Official Title: A Phase 2, Randomized, Double-Blind, Placebo-Controlled, Dose-Ranging Study of the Efficacy and Safety of INCB054707 in Participants With Hidradenitis Suppurativa

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Statistical Analysis Plan

INCB 54707-204

A Phase 2, Randomized, Double-Blind, Placebo-Controlled, Dose-Ranging Study of the Efficacy and Safety of INCB054707 in Participants With Hidradenitis Suppurativa

IND Number:	**137,156**
EudraCT Number:	**2020-001981-13**
Sponsor:	**Incyte Corporation** **1801 Augustine Cut-Off** **Wilmington, DE 19803** **United States**
Protocol Version:	**Protocol Amendment 1 dated 10 SEP 2021**
CRF Approval Date:	**27 JUL 2020**
SAP Version:	**Original**
SAP Author:	[redacted] **Biostatistics**
Date of Plan:	**12 OCT 2021**

This study is being conducted in compliance with Good Clinical Practice, including the archiving of essential documents.

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LIST OF ABBREVIATIONS

Abbreviations	Definition
AE	adverse event
ALT	alanine aminotransferase
AN	abscess and inflammatory nodule
ANF	abscess, inflammatory nodule, and draining fistula
AST	aspartate aminotransferase
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
CTCAE	Common Terminology Criteria for Adverse Events
DILI	Drug Induced Liver Injury
DLQI	Dermatology Life Quality Index
DMC	data monitoring committee
ECG	electrocardiogram
eCRF	electronic case report form
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
HDL	high-density lipoprotein
[redacted]	[redacted]
[redacted]	[redacted]
HS	hidradenitis suppurativa
IHS4	International Hidradenitis Suppurativa Severity Score System
ITT	intent-to-treat
LDL	low-density lipoprotein
LTE	long-term extension
MedDRA	Medical Dictionary for Regulatory Activities
MMRM	mixed model repeated measures
NCI	National Cancer Institute
NRI	non-responder imputation
[redacted]	[redacted]
OLE	open-label extension
PC	placebo-controlled
[redacted]	[redacted]
[redacted]	[redacted]
PP	per protocol

[redacted]	[redacted]
PT	preferred term
QALYs	quality-adjusted life years
QD	once daily
QTcF	Fridericia's corrected QT interval
SAP	Statistical Analysis Plan
SOC	system organ class
[redacted]	[redacted]
TEAE	treatment-emergent adverse event
[redacted]	[redacted]
ULN	upper limit of normal
[redacted]	[redacted] a

1. INTRODUCTION

This is a Phase 2, multicenter, parallel group, placebo-controlled, double-blind, randomized study to evaluate the efficacy and safety of INCB054707 (15, 45, and 75 mg QD) over a 16-week PC period. Upon completion of the 16-week PC period, participants will continue for 36 weeks of OLE period (INCB054707 75 mg QD). At the end of the OLE period, all eligible participants have the option to continue treatment for additional 48 weeks in an LTE period, to collect long-term safety and efficacy data for a total of 104 weeks. A safety follow-up visit will be conducted approximately 4 weeks after the last dose of study drug.

The purpose of this SAP is to provide details of the statistical analyses that have been outlined in the Study INCB 54707-204 Protocol.

2. STUDY INFORMATION, OBJECTIVES, AND ENDPOINTS

2.1. Protocol and Case Report Form Version

This SAP is based on INCB 054707-204 Protocol Amendment 1 dated 10 SEP 2021 and CRFs approved 27 JUL 2020. Unless superseded by an amendment, this SAP will be effective for all subsequent Protocol amendments and eCRF versions.

2.2. Study Objectives and Endpoints

Table 1 presents the objectives and endpoints.

Table 1: Objectives and Endpoints

Objectives	Endpoints
Primary	
To determine the efficacy of INCB054707	• Mean change of AN count at Week 16 relative to baseline.
Secondary	
To further evaluate the efficacy of INCB054707	• **Key secondary endpoint:** Proportion of participants who achieve HiSCR at Week 16. Hidradenitis suppurativa clinical response is defined as at least a 50% decrease from baseline in AN count with no increase in the number of abscesses or draining fistulas. • Proportion of participants who achieve HiSCR at each visit from Weeks 2 to 12. • Proportion of participants who achieve at least a 75% decrease from baseline in AN count with no increase in the number of abscesses or draining fistulas from Weeks 2 to 16. • Mean change from baseline in the severity of the disease, as assessed by the IHS4 score, from Weeks 2 to 16. • Proportion of participants achieving AN50, AN75, AN90, and AN100 (at least 50%, 75%, 90%, and 100% reduction in AN count relative to baseline, respectively) from Weeks 2 to 16. • Mean change in AN count at Weeks 2 to 12, relative to baseline. • Proportion of participants with a total AN count of 0 to 2 from Weeks 2 to 16. • Mean change in draining fistula count from Weeks 2 to 16, relative to baseline. • Mean change in ANF count from Weeks 2 to 16, relative to baseline.

Table 1: Objectives and Endpoints (Continued)

Objectives	Endpoints
To evaluate the safety and tolerability of INCB054707	• Frequency and severity of AEs, including the evaluation of clinical laboratory results, vital signs, ECGs, and the results of physical examinations.
[redacted]	
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

Table 1: Objectives and Endpoints (Continued)

Objectives	Endpoints
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

Table 1: Objectives and Endpoints (Continued)

Objectives	Endpoints
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

Table 1: Objectives and Endpoints (Continued)

Objectives	Endpoints
[redacted]	[redacted]
[redacted]	[redacted]

Table 1: Objectives and Endpoints (Continued)

Objectives	Endpoints
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

Table 1: Objectives and Endpoints (Continued)

Objectives	Endpoints
[redacted]	[redacted]

3. STUDY DESIGN

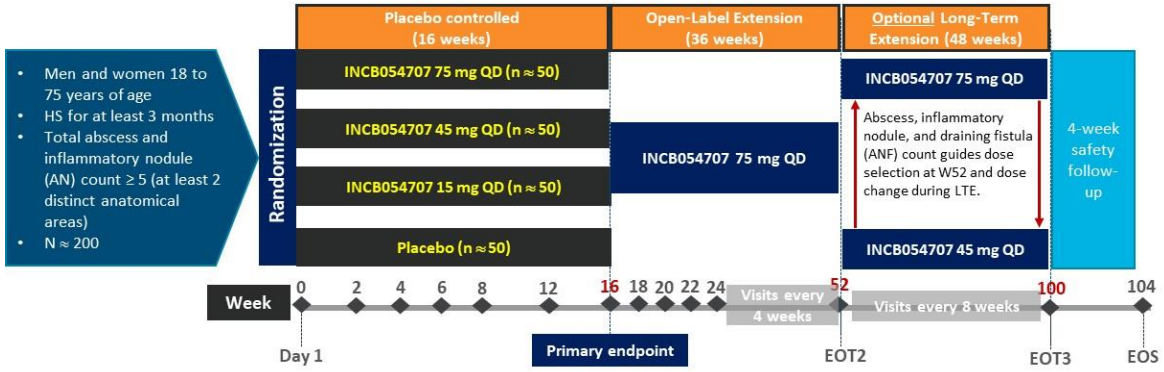
This is a Phase 2, multicenter, randomized, parallel group, placebo-controlled, dose-ranging study to evaluate the efficacy and safety of INCB054707 (15, 45, and 75 mg QD) over a 16-week PC period followed by a 36-week OLE period (INCB054707 75 mg QD) and an additional optional 48-week LTE period. The study will enroll men or women aged 18 to 75 years who have been diagnosed with HS (Hurley Stage I, II, or III) for at least 3 months with a total AN count of at least 5 and inflammatory lesions that affect at least 2 distinct anatomical areas.

Participants will undergo screening within 30 days prior to randomization. Participants who continue to meet eligibility criteria at baseline will have Day 1 (Week 0) assessments and will be randomized to 1 of 4 treatment groups. Participants will be stratified based on geographical region (North America and outside of North America) and disease severity (Hurley Stages I, II, and III) with no more than 25% of the total number of participants as Hurley Stage III.

Participants will receive double-blinded study treatment of placebo or 1 of 3 doses of INCB054707 (15, 45, or 75 mg) QD for 16 weeks. At Week 16, participants will enter the 36-week OLE period (INCB054707 75 mg QD). At the completion of the OLE period, all eligible participants will have the option to continue treatment for an additional 48-week LTE period. A safety follow-up visit will be scheduled approximately 4 weeks after the end of OLE period (Week 56 visit) for participants who do not continue into the LTE period, or the LTE period (Week 104 visit) for participants who continue into the LTE period.

The study schema is shown below in Figure 1.

Figure 1: Study Design Schema



The primary analysis will occur after the primary database lock, when all participants have completed or discontinued from the placebo-controlled, double-blind treatment period.

The final analysis will occur when all participants have completed or withdrew from the study.

3.1. Randomization

Approximately 200 participants will be randomized 1:1:1:1 to 1 of 3 INCB054707 treatment groups or the placebo group (approximately 50 participants per group).

Participant randomization will be stratified based on geographical region (North America and outside of North America) and disease severity (Hurley Stages I, II, and III) with no more than 25% of the total number of participants as Hurley Stage III.

[redacted]

3.4. Schedule of Assessments

Refer to Protocol Amendment 1 dated 10 SEP 2021 for a full description of all study procedures and assessment schedules for this study.

4. DATA HANDLING DEFINITIONS AND CONVENTIONS

4.1. Scheduled Study Evaluations and Study Periods

4.1.1. Day 1

Day 1 is defined in Table 2 for each period, and combination of periods specified. Note that the treatment groups for each period are described in Section 5.2.

Table 2: Definition of Day 1

Treatment Period	Treatment Groups	Day 1
PC period	Placebo INCB054707 15 mg INCB054707 45 mg INCB054707 75 mg	The day of the first dose of study drug (INCB054707 or placebo) administered to the participants in the PC period.
OLE period	Placebo to INCB054707 75 mg INCB054707 15 mg to 75 mg INCB054707 45 mg to 75 mg INCB054707 75 mg	The day of the first dose of study drug (INCB054707 75 mg) administered to the participants in the OLE period
Throughout study participation up to Week 52	INCB054707 75 mg	The day of the first dose of study drug (INCB054707 75 mg) administered to the participants in the PC period
LTE period	INCB054707 ≤ 45 mg INCB054707 ≥ 60 mg	The day of the first dose of study drug (INCB054707) administered to the participants in the LTE period

For randomized participants not treated with any study drug, Day 1 is defined as the day of randomization.

4.1.2. Study Day

If a visit/reporting date is on or after Day 1, then the study day at the visit/reporting date will be calculated as

Day # = (visit/reporting date – Day 1 date + 1).

If the visit/reporting date is before Day 1, then the study day at the visit/reporting date will be calculated as

Day # = (visit/reporting date – Day 1 date).

A study day of –1 indicates 1 day before Day 1.

4.1.3. Baseline Value

Baseline is the last nonmissing measurement obtained before the first administration of INCB054707 or placebo in the PC period, unless otherwise defined.

For randomized participants not treated with any study drug, baseline is defined as the last nonmissing assessment before or on the day of randomization for all parameters.

For participants who continue in the OLE period, baseline is defined as follows:

- For efficacy evaluation, baseline is the last nonmissing measurement obtained before the first administration of study drug in the PC period, unless otherwise defined.
- For safety evaluation in the OLE period:
  - For participants who cross over from the placebo group or the INCB054707 15 or 45 mg groups to INCB054707 75 mg, baseline is the last nonmissing measurement obtained before the first administration of INCB054707 75 mg in the OLE period.
  - For participants who take INCB054707 75 mg throughout study participation up to Week 52, baseline is the last nonmissing measurement obtained before the first administration of study drug in the PC period.

For participants who continue in the LTE period, baseline is defined as follows:

- For efficacy evaluation, baseline is the last nonmissing measurement obtained before the first administration of study drug in the PC period, unless otherwise defined.
- For safety evaluation in the LTE period, baseline is the last nonmissing measurement obtained before the first administration of INCB054707 in the LTE period.

When scheduled assessments and unscheduled assessments occur on the same day and the time of the assessment or time of first dose is not available, use the following convention to determine baseline:

- If both a scheduled and an unscheduled visit are available on the day of the first dose and the time is missing, use the scheduled assessment as baseline.
- If all scheduled assessments are missing on the day of the first dose and an unscheduled assessment is available, use the unscheduled assessment as baseline.

4.1.4. Handling of Missing and Incomplete Dates

In general, values for missing dates will not be handled unless methods for handling missing dates are specified in this section or relevant sections. The original reported dates collected on the eCRF should be used in all relevant listings. The following rules will be used for handling partial dates for analyses requiring dates.

When calculating the time since diagnosis of HS, a partial HS diagnosis date will be handled as follows in the calculation:

- If only the day is missing, then the first day of the month will be used.
- If both the month and day are missing, then 01 JAN of the year will be used.
- If the diagnosis date is completely missing, then the time since diagnosis will not be calculated.

When the date of the last dose is used in deriving variables such as duration of treatment or TEAE flag, a missing or partial date of the last dose will be handled as follows:

- If only the day is missing, then the earlier date of the last day of the month or the date that the participant discontinued treatment will be used.
- If both the month and day are missing, then the earlier date of 31 DEC of the year or the date that the participant discontinued treatment will be used.
- Otherwise, the date that the participant discontinued treatment will be used as the date of the last dose.

For response endpoints, all nonresponders, as well as all participants who are missing postbaseline values, will be defined as nonresponders for the NRI analysis.

For continuous endpoints, any participant who is missing postbaseline values may have missing data handled using MMRM under the missing-at-random assumption. Mixed model repeated measures implicitly adjusts for missing data through a variance-covariance structure.

For other endpoints, missing observations will be handled as detailed in the specific sections addressing each analysis.

4.2. Variable Definitions

The following variables will only be calculated if not reported on the eCRF.

4.2.1. Body Mass Index

Body mass index will be calculated as follows:

BMI (kg/m^2) = [weight (kg)] / [height (m)]^2.

4.2.2. Prior and Concomitant Medication

Prior medication is defined as any nonstudy medication started before the first dose of INCB054707 or placebo in the PC period.

In the PC period, concomitant medication is defined as any nonstudy medication that is started accordingly:

- Before the date of first administration of INCB054707 or placebo in the PC period and is ongoing throughout the study or ends on/after the date of first study drug administration during the PC period.
- On/after the date of first administration of INCB054707 or placebo in the PC period and is ongoing or ends during the PC period.

In the OLE period, concomitant medication is defined as any nonstudy medication that is started accordingly:

- Before the date of first administration of INCB054707 75 mg in the OLE period and is ongoing throughout the study or ends on/after the date of first study drug administration during the OLE period.
- On/after the date of first administration of INCB054707 75 mg in the OLE period and is ongoing or ends during the OLE period.

In the LTE period, concomitant medication is defined as any nonstudy medication that is started accordingly:

- Before the date of first administration of INCB054707 in the LTE period and is ongoing throughout the study or ends on/after the date of first study drug administration during the LTE period.
- On/after the date of first administration of INCB054707 in the LTE period and is ongoing or ends during the LTE period.

A prior medication could also be classified as "both prior and concomitant medication" if the end date is on or after first dose of INCB054707 or placebo. In the listing, it will be indicated whether a medication is only prior, only concomitant, or both prior and concomitant.

For the purposes of analysis, all medications will be considered concomitant medications unless the medications can unequivocally be defined as not concomitant.

5. STATISTICAL METHODOLOGY

5.1. General Methodology

Unless otherwise noted, SAS® software (SAS Institute Inc, Cary, NC; v9.1 or later) will be used for the generation of all tables, graphs, and statistical analyses. Descriptive summaries for continuous variables will include but not be limited to the number of observations, mean, standard deviation, median, minimum, and maximum. Descriptive summaries for categorical variables will include the number and percentage of participants in each category.

5.2. Treatment Groups

This is a randomized, double-blind, placebo-controlled, dose-ranging study followed by an open-label extension period, and an optional long-term extension period. Table summaries, unless otherwise indicated, will present data by treatment groups. The results will be summarized and presented separately for the PC period, the OLE period, and the LTE period, unless otherwise specified.

For the PC period, the treatment groups will be placebo and INCB054707 15 mg, 45 mg, and 75 mg.

For the OLE period, the participants will be grouped into the following groups according to the treatment group they received during the PC period:

- Placebo to INCB054707 75 mg
- INCB054707 15 mg to 75 mg
- INCB054707 45 mg to 75 mg
- INCB054707 75 mg

For the LTE period, the participants will be grouped into the following groups according to the initial INCB054707 dose group they received in the LTE period:

- INCB054707 ≤ 45 mg
- INCB054707 ≥ 60 mg

5.3. Analysis Populations

5.3.1. Intent-to-Treat Population

All participants who were randomized to the study constitute the ITT population. Treatment groups for this population will be defined according to the treatment assignment at the time of randomization regardless of the actual study treatment the participant might apply during his/her participation in the PC period.

The ITT population will be used for the summary of demographics, baseline characteristics, participant disposition, and analyses of all efficacy data in the PC period.

5.3.2. Per Protocol Population

Participants in the ITT population who are considered to be sufficiently compliant with the Protocol compose the PP population. The determination of participants being considered for exclusion from the PP population by the clinical team will be prepared and signed before unblinding and database lock.

The PP population will be used in the supportive sensitivity analysis for the primary efficacy endpoint.

5.3.3. Safety Population

The safety population will include all participants who received at least 1 dose of INCB054707 or placebo during the PC period. Treatment groups for this population will be determined according to the actual treatment the participant received on Day 1 regardless of assigned study treatment.

All safety analyses for the PC period will be conducted using the safety population.

5.3.4. Open-Label Evaluable Population

All analyses for the OLE period will be conducted with the open-label evaluable population, which includes all participants who received at least 1 dose of INCB054707 75 mg during the OLE period.

5.3.5. Long-Term Evaluable Population

All analyses for the LTE period will be conducted with the long-term evaluable population, which includes all participants who received at least 1 dose of INCB054707 during the LTE period.

[redacted]

6. BASELINE, EXPOSURE, AND DISPOSITION

Appendix A provides a list of data displays. Sample data displays are included in a separate document.

6.1. Demographics, Baseline Characteristics, and Disease History

The demographics, baseline characteristics, and disease history will be summarized by treatment groups and overall.

6.1.1. Demographics and Baseline Characteristics

The following demographics will be summarized for the ITT population, the open-label evaluable population, and the long-term evaluable population: age, sex, race, ethnicity, weight, height, BMI, BMI category (< 25 kg/m^2, ≥ 25 to < 30 kg/m^2, ≥ 30 to < 40 kg/m^2, ≥ 40 to < 50 kg/m^2, ≥ 50 kg/m^2), and geographic region (North America, Outside of North America).

The following demographics will be summarized for the ITT population only: tobacco use (never used, current user, former user), cannabis use (never used, current user, former user), and alcohol use (yes, no).

6.1.2. Baseline Disease Characteristics and Disease History

The following baseline disease characteristics and disease history summarized for all participants in the ITT population include but are not limited to:

- Disease duration (years)
- Prior therapy or surgical intervention administered for HS [redacted]
- HS family history
- Comorbidities [redacted]
- Hurley stage (Stage I, Stage II, Stage III) (See Section 7.2.5 for patient overall Hurley stage)
- AN count
- AN count category [redacted]
- ANF count
- Inflammatory nodule count
- Abscess count
- Draining fistula count
- Draining fistula count category [redacted]
- Number of anatomical areas with abscess, inflammatory nodule or draining fistula [redacted]

- IHS4 score

Note: Disease duration (years) will be calculated as follows:

Disease duration (years) = (date of randomization – date of initial HS diagnosis + 1) / 365.25.

6.1.3. Medical History

For participants in the ITT population, medical history will be summarized by assigned treatment groups. This summary will include the number and percentage of participants with medical history for each body system/organ class as documented on the eCRF.

6.2. Disposition of Participant

The following categories will be summarized by treatment groups and overall for the ITT population in the PC period:

- Number (%) of participants who were randomized
- Number (%) of participants who were treated in the PC period
- Number (%) of participants who completed treatment in the PC period through Week 16
- Number (%) of participants who discontinued study treatment with a primary reason for discontinuation in the PC period
- Number (%) of participants who withdrew from the study with a primary reason for withdrawal in the PC period

The number of participants enrolled by country and/or site will also be provided by treatment group and overall.

The following categories will be summarized by treatment groups and overall for the open-label evaluable population in the OLE period:

- Number (%) of participants who were treated in the OLE period
- Number (%) of participants who completed treatment in the OLE period through Week 52
- Number (%) of participants who discontinued the study treatment with a primary reason for discontinuation in the OLE period
- Number (%) of participants who completed the study through Week 56
- Number (%) of participants who withdrew from the study with a primary reason for withdrawal in the OLE period

The following categories will be summarized by treatment groups and overall for the long-term evaluable population in the LTE period:

- Number (%) of participants who were treated in the LTE period
- Number (%) of participants who completed treatment in the LTE period through Week 100
- Number (%) of participants who discontinued the study treatment with a primary reason for discontinuation in the LTE period
- Number (%) of participants who completed the study through Week 104
- Number (%) of participants who withdrew from the study with a primary reason for withdrawal in the LTE period

6.3. Protocol Deviations

Protocol deviations recorded on the eCRF will be summarized by treatment groups and overall for ITT population in the PC period, open-label evaluable population in the OLE period, and long-term evaluable population in the LTE period, and listed.

6.4. Exposure

For participants in the safety population in the PC period, the open-label evaluable population in the OLE period, those who take INCB054707 75 mg throughout study participation up to Week 52, and the long-term evaluable population in the LTE period, study drug exposure in terms of duration of treatment with study drug will be summarized by treatment groups descriptively as follows:

- **Duration of treatment with study drug (days):** date of last dose of study drug – date of first dose of study drug + 1.

Note that the date of first and last dose of study drug are period-specific and defined in Table 3.

Table 3: Definition of First and Last Dose Date

Treatment Period	Treatment Group	First Dose Date	Last Dose Date
PC period	Placebo INCB054707 15 mg INCB054707 45 mg INCB054707 75 mg	Date that the first dose of study drug (INCB054707 or placebo) was administered to the participants in the PC period	Date that the last dose of study drug (INCB054707 or placebo) is administered to the participants in the PC period
OLE period	Placebo to INCB054707 75 mg INCB054707 15 mg to 75 mg INCB054707 45 mg to 75 mg INCB054707 75 mg	Date that the first dose of study drug (INCB054707 75 mg) was administered to the participants in the OLE period	Date that the last dose of study drug (INCB054707 75 mg) is administered to the participants in the OLE period
Throughout study participation up to Week 52	INCB054707 75 mg	Date that the first dose of study drug (INCB054707 75 mg) was administered to the participants in the PC period	Date that the last dose of study drug (INCB054707 75 mg) is administered to the participants throughout study participation up to Week 52
LTE period	INCB054707 ≤ 45 mg INCB054707 ≥ 60 mg	Date that the first dose of study drug (INCB054707) was administered to the participants in the LTE period	Date that the last dose of study drug (INCB054707) is administered to the participants in the LTE period

In addition, for the safety population in the PC period and the open-label evaluable population in the OLE period, average daily dose of INCB054707 and total actual dose of INCB054707 taken will be summarized by treatment groups descriptively as follows:

- **Average daily dose of INCB054707 (mg/day):** total actual INCB054707 dose taken (mg) / [duration of treatment with study drug (days) – number of interrupted days with study drug].
- **Total actual dose of INCB054707 taken (mg) will be calculated as:** (total number of tablets dispensed – total number of tablets returned) ×15 (mg/tablet) × p_T

  Where p_T denotes the proportion of INCB054707 among the 5 tablets taken daily with $p_T = 0$ (0/5) for placebo group, 1/5 for INCB054707 15 mg group, 3/5 for INCB054707 45 mg group, and 1 (5/5) for INCB054707 75 mg group.

Total number of tablets dispensed and returned in each period is based on information entered on the Drug Accountability eCRF. If there is dispensed drug that has not been returned yet, the actual dose taken starting from the dispense date of the unreturned drug will be imputed by the dose taken as reported on the Dosing eCRF.

6.5. Study Drug Compliance

For participants in the safety population, the open-label evaluable population, and the long-term evaluable population, overall compliance (%) for INCB05707/placebo will be calculated for all participants as follows:

compliance (%) = 100 × [total dose actually taken (in the specific period)] / [total prescribed dose].

Total prescribed dose is defined as the sum of the doses prescribed by the investigator accounting for dose modifications.

Total dose actually taken will be calculated as: total number of tablets dispensed – total number of tablets returned (see Section 6.4 for details on total number of tablets dispensed and returned).

6.6. Prior and Concomitant Medication

Prior medications and concomitant medications will be coded using the WHO Drug Dictionary. The number and percentage of participants in the ITT during the PC period for each prior and concomitant medication will be summarized by treatment groups and overall by WHO drug class and WHO drug preferred term. For the open-label evaluable population in the OLE period and the long-term evaluable population in the LTE period, only concomitant medications will be summarized by treatment groups and overall by WHO drug class and WHO drug preferred term.

7. EFFICACY

Appendix A provides a list of data displays. Sample data displays are included in a separate document.

7.1. General Considerations

For participants who enter the OLE period and do not continue in the LTE period, all by-visit analyses for open-label evaluable population will include the follow-up period if the data are available, unless otherwise specified.

For participants who continue into the LTE period, all by-visit analyses for long-term evaluable population will include the follow-up period if the data are available, unless otherwise specified.

Unless otherwise stated, the strata identified in the randomization process will be used in all efficacy analyses.

7.2. Efficacy Parameters

An example of the lesion count worksheet is provided in the Study Manual and will be used for assessment of AN and ANF counts, HiSCR, IHS4, [redacted] and Hurley Stage. It includes assessment of 7 anatomic regions:

7.2.1. AN and ANF Counts

The AN count is defined as the sum of abscess and inflammatory nodule counts. The AN results will be used to calculate change in AN count relative to baseline, as well as AN50, AN75, AN90, and AN100, defined respectively as at least a 50%, 75%, 90%, and 100% decrease in AN count relative to baseline.

The ANF count is defined as the sum of abscess, inflammatory nodule, and draining fistula counts. The ANF results will be used to calculate the change in ANF count relative to baseline.

7.2.2. Hidradenitis Suppurativa Clinical Response

A HiSCR definition is based on the following criteria relative to the baseline at each visit:

- at least 50% reduction in AN count,
- no increase in abscess count, and
- no increase in draining fistula count.

HiSCR75 is defined as at least 75% reduction from baseline in AN count with no increase in the number of abscesses or draining fistulas.

HiSCR90 is defined as at least 90% reduction from baseline in AN count with no increase in the number of abscesses or draining fistulas.

7.2.3. International Hidradenitis Suppurativa Severity Score System

The IHS4 (Zouboulis et al 2017) is a composite, dynamic score and validated tool used to determine HS severity. The total IHS4 score can be calculated as:

IHS4 (points) = (number of inflammatory nodules × 1) + (number of abscesses × 2) + (number of draining tunnels [draining fistulae/sinuses] × 4)

And the IHS4 category is defined as:

Mild HS: ≤ 3points; Moderate HS: 4-10 points; Severe HS: ≥11 points.

[redacted]

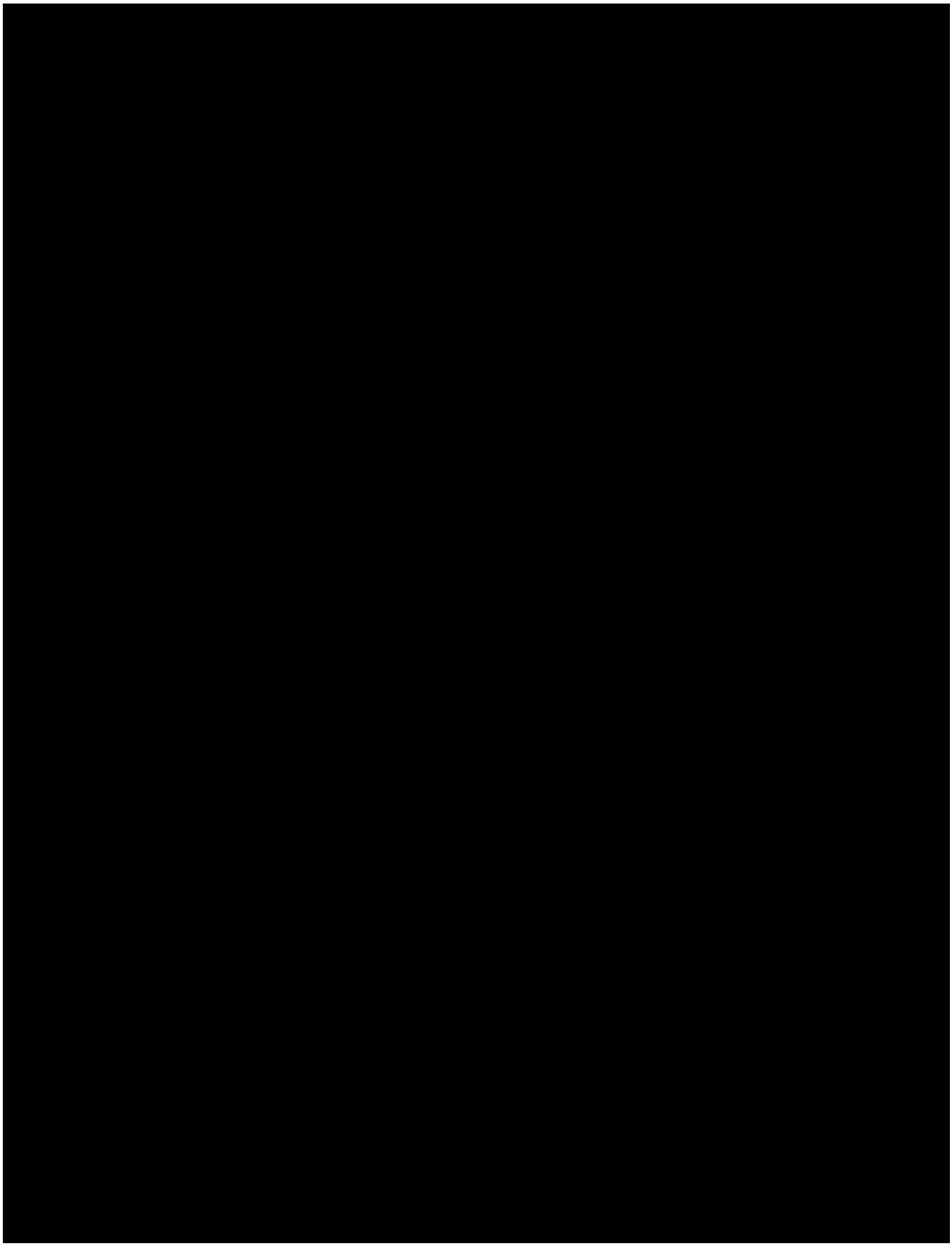
7.2.5. Hurley Stages of Hidradenitis Suppurativa

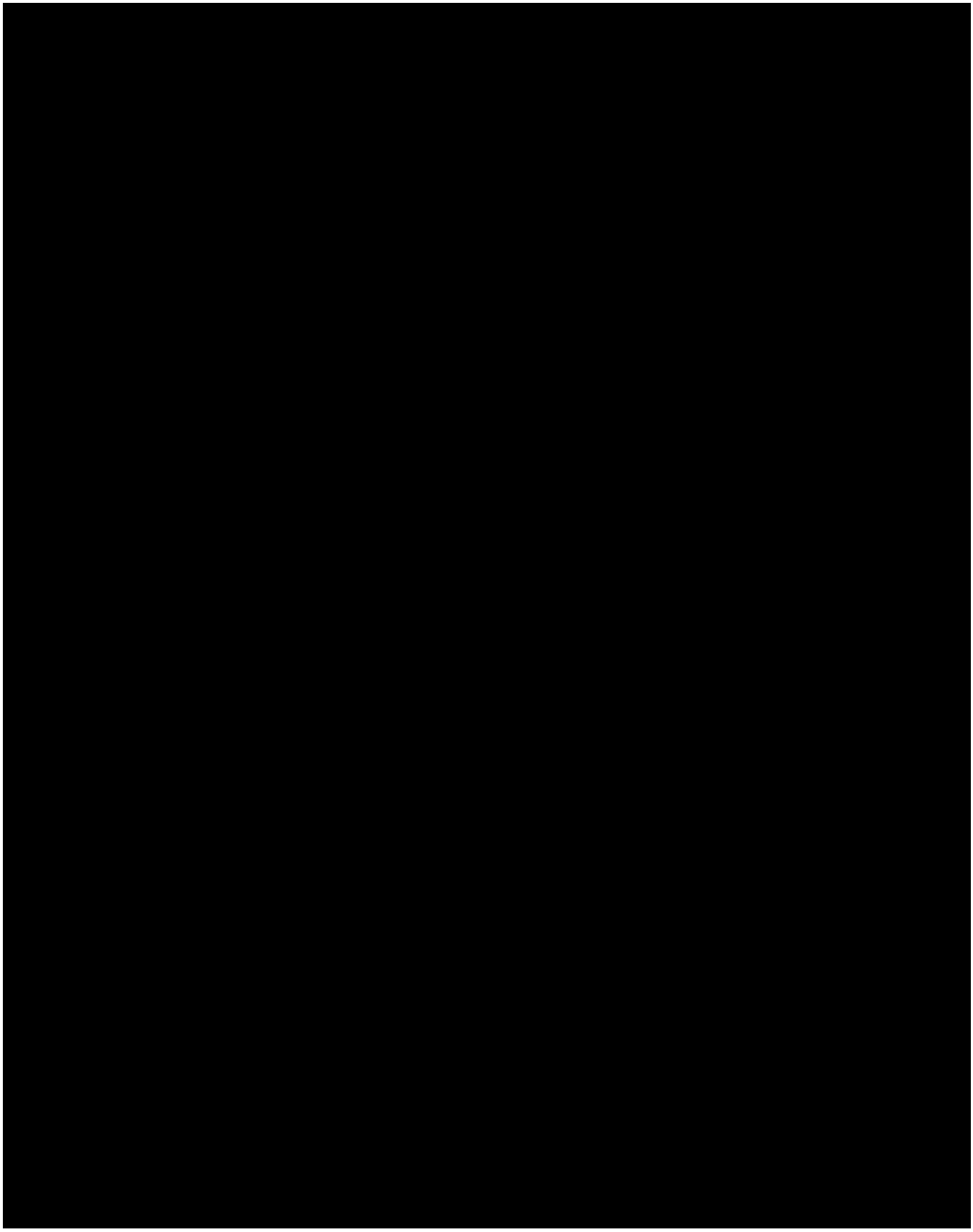
The Hurley Stages are defined in Table 4. The investigator (or designee) will determine the Hurley Stage in each affected anatomical region at the designated study visits. If more than 1 stage is present in the region, the worst stage in that region should be documented. The participant will be assigned an overall Hurley Stage corresponding to the stage of the worst involved anatomical region.

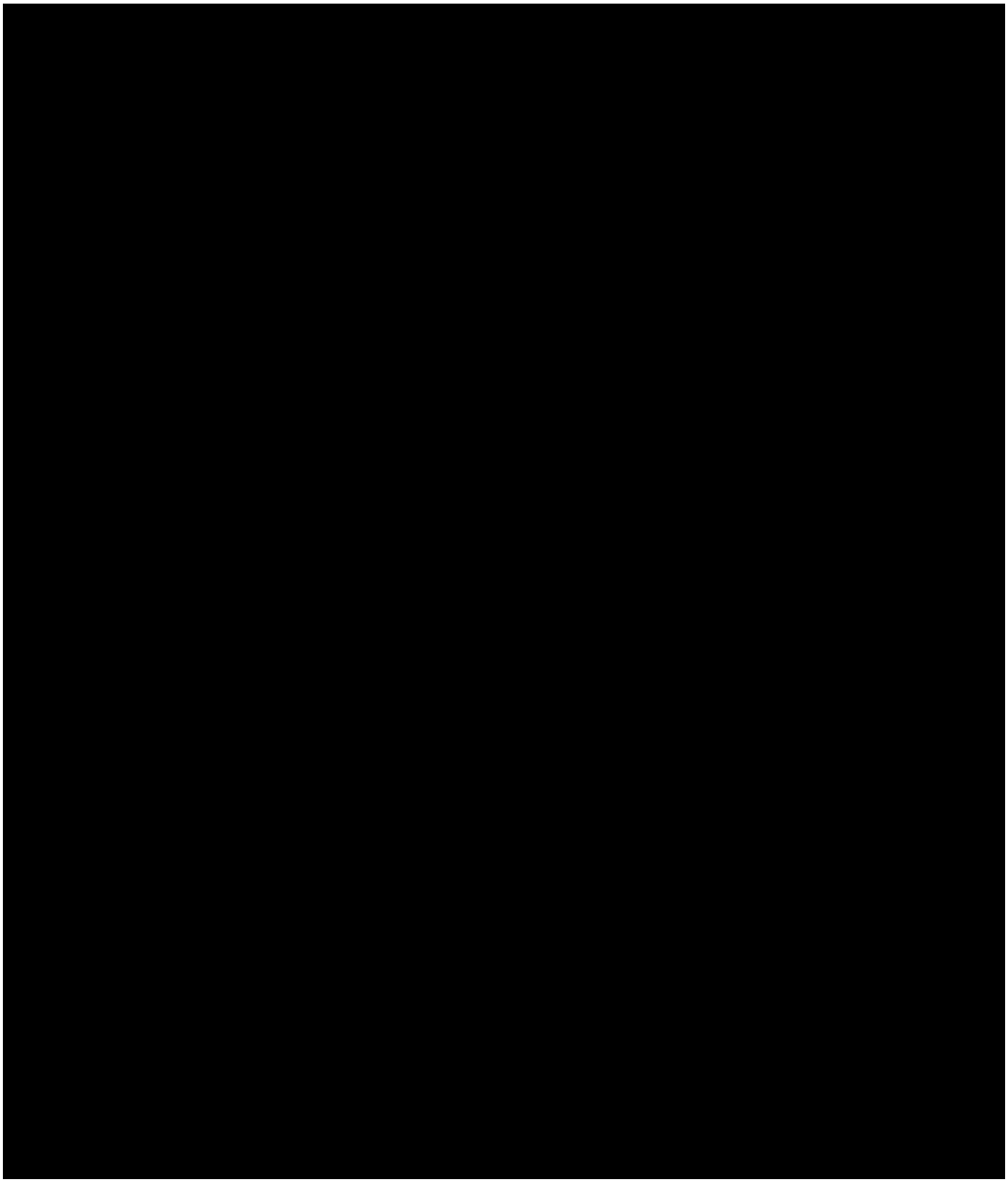
Table 4: Hurley Stages of Hidradenitis Suppurativa

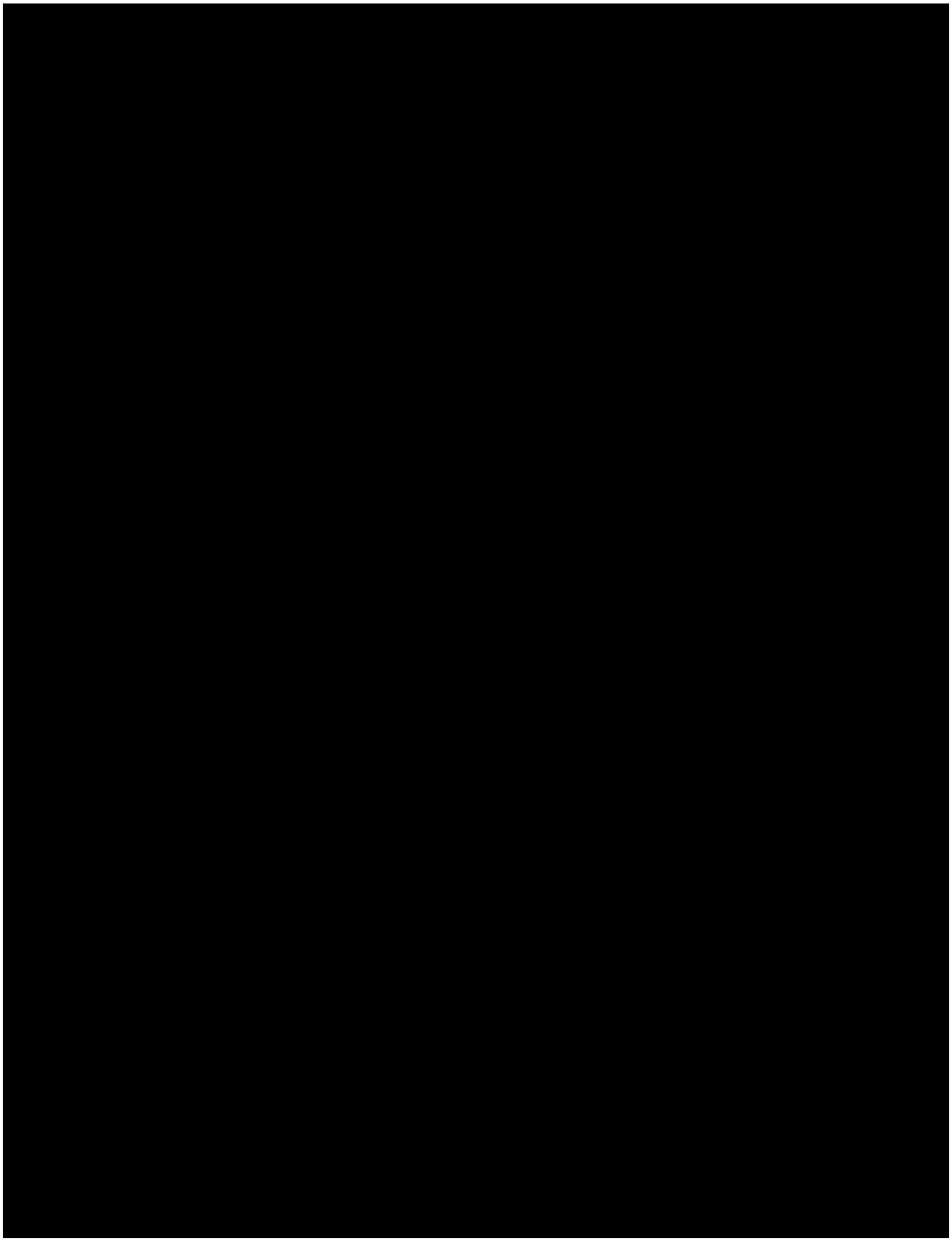
Hurley Stage	Description
I	Abscess formation, single or multiple, without sinus tracts and cicatrization (scarring).
II	One or more widely separated recurrent abscesses with tract formation and cicatrization (scarring).
III	Multiple interconnected tracts and abscesses across the entire area, with diffuse or near diffuse involvement.

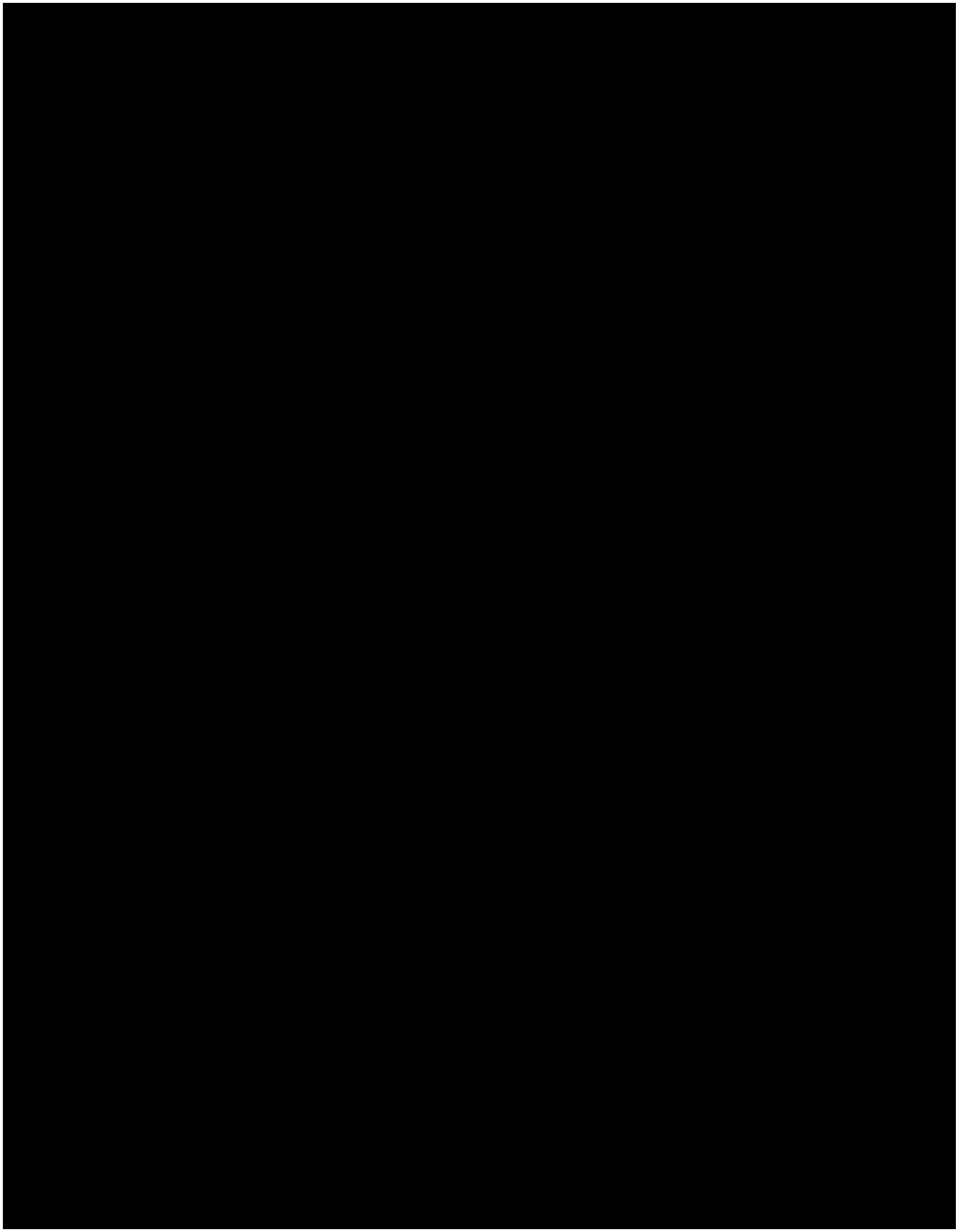
[redacted]











7.3. Efficacy Hypotheses

The primary hypothesis is that INCB054707 75 mg is superior to placebo at Week 16 on mean change from baseline in AN in participants with HS. Assuming μ_T is the mean change from baseline at Week 16 in AN count in INCB054707 75 mg group and μ_C is the mean change from baseline at Week 16 in AN count in placebo group, the primary hypothesis of the study are as follows:

- H_0 (null hypothesis): $\mu_T = \mu_C$
- H_A (alternative hypothesis): $\mu_T \neq \mu_C$

7.4. Analysis of the Primary Efficacy Parameter

The primary efficacy endpoint is the mean change of AN count at Week 16 relative to baseline.

7.4.1. Primary Efficacy Analysis

[redacted]

7.4.2. Subgroup Analyses for Primary Endpoint

Subgroups will be formed based on the following participant characteristics and baseline variables for those participants whose data are available:

- Geographic region (North America, Outside of North America)
- Baseline Hurley Stage (Stage I, Stage II, Stage III)

The primary efficacy endpoint will be summarized using descriptive statistics based on the ITT population for the subgroups defined above.

7.4.3. Sensitivity and Supportive Analyses for Primary Endpoint

The primary endpoint will be analyzed using the PP population as a sensitivity analysis to the ITT.

7.5. Analysis of the Secondary Efficacy Parameters

7.5.1. Analysis of the Key Secondary Efficacy Endpoint

The key secondary efficacy endpoint is proportion of participants who achieve HiSCR at Week 16 will be conducted for the ITT population.

[redacted]

7.5.2. Analysis of Other Secondary Efficacy Endpoints

All other secondary efficacy endpoints are listed in Table 1 and will be summarized using descriptive statistics based on the ITT population.

For categorical measurements, summary statistics will include sample size, frequency, and percentages. For continuous measurements, summary statistics will include sample size, mean, median, standard deviation, minimum, and maximum. Summary statistics for continuous measures will be provided for baseline, the actual measurements at each visit, and the change from baseline at each visit.

[redacted]

7.7. Analysis of Additional Efficacy Parameters

The following additional efficacy endpoints will be summarized descriptively based on the ITT population in the PC period, the open-label evaluable population in the OLE period, and the long-term evaluable population in the LTE period:

- Proportion of participants in each category of Hurley Stage at each scheduled visit
- Proportion of participants with Hurley Stage change from baseline at each scheduled visit
- Mean percent change from baseline in AN count at each scheduled visit
- [redacted]
- Proportion of participants achieving HiSCR90 at each scheduled visit

9. SAFETY AND TOLERABILITY

Appendix A provides a list of data displays. Sample data displays are included in a separate document.

9.1. General Considerations

The analyses in this section will be provided for the safety population in the PC period, the open-label evaluable population in the OLE period, and the long-term evaluable population in the LTE period, unless otherwise specified. Summary tables may be replaced with listings when appropriate. For instance, an AE frequency table may be replaced with a listing if it only contains a few unique preferred terms reported on relatively few participants.

9.2. Adverse Events

9.2.1. Adverse Event Definitions

A TEAE is any AE either reported for the first time or worsening of a pre-existing event after the first dose of study drug until the end of the safety follow-up.

TEAE in each period is any AE with a start time after the first dose of study drug in each period and until the end of the safety follow-up, or prior to the first dose in the subsequent period for participants who entered in to the subsequent period. Analysis of AEs (as discussed below) will be limited to TEAEs, but data listings will include all AEs regardless of their timing in relation to study drug administration. For purposes of analysis, all AEs will be considered TEAEs unless the AE can unequivocally be defined as not treatment-emergent.

Adverse events will be tabulated by MedDRA PT and SOC. Severity of AEs will be graded using the NCI CTCAE v5.0. The CTCAE reporting guidelines and grading details are available on the Cancer Therapy Evaluation Program website.

The subset of AEs considered by the investigator to be related to study drug will be considered to be treatment-related AEs. If the investigator does not specify the relationship of the AE to study drug, the AE will be considered to be treatment-related. The incidence of AEs and treatment-related AEs will be tabulated. In addition, serious TEAEs will also be tabulated.

9.2.2. Adverse Event Summaries

AE will be summarized by treatment groups for the safety population in the PC period, the open-label evaluable population in the OLE period, participants who take INCB054707 75 mg throughout study participation up to Week 52, and the long-term evaluable population in the LTE period.

An overall summary of AEs will include the following:

- Number (%) of participants reporting any TEAEs
- Number (%) of participants reporting any serious TEAEs
- Number (%) of participants reporting any Grade 3 or higher TEAEs
- Number (%) of participants reporting any treatment-related TEAEs
- Number (%) of participants who temporarily interrupted study treatment because of TEAEs
- Number (%) of participants who permanently discontinued study treatment because of TEAEs
- Number (%) of participants who had a fatal TEAE

The following summaries will be produced by MedDRA term (if 10 or fewer subjects appear in a table, a listing may be appropriate):

- Summary of TEAEs by MedDRA SOC and PT
- Summary of TEAEs by MedDRA PT in decreasing order of frequency
- Summary of TEAEs by MedDRA SOC, PT, and maximum severity
- Summary of TEAEs by MedDRA SOC, PT, and CTCAE grade category
- Summary of Grade 3 or higher TEAEs by MedDRA SOC and PT
- Summary of Grade 3 or higher TEAEs by MedDRA PT in decreasing order of frequency
- Summary of serious TEAEs by MedDRA SOC and PT
- Summary of serious TEAEs by MedDRA PT in decreasing order of frequency
- Summary of treatment-related TEAEs by MedDRA SOC and PT
- Summary of treatment-related TEAEs by MedDRA PT in decreasing order of frequency
- Summary of Grade 3 or higher treatment-related TEAEs by MedDRA SOC and PT

- Summary of treatment-related serious TEAEs by MedDRA SOC and PT
- Summary of TEAEs with a fatal outcome by MedDRA SOC and PT
- Summary of TEAEs leading to dose reduction by MedDRA SOC and PT
- Summary of TEAEs leading to dose interruption by MedDRA SOC and PT
- Summary of TEAEs leading to discontinuation of study drug by MedDRA SOC and PT
- Summary of TEAEs requiring concomitant medications by MedDRA SOC and PT

9.3. Clinical Laboratory Tests

9.3.1. Laboratory Value Definitions

Laboratory values, change from baseline values, and percent change from baseline values will be summarized descriptively by visit, and non-numeric test values will be tabulated when necessary. Baseline will be determined according to Section 4.1.3. The last record before administration in the highest priority will be considered the baseline record. For baseline laboratory candidates with the same date and time in the same priority category, additional rules may be provided after consultation with the medical monitor to delineate which value will be defined as baseline.

9.3.2. Laboratory Value Summaries

All test results and associated normal ranges from central laboratories will be reported in SI units. All tests with numeric values will have a unique unit per test. Any laboratory test results and associated normal ranges from local laboratories will be converted to SI units.

When there are multiple laboratory nonmissing values for a participant's particular test within a visit window, the laboratory value with the smallest laboratory sequence number will be used in by-visit summaries. [redacted]

For test results that will be summarized with available normal ranges, the number and percentage of participants with laboratory values being low (but never high), normal, high (but never low), and both low and high will be calculated for each test. This shift summary will be produced for each test. The denominator for the percentage calculation will use the number of participants in the baseline category (ie, low, high, normal, missing) as the denominator for the percentage in each of the categories during the study.

Severity grades will be assigned to laboratory test values based on the numerical component of CTCAE v5. Shift tables will also be presented showing change in CTCAE grade from baseline to the worst grade postbaseline. Separate summaries for abnormally high and abnormally low laboratory values will be provided when the laboratory parameter has both high and low grading criteria. The denominator for the percentage calculation will be the number of participants in the baseline category. The number of participants who experienced worsening of laboratory abnormalities will be summarized by maximum severity.

9.3.3. Potentially Clinically Important Laboratory Values

Criteria for potentially clinically important laboratory values are listed in Table 5 below.

[redacted]

[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

Note that combination of values need to be measured on the same day.

The number and percentage of participants with postbaseline liver specific function test values that meet each of the above criteria will be presented at each scheduled visit by treatment groups. Participants with potential DILI events will also be listed.

9.4. Vital Signs

Values at each scheduled visit, change, and percentage change from baseline for vital signs, including systolic blood pressure, diastolic blood pressure, pulse, respiratory rate, and body temperature will be summarized descriptively.

Normal ranges for vital sign values are defined in Table 6. For participants exhibiting vital sign abnormalities, the abnormal values will be listed along with their assigned treatment group. Alert vital signs are defined as an absolute value outside the defined normal range and percentage change greater than 25%. Note that the definition of alert vital signs does not apply to body temperature. The abnormal values for participants exhibiting alert vital sign abnormalities will be listed.

9.5. Electrocardiograms

Twelve-lead ECGs including PR, QT, QRS and QTcF intervals will be obtained for each participant during the study. Values at each scheduled visit, change, and percentage change from baseline will be summarized for each ECG parameter. Baseline will be determined as the average of all nonmissing values before the first administration of INCB054707 or placebo.

Normal ranges for ECG values are defined in Table 7. ECG values will also be considered abnormal if the absolute percentage change from baseline is more than 25% (30% for QRS interval). Participants exhibiting ECG abnormalities will be listed with study visit and assigned treatment group. Abnormal values for participants with alert ECG values, defined as both the absolute value and the percentage change from baseline being outside normal ranges, will be identified and listed. Outliers of QT and QTcF values, defined as absolute values > 450 millisecond, > 500 millisecond, or change from baseline > 30 millisecond, will be summarized.

10. CHANGES AND MODIFICATIONS TO THE ANALYSIS PLAN

All versions of the SAP are listed in Table 8.

Table 8: Statistical Analysis Plan Versions

SAP Version	Date
Original	12 OCT 2021

10.1. Changes to Protocol-Defined Analyses

[redacted]

10.2. Changes to the Statistical Analysis Plan

Not applicable.

11. REFERENCES

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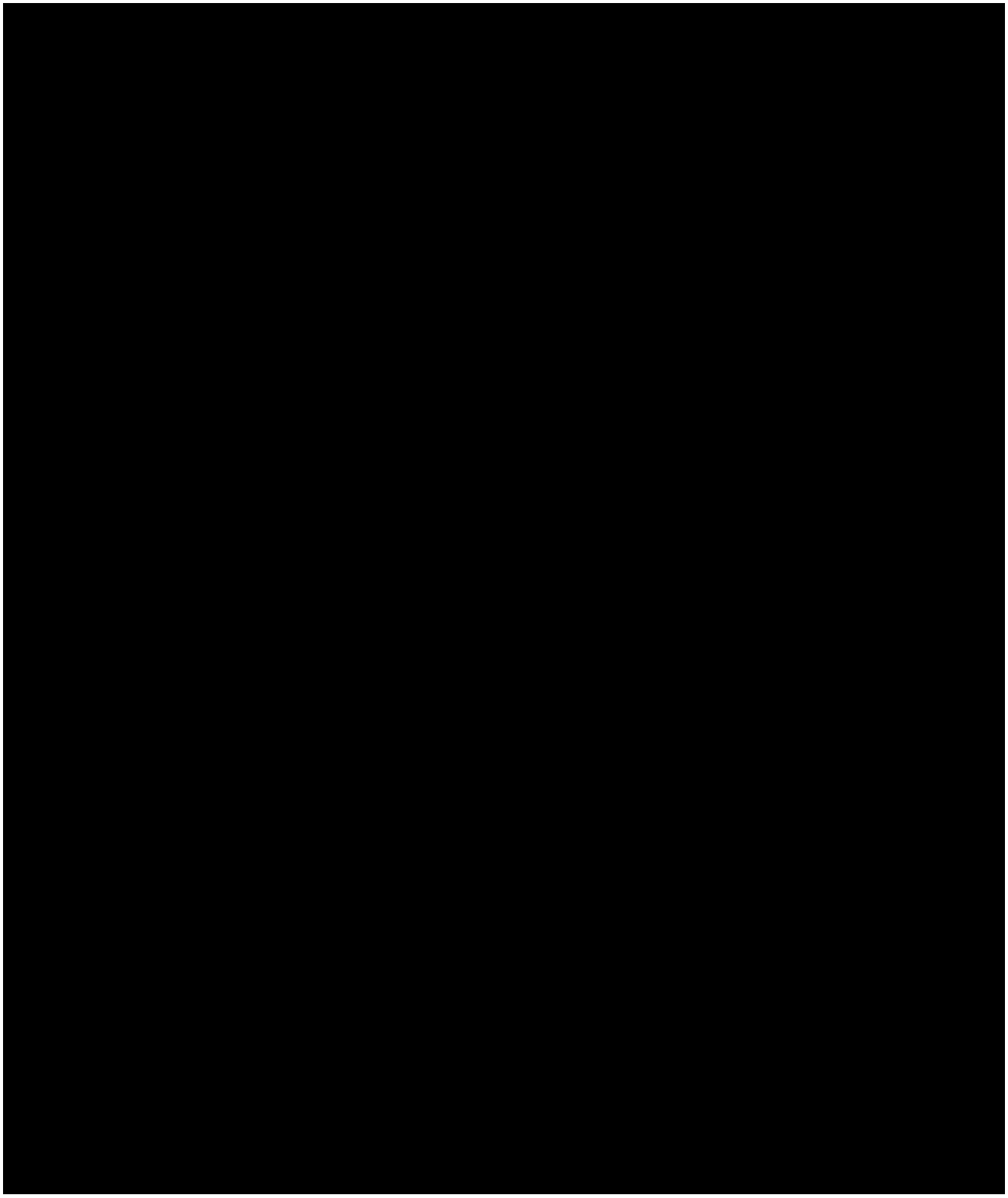

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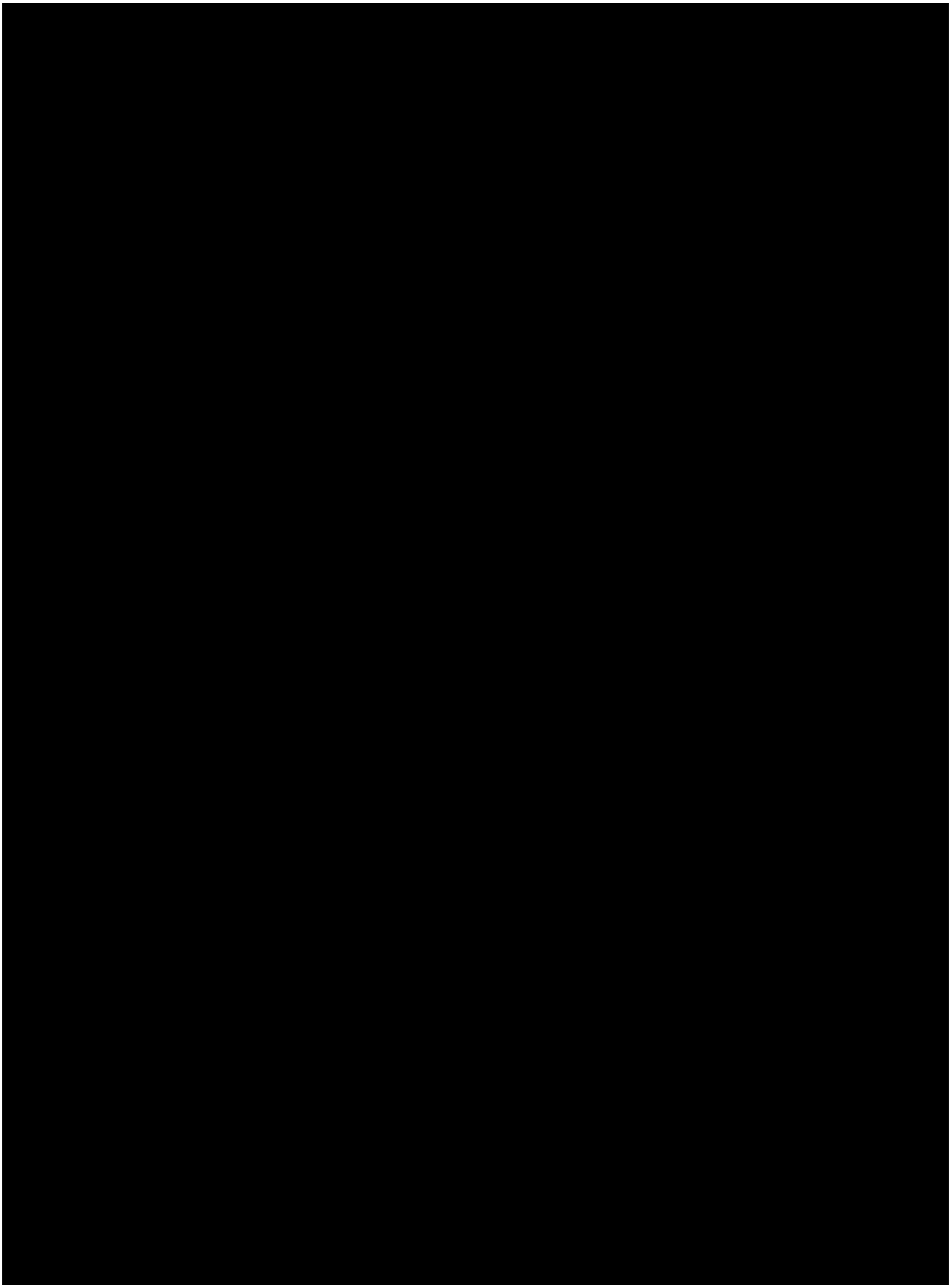

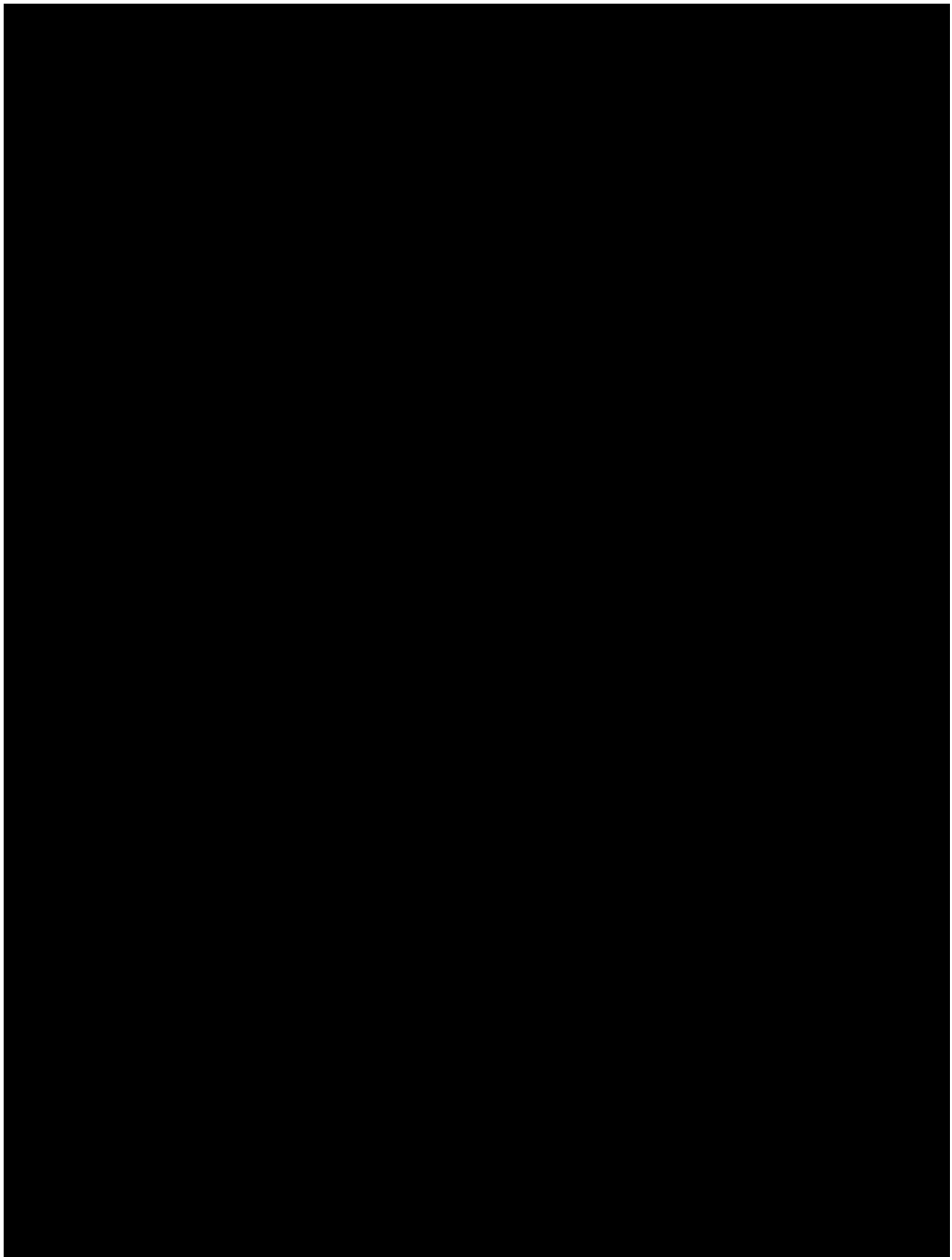

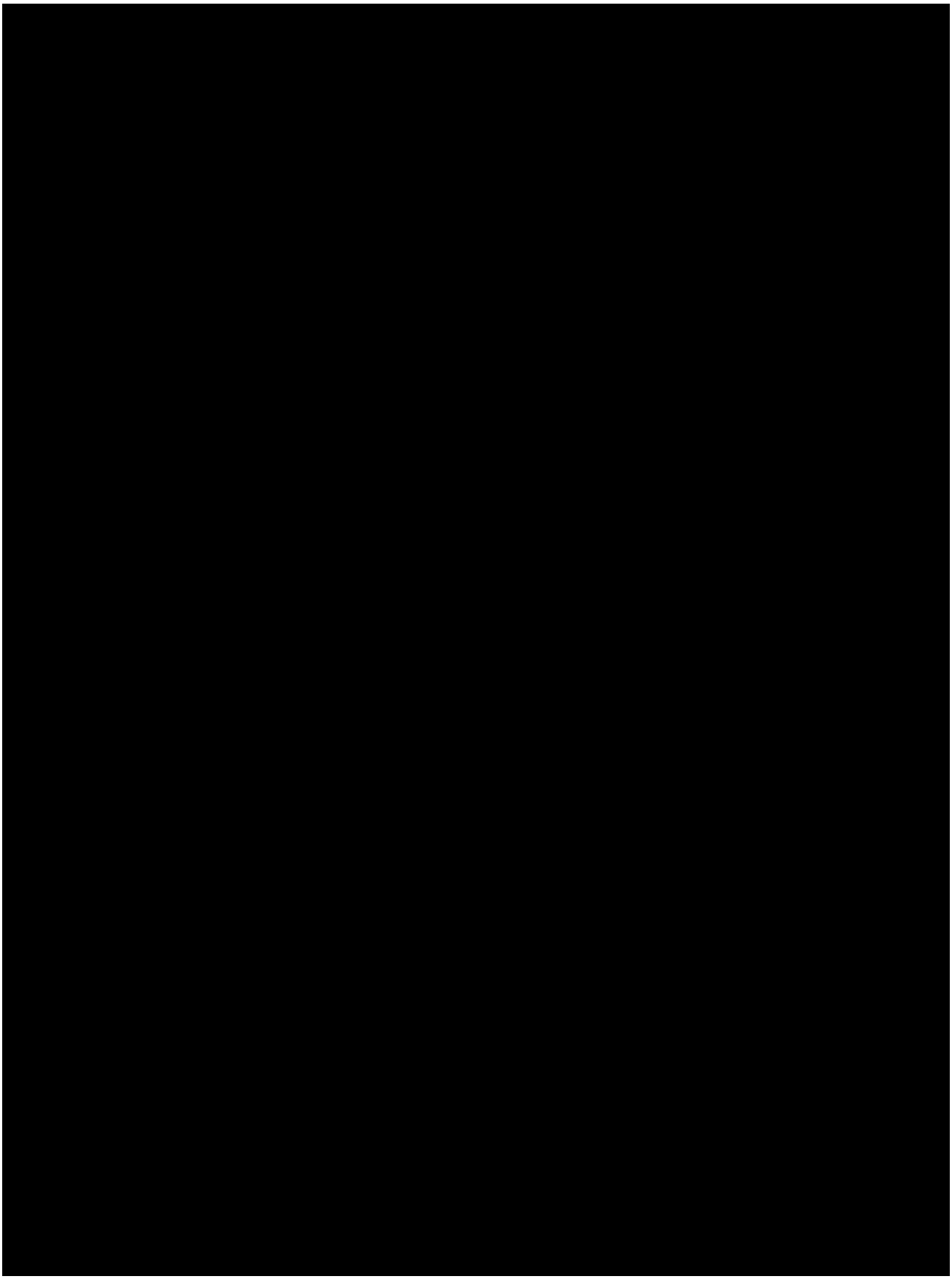

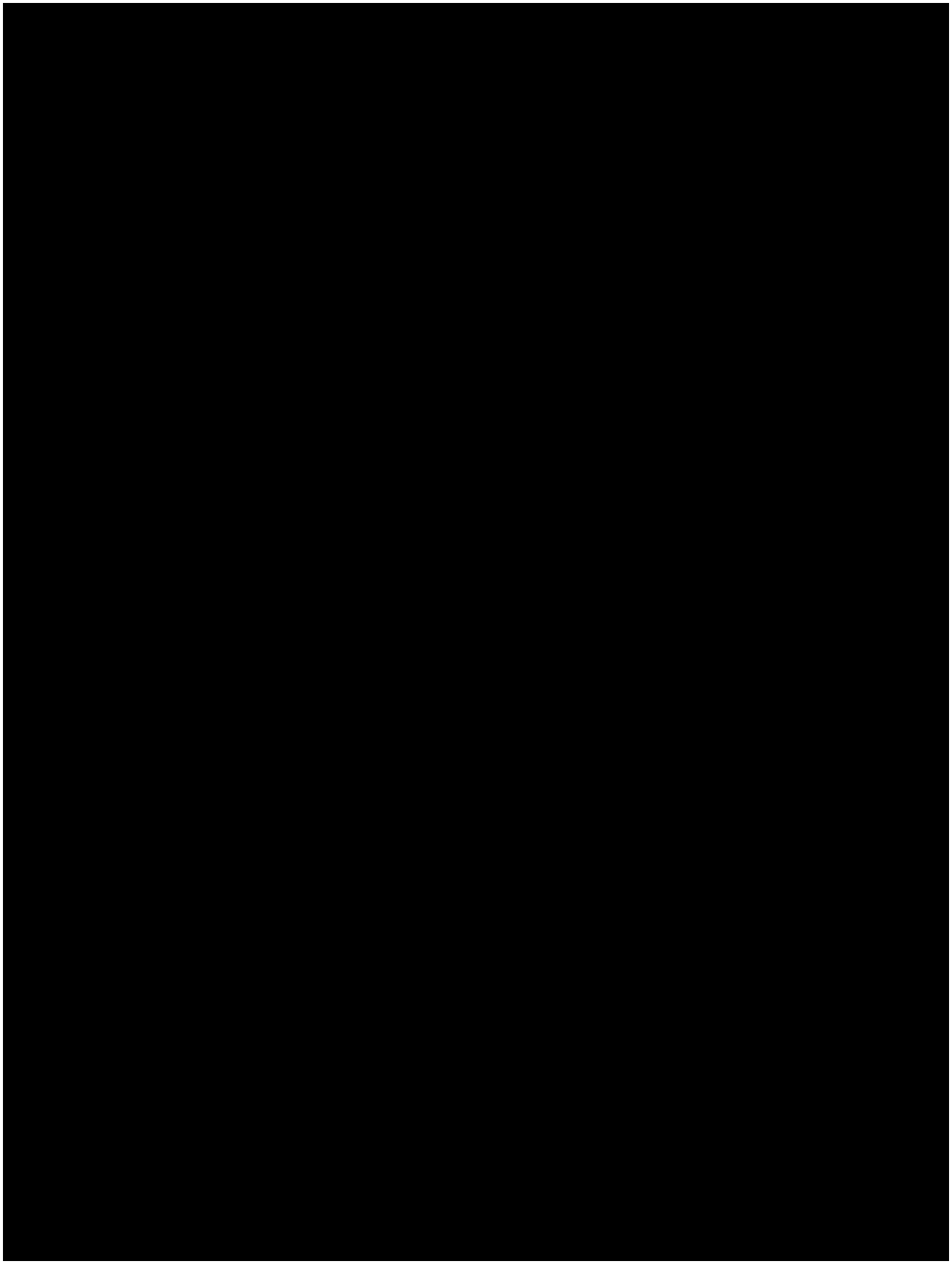

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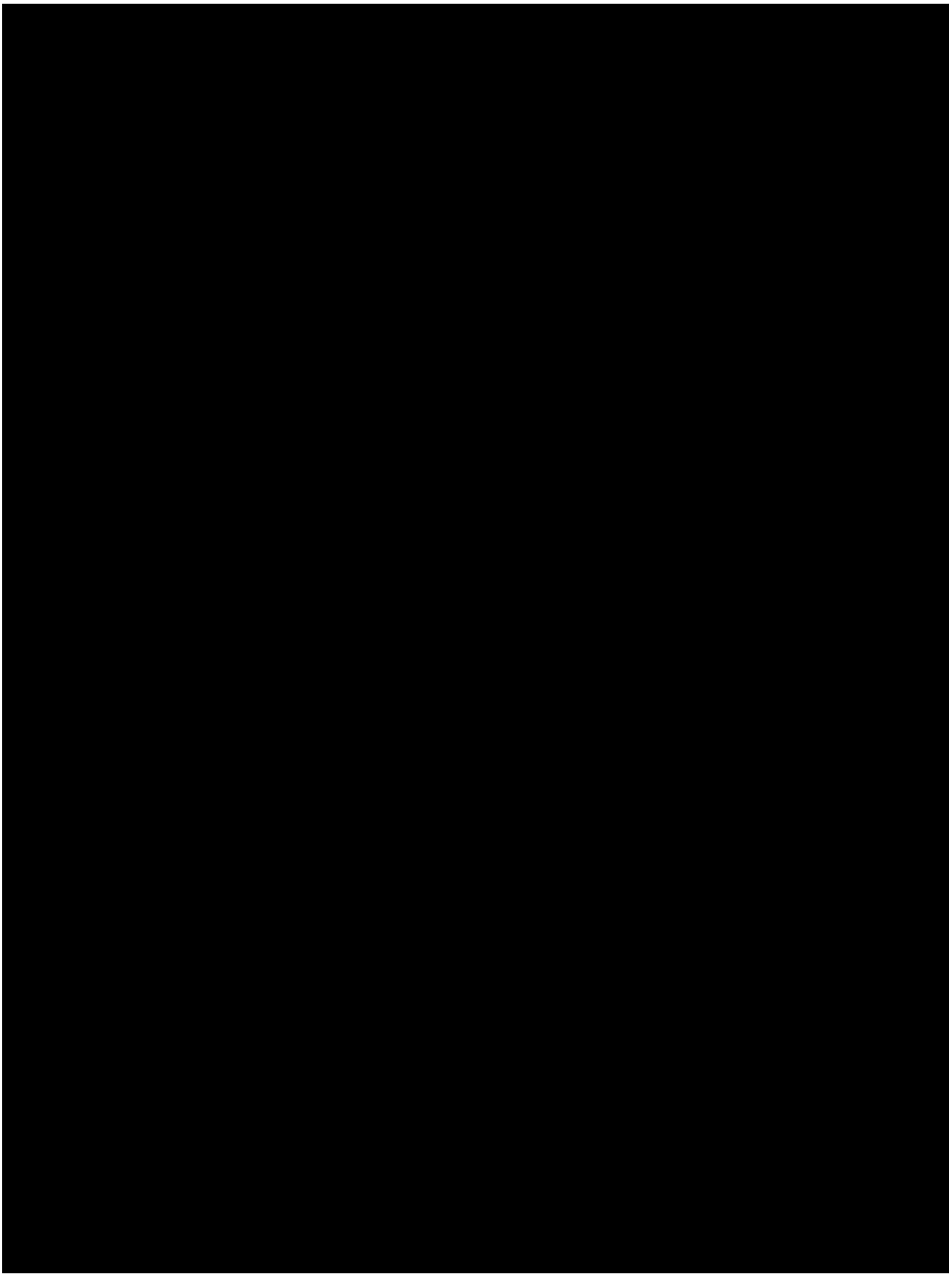

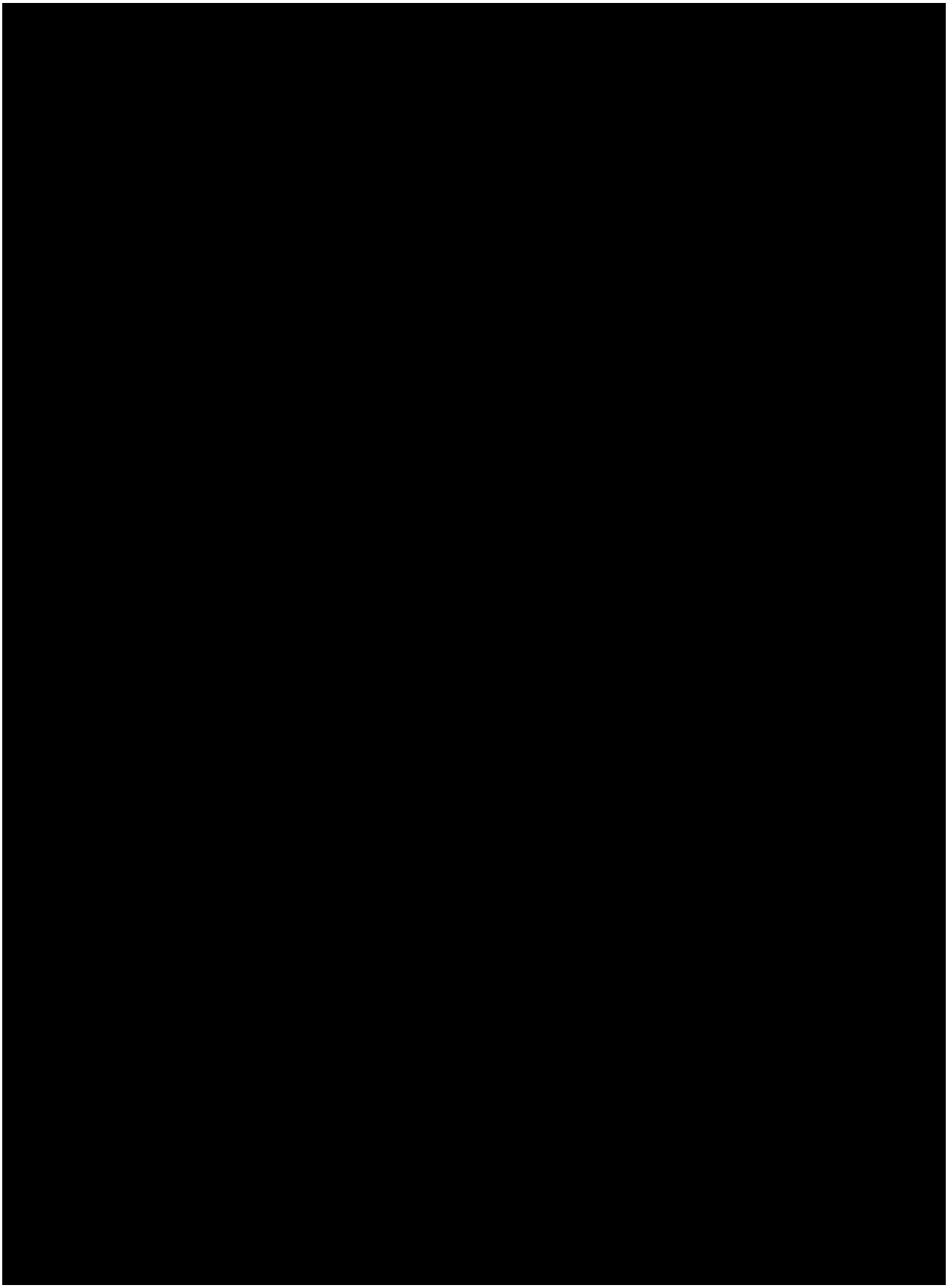

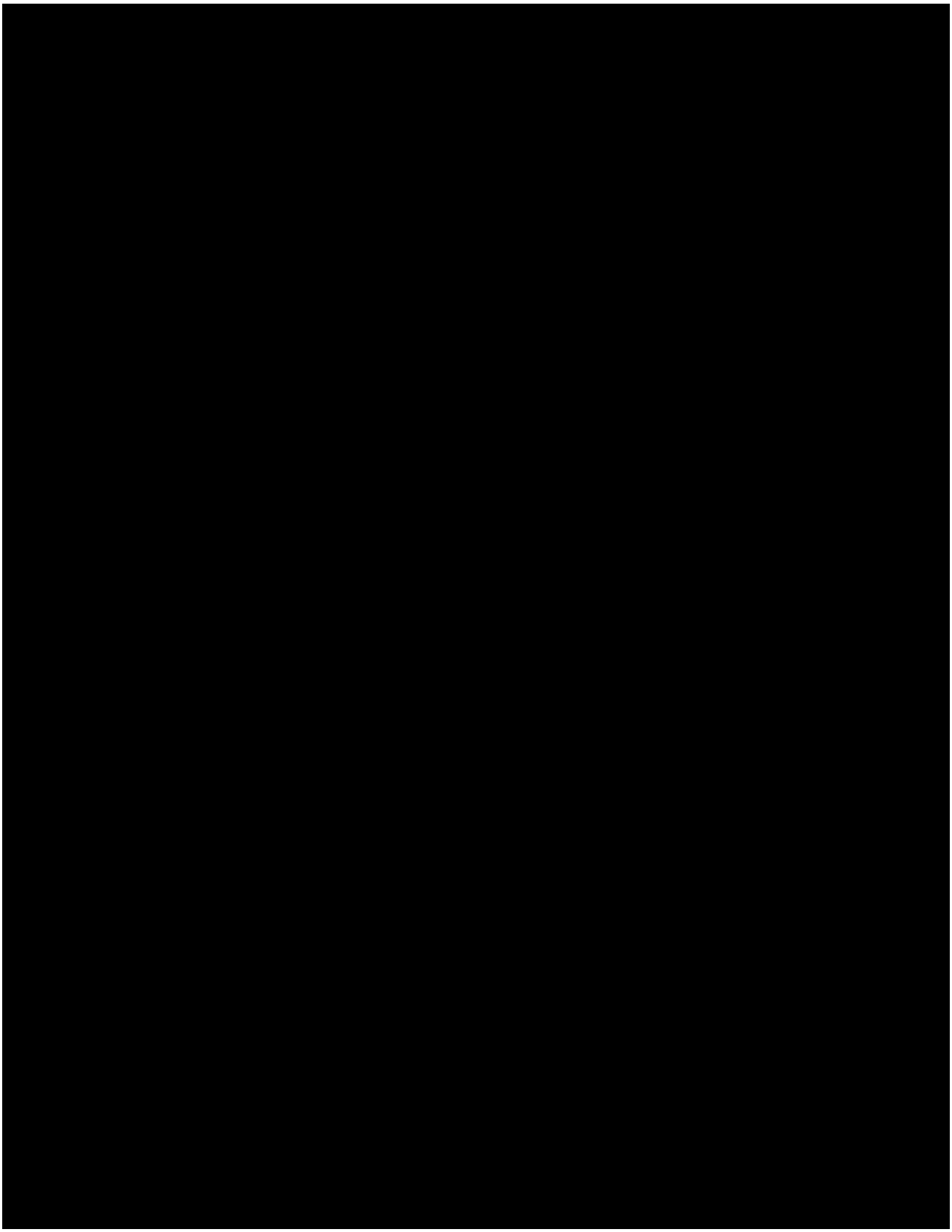

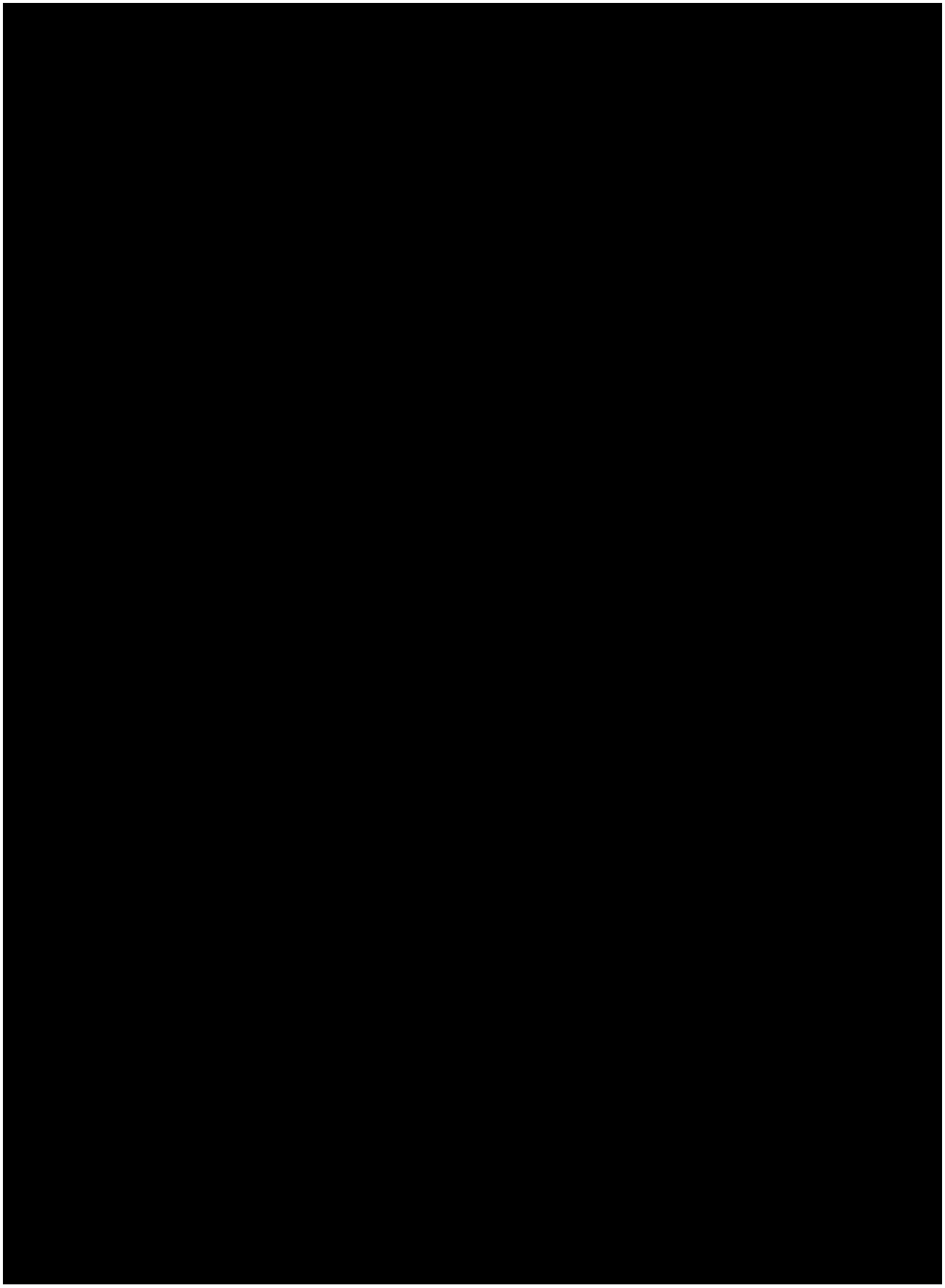

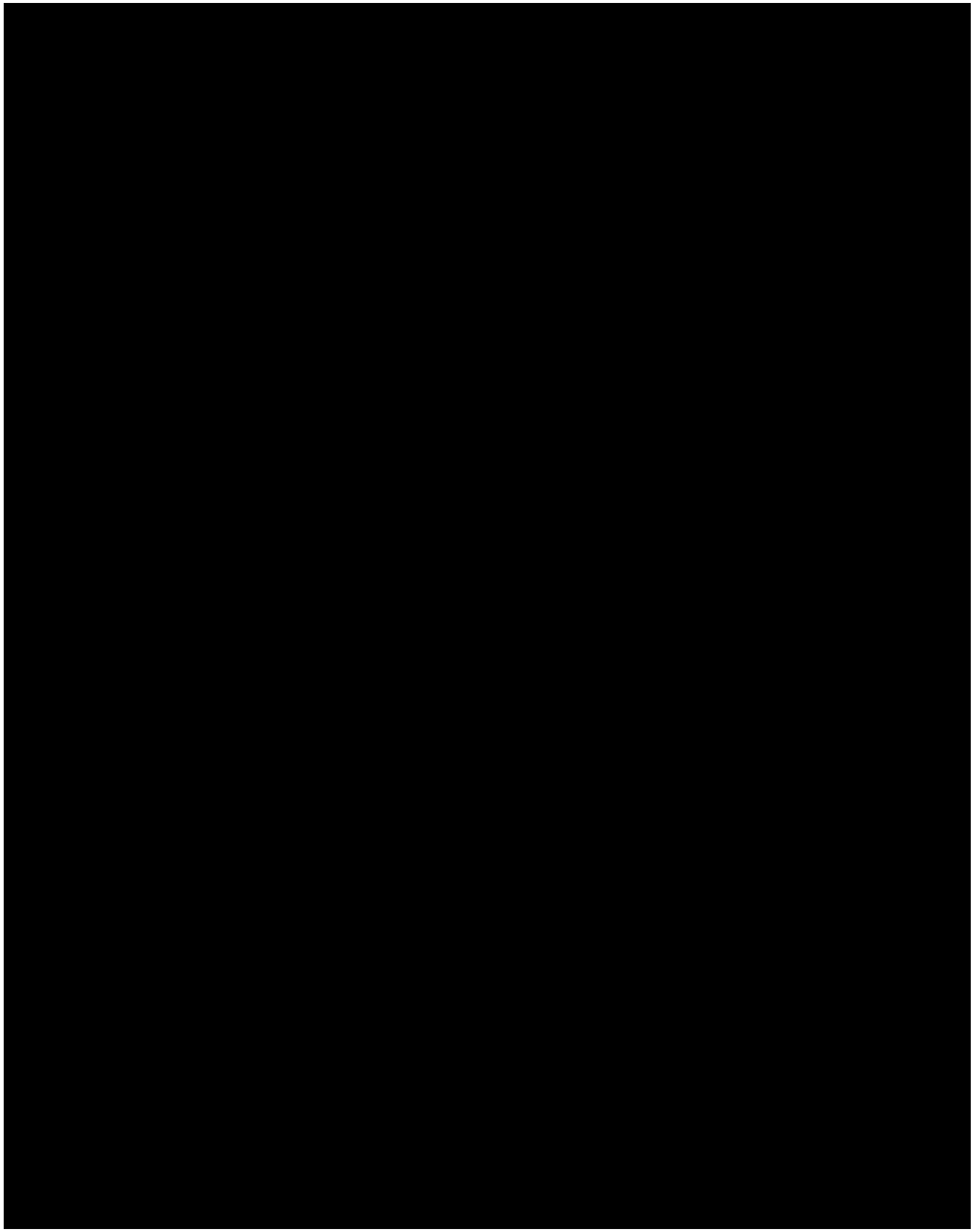

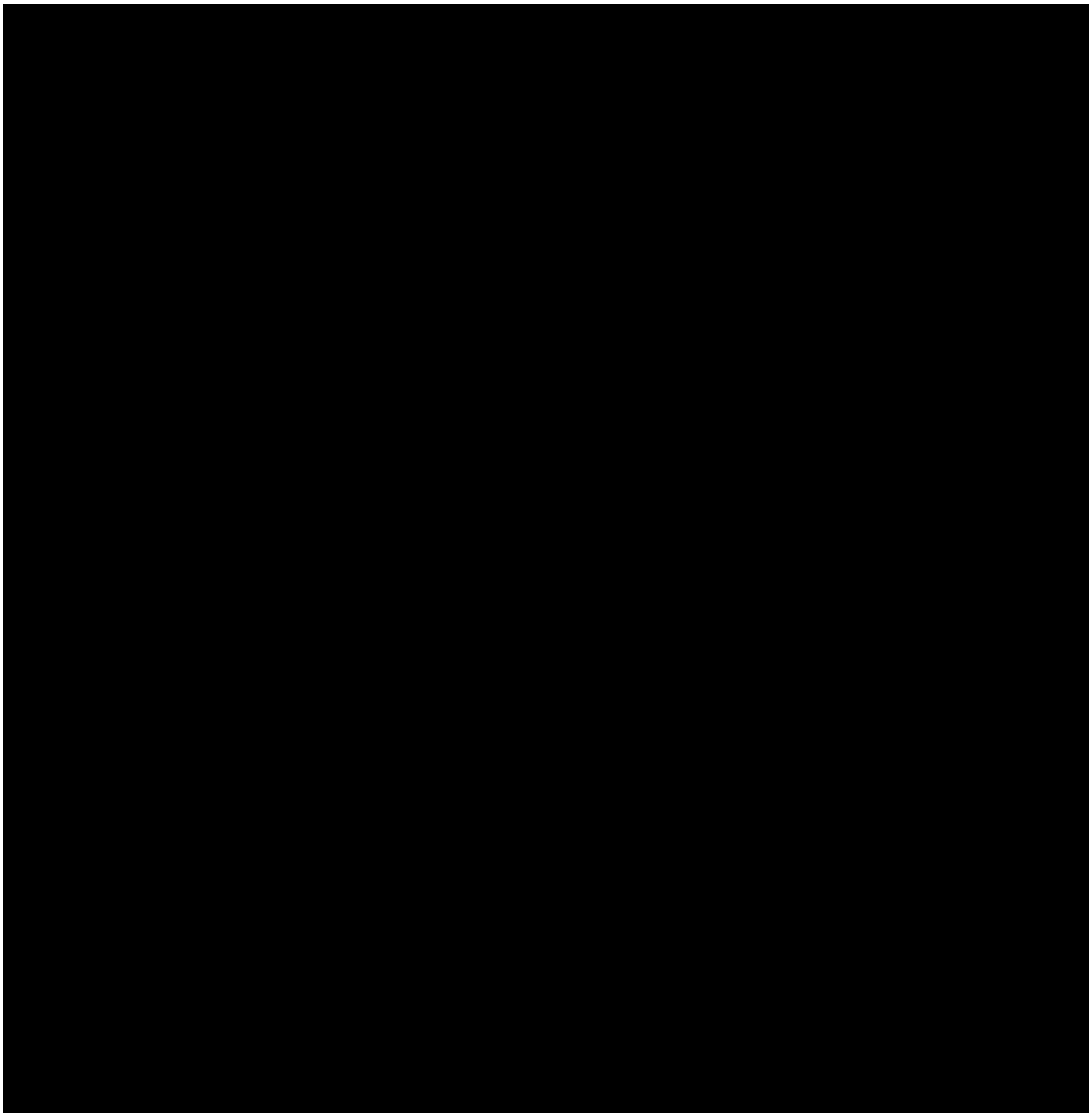

Figures