Official Title: **A Phase 1/2 Study of INCB053914 in Subjects With Advanced Malignancies**

NCT Number: NCT02587598

Document Date: Statistical Analysis Plan: 25 August 2017

16.1.9 DOCUMENTATION OF STATISTICAL METHODS

The document(s) presented below are enclosed.

Statistical Analysis Plan	25 AUG 2017

STATISTICAL ANALYSIS PLAN

INCB 53914-101 / NCT02587598

A Phase 1/2 Study of INCB053914 in Subjects With Advanced Malignancies

IND Number:	**126,097**
Sponsor:	**Incyte Corporation** **1801 Augustine Cut-Off** **Wilmington, DE 19803**
Protocol Version:	**Protocol Amendment 6 dated 15 Mar 2017**
CRF Approval Date:	**27 JUN 2017**
SAP Version:	**Original**
SAP Author:	[redacted], [redacted]
Date of Plan:	**25 AUG 2017**

This study is being conducted in compliance with good clinical practice, including the archiving of essential documents.

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LIST OF ABBREVIATIONS

Abbreviation	Term
aCML	atypical chronic myeloid leukemia
AE	adverse event
ALP	alkaline phosphatase
ALT	alanine aminotransferase
AML	acute myeloid leukemia
AST	aspartate aminotransferase
AUC_{0-t}	AUC from time zero (predose) to time of last observed quantifiable concentration within a subject across all treatments
BID	twice daily
BOR	best overall response
bpm	beats per minute
BSA	body surface area
CCyR	complete cytogenetic response
CI	confidence interval
Cl/F	oral dose clearance
CLL	chronic lymphocytic leukemia
C_{max}	maximum observed concentration
C_{min}	minimum observed concentration
CMML	chronic myelomonocytic leukemia
CMR	complete molecular response
CR	complete remission/response
CRF	case report form
CRi	complete remission with incomplete hematologic recovery
CRp	complete remission with incomplete platelet recovery
CT	computed tomography
CTCAE	Common Terminology Criteria for Adverse Events
CTEP	Cancer Therapy Evaluation Program
C-TG	combination treatment group
DLBCL	diffuse large B-cell lymphoma
DLT	dose-limiting toxicity

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Abbreviation	Term
[redacted]	[redacted]
ECG	electrocardiogram
ECOG	Eastern Cooperative Oncology Group
eCRF	electronic case report form
[redacted]	[redacted]
ELN	European LeukemiaNet
EOT	end of treatment
[redacted]	[redacted]
FAS	full analysis set
FDA	Food and Drug Administration
FISH	fluorescence *in situ* hybridization
HI	hematologic improvement
HI-E	hematologic improvement – erythroid response
HI-N	hematologic improvement – neutrophil response
HI-P	hematologic improvement – platelet response
I-DAC	intermediate-dose cytarabine
IV	intravenously
IWCLL	International Workshop on Chronic Lymphocytic Leukemia
IWG	International Working Group
IWG-MRT	International Working Group-Myeloproliferative Neoplasms Research and Treatment
KM	Kaplan-Meier
LCM	left costal margin
L-DAC	low-dose cytarabine
MDS	myelodysplastic syndrome
MedDRA	Medical Dictionary for Regulatory Activities
MF	myelofibrosis
MLFS	morphologic leukemia-free state
MM	multiple myeloma
MPN	myeloproliferative neoplasms
[redacted]	[redacted]
MPN-U	myeloproliferative neoplasms unclassifiable

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Abbreviation	Term
MR	minimal response
MRI	magnetic resonance imaging
MTD	maximum tolerated dose
NA	not assessed
NCI	National Cancer Institute
NE	nonevaluable
NONMEM	nonlinear mixed-effect modeling
ORR	objective remission/response rate
[redacted]	[redacted]
PAD	pharmacologically active dose
pBAD	phosphorylated Bcl-2–associated death promoter protein
PCyR	partial cytogenetic response
PD	pharmacodynamics
PET	probability of early termination
PET-MF	post-essential thrombocythemia myelofibrosis
[redacted]	[redacted]
[redacted]	[redacted]
PIM	proviral integration site of Moloney murine leukemia virus
PK	pharmacokinetic
PMF	primary myelofibrosis
PMR	partial molecular response
PP	per protocol
PPV-MF	post-polycythemia vera myelofibrosis
PR	partial remission/response
PT	preferred term
QD	once daily
QRS	Combination of three of the graphical deflections on an ECG. It is usually the central and most visually obvious part of the tracing. It corresponds to the depolarization of the right and left ventricles of the human heart.
QTcF	QT interval corrected using the Fridericia formula
RARS-T	refractory anemia with ring sideroblasts and thrombocytosis
RD	relapse disease
RNA	ribonucleic acid

Abbreviation	Term
RP2D	recommended Phase 2 dose
RR	ECG interval from the beginning of a QRS complex to the beginning of the next QRS complex
SAE	serious adverse event
SAP	statistical analysis plan
SC	subcutaneously
sCR	stringent complete response
SD	stable disease
SI units	International System of Units
SOC	system organ class
TEAE	treatment-emergent adverse event
TGA	Treatment Group A
TGB	Treatment Group B
TGC	Treatment Group C
T_{max}	time of occurrence of C_{max}
UE	unable to evaluable
VGPR	very good partial response
WBC	white blood cell
WHO	World Health Organization

1. INTRODUCTION

This is an open-label, dose-escalation study of the pan-PIM kinase inhibitor INCB053914 as monotherapy and in combination with standard-of-care agents in subjects with advanced malignancies. The study will be conducted in 4 parts: Parts 1 and 2 will evaluate INCB053914 as monotherapy, and Parts 3 and 4 will evaluate INCB053914 in combination with cytarabine, azacitidine, or ruxolitinib. Section 1 of the Protocol provides a detailed description of the investigational product, target patient population, rationale for doses to be examined, and potential risks and benefits of treatment with INCB053914 and selected standard-of-care agents.

The purpose of this SAP is to provide details of the statistical analyses that have been outlined in the Study INCB 53914-101 Protocol. The scope of this plan includes the interim and final analyses that are planned and will be executed by the Department of Biostatistics or designee, and the analyses of PK.

2. STUDY INFORMATION, OBJECTIVES, AND ENDPOINTS

2.1. Protocol and Case Report Form Version

This SAP is based on INCB 53914-101 Protocol Amendment 6 dated 15 MAR 2017 and CRFs approved 27 JUN 2017. Unless superseded by an amendment, this SAP will be effective for all subsequent Protocol amendments and CRF versions.

2.2. Study Objectives

2.2.1. Primary Objectives

- All parts: To evaluate the safety and tolerability of INCB053914 as a monotherapy and in combination with standard-of-care agents in subjects with advanced malignancies.
- Part 4 only:
  - To evaluate the efficacy of INCB053914 in combination with cytarabine in subjects with relapsed or refractory AML based on ORR.
  - To evaluate the efficacy of INCB053914 in combination with azacitidine in subjects with newly diagnosed AML who are 65 years or older and unfit for intensive chemotherapy based on ORR.

2.2.2. Secondary Objectives

- All parts: To evaluate the PK of INCB053914 when administered alone in the fasted state, the effect of food on the INCB053914 PK, and the PK when administered in combination with SOC agents in the fasted state.
- All parts: To assess the PD of INCB053914 as a monotherapy and in combination with standard-of-care agents in subjects with advanced malignancies.

[redacted]

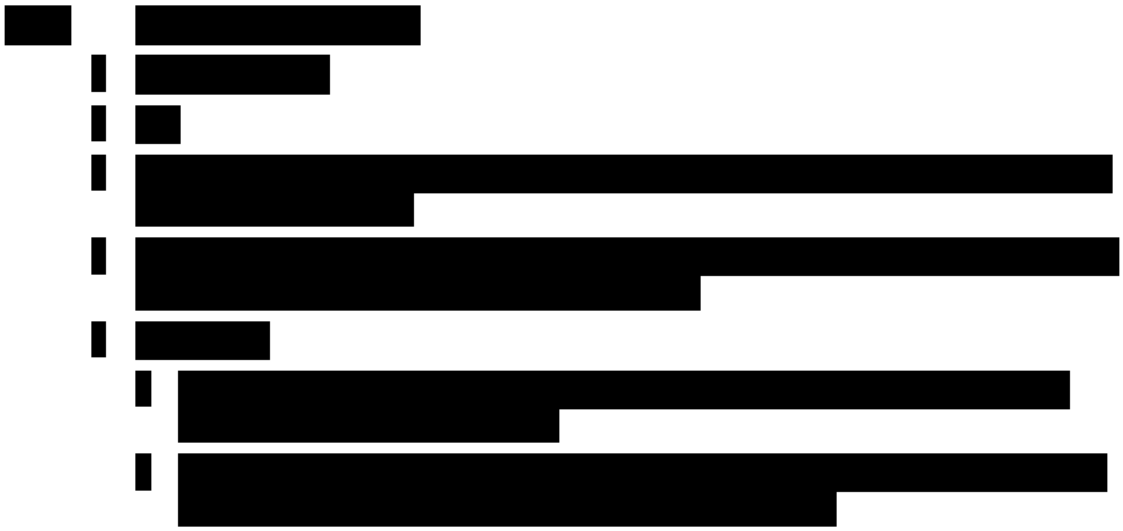
2.3. Study Endpoints

2.3.1. Primary Endpoints

- Safety and tolerability will be assessed by monitoring frequency, duration, and severity of AEs and DLTs; through physical examinations; by evaluating changes in vital signs and ECGs; and through clinical laboratory blood and urine sample evaluations.
- Part 4 only: ORR, defined as the proportion of subjects who achieve CR or CRi.

2.3.2. Secondary Endpoints

- PK of INCB053914, including C_{max}, T_{max}, C_{min}, AUC_{0-t}, Cl/F at timepoints specified in the Protocol, Section 6.
- PD profile of INCB053914 defined by pBAD.
- [redacted]



3. STUDY DESIGN

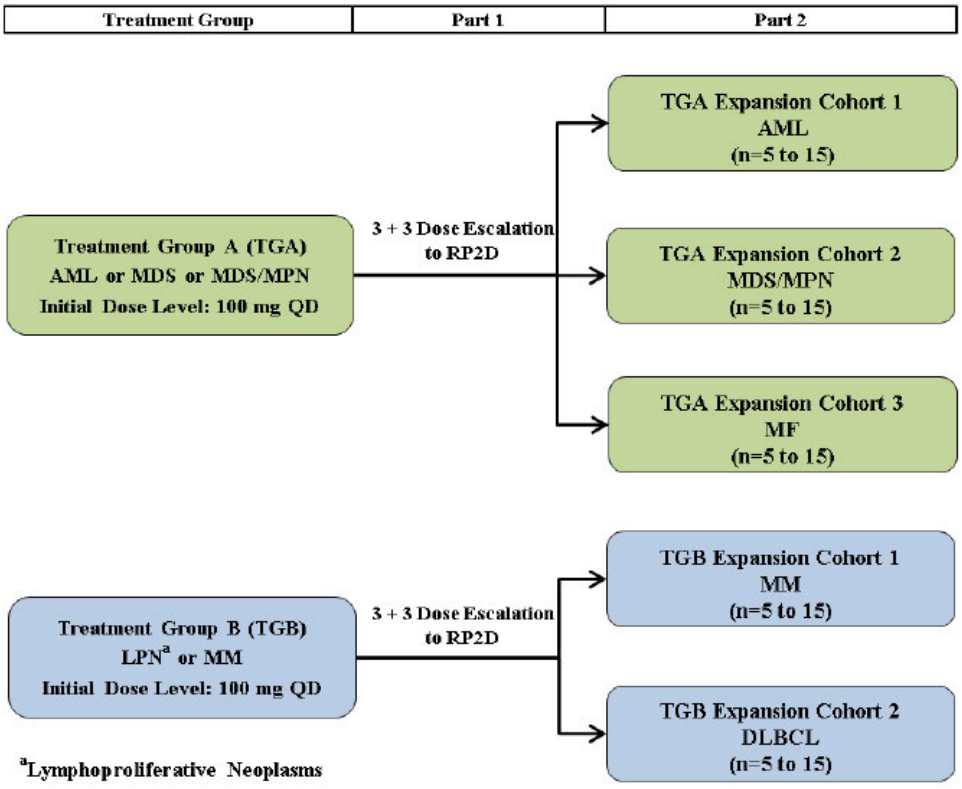
This is an open-label, dose-escalation study of the PIM kinase inhibitor INCB053914 as monotherapy and in combination with standard-of-care agents in subjects with advanced malignancies. Subjects will receive INCB053914 in 21- or 28-day cycles (as applicable to regimen schedules) until withdrawal criteria are met. Alternative administration schedules may be assessed if indicated by emerging safety, PK, or PD data. The study will be conducted in 4 parts: Parts 1 and 2 will evaluate INCB053914 as monotherapy (Figure 1) and Parts 3 and 4 will evaluate INCB053914 in combination with select standard-of-care agents (Figure 2).

Part 1 (monotherapy dose escalation) will be conducted in 2 disease-specific treatment groups (TGA and TGB, respectively) and will determine the MTD of INCB053914 and/or a tolerated PAD (defined as a plasma concentration exceeding average PK that is projected to inhibit pBAD level > 50% for approximately 12 hours) that will be taken forward into Part 2 of the study (ie, the RP2D). Treatment Group A will include acute leukemia, high-risk MDS, and MDS/MPNs (including aCML, CMML, MDS/MPN-U, and RARS-T). Treatment Group B will include MM, lymphoma, and other lymphoproliferative neoplasms. Dose escalation for TGA and TGB will proceed independently, with each treatment group following a 3 + 3 design. At least 3 subjects will be enrolled and treated in each cohort. If no DLTs are observed in the initial 3 subjects, the next cohort will begin enrollment at the next higher dose level. If 1 DLT is observed in the first 3 subjects, 3 additional subjects will be enrolled in that cohort. If a DLT occurs in one-third or more of the total cohort (ie, $\geq$ 2 of 6 subjects), then the MTD will be deemed to have been exceeded, and the next lower dose level will be deemed to be the MTD. Thus, the MTD will be defined as 1 dose level below that at which one-third or more of subjects in a particular cohort report DLTs. If the first cohort exceeds the MTD, a dose de-escalation will be considered.

Part 2 (monotherapy dose expansion) will further evaluate the safety, efficacy, PK, and PD of the RP2D in specific disease indications in which PIM kinases are particularly relevant, including leukemias and myeloproliferative and lymphoproliferative disorders, such as AML, MDS/MPN, MF, MM, and DLBCL. The 5 expansion cohorts are as follows:

- **TGA Expansion Cohort 1 (TGA A1):** At least 5 and up to approximately 15 subjects with AML will be enrolled and treated at the RP2D identified in Part 1 TGA.
- **TGA Expansion Cohort 2 (TGA A2):** At least 5 and up to approximately 15 subjects with MDS/MPN (including aCML, CMML, MDS/MPN-U, and RARS-T) will be enrolled and treated at the RP2D identified in Part 1 TGA.
- **TGA Expansion Cohort 3 (TGA A3):** At least 5 and up to approximately 15 subjects with MF will be enrolled and treated at the RP2D identified in Part 1 TGA.
- **TGB Expansion Cohort 1 (TGB B1):** At least 5 and up to approximately 15 subjects with MM will be enrolled and treated at the RP2D identified in Part 1 TGB.
- **TGB Expansion Cohort 2 (TGB B2):** At least 5 and up to approximately 15 subjects with DLBCL will be enrolled and treated at the RP2D identified in Part 1 TGB.

Figure 1: Monotherapy Study Design



Part 3 (combination dose-finding) will consist of up to 3 disease-specific combination treatment groups (C-TGA, C-TGB, and C-TGC) and will determine the MTD and/or a tolerated PAD of INCB053914 in combination with the selected standard-of-care agents. The combination dose-finding will use a 3 + 3 design to identify an optimal dose regimen in up to 3 different combination expansion cohorts. The possible combination expansion cohorts are as follows:

- **Combination Treatment Group A (C-TGA):** INCB053914 + cytarabine in subjects with relapsed/refractory AML.
- **Combination Treatment Group B (C-TGB):** INCB053914 + azacitidine in subjects with relapsed/refractory AML or elderly subjects (≥ 65 years) with newly diagnosed AML (*de novo* or secondary) who are unfit to receive intensive chemotherapy.
- **Combination Treatment Group C (C-TGC):** INCB053914 + ruxolitinib in subjects with primary or secondary MF (PPV-MF or PET-MF) who have had an inadequate response to ruxolitinib monotherapy, defined as follows:
  - Palpable spleen of > 10 cm below the left subcostal margin on physical examination at the screening visit OR
  - Palpable splenomegaly of 5 to 10 cm below left subcostal margin on physical examination and active symptoms of MF at the screening visit as demonstrated by presence of 1 symptom score ≥ 5 or 2 symptom scores ≥ 3 using the Screening Symptom Form (Appendix N).

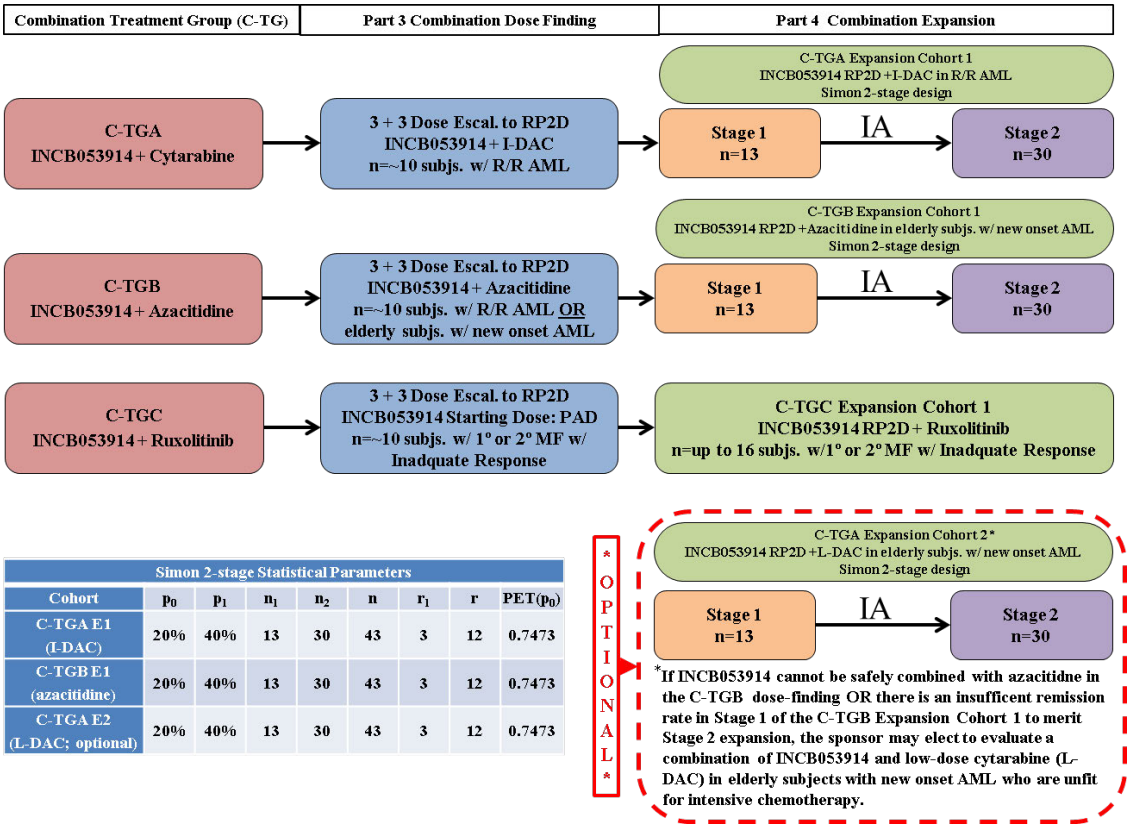
Between 3 and up to approximately 10 subjects will be enrolled into cohorts under each of the SOC treatment groups, C-TGA, C-TGB, and C-TGC, as described above. Dose-finding for C-TGA, C-TGB, and C-TGC will proceed independently, with each treatment group following a 3 + 3 cohort design. At least 3 subjects will be enrolled and treated at each dose level. If no DLTs are observed in the initial 3 subjects, the next cohort will begin enrollment at the next higher dose level of INCB053914. If 1 DLT is observed in the first 3 subjects, 3 additional subjects will be enrolled in that cohort. If a DLT occurs in one-third or more of the total cohort (ie, ≥ 2 of 6 subjects), then the MTD will be deemed to have been exceeded, and the next lower dose level will be deemed to be the MTD. Thus, the MTD will be defined as 1 INCB053914 dose level below that at which one-third or more of subjects in a particular cohort report DLTs. If the first cohort exceeds the MTD, a dose de-escalation of INCB053914 will be considered.

Part 4 (combination dose expansion) will further evaluate the safety, efficacy, PK, and PD of the selected combination dose regimens identified in Part 3 in up to 3 expansion cohorts in specific indications relevant to the drug combinations (2 AML; 1 MF). The 2 AML expansion cohorts will use a Simon 2-stage design to evaluate the efficacy of the combination regimens.

- **C-TGA Expansion Cohort 1 (C-TGA E1)** will enroll relapsed/refractory (r/r) AML subjects who will be treated with INCB053914 in combination with I-DAC using the regimen identified in Part 3. This cohort will use a Simon 2-stage design. If an insufficient number of responders is observed in the cohort at Stage 1, further enrollment in the cohort will be terminated.

- **C-TGB Expansion Cohort 1 (C-TGB E1)** will enroll subjects with newly diagnosed AML (*de novo* or secondary) who are ≥ 65 years at screening and unfit to receive intensive chemotherapy and who will be treated with INCB053914 in combination with azacitidine using the regimen identified in Part 3. This cohort will use a Simon 2-stage design. If an insufficient number of responders is observed in the cohort at Stage 1, further enrollment in the cohort will be terminated.
- **C-TGC Expansion Cohort 1 (C-TGC E1)** will enroll up to 16 subjects with PMF or secondary MF (PPV-MF or PET-MF) who have had an inadequate response to ruxolitinib monotherapy and who will be treated with INCB053914 in combination with ruxolitinib using the dose identified in Part 3.
- **Optional C-TGA Expansion Cohort 2 (C-TGA E2):** If the Part 3 C-TGB dose-finding does not yield a tolerable combination of INCB053914 and azacitidine, or if the Part 4 C-TGB E1 Simon Stage 1 does not yield favorable efficacy data, then the sponsor may elect to evaluate INCB053914 in combination with a L-DAC regimen in this population. This option will use an INCB053914 dose deemed tolerable in combination with I-DAC and will reference safety and tolerability data obtained from the Part 3 C-TGA dose-finding. If the sponsor and investigators believe that the optimal dose regimen of INCB053914 in combination with L-DAC will be different from that of INCB053914 in combination I-DAC, a separate dose-finding cohort will be initiated to identify the optimal dose regimen of INCB053914 in combination with L-DAC.

Figure 2: Combination Therapy Study Design



Simon 2-stage Statistical Parameters								
Cohort	p_0	p_1	n_1	n_2	n	r_1	r	PET(p_0)
C-TGA E1 (I-DAC)	20%	40%	13	30	43	3	12	0.7473
C-TGB E1 (azacitidine)	20%	40%	13	30	43	3	12	0.7473
C-TGA E2 (L-DAC; optional)	20%	40%	13	30	43	3	12	0.7473

3.1. Control of Type I Error

For the primary efficacy endpoint in Part 4, the 1-sided Type I error will be controlled at 0.05 for each individual cohort expansion. Note that this level of significance does not account for the multiple expansion cohorts. For other endpoints, CIs will be reported at a 95% confidence level.

3.2. Sample Size Considerations

3.2.1. Sample Size in Part 1

In Part 1, a 3 + 3 dose escalation design will be used in 2 disease-specific treatment groups. Dose escalation for the 2 treatment groups will proceed independently. A minimum of 3 and up to 6 evaluable subjects will be enrolled at each dose level. The total sample size in Part 1 will depend on the frequency of DLTs and the number of dose levels tested before the MTD or PAD is reached.

3.2.2. Sample Size in Part 2

In Part 2, up to 5 expansion cohorts will consist of at least 5 and up to approximately 15 subjects each treated at the RP2D identified in the corresponding Part 1 treatment group. With 5 subjects

enrolled, there is an 83% probability of observing at least 1 responder if the true underlying response rate is 30%.

3.2.3. Sample Size in Part 3

In Part 3, a 3 + 3 design will be used in up to 3 disease-specific treatment groups to identify an optimal dose regimen. Dose escalation for 3 treatment groups will proceed independently. A minimum of 3 and up to 6 subjects will be enrolled in each dose cohort. The total number of subjects will depend on the frequency of DLTs and the number of dose levels tested before the MTD or PAD is reached.

3.2.4. Sample Size in Part 4

In Part 4, up to 4 expansion cohorts will be included to further evaluate the safety, tolerability, efficacy, PK, and PD of RP2Ds selected from Part 3.

3.2.4.1. Sample Size in C-TGA and C-TGB

A Simon 2-stage design (Simon 1989; see Table 1) will be used for combination expansion cohorts C-TGA E1, C-TGB E1, and the optional C-TGA E2. The response rates for the historical control (p_0), desired response rates for the combination (p_1), number of subjects needed in Stage 1 (n_1) and Stage 2 (n_2), total number of subjects in both stages (n), first stage threshold to declare cohort undesirable (r_1), upper limit of the number of responses in n patients such that futility of the drug is concluded (r), and PET under p_0 (PET[p_0]) are provided for each of these expansion cohorts. The calculation is based on a 1-sided Type I error of 0.05 and power of 80%.

Table 1: Simon 2-Stage Design

Cohort	p_0	p_1	n_1	n_2	n	r_1	r	PET[p_0]
C-TGA E1	20%	40%	13	30	43	3	12	0.7473
C-TGB E1	20%	40%	13	30	43	3	12	0.7473
C-TGA E2 (optional)	20%	40%	13	30	43	3	12	0.7473

3.2.4.2. Sample Size in C-TGC

Up to 16 subjects will be enrolled in the C-TGC E1 cohort. The sign test will be used to evaluate change and percentage change from baseline in spleen volume by MRI or CT in applicable subjects with a 1-sided Type I error of 0.05. Assuming the percentage reduction is normally distributed with a mean of 15 and standard deviation of 14.5, the test has 92.2% power to indicate whether additional development is warranted.

3.3. Schedule of Assessments

See Protocol Amendment 6 dated 15 MAR 2017 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

For monotherapy, Day 1 is the date that the first dose of INCB053914 is administered to the subjects.

For combination therapy, Day 1 is the date that the first dose of any of the study drugs (INCB053914, cytarabine, azacitidine, or ruxolitinib) is administered to the subjects.

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

For monotherapy, baseline is the last nonmissing measurement obtained before the first administration of INCB053914.

For combination therapy, baseline is the last nonmissing measurement obtained before the first administration of INCB053914, cytarabine, azacitidine, or ruxolitinib.

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 Data

In general, values for missing data will not be imputed unless methods for handling missing data are specified in this section or relevant sections.

Missing or partial disease/cancer diagnosis date will be handled as follows:

- If only the day is missing, then the imputed day will be the first of the month.
- If both the month and day are missing, then the imputed day and month will be 01 JAN.
- No imputation will be done if the date is completely missing.

Missing or partial date of last dose will be handled as follows:

- If only the day is missing, then the imputed date of the last dose will be the earlier date of the first day of the month or the date that the subject discontinued treatment.
- Otherwise, the date that the subject discontinued treatment will be used as the date of the last dose.

For relevant efficacy endpoints, partial death date will be imputed as follows:

- If mmyyyy for the last contact date = mmyyyy for the death date, then the death date will be set to the day after the last contact date.
- If mmyyyy for the last contact date < mmyyyy for the death date, then the death date will be set to the first day of the death month.
- Otherwise, the partial death date will not be imputed.

For prior and concomitant medications:

The start/stop dates recorded in the eCRF by the investigator and his or her research staff will be used to identify when a concomitant medication was taken during the study. Any missing start date must be queried for resolution. Unresolved missing start dates will be handled as follows:

- If the date is completely missing, the medication will be considered both prior and concomitant.
- If only the day is missing, and the last day of the month is before the first dose date on Day 1, then the concomitant medication will be considered as starting before Day 1, and the incomplete date will be imputed as the last day of the month.
- If only the day is missing, and the first day of the month is after the first dose date on Day 1, then the concomitant medication will be considered as starting after Day 1, and the incomplete date will be imputed as the first day of the month.
- If only the day is missing, and the month is equal to the month of the first dose date on Day 1, then the incomplete date will be imputed as the first day of the month.
- If both the month and day are missing, and the last day of the year is before the first dose date on Day 1, then the concomitant medication will be considered as starting before Day 1, and the incomplete date will be imputed as the last day of the year. Otherwise, the incomplete date will be imputed as the first day of the year.

4.1.5. Cycle Length and Duration

Cycle 1 Day 1 is the day that the first dose of study drug is administered. For monotherapy, the scheduled cycle length is 21 days for Parts 1 and 2 (all treatment groups/cohorts). For combination therapy, the scheduled cycle length is 21 days for the Part 3 C-TGA, Part 3 C-TGC, Part 4 C-TGA E1, and Part 4 C-TGC E1 cohorts and 28 days for the Part 3 C-TGB, Part 4 C-TGA E2, and Part 4 C-TGB E1 cohorts.

Actual Day 1 of subsequent cycles will correspond with the first day of administration of INCB059314 or standard-of-care agent in that cycle; thus, treatment cycles may become out of sync with the originally planned schedule, and cycle length may be different from 21 or 28 days. The date of the Day 1 of subsequent cycles recorded in the eCRF will be used as the Day 1 of subsequent cycles.

In the Part 3 C-TGA and Part 4 C-TGA E1 (cytarabine) cohorts, cytarabine treatment will be administered in 3 possible periods anchored to the 21-day INCB053914 cycles.

- **First Induction Cycle:** Subjects will initially receive a 21-day induction cycle.
- **Second Induction Cycle (optional):** At the discretion of the investigator, a second induction cycle may be started between 15 days and 8 weeks after initiation of Cycle 1 in subjects with residual leukemia upon bone marrow assessment during initial induction. Treatment in the second induction cycle may not initiate until all drug-related toxic effects have resolved to ≤ Grade 1.
- **Consolidation Phase:** At the discretion of the investigator, up to 2 additional cycles may be given as consolidation therapy in subjects who achieve complete remission or CRp recovery.

The start of subsequent induction or consolidation cycles of I-DAC should be coordinated with the Day 1 of a 21-day INCB053914 cycle when feasible.

4.2. Variable Definitions

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

4.2.1. Age

Subject age will be calculated as the integer part of the number of years from date of birth to the date of signing the informed consent form, using the following formula:

Age = integer part of (date of informed consent – date of birth + 1) / 365.25

4.2.2. Body Surface Area

Body surface area will be calculated based on the Mosteller (1987) formula as follows:

$$BSA\ (m^2) = \{[weight\ (kg) \times height\ (cm)] / 3600\}^{1/2}$$

Sites will also record the BSA calculated per institutional standards.

4.2.3. Prior and Concomitant Medication

Prior medication is defined as any nonstudy medication started before the first dose of INCB053914, cytarabine, azacitidine, or ruxolitinib.

Concomitant medication is defined as any nonstudy medication that is started accordingly:

- Before the date of first administration of INCB053914, cytarabine, azacitidine, or ruxolitinib and is ongoing throughout the study or ends on/after the date of first study drug administration.
- On/after the date of first administration of INCB053914, cytarabine, azacitidine, or ruxolitinib and is ongoing or ends during the course of study drug administration.

A nonstudy medication can also be classified as "both prior and concomitant" if the start date is before and the end date is on or after first dose of INCB053914, cytarabine, azacitidine, or ruxolitinib. The listing will indicate whether a medication is prior-only, concomitant-only, or both prior and concomitant.

For the purposes of analysis, all nonstudy 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; Version 9.4 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 subjects in each category.

Interim analyses are planned for this study as defined in Section 11.

5.2. Treatment Groups

This is an open-label, dose-escalation study of the PIM kinase inhibitor INCB053914 as monotherapy and in combination with standard-of-care agents in subjects with advanced malignancies. The study will be conducted in 4 parts: Parts 1 and 2 will evaluate INCB053914 as monotherapy and Parts 3 and 4 will evaluate INCB053914 in combination with select standard-of-care agents.

In Part 1, subjects will be enrolled in 1 of 2 treatment groups. The initial dose level in each treatment group will be 100 mg QD, with dose increases up to 2-fold until a Grade 2 toxicity that has a reasonable possibility of being related to INCB053914 is observed in that treatment group or until a total daily dose of 300 mg has been reached in that treatment group, after which dose increases will be limited to ≤ 50%. Alternate administration, such as intermediate doses, alternate dose regimens, or alternate formulations, may also be implemented depending on emerging PK, PD, and safety results.

In Part 2, subjects will be enrolled in up to 5 expansion cohorts (TGA A1, TGA A2, TGA A3, TGB B1, and TGB B2), as defined in Section 3, at the RP2Ds identified in Part 1.

Part 3 will comprise up to 3 disease-specific treatment groups: C-TGA, C-TGB, and C-TGC, as defined in Section 3. The starting dose of INCB053914 in the combination treatment groups will be a PAD and a dose level below the highest tolerated dose of INCB053914 monotherapy identified in Part 1 of this study. As of the most recent data cutoff date (at the time of Amendment 6), the highest tolerated dose of INCB053914 monotherapy was 80 mg BID, which also met the Protocol-defined criteria for a PAD; thus the starting dose for Part 3 will be 65 mg BID (Dose Level 1 dose). The INCB053914 dose used in Part 3 will never exceed the monotherapy MTD dose to be identified in Part 1 of the study.

Table 2, Table 3, and Table 4 summarize the dose regimens to be used in the standard-of-care combination dose-finding cohorts. An alternative starting dose and/or subsequent INCB053914 doses may be selected pending emerging Part 1 safety, PK, and PD data.

Table 2: Planned C-TGA Combination Dose-Finding Cohorts

Dose Level	I-DAC Dose	INCB053914 Dose[a]	Treatment Group
-1	1 g/m^2; given as 2-hour infusion on Days 1-5[b]	50 mg BID	C-TGA 50 mg BID
1 (starting dose)	1 g/m^2; given as 2-hour infusion on Days 1-5	65 mg BID	C-TGA 65 mg BID
2	1 g/m^2; given as 2-hour infusion on Days 1-5	80 mg BID	C-TGA 80 mg BID
3	1 g/m^2; given as 2-hour infusion on Days 1-5	100 mg BID	C-TGA 100 mg BID

BID = twice daily; I-DAC = intermediate-dose cytarabine; PD = pharmacodynamic; PK = pharmacokinetic.
[a] INCB053914 starting dose and subsequent cohort doses may change based on emerging Part 1 safety, PK, and PD data.
[b] I-DAC is given on Days 1-5 of all treatment cycles where cytarabine is given.

Table 3: Planned C-TGB Combination Dose-Finding Cohorts

Dose Level	Azacitidine Dose	INCB053914 Dose[a]	Treatment Group
-1	75 mg/m^2 SC or IV; given on Days 1-5 and 8-9 of a 28-day cycle	50 mg BID	C-TGB 50 mg BID
1 (starting dose)	75 mg/m^2 SC or IV; given on Days 1-5 and 8-9 of a 28-day cycle	65 mg BID	C-TGB 65 mg BID
2	75 mg/m^2 SC or IV; given on Days 1-5 and 8-9 of a 28-day cycle	80 mg BID	C-TGB 80 mg BID
3	75 mg/m^2 SC or IV; given on Days 1-5 and 8-9 of a 28-day cycle	100 mg BID	C-TGB 100 mg BID

BID = twice daily; IV = intravenous; PD = pharmacodynamic; PK = pharmacokinetic; SC = subcutaneous.
[a] INCB053914 starting dose and subsequent cohort doses may change based on emerging Part 1 safety, PK, and PD data.

Table 4: Planned C-TGC Dose-Finding Cohorts

Dose Level	Ruxolitinib Dose	INCB053914 Dose[a]	Treatment Group
-1	Subject's current stable dose (between 5 mg BID and 25 mg BID)	50 mg BID	C-TGC 50 mg BID
1 (starting dose)	Subject's current stable dose (between 5 mg BID and 25 mg BID)	65 mg BID	C-TGC 65 mg BID
2	Subject's current stable dose (between 5 mg BID and 25 mg BID)	80 mg BID	C-TGC 80 mg BID
3	Subject's current stable dose (between 5 mg BID and 25 mg BID)	100 mg BID	C-TGC 100 mg BID

BID = twice daily; PD = pharmacodynamic; PK = pharmacokinetic.
[a] INCB053914 starting dose and subsequent cohort doses may change based on emerging Part 1 safety, PK, and PD data.

Part 4 will enroll up to 4 expansion cohorts: C-TGA E1, C-TGB E1, C-TGC E1, and C-TGA E2 (optional) as defined in Section 3.

Data will be summarized by treatment group by dose level in Parts 1 and 3 and by treatment group in Parts 2 and 4. In the event that several dose regimens tested are deemed substantially below the MTD, these doses may be combined for summary purposes.

5.3. Analysis Populations

5.3.1. Full Analysis Set

The FAS includes all subjects enrolled in the study who received at least 1 dose of any drug involved in the study and have at least 1 postbaseline assessment or who discontinued treatment. All efficacy analyses will be based on the FAS. Parts 2 and 4 demographics, baseline characteristics, and subject disposition data will be based on the FAS.

Specific analysis populations to be used for tumor type or drug-specific tables include the following subgroups.

- Part 2 AML FAS population
- Part 2 MDS/MPN FAS population
- Part 2 MF FAS population
- Part 2 MM FAS population
- Part 2 DLBCL FAS population
- Part 3 cytarabine FAS population
- Part 3 azacitidine FAS population
- Part 3 ruxolitinib FAS population
- Part 4 AML FAS population
- Part 4 MF FAS population

5.3.2. Per Protocol Population

Subjects in the FAS population who are considered to be sufficiently compliant with the Protocol comprise the PP population.

The following procedures will be performed to identify those subjects who are to be excluded from the PP population before the database finalization:

- Clinical review of Protocol deviations/violations
- Clinical review of concomitant medications (prohibited medications) as defined in Section 5.2.8 of the Protocol
- Clinical review of the dose administration and drug accountability listing

5.3.3. Safety Population

The safety population includes all subjects enrolled in the study who received at least 1 dose of any drug involved in the study. All safety analyses, Parts 1 and 3 demographics, baseline characteristics, and subject disposition data will be based on the safety population.

Specific analysis populations to be used for tumor type or drug-specific tables include the following subgroups.

- Part 1 AML safety population
- Part 1 other leukemia safety population
- Part 1 MDS safety population
- Part 1 MDS/MPN safety population
- Part 1 MM safety population
- Part 1 lymphoma safety population
- Part 2 AML safety population
- Part 2 MDS/MPN safety population
- Part 2 MF safety population
- Part 2 MM safety population
- Part 2 DLBCL safety population
- Part 3 cytarabine safety population
- Part 3 azacitidine safety population
- Part 3 ruxolitinib safety population
- Part 4 AML safety population
- Part 4 MF safety population

5.3.4. PK/PD Evaluable Population

The PK evaluable population includes those in the safety population who have at least 1 valid PK measurement. The study pharmacokineticist will review data listings of study drug administration and sample records to identify subjects to be excluded from analyses of PK data.

The PD evaluable population includes those in the safety population who have at least 1 valid PD measurements at both pre- and postdose. The study research investigator will review data listings of PD data and sample records to identify subjects to be excluded from analyses of PD data.

6. BASELINE, EXPOSURE, AND DISPOSITION VARIABLES AND ANALYSES

Appendix A provides a list of data displays.

6.1. Baseline and Demographics, Physical Characteristics, and Disease History

6.1.1. Demographics

Age, race, sex, and ethnicity will be summarized by treatment group and dose level for the safety population in Parts 1 and 3 and by treatment group for the FAS population in Parts 2 and 4.

6.1.2. Baseline Disease Characteristics and Disease History

For each tumor type, primary tumor histology, date of initial diagnosis, stage at initial diagnosis, current stage of disease, current site of disease, and tumor markers will be summarized for all subjects in the safety population by treatment group by dose level in Parts 1 and 3 and for all subjects in the FAS population by treatment group in Parts 2 and 4.

ECOG performance status will be summarized for all subjects in the safety population by treatment group and dose level in Parts 1 and 3 and for all subjects in the FAS by treatment group in Parts 2 and 4.

6.1.3. Other Baseline Characteristics

Height and weight will be summarized by treatment group and dose level for the safety population in Parts 1 and 3 and by treatment group for the FAS population in Parts 2 and 4.

6.1.4. Prior Disease Therapy

The number of prior systemic cancer therapy regimens will be summarized for the safety population by treatment group and dose level in Parts 1 and 3 and for the FAS population by treatment group in Parts 2 and 4. Regimen name, best response, reason for discontinuation, and date of relapse/progression will be listed.

The number of subjects who received prior radiation will be summarized for the safety population by treatment group and dose level in Parts 1 and 3 and for the FAS population by treatment group in Parts 2 and 4. Radiotherapy type, body site, start and stop date, reason for regimen, best response, number of fractions received, and total dose will be listed.

The number of subjects who had prior surgery or surgical procedure for the malignancies under study will be summarized for the safety population by treatment group and dose level in Parts 1 and 3 and for the FAS population by treatment group in Parts 2 and 4. Date and description of the surgery/procedure will be listed.

The number of subjects who had a hematopoietic stem cell transplant will be summarized for the safety population by treatment group and dose level in Parts 1 and 3 and for the FAS population by treatment group in Parts 2 and 4. Date of transplant, type of transplant, source of cells, line of therapy, best response, and conditioning regimen name will be listed.

6.1.5. General Medical History

Medical history will be summarized for subjects in the Parts 1 and 3 safety population by treatment group and dose level and for subjects in Parts 2 and 4 FAS population by treatment group. This summation will include the number and percentage of subjects with significant medical history for each body system/organ class as documented on the eCRF.

6.2. Disposition of Subjects

The number and percentage of subjects who were enrolled, were treated, discontinued study treatment with a primary reason for discontinuation, and withdrew from the study with a primary reason for withdrawal will be summarized for the subjects in Parts 1 and 3 safety population by treatment group and dose level and for the subjects in Parts 2 and 4 FAS population by treatment group. The number of subjects enrolled by site will also be provided by treatment group for Parts 1 and 3 and by treatment group for Parts 2 and 4.

6.3. Protocol Deviations and Violations

Protocol deviations and violations recorded on the eCRF will be presented in the subject data listings.

6.4. Exposure

For subjects in the safety population, exposure to INCB053914, cytarabine, azacitidine, or ruxolitinib will be summarized descriptively as follows.

6.4.1. Exposure for INCB053914

- **Duration of treatment (days):** Date of last dose of INCB053914 – date of first dose of INCB053914 + 1.
- **Total dose administered (mg):** Sum of INCB053914 doses administered (mg) across cycles.
- **Average Daily Dose (mg/day):** Total dose administered (mg) / duration of treatment (days).

6.4.2. Exposure for Cytarabine

6.4.2.1. Exposure for Intermediate-Dose Cytarabine

- **Total number of infusions:** Total number of infusions per subject with a nonzero dose of I-DAC.
- **Dose administered per cycle (g/m^2):** The actual dose administered (g/m^2) per cycle.

- **Total dose administered (g/m^2):** Sum of the BSA-adjusted cumulative dose of I-DAC that has been administered to the subject.

  For an infusion i, let C_i be the concentration (g/mL) of I-DAC and V_i be the total volume administered (in mL) reported on the I-DAC dosing eCRF; let B be the subject's baseline BSA (m^2) and N be the total number of infusions

  $$\text{Total dose administered (g/m}^2\text{)} = \sum_{i=1}^{N} \frac{C_i \times V_i}{B}$$

- **Average dose (g/m^2):** Total dose administered (g/m^2) divided by the total number of infusions.

6.4.2.2. Exposure for Low-Dose Cytarabine

- **Total number of administrations:** Total number of injections per subject with a nonzero dose of L-DAC.
- **Dose administered per cycle (mg):** Actual dose administered (mg) per cycle.
- **Total dose administered (mg):** Sum of L-DAC doses administered (mg) across cycles.
- **Average dose (mg):** Total dose administered (mg) divided by the total number of injections.

6.4.3. Exposure for Azacitidine

- **Total number of administrations:** Total number of infusions and injections per subject with a nonzero dose of azacitidine.
- **Dose administered per cycle (mg/m^2):** Actual dose administered (mg/m^2) per cycle.
- **Total dose administered (mg/m^2):** Sum of the BSA-adjusted cumulative dose of azacitidine that has been administered to the subject.

  For an infusion/injection i, let C_i be the concentration (mg/mL) of azacitidine and V_i be the total volume administered (mL) reported on the azacitidine dosing eCRF if the ith administration is through IV; let M_i be the actual dose administered (mg) if the ith administration is through SC. Let

  $$I_{IV,i} = \begin{cases} 1, & \text{administered throught IV} \\ 0, & \text{administered throught SC} \end{cases}$$

  $$I_{SC,i} = \begin{cases} 1, & \text{administered throught SC} \\ 0, & \text{administered throught IV} \end{cases}$$

  Suppose B is the subject's baseline BSA (m^2) and N is the total number of infusions and injections:

  $$\text{Total dose administered (mg/m}^2\text{)} = \sum_{i=1}^{N} (C_i \times V_i \times I_{IV,i} + M_i \times I_{SC,i})/B.$$

- **Average dose (mg/m^2):** Total dose administered (mg/m^2) divided by the total number of injections and infusions.

6.4.4. Exposure for Ruxolitinib

- **Duration of treatment (days):** Date of last dose of ruxolitinib – date of first dose of ruxolitinib + 1.
- **Total dose administered (mg):** Sum of ruxolitinib administered (mg) across cycles.
- **Average Daily Dose (mg/day):** Total dose administered (mg) divided by the duration of treatment in days.

6.5. Study Drug Compliance

For subjects in the safety population, overall compliance (%) for INCB053914 will be calculated for all subjects as

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

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

The total actual dose taken will be calculated based on information entered on the drug accountability eCRF. If there is dispensed drug that has not been returned at the time of the analysis, the dispensed drug will not be counted in the compliance.

Compliance data for ruxolitinib will not be collected, and compliance calculations are not required for IV or SC administered agents.

6.6. Prior and Concomitant Medication

For subjects in the safety population, prior medications and concomitant medications will be coded using the WHO Drug Dictionary and summarized by WHO drug class and WHO drug term. Results will be summarized as number and percentage of subjects with prior and concomitant medications by PT and WHO drug class, for each treatment group and dose level in Parts 1 and 3 and for each treatment group in Parts 2 and 4.

7. EFFICACY

Appendix A provides a list of data displays.

7.1. General Considerations

Efficacy endpoints of this study include ORR, by investigator assessment using the disease specific response criteria in Section 7.3. Listings of response assessment at each visit will be provided.

7.2. Efficacy Hypotheses

In Part 4, the Simon 2-stage design will be applied to C-TGA E1, C-TGB E1, and an optional C-TGA E2 independently in testing the null hypothesis that the true ORR is less than or equal to the clinically insignificant response rates of 20% against the alternative hypothesis that the true ORR is equal to the target ORR of 40%.

7.3. Response Criteria

The following disease response criteria will be used for each of the malignancies included in this study:

- AML: IWG Response Criteria for AML (Cheson et al 2003; Appendix B)

[redacted]

7.4. Analysis of the Efficacy Parameters

7.4.1. Acute Myeloid Leukemia

7.4.1.1. Response Assessment

Disease assessment for AML subjects will be performed following the International Working Group Response Criteria for Acute Myeloid Leukemia (Cheson et al 2003). The investigator's assessment will be used to determine responses and will be logged into the eCRF.

Response status per investigator's assessment for AML will be recorded in terms of 3 aspects: 1) altering the natural history of the disease, 2) cytogenetic response, and 3) molecular response. For altering the natural history of the disease, response status will be recorded at each response assessment as CR, CRi, MLFS, PR, peripheral blood blast response, SD, treatment failure, relapse, or progressive disease. For cytogenetic response, response status will be recorded at each response assessment visit as CCyR, PCyR, no response, NA, or not applicable. For molecular response, response status will be recorded at each response assessment visit as CMR, PMR, no response, NA, or not applicable.

7.4.1.2. Best Overall Response and Objective Remission Rate

7.4.1.2.1. Altering the Natural History of the Disease

For AML, BOR based on altering the natural history of the disease is the best response recorded before and including the first event which consists of treatment failure, relapse, or progressive disease, in the order of CR, CRi, MLFS, PR, peripheral blood blast response, SD, and event. A subject is considered a responder if they have a BOR of CR, CRi, MLFS, PR, or peripheral blood blast response.

The ORR for AML is defined as the proportion of responders based on altering the natural history of the disease. Subjects who do not have sufficient baseline information will be included in the denominators in the calculations of ORR.

Best overall response will be summarized descriptively. The ORR will be estimated with 95% CIs. Confidence intervals will be calculated based on the exact method for binomial distributions.

7.4.1.2.2. Cytogenetic Response

Cytogenetic response is applicable for subjects with abnormal karyotype at baseline. Best overall response for cytogenetic response is the best response recorded before and including the time when the first event of treatment failure, relapse, or progressive disease based on altering the natural history of the disease occurs, in the order of CCyR, PCyR, no response, and NA.

BOR for cytogenetic response will be summarized descriptively. Subjects with abnormal karyotype at baseline will be included in the denominators in the summary of BOR.

7.4.1.2.3. Molecular Response

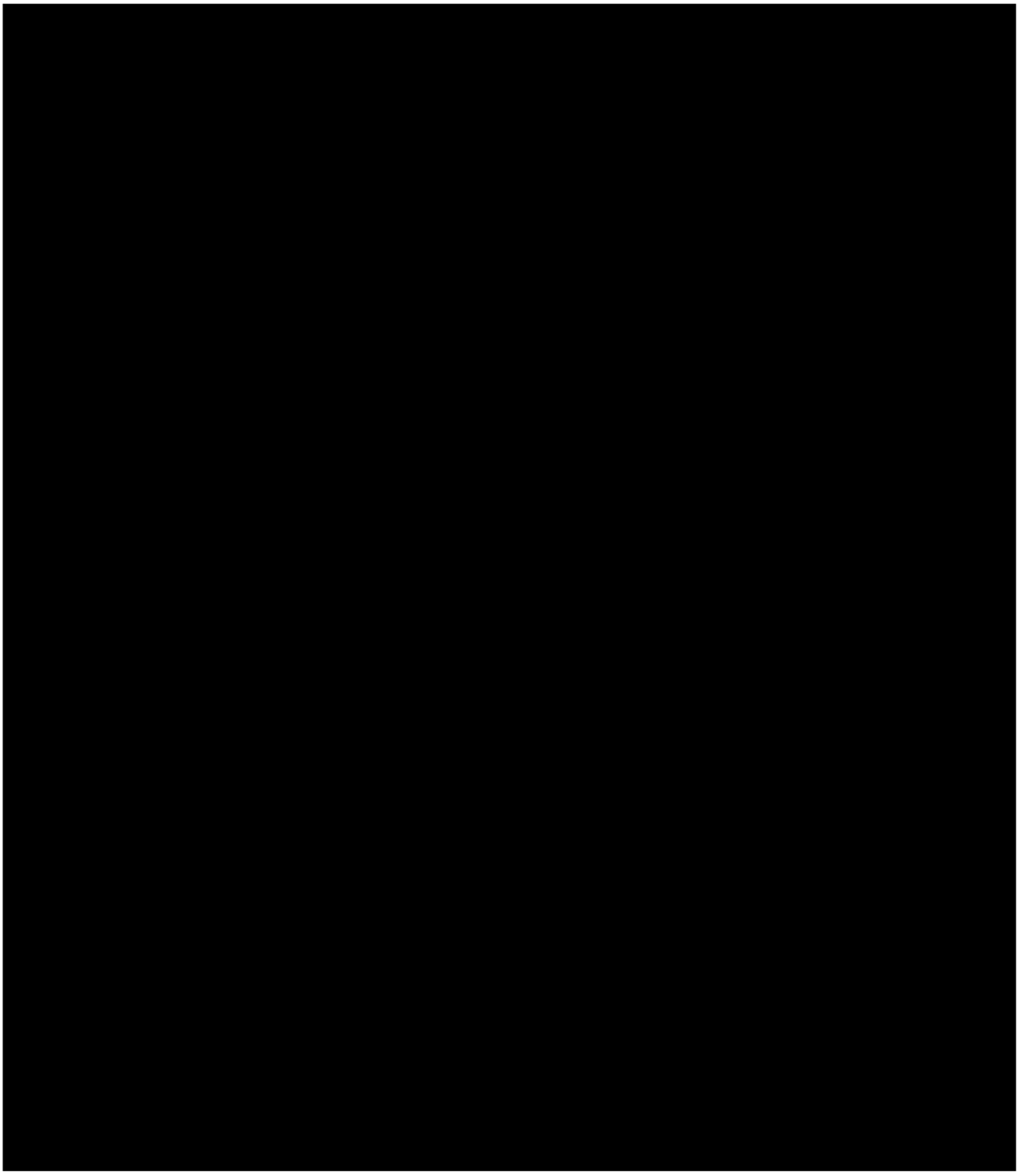
Molecular response is applicable for subjects with molecular abnormality at baseline. Best overall response for molecular response is the best response recorded before and including the time when the first event of treatment failure, relapse, or progressive disease based on altering the natural history of the disease occurs, in the order of CMR, PMR, no response, and NA.

Best overall response for molecular response will be summarized descriptively. Subjects with molecular abnormality at baseline will be included in the denominators in the summary of BOR.

[redacted]

[redacted]

[redacted]



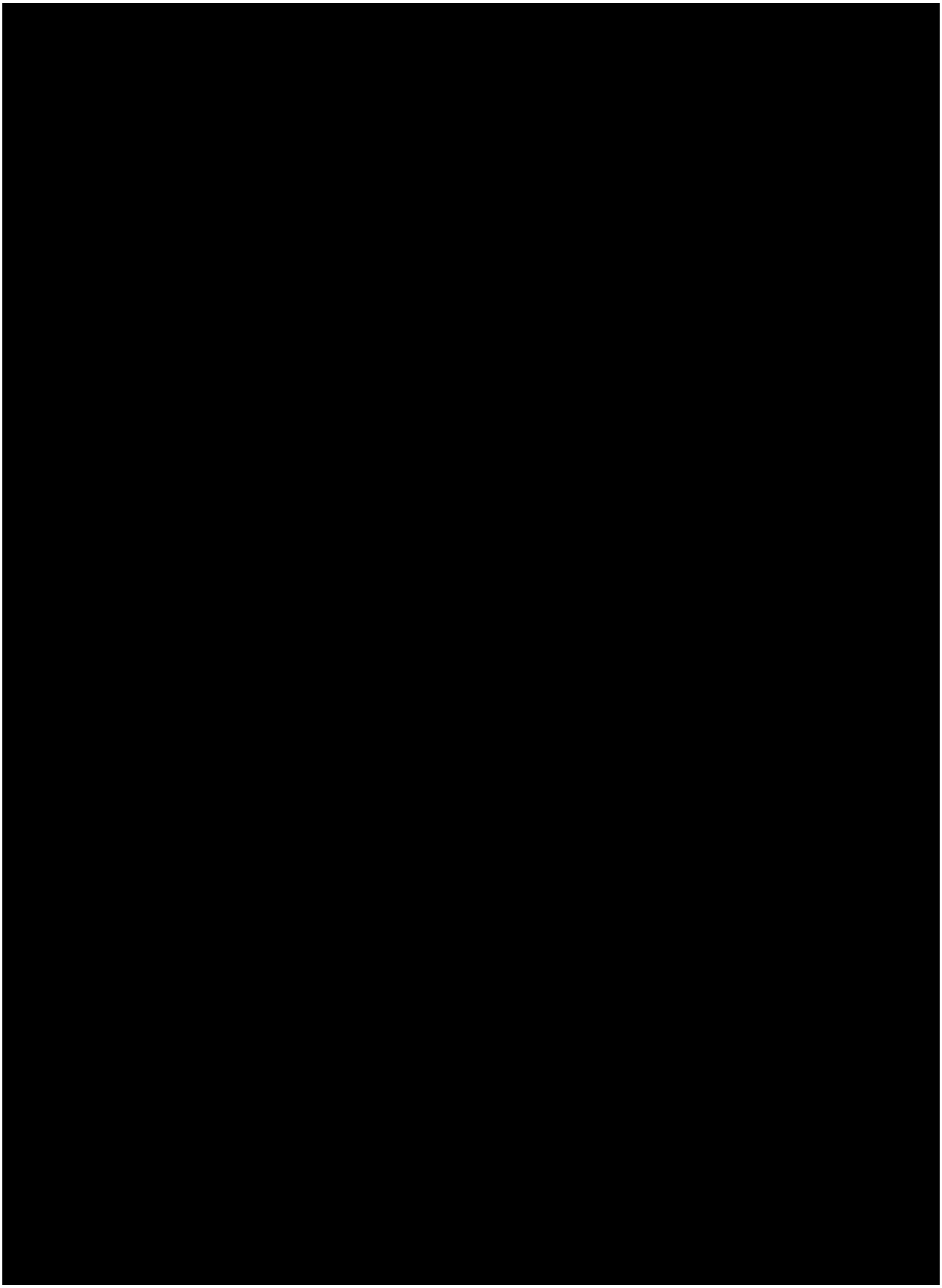
[redacted]

7.4.5. Myelofibrosis

[redacted]

[redacted]

[redacted]



8. PHARMACOKINETIC ANALYSES

The following PK parameters will be calculated from the blood plasma concentrations of INCB053914 using standard noncompartmental (model-independent) PK methods: C_{max}, t_{max}, C_{min}, AUC_{0-t}, and Cl/F. Pharmacokinetic calculations will be performed, if appropriate, using commercial software such as WinNonlin® (Pharsight Corporation, Mountain View, CA). Nominal times will be used in all cases, except when the difference between the actual time and nominal time is greater than 15 minutes for samples collected up to 4 hours after administration and greater than 30 minutes for samples collected more than 4 hours after administration; in these cases, actual time will be used for PK analysis.

If there is a sufficient amount of plasma concentration data from this study, the data will be analyzed by standard population PK methods using appropriate software (eg, NONMEM).

9. PHARMACODYNAMIC ANALYSES

Biomarker assessments in this study include the analysis of INCB053914 defined by pBAD promoter protein; [redacted]

Pharmacodynamics parameters will be summarized descriptively.

10. SAFETY AND TOLERABILITY

Appendix A provides a list of data displays.

10.1. General Considerations

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 PTs reported on relatively few subjects.

All AEs reported on the eCRF will be included in the summaries unless otherwise required by the study.

10.2. Adverse Events

10.2.1. Adverse Event Definitions

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

Adverse events will be tabulated by MedDRA PT and SOC. Severity of AEs will be graded using the NCI CTCAE. The CTCAE version 4.03 is used for this study. The CTCAE reporting guidelines and grading details are available on the CTEP 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, SAEs will also be tabulated.

Any missing onset date, causality, or severity must be queried for resolution. Unresolved missing causality and severity will be handled according to the following rules:

- An unresolved missing causality will be considered treatment-related.
- An unresolved missing severity will be identified as an unknown severity.

For purposes of analysis, all AEs will be considered TEAEs unless the AE can unequivocally be defined as not treatment emergent.

10.2.2. Dose-Limiting Toxicities

The number of subjects with DLTs and the type of DLT will be listed by dose level.

10.2.3. Maximum Tolerated Dose

In Part 1 and Part 3 of the study, the MTD will be defined as 1 dose level below that at which one-third of subjects or more in a particular cohort have DLTs.

10.2.4. Adverse Events of Special Interest

Adverse events of special interest include treatment-emergent ALT, AST, ALP, and bilirubin elevations and treatment-emergent AEs related to liver toxicities.

Number (%) of subjects reporting any treatment-emergent ALT, AST, ALP, and bilirubin will be summarized by grade. Any AEs related to liver toxicity will be identified using standard MedDRA queries.

10.2.5. Adverse Event Summaries

An overall summary of AEs by treatment group will include the following:

- Number (%) of subjects reporting any TEAEs
- Number (%) of subjects reporting any DLTs
- Number (%) of subjects reporting any SAEs
- Number (%) of subjects reporting any Grade 3 or 4 TEAEs
- Number (%) of subjects reporting any TEAEs related to INCB053914
- Number (%) of subjects reporting any TEAEs related to cytarabine
- Number (%) of subjects reporting any TEAEs related to azacitidine
- Number (%) of subjects reporting any TEAEs related to ruxolitinib
- Number (%) of subjects who temporarily interrupted INCB053914 because of TEAEs
- Number (%) of subjects who temporarily interrupted cytarabine because of TEAEs
- Number (%) of subjects who temporarily interrupted azacitidine because of TEAEs
- Number (%) of subjects who temporarily interrupted ruxolitinib because of TEAEs
- Number (%) of subjects who permanently discontinued INCB053914 because of TEAEs
- Number (%) of subjects who permanently discontinued cytarabine because of TEAEs
- Number (%) of subjects who permanently discontinued azacitidine because of TEAEs
- Number (%) of subjects who permanently discontinued ruxolitinib because of TEAEs
- Number (%) of subjects with INCB053914 dose reductions because of TEAEs
- Number (%) of subjects with cytarabine dose reductions because of TEAEs

- Number (%) of subjects with azacitidine dose reductions because of TEAEs
- Number (%) of subjects with ruxolitinib dose reductions because of TEAEs
- Number (%) of subjects who had a fatal TEAE
- Number (%) of subjects who withdrew from study because of an 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 SOC and PT
- Summary of TEAEs by PT in decreasing order of frequency
- Summary of TEAEs by SOC, PT, and maximum severity
- Summary of Grade 3 or 4 TEAEs by SOC and PT
- Summary of INCB053914 treatment-related AEs by SOC and PT
- Summary of cytarabine treatment-related AEs by SOC and PT
- Summary of azacitidine treatment-related AEs by SOC and PT
- Summary of ruxolitinib treatment-related AEs by SOC and PT
- Summary of Grade 3 or 4 INCB053914 treatment-related AEs by SOC and PT
- Summary of Grade 3 or 4 cytarabine treatment-related AEs by SOC and PT
- Summary of Grade 3 or 4 azacitidine treatment-related AEs by SOC and PT
- Summary of Grade 3 or 4 ruxolitinib treatment-related AEs by SOC and PT
- Summary of INCB053914 treatment-related AEs by SOC, PT, and maximum severity
- Summary of cytarabine treatment-related AEs by SOC, PT, and maximum severity
- Summary of azacitidine treatment-related AEs by SOC, PT, and maximum severity
- Summary of ruxolitinib treatment-related AEs by SOC, PT, and maximum severity
- Summary of TEAEs leading to death by SOC and PT
- Summary of treatment-emergent SAEs by SOC and PT
- Summary of treatment-emergent SAEs by PT in descending order of frequency
- Summary of treatment-emergent non-SAE by SOC and PT
- Summary of INCB053914 treatment-related SAEs by SOC and PT
- Summary of cytarabine treatment-related SAEs by SOC and PT
- Summary of azacitidine treatment-related SAEs by SOC and PT
- Summary of ruxolitinib treatment-related SAEs by SOC and PT
- Summary of TEAEs leading to INCB053914 dose reduction by SOC and PT
- Summary of TEAEs leading to cytarabine dose reduction by SOC and PT

- Summary of TEAEs leading to azacitidine dose reduction by SOC and PT
- Summary of TEAEs leading to ruxolitinib dose reduction by SOC and PT
- Summary of TEAEs leading to INCB053914 dose interruption by SOC and PT
- Summary of TEAEs leading to cytarabine dose interruption by SOC and PT
- Summary of TEAEs leading to azacitidine dose interruption by SOC and PT
- Summary of TEAEs leading to ruxolitinib dose interruption by SOC and PT
- Summary of TEAEs leading to discontinuation of INCB053914 by SOC and PT
- Summary of TEAEs leading to discontinuation of cytarabine by SOC and PT
- Summary of TEAEs leading to discontinuation of azacitidine by SOC and PT
- Summary of TEAEs leading to discontinuation of ruxolitinib by SOC and PT
- Summary of TEAEs of special interest by SOC and PT

10.3. Clinical Laboratory Tests

10.3.1. Laboratory Value Definitions

Laboratory values and change from baseline values will be summarized descriptively by visit. The baseline value will be determined using the nonmissing values collected before the first dose, prioritizing scheduled assessments for baseline identification over unscheduled visits. 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.

Laboratory test values outside the normal range will be assessed for severity based on CTCAE grade or similar criteria where clinical intervention is required for CTCAE grading. The incidence of abnormal laboratory values and shift tables relative to baseline will be tabulated.

10.3.2. Laboratory Value Summaries

All test results and associated normal ranges from local 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. For the limited number of cases where the associated normal ranges from a local laboratory cannot be obtained despite due diligence, if query is unsuccessful at resolving issue and analysis is mandatory, then the clinical scientist and medical monitor may provide a suitable normal range to be used in determining CTCAE grading to facilitate reporting the test results.

When there are multiple laboratory nonmissing values for a subject's particular test within a visit window, the convention described in Table 9 will be used to determine the record used for by-visit tabulations and summaries.

Table 9: Identification of Records for Postbaseline By-Visit Summaries

Priority	Laboratory Visit	Proximity to Visit Window	Tiebreaker
1	Scheduled	In-window	Use smallest laboratory sequence number
2	Unscheduled	In-window	
3	Scheduled	Out-of-window	

Numeric laboratory values will be summarized descriptively in SI units, and non-numeric test values will be tabulated when necessary. In addition, line graphs will be provided for hemoglobin, platelet, WBC, and neutrophil counts.

For test results that will be summarized with available normal ranges, the number and percentage of subjects with the 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 for the safety population. The denominator for the percentage calculation will use the number of subjects in the baseline category (ie, low, high, normal, missing) as the denominator for the percentage in each of the categories during the treatment period.

For all gradable laboratory parameters, shift tables will be presented showing change in CTCAE grade from baseline to worst grade postbaseline for all treatment-emergent laboratory AEs. The number and percentage of subjects with normal laboratory values, and the laboratory values of Grade 1, 2, 3, or 4 will be calculated for each treatment group according to the largest treatment-emergent worsening of laboratory grade. 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 subjects in the baseline category.

In cases where differentials of hematology parameters are obtained without corresponding absolute count data, efforts will be made to investigate if the conversion to an absolute value will lead to additional abnormalities. This will be discussed with the clinical team regarding appropriate documentation and action.

10.4. Vital Signs

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

Criteria for clinically notable vital sign abnormalities are defined in Table 10. The abnormal values for subjects exhibiting clinically notable vital sign abnormalities will be listed along with their assigned treatment group. An alert vital sign is defined as an absolute value outside the defined range and percentage change greater than 25%. The abnormal values for subjects exhibiting alert vital sign abnormalities will be listed.

Table 10: Criteria for Clinically Notable Vital Sign Abnormalities

Parameter	High Threshold	Low Threshold
Systolic blood pressure	> 155 mmHg	< 85 mmHg
Diastolic blood pressure	> 100 mmHg	< 40 mmHg
Pulse	> 100 bpm	< 45 bpm
Body temperature	> 38ºC	< 35.5ºC
Respiratory rate	> 24 breaths/min	< 8 breaths/min

10.5. Electrocardiograms

Twelve-lead ECGs including heart rate, pulse rate, QRS, QT, QTcF, and RR intervals will be obtained for each subject 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 study drug administration. Electrocardiograms conducted prior to dose administration (establishing the baseline for the day) should be performed in triplicate.

Criteria for clinically notable ECG abnormalities are defined in Table 11. Subjects exhibiting clinically notable ECG abnormalities will be listed with study visit and assigned treatment group. Abnormal values for subjects 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.

Table 11: Criteria for Clinically Notable Electrocardiogram Abnormalities

Parameter	High Threshold	Low Threshold
QTcF	> 460 ms	< 295 ms
Pulse Rate	> 220 ms	< 75 ms
QRS	> 120 ms	< 50 ms
QT	> 500 ms	< 300 ms
RR	> 1330 ms	< 600 ms

QTcF = Fridericia correction.

Twelve-lead ECGs will be obtained for each subject during the study. Electrocardiogram abnormalities, both at baseline and postbaseline visits, will be tabulated by treatment group. Incidences of abnormalities will be listed with study visit, assigned treatment group, and a description of the abnormality.

11. INTERIM ANALYSES

There are no planned, formal interim analyses for Parts 1, 2, and 3. Periodic review of accrued clinical data will be conducted by Incyte and provided to study investigators via teleconferences at the end of each part. Based on review of the most current safety data, the sponsor (in consultation with the study investigators and using the dose-escalation/de-escalation rules) will determine if, and at what dose, additional subjects should be treated in the study.

In Part 4, there are up to 3 planned interim analyses for futility in C-TGA E1, C-TGB E1, and the optional C-TGA E2. The Simon 2-stage design will be applied to each expansion cohort independently. During Stage 1, 13 subjects will be enrolled into each expansion cohort. If 3 or fewer of the first 13 evaluable subjects achieve an objective response, the cohort will be terminated for futility. In any cohort that exceeds this number of responders, additional subjects will be enrolled for Stage 2 evaluation.

Based on this early termination rule, the PET is 0.7473 under the assumption of a 20% historical control response rate; the PET is 0.1686 under the assumption of a 40% desired response rate. The PET for Stage 1 is summarized in Table 12.

Table 12: Probability of Early Termination at Stage 1 for Simon 2-Stage Design

True Response Rate	Probability of Early Termination at Stage 1
15%	88.2%
20%	74.7%
25%	58.4%
30%	42.1%
35%	27.8%

The interim analysis for each expansion cohort will be conducted once the first postbaseline bone marrow biopsies for Stage 1 subjects within the cohort are available. Enrollment will not continue unless a sufficient number of responders (> 3 responders) has been observed.

12. CHANGES AND MODIFICATIONS TO THE ANALYSIS PLAN

All versions of the SAP are listed in Table 13.

Table 13: Statistical Analysis Plan Versions

SAP Version	Date
Original	25 AUG 2017

13. REFERENCES

Blade J, Samson D, Reece D, et al. Criteria for evaluating disease response and progression in patients with multiple myeloma treated by high-dose therapy and haemopoietic stem cell transplantation: Myeloma Subcommittee of the EBMT, European Group for Blood and Marrow Transplant. Br J Haematol 1998;102:1115-1123.

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Simon R. Optimal two-stage designs for phase II clinical trials. Control Clin Trials 1989;10:1-10.

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Tefferi A, Cervantes F, Mesa R, et al. Revised response criteria for myelofibrosis: International Working Group-Myeloproliferative Neoplasms Research and Treatment (IWG-MRT) and European LeukemiaNet (ELN) consensus report. Blood 2013;122:1395-1398.

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APPENDIX A. PLANNED TABLES AND FIGURES

This appendix provides a list of the planned tables and figures for the Clinical Study Report. Standard tables will follow the conventions in the Standard Safety Tables initial version. Shells are provided for all tables. In-text tables are identical in structure and content as appendix tables, but follow a Rich Text Format.

The list of tables, figures, and listings and the shells are to be used as guideline. Modifications of the list or shells that do not otherwise affect the nature of the analysis will not warrant an amendment to the SAP.

Tables

Table No.	Title	Population	Standard	In-Text
1.1.1.1	Analysis Populations	Part 1 Safety	X	X
1.1.1.2	Analysis Populations	Part 2 FAS	X	X
1.1.1.3	Analysis Populations	Part 3 Safety	X	X
1.1.1.4	Analysis Populations	Part 4 FAS	X	X
1.1.2.1	Summary of Subject Disposition	Part 1 Safety	X	X
1.1.2.2	Summary of Subject Disposition	Part 2 FAS	X	X
1.1.2.3	Summary of Subject Disposition	Part 3 Safety	X	X
1.1.2.4	Summary of Subject Disposition	Part 4 FAS	X	X
1.1.3.1	Summary of Number of Subjects Enrolled by Site	Part 1 Safety	X	
1.1.3.2	Summary of Number of Subjects Enrolled by Site	Part 2 FAS	X	
1.1.3.3	Summary of Number of Subjects Enrolled by Site	Part 3 Safety	X	
1.1.3.4	Summary of Number of Subjects Enrolled by Site	Part 4 FAS	X	
1.2.1	Summary of Demographics	Part 1 Safety	X	X
1.2.2	Summary of Demographics	Part 2 FAS	X	X
1.2.3	Summary of Demographics	Part 3 Safety	X	X
1.2.4	Summary of Demographics	Part 4 FAS	X	X
1.3.1.1	Summary of Acute Myeloid Leukemia History and Baseline Disease Characteristics	Part 1 AML Safety		X
1.3.1.2	Summary of Leukemia History and Baseline Disease Characteristics	Part 1 Leukemia Safety		X
1.3.1.3	Summary of Myelodysplastic Syndrome History and Baseline Disease Characteristics	Part 1 MDS Safety		X
1.3.1.4	Summary of Myelodysplastic Syndrome/Myeloproliferative Neoplasm History and Baseline Disease Characteristics	Part 1 MDS/MPN Safety		X
1.3.1.5	Summary of Multiple Myeloma History and Baseline Disease Characteristics	Part 1 MM Safety		X
1.3.1.6	Summary of Lymphoma History and Baseline Disease Characteristics	Part 1 Lymphoma Safety		X
1.3.1.7	Summary of Myelofibrosis History and Baseline Disease Characteristics	Part 1 MF Safety		
1.3.2.1	Summary of Acute Myeloid Leukemia History and Baseline Disease Characteristics	Part 2 AML FAS		X

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Table No.	Title	Population	Standard	In-Text
1.3.2.2	Summary of Myelodysplastic Syndrome/Myeloproliferative Neoplasm History and Baseline Disease Characteristics	Part 2 MDS/MPN FAS		X
1.3.2.3	Summary of Myelofibrosis History and Baseline Disease Characteristics	Part 2 MF FAS		X
1.3.2.4	Summary of Multiple Myeloma History and Baseline Disease Characteristics	Part 2 MM FAS		X
1.3.2.5	Summary of DLBCL History and Baseline Disease Characteristics	Part 2 DLBCL FAS		X
1.3.3.1	Summary of Acute Myeloid Leukemia History and Baseline Disease Characteristics	Part 3 Cytarabine Safety		X
1.3.3.2	Summary of Acute Myeloid Leukemia History and Baseline Disease Characteristics	Part 3 Azacitidine Safety		
1.3.3.3	Summary of Myelofibrosis History and Baseline Disease Characteristics	Part 3 Ruxolitinib Safety		
1.3.4.1	Summary of Acute Myeloid Leukemia History and Baseline Disease Characteristics	Part 4 AML FAS		X
1.3.4.2	Summary of Myelofibrosis History and Baseline Disease Characteristics	Part 4 MF FAS		X
1.4.1.1	Summary of Prior Cancer Therapy	Part 1 Safety		
1.4.1.2	Summary of Prior Cancer Therapy	Part 2 FAS		
1.4.1.3	Summary of Prior Cancer Therapy	Part 3 Safety		
1.4.1.4	Summary of Prior Cancer Therapy	Part 4 FAS		
1.4.2.1	Summary of Hematopoietic Stem Cell Transplant	Part 1 Safety		
1.4.2.2	Summary of Hematopoietic Stem Cell Transplant	Part 2 FAS		
1.4.2.3	Summary of Hematopoietic Stem Cell Transplant	Part 3 Safety		
1.4.2.4	Summary of Hematopoietic Stem Cell Transplant	Part 4 FAS		
1.4.3.1	Summary of Prior Medications	Part 1 Safety	X	
1.4.3.2	Summary of Prior Medications	Part 2 FAS	X	
1.4.3.3	Summary of Prior Medications	Part 3 Safety	X	
1.4.3.4	Summary of Prior Medications	Part 4 FAS	X	
1.4.4.1	Summary of Concomitant Medications	Part 1 Safety	X	
1.4.4.2	Summary of Concomitant Medications	Part 2 FAS	X	
1.4.4.3	Summary of Concomitant Medications	Part 3 Safety	X	
1.4.4.4	Summary of Concomitant Medications	Part 4 FAS	X	
1.5.1	Summary of General Medical History	Part 1 Safety	X	
1.5.2	Summary of General Medical History	Part 2 FAS	X	
1.5.3	Summary of General Medical History	Part 3 Safety	X	
1.5.4	Summary of General Medical History	Part 4 FAS	X	
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[redacted]	[redacted]	[redacted]		
[redacted]	[redacted]	[redacted]		[redacted]
2.1.3.1	Summary of Response – Acute Myeloid Leukemia	Part 4 AML FAS		X
[redacted]	[redacted]	[redacted]		
[redacted]	[redacted]	[redacted]		
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3.1.1.1	Summary of Exposure to INCB053914	Part 1 Safety	X	X
3.1.1.2	Summary of Exposure to INCB053914	Part 2 Safety	X	X
3.1.1.3.1	Summary of Exposure to INCB053914	Part 3 INCB053914 Safety	X	X
3.1.1.3.2	Summary of Exposure to Cytarabine	Part 3 Cytarabine Safety	X	X
3.1.1.3.3	Summary of Exposure to Azacitidine	Part 3 Azacitidine Safety	X	X
3.1.1.3.4	Summary of Exposure to Ruxolitinib	Part 3 Ruxolitinib Safety	X	X
3.1.1.4.1	Summary of Exposure to INCB53914	Part 4 INCB053914 Safety	X	X
3.1.1.4.2	Summary of Exposure to Intermediate-Dose Cytarabine	Part 4 Intermediate-Dose Cytarabine Safety	X	X
3.1.1.4.3	Summary of Exposure to Azacitidine	Part 4 Azacitidine Safety	X	X
3.1.1.4.4	Summary of Exposure to Ruxolitinib	Part 4 Ruxolitinib Safety	X	X
3.1.2.1	Summary of INCB053914 Compliance	Part 1 INCB053914 Safety	X	X
3.1.2.2	Summary of INCB053914 Compliance	Part 2 INCB053914 Safety	X	X
3.1.2.3	Summary of INCB053914 Compliance	Part 3 INCB053914 Safety	X	X
3.1.2.4	Summary of INCB053914 Compliance	Part 4 INCB053914 Safety	X	X
3.2.1.1	Overall Summary of Treatment-Emergent Adverse Events	Part 1 Safety	X	X

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Table No.	Title	Population	Standard	In-Text
3.2.1.2	Overall Summary of Treatment-Emergent Adverse Events	Part 2 Safety	X	X
3.2.1.3	Overall Summary of Treatment-Emergent Adverse Events	Part 3 Safety	X	X
3.2.1.4	Overall Summary of Treatment-Emergent Adverse Events	Part 4 Safety	X	X
3.2.2.1	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Part 1 Safety	X	X
3.2.2.2	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Part 2 Safety	X	X
3.2.2.3	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Part 3 Safety	X	X
3.2.2.4	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Part 4 Safety	X	X
3.2.3.1	Summary of Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	Part 1 Safety	X	X
3.2.3.2	Summary of Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	Part 2 Safety	X	X
3.2.3.3	Summary of Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	Part 3 Safety	X	X
3.2.3.4	Summary of Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency	Part 4 Safety	X	X
3.2.4.1	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class, Preferred Term, and Maximum Severity	Part 1 Safety	X	
3.2.4.2	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class, Preferred Term, and Maximum Severity	Part 2 Safety	X	
3.2.4.3	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class, Preferred Term, and Maximum Severity	Part 3 Safety	X	
3.2.4.4	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class, Preferred Term, and Maximum Severity	Part 4 Safety	X	
3.2.5.1	Summary of Grade 3 or 4 Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Part 1 Safety	X	X
3.2.5.2	Summary of Grade 3 or 4 Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Part 2 Safety	X	X
3.2.5.3	Summary of Grade 3 or 4 Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Part 3 Safety	X	X
3.2.5.4	Summary of Grade 3 or 4 Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Part 4 Safety	X	X

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Table No.	Title	Population	Standard	In-Text
3.2.6.1	Summary of INCB053914 Treatment-Related Adverse Events by MedDRA System Organ Class and Preferred Term	Part 1 INCB053914 Safety	X	
3.2.6.2	Summary of INCB053914 Treatment-Related Adverse Events by MedDRA System Organ Class and Preferred Term	Part 2 INCB053914 Safety	X	
3.2.6.3	Summary of INCB053914 Treatment-Related Adverse Events by MedDRA System Organ Class and Preferred Term	Part 3 INCB053914 Safety	X	
3.2.6.4	Summary of INCB053914 Treatment-Related Adverse Events by MedDRA System Organ Class and Preferred Term	Part 4 INCB053914 Safety	X	
3.2.6.5	Summary of Cytarabine Treatment-Related Adverse Events by MedDRA System Organ Class and Preferred Term	Part 3 Cytarabine Safety	X	
3.2.6.6	Summary of Azacitidine Treatment-Related Adverse Events by MedDRA System Organ Class and Preferred Term	Part 3 Azacitidine Safety	X	
3.2.6.7	Summary of Ruxolitinib Treatment-Related Adverse Events by MedDRA System Organ Class and Preferred Term	Part 3 Ruxolitinib Safety	X	
3.2.6.8	Summary of Cytarabine/Azacitidine/Ruxolitinib Treatment-Related Adverse Events by MedDRA System Organ Class and Preferred Term	Part 4 Safety	X	
3.2.7.1	Summary of Grade 3 or 4 INCB053914 Treatment-Related Adverse Events by MedDRA System Organ Class and Preferred Term	Part 1 INCB053914 Safety	X	
3.2.7.2	Summary of Grade 3 or 4 INCB053914 Treatment-Related Adverse Events by MedDRA System Organ Class and Preferred Term	Part 2 INCB053914 Safety	X	
3.2.7.3	Summary of Grade 3 or 4 INCB053914 Treatment-Related Adverse Events by MedDRA System Organ Class and Preferred Term	Part 3 INCB053914 Safety	X	
3.2.7.4	Summary of Grade 3 or 4 INCB053914 Treatment-Related Adverse Events by MedDRA System Organ Class and Preferred Term	Part 4 INCB053914 Safety	X	
3.2.7.5	Summary of Grade 3 or 4 Cytarabine Treatment-Related Adverse Events by MedDRA System Organ Class and Preferred Term	Part 3 Cytarabine Safety	X	
3.2.7.6	Summary of Grade 3 or 4 Azacitidine Treatment-Related Adverse Events by MedDRA System Organ Class and Preferred Term	Part 3 Azacitidine Safety	X	
3.2.7.7	Summary of Grade 3 or 4 Ruxolitinib Treatment-Related Adverse Events by MedDRA System Organ Class and Preferred Term	Part 3 Ruxolitinib Safety	X	
3.2.7.8	Summary of Grade 3 or 4 Cytarabine/Azacitidine/Ruxolitinib Treatment-Related Adverse Events by MedDRA System Organ Class and Preferred Term	Part 4 Safety	X	

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Table No.	Title	Population	Standard	In-Text
3.2.8.1	Summary of INCB053914 Treatment-Related Adverse Events by MedDRA System Organ Class, Preferred Term, and Maximum Severity	Part 1 INCB053914 Safety	X	
3.2.8.2	Summary of INCB053914 Treatment-Related Adverse Events by MedDRA System Organ Class, Preferred Term, and Maximum Severity	Part 2 INCB053914 Safety	X	
3.2.8.3	Summary of INCB053914 Treatment-Related Adverse Events by MedDRA System Organ Class, Preferred Term, and Maximum Severity	Part 3 INCB053914 Safety	X	
3.2.8.4	Summary of INCB053914 Treatment-Related Adverse Events by MedDRA System Organ Class, Preferred Term, and Maximum Severity	Part 4 INCB053914 Safety	X	
3.2.8.5	Summary of Cytarabine Treatment-Related Adverse Events by MedDRA System Organ Class, Preferred Term, and Maximum Severity	Part 3 Cytarabine Safety	X	
3.2.8.6	Summary of Azacitidine Treatment-Related Adverse Events by MedDRA System Organ Class, Preferred Term, and Maximum Severity	Part 3 Azacitidine Safety	X	
3.2.8.7	Summary of Ruxolitinib Treatment-Related Adverse Events by MedDRA System Organ Class, Preferred Term, and Maximum Severity	Part 3 Ruxolitinib Safety	X	
3.2.8.8	Summary of Cytarabine/Azacitidine/Ruxolitinib Treatment-Related Adverse Events by MedDRA System Organ Class, Preferred Term, and Maximum Severity	Part 4 Safety	X	
3.2.9.1	Summary of Treatment-Emergent Adverse Events With a Fatal Outcome by MedDRA System Organ Class and Preferred Term	Part 1 Safety	X	X
3.2.9.2	Summary of Treatment-Emergent Adverse Events With a Fatal Outcome by MedDRA System Organ Class and Preferred Term	Part 2 Safety	X	X
3.2.9.3	Summary of Treatment-Emergent Adverse Events With a Fatal Outcome by MedDRA System Organ Class and Preferred Term	Part 3 Safety	X	X
3.2.9.4	Summary of Treatment-Emergent Adverse Events With a Fatal Outcome by MedDRA System Organ Class and Preferred Term	Part 4 Safety	X	X
3.2.10.1	Summary of Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Part 1 Safety	X	X
3.2.10.2	Summary of Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Part 2 Safety	X	X
3.2.10.3	Summary of Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Part 3 Safety	X	X
3.2.10.4	Summary of Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Part 4 Safety	X	X

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Table No.	Title	Population	Standard	In-Text
3.2.11.1	Summary of Serious Treatment-Emergent Adverse Events by Preferred Term in Decreasing Order of Frequency	Part 1 Safety	X	X
3.2.11.2	Summary of Serious Treatment-Emergent Adverse Events by Preferred Term in Decreasing Order of Frequency	Part 2 Safety	X	X
3.2.11.3	Summary of Serious Treatment-Emergent Adverse Events by Preferred Term in Decreasing Order of Frequency	Part 3 Safety	X	X
3.2.11.4	Summary of Serious Treatment-Emergent Adverse Events by Preferred Term in Decreasing Order of Frequency	Part 4 Safety	X	X
3.2.12.1	Summary of Non-Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Part 1 Safety	X	X
3.2.12.2	Summary of Non-Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Part 2 Safety	X	X
3.2.12.3	Summary of Non-Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Part 3 Safety	X	X
3.2.12.4	Summary of Non-Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term	Part 4 Safety	X	X
3.2.13.1	Summary of INCB053914 Treatment-Related Serious Adverse Events by MedDRA System Organ Class and Preferred Term	Part 1 INCB053914 Safety	X	X
3.2.13.2	Summary of INCB053914 Treatment-Related Serious Adverse Events by MedDRA System Organ Class and Preferred Term	Part 2 INCB053914 Safety	X	X
3.2.13.3	Summary of INCB053914 Treatment-Related Serious Adverse Events by MedDRA System Organ Class and Preferred Term	Part 3 INCB053914 Safety	X	X
3.2.13.4	Summary of INCB053914 Treatment-Related Serious Adverse Events by MedDRA System Organ Class and Preferred Term	Part 4 INCB053914 Safety	X	X
3.2.13.5	Summary of Cytarabine Treatment-Related Serious Adverse Events by MedDRA System Organ Class and Preferred Term	Part 3 Cytarabine Safety	X	X
3.2.13.6	Summary of Azacitidine Treatment-Related Serious Adverse Events by MedDRA System Organ Class and Preferred Term	Part 3 Azacitidine Safety	X	X
3.2.13.7	Summary of Ruxolitinib Treatment-Related Serious Adverse Events by MedDRA System Organ Class and Preferred Term	Part 3 Ruxolitinib Safety	X	X
3.2.13.8	Summary of Cytarabine/Azacitidine/Ruxolitinib Treatment-Related Serious Adverse Events by MedDRA System Organ Class and Preferred Term	Part 4 Safety	X	X

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Table No.	Title	Population	Standard	In-Text
3.2.14.1	Summary of Treatment-Emergent Adverse Events Leading to INCB053914 Dose Reduction by MedDRA System Organ Class and Preferred Term	Part 1 INCB053914 Safety	X	
3.2.14.2	Summary of Treatment-Emergent Adverse Events Leading to INCB053914 Dose Reduction by MedDRA System Organ Class and Preferred Term	Part 2 INCB053914 Safety	X	
3.2.14.3	Summary of Treatment-Emergent Adverse Events Leading to INCB053914 Dose Reduction by MedDRA System Organ Class and Preferred Term	Part 3 INCB053914 Safety	X	
3.2.14.4	Summary of Treatment-Emergent Adverse Events Leading to INCB053914 Dose Reduction by MedDRA System Organ Class and Preferred Term	Part 4 INCB053914 Safety	X	
3.2.14.5	Summary of Treatment-Emergent Adverse Events Leading to Cytarabine Dose Reduction by MedDRA System Organ Class and Preferred Term	Part 3 Cytarabine Safety	X	
3.2.14.6	Summary of Treatment-Emergent Adverse Events Leading to Azacitidine Dose Reduction by MedDRA System Organ Class and Preferred Term	Part 3 Azacitidine Safety	X	
3.2.14.7	Summary of Treatment-Emergent Adverse Events Leading to Ruxolitinib Dose Reduction by MedDRA System Organ Class and Preferred Term	Part 3 Ruxolitinib Safety	X	
3.2.14.8	Summary of Treatment-Emergent Adverse Events Leading to Cytarabine/Azacitidine/Ruxolitinib Dose Reduction by MedDRA System Organ Class and Preferred Term	Part 4 Safety	X	
3.2.15.1	Summary of Treatment-Emergent Adverse Events Leading to INCB053914 Dose Interruption by MedDRA System Organ Class and Preferred Term	Part 1 INCB053914 Safety	X	
3.2.15.2	Summary of Treatment-Emergent Adverse Events Leading to INCB053914 Dose Interruption by MedDRA System Organ Class and Preferred Term	Part 2 INCB053914 Safety	X	
3.2.15.3	Summary of Treatment-Emergent Adverse Events Leading to INCB053914 Dose Interruption by MedDRA System Organ Class and Preferred Term	Part 3 INCB053914 Safety	X	
3.2.15.4	Summary of Treatment-Emergent Adverse Events Leading to INCB053914 Dose Interruption by MedDRA System Organ Class and Preferred Term	Part 4 INCB053914 Safety	X	
3.2.15.5	Summary of Treatment-Emergent Adverse Events Leading to Cytarabine Dose Interruption by MedDRA System Organ Class and Preferred Term	Part 3 Cytarabine Safety	X	
3.2.15.6	Summary of Treatment-Emergent Adverse Events Leading to Azacitidine Dose Interruption by MedDRA System Organ Class and Preferred Term	Part 3 Azacitidine Safety	X	
3.2.15.7	Summary of Treatment-Emergent Adverse Events Leading to Ruxolitinib Dose Interruption by MedDRA System Organ Class and Preferred Term	Part 3 Ruxolitinib Safety	X	
3.2.15.8	Summary of Treatment-Emergent Adverse Events Leading to Cytarabine/Azacitidine/Ruxolitinib Dose Interruption by MedDRA System Organ Class and Preferred Term	Part 4 Safety	X	

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Table No.	Title	Population	Standard	In-Text
3.2.16.1	Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of INCB053914 by MedDRA System Organ Class and Preferred Term	Part 1 INCB053914 Safety	X	X
3.2.16.2	Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of INCB053914 by MedDRA System Organ Class and Preferred Term	Part 2 INCB053914 Safety	X	X
3.2.16.3	Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of INCB053914 by MedDRA System Organ Class and Preferred Term	Part 3 INCB053914 Safety	X	X
3.2.16.4	Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of INCB053914 by MedDRA System Organ Class and Preferred Term	Part 4 INCB053914 Safety	X	X
3.2.16.5	Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of Cytarabine by MedDRA System Organ Class and Preferred Term	Part 3 Cytarabine Safety	X	
3.2.16.6	Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of Azacitidine by MedDRA System Organ Class and Preferred Term	Part 3 Azacitidine Safety	X	
3.2.16.7	Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of Ruxolitinib by MedDRA System Organ Class and Preferred Term	Part 3 Ruxolitinib Safety	X	
3.2.16.8	Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of Cytarabine/Azacitidine/Ruxolitinib by MedDRA System Organ Class and Preferred Term	Part 4 Safety	X	
3.2.17.1	Summary of Treatment-Emergent Adverse Events of Special Interest by MedDRA System Organ Class and Preferred Term	Part 1 Safety	X	
3.2.17.2	Summary of Treatment-Emergent Adverse Events of Special Interest by MedDRA System Organ Class and Preferred Term	Part 2 Safety	X	
3.2.17.3	Summary of Treatment-Emergent Adverse Events of Special Interest by MedDRA System Organ Class and Preferred Term	Part 3 Safety	X	
3.2.17.4	Summary of Treatment-Emergent Adverse Events of Special Interest by MedDRA System Organ Class and Preferred Term	Part 4 Safety	X	
3.3.1.1	Summary of Laboratory Values – Hematology	Part 2 Safety	X	
3.3.1.2	Summary of Laboratory Values – Hematology	Part 4 Safety	X	
3.3.2.1	Shift Summary of Hematology Values To the Worst Abnormal Value	Part 1 Safety	X	
3.3.2.2	Shift Summary of Hematology Values To the Worst Abnormal Value	Part 2 Safety	X	
3.3.2.3	Shift Summary of Hematology Values To the Worst Abnormal Value	Part 3 Safety	X	
3.3.2.4	Shift Summary of Hematology Values To the Worst Abnormal Value	Part 4 Safety	X	
3.3.3.1	Shift Summary of Hematology Laboratory Values in CTC Grade To the Worst Abnormal Value	Part 1 Safety	X	X

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Table No.	Title	Population	Standard	In-Text
3.3.3.2	Shift Summary of Hematology Laboratory Values in CTC Grade To the Worst Abnormal Value	Part 2 Safety	X	X
3.3.3.3	Shift Summary of Hematology Laboratory Values in CTC Grade To the Worst Abnormal Value	Part 3 Safety	X	X
3.3.3.4	Shift Summary of Hematology Laboratory Values in CTC Grade To the Worst Abnormal Value	Part 4 Safety	X	X
3.3.4.1	Summary of Laboratory Values – Chemistry	Part 2 Safety	X	X
3.3.4.2	Summary of Laboratory Values – Chemistry	Part 4 Safety	X	X
3.3.5.1	Shift Summary of Chemistry Values To the Worst Abnormal Value	Part 1 Safety	X	
3.3.5.2	Shift Summary of Chemistry Values To the Worst Abnormal Value	Part 2 Safety	X	
3.3.5.3	Shift Summary of Chemistry Values To the Worst Abnormal Value	Part 3 Safety	X	
3.3.5.4	Shift Summary of Chemistry Values To the Worst Abnormal Value	Part 4 Safety	X	
3.3.6.1	Shift Summary of Chemistry Laboratory Values in CTC Grade To the Worst Abnormal Value	Part 1 Safety	X	X
3.3.6.2	Shift Summary of Chemistry Laboratory Values in CTC Grade To the Worst Abnormal Value	Part 2 Safety	X	X
3.3.6.3	Shift Summary of Chemistry Laboratory Values in CTC Grade To the Worst Abnormal Value	Part 3 Safety	X	X
3.3.6.4	Shift Summary of Chemistry Laboratory Values in CTC Grade To the Worst Abnormal Value	Part 4 Safety	X	X
3.3.7.1	Summary of Laboratory Values – Coagulation	Part 2 Safety	X	
3.3.7.2	Summary of Laboratory Values – Coagulation	Part 4 Safety	X	
3.3.8.1	Shift Summary of Coagulation Values To the Worst Abnormal Value	Part 1 Safety	X	
3.3.8.2	Shift Summary of Coagulation Values To the Worst Abnormal Value	Part 2 Safety	X	
3.3.8.3	Shift Summary of Coagulation Values To the Worst Abnormal Value	Part 3 Safety	X	
3.3.8.4	Shift Summary of Coagulation Values To the Worst Abnormal Value	Part 4 Safety	X	
3.3.9.1	Summary of Treatment-Emergent Worsening of Liver Function Values	Part 1 Safety		
3.3.9.2	Summary of Treatment-Emergent Worsening of Liver Function Values	Part 2 Safety		
3.3.9.3	Summary of Treatment-Emergent Worsening of Liver Function Values	Part 3 Safety		
3.3.9.4	Summary of Treatment-Emergent Worsening of Liver Function Values	Part 4 Safety		
3.4.1.1	Summary of Systolic Blood Pressure	Part 2 Safety	X	
3.4.1.2	Summary of Systolic Blood Pressure	Part 4 Safety	X	
3.4.2.1	Summary of Diastolic Blood Pressure	Part 2 Safety	X	
3.4.2.2	Summary of Diastolic Blood Pressure	Part 4 Safety	X	
3.4.3.1	Summary of Respiration Rate	Part 2 Safety	X	
3.4.3.2	Summary of Respiration Rate	Part 4 Safety	X	

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Table No.	Title	Population	Standard	In-Text
3.4.4.1	Summary of Body Temperature	Part 2 Safety	X	
3.4.4.2	Summary of Body Temperature	Part 4 Safety	X	
3.4.5.1	Summary of Weight	Part 2 Safety	X	
3.4.5.2	Summary of Weight	Part 4 Safety	X	
3.4.6.1	Summary of Pulse Rate	Part 2 Safety	X	
3.4.6.2	Summary of Pulse Rate	Part 4 Safety	X	
3.5.1.1	Summary of PR Interval (ms) From 12-Lead ECG	Part 1 Safety	X	
3.5.1.2	Summary of PR Interval (ms) From 12-Lead ECG	Part 2 Safety	X	
3.5.1.3	Summary of PR Interval (ms) From 12-Lead ECG	Part 3 Safety	X	
3.5.1.4	Summary of PR Interval (ms) From 12-Lead ECG	Part 4 Safety	X	
3.5.2.1	Summary of QRS Interval (ms) From 12-Lead ECG	Part 1 Safety	X	
3.5.2.2	Summary of QRS Interval (ms) From 12-Lead ECG	Part 2 Safety	X	
3.5.2.3	Summary of QRS Interval (ms) From 12-Lead ECG	Part 3 Safety	X	
3.5.2.4	Summary of QRS Interval (ms) From 12-Lead ECG	Part 4 Safety	X	
3.5.3.1	Summary of QT Interval (ms) From 12-Lead ECG	Part 1 Safety	X	
3.5.3.2	Summary of QT Interval (ms) From 12-Lead ECG	Part 2 Safety	X	
3.5.3.3	Summary of QT Interval (ms) From 12-Lead ECG	Part 3 Safety	X	
3.5.3.4	Summary of QT Interval (ms) From 12-Lead ECG	Part 4 Safety	X	
3.5.4.1	Summary of QTcF Interval (ms) From 12-Lead ECG	Part 1 Safety	X	
3.5.4.2	Summary of QTcF Interval (ms) From 12-Lead ECG	Part 2 Safety	X	
3.5.4.3	Summary of QTcF Interval (ms) From 12-Lead ECG	Part 3 Safety	X	
3.5.4.4	Summary of QTcF Interval (ms) From 12-Lead ECG	Part 4 Safety	X	
3.5.5.1	Summary of RR Interval (ms) From 12-Lead ECG	Part 1 Safety	X	
3.5.5.2	Summary of RR Interval (ms) From 12-Lead ECG	Part 2 Safety	X	
3.5.5.3	Summary of RR Interval (ms) From 12-Lead ECG	Part 3 Safety	X	
3.5.5.4	Summary of RR Interval (ms) From 12-Lead ECG	Part 4 Safety	X	
3.5.6.1	Summary of Heart Rate (bpm) From 12-Lead ECG	Part 1 Safety	X	
3.5.6.2	Summary of Heart Rate (bpm) From 12-Lead ECG	Part 2 Safety	X	
3.5.6.3	Summary of Heart Rate (bpm) From 12-Lead ECG	Part 3 Safety	X	
3.5.6.4	Summary of Heart Rate (bpm) From 12-Lead ECG	Part 4 Safety	X	
3.5.7.1	Summary of Outliers of QT, QTcB, and QTcF Interval Values From 12-Lead ECG	Part 1 Safety	X	X
3.5.7.2	Summary of Outliers of QT, QTcB, and QTcF Interval Values From 12-Lead ECG	Part 2 Safety	X	X
3.5.7.3	Summary of Outliers of QT, QTcB, and QTcF Interval Values From 12-Lead ECG	Part 3 Safety	X	X
3.5.7.4	Summary of Outliers of QT, QTcB, and QTcF Interval Values From 12-Lead ECG	Part 4 Safety	X	X
3.6.1.1	Summary of Pharmacodynamic Markers	Parts 1 and 2 PD Evaluable		
3.6.1.2	Summary of Pharmacodynamic Markers	Parts 3 and 4 PD Evaluable		
3.6.2.1	Summary of Categorized Percentage Change From Baseline in Pharmacodynamic Markers	Parts 1 and 2 PD Evaluable		

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Table No.	Title	Population	Standard	In-Text
3.6.2.2	Summary of Categorized Percentage Change From Baseline in Pharmacodynamic Markers	Parts 3 and 4 PD Evaluable		
3.6.3.1	Summary of Flow Cytometry	Parts 1 and 2 PD Evaluable		
3.6.3.2	Summary of Flow Cytometry	Parts 3 and 4 PD Evaluable		

Figures

Figure No.	Title
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
4.3.1	Line Graph of Selected Laboratory Values by Study Visit
4.3.2	Box-and-Whisker Plot of Selected Laboratory Values by Study Visit

Listings

Listing No.	Title
2.1.1	Subject Enrollment and Disposition Status
2.1.2	Subject Inclusion and Exclusion Criteria Violations
2.2.1	Protocol Deviations and Violations
2.3.1	Analysis Population
2.4.1	Demographic and Baseline Disease Characteristics
2.4.2	Disease History
2.4.3	Prior Radiation Treatment
2.4.4	Prior Systemic Therapy
2.4.5	Prior Surgery or Surgical Procedure
2.4.6	Prior Stem Cell Transplant
2.4.7	General Medical History
2.4.8	Prior and Concomitant Medication
2.5.1	Study Drug Compliance
2.6.1.1	Best Overall Response, [redacted] – Acute Myeloid Leukemia
2.6.1.2	Best Overall Response, [redacted] – Leukemia
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
2.6.2.1	Overall Response Assessment by Visit – Acute Myeloid Leukemia
2.6.2.2	Overall Response Assessment by Visit – Leukemia
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
2.6.3.1	ECOG status

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Listing No.	Title
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
2.7.1	Study Drug Administration
2.7.2	Adverse Events
2.7.3	Dose-Limiting Toxicities
2.7.4	Serious Adverse Events
2.7.5	Grade 3 and Higher Adverse Events
2.7.6	Fatal Adverse Events
2.7.7.1	INCB053914 Treatment-Related Adverse Events
2.7.7.2	Any Other Study Drug Treatment-Related Adverse Events
2.7.8.1	Adverse Events Leading to Interruption, Reduction, or Discontinuation of INCB053914, Cytarabine, Azacitidine, or Ruxolitinib
2.7.8.2	Adverse Events Leading to Interruption, Reduction, or Discontinuation of Any Other Study Drug
2.7.9	Adverse Events Leading to Withdrawal From Study
2.7.10	Death
2.8.1.1	Clinical Laboratory Values – Hematology
2.8.1.2	Clinical Laboratory Values – Chemistry
2.8.1.3	Clinical Laboratory Values – Urinalysis
2.8.1.4	Clinical Laboratory Values – Coagulation
2.8.1.5	Abnormal Clinical Laboratory Values
2.8.2.1	PK Blood Sampling Times
2.8.2.2	PK Urine Sampling Times
2.9.1	Vital Signs
2.9.2	Abnormal Vital Sign Values
2.9.3	Alert Vital Sign Values
2.10.1	12-Lead ECG Values
2.10.2	Abnormal 12-Lead ECG Values
2.10.3	Alert 12-Lead ECG Values
2.11.1	Physical Examinations

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APPENDIX B. INTERNATIONAL WORKING GROUP RESPONSE CRITERIA FOR ACUTE MYELOID LEUKEMIA

Response Category	Response Definition
Complete remission (CR)[1]	Bone marrow blasts < 5 percent; absence of blasts with Auer rods; absence of extramedullary disease; absolute neutrophil count > 1.0×10^9/L (1000/μL); platelet count >100×10^9/L (100,000/μL); independence of red cell transfusions
CR with incomplete recovery (CRi)	All CR criteria except for residual neutropenia (< 1.0×10^9/L [1000/μL]) or thrombocytopenia (< 100×10^9/L [100,000/μL])
Morphologic leukemia-free state	Bone marrow blasts < 5 percent; absence of blasts with Auer rods; absence of extramedullary disease; no hematologic recovery required
Partial remission (PR)	All hematologic criteria of CR; decrease of bone marrow blast percentage to 5 to 25 percent; and decrease of pretreatment bone marrow blast percentage by at least 50 percent
Cytogenetic CR (CRC)	Reversion to a normal karyotype at the time of morphologic CR (or CRi) in cases with an abnormal karyotype at the time of diagnosis; based on the evaluation of 20 metaphase cells from bone marrow
Molecular CR (CRm)	No standard definition; depends on molecular target
Treatment failure	
Resistant disease (RD)	Failure to achieve CR or CRi or PR (Phase 1 trials); only includes patients surviving ≥ 7 days following completion of initial treatment, with evidence of persistent leukemia by blood and/or bone marrow examination
Death in aplasia	Deaths occurring ≥ 7 days following completion of initial treatment while cytopenic; with an aplastic or hypoplastic bone marrow obtained within 7 days of death, without evidence of persistent leukemia
Death from indeterminate cause	Deaths occurring before completion of therapy, or < 7 days following its completion; or deaths occurring ≥ 7 days following completion of initial therapy with no blasts in the blood, but no bone marrow examination available
Relapse[2]	Bone marrow blasts ≥ 5 percent; or reappearance of blasts in the blood; or development of extramedullary disease

[1] All criteria need to be fulfilled; marrow evaluation should be based on a count of 200 nucleated cells in an aspirate with spicules; if ambiguous, consider repeat exam after 5 to 7 days; flow cytometric evaluation may help to distinguish between persistent leukemia and regenerating normal marrow; a marrow biopsy should be performed in cases of dry tap, or if no spicules are obtained; no minimum duration of response required.

[2] In cases with low blast percentages (5 to 10 percent), a repeat marrow should be performed to confirm relapse. Appearance of new dysplastic changes should be closely monitored for emerging relapse. In a patient who has been recently treated, dysplasia or a transient increase in blasts may reflect a chemotherapy effect and recovery of hematopoiesis. Cytogenetics should be tested to distinguish true relapse from therapy-related MDS/AML.

Source: Cheson et al 2003.

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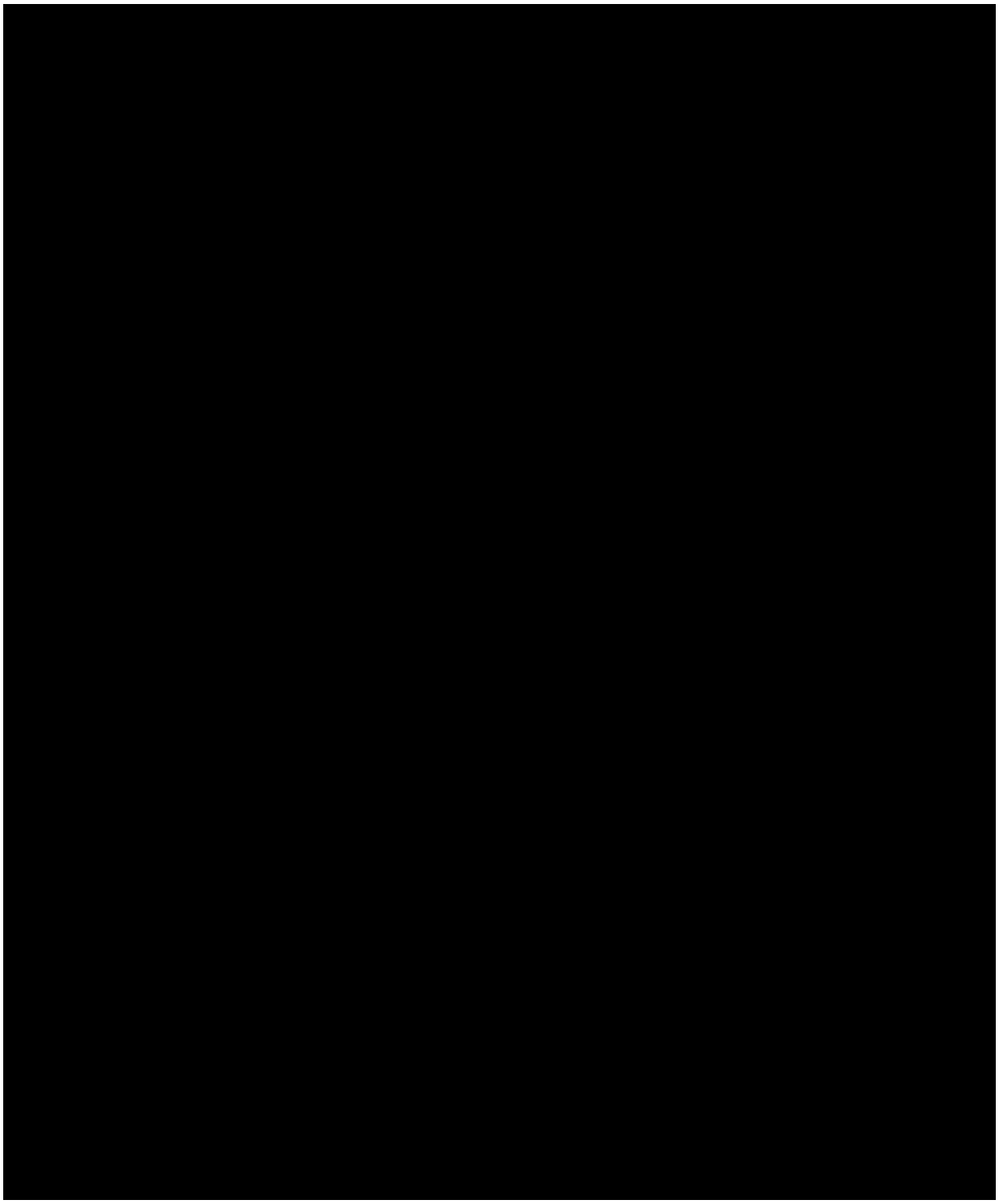

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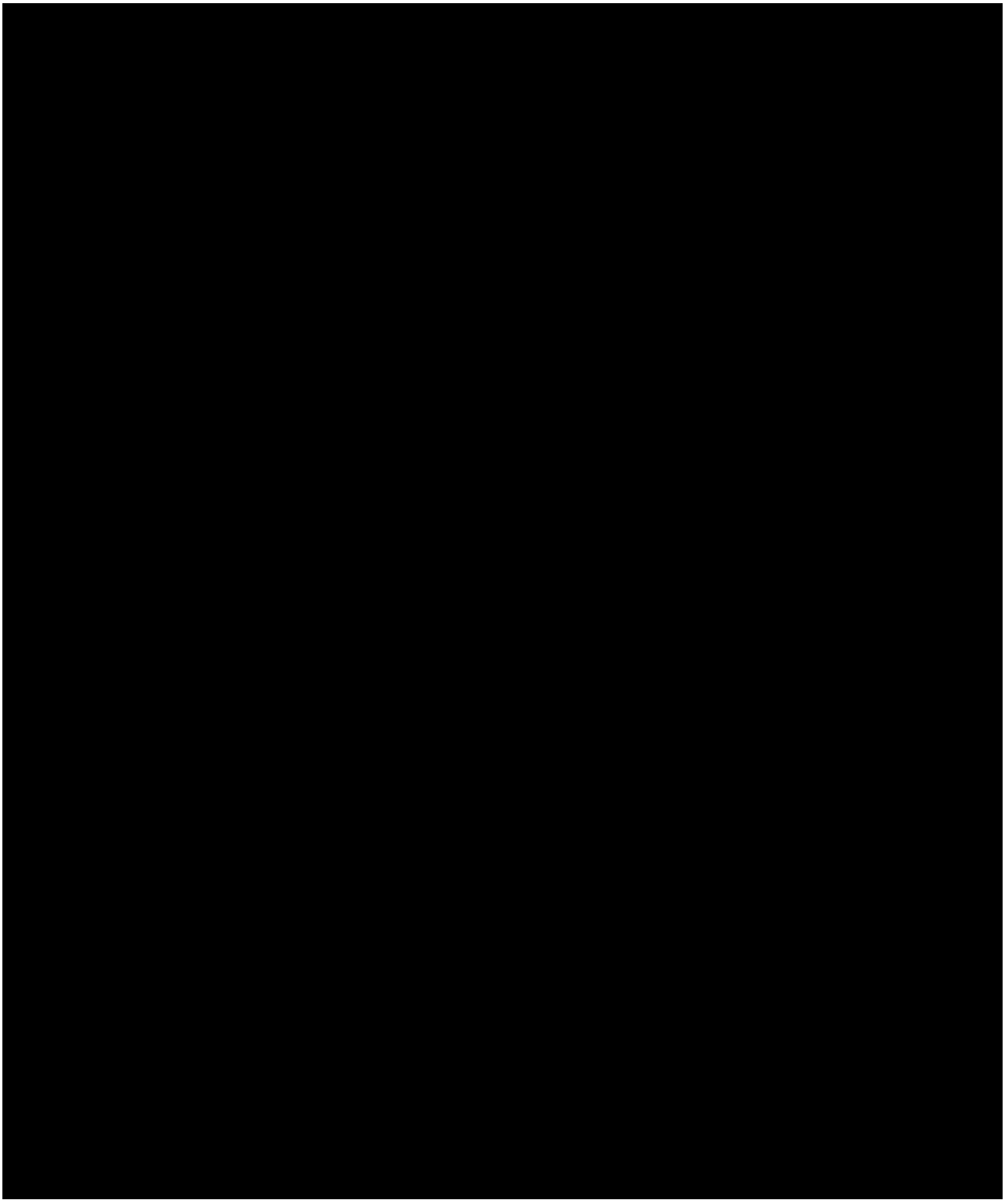

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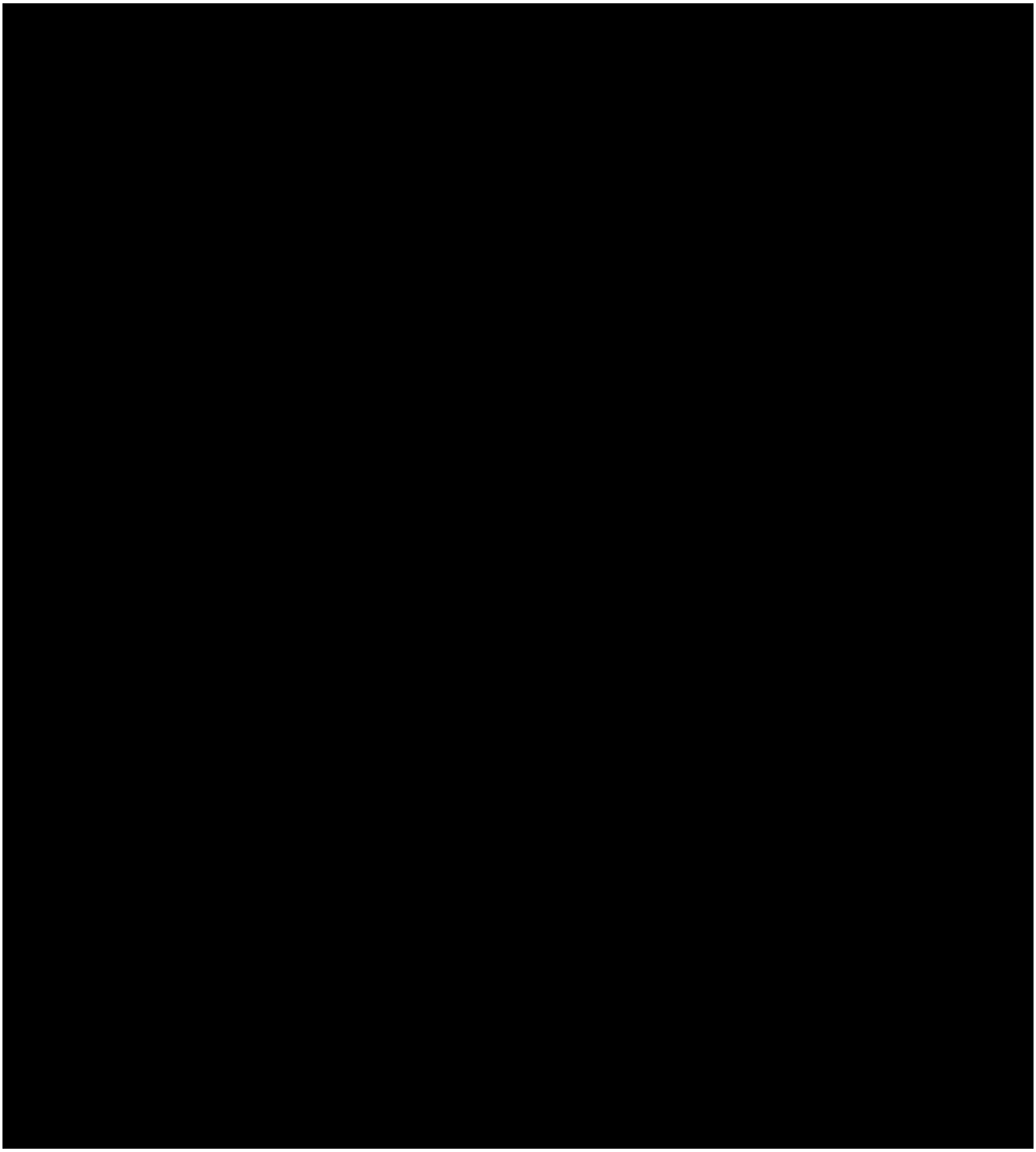

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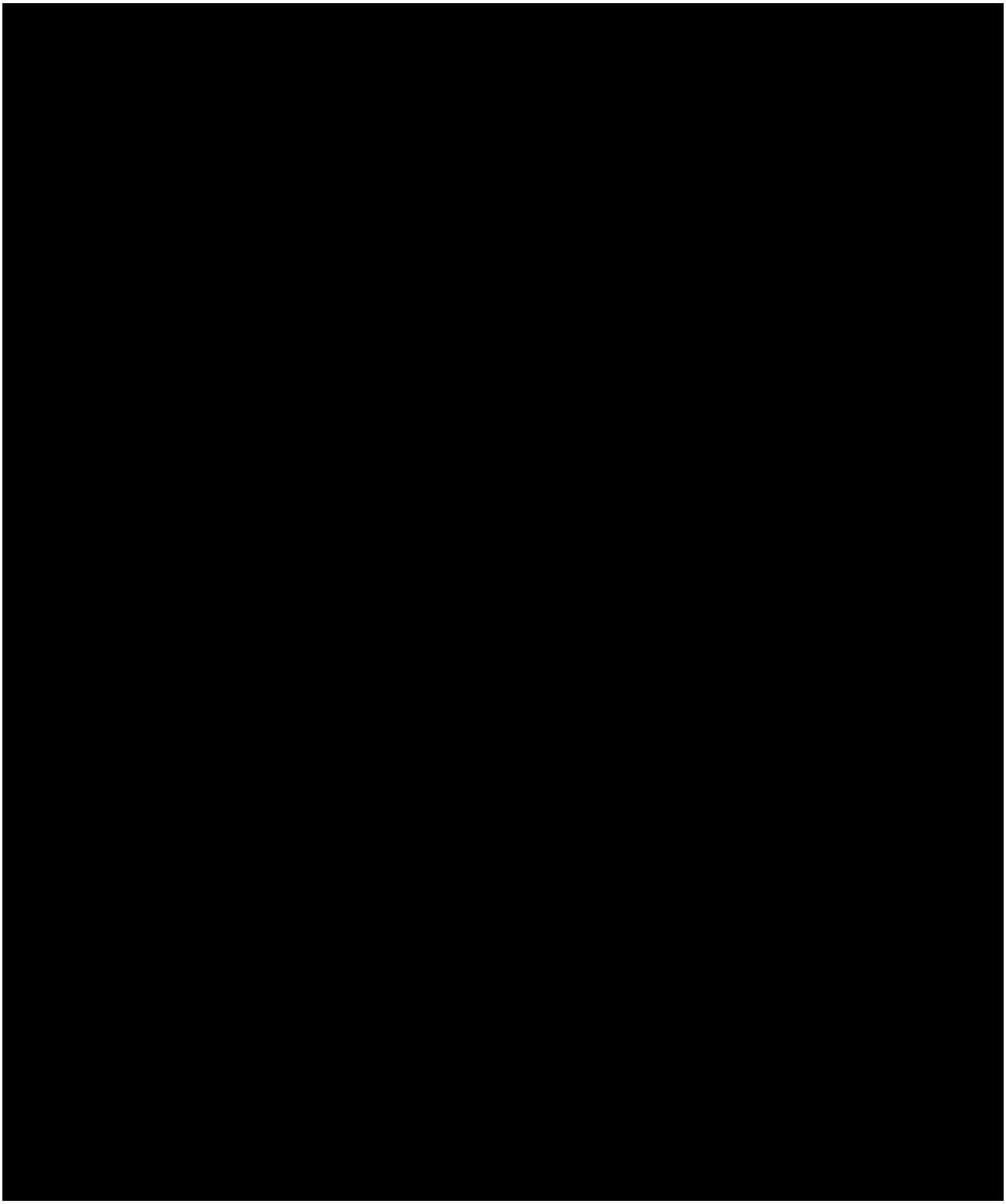

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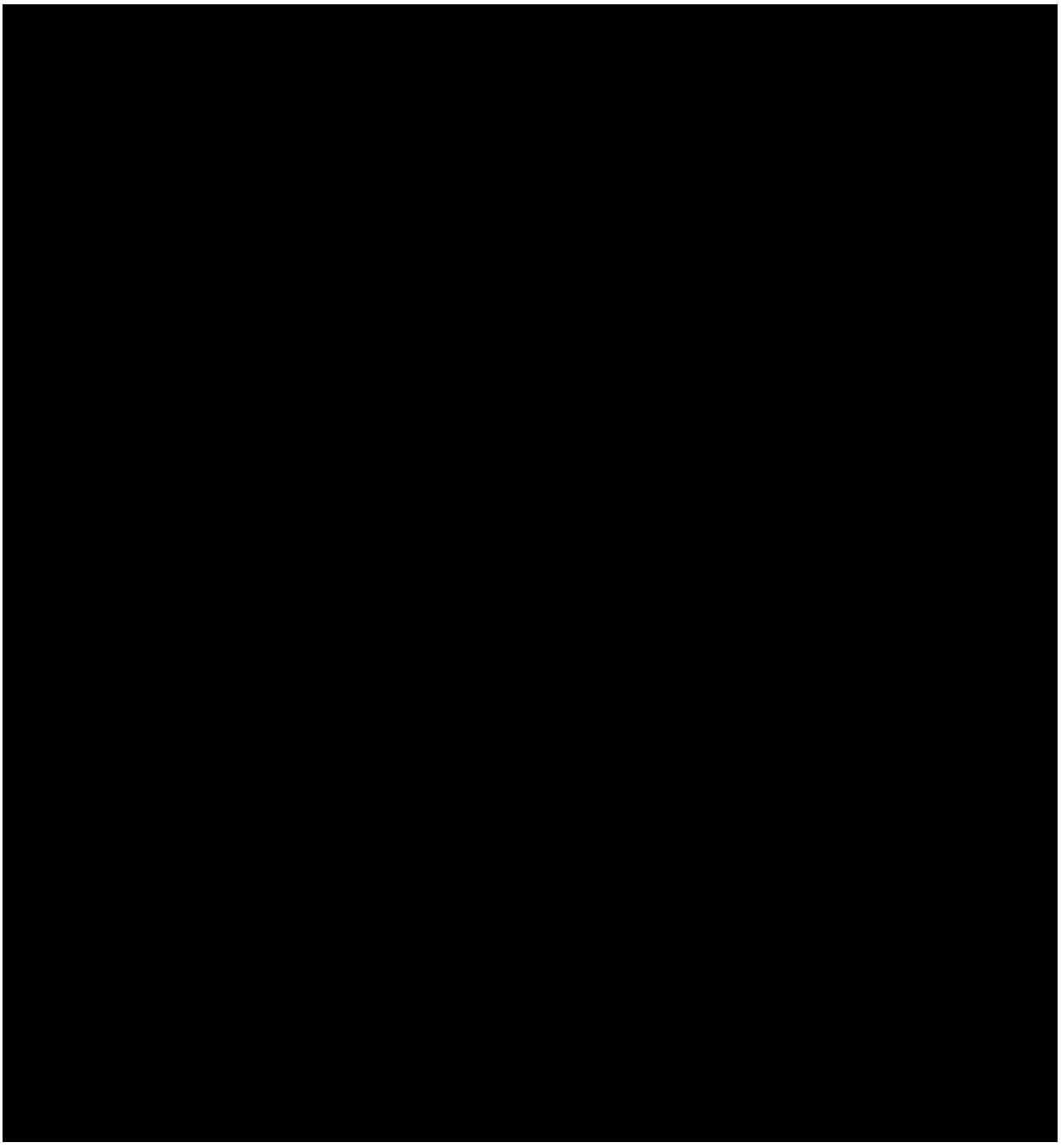

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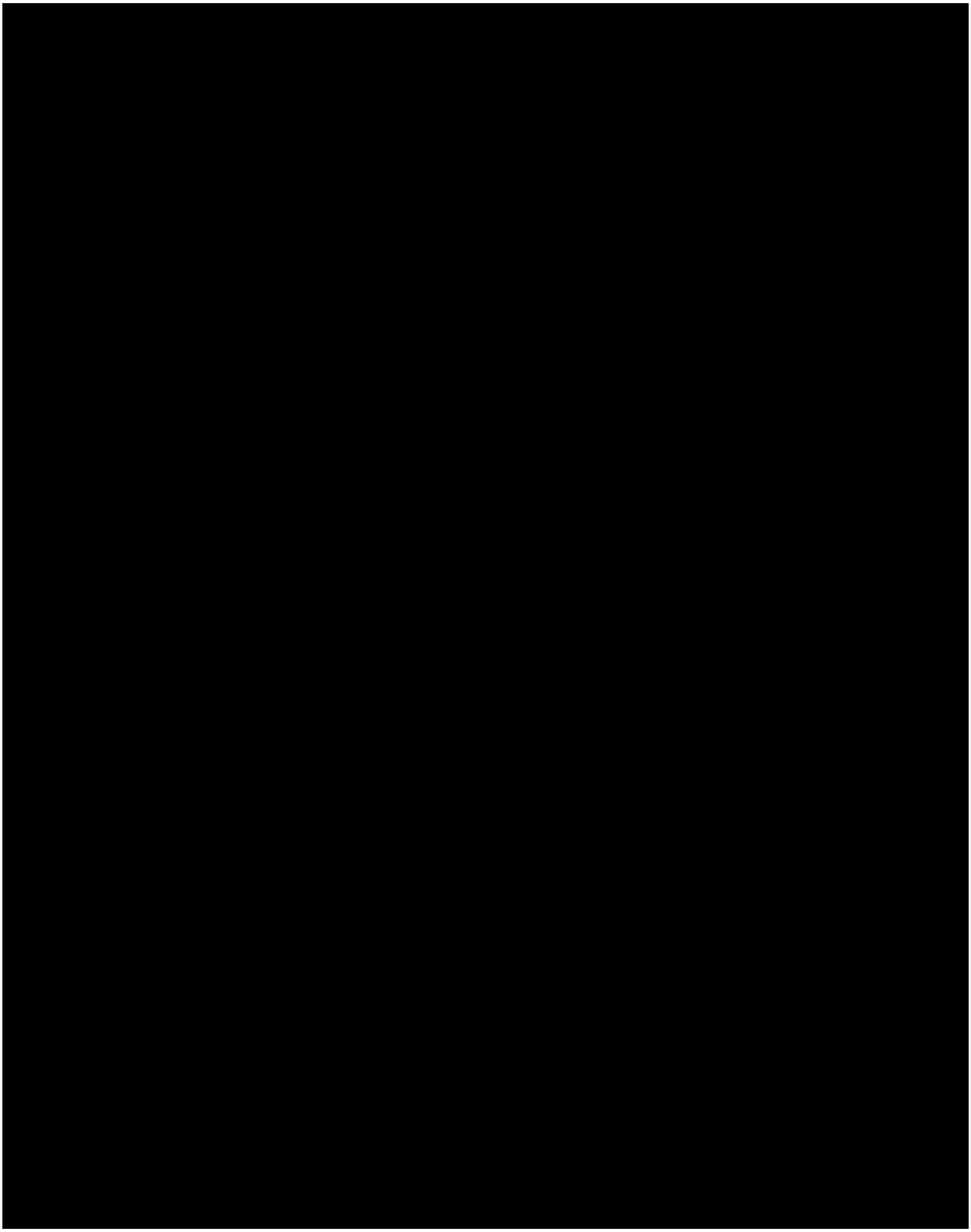

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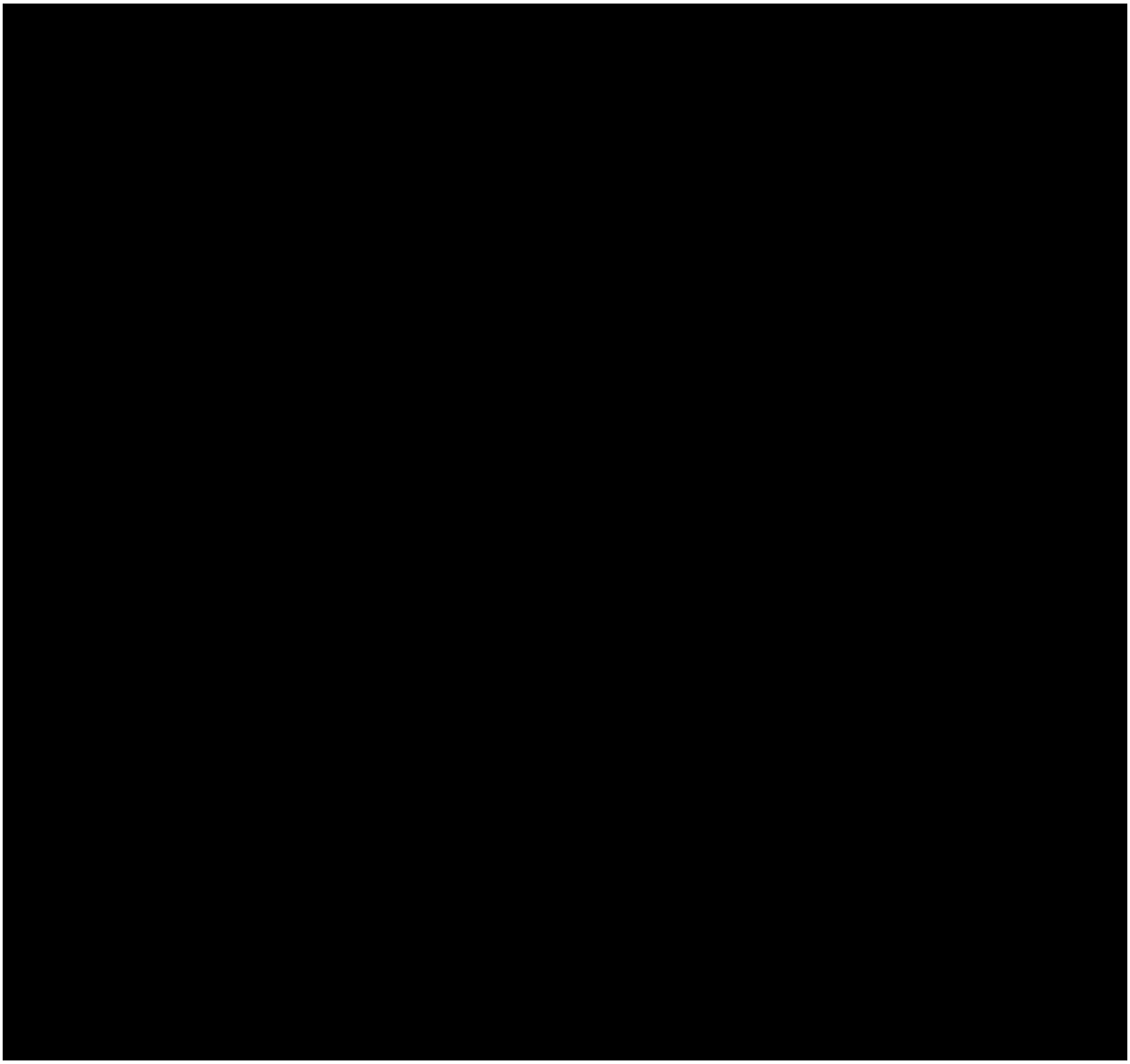

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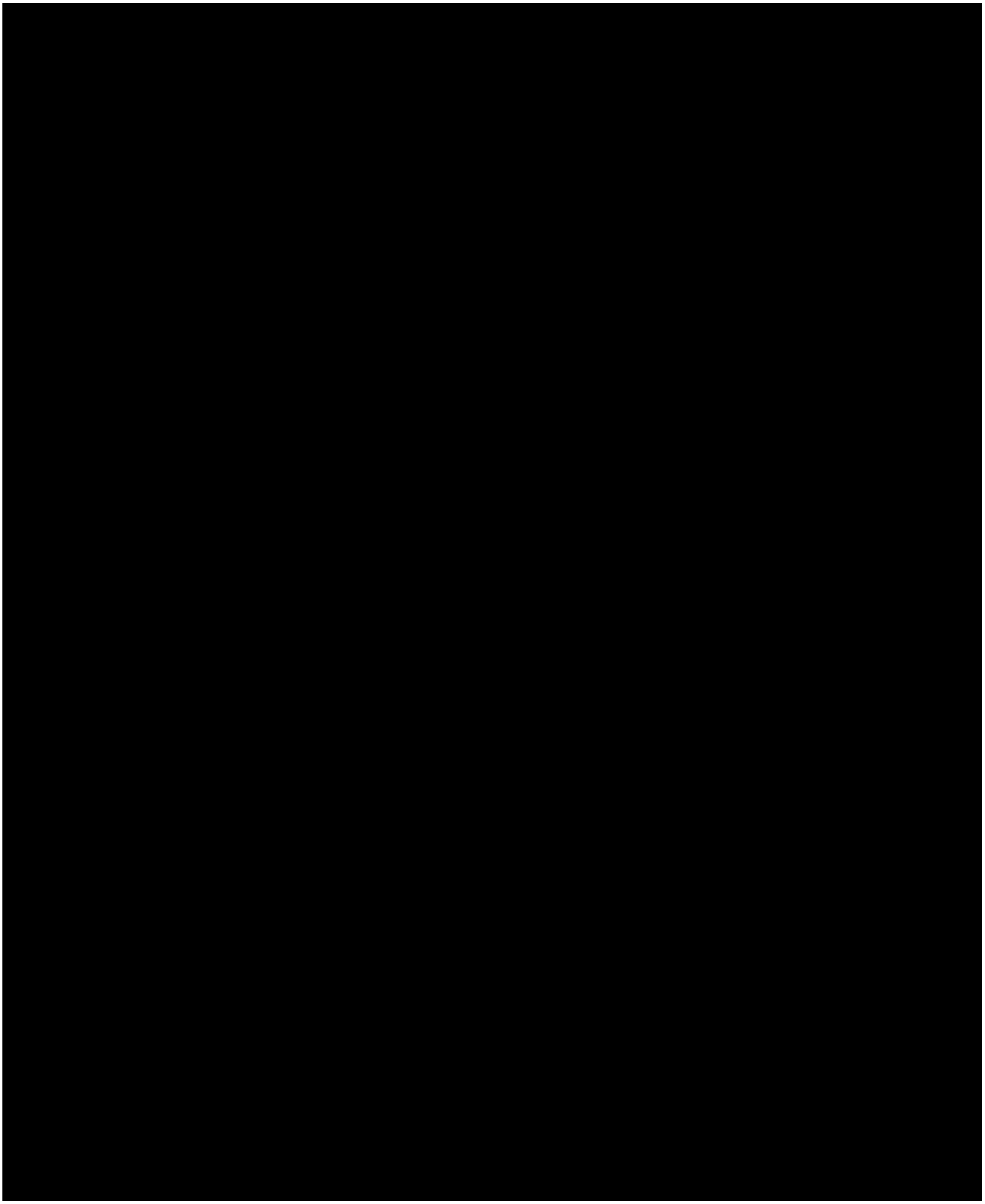

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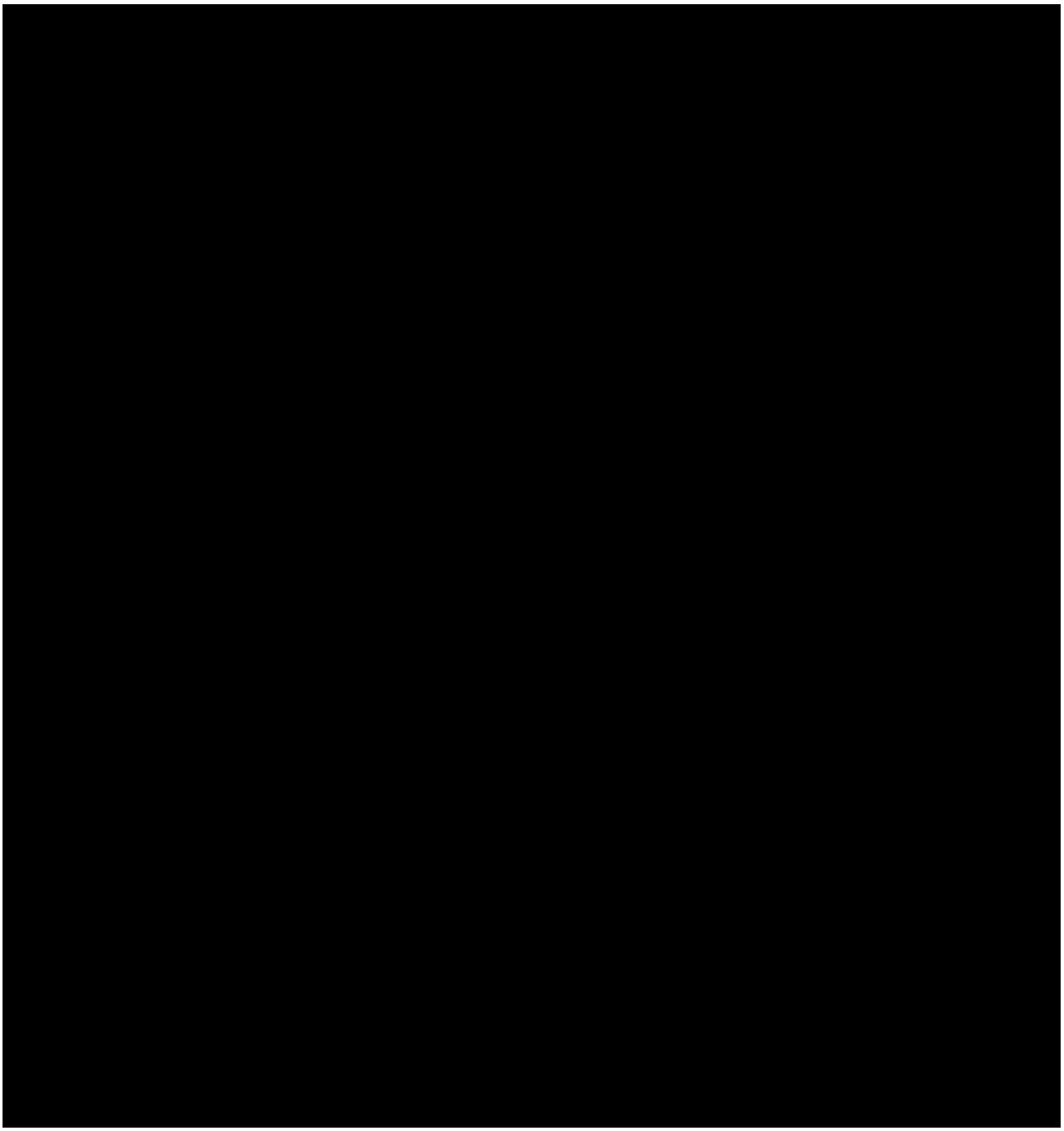

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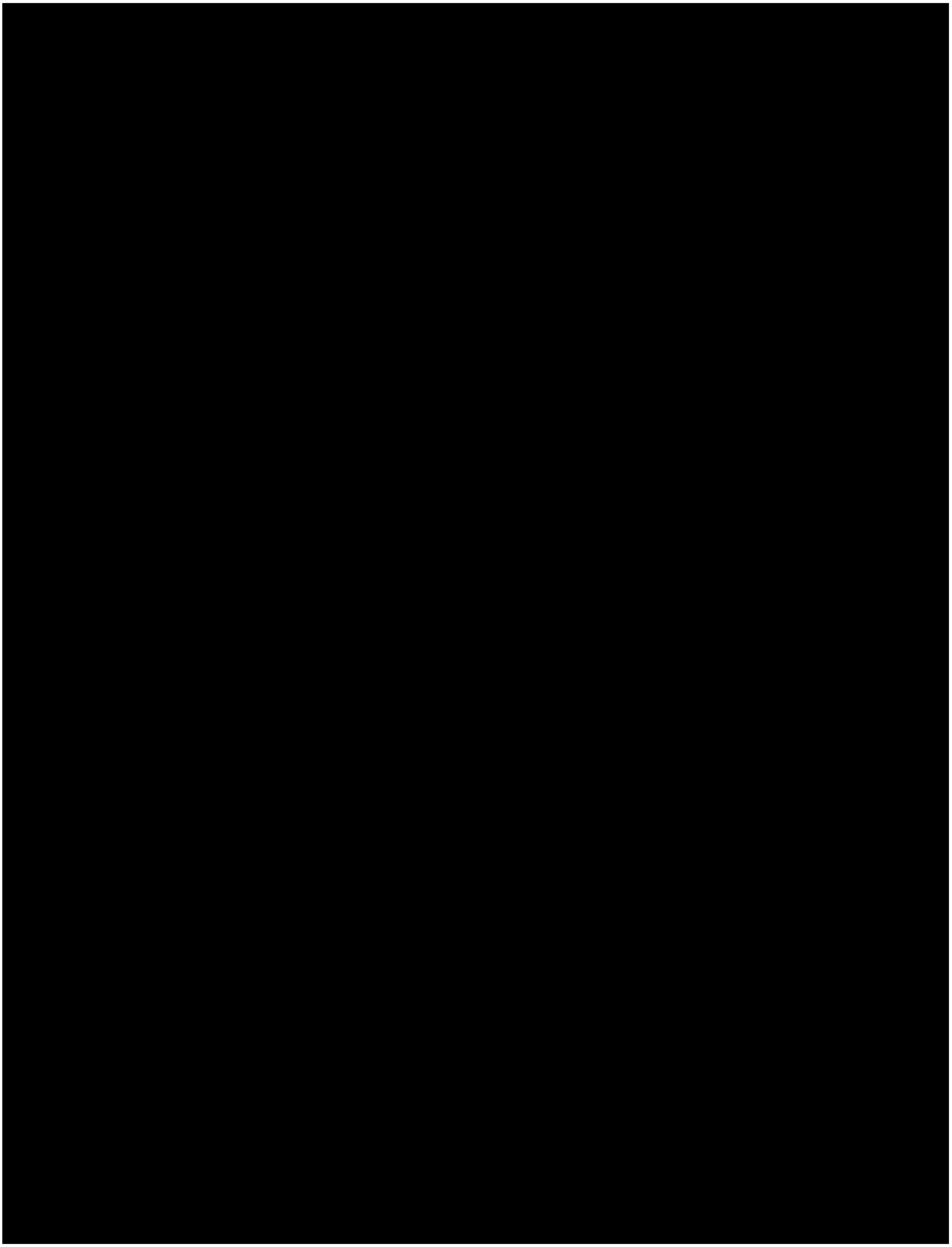

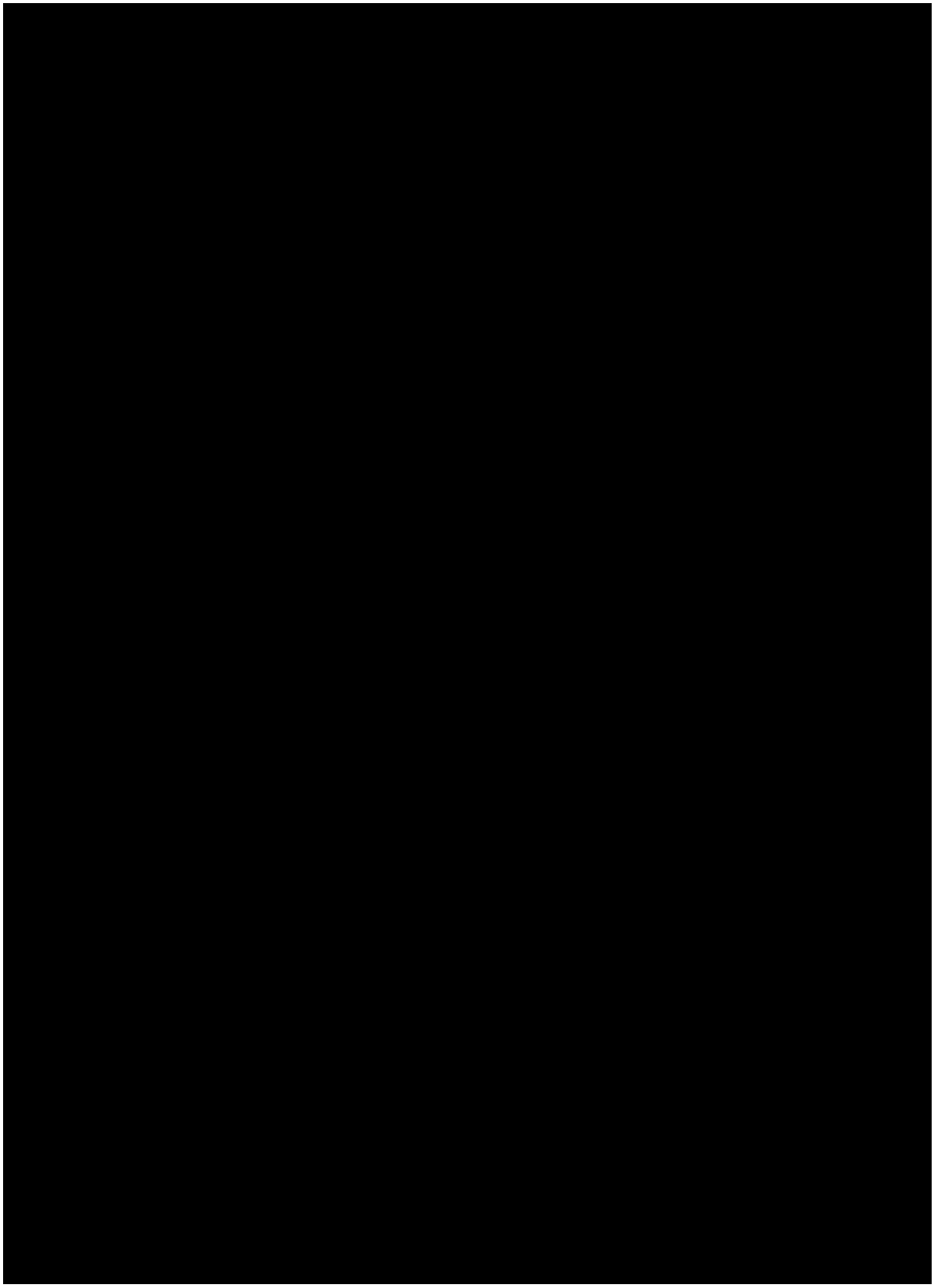

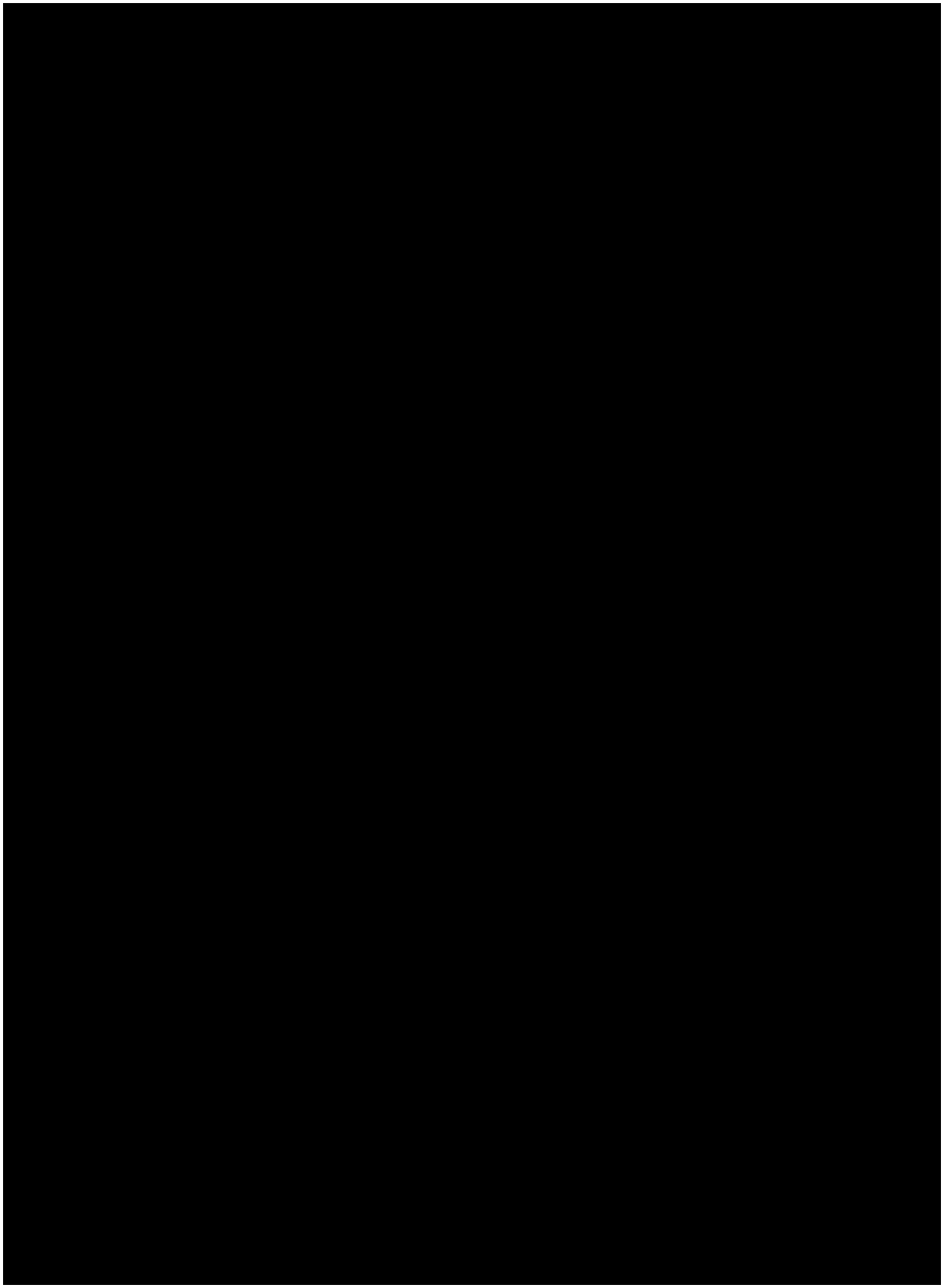

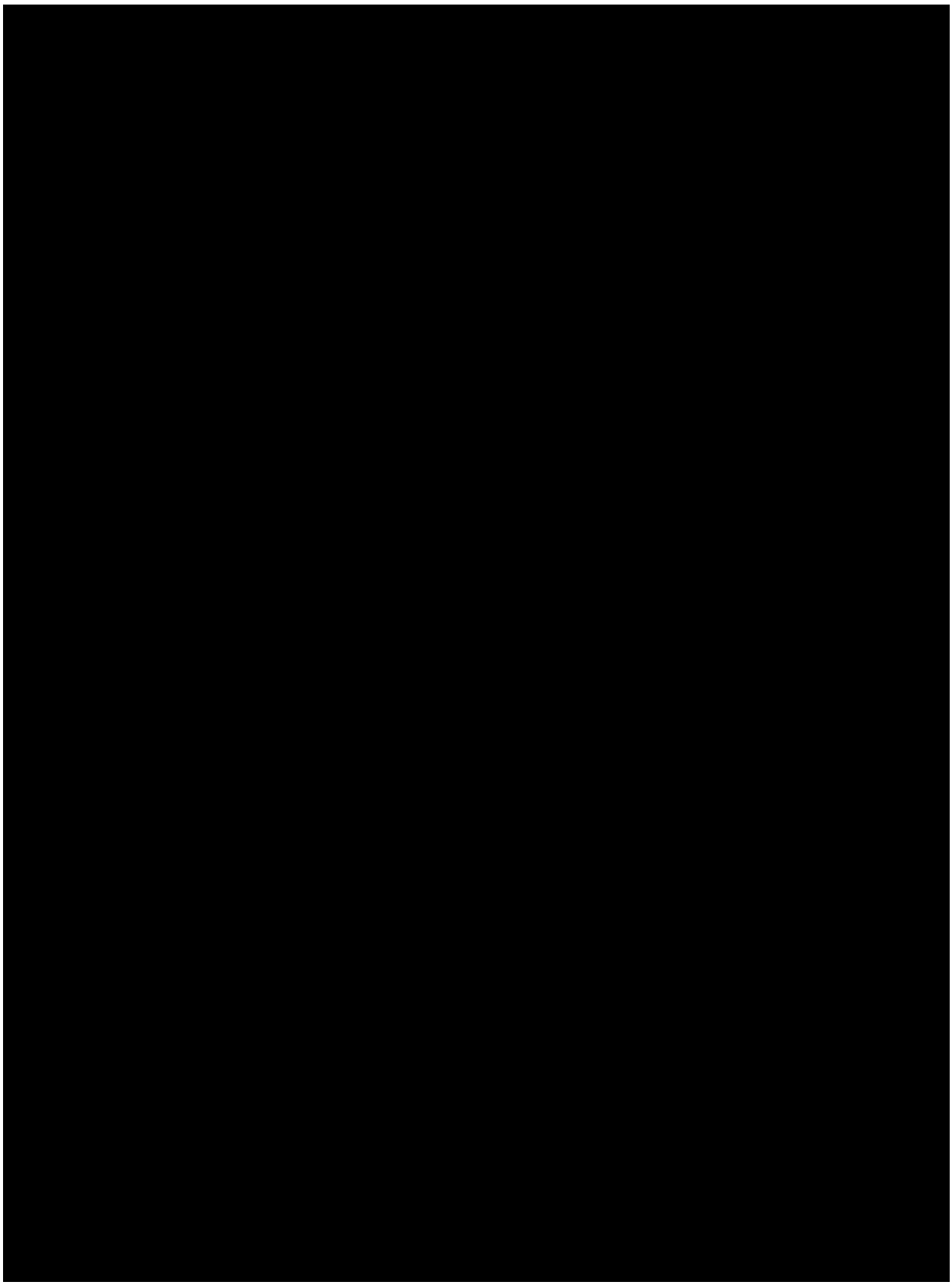

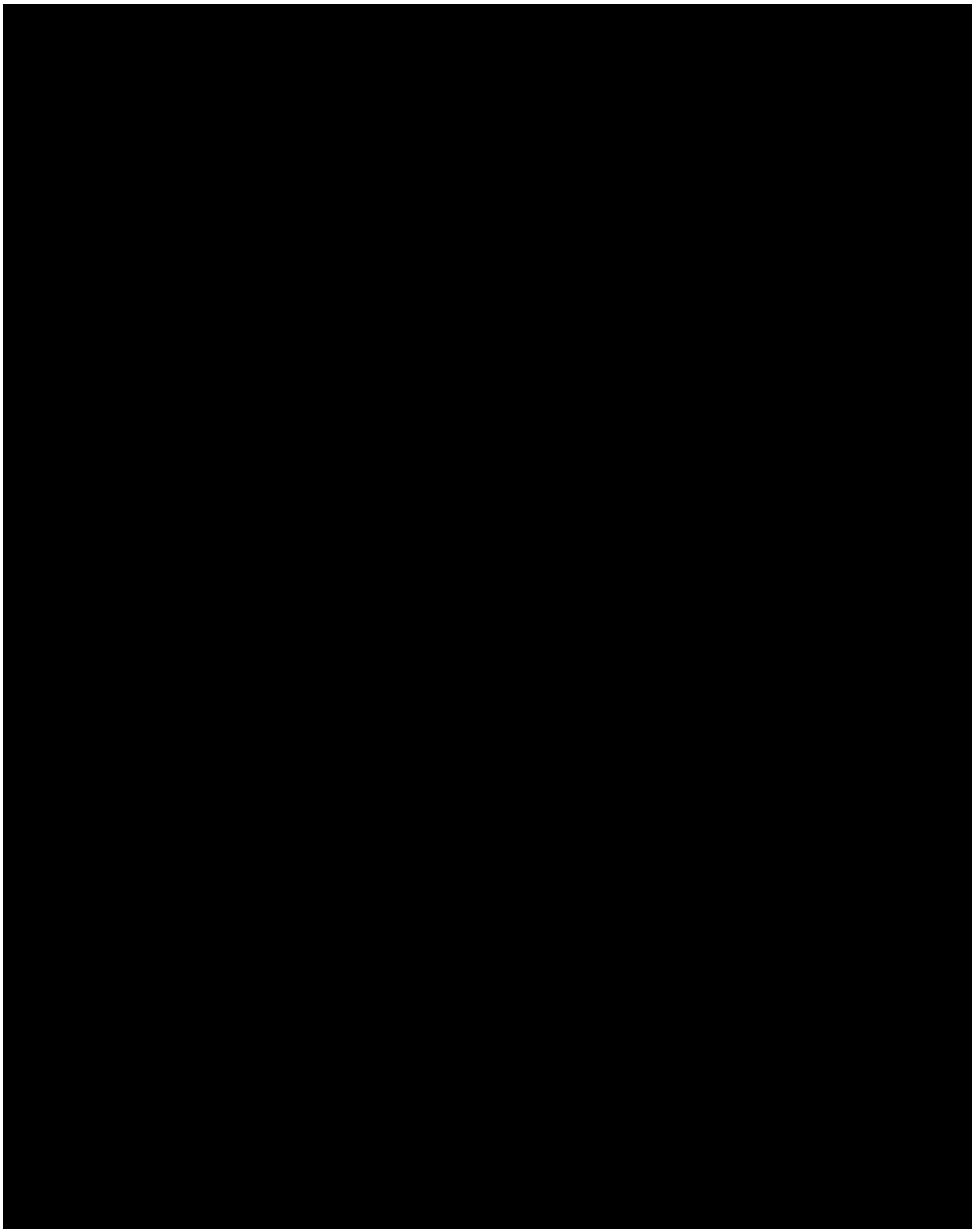

APPENDIX N. SCREENING SYMPTOM FORM

Instructions to Subjects: Please answer all questions to the best of your ability, based on your memory **over the past 7 days (1 week)**. There is no right or wrong answer.

1. During the past 7 days, how severe were your worst night sweats (or feeling hot or flushed) due to MF?	0 (Absent) 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
2. During the past 7 days, how severe was your worst itchiness due to MF?	0 (Absent) 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
3. During the past 7 days, how severe was your worst abdominal discomfort (feel uncomfortable, pressure or bloating) due to MF?	0 (Absent) 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
4. During the past 7 days, how severe was your worst pain under the ribs on the left side due to MF?	0 (Absent) 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
5. During the past 7 days, what was the worst feeling of fullness (early satiety) you had after beginning to eat, due to MF?	0 (Absent) 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
6. During the past 7 days, how severe was your worst bone or muscle pain due to MF (diffuse, not joint or arthritis pain)?	0 (Absent) 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)
7. During the past 7 days, what was the worst degree of inactivity (including work and social activities) you had due to MF?	0 (Absent) 1 2 3 4 5 6 7 8 9 10 (Worst Imaginable)

Investigators/Site Staff:

Please complete the table below to confirm the criterion used to confirm the subject's eligibility in the trial based on an assessment of his/her active symptoms of myelofibrosis.

ELIGIBILITY CRITERION	CONFIRMATION
A symptom score of at least 5 on at least 1 of the symptoms	□ Yes □ No
A symptom score of 3 or greater on at least 2 of the symptoms	□ Yes □ No

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