, efficacy, PK, [redacted] for EQ101. Treatment will be weekly IV doses of the current formulation used in the previously concluded studies. This study will not include a control group given the recent completion of multiple Phase 2 and Phase 3 studies in a similar AA population that have provided historic data characterising the consistent and low placebo rates in this population. The current nonclinical toxicology studies (13-week studies completed with mice and cynomolgus monkeys) and prior clinical studies support the selected dose (2 mg/kg) and the treatment period of up to 24 weeks. [redacted]

Endpoints were selected to focus on the safety and tolerability of EQ101 in this AA population, as well as PK [redacted] markers in order to inform on dosing for future studies and characterise the drug-response profile in subjects with AA.

Efficacy endpoints will focus on regrowth of hair by percent and absolute changes in Severity of Alopecia Tool (SALT) score and reaching improvements in SALT scores (Improvement of SALT by 50% [$SALT_{50}$] and Improvement of SALT by 75% [$SALT_{75}$]). Efficacy endpoints will also include measures of scalp, eyebrow, eyelash and body hair regrowth and patient-reported outcomes (PROs). The study population will be those with at least 35% scalp hair loss to focus on subjects with the greatest unmet need but have lower likelihood of spontaneous regrowth. However, the current hair loss episode must be < 7 years in order to ensure that the hair loss could be reversible.

[redacted]

A maximum of approximately 25% of the total study population will have AT/AU in order to assess some subjects with complete hair loss in addition to those with incomplete hair loss. Similarly, a maximum of approximately 25% of the total study population will have 35% to < 50% of scalp hair loss to ensure that this PoC study assesses subjects with different severities of scalp hair loss.

The study includes a follow-up visit approximately 4 weeks after the last administration of the study drug. This will allow blood sample collection for the assessment of PK [redacted] during EQ101 washout, as well as the sustainability of the clinical response.

1.4.1. Justification for Dose

The dose of 2 mg/kg has been selected for this Phase 2 PoC study based on the safety profile, the exposure-response relationship, and the efficacy [redacted] conducted in the previous Phase 1 and Phase 2 studies of EQ101:

- [redacted]
- [redacted]
- [redacted]

There were no DLTs and a maximum tolerated dose (MTD) was not reached at any dose level tested in any of the human studies.

A review of data from Phase 1 healthy subjects who received EQ101 indicated a half-life of [redacted]

1.5. Potential Risks and Benefits

1.5.1. Potential Risks

No significant medical risks to subjects have been identified from clinical and nonclinical studies conducted thus far with EQ101 [redacted]

[redacted]

1.5.3. Overall Risk and Benefit Conclusion

Considering the preclinical and clinical efficacy demonstrated and the favourable safety profile in studies to date, the benefit/risk profile of EQ101 for the treatment of AA is considered positive.

[redacted]

2. STUDY OBJECTIVES AND ENDPOINTS

2.1. Study Objectives

2.1.1. Primary Objective

The primary objective of the study is to evaluate the safety and tolerability of EQ101 in adult subjects with moderate to severe AA over a 24-week treatment period.

2.1.2. Secondary Objectives

The secondary objectives of the study are:

- to evaluate the efficacy of EQ101 in adult subjects with moderate to severe AA over a 24-week treatment period;
- to characterise the PK of EQ101 in adult subjects with moderate to severe AA;
- [redacted]
- [redacted]

2.2. Study Endpoints

2.2.1. Primary Endpoints

The primary endpoints of the study are:

- incidence, severity, and relationship of TEAEs, SAEs, TEAEs leading to discontinuation of study treatment;
- changes in vital sign measurements;
- changes in ECG parameters; and
- changes in clinical laboratory results.

2.2.2. Primary Efficacy Endpoint

The primary efficacy endpoint is the percent change from Baseline in SALT score at Week 24.

2.2.3. Secondary Efficacy Endpoints

The secondary efficacy endpoints are:

- percent change from Baseline in SALT score at Weeks 4, 8, 12, 16, and 20;
- change from Baseline in SALT score at Weeks 4, 8, 12, 16, 20, and 24;
- percentages of subjects with a SALT $\leq$ 20 and those with a SALT $\leq$ 10 at Weeks 4, 8, 12, 16, 20, and 24;
- percentages of subjects achieving 50% improvement of SALT ($SALT_{50}$) and those achieving 75% improvement of SALT ($SALT_{75}$) from Baseline at Weeks 4, 8, 12, 16, 20, and 24;
- times to SALT score improvement of 50% ($SALT_{50}$) and SALT score improvement of 75% ($SALT_{75}$);

- percentage of subjects achieving ClinRO Measure for eyebrow (EB) Hair Loss 0 or 1 with ≥ 2-point improvement from Baseline among subjects with ClinRO Measure for EB Hair Loss ≥2 at Baseline at Weeks 4, 8, 12, 16, 20, and 24;
- percentage of subjects achieving ClinRO Measure for eyelash (EL) Hair Loss 0 or 1 with ≥ 2-point improvement from Baseline among subjects with ClinRO Measure for EL Hair Loss ≥2 at Baseline at Weeks 4, 8, 12, 16, 20, and 24;
- percentage of subjects achieving ClinRO Measure for Body Hair Loss 0 or 1 with ≥ 2-point improvement from Baseline among subjects with ClinRO Measure for Body Hair Loss ≥2 at Baseline and Week 24;
- percentage of subjects with Scalp Hair Assessment PRO of 0 or 1 with a ≥ 2-point improvement from Baseline among subjects with a score of ≥ 3 at Baseline at Weeks 4, 8, 12, 16, 20, and 24;
- percentage of subjects achieving PRO measure for EB 0 or 1 with ≥ 2-point improvement from Baseline among subjects with PRO measure for EB ≥2 at Baseline at Weeks 4, 8, 12, 16, 20, and 24;
- percentage of subjects achieving PRO measure for EL 0 or 1 with ≥2-point improvement from Baseline among subjects with PRO measure EL ≥2 at Baseline at Weeks 4, 8, 12, 16, 20, and 24;
- percentage of subjects achieving PRO measure for Body Hair 0 or 1 with ≥ 2-point improvement from Baseline among subjects with PRO measure Body Hair ≥ 2 at Baseline and Week 24.

2.2.4. PK Endpoints

PK endpoints to be evaluated include (but are not limited to):

- plasma concentrations of EQ101 at Visit Days 1, 8, 15, 22, 29, 57, 85, 113, 141, 169, 197 (Baseline/Week 0 and Weeks 1, 2, 3, 4, 8, 12, 16, 20, 24, and 28), and
- incidence of antidrug antibody (ADA) at Visit Days 1, 29, 85, 141, 169, and 197 (Baseline/Week 0 and Weeks 4, 12, 20, 24, and 28).

3. INVESTIGATIONAL PLAN

3.1. Overall Study Design and Plan

This is a multicenter, Phase 2, open-label PoC study of EQ101 in adult subjects with at least 35% scalp hair loss due to AA. Approximately, 30 subjects will be enrolled in the study. During the 24-week treatment period, subjects will be dosed once weekly with EQ101 2 mg/kg IV. Subjects then will be followed up for an additional 4 weeks.

Eligible subjects must be between the ages of 18 and 60 years, have a clinical diagnosis of AA with a scalp hair loss of ≥ 35% at Screening and Baseline. There will be no more than approximately 25% of subjects with AT and/or AU and no more than approximately 25% of subjects with 35% to < 50% scalp hair loss. In addition, each subject's current hair loss episode must have lasted at least 6 months but not more than 7 years and there can be no appreciable improvement in terminal hair regrowth within 6 months of Baseline. See Study Population (Section 4.1) below for a full description of inclusion and exclusion criteria.

Safety, efficacy, PK, [redacted] assessments will be made during the study. Safety assessments will include AEs (i.e., type, severity, frequency, seriousness, causality) and clinical safety lab results. Efficacy measurements will include Clinical Investigator assessments (e.g., SALT, ClinRO for EB, EL and body hair changes) and assessments made by study subjects (e.g., Scalp Hair Assessment PRO, and PRO measures for EB, EL and body hair changes).

3.2. Blinding

Not applicable. This is an open-label study.

3.3. Study Duration

The maximum duration of study participation for each subject (from Screening through the last scheduled follow-up visit at Week 28) will be 232 days (33 weeks). Following a screening period of up to 35 days, subjects will be enrolled and dosed weekly with EQ101 during the 24-week treatment period, followed by a 4-week post-treatment follow-up period. For regulatory reporting purposes, the end of the study is defined as the date of the last subject's final visit.

4. STUDY POPULATION AND WITHDRAWAL OF SUBJECTS

4.1. Study Population

Approximately 30 subjects will be enrolled. (No more than approximately 25% of the study population will be comprised of subjects with 35% to < 50% scalp hair loss; also, no more than approximately 25% of the study population will be comprised of subjects with AT and/or AU)

4.1.1. Subject Inclusion Criteria

Subjects are required to meet all of the following inclusion criteria in order to be eligible for study enrolment:

1. Male or female adults aged 18 – 60 years, inclusive
2. Subjects have AA, meeting all of the following criteria:
    a. Clinical diagnosis of AA with no other aetiology of hair loss (e.g., telogen effluvium, androgenetic alopecia, etc.);
    b. At least 35% scalp hair loss, as defined by a SALT score ≥ 35, at Screening and Baseline. (No more than approximately 25% of the study population will be comprised of subjects with 35% to < 50% scalp hair loss; also, no more than approximately 25% of the study population will be comprised of subjects with AT and/or AU);
    c. Current episode of hair loss lasting at least 6 months and not exceeding 7 years at the time of Screening; and
    d. No appreciable change (i.e., ≥ 10-point improvement in SALT) in terminal hair regrowth within 6 months of the baseline visit.
3. Provide written informed consent.
4. Are willing and able to comply with scheduled visits, treatment plan, laboratory tests, and other study procedures.
5. Female subjects must:
    a. Be of nonchildbearing potential (i.e., surgically sterilised [hysterectomy, bilateral salpingectomy, bilateral oophorectomy]) at least 6 weeks before the screening visit or postmenopausal (where postmenopausal is defined as no menses for 12 months without an alternative medical cause and a follicle-stimulating hormone (FSH) level > 40 IU/L at the screening visit); OR
    b. If of childbearing potential, must have a negative pregnancy test at Screening (blood test) and before the first study drug administration (Day 1 urine test). Subject must agree not to attempt to become pregnant, must not donate ova, and must use a highly effective contraceptive method [redacted] from signing the consent form, until at least 60 days after the last dose of study drug; and
    c. Must not be breastfeeding.
6. Male subjects must agree not to donate sperm and, if engaging in sexual intercourse with a female partner who could become pregnant, must agree to use a condom in addition to having the female partner use a highly effective contraceptive method [redacted] between signing consent, during the study, and at least 150 days after the last dose of study drug.

[redacted]

4.1.2. Subject Exclusion Criteria

Subjects are ineligible for enrolment and excluded from the study if any of the following criteria apply:

1. Known history of, or currently experiencing, male pattern androgenetic alopecia (Hamilton Norwood ≥ 3 vertex) or female pattern hair loss (Sinclair stage ≥ 3).
2. Currently experiencing any other types of alopecia (including, but not limited to traction or scarring alopecia, telogen effluvium, or diffuse type of AA).
3. History of scalp hair transplantation.
4. Other scalp disease that may impact AA assessment or require topical treatment (including, but not limited to scalp psoriasis, seborrheic dermatitis, actinic keratosis).
5. Unwilling to maintain a consistent hair style, including shampoo and hair products (including hair dye, process, and timing to hair appointments), and to refrain from weaves or extensions throughout the course of the study, or shaving of scalp hair for 12 days preceding a SALT assessment.
6. Use of adhesive or difficult to remove hairpiece or wigs during the study (except banded perimeter wigs).
7. Have undergone significant trauma or major surgery within 8 weeks of the first dose of study drug or considered in imminent need for surgery or with elective surgery scheduled to occur during the study.
8. Donation of blood in excess of 500 mL within 8 weeks prior to the baseline visit.
9. Participation in other clinical studies involving investigational drug(s) within 4 weeks or within 5 half-lives (if known), whichever is longer, prior to the baseline visit and/or during study participation.
10. History of alcohol, medication, or illicit drug abuse within 1 year before the baseline visit.
11. Use of any live or live attenuated vaccinations within 90 days prior to the first study drug administration except for vaccines for influenza. It is noted that messenger ribonucleic acid (mRNA) or adeno-associated virus (AAV)-based COVID-19 vaccinations are permitted at any stage throughout the study.
12. Treatment with an oral JAK inhibitor within 6 months prior to the baseline visit.
13. Have previously been treated with an oral JAK inhibitor for AA for at least 12 weeks without achieving at least a 25% improvement in SALT score.
14. Have been treated with any cell-depleting agents including but not limited to rituximab: within 6 months of the baseline visit, or 5 half-lives (if known), or until lymphocyte count returns to normal, whichever is longer.
15. Have been treated with any biologics (e.g., adalimumab, atlizumab, canakinumab, certolizumab, fontolizumab, golimumab, infliximab, mepolizumab, secukinumab, tocilizumab, ustekinumab, etanercept, ixekizumab, tildrakizumab, dupilumab, tralokinumab) within 12 weeks or 5 half-lives of the baseline visit, whichever is longer.
16. Have been treated with any oral immune suppressants (e.g., cyclosporine A, azathioprine, methotrexate, sulfasalazine, systemic corticosteroids, mycophenolate mofetil) within 8 weeks of the baseline visit.

[redacted]

17. Have received intralesional injections of corticosteroid or platelet-rich plasma (PRP) in the scalp within 6 weeks of the baseline visit.
18. Have used phototherapy [e.g., ultraviolet B (UVB), psoralen ultraviolet A (PUVA)], contact sensitisers, contact irritants, or cryotherapy within 4 weeks of the baseline visit.
19. Have used topical treatments applied to the scalp, eyebrows, or eyelashes (e.g., corticosteroid cream; JAK inhibitors; medicated shampoo; minoxidil (Rogaine); or herbal hair care that could affect AA) within 4 weeks of the baseline visit.
20. Have current or recent history of clinically significant severe, progressive, or uncontrolled renal (including, but not limited to active renal disease or recent kidney stones), hepatic, haematological, gastrointestinal, metabolic, endocrine, pulmonary, cardiovascular, psychiatric, immunologic/rheumatologic or neurologic disease; or have any other severe acute or chronic medical or psychiatric condition or laboratory abnormality that may increase the risk associated with study participation or study drug administration, or interfere with the interpretation of study results in the judgement of the Investigator or Sponsor, would make the subject inappropriate for entry into this study.
21. Have a known immunodeficiency disorder or a first-degree relative with a hereditary immunodeficiency.
22. History of solid organ or haematological transplantation.
23. History of a lymphoproliferative disease or malignancy, other than adequately treated non-melanoma skin cancer or cervical carcinoma with no evidence of recurrence.
24. Have active acute or chronic infection including:

    COVID-19 infection, infection requiring treatment with systemic antibiotics, antivirals, antiparasitics, antiprotozoals, or antifungals within 14 days before the first dose of study drug or a major episode of infection that required hospitalisation or treatment with IV antibiotics within 60 days before the baseline visit. Or serologic evidence of HBsAg, HCV or HIV, including during screening.
25. Abnormalities in clinical laboratory tests at Screening, as confirmed by a single repeat, if deemed necessary:
    a. Absolute neutrophil count (ANC) $<1.0 \times 10^9$/L.
    b. Liver function tests (LFTs including ALT and AST) >3 x upper limit of normal (ULN).
    c. Total bilirubin >1.5 times ULN (unless isolated Gilbert's syndrome)
    d. Serum creatinine >1.5 ULN.

4.1.3. Lifestyle Considerations

In order to participate in the study, subjects must follow these lifestyle guidelines and restrictions throughout the study.

- Agree to use appropriate contraception methods [redacted]
- Agree to maintain a consistent hair style, including shampoo and hair products (including hair dye, process, and timing to hair appointments), and to refrain from weaves or extensions throughout the course of the study, or shaving of scalp hair for 12 days preceding a SALT assessment.

[redacted]

- For subjects who undergo colour application to their hair, it is recommended that the colour application not be performed within 3 days prior to the scheduled study visits, if possible. Hair colouring should remain consistent throughout study.
- Agree not to use adhesive or difficult to remove hairpiece or wigs during the study.
- Mascara and false eyelashes are allowed but must be removed prior to clinical assessments during the study. The use of false eyelashes with adhesive should be discouraged, where possible, due to the risk of eyelash loss during removal.
- Hair transplants and tattooing of scalp, eyebrows, or eyelashes, including procedures such as microblading, are not permitted during the study.

4.1.4. Screen Failures

If appropriate, subjects may be rescreened and will be assigned a new unique subject identifier.

4.2. Method of Assigning Subjects to Treatment Groups

Subjects who meet the eligibility criteria will receive 2 mg/kg IV of EQ101 in an open-label fashion.

4.3. Treatment Discontinuation, Study Withdrawal, and Replacement

Study sites could be terminated for the following reasons:

- Failure of the Investigator to comply with the protocol, the requirements of the Independent Ethics Committee (IEC) or local health authorities, the Sponsor's procedures, or Good Clinical Practice (GCP) guidelines.
- Inadequate recruitment of participants by the Investigator.

4.3.1. Discontinuation of Study Drug

Subjects should be encouraged to complete study treatment. If 3 or more study doses are missed or planned to be missed, or if 2 consecutive doses are missed or planned to be missed, the Investigator in conjunction with the Sponsor study team should determine whether study drug should be discontinued permanently.

If study treatment is permanently discontinued, the subject should follow up at the next scheduled visit for end of treatment (EOT) assessments. An end of study (EOS) visit should occur approximately 4 weeks after their final study drug dose.

A subject is considered to have completed the study if he/she has completed the follow-up visit at Week 28 (Day 197).

Study drug must be discontinued if any of the following events occur:

- Subject receives or plans to receive a prohibited therapy (see Section 5.3) consistently over the course of the study.
- Subject has ≥ Grade 3 hypersensitivity reactions or anaphylaxis due to study drug per Common Terminology Criteria for Adverse Events (CTCAE) criteria. [redacted]
- Noncompliance with study procedures and expectations.

- Subject becomes pregnant.
- Subject withdraws consent.

Other reasons study drug may be discontinued include:

- AE (the specific AE should be identified on the electronic case report form [eCRF]).
- Investigator's decision.
- Sponsor's decision.

The date and the primary reason for study drug discontinuation will be recorded on the eCRF. If a subject discontinues study drug because of an AE, the Sponsor and/or designee must be notified by email or phone as soon as possible, and the specific AE leading to study drug discontinuation should also be identified on the eCRF.

4.3.2. Withdrawal From the Study

Subjects may withdraw from the study at any time at their own request or may be withdrawn at any time at the discretion of the Investigator for safety, behavioural, or compliance reasons.

The date and the primary reason for study withdrawal will be recorded on the eCRF. If a subject is withdrawn from the study because of an AE, the Sponsor and/or designee must be notified by email or phone within 48 hours, and the specific AE leading to study withdrawal should also be identified on the eCRF.

If subjects discontinue treatment for any reason, they should complete an EOT visit at their next scheduled visit, and then have an EOS visit approximately 4 weeks following their last study drug dose.

4.3.3. Subject Replacement

Subjects that terminate study treatment early may be replaced as appropriate to meet the objectives of the study.

[redacted]

5. STUDY TREATMENT

Study drug is defined as EQ101 and will be supplied by the Sponsor [redacted]

5.1. Study Drug

[redacted]

5.1.6. Modification of Dose and/or Treatment Schedule

There are no dose modifications to study drug during this study. Subjects should be encouraged to complete all dosing and visits.

[redacted]

5.1.7. Study Drug Compliance

If subjects have missed or plan to miss ≥3 doses of study drug or 2 consecutive doses, the Investigator in conjunction with the Sponsor study team should discuss whether a subject should permanently discontinue study drug.

5.1.8. Study Drug Accountability

The site will maintain the following records: receipt of shipments, dispensation to subjects, and destruction or return of partially used, or unused study drug. Upon completion or early termination (ET) of the study, all unused and partially used (if allowed by site/institutional procedure to be retained) study drug must be returned to the Sponsor or designee, unless the Sponsor authorises the study site to destroy study drug.

5.2. Additional Protocol Required Medication

There are no additional protocol required medications.

[redacted]

6. STUDY PROCEDURES AND ASSESSMENTS

The following sections describe the study procedures and assessments that will be performed during the study. [redacted]

6.1. Medical History and Demographics

6.1.1. Medical History

A complete medical history and information on the subject's concurrent medical conditions will be obtained.

All findings will be recorded on the Medical History eCRF.

Details of the diagnosis and previous treatment for AA will be collected. This may include details of locations and timing of hair loss and regrowth.

6.1.2. Demographics

Demographic information collected will include age, sex, race, and ethnicity. Where local regulations do not permit certain demographic data to be collected, collection of those data will not be required.

6.2. Prior and Concomitant Therapy

All medications taken by subjects between signing the informed consent form (ICF) and the end of the study will be recorded in the subject's eCRF. The name, dose, route, and start and stop dates of concomitant medications must be recorded. Medications include prescription and over-the-counter medications (including herbal products and vitamins). For subjects entering on a stable dose of permitted medication, any change in dose should also be recorded.

Previous treatments for AA will be recorded.

6.3. Safety Assessments

This section provides information on AE collection. Safety monitoring and reporting procedures are addressed in Section 8.

While pregnancy is not considered an AE, all cases of fetal drug exposure via a maternal parent as study subject or pregnancy of a partner of a male study subject will be reported immediately to the Sponsor (refer to Section 8.2.3 for reporting requirements).

6.3.1. Adverse Events

An **AE** is any untoward medical occurrence in a clinical study participant administered a pharmaceutical product and which does not necessarily have a causal relationship with this treatment.

An AE can therefore be any unfavourable and unintended sign (including an abnormal laboratory finding), symptom, or disease temporally associated with the use of a medicinal (investigational) product, whether or not related to the medicinal (investigational) product (definition per International Council for Harmonisation [ICH]). Pre-existing events, which increase in frequency or severity or change in nature during or because of use of a drug in human clinical studies, will also be considered as AEs. AEs may also include pre- or post-treatment complications that occur as a result of protocol-mandated procedures (e.g., invasive procedures such as biopsies).

AEs will be monitored throughout the entire study. Investigators will ask the subjects at each visit if they have experienced any untoward occurrence since the last study visit. All AEs will be recorded on the CRFs provided, including: a description of the event, severity, time of occurrence, duration, any action (e.g., treatment and follow-up tests), outcome, and the Investigator's assessment of the relationship to the study treatment.

From the time of signing the ICF through the first study drug administration, all SAEs and nonserious AEs related to protocol-mandated procedures (including medication washout performed specifically for the study) will be recorded on the SAE/AE eCRF. All other untoward medical occurrences observed during Screening, including exacerbation or changes in the medical and surgical history, will be captured on the medical and surgical history eCRF. An AE does not include:

- medical or surgical procedures (i.e., surgery, endoscopy, tooth extraction, transfusion); the condition that leads to the procedure is an AE;
- pre-existing diseases or conditions present or detected prior to start of study drug administration which do not worsen;
- situations where an untoward medical occurrence has not occurred (i.e., hospitalisation for elective surgery [prolongation of hospitalisation is an AE], social and /or convenience admissions); or
- overdose of either study drug or concomitant medication without any signs or symptoms, unless the subject is hospitalised for observation.

A clinical abnormality that meets any of the following criteria should be reported as an AE:

- has accompanying symptoms and signs;
- requires additional diagnostic tests or therapeutic measures (e.g., surgical intervention);
- leads to a change in study drug dosing regimen (e.g., dose delay, discontinuation) or study termination; or
- is considered clinically significant by the Principal Investigator (PI).

Any AE where a causal relationship with the study drug is a reasonable possibility (possibly/probably or definitely related) is referred to as an **adverse drug reaction**.

An **SAE** is any AE that, at any dose:

- results in death;
- is life-threatening (the term 'life-threatening' in the definition of 'serious' refers to an event/reaction in which the participant was at risk of death at the time of the event/reaction; it does not refer to an event/reaction which hypothetically might have caused death, if it were more severe);
- requires inpatient hospitalisation or prolongation of an existing hospitalisation (only hospitalisations that are longer than expected based on PI judgement, will be considered prolonged hospitalisations);
- results in persistent or significant disability/incapacity (an AE that results in a substantial disruption of a person's ability to conduct normal life functions); or

- is a congenital anomaly/birth defect (a congenital anomaly/birth defect that occurs in the offspring of a participant exposed to the study drug).

Medical and scientific judgement should be exercised in deciding whether other situations should be considered serious, such as important medical events that may not be immediately life-threatening or result in death or hospitalisation but might jeopardise the participant or might require medical or surgical intervention to prevent one of the other outcomes listed in the above definition. These should also be considered serious.

Examples of such events are intensive treatment in an emergency room or at home for allergic bronchospasm, blood dyscrasias or convulsions that do not result in hospitalisation, or development of drug dependency or drug abuse.

A sudden unexpected serious adverse reaction (SUSAR) is an AE that meets all the following criteria:

- is serious;
- there is at least a reasonable possibility of a causal relationship between the event and the study drug;
- is considered unexpected (i.e., the event is not listed in the Investigator's Brochure [IB] or is not listed at the specificity or severity that has been observed). For example, under this definition, hepatic necrosis would be unexpected (by virtue of greater severity) if the IB referred only to elevated hepatic enzymes or hepatitis. Similarly, cerebral thromboembolism and cerebral vasculitis would be unexpected (by virtue of greater specificity) if the IB listed only cerebral vascular accidents. "Unexpected" as used in this definition, also refers to AEs that are mentioned in the IB as occurring with a class of drugs or are anticipated from the pharmacological properties of the drug but are not specifically mentioned as occurring with the particular drug under investigation.

6.3.2. Evaluating AEs and SAEs

6.3.2.1. Assessment of Severity

The PI will make an assessment of severity for each AE and SAE reported during the study. The assessment will be based on the PI's clinical judgement. The intensity of each AE and SAE will be graded using the most current version of the National Cancer Institute (NCI) CTCAE 5-point scale [redacted]

[redacted]

6.3.2.2. Assessment of Causality

The PI will make an assessment as to the relationship between the study treatment and the occurrence of each AE/SAE. The PI will use clinical judgement to determine whether or not the AE/SAE is causally related to the study treatment(s). Alternative causes, such as natural history of an underlying medical condition, concomitant therapy, other risk factors, and the temporal relationship of the event to the study treatment will be considered and investigated. The PI will also consult the IB (or the product information sheet in instances where the study treatment is an approved agent) in the determination of his/her assessment.

[redacted]

[redacted]

The causality assessment is one of the criteria used when determining regulatory reporting requirements, therefore, the PI must make an assessment of causality based on all available information for every event prior to transmission of the SAE form to the Sponsor. The PI may change his/her opinion regarding causality in light of follow-up information and amend the SAE form and the eCRF accordingly.

6.3.3. Action Taken and Outcome

For all AEs reported, the actions taken, and outcomes must be specified and documented in the appropriate forms.

Actions taken may include but are not limited to the following:

Action(s) taken with study drug:

- Dose not changed
- Dose reduced
- Drug withdrawn

[redacted]

6.3.4. Procedures and Time Period for Detecting Adverse Events

The PI (or designee) is responsible for detection, recording and reporting of events that meet the criteria and definition of AEs.

As a consistent method of soliciting AEs, the participant shall be asked a nonleading question such as: “How do you feel?”

Detection and recording of study-related AEs and SAEs extend from the time of first dose until completion of the last study-related procedure (including follow-up for safety assessments).

Any change in health status that is reported or observed after informed consent but prior to starting study treatment, will be documented as medical history.

Any pre-existing conditions or signs and/or symptoms present in a volunteer prior to any involvement in the study (i.e., before informed consent) should be recorded as medical history. In addition, any change in health status, which is reported after informed consent but started prior to informed consent, will be documented as medical history. Any worsening of a pre-existing condition that occurs following informed consent, but prior to commencing study treatment, will be recorded as medical history. Any worsening of a pre-existing condition that occurs following the first administration study treatment, will be recorded as an AE/SAE.

A post-study AE/SAE is defined as any event that occurs outside of the nominal AE/SAE study detection period. Investigators are not obligated to actively seek AEs/SAEs in former study

[redacted]

participants. However, if the PI learns of any SAE, including a death, at any time after a participant has completed the study and he/she considers the event reasonably related to the study treatment, the PI will promptly notify the Sponsor.

Participants must be provided with an "Emergency Wallet Card" indicating the name of the study treatment, the study number, the PI's name, an emergency contact number, and, if applicable, excluded concomitant medications.

6.3.5. Recording of AEs and SAEs

All AEs, regardless of seriousness, severity, or presumed relationship to study treatment, must be recorded using medical terminology in the eCRF and/or other sources. Whenever possible, diagnoses should be given when signs and symptoms are due to a common aetiology (e.g., cough, runny nose, sneezing, sore throat, and head congestion may be reported as "upper respiratory infection"). Investigators must record in the eCRF the date of onset of the event, their opinion concerning the relationship of the AE to the study treatment, severity of the event, whether the event is serious or nonserious, actions taken to manage the event, the outcome of the event, and date of resolution where applicable.

Any increase to the severity of an AE must be recorded as a separate AE, ensuring that the end date and time of the preceding AE matches the start date and time of the subsequent AE, so that the overall duration of the AE is continuous.

6.3.6. Physical Examinations

Complete physical examinations will include an assessment of skin, head and neck, lungs, cardiovascular system, nervous system, abdomen, thyroid, lymph nodes, and extremities. Targeted physical examinations will include an evaluation of the skin and areas impacted by AA including the scalp, eyelashes, eyebrows, and fingernails (i.e. pitting, koilonychia -rough nails), and any new subject complaints or changes from Baseline for AE assessments. Additionally, lymph node and cardiopulmonary exams should be conducted.

Physical examination findings prior to the first dose of study drug will be recorded on the Medical History eCRF; clinically significant findings after the first dose of study drug will be recorded as AEs.

6.3.7. Vital Sign Measurements

Vital sign measurements will include temperature, systolic and diastolic blood pressure, and pulse. Subjects should be in a rested, calm state for at least 5 minutes before vital signs are collected, as much as possible.

On dosing days, vital signs will be assessed prior to dosing and 30 minutes (± 10 minutes) following the administration of study drug at a minimum.

[redacted]

6.3.8. 12-Lead Electrocardiogram

Standard digital 12-lead ECGs will be performed. On dosing days, a 12-lead ECG will be performed pre-dose. On Day 1, there will also be an ECG 30 minutes (±10 minutes) post-dose.

[redacted]

Subjects should be in the supine position in a rested, calm state for at least 5 minutes before ECGs are performed.

The Investigator (or designated study site physician) will review all ECG results and document any relevant findings.

The original ECG results will be retained with the subject's source documents. Copies of all source ECG data and tracings must be made available to the Sponsor, if requested.

6.3.9. Clinical Safety Laboratory Tests

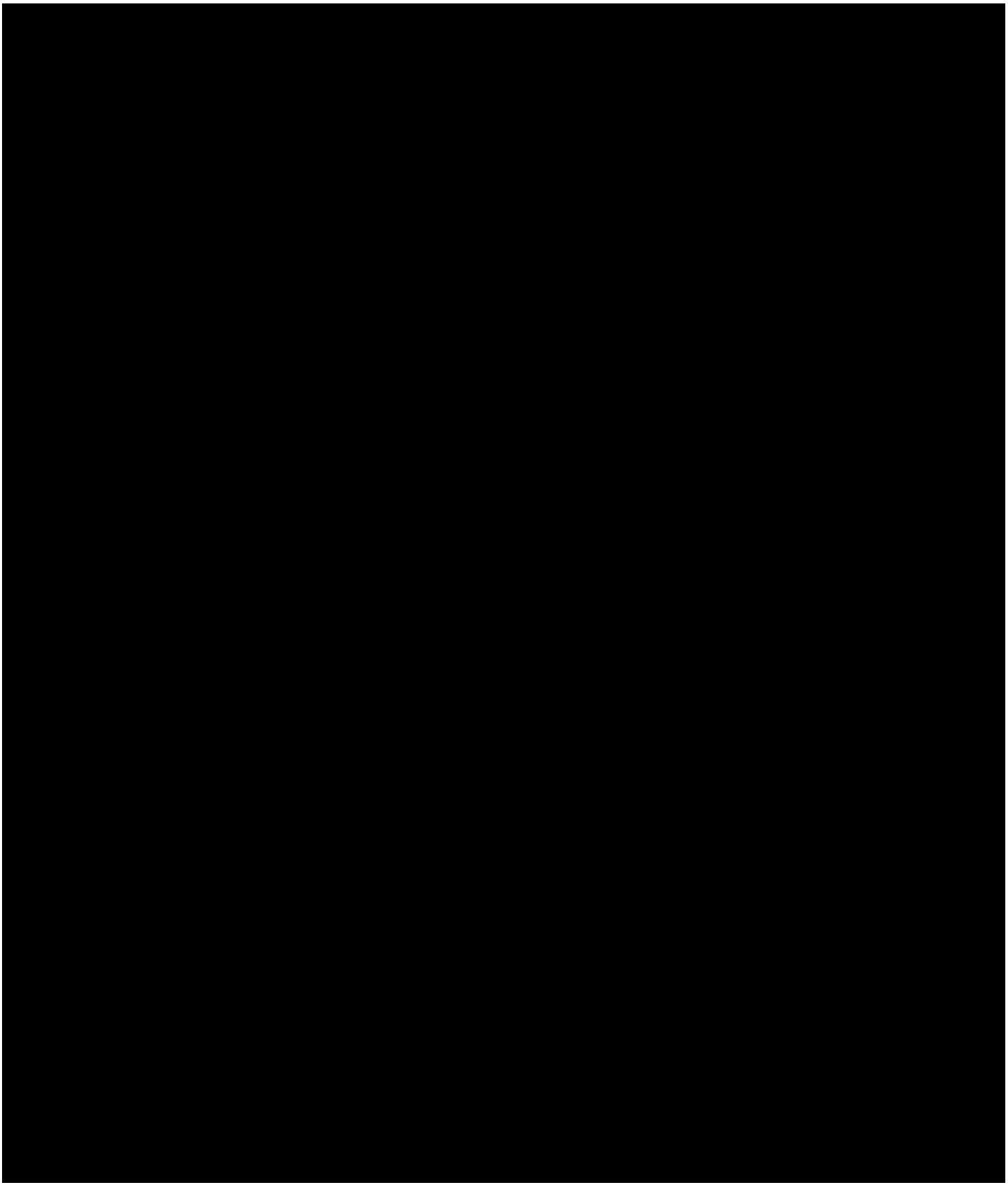
Blood and urine samples will be collected for safety laboratory tests (haematology, serum chemistry, coagulation, urinalysis, and viral studies). [redacted]

Pre-dose safety laboratory results (i.e., haematology, coagulation, serum chemistry including LFTs, urinalysis) and those for eligibility (i.e., liver function tests) must be performed prior to Day 1 dosing.

All scheduled laboratory safety tests, unless specified, will be performed at a central laboratory.

Laboratory results will be reviewed by the Investigator (or designee). The Investigator may repeat a laboratory test or request additional tests to verify the results of the original laboratory test. In general, abnormal laboratory findings without clinical significance (based on the Investigator's judgement) will not be recorded as AEs. Laboratory values should be reported as AEs at the Investigator's discretion. When applicable, clinical sequelae (not the laboratory abnormality) can be recorded as the AE.

Detailed instructions on sample collection, processing, storage, and shipping procedures are provided in the Laboratory Manual.



[redacted]

6.3.10. COVID-19

A COVID-19 polymerase chain reaction (PCR) or rapid antigen test (RAT) test should be performed on Day 1 prior to dosing. A COVID-19 PCR or RAT may be performed at any time during the study at the discretion of the Investigator, if clinically indicated, or if required by local regulations.

6.3.11. ADA and Neutralising ADA Assessments

Plasma samples will be obtained pre-dose at scheduled timepoints [redacted] during the study to assess the presence of treatment-emergent ADAs against EQ101. If a subject has a positive result for ADAs, a neutralising ADA assay will be performed on the same sample. ADA sampling can also be requested by the Sponsor at an unscheduled visit to further assess the relationship between immunogenicity and safety in individual subjects.

6.3.12. Pregnancy Testing

Pregnancy tests are required to be done (if applicable) [redacted]. For female subjects of childbearing potential, 2 negative pregnancy tests are required before receiving study treatment(s): 1 negative serum pregnancy test at Screening and 1 urine pregnancy test at the baseline visit immediately before study treatment administration. Pregnancy tests will also be repeated at visits specified in the Schedule of Events (SoE). In the case of a positive confirmed pregnancy, the subject will be withdrawn from administration of study drug but may remain in the study for follow-up.

6.4. PK Assessments

Blood samples will be collected for analysis of EQ101 concentrations. Instructions for collection, processing, storage, and shipping of PK samples will be provided in the study Laboratory Manual.

Samples will be assayed by a validated method, which is specific for the determination of EQ101 components.

Sample processing and storage details will be provided in the study Laboratory Manual.

On Day 1, samples should be collected both pre-dose and 45 minutes (±15 minutes) after the study drug administration.

All other PK samples should be taken prior to dosing as outlined in the Schedule of Events.

[redacted]

[redacted]

6.6.2. Photographs of the Scalp, Eyebrows and Eyelashes

All sites will obtain photographs of the scalp (4 planes), 1 frontal view of the face and scalp, and photographs of the eyebrows/eyelashes at Baseline (Day 1) and every 4 weeks and Week 24/EOT and EOS visits. Camera equipment, necessary ancillary materials, and a study-specific photography manual will be provided to all sites by the Sponsor or designee as needed. The following photographs will be obtained by trained site personnel under similar lighting conditions and magnifications, and per instructions provided during training and as outlined in the photographic procedure manual:

- 4-plane views of the scalp, including each side, back, and top of head.
- 1 frontal view of the face and scalp.
- Photographs of the eyebrows/eyelashes will be taken from subjects with eyelash and/or eyebrow loss (ClinRO Measure for Eyebrow and/or Eyelash Hair Loss ≥ 1).

6.6.3. Photographs of Body Hair and/or Fingernails (Optional, at Participating Site/s)

The following photographs may be obtained from subjects that have provided the relevant written informed consent for optional body hair and/or fingernail photographs:

- If applicable, optional photographs of body hair (growth or regrowth) may also be taken in subjects with hair loss on the trunk and limbs. Subjects with AA localised to the scalp are not eligible to participate in this optional assessment.
- If applicable, optional photographs of fingernails may be taken in subjects with identified fingernail changes (i.e. pitting, koilonychia -rough nails).

[redacted]

6.6.4. Research Use of Stored Human Samples, Specimens, or Data

De-identified data obtained from this study may be shared with academic institutions after study completion if such sharing is permitted by local regulations. Furthermore, any remaining samples may be stored for future analysis to support understanding of biomarkers for disease state, progression, and response to treatment as new discoveries emerge.

No genetic testing will be performed on any of these stored samples. Subjects will be asked to consent to the storage and use of these samples and data for future use during the consent process.

6.7. Efficacy Assessments

Efficacy measures will be collected for all subjects. Efficacy measures include SALT score [redacted] ClinRO measures for EB, EL and body hair loss evaluated by the Investigator and PRO measures. The Scalp PRO tool and ClinRO/PRO measures for EB and EL hair loss are validated outcome measures [redacted]

The SALT and ClinRO assessments should be performed by the trained Investigator/sub-Investigator. Prior to enrolling subjects, the evaluator (s) will be trained in the use of the efficacy scale to ensure that it is scored consistently at each site and across all sites. Training will be standardised and documented for all Investigators. Assessments should be performed in a well-lit room under consistent lighting at each study visit. Whenever possible, the evaluator(s) performing the efficacy assessments at an individual study site should perform these evaluations for all subjects throughout the study. If it is not possible to use the same evaluator to follow a given subject, the Sponsor recommends that evaluations between the primary and subsequent evaluator overlap (both evaluators should examine the subject together and discuss findings) for at least 1 visit.

[redacted]

6.7.1. SALT Score

AA severity will be evaluated using the SALT based on scalp terminal hair loss [redacted]

The SALT uses a visual aid which divides the scalp hair into 4 areas with the top of the scalp representing 40% of total scalp surface area, the posterior/back of the scalp 24%, and the right and left sides of the scalp representing 18% each. The percentage of hair loss in each area is determined and is multiplied by the percentage of scalp covered by that area. The total sum of the 4 products of each area gives the SALT score [redacted]

Subject must have a SALT score of ≥35 at Screening and Baseline to be eligible for the study. An independent reviewer may review the photos to confirm the SALT scores.

6.7.2. ClinRO Measure for Eyebrow Hair Loss™

ClinRO Measure for EB Hair Loss™ is the Investigator's assessment of the subject's overall severity of EB hair loss. The assessment uses a 4-point response scale ranging from 0 (full coverage/no hair loss) to 3 (no notable EB hair). The ClinRO Measure for EB Hair Loss™ rating scale [redacted]

[redacted]

6.7.3. ClinRO Measure for Eyelash Hair Loss™

ClinRO Measure for EL Hair Loss™ is the Investigator's assessment of the subject's overall severity of EL hair loss. The assessment uses a 4-point response scale ranging from 0 (ELs form a continuous line along eyelids on both eyes) to 3 (no notable ELs). The ClinRO Measure for EL Hair Loss™ rating scale [redacted]

6.7.4. ClinRO Measure for Body Hair Loss

ClinRO Measure for Body Hair Loss is the Investigator's assessment of the subject's overall severity of Body hair loss. The assessment uses a 5 category response options: 0 = No missing hair (0% of body is missing hair); 1 = A limited area (1% to 20% of body is missing hair); 2 = A moderate area (21% to 49% of body is missing hair); 3 = A large area (50% to 94% of body is missing hair); and 4 = Nearly all or all (95% to 100% of body is missing hair). The ClinRO Measure for Body Hair Loss rating scale [redacted]

Body hair assessment should include armpits, pubic hair and beard (scalp, eyebrows, and eyelashes are excluded).

6.7.5. Patient-Reported Outcomes (PRO)

Patient-reported outcomes will include Scalp Hair Assessment PRO™, PRO Measure for EB™, PRO Measure for EL™, PRO Measure for Body Hair.

6.7.5.1. Scalp Hair Assessment PRO™

Subjects will assess the severity of their scalp hair loss using the 5-point Scalp Hair Assessment PRO™ scale [redacted] The Scalp Hair Assessment PRO is comprised of 5 category response options: 0 = No missing hair (0% of my scalp is missing hair; I have a full head of hair); 1 = A limited area (1% to 20% of my scalp is missing hair); 2 = A moderate area (21% to 49% of my scalp is missing hair); 3 = A large area (50% to 94% of my scalp is missing hair); and 4 = Nearly all or all (95% to 100% of my scalp is missing hair).

6.7.5.2. PRO Measure for Eyebrows™

Subject's self-assessment of the overall severity of EB hair loss is measured by a 4-point scale, [redacted] This assessment uses a 4-point response scale, ranging from 0 (full EBs on each eye) to 3 (no or barely any EB hairs).

6.7.5.3. PRO Measure for Eyelashes™

Subject's self-assessment of the overall severity of EL hair loss is measured by a 4-point scale [redacted] This assessment uses a 4-point response scale, ranging from 0 (full ELs on each eyelid) to 3 (no or barely any EL hairs).

6.7.5.4. PRO Measure for Body Hair

Subjects will assess the severity of their body hair loss using the 5-point Body Hair Assessment PRO scale [redacted] The Body Hair Assessment PRO is comprised of 5 category response options: 0 = No missing hair (0% of my body is missing hair, I have a normal amount of body

[redacted]

hair); 1 = A limited area (1% to 20% of my body is missing hair); 2 = A moderate area (21% to 49% of my body is missing hair); 3 = A large area (50% to 94% of my body is missing hair); and 4 = Nearly all or all (95% to 100% of my body is missing hair).

Body hair assessment should include armpits, pubic hair and beard (scalp, eyebrows and eyelashes are excluded).

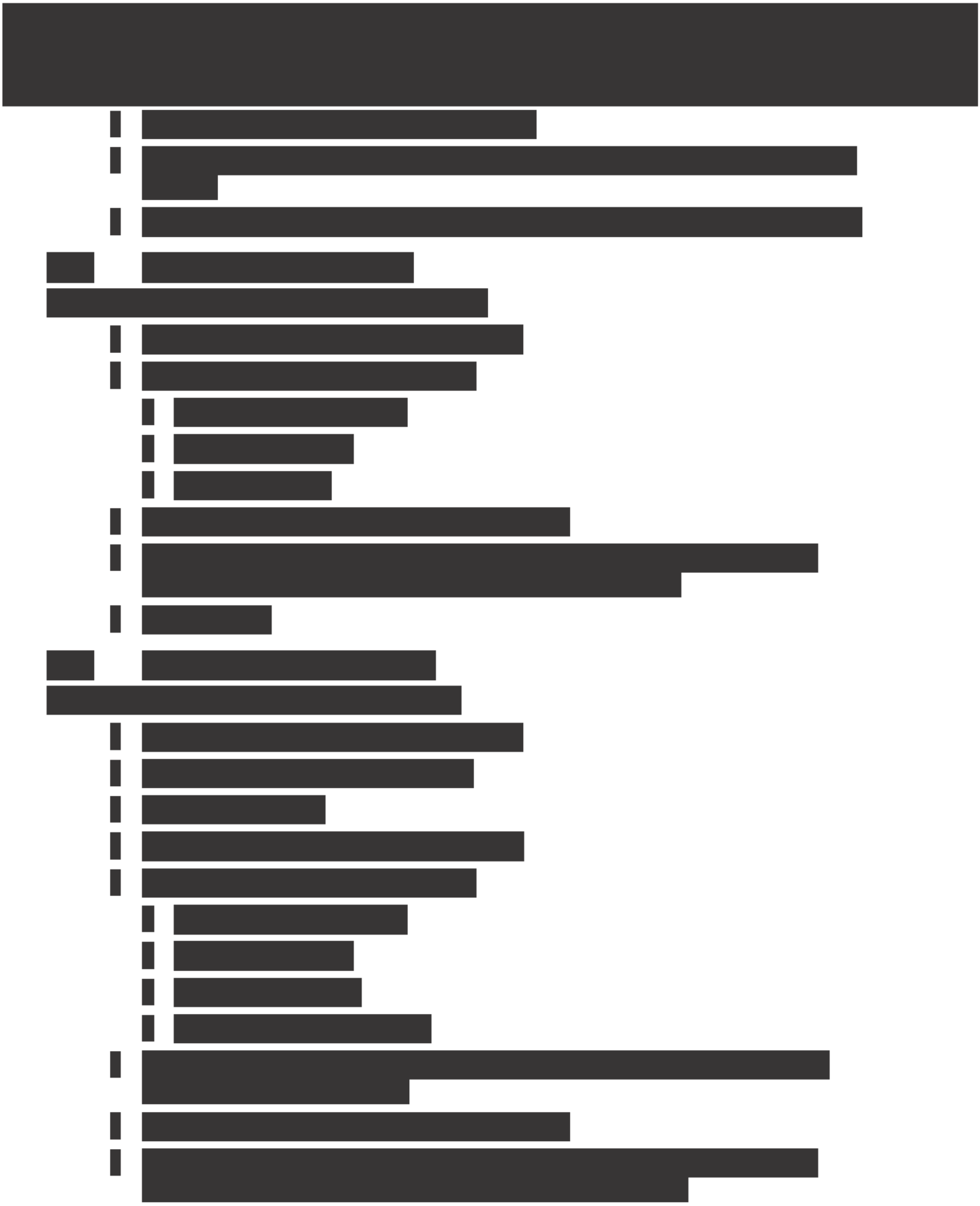
[redacted]

7. STUDY ACTIVITIES

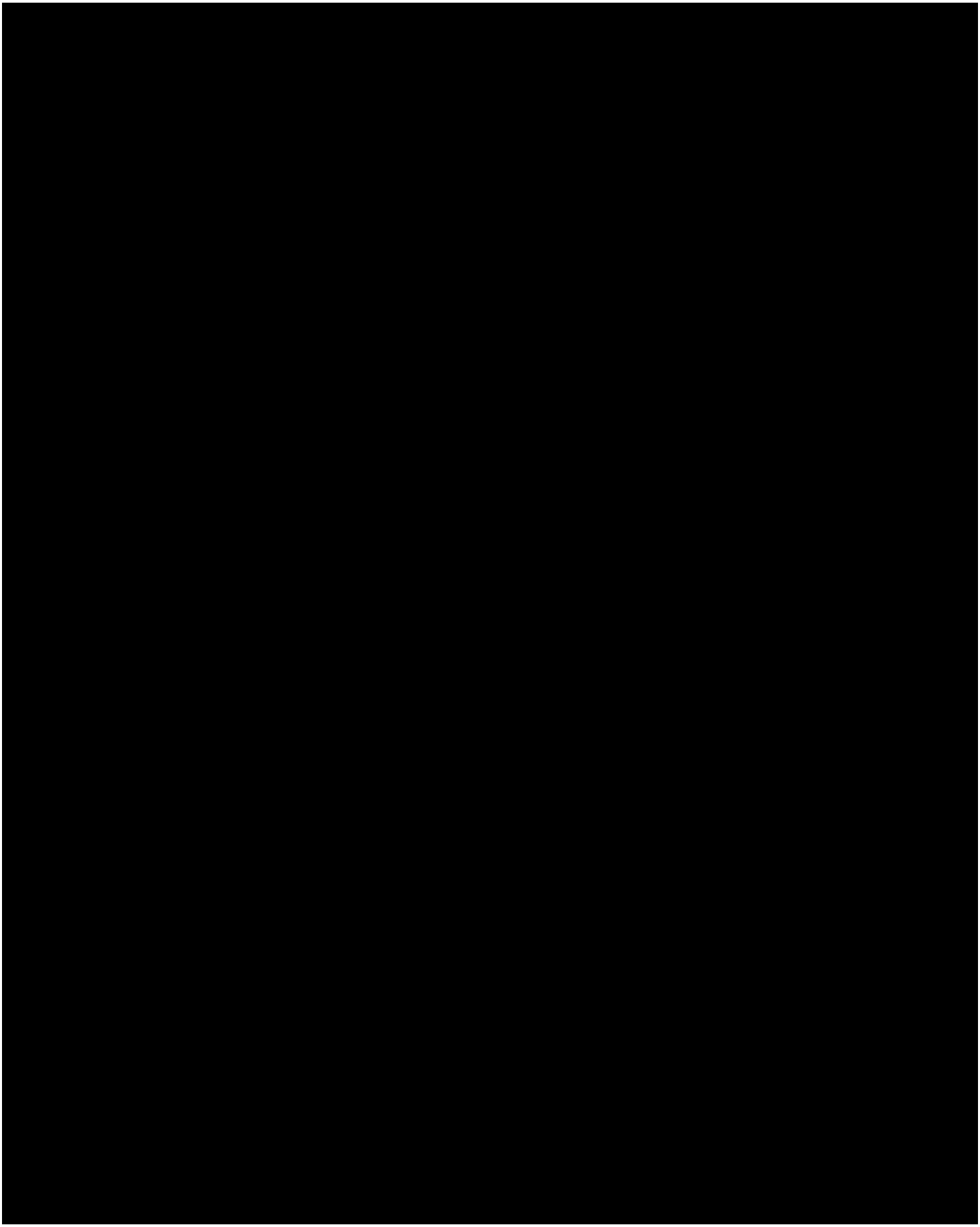
[redacted]

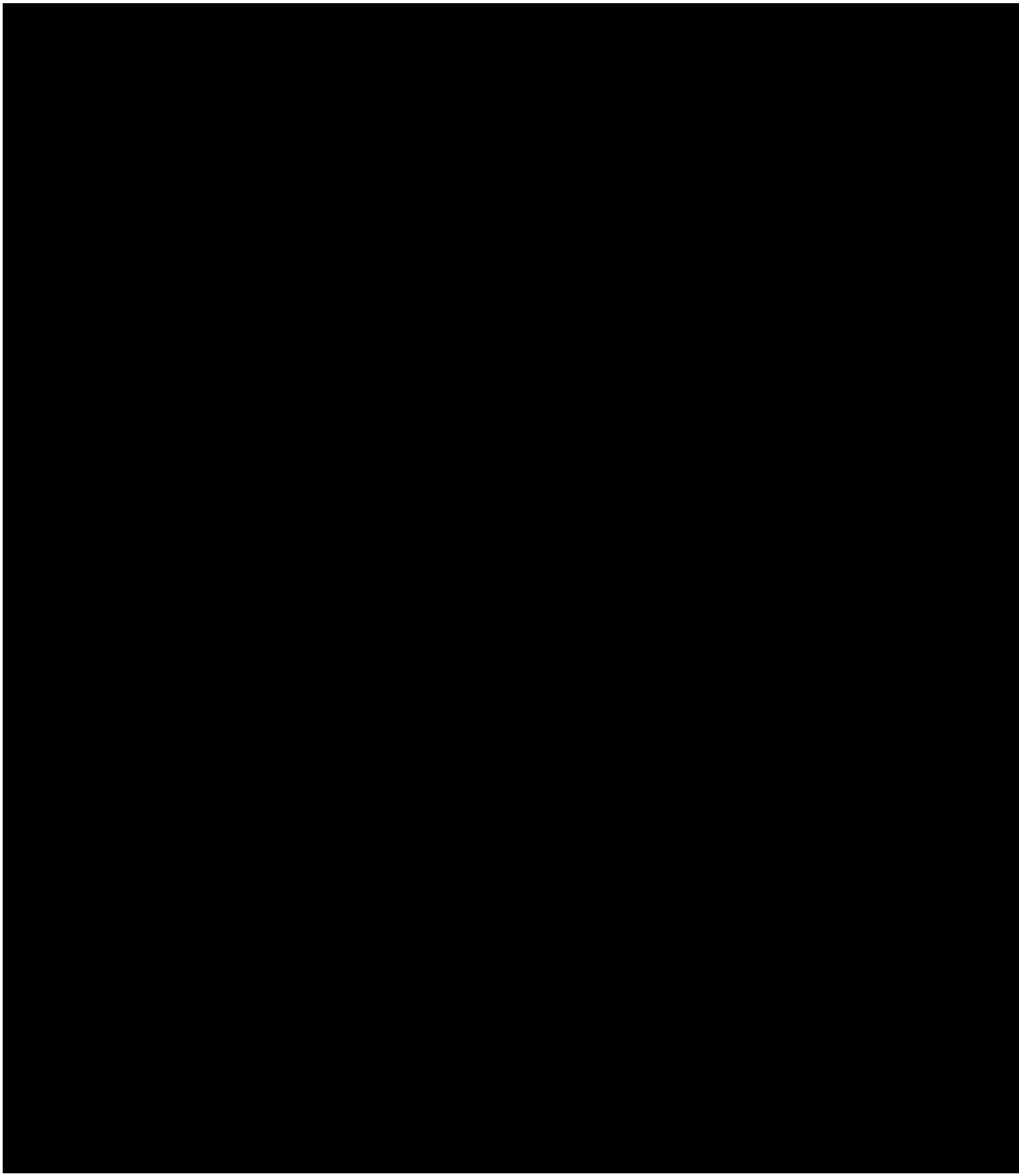
Unless there is a safety concern, every effort should be made to avoid protocol deviations by completing procedures and assessments according to the protocol guidance. Procedures and assessments should be made in the order listed in this section below.

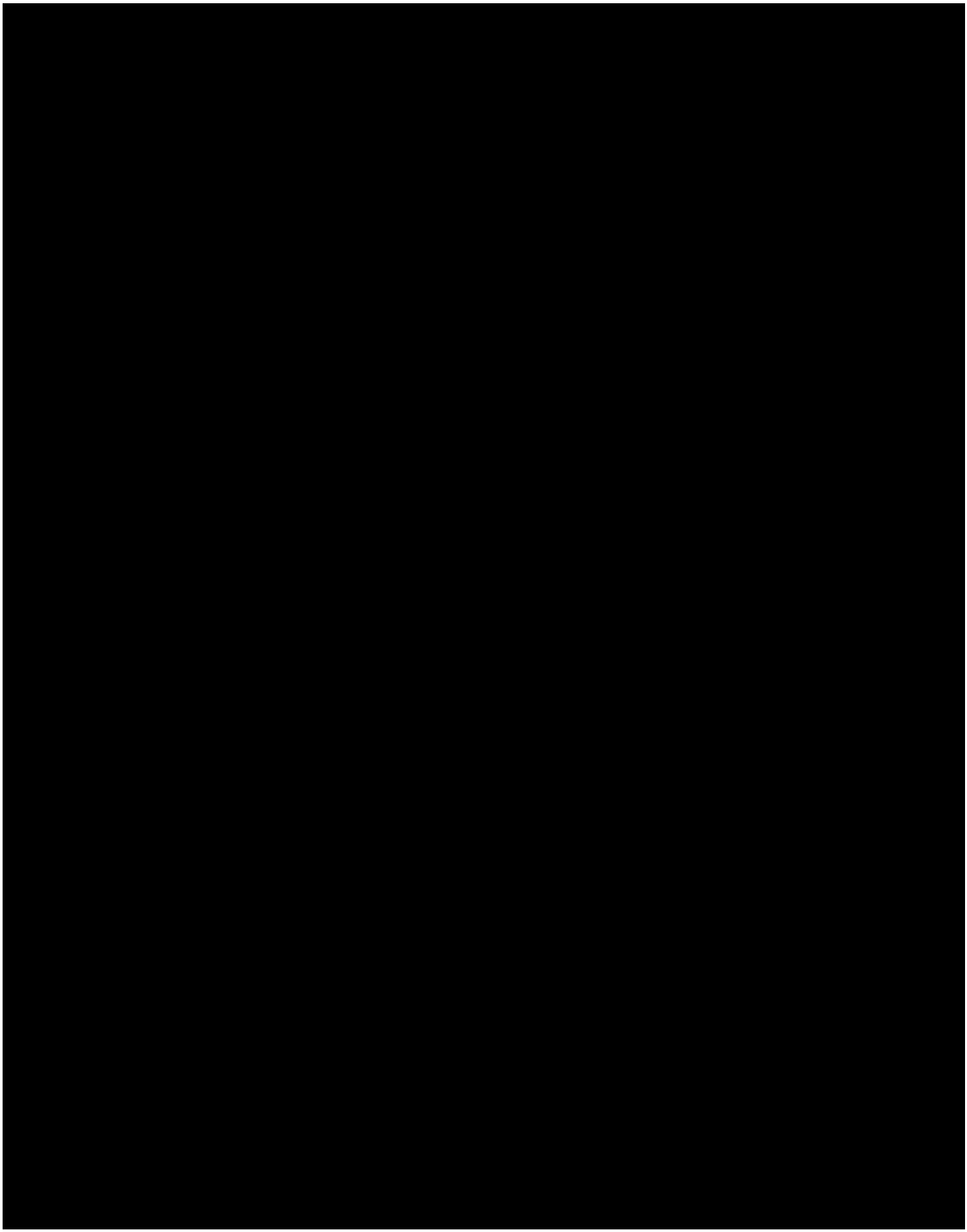
Unscheduled visits and assessments should be performed if clinically indicated in the opinion of the Investigator. The results of any unscheduled assessments should be recorded on an eCRF.

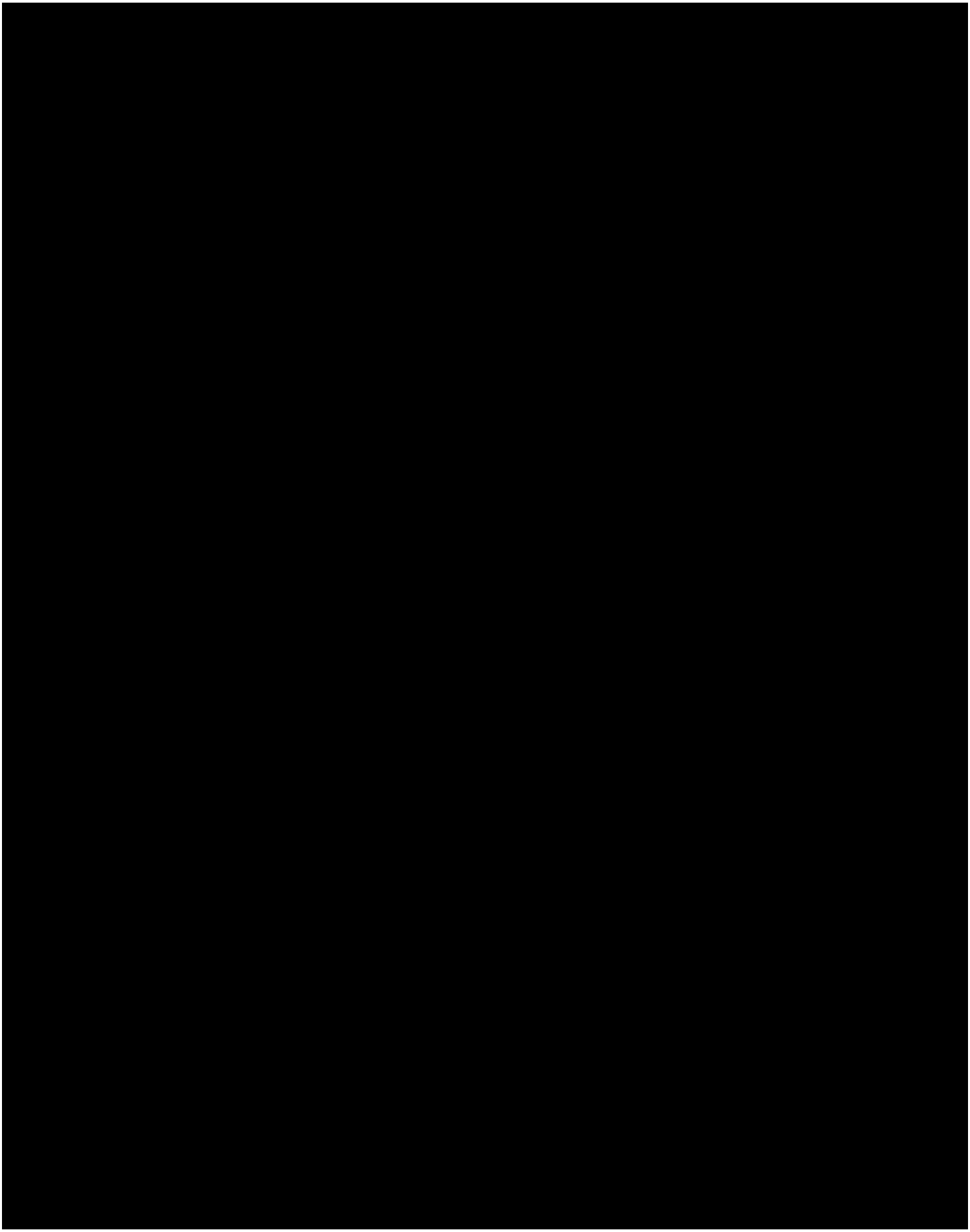


[redacted]









8. SAFETY MONITORING AND REPORTING PROCEDURES

8.1. Safety Monitoring

Study subjects will be under close medical supervision by the Investigator throughout the study.

Study drug will be administered at the study site. Following study drug administration, vital signs will be monitored and subjects will be monitored for toxicity.

The Sponsor and/or Medical Monitor will regularly review the safety data during the study.

Infusion-related reactions and hypersensitivity reactions require close monitoring, as they have occurred with IV infusions of immunomodulators.

Subjects that test positive for COVID-19 while in the study should notify the study site personnel. Site personnel should contact the Medical Monitor to determine any impact on dosing schedule or further participation in the study.

8.1.1. Infusion-Related Reactions and Hypersensitivity Reactions (Including Anaphylaxis)

Infusion-related reactions and hypersensitivity reactions could include symptoms such as fever, chills, and/or rash at or following the IV infusion of EQ101.

If infusion-related or hypersensitivity reactions occur during study drug IV administration, the infusion may be paused, and the subject should be treated for the reaction as clinically indicated, such as with additional antihistamines (H1 ± H2 blocker) and/or topical or systemic corticosteroids. The infusion may be continued when appropriate if safe to do so, at the Investigator's discretion. Hypersensitivity reactions will be evaluated by the "Immune System Disorders" section of the CTCAE criteria ([redacted]. To identify cases of anaphylaxis, the National Institute for Allergy and Infectious Diseases definition will be used [redacted]

Subjects who develop anaphylaxis or a CTCAE criteria ≥Grade 3 hypersensitivity event based on the Immune System Disorders section (i.e., allergic reaction or serum sickness) that is determined by the Investigator to be related to study drug must immediately and permanently discontinue study drug. Immediate treatment and support should be given such as with oxygen, bronchodilators, steroids, epinephrine, etc., in accordance with Investigator/local standard of care.

8.2. Reporting Procedures

8.2.1. Reporting Serious Adverse Events

The PI must notify the study Sponsor within 24 hours of becoming aware of the occurrence of an SAE including SUSARs through the process described below.

Information regarding SAEs will be transmitted to the Sponsor's safety vendor within 24 hours of becoming aware of the occurrence of an SAE. SAEs should be reported on a paper SAE form. The SAE form must be completed and signed by a member of the investigational staff and the PI and transmitted to the Sponsor's safety vendor [redacted] Any new or updated clinical information on the SAE will be recorded on a new SAE form and sent to the Sponsor's safety

[redacted]

vendor within 24 hours of the information being available. Receipt of the SAE form must be confirmed by recipient.

[redacted]

It is the responsibility of the Sponsor to assess the expectedness of an SAE in order to determine whether a reported SAE fits the classification of a SUSAR. The PI's opinion regarding the assessment of expectedness (if provided) and causality will be taken into account in the Sponsor's determination of the SAE as a SUSAR. The causality assessment given by the PI cannot be downgraded by the Sponsor. Both the Sponsor's and PI's causality assessment will be considered to determine expedited reportability of an SAE as a SUSAR.

The PI must report SUSARs to the IEC/ Institutional Review Board (IRB) that approved the protocol in accordance with the IEC/IRB safety reporting procedures.

SAEs (including SUSARs) will be reported to competent authorities in accordance with national requirements. The Sponsor assumes responsibility for appropriate reporting of SAEs (including SUSARs) to the regulatory authorities as described in the Safety Reporting Plan.

8.2.2. Follow-up of AEs and SAEs

Following initial observation of an AE/SAE, the PI is required to proactively follow progress of the relevant participant. Any information obtained in relation to the status of the AE/SAE and the condition of the participant must be appropriately documented in the eCRF and in a follow-up SAE form/eCRF where required.

All AEs and SAEs documented at a previous visit/contact that are designated as ongoing, will be reviewed at subsequent visits/contacts. Any AEs/SAEs that have not resolved by the end of the study, or that have not resolved upon discontinuation of the participant's involvement in the study, must be followed until any of the following occurs:

The event resolves:

- The event stabilises.
- The event returns to Baseline, if a Baseline value is available.
- The event can be attributed to agents other than the study treatment or to factors unrelated to study conduct.
- It becomes unlikely that any additional information can be obtained (participant or health care practitioner refusal to provide additional information, lost to follow-up after demonstration of due diligence with follow-up efforts).

The PI will ensure that AE/SAE follow-up includes any supplemental investigations as may be indicated to elucidate the nature and/or causality of the event. This may include additional

[redacted]

laboratory tests or investigations, histopathological examinations, or consultation with other health care professionals.

The Sponsor may request that the PI perform or arrange for the conduct of supplemental measurements and/or evaluations to elucidate as fully as possible the nature and/or causality of the AE/SAE. If a participant dies during participation in the study or during a recognised follow-up period, the Sponsor will be provided with a copy of any post-mortem findings, including histopathology.

New or updated information will be recorded on a new SAE form and sent to the Sponsor. Due to the COVID-19 pandemic, PIs must also ensure compliance with local governing legislation and reporting requirements associated with COVID-19 infections.

8.2.3. Pregnancy Reporting

In instances of pregnancies or suspected pregnancies, including a positive pregnancy test, identified or reported for any female participant (or male participant's female partner), regardless of age, following administration of study treatment, the pregnant female participant (or the male participant's female partner) will be advised to notify her healthcare provider. Study drug administration will be discontinued immediately in the event of a reported (or suspected) pregnancy in a female participant (or male participant's female partner).

The PI will notify the Sponsor and the Sponsor's designated study safety officer of this event and document the exposure in utero (EIU) on the Pregnancy form as described in the study Pregnancy Report Form Completion Guidelines.

Informed consent will be sought from the pregnant female participant (or male participant's female partner) in order to allow for the PI to conduct follow-up access and review of relevant medical records throughout the gestational period and on the infant following delivery. The PI shall follow up newborn infants that have been exposed to study drug in utero for a minimum of 12 months. Upon discovery of any congenital anomalies (or neonatal deaths) the PI shall submit a follow-up report to the Sponsor (and the Sponsor's designated study safety officer) using an SAE paper form (as per study SAE Report Form Completion Guidelines) including information regarding the status of the newborn. A miscarriage or abortion or any congenital anomaly diagnosed in the infant exposed in utero shall also be reported by the PI to the Sponsor's safety vendor using an SAE form.

[redacted]

9. STATISTICAL METHODS

9.1. General Considerations

Data will be summarised using descriptive statistics (n, mean, median, standard deviation, minimum, maximum) for continuous variables and frequencies and percentages for discrete variables. Time to event variables will be summarised using the Kaplan-Meier method. All data summaries and listings will be produced using the SAS® software Version 9.4 or higher. A separate statistical analysis plan (SAP) will be prepared describing more details.

[redacted]

9.3. Analysis Populations

Safety Population: Consists of all subjects who receive at least one dose of study drug.

PK Analysis Population: Subjects in the safety population who have at least one measurable post-EQ101 exposure concentration.

[redacted]

9.4. Statistical Analysis Methods

9.4.1. Safety Analyses

AEs will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) for the purposes of summarisation. TEAEs, AEs that start during or after the first dose of study drug or AEs with an onset prior to the first dose of study drug that worsen after study drug administration, will be summarised by system organ class (SOC) and preferred term (PT). Treatment-emergent serious AEs (TESAEs), TEAEs leading to treatment discontinuation, and TEAEs with an outcome of death will be summarised similarly. In addition, TEAEs will be further summarised by worst severity grade and relationship to study drug, AEs of special interest (AESI) will be summarised by SOC, PT, and worst severity grade.

Clinical laboratory data will be summarised descriptively including observed values at collection timepoints and change from Baseline. All laboratory parameters that can be graded using CTCAE v5.0 will be graded. Other safety measures including vital signs and physical examination findings will be listed and summarised as appropriate.

9.4.2. Efficacy Analyses

Efficacy measures will be collected for all subjects. Efficacy measures include the SALT score [redacted] ClinRO measures for EB, EL and body hair loss evaluated by the Investigator and PRO measures. The Scalp PRO tool and ClinRO/PRO measures for EB and EL hair loss are

[redacted]

validated outcome measures [redacted] Efficacy endpoints will be summarised in the safety population using methods described in the General Considerations section.

9.4.3. Pharmacokinetic (PK) Analyses

Plasma concentrations of EQ101 will be reported as listings for individual subjects and also as statistical summaries grouped by the scheduled timepoint. The statistical summary will include mean, standard deviation (SD), coefficient of variation (CV%), maximum, minimum, median, geometric mean, and geometric CV%.

Plasma concentrations of EQ101 from this study may be included in a population PK analysis in order to generate PK parameters that will be documented in a separate Population PK Report

[redacted]

10. ADMINISTRATIVE CONSIDERATIONS

10.1. DATA HANDLING AND RECORDKEEPING

10.1.1. Privacy of Personal Data

In order to maintain subject privacy, all eCRFs, study treatment accountability records, study reports and communications will identify subjects by only their assigned subject study number. The PI will grant monitor(s) and auditor(s) from the Sponsor (or designee) and regulatory authorities access to the subject's original medical records for verification of data gathered on the eCRF and for the purposes of auditing the data collection process. The subject's confidentiality will be maintained at all times and will not be made publicly available to the extent permitted by the applicable laws and regulations.

10.1.2. Screening/Enrolment Logs and Privacy

The PI is required to complete a subject enrolment log to permit reference to each subject during and after the study. Any log identifying study subject identity will be treated as confidential and will be filed by the PI in the Investigator Site File (ISF). This document will be reviewed by the Study Monitor for completeness. To ensure subject confidentiality, if such a log is required to be distributed to the Sponsor, it must first have any personal details (e.g., name, initials, date of birth) redacted.

The PI must also complete a volunteer screening log, which reports on all volunteers who were assessed to determine eligibility for inclusion in the study.

10.1.3. Source Documentation

Source documentation must be prepared and available to capture at a minimum the following aspects and parameters:

- adherence to protocol procedures;
- participant study reference number(s);
- informed consent procedures;
- eligibility assessments;
- protocol specified schedules and assessments;
- dates of visits;
- safety observations including reporting and follow up of AEs;
- drug receipt/dispensing/return records;
- study treatment administration information;
- date of participant completion;
- discontinuation from treatment, or withdrawal from the study, and the reason if appropriate;

Specific items required as source documents will be reviewed with the PI before the study.

The author of an entry in the source documents must be identifiable. Worksheets may be used for the capture of some data to facilitate completion of the eCRF. Any such worksheets will become part of the subjects' source documentation.

Following the ICH-GCP guidelines, direct access to source documentation and medical records must be allowed for the purpose of verifying that the data recorded in the eCRF are consistent with the original source data.

10.1.4. Electronic Case Report Form

An eCRF entry must be completed for each subject who signs consent and commences screening for the study. For reasons of confidentiality, the name and initials of the subject should not appear in the eCRF. All eCRF entries, corrections, and alterations must be made by the PI or other authorised study-site personnel.

Data entry into the eCRF will be conducted throughout study conduct according to the Sponsor's (or delegate) instructions and reviewed by the Sponsor (or delegate) to determine their acceptability. If necessary, eCRF queries will be raised by the Sponsor (or delegate) relating to eCRF data entries. The PI or authorised study site staff must address all eCRF queries raised.

10.1.5. Recordkeeping and Retention of Records

In compliance with the ICH/GCP guidelines, the PI/institution will maintain all source documents that support the data collected from each subject, as well as all study documents as specified in ICH/GCP Section 8, Essential Documents for the Conduct of a Clinical Trial. The PI/institution will take measures to prevent accidental or premature destruction of these documents.

Following closure of the study, the PI must maintain all site study records in a safe and secure location. The records must be maintained to allow easy and timely retrieval, when needed (e.g., audit or inspection) and whenever feasible, to allow any subsequent review of data in conjunction with assessment of the facility, supporting systems and staff. When permitted by local laws/regulations or institutional policy, some or all of these records can be maintained in a format other than hard copy (e.g., microfiche, scanned, electronic); however, caution needs to be exercised before such action is taken. The PI must ensure that all reproductions are legible and are a true and accurate copy of the original and meet accessibility and retrieval standards, including re-generating a hard copy, if required. Furthermore, the PI must ensure there is an acceptable back-up of these reproductions and that an acceptable quality control process exists for making these reproductions.

The Sponsor will inform the PI of the time period for retaining these records to comply with all applicable regulatory requirements. The minimum retention time will meet the strictest standard applicable to that site for the study, as dictated by any institutional requirements or local laws or regulations, or the study Sponsor, standards/procedures; otherwise, the retention period will default to 15 years.

If the responsible PI retires, relocates, or for other reasons withdraws from the responsibility of keeping the study records, custody must be transferred to a person who will accept the

responsibility. The Sponsor must be notified in writing of the name and address of the new custodian.

Under no circumstance shall the PI relocate or dispose of any study documents before having obtained written approval from the Sponsor.

If it becomes necessary for the Sponsor or the appropriate regulatory authority to review any documentation relating to this study, the PI must permit access to all study documentation.

The material to be stored shall include, but is not limited to, the following:

- signed and dated copy of the IEC/IRB approved version of the study protocol and any amended IEC/IRB approved versions;
- signed and dated letter of IEC/IRB approval(s), letter of constitution of the IEC/IRB and copies of any other correspondence relevant to the study with the IEC/IRB or regulatory authorities;
- IEC/IRB approved participant informed consent forms (PICFs);
- current *curriculum vitae* (signed and dated) of the PI and co-workers with major responsibilities in the trial;
- Site Signature and Delegation of Responsibility Log;
- Financial Disclosure Form(s);
- blank copy of the study eCRF;
- signed PICFs;
- laboratory reference ranges (signed and dated);
- final Clinical Study Report; and
- clinical raw data including the Source Data Forms, all clinical laboratory report forms, subject eCRF, drug accountability forms, and dispensing records.

10.2. ETHICS AND REGULATORY COMPLIANCE

10.2.1. Investigator Responsibilities

The PI must conduct the clinical study in accordance with the IEC/IRB approved study protocol, current ICH guidelines for GCP, and applicable regulatory and legal requirements. Good Clinical Practice is an international ethical and scientific quality standard for designing, conducting, recording, and reporting studies that involve the participation of human subjects. Compliance with this standard provides public assurance that the rights, safety, and well-being of study subjects are protected, consistent with the principles that originated in the Declaration of Helsinki, and that the clinical study data are credible.

10.2.2. Ethics Committee and Regulatory Authority Approval

This study protocol and any amendment(s) must be submitted to the appropriate ethics committee(s)/relevant competent authority in each respective country, as required. The Sponsor

(or designee) is responsible for regulatory submissions. This clinical study may not be initiated until all local regulatory requirements are met.

Before the start of the study, a written favourable opinion or approval must be received from the ethics committee/relevant competent authority. To achieve this, the Investigator or the Sponsor will submit to the ethics committee and regulatory authorities, as required by local regulations, current and complete copies of relevant documents.

The written favourable opinion or approval must be dated and must clearly identify the documents reviewed, which should include the final protocol and any amendments, the ICF, applicable recruiting materials, and any subject compensation program.

During the study, the Investigator or Sponsor (or designee), as required, will submit the following for ethics committee review or opinion/approval:

1. Revisions or updates of documents previously submitted to the ethics committee, and
2. Relevant new information or documents, as required:
    a. Summaries of the status of the study (at least annually or at intervals stipulated in guidelines of the ethics committee).
    b. Reports of AEs that are serious, unlisted, and associated with the investigational drug.
    c. Deviations from or changes to the study protocol to eliminate immediate hazards to the subjects.

When and where required by local regulations, before implementation of any change, study protocol amendments and revised documents must receive ethics committee favourable opinion or approval.

The ethics committee will be given official notification of the study completion.

10.2.3. Informed Consent

Informed consent will be obtained before any volunteer can participate in the study. The written ICF must also be signed and dated by the person who conducted the informed consent procedure. The consent form must be signed before performance of any study-related activity. The contents and process of obtaining informed consent will be in accordance with all applicable regulatory requirements and adhere to ICH/GCP guidelines and the requirements in the Declaration of Helsinki. Study participation includes any and all screening and training procedures, as well as any washout of excluded medications.

It is the responsibility of the PI (or the delegate who conducted the informed consent procedure) to obtain a voluntary signed and dated informed consent from each individual participating in this study after adequate explanation of the aims, methods, objectives, and potential hazards of participating in the study. The PI (or delegate) must also explain to the volunteers that they are completely free to refuse to enter the study or to withdraw from it at any time. All eligible volunteers must receive a full explanation, in layman's terms, of the aims of the study, the discomfort, risks and potential benefits in taking part as well as of insurance and other procedures for compensation in case of injury. It will be explained that the study is for research purposes only and is not expected to provide any therapeutic benefit to the individual. It will be pointed out that they can withdraw from the study at any time without prejudice. Each subject

will acknowledge receipt of this information by giving written informed consent for participation in the study. All subjects will be given a copy of the signed PICF to retain.

Should a protocol amendment become necessary, the PICF may need to be revised to reflect the changes to the protocol. It is the responsibility of the Sponsor (or delegate) to ensure that an amended PICF is reviewed and has received favourable opinion from IEC/IRB, and the Investigator has to ensure that the amended PICF is signed by all subjects subsequently entered in the study and those currently in the study, if affected by the amendment.

10.2.4. Emergency Contact with Principal Investigator

Suitable arrangements must be made for subjects to make contact with the PI or medically trained nominee in the event of an emergency.

10.2.5. Pandemic Preparedness

Clinical sites should have in place procedures and strategies to accommodate the current COVID-19 pandemic (or other pandemics as appropriate). Such procedures should include requirements in relation to criteria such as:

- attendance (e.g., who is permitted to be on site during a pandemic, limitations, records of attendance, plans for suppliers and deliveries);
- physical layout (e.g., physical distancing requirements and signage);
- flexibility (e.g., procedures for scaling, ability to respond to outbreak);
- support for remote interactions with Sponsors and study teams (e.g., communication including infrastructure);
- local environment (e.g., contact with local health authorities, ability to access up-to-date pandemic information); and
- any other relevant criteria.

10.2.6. Notification of the General Practitioner

It is recommended that the investigator inform the subject's primary physician about the subject's participation in the trial if the subject has a primary physician and if the subject agrees to the primary physician being informed.

10.2.7. Clinical Laboratory Certification and Reference Ranges

Before the initiation of this study, the PI, or nominee, will obtain a copy of the certification form, with certification number and expiration date for all clinical laboratories used in the study. Reference ranges for each clinical laboratory test used in this study will be obtained from the appropriate laboratory, which will perform the test for the study.

10.2.8. Study Completion/Site Closure

The study is considered completed at the last contact of the last subject involved in the study. The final data from the investigational site will be sent to the Sponsor (or designee) in the time

frame specified in the Clinical Trial Agreement. Investigational sites will be closed upon study completion. An investigational site is considered closed when all required documents and study supplies have been collected and a site closure visit has been performed by the Sponsor (or delegate).

10.2.9. Termination of the Study

The Sponsor reserves the right to discontinue the study at any time. Reasons will be provided in the event of this happening. The PI reserves the right to discontinue the study for safety reasons at any time in consultation with the Sponsor.

10.2.10. End of Study and Regulatory Notification

At the end of the study, the IEC/IRB and relevant regulatory authorities will be notified by the Sponsor (or delegate) according to applicable IEC/IRB and regulatory requirements.

10.3. QUALITY CONTROL AND ASSURANCE

10.3.1. Study Monitoring

The Sponsor is responsible for assuring the proper conduct of the study with regard to protocol adherence and validity of the data recorded in the eCRF.

During the course of the study, the Sponsor (or designee) will visit the study site and/or perform remote monitoring at regular intervals. The PI must make themselves available to the Study Monitor during an on-site (or remote) monitoring visit to enable discussion on any arising issues relating to the study. The purpose of the monitoring (on site or remote) is to ensure that the eCRF is completed correctly, the protocol is being adhered to, the source data are verified, and drug accountability is performed.

The PI agrees to allow the Study Monitor direct access to relevant source documents (original documents, data, and records). Direct access includes permission to examine, analyse, verify, and reproduce any record(s) and report(s) that are important to evaluation of the clinical study. The PI also agrees to allocate his/her time and the time of his/her staff to the Monitor to discuss findings and any relevant issues.

Subject confidentiality must be maintained during any monitoring activities conducted by the Sponsor (or delegate).

In accordance with applicable regulations and ICH/GCP, a Study Monitor who will contact the site to organise an on-site (or remote) visit prior to subject enrolment to review the protocol and data collection procedures with site staff. In addition, the assigned Study Monitor will periodically contact the site, including conducting on-site (or remote) visits. The extent, nature and frequency of on-site visits will be based on such considerations as the study objectives and/or endpoints, the purpose of the study, study design complexity, and enrolment rate.

During these site visits, the Study Monitor will:

- check the progress of the study;
- review study data collected;

- conduct source document verification;
- identify any issues and address their resolution;
- check study treatment accountability records;
- review biological samples collected for the study and ensure that they are labelled and stored correctly; and
- verify that:
  - data are authentic, accurate, and complete;
  - safety and rights of subjects are being protected; and
  - study is conducted in accordance with the currently approved protocol (and any amendments), ICH/GCP, and all applicable regulatory requirements.

At study closure, a Study Monitor will conduct the following activities in conjunction with the PI or site staff as appropriate:

- Ensure that all data queries have been resolved.
- Conduct final accountability and reconciliation for study treatment supplies including inventory and final disposition (e.g., destruction, shipping to repository, etc.).
- Review site study records for completeness.

A Study Monitor will be assigned to visit the site pharmacy during the study and at study completion, to review the randomisation schedule in comparison to the dispensing log in order to verify correct randomisation of study drug.

10.3.2. Quality Assurance and Quality Control

To ensure compliance with ICH/GCP and all applicable regulatory requirements, the Sponsor (or a designated third party), may conduct a quality assurance audit of the study site. Regulatory agencies may also conduct a regulatory inspection of this study. Such audits/inspections can occur at any time during or after completion of the study. If an audit or inspection occurs, the PI and institution agree to notify the Sponsor as soon as possible following awareness of an impending regulatory inspection. The Investigator and Institution agree to allow the auditor/inspector direct access to all relevant documents and allocate his/her time and the time of his/her staff to the auditor/inspector to discuss findings and any relevant issues.

The Sponsor (or delegate) will perform the quality assurance and quality control activities for this study; however, responsibility for the accuracy, completeness, and reliability of the study data presented to the Sponsor lies with the PI (and delegate(s)) generating the data.

Prior to the study initiation, the Sponsor (or delegate) will explain the protocol, the IB, and eCRF to the PI and the site staff involved in this study. In addition, the assigned Study Monitor will be available to explain applicable regulations and to answer any questions regarding the conduct of the study.

[redacted]

10.3.3. Data Quality Control

Steps to be taken to ensure the accuracy and reliability of data include the selection of qualified Investigators and appropriate study centres, review of protocol procedures with the PI and associated personnel before the study, and periodic monitoring visits by the Sponsor (or delegate). Written instructions will be provided for collection, preparation, and shipment of biological samples collected for the purposes of this study. Electronic case report form completion training will be conducted with study personnel before the start of the study. The Study Monitor will review electronic data for accuracy and completeness during on-site (or remote) monitoring visits and any discrepancies will be resolved with the PI or designee, as appropriate. The data will be entered into the clinical study eCRF and verified for accuracy.

[redacted]

10.5. STUDY PROTOCOL GUIDELINES

[redacted]

10.5.2. Protocol Waivers

Protocol waivers will not be granted by the Sponsor in this study.

[redacted]

[redacted]

10.6. INTELLECTUAL PROPERTY, CONFIDENTIALITY AND PUBLICATIONS

10.6.1. Ownership

All information provided by the Sponsor and all data and information generated by the clinical facility staff as part of the study (other than a subject's medical records), are the sole property of the Sponsor.

All rights, title and interests in any inventions, know-how or other intellectual or industrial property rights which are conceived or reduced to practice by clinical facility staff during the course of or as a result of the study are the sole property of the Sponsor and are hereby assigned to Equillium.

If a written contract for the conduct of the study which includes ownership provisions inconsistent with this statement is executed between the Sponsor and the clinical facility, that contract's ownership provisions shall apply rather than this statement.

10.6.2. Confidentiality

All information provided by the Sponsor and all data and information generated by the clinical facility as part of the study will be kept confidential by the PI and other site staff. The PI or other site personnel will not use this information and data for any purpose other than conducting the study. These restrictions do not apply to:

3. information which becomes publicly available through no fault of the PI or site staff;
4. information which it is necessary to disclose in confidence to an IEC/IRB solely for the evaluation of the study;
5. information which it is necessary to disclose in order to provide appropriate medical care to a study participant; or
6. study results which may be published as described in the Publication Policy (Section 10.6.3).

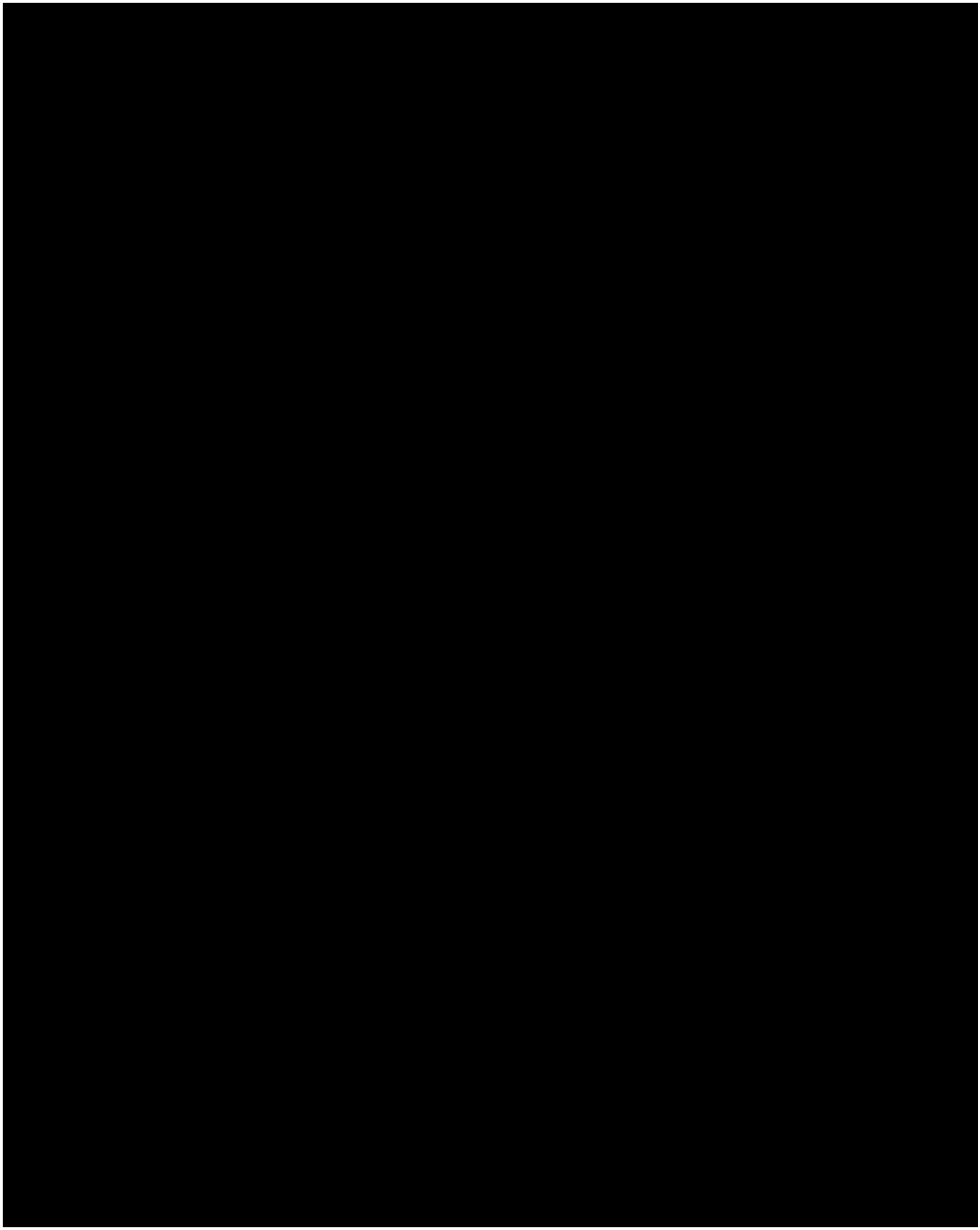
If a written contract for the conduct of the study, which includes confidentiality provisions inconsistent with this statement, is executed, that contract's confidentiality provisions shall apply rather than this statement.

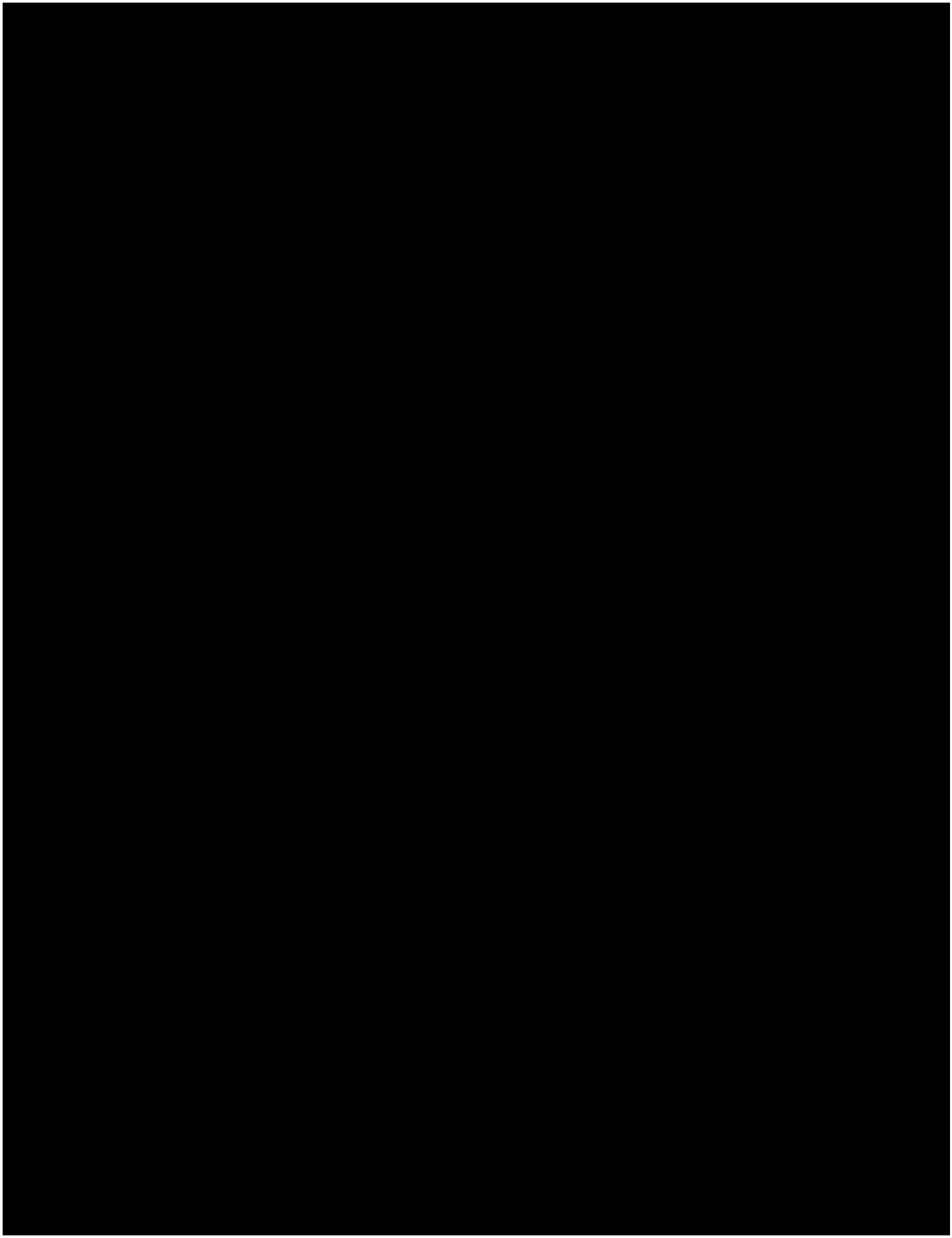
10.6.3. Publication Policy

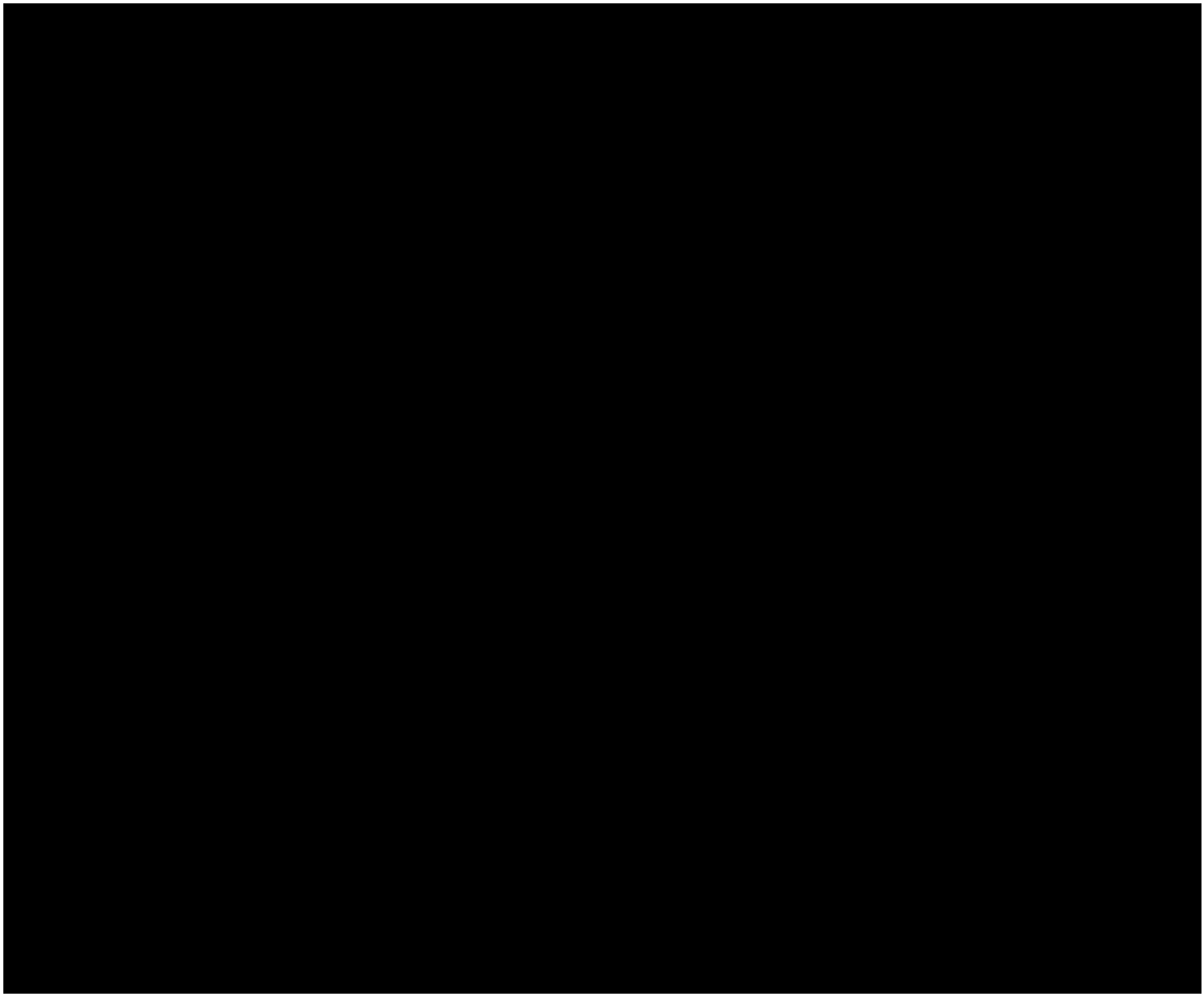
The Sponsor plans to publish the results of this study at an appropriate time. No publication of the results shall take place without the express consent of the Sponsor. Prior to submitting for any publication, presentation, use for instructional purposes or otherwise disclosing the study results generated by the site (collectively, a "Publication"), the PI shall provide the Sponsor with a copy of the proposed publication and allow the Sponsor a period of at least sixty (60) days [or for abstracts, at least fifteen (15) working days] to review the proposed publication. Proposed publications shall not include Sponsor confidential information.

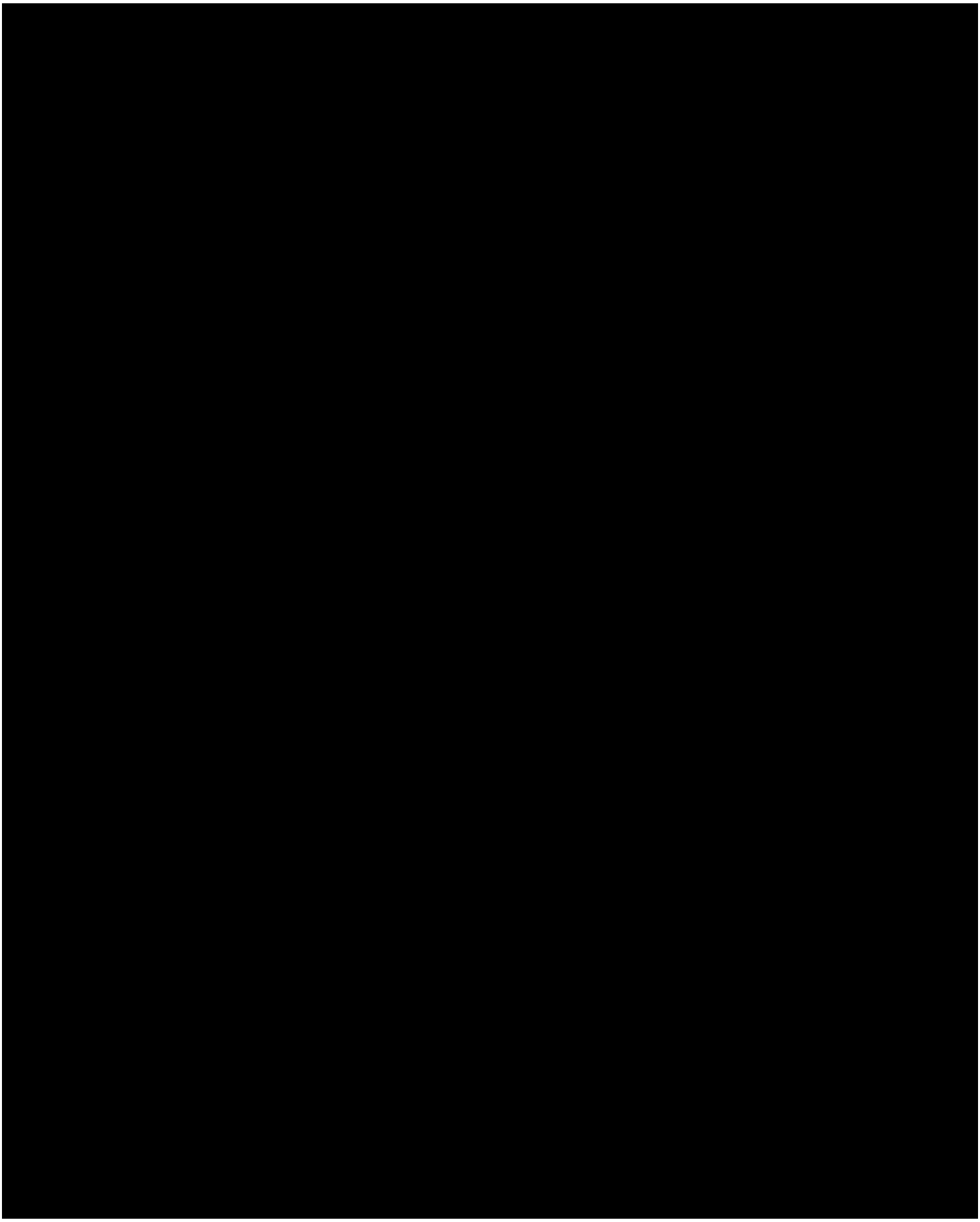
At the request of the Sponsor, the submission or other disclosure of a proposed publication will be delayed for a sufficient length of time to allow the Sponsor to seek patent or similar protection of any inventions, know-how or other intellectual or industrial property rights disclosed in the proposed publication.

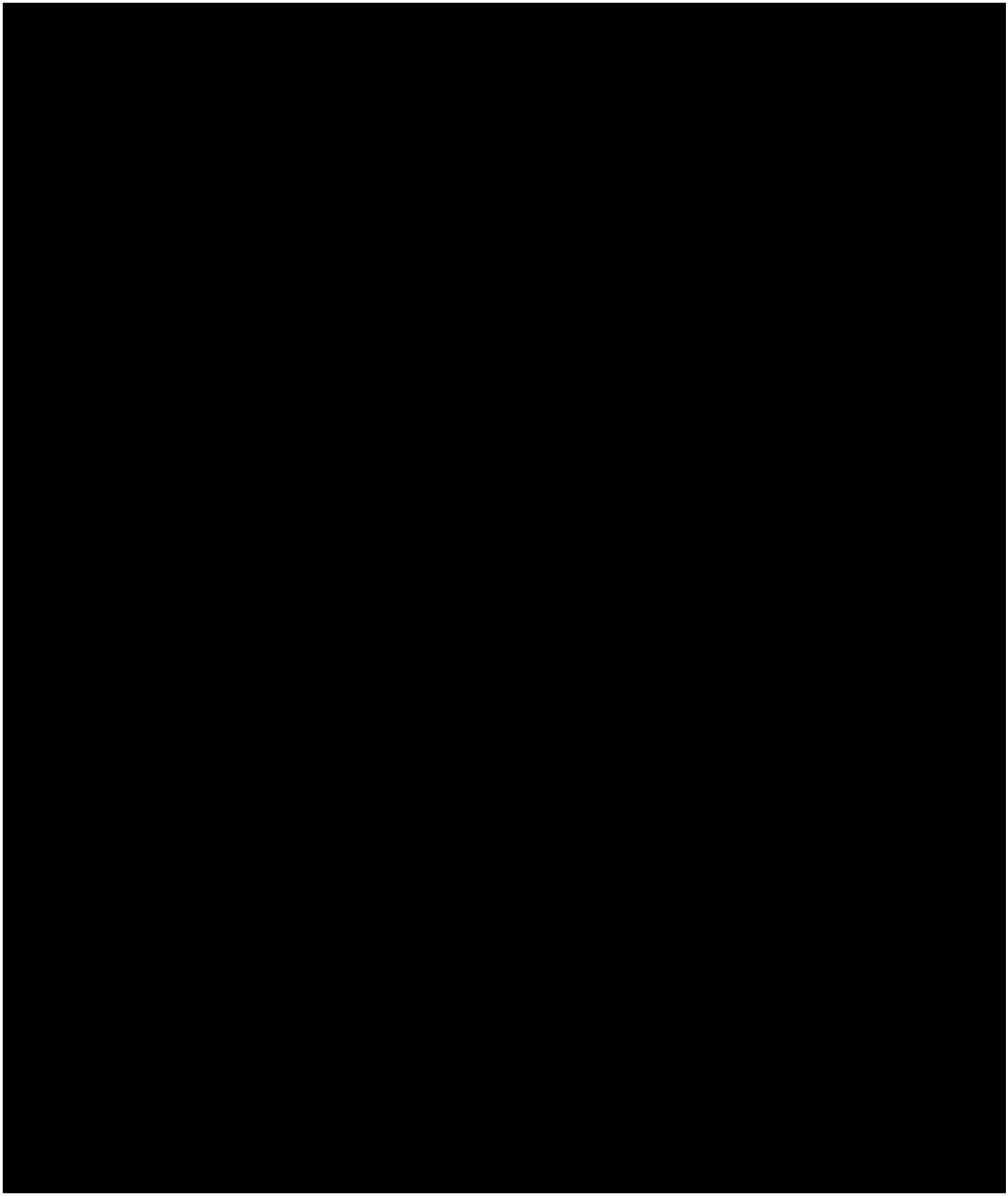
If a written contract for the conduct of the study, which includes publication provisions inconsistent with the statement is executed, that contract's publication provisions shall apply rather than this statement.

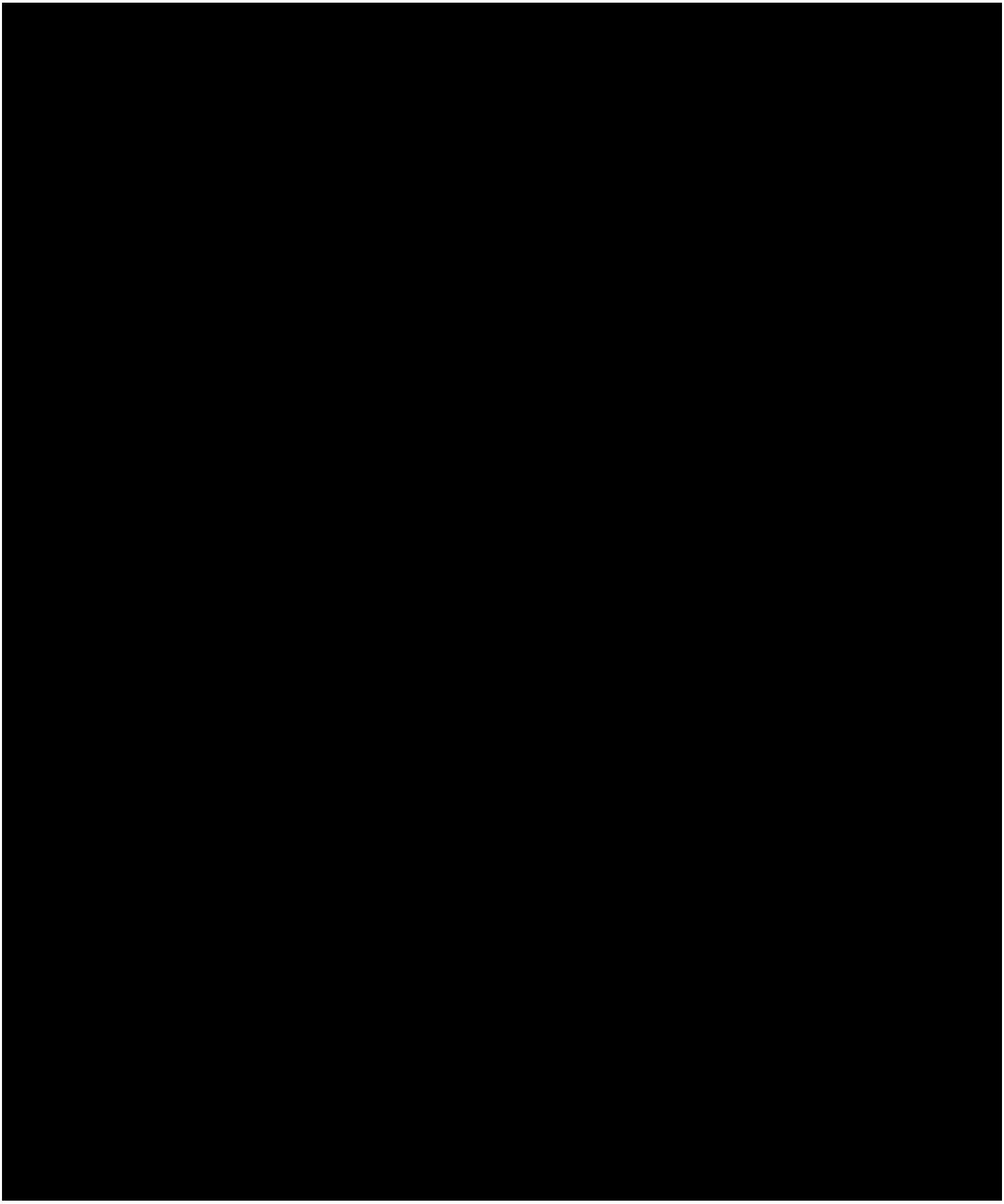


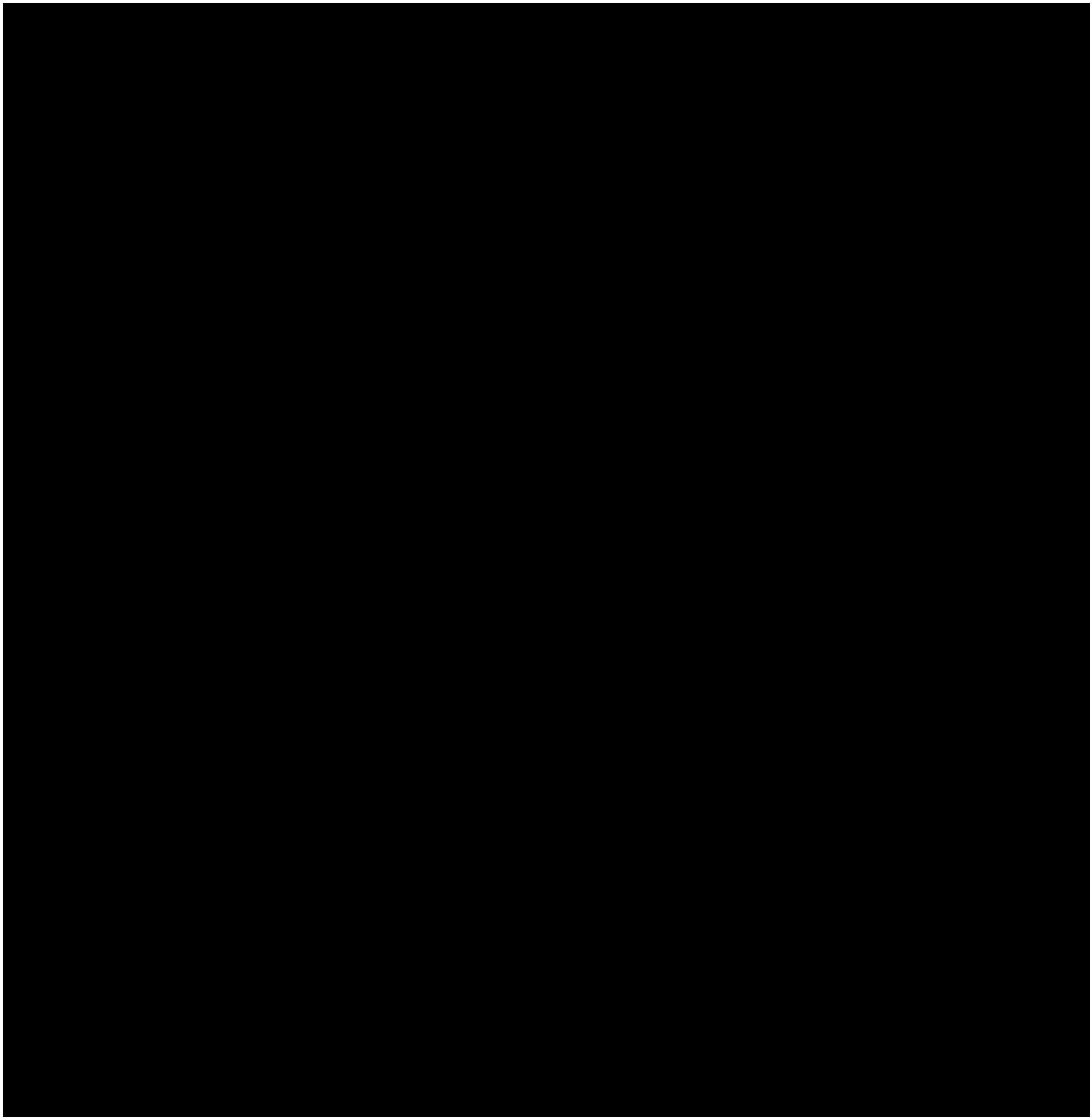












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