Official Title of Study:

An Open-label, Multi-center Extension Study to Evaluate the Long-term Safety and Efficacy of Deucravacitinib in Participants with Moderate to Severe Crohn's Disease or Moderate to Severe Ulcerative Colitis

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CLINICAL PROTOCOL IM011077

An Open-label, Multi-center Extension Study to Evaluate the Long-term Safety and Efficacy of Deucravacitinib in Participants with Moderate to Severe Crohn's Disease or Moderate to Severe Ulcerative Colitis

Short Title: Long-term Safety and Efficacy of Deucravacitinib in Participants with Crohn's Disease or Ulcerative Colitis

Protocol Amendment 01

Incorporates Administrative Letters 01 and 02

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DOCUMENT HISTORY

Document	Date of Issue	Summary of Change
Protocol Amendment 01	04-Mar-2022	The purpose for Protocol Amendment 01 is to include the following updates: • Added individual Day 1 Schedule of Activities (Section 2) tables for each parent study. • Clarified study procedures that may need to be repeated based on the timing of entering Study IM011077. • Clarified Prohibited Prior and Concomitant Medications. • Clarified Exclusion Criteria. • Clarified timing for first dose of study treatment in Study IM011077. • [redacted] • Added additional Hematology testing for routine safety laboratory assessments. • Added additional investigational laboratory testing for participants with abnormal Hematology results that meet the discontinuation criteria. • Added information to clarify the collection of Adverse Events and Medical History. • Added preventative care for inflammatory bowel disease (IBD) to the Safety Section. • Updated BMS-986165 to "deucravacitinib" throughout document. • Incorporated HEOR editorial updates. • Revised or removed language related to Screening, Randomization, and Lead-In Period to align with the protocol design. • Added language for periodic surveillance for IBD-associated colonic dysplasia or screening for colorectal carcinoma.
Administrative Letter 02	15-Sep-2021	Study personnel updated
Administrative Letter 01	23-Feb-2021	• Corrected erroneous cross-references to the Schedule of Activities in Sections 9.1.6 and 9.4.4 • Clarifies typographical error in Section 9.1.6
Original Protocol	25-Nov-2020	Not applicable

OVERALL RATIONALE FOR PROTOCOL AMENDMENT 01:

The purpose for Protocol Amendment 01 is to include the following updates:

- Added individual Day 1 Schedule of Activities (Section 2) tables for each parent study.
- Clarified study procedures that may need to be repeated based on the timing of entering Study IM011077.
- Clarified Prohibited Prior and Concomitant Medications.
- Clarified Exclusion Criteria.
- Clarified timing for first dose of study treatment in Study IM011077.
- [redacted]
- Added additional Hematology testing for routine safety laboratory assessments.
- Added additional investigational laboratory testing for participants with abnormal Hematology results that meet discontinuation criteria.
- Added information to clarify the collection of Adverse Events and Medical History.
- Added preventative care for inflammatory bowel disease (IBD) to the Safety Section.
- Updated BMS-986165 to "deucravacitinib" throughout document.
- Incorporated health economics and outcomes research editorial updates.
- Revised or removed language related to Screening, Randomization, and Lead-In Period to align with the protocol design.
- Added language for periodic surveillance for IBD-associated colonic dysplasia or screening for colorectal carcinoma.

SUMMARY OF KEY CHANGES FOR PROTOCOL AMENDMENT 01		
Section Number & Title	**Description of Change**	**Brief Rationale**
Title Page	Updated the Name and Contact information of the Medical Monitor and Clinical Scientist.	Updated per Administrative Letter 02.
Section 2: Schedule of Activities	• Added Table 2-1: Day 1 Procedural Outline IM011077 From Parent Study IM011023 - Crohn's Disease. • Deleted Day 1 column from Table 2-2: Year 1 Procedural Outline (IM011077) - Crohn's Disease.	• To clarify Day 1 procedures for participants from parent study IM011023. • Deleted column because we made a separate table for Day 1.

SUMMARY OF KEY CHANGES FOR PROTOCOL AMENDMENT 01		
Section Number & Title	**Description of Change**	**Brief Rationale**
	• Added Table 2-4: Day 1 Procedural Outline IM011077 From Parent Study IM011024 - Ulcerative Colitis. • Added Table 2-5: Day 1 Procedural Outline IM011077 From Parent Study IM011027 - Ulcerative Colitis. • Deleted Day 1 column from Table 2-6: Year 1 Procedural Outline (IM011077) - Ulcerative Colitis.	• To clarify Day 1 procedures for participants from parent study IM011024. • To clarify Day 1 procedures for participants from parent study IM011127. • Deleted column because we made a separate table for Day 1.
Section 5.1.1: Qualification and Enrollment into Study	Added text for clarification of same-day transition between the parent study end of treatment and Day 1 of Study IM011077. As well as. deleted text regarding the number of days from which a participant would be ineligible for this study after last visit in the prior study. Added text clarifying that certain procedures may or may not be repeated depending on timing of entering Study IM011077, after informed consent.	To clarify the protocol-allowed number of days between the parent study End of Treatment Visit and Study IM011077. To clarify if the Day 1 procedures need to be repeated as per the number of days between the parent study End of Treatment Visit and Day 1.
Section 5.1.2: Treatment Period	Added text stating that the morning dose of study treatment on Day 1, should be taken at the site from Study IM011-077. Added additional information for participants who wish to	To clarify Day 1 dosing. For accuracy and to ensure that participants who discontinue the study complete the safety follow-up visit.

SUMMARY OF KEY CHANGES FOR PROTOCOL AMENDMENT 01		
Section Number & Title	**Description of Change**	**Brief Rationale**
	discontinue from study treatment.	
Section 5.1.3: Follow-up Period	Added additional information for participants who wish to discontinue from study treatment.	For accuracy and to ensure that participants who discontinue the study complete the safety follow-up visit.
Section 5.1.4: Treatment Failure	Added a fifth definition of treatment failure to exclude participants requiring [redacted]	Added to further specify treatment failure.
Section 6.2: Exclusion Criteria	• Deleted text under criterion 1) b). • Added and deleted text under criterion 3) a) for antibiotic use and deleted text under criterion 3) b). • Added text under criteria 4) a) and deleted text under 4) c) and d) and added additional criterion 4) e). • Deleted text under criteria 5) a), c), and d) and added text under criterion 5) e).	• 1) b) Deleted criterion does not apply to extension study. • 3) a) To clarify prophylactic antibiotic use should be discussed with the BMS Medical Monitor/designee. • 3) b) Deleted criterion, does not apply to extension study. • 4) a) To clarify prohibited concomitant medications are exclusionary until Day 1 • 4) c) and d) Deleted criteria, does not apply to extension study. • 5) a) [redacted] • 5) c) Deleted criterion, does not apply to extension study. • 5) d) Deleted criterion, does not apply to extension study.

SUMMARY OF KEY CHANGES FOR PROTOCOL AMENDMENT 01		
Section Number & Title	**Description of Change**	**Brief Rationale**
	• Added text under criteria 7) a).	• 5) e) To clarify laboratory testing at the second to last visit in the parent study or most current result available prior to Day 1 needs to be assessed for exclusion criterion. • 7) a) To clarify participants with Nonmelanoma Skin Cancer are not excluded.
Section 6.4: Enrollment Failures	Replaced "screen" for "enrollment."	For accuracy since study does not have a Screening Period.
Section 6.4.1: Retesting During Lead-in Period	Deleted this section.	For accuracy as study does not have a Lead-in Period.
Section 7.2: Method of Treatment Assignment	Adjusted the text describing the number assignment process for participants.	To eliminate repetitious information stated in Section 7.2.
Section 7.7.1: Prohibited Treatments	Added text to Table 7.7.1-1: Summary of Prohibited Concomitant Medications.	To clarify in the notes the timing and criteria of prohibited concomitant medications.
Section 8.1: Discontinuation From Study Treatment	Added text to clarify laboratory test result abnormalities regarding Hemoglobin levels.	For participant safety.
Section 8.1.1: Temporary Discontinuation From Study Treatment	Deleted text regarding restarting study treatment.	To eliminate repetitious information stated in Section 8.1.1.
Section 9: Study Assessments and Procedures	Deleted text referring to screening evaluations. Added text describing the information collected from this study will be used to help understand certain health conditions.	For accuracy. Study does not have a Screening Period. To clarify how the study data collected will be used.

SUMMARY OF KEY CHANGES FOR PROTOCOL AMENDMENT 01		
Section Number & Title	**Description of Change**	**Brief Rationale**
Section 9.1.4.2: Ulcerative Colitis	Added text elaborating when the modified Mayo score is to be calculated.	Added to clarify as to which study's end of treatment visit may be used.
[redacted]		
Section 9.1.6: Laboratory Assessments	Added text stating additional tests that are recommended to exclude infectious causes of disease exacerbation.	Updated per Administrative Letter 01.
Section 9.2.1: Time Period and Frequency for Collecting AE and SAE Information	Added information regarding the timepoints at which adverse events (AEs) will be collected and reported.	For clarity.
Section 9.4.1: Preventative Care	Added new section for up-to-date preventative care for IBD.	For participant safety due to length of study.
Section 9.4.2: Physical Examinations	Added text referring to schedules for targeted physical examination in Section 2.	To clarify when targeted physical examinations should be performed during the study and added skin examination to the targeted physical examination.
Section 9.4.3: Vital Signs	Added information and description of vital signs to be collected.	To clarify method for collecting vital signs.
Section 9.4.5: Clinical Safety Laboratory Assessments	Added more Hematology Parameters to be assessed in Table 9.4.5-1: Summary of Laboratory Parameters Used to Assess Clinical Safety.	For participant safety.
Section 9.4.7: Imaging Safety Assessment	Added text referencing Section 9.4.1 for periodic surveillance for IBD associated colonic dysplasia or screening for colorectal carcinoma.	For participant safety.

SUMMARY OF KEY CHANGES FOR PROTOCOL AMENDMENT 01		
Section Number & Title	**Description of Change**	**Brief Rationale**
Section 9.5: Pharmacokinetics	Added new footnotes to Table 9.5-1: Pharmacokinetic Sampling Schedule for All Participants (Study IM011077).	To clarify Day 1 dosing and the drawing of the pre-dose samples.
[redacted]		
Section 10.4.2: Safety Analyses	Deleted text stating that "participants will be summarized according to the treatment they receive in their parent trial."	The statement was redundant.
Section 10.4.2.1: Adverse Events	Added information regarding the timepoints at which AEs will be collected and reported.	For clarity.
Appendix 2: Study Governance Considerations	Updated language for monitoring.	This was done to align with standard language updates to the Protocol Model Document.
[redacted]		

SUMMARY OF KEY CHANGES FOR PROTOCOL AMENDMENT 01		
Section Number & Title	**Description of Change**	**Brief Rationale**
		[redacted]
All	Changed the drug name from "BMS-986165" to "deucravacitinib" here and throughout the protocol.	Updated as per the Deucravacitinib Usage Guidance (updated January 2021).

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1 SYNOPSIS

Protocol Title: An Open-label, Multi-center Extension Study to Evaluate the Long-term Safety and Efficacy of Deucravacitinib in Participants with Moderate to Severe Crohn's Disease or Moderate to Severe Ulcerative Colitis

Short Title: Long-term Safety and Efficacy of Deucravacitinib in Participants with Crohn's Disease or Ulcerative Colitis

Study Phase: 2

Rationale:

IM011077 is an open-label, long-term extension study designed to evaluate the long-term safety and efficacy of deucravacitinib (BMS-986165) 6 mg twice daily (BID) in participants who have previously been enrolled in a Phase 2 deucravacitinib study for moderate to severe Crohn's disease (CD) (Study IM011023) or moderate to severe ulcerative colitis (UC) (Studies IM011024 and IM011127).

[redacted]

Study Population: Adults with CD or UC who have completed participation in a preceding study, including Studies IM011023, IM011024, or IM011127, may be eligible to enroll in Study IM011077.

Objectives and Endpoints - Crohn's Disease

Objective	Endpoint
Primary	
• To assess the safety and tolerability of long-term use of deucravacitinib in participants with moderate to severe CD.	• Number and proportion of participants experiencing AEs, SAEs, AEs leading to study discontinuation, and AEIs. • Number and proportion of participants experiencing abnormalities in laboratory testing, ECG, and vital sign parameters over time. • Changes from Day 1 for laboratory testing, ECG, and vital signs.
Exploratory	
[redacted]	

Objective	Endpoint
[redacted]	

Abbreviations: AE = adverse event; AEI = adverse event of interest; CD = Crohn's disease; ECG = electrocardiogram; [redacted] SAE = serious adverse event; [redacted]

Objectives and Endpoints - Ulcerative Colitis:

Objective	Endpoint
Primary	
• To assess the safety and tolerability of long-term use of deucravacitinib in participants with moderate to severe UC.	• Number and proportion of participants experiencing AEs, SAEs, AEs leading to study discontinuation, and AEIs. • Number and proportion of participants experiencing abnormalities in laboratory testing, ECG, and vital sign parameters over time. • Changes from baseline for laboratory testing, ECG, and vital signs.
Exploratory	

Objective	Endpoint
[redacted]	

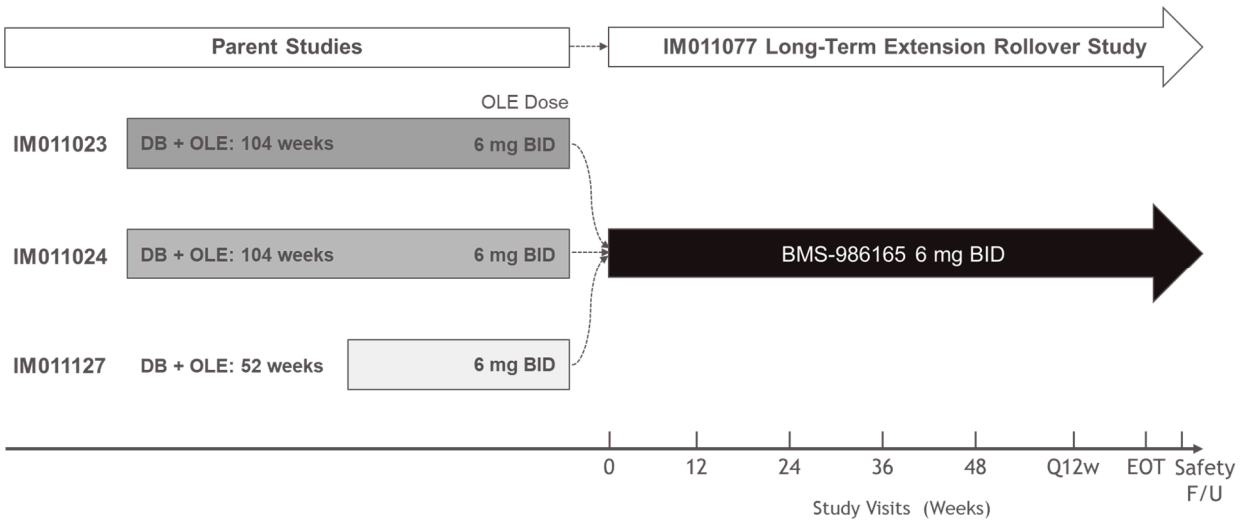
Abbreviations: AE = adverse event; AEI = adverse event of interest; ECG = electrocardiogram; [redacted] SAE = serious adverse event; [redacted] UC = ulcerative colitis; [redacted]

Overall Design:

This is an open-label, multi-center study to evaluate the long-term safety and tolerability of deucravacitinib in participants with moderate to severe CD or moderate to severe UC who have completed one of the applicable parent studies (IM011023, IM011024, and IM011127), are likely to safely derive a clinical benefit from ongoing treatment with deucravacitinib, and are willing and able to participate. Participants will receive deucravacitinib 6 mg BID by mouth (PO) in a tablet formulation.

The study design schematic is presented in the figure below.

Study Design Schematic



Abbreviations: BID = twice daily; BMS-986165 = deucravacitinib; DB = double-blind; EOT = end of treatment; F/U = follow-up; OLE = open-label extension; Q12W = every 12 weeks.

Number of Participants: Approximately 300 participants are expected to rollover from the parent studies into Study IM011077. All participants must have completed 1 of the parent studies (Studies IM011023, IM011024, or Study IM011127) and must meet all eligibility criteria.

Treatment Arms and Duration:

Participants will receive deucravacitinib 6 mg BID PO in a tablet formulation.

The duration of the study is approximately 296 weeks (2,072 day) as follows:

- Qualification and enrollment: up to 28 days
- Open-label study period: 288 weeks (2,017 days)
- Post-treatment follow-up period: 4 weeks (28 days)

Study Treatment:

Study Drug for IM011077		
Medication	**Potency**	**IP/Non-IP**
Deucravacitinib (BMS-986165)	6 mg	IP

Abbreviation: IP = Investigational Product.

Data Monitoring Committee: Yes

2 SCHEDULE OF ACTIVITIES

Table 2-1: Day 1 Procedural Outline IM011077 From Parent Study IM011023 - Crohn's Disease

Procedure	Day 1		Notes
Visit Window (n days from parent study EOT)	**< 14**	**≥ 14 through ≤ 28** [a]	
Eligibility and Disease Assessments			
Informed Consent	X	X	Appendix 2 (Study Governance)
Inclusion/Exclusion Criteria	X	X	Section 6 (Study Population)
Obtain Participant Number (IRT)	X	X	Section 7.2 (Method of Treatment Assignment)
Tobacco/e-Cigarette Use	X	X	Section 6.3.2 (Tobacco and e-Cigarettes)
Medical History[b]	X	X	Section 9.2.1
Concomitant Medication Use [c]	PSEOT [k]	X	Section 7.7 (Concomitant Therapy)
Physical Examination			
Physical Examination	PSEOT [k]	X	Section 9.4.2 (Physical Examinations)
Vital Signs (heart rate, blood pressure, temperature)	PSEOT [k]	X	Includes body temperature and seated blood pressure and heart rate. Blood pressure and heart rate should be measured after the participant has been resting quietly for at least 5 minutes.
Height	X	X	The height measurement should not be collected at Day 1. This height measurement should be carried over from the parent study screening visit and entered into Study IM011077 database (eg, eCRF).
Weight	PSEOT [k]	X	
[redacted]			

Table 2-1: Day 1 Procedural Outline IM011077 From Parent Study IM011023 - Crohn's Disease

Procedure	Day 1		Notes
Visit Window (n days from parent study EOT)	**< 14**	**≥ 14 through ≤ 28** [a]	
ECG	PSEOT [k]	X	Section 9.4.4 (Electrocardiograms)
Blood, Urine, and Fecal Tests			
Hematology and Chemistry	PSEOT [k]	X	Section 9.4.5 (Clinical Safety Labs)
Calculate eGFR	X	X	Exclusion Criterion 5(e)(ii)
Coagulation	PSEOT [k]	X	
Fasting Lipid Panel and Glucose	PSEOT [k]	X	Section 9.4.5 (Clinical Safety Labs)
Tuberculosis Risk Assessment [redacted]	X	X	Appendix 5 (TB)
[redacted]			
FSH	X	X	Appendix 4
Urine Pregnancy Test [f]	PSEOT [k]	X	Section 9.2.5 (Pregnancy); Section 9.4.5 (Clinical Safety Labs); Appendix 4
Urinalysis and Urine Chemistry	X	X	Section 9.4.5 (Clinical Safety Labs)
Pharmacokinetic Assessments	PSEOT [k]	X	See Table 9.5-1 for sample collection details.
[redacted]			

Table 2-1: Day 1 Procedural Outline IM011077 From Parent Study IM011023 - Crohn's Disease

Procedure	Day 1		Notes
Visit Window (n days from parent study EOT)	**< 14**	**≥ 14 through ≤ 28** [a]	
Endoscopy and Endoscopic Biopsies			
Endoscopy (ileocolonoscopy)	PSEOT		Section 9.1.1 (Endoscopies and Biopsies)
[redacted]			
Additional Efficacy Assessments			
[redacted]			
Health-Outcomes Assessments			
Register and Train Participant on Slate Device	X		
[redacted]			
Safety Assessment (in addition to the above)			
SAE Assessment	PSEOT [k]	X	Section 9.2 (AEs); Appendix 3
AE Assessment	PSEOT [k]	X	Section 9.2 (AEs); Appendix 3

Table 2-1: Day 1 Procedural Outline IM011077 From Parent Study IM011023 - Crohn's Disease

Procedure	Day 1		Notes
Visit Window (n days from parent study EOT)	**< 14**	**≥ 14 through ≤ 28** [a]	
Study Treatment			
Dispense Study Treatment	X		deucravacitinib
Clinic Study Treatment Administration [j]	X		Section 9.5 (Pharmacokinetics)

Abbreviations: AE = adverse event; [redacted] BMS = Bristol-Myers Squibb; [redacted] ECG = electrocardiogram; [redacted] eCRF = electronic case report form; EOT = end of treatment; eGFR = estimated glomerular filtration rate; FSH = follicle-stimulating hormone; [redacted] IEC = Independent Ethics Committee; [redacted] IP = Investigational Product; IRB = Institutional Board Review; IRT = interactive response technology; n = number; [redacted] PSEOT = parent study end of treatment; [redacted] SAE = serious adverse event; [redacted] TB = tuberculosis; [redacted] WOCBP = women of childbearing potential.

[a] If same-day transition does not occur between the parent study EOT and Day 1 of Study IM011077; participants should enter the study within [redacted] of the last visit of the parent study and assessments should be repeated as indicated. If the number of days since the last visit of the parent study exceeds [redacted], participants are not eligible for participation in this study. The only exception to this [redacted] is when the delay is due to clinical or regulatory issues (eg, resolution or treatment for an otherwise exclusionary AE or clinical laboratory value, or delayed IRB/IEC approval), investigators must discuss a participant's continued participation with the BMS Medical Monitor/designee prior to enrolling the participant.

[b] Medical History will consist of medical history and adverse events from parent Study IM011023. Parent Study AEs that have either resolved or are ongoing [redacted] after the PSEOT visit will be considered medical history in Study IM011077. These data will need to be manually entered into the Study IM011077 database (eg, eCRFs).

[c] Concomitant Medications taken within [redacted] of Day 1 will need to be manually entered into the Study IM011077 database (eg, eCRFs).

[redacted]

[redacted]

[f] Serum pregnancy test can be performed as an alternative to urine pregnancy test, based on the clinical judgment of the investigator. A serum pregnancy test should be performed prior to IP administration in WOCBP where a urine pregnancy test does not adequately exclude a clinical suspicion of pregnancy.

[redacted]

j On Day 1, after informed consent, study treatment should be taken from Study IM011077.

k Assessment will be performed during the PSEOT visit per protocol. Any missing data should be collected on Day 1.

Table 2-2: Year 1 Procedural Outline (IM011077) - Crohn's Disease

Procedure	Week 12 (Day 85)	Week 24 (Day 169)	Week 36 (Day 253)	Week 48 (Day 337) (or ET)	Final Safety Visit (28 days after ET)	Notes
Visit Window (± n days)	**14**	**14**	**14**	**14**	**3**	
Eligibility and Disease Assessments						
Tobacco/e-Cigarette Use	X	X	X	X	X	Section 6.3.2 (Tobacco and e-Cigarettes)
Concomitant Medication Use	X	X	X	X	X	Section 7.7 (Concomitant Therapy)
Physical Examination						
Physical Examination				X	X	Section 9.4.2 (Physical Examinations)
Targeted Physical Examination	X	X	X			Section 9.4.2 (Physical Examinations)
Vital Signs (heart rate, blood pressure, temperature)	X	X	X	X	X	Includes body temperature and seated blood pressure and heart rate. Blood pressure and heart rate should be measured after the participant has been resting quietly for at least 5 minutes.
Weight	X	X	X	X	X	
[redacted]						
ECG				X	X [a]	Section 9.4.4

Table 2-2: Year 1 Procedural Outline (IM011077) - Crohn's Disease

Procedure	Week 12 (Day 85)	Week 24 (Day 169)	Week 36 (Day 253)	Week 48 (Day 337) (or ET)	Final Safety Visit (28 days after ET)	Notes
Blood, Urine, and Fecal Tests						
Hematology and Chemistry	X	X	X	X	X	Section 9.4.5 (Clinical Safety Labs)
Coagulation				X	X	
Fasting Lipid Panel and Glucose				X		Section 9.4.5 (Clinical Safety Labs)
Tuberculosis Risk Assessment [redacted]				X		Appendix 5 (TB)
[redacted]						
Urine Pregnancy Test [d]	X	X	X	X	X	Section 9.2.5 (Pregnancy); Section 9.4.5 (Clinical Safety Labs); Appendix 4
Urinalysis and Urine Chemistry	X			X	X	Section 9.4.5 (Clinical Safety Labs)
Pharmacokinetic Assessments	See Table 9.5-1 for sample collection details.					

Table 2-2: Year 1 Procedural Outline (IM011077) - Crohn's Disease

Procedure	Week 12 (Day 85)	Week 24 (Day 169)	Week 36 (Day 253)	Week 48 (Day 337) (or ET)	Final Safety Visit (28 days after ET)	Notes
[redacted]						
Endoscopy and Endoscopic Biopsies						
Endoscopy (ileocolonoscopy) [f]				X		Section 9.1.1 (Endoscopies and Biopsies)
[redacted]						
Additional Efficacy Assessments						
[redacted]						
Health-Outcomes Assessments						
[redacted]						

Table 2-2: Year 1 Procedural Outline (IM011077) - Crohn's Disease

Procedure	Week 12 (Day 85)	Week 24 (Day 169)	Week 36 (Day 253)	Week 48 (Day 337) (or ET)	Final Safety Visit (28 days after ET)	Notes
Safety Assessment (in addition to the above)						
SAE Assessment	X	X	X	X	X	Section 9.2 (AEs); Appendix 3
AE Assessment	X	X	X	X	X	Section 9.2 (AEs); Appendix 3
Study Treatment						
Dispense Study Treatment	X	X	X	X [i]		deucravacitinib
Clinic Study Treatment Administration	X	X	X	X		Section 9.5 (Pharmacokinetics)
Review Study Treatment Compliance	X	X	X	X		Section 7.6 (Treatment Compliance)

Abbreviations: AE = adverse event; [redacted] ECG = electrocardiogram; [redacted] EOT = end of treatment; ET = early termination; FSH = follicle-stimulating hormone; [redacted] IRT = interactive response technology; n = number; [redacted] SAE = serious adverse event; [redacted] TB = tuberculosis; [redacted] WOCBP = women of childbearing potential.

[a] Required only if ECG at ET is abnormal.

[redacted]

[d] Serum pregnancy test can be performed as an alternative to urine pregnancy test, based on the clinical judgment of the investigator. A serum pregnancy test should be performed prior to study treatment administration in WOCBP where a urine pregnancy test does not adequately exclude a clinical suspicion of pregnancy.

[redacted]

f [redacted]

[redacted]

i Study treatment will not be dispensed at the EOT or ET visit.

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

Table 2-3: Long-term Procedural Outline (IM011077) - Crohn's Disease

Procedure		Q1	Q2	Q3	Q4	ET	Final Safety Visit (28 days after EOT or ET)	Notes
	Year 2	Week 60 (Day 421)	Week 72 (Day 505)	Week 84 (Day 589)	Week 96 (Day 673)			
	Year 3	Week 108 (Day 757)	Week 120 (Day 841)	Week 132 (Day 925)	Week 144 (Day 1,009)			
	Year 4	Week 156 (Day 1,093)	Week 168 (Day 1,177)	Week 180 (Day 1,261)	Week 192 Day (1,345)			
	Year 5	Week 204 (Day 1,429)	Week 216 (Day 1,513)	Week 228 (Day 1,597)	Week 240 (Day 1,681)			
	Year 6	Week 252 (Day 1,765)	Week 264 (Day 1,849)	Week 276 (Day 1,933)	Week 288 (Day 2,017) EOT			
Visit Window (± n days)		14	14	14	14		3	
Disease Assessments								
Concomitant Medication Use		X	X	X	X		X	Section 7.7 (Concomitant Therapy)
Tobacco/e-Cigarette Use		X	X	X	X		X	Section 6.3.2 (Tobacco and e-Cigarettes)
Physical Examination								
Physical Examination					X		X	Section 9.4.2 (Physical Examinations)
Targeted Physical Examination		X	X	X				Section 9.4.2 (Physical Examinations)
Vital Signs		X	X	X	X		X	Includes body temperature and seated blood pressure and heart rate. Blood pressure and heart rate should be measured after the participant has been resting quietly for at least 5 minutes.
Weight		X	X	X	X		X	

Table 2-3: Long-term Procedural Outline (IM011077) - Crohn's Disease

Procedure		Q1	Q2	Q3	Q4	ET	Final Safety Visit (28 days after EOT or ET)	Notes
	Year 2	Week 60 (Day 421)	Week 72 (Day 505)	Week 84 (Day 589)	Week 96 (Day 673)			
	Year 3	Week 108 (Day 757)	Week 120 (Day 841)	Week 132 (Day 925)	Week 144 (Day 1,009)			
	Year 4	Week 156 (Day 1,093)	Week 168 (Day 1,177)	Week 180 (Day 1,261)	Week 192 Day (1,345)			
	Year 5	Week 204 (Day 1,429)	Week 216 (Day 1,513)	Week 228 (Day 1,597)	Week 240 (Day 1,681)			
	Year 6	Week 252 (Day 1,765)	Week 264 (Day 1,849)	Week 276 (Day 1,933)	Week 288 (Day 2,017) EOT			
Visit Window (± n days)		14	14	14	14		3	
[redacted]								
ECG					X		X [a]	Section 9.4.4 (Electrocardiograms)
Blood , Urine, and Fecal Tests								
Hematology and Chemistry		X	X	X	X		X	Section 9.4.5 (Clinical Safety Labs)
Coagulation					X		X	Section 9.4.5 (Clinical Safety Labs)
Fasting Lipid Panel and Glucose					X			Section 9.4.5 (Clinical Safety Labs)
Tuberculosis Risk Assessment [redacted]					X			Appendix 5 (TB)
[redacted]								

Table 2-3: Long-term Procedural Outline (IM011077) - Crohn's Disease

Procedure		Q1	Q2	Q3	Q4	ET	Final Safety Visit (28 days after EOT or ET)	Notes
	Year 2	Week 60 (Day 421)	Week 72 (Day 505)	Week 84 (Day 589)	Week 96 (Day 673)			
	Year 3	Week 108 (Day 757)	Week 120 (Day 841)	Week 132 (Day 925)	Week 144 (Day 1,009)			
	Year 4	Week 156 (Day 1,093)	Week 168 (Day 1,177)	Week 180 (Day 1,261)	Week 192 Day (1,345)			
	Year 5	Week 204 (Day 1,429)	Week 216 (Day 1,513)	Week 228 (Day 1,597)	Week 240 (Day 1,681)			
	Year 6	Week 252 (Day 1,765)	Week 264 (Day 1,849)	Week 276 (Day 1,933)	Week 288 (Day 2,017) EOT			
Visit Window (± n days)		14	14	14	14		3	
[redacted]								
Urine Pregnancy Test [d]		X	X	X	X		X	Section 9.2.5 (Pregnancy); Section 9.4.5 (Clinical Safety Labs); Appendix 4
Urinalysis and Urine Chemistry					X		X	Section 9.4.5 (Clinical Safety Labs)
Pharmacokinetic Assessments		See Table 9.5-1 for sample collection details.						
[redacted]								
Endoscopy and Endoscopic Biopsies								
Endoscopy (ileocolonoscopy) [f]					X			Section 9.1.1 (Endoscopies and Biopsies)

Table 2-3: Long-term Procedural Outline (IM011077) - Crohn's Disease

Procedure		Q1	Q2	Q3	Q4	ET	Final Safety Visit (28 days after EOT or ET)	Notes
	Year 2	Week 60 (Day 421)	Week 72 (Day 505)	Week 84 (Day 589)	Week 96 (Day 673)			
	Year 3	Week 108 (Day 757)	Week 120 (Day 841)	Week 132 (Day 925)	Week 144 (Day 1,009)			
	Year 4	Week 156 (Day 1,093)	Week 168 (Day 1,177)	Week 180 (Day 1,261)	Week 192 Day (1,345)			
	Year 5	Week 204 (Day 1,429)	Week 216 (Day 1,513)	Week 228 (Day 1,597)	Week 240 (Day 1,681)			
	Year 6	Week 252 (Day 1,765)	Week 264 (Day 1,849)	Week 276 (Day 1,933)	Week 288 (Day 2,017) EOT			
Visit Window (± n days)		14	14	14	14		3	
[redacted]								
Additional Efficacy Assessments								
[redacted]								
Health-Outcomes Assessments and Medical Resource Utilization								
[redacted]								

Table 2-3: Long-term Procedural Outline (IM011077) - Crohn's Disease

Procedure		Q1	Q2	Q3	Q4	ET	Final Safety Visit (28 days after EOT or ET)	Notes
	Year 2	Week 60 (Day 421)	Week 72 (Day 505)	Week 84 (Day 589)	Week 96 (Day 673)			
	Year 3	Week 108 (Day 757)	Week 120 (Day 841)	Week 132 (Day 925)	Week 144 (Day 1,009)			
	Year 4	Week 156 (Day 1,093)	Week 168 (Day 1,177)	Week 180 (Day 1,261)	Week 192 Day (1,345)			
	Year 5	Week 204 (Day 1,429)	Week 216 (Day 1,513)	Week 228 (Day 1,597)	Week 240 (Day 1,681)			
	Year 6	Week 252 (Day 1,765)	Week 264 (Day 1,849)	Week 276 (Day 1,933)	Week 288 (Day 2,017) EOT			
Visit Window (± n days)		14	14	14	14		3	
[redacted]								
Safety Assessments (in addition to the above)								
SAE Assessment		X	X	X	X		X	Section 9.2 (AEs); Appendix 3
AE Assessment		X	X	X	X		X	Section 9.2 (AEs); Appendix 3
Study Treatment								
Dispense Study Treatment		X	X	X	X[i]			deucravacitinib
Clinic Study Treatment Administration		X	X	X	X			Section 9.5 (Pharmacokinetics)
Review Study Treatment Compliance		X	X	X	X			Section 7.6 (Treatment Compliance)

Abbreviations: AE = adverse event; [redacted] ECG = electrocardiogram; [redacted] EOT = end of treatment; ET = early termination; [redacted]

[redacted]
n = number;
[redacted] SAE = serious adverse event;
[redacted] TB = tuberculosis;
[redacted] WOCBP = women of childbearing potential.

[a] Required only if ECG at ET is abnormal.

[redacted]

[d] Serum pregnancy test can be performed as an alternative to urine pregnancy test, based on the clinical judgment of the investigator. A serum pregnancy test should be performed prior to study treatment administration in WOCBP where a urine pregnancy test does not adequately exclude a clinical suspicion of pregnancy.

[redacted]

[f] [redacted]

[redacted]

[i] Study treatment will not be dispensed at the EOT or ET visit.

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

Table 2-4: Day 1 Procedural Outline IM011077 From Parent Study IM011024 - Ulcerative Colitis

Procedure	Day 1		Notes
Visit Window (n days from parent study EOT)	**<14**	**≥ 14 through ≤ 28** [a]	
Eligibility and Disease Assessments			
Informed Consent	X	X	Appendix 2 (Study Governance)
Inclusion/Exclusion Criteria	X	X	Section 6 (Study Population)
Obtain Participant Number (IRT)	X	X	Section 7.2 (Method of Treatment Assignment)
Tobacco/e-Cigarette Use	PSEOT [k]	X	Section 6.3.2 (Tobacco and e-Cigarettes)
Medical History [b]	X	X	Section 9.2.1
Concomitant Medication Use [c]	PSEOT [k]	X	Section 7.7 (Concomitant Therapy)
Physical Examination			
Physical Examination	PSEOT [k]	X	Section 9.4.2 (Physical Examinations)
Vital Signs (heart rate, blood pressure, temperature)	PSEOT [k]	X	Includes body temperature and seated blood pressure and heart rate. Blood pressure and heart rate should be measured after the participant has been resting quietly for at least 5 minutes.
Height	X	X	The height measurement should not be collected at Day 1. This height measurement should be carried over from the parent study screening visit and entered into Study IM011077 database (eg, eCRF).
Weight	PSEOT [k]	X	

Table 2-4: Day 1 Procedural Outline IM011077 From Parent Study IM011024 - Ulcerative Colitis

Procedure	Day 1		Notes
Visit Window (n days from parent study EOT)	**<14**	**≥ 14 through ≤ 28** [a]	
[redacted]			
ECG	PSEOT [k]	X	Section 9.4.4 (Electrocardiograms)
Blood, Urine, and Fecal Tests			
Hematology and Chemistry	PSEOT [k]	X	Section 9.4.5 (Clinical Safety Labs)
Calculate eGFR	X	X	Exclusion Criterion 5(e)(ii)
Coagulation	X	X	Section 9.4.5 (Clinical Safety Labs)
Fasting Lipid Panel and Glucose	PSEOT [k]	X	Section 9.4.5 (Clinical Safety Labs)
Tuberculosis Risk Assessment [redacted]	X	X	Appendix 5 (TB)
[redacted]			

Table 2-4: Day 1 Procedural Outline IM011077 From Parent Study IM011024 - Ulcerative Colitis

Procedure	Day 1		Notes
Visit Window (n days from parent study EOT)	**<14**	**≥ 14 through ≤ 28** [a]	
FSH	X	X	Appendix 4
Urine Pregnancy Test [f]	PSEOT [k]	X	Section 9.2.5 (Pregnancy); Section 9.4.5 (Clinical Safety Labs); Appendix 4
Urinalysis and Urine Chemistry	PSEOT [k]	X	Section 9.4.5 (Clinical Safety Labs)
Pharmacokinetic Assessments	PSEOT [k]	X	See Table 9.5-1 for sample collection details.
[redacted]			
Endoscopy and Endoscopic Biopsies			
Endoscopy (colonoscopy/sigmoidoscopy)	PSEOT		Section 9.1.1 (Endoscopies and Biopsies)
[redacted]			
Additional Efficacy Assessments			
Site Calculates the Modified Mayo Score [h]	PSEOT		Section 9.1.4 (Disease Activity Indices); Appendix 13 (Mayo)
[redacted]			

Table 2-4: Day 1 Procedural Outline IM011077 From Parent Study IM011024 - Ulcerative Colitis

Procedure	Day 1		Notes
Visit Window (n days from parent study EOT)	**<14**	**≥ 14 through ≤ 28** [a]	
Health-Outcomes Assessments			
Register and Train Participant on Slate Device	X		
[redacted]			
Safety Assessment (in addition to the above)			
SAE Assessment	PSEOT [k]	X	Section 9.2 (AEs); Appendix 3
AE Assessment	PSEOT [k]	X	Section 9.2 (AEs); Appendix 3
Study Treatment			
Dispense Study Treatment	X		deucravacitinib
Clinic Study Treatment Administration [j]	X		Section 9.5 (Pharmacokinetics)

Abbreviations: AE = adverse event; [redacted] BMS = Bristol-Myers Squibb; [redacted] ECG = electrocardiogram; [redacted] eCRF = electronic case report form; eGFR = estimated glomerular filtration rate; EOT = end of treatment; FSH = follicle-stimulating hormone; [redacted] IEC = Independent Ethics Committee; [redacted] IP = Investigational Product; IRB = Institutional Review Board; IRT = interactive response technology; n = number; PSEOT = parent study end of treatment; [redacted] SAE = serious adverse event; [redacted] TB = tuberculosis; [redacted] WOCBP = women of childbearing potential.

[a] If same-day transition does not occur between the parent study EOT and Day 1 of Study IM011077; participants should enter the study within [redacted] of the last visit of the parent study and assessments should be repeated as indicated. If the number of days since the last visit of the parent study exceeds [redacted], participants are not eligible for participation in this study. The only exception to this [redacted] is when the delay is due to clinical or regulatory issues (eg, resolution or treatment for an otherwise exclusionary AE or clinical laboratory value, or delayed IRB /IEC, investigators must discuss a participant's continued participation with the BMS Medical Monitor/designee prior to enrolling the participant.

[b] Medical History will consist of medical history and adverse events from parent Study IM011024. Parent Study AEs that have either resolved or are ongoing [redacted] after the PSEOT visit will be considered medical history in Study IM011077. These data will need to be manually entered into the Study IM011077 database (eg, eCRFs).

[c] Concomitant Medications taken within [redacted] of Day 1 will need to be manually entered into the Study IM011077 database (eg, eCRFs).

[redacted]

[redacted]

[f] Serum pregnancy test can be performed as an alternative to urine pregnancy test, based on the clinical judgment of the investigator. A serum pregnancy test should be performed prior to IP administration in WOCBP where a urine pregnancy test does not adequately exclude a clinical suspicion of pregnancy.

[redacted]

[h] The modified Mayo score calculated at this visit may be used for eligibility assessment if the score is not available from the central reader.

[redacted]

[j] On Day 1, after informed consent, study treatment should be taken from Study IM011077.

[k] Assessment will be performed during the PSEOT visit per protocol. Any missing data should be collected on Day 1.

Table 2-5: Day 1 Procedural Outline IM011077 From Parent Study IM011127- Ulcerative Colitis

Procedure	Day 1		Notes
Visit Window (n days from parent study EOT)	**<14**	**≥ 14 through ≤ 28** [a]	
Eligibility and Disease Assessments			
Informed Consent	X	X	Appendix 2 (Study Governance)
Inclusion/Exclusion Criteria	X	X	Section 6 (Study Population)
Obtain Participant Number (IRT)	X	X	Section 7.2 (Method of Treatment Assignment)
Tobacco/e-Cigarette Use	PSEOT [k]	X	Section 6.3.2 (Tobacco and e-Cigarettes)
Medical History [b]	X	X	Section 9.2.1
Concomitant Medication Use [c]	PSEOT [k]	X	Section 7.7 (Concomitant Therapy)
Physical Examination			
Physical Examination	PSEOT [k]	X	Section 9.4.2 (Physical Examinations)
Vital Signs (heart rate, blood pressure, temperature)	PSEOT [k]	X	Includes body temperature and seated blood pressure and heart rate. Blood pressure and heart rate should be measured after the participant has been resting quietly for at least 5 minutes.
Height	X	X	The height measurement should not be collected at Day 1. This height measurement should be carried over from the parent study screening visit and entered into Study IM011077 database (eg, eCRF).
Weight	PSEOT [k]	X	
[redacted]			

Table 2-5: Day 1 Procedural Outline IM011077 From Parent Study IM011127- Ulcerative Colitis

Procedure	Day 1		Notes
Visit Window (n days from parent study EOT)	**<14**	**≥ 14 through ≤ 28** [a]	
[redacted]			
ECG	PSEOT [k]	X	Section 9.4.4 (Electrocardiograms)
Blood, Urine, and Fecal Tests			
Hematology and Chemistry	PSEOT [k]	X	Section 9.4.5 (Clinical Safety Labs)
Calculate eGFR	X	X	Exclusion Criterion 5(e)(ii)
Coagulation	PSEOT [k]	X	Section 9.4.5 (Clinical Safety Labs)
Fasting Lipid Panel and Glucose	PSEOT [k]	X	Section 9.4.5 (Clinical Safety Labs)
Tuberculosis Risk Assessment [redacted]	X	X	Appendix 5 (TB)
[redacted]			
FSH	X	X	Appendix 4
Urine Pregnancy Test [f]	PSEOT [k]	X	Section 9.2.5 (Pregnancy); Section 9.4.5 (Clinical Safety Labs); Appendix 4

Table 2-5: Day 1 Procedural Outline IM011077 From Parent Study IM011127- Ulcerative Colitis

Procedure	Day 1		Notes
Visit Window (n days from parent study EOT)	**<14**	**≥ 14 through ≤ 28** [a]	
Urinalysis and Urine Chemistry	PSEOT [k]	X	Section 9.4.5 (Clinical Safety Labs)
Pharmacokinetic Assessments	PSEOT [k]	X	See Table 9.5-1 for sample collection details.
[redacted]			
Endoscopy and Endoscopic Biopsies			
Endoscopy (colonoscopy/sigmoidoscopy)	PSEOT		Section 9.1.1 (Endoscopies and Biopsies)
[redacted]			
Additional Efficacy Assessments			
Site Calculates the Modified Mayo Score [h]	PSEOT		Section 9.1.4 (Disease Activity Indices); Appendix 13 (Mayo)
[redacted]			
Health-Outcomes Assessments			
Register and Train Participant on Slate Device	X		

Table 2-5: Day 1 Procedural Outline IM011077 From Parent Study IM011127- Ulcerative Colitis

Procedure	Day 1		Notes
Visit Window (n days from parent study EOT)	**<14**	**≥ 14 through ≤ 28** [a]	
[redacted]			
Safety Assessment (in addition to the above)			
SAE Assessment	PSEOT [k]	X	Section 9.2 (AEs); Appendix 3
AE Assessment	PSEOT [k]	X	Section 9.2 (AEs); Appendix 3
Study Treatment			
Dispense Study Treatment	X		deucravacitinib
Clinic Study Treatment Administration [j]	X		Section 9.5 (Pharmacokinetics)

Abbreviations: AE = adverse event; [redacted] BMS = Bristol-Myers Squibb; [redacted] ECG = electrocardiogram; [redacted] eCRF = electronic case report case; eGFR = estimated glomerular filtration rate; EOT = end of treatment; FSH = follicle-stimulating hormone; [redacted] IBD = inflammatory bowel disease; [redacted] IEC = Independent Ethics Committee; [redacted] IP = Investigational Product; IRB = Institutional Review Board; IRT = interactive response technology; n = number; PSEOT = parent study end of treatment; [redacted] SAE = serious adverse event; [redacted] TB = tuberculosis; [redacted] WOCBP = women of childbearing potential.

[a] If same-day transition does not occur between the parent study EOT and Day 1 of Study IM011077; participants should enter the study within [redacted] of the last visit of the parent study and assessments should be repeated as indicated. If the number of days since the last visit of the parent study exceeds [redacted], participants are not eligible for participation in this study. The only exception to this [redacted] is when the delay is due to clinical or regulatory issues (eg, resolution or treatment for an otherwise exclusionary AE or clinical laboratory value, or delayed IRB/IEC approval), investigators must discuss a participant's continued participation with the BMS Medical Monitor/designee prior to enrolling the participant.

[b] Medical History will consist of medical history and adverse events from parent Study IM011127. Parent Study AEs that have either resolved or are ongoing after the PSEOT visit will be considered medical history in Study IM011077. These data will need to be manually entered into the Study IM011077 database (eg, eCRFs).

[c] Concomitant Medications taken within of Day 1 will need to be manually entered into the Study IM011077 database (eg, eCRFs).

[f] Serum pregnancy test can be performed as an alternative to urine pregnancy test, based on the clinical judgment of the investigator. A serum pregnancy test should be performed prior to IP administration in WOCBP where a urine pregnancy test does not adequately exclude a clinical suspicion of pregnancy.

[h] The modified Mayo score calculated at this visit may be used for eligibility assessment if the score is not available from the central reader.

[j] On Day 1, after informed consent, study treatment should be taken from Study IM011077.

[k] Assessment will be performed during the PSEOT visit per protocol. Any missing data should be collected on Day 1.

Table 2-6: Year 1 Procedural Outline (IM011077) - Ulcerative Colitis

Procedure	Week 12 (Day 85)	Week 24 (Day 169)	Week 36 (Day 253)	Week 48 (Day 337) (or ET)	Final Safety Visit (28 days after ET)	Notes
Visit Window (± n days)	**14**	**14**	**14**	**14**	**3**	
Eligibility and Disease Assessments						
Tobacco/e-Cigarette Use	X	X	X	X	X	Section 6.3.2 (Tobacco and e-Cigarettes)
Concomitant Medication Use	X	X	X	X	X	Section 7.7 (Concomitant Therapy)
Physical Examination						
Physical Examination				X	X	Section 9.4.2 (Physical Examinations)
Targeted Physical Examination	X	X	X			Section 9.4.2 (Physical Examinations)
Vital Signs (heart rate, blood pressure, temperature)	X	X	X	X	X	Includes body temperature and seated blood pressure and heart rate. Blood pressure and heart rate should be measured after the participant has been resting quietly for at least 5 minutes.
Weight	X			X	X	
[redacted]						
ECG				X	X [a]	Section 9.4.4 (Electrocardiograms)
Blood, Urine, and Fecal Tests						
Hematology and Chemistry	X	X	X	X	X	Section 9.4.5 (Clinical Safety Labs)
Coagulation				X	X	Section 9.4.5 (Clinical Safety Labs)
Fasting Lipid Panel and Glucose				X		Section 9.4.5 (Clinical Safety Labs)

Table 2-6: Year 1 Procedural Outline (IM011077) - Ulcerative Colitis

Procedure	Week 12 (Day 85)	Week 24 (Day 169)	Week 36 (Day 253)	Week 48 (Day 337) (or ET)	Final Safety Visit (28 days after ET)	Notes
Visit Window (± n days)	**14**	**14**	**14**	**14**	**3**	
Tuberculosis Risk Assessment [redacted]				X		Appendix 5 (TB)
[redacted]						
Urine Pregnancy Test [d]	X	X	X	X	X	Section 9.2.5 (Pregnancy); Section 9.4.5 (Clinical Safety Labs); Appendix 4
Urinalysis and Urine Chemistry	X			X	X	Section 9.4.5 (Clinical Safety Labs)
Pharmacokinetic Assessments	See Table 9.5-1 for sample collection details.					
[redacted]						
Endoscopy and Endoscopic Biopsies						
Endoscopy (colonoscopy/sigmoidoscopy) [f]				X		Section 9.1.1 (Endoscopies and Biopsies)
[redacted]						

Table 2-6: Year 1 Procedural Outline (IM011077) - Ulcerative Colitis

Procedure	Week 12 (Day 85)	Week 24 (Day 169)	Week 36 (Day 253)	Week 48 (Day 337) (or ET)	Final Safety Visit (28 days after ET)	Notes
Visit Window (± n days)	**14**	**14**	**14**	**14**	**3**	
[redacted]						
Additional Efficacy Assessments						
[redacted]						
Health-Outcomes Assessments						
[redacted]						

Table 2-6: Year 1 Procedural Outline (IM011077) - Ulcerative Colitis

Procedure	Week 12 (Day 85)	Week 24 (Day 169)	Week 36 (Day 253)	Week 48 (Day 337) (or ET)	Final Safety Visit (28 days after ET)	Notes
Visit Window (± n days)	**14**	**14**	**14**	**14**	**3**	
Safety Assessment (in addition to the above)						
SAE Assessment	X	X	X	X	X	Section 9.2 (AEs); Appendix 3
AE Assessment	X	X	X	X	X	Section 9.2 (AEs); Appendix 3
Study Treatment						
Dispense Study Treatment	X	X	X	X [h]		deucravacitinib
Clinic Study Treatment Administration	X	X	X	X		Section 9.5 (Pharmacokinetics)
Review Study Treatment Compliance	X	X	X	X		Section 7.6 (Treatment Compliance)

Abbreviations: AE = adverse event; [redacted] ECG = electrocardiogram; [redacted] EOT = end of treatment; ET = early termination; FSH = follicle-stimulating hormone; [redacted] IRT = interactive response technology; n = number; [redacted] SAE = serious adverse event; [redacted] TB = tuberculosis; [redacted] WOCBP = women of childbearing potential.

[a] Required only if ECG at ET is abnormal.

[redacted]

[redacted]

[d] Serum pregnancy test can be performed as an alternative to urine pregnancy test, based on the clinical judgment of the investigator. A serum pregnancy test should be performed prior to study treatment administration in WOCBP where a urine pregnancy test does not adequately exclude a clinical suspicion of pregnancy.

[redacted]

f [redacted]

[redacted]

h Study treatment will not be dispensed at the ET visit.

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

Table 2-7: Long-term Procedural Outline (IM011077) - Ulcerative Colitis

Procedure		Q1	Q2	Q3	Q4	ET	Final Safety Visit (28 days after EOT or ET)	Notes
	Year 2	Week 60 (Day 421)	Week 72 (Day 505)	Week 84 (Day 589)	Week 96 (Day 673)			
	Year 3	Week 108 (Day 757)	Week 120 (Day 841)	Week 132 (Day 925)	Week 144 (Day 1,009)			
	Year 4	Week 156 (Day 1,093)	Week 168 (Day 1,177)	Week 180 (Day 1,261)	Week 192 Day (1,345)			
	Year 5	Week 204 (Day 1,429)	Week 216 (Day 1,513)	Week 228 (Day 1,597)	Week 240 (Day 1,681)			
	Year 6	Week 252 (Day 1,765)	Week 264 (Day 1,849)	Week 276 (Day 1,933)	Week 288 (Day 2,017)/ EOT			
Visit Window (± n days)		14	14	14	14		3	
Disease Assessments								
Concomitant Medication Use		X	X	X	X		X	Section 7.7 (Concomitant Therapy)
Tobacco/e-Cigarette Use		X	X	X	X		X	Section 6.3.2 (Tobacco and e-Cigarettes)
Physical Examination								
Physical Examination					X		X	Section 9.4.2 (Physical Examinations)
Targeted Physical Examination		X	X	X				Section 9.4.2 (Physical Examinations)
Vital Signs		X	X	X	X		X	Includes body temperature and seated blood pressure and heart rate. Blood pressure and heart rate should be measured after the participant has been resting quietly for at least 5 minutes.
Weight					X		X	

Table 2-7: Long-term Procedural Outline (IM011077) - Ulcerative Colitis

Procedure		Q1	Q2	Q3	Q4	ET	Final Safety Visit (28 days after EOT or ET)	Notes
	Year 2	Week 60 (Day 421)	Week 72 (Day 505)	Week 84 (Day 589)	Week 96 (Day 673)			
	Year 3	Week 108 (Day 757)	Week 120 (Day 841)	Week 132 (Day 925)	Week 144 (Day 1,009)			
	Year 4	Week 156 (Day 1,093)	Week 168 (Day 1,177)	Week 180 (Day 1,261)	Week 192 Day (1,345)			
	Year 5	Week 204 (Day 1,429)	Week 216 (Day 1,513)	Week 228 (Day 1,597)	Week 240 (Day 1,681)			
	Year 6	Week 252 (Day 1,765)	Week 264 (Day 1,849)	Week 276 (Day 1,933)	Week 288 (Day 2,017)/ EOT			
Visit Window (± n days)		14	14	14	14		3	
[redacted]								
ECG					X		X [a]	Section 9.4.4 (Electrocardiograms)
Blood, Urine, and Fecal Tests								
Hematology and Chemistry		X	X	X	X		X	Section 9.4.5 (Clinical Safety Labs)
Coagulation					X		X	Section 9.4.5 (Clinical Safety Labs)
Fasting Lipid Panel and Glucose					X			Section 9.4.5 (Clinical Safety Labs)
Tuberculosis Risk Assessment [redacted]					X			Appendix 5 (TB)

Table 2-7: Long-term Procedural Outline (IM011077) - Ulcerative Colitis

Procedure		Q1	Q2	Q3	Q4	ET	Final Safety Visit (28 days after EOT or ET)	Notes
	Year 2	Week 60 (Day 421)	Week 72 (Day 505)	Week 84 (Day 589)	Week 96 (Day 673)			
	Year 3	Week 108 (Day 757)	Week 120 (Day 841)	Week 132 (Day 925)	Week 144 (Day 1,009)			
	Year 4	Week 156 (Day 1,093)	Week 168 (Day 1,177)	Week 180 (Day 1,261)	Week 192 Day (1,345)			
	Year 5	Week 204 (Day 1,429)	Week 216 (Day 1,513)	Week 228 (Day 1,597)	Week 240 (Day 1,681)			
	Year 6	Week 252 (Day 1,765)	Week 264 (Day 1,849)	Week 276 (Day 1,933)	Week 288 (Day 2,017)/ EOT			
Visit Window (± n days)		14	14	14	14		3	
[redacted]								
Urine Pregnancy Test [d]		X	X	X	X		X	Section 9.2.5 (Pregnancy); Section 9.4.5 (Clinical Safety Labs); Appendix 4
Urinalysis and Urine Chemistry					X		X	Section 9.4.5 (Clinical Safety Labs)
Pharmacokinetic Assessments		See Table 9.5-1 for sample collection details.						

Table 2-7: Long-term Procedural Outline (IM011077) - Ulcerative Colitis

Procedure		Q1	Q2	Q3	Q4	ET	Final Safety Visit (28 days after EOT or ET)	Notes
	Year 2	Week 60 (Day 421)	Week 72 (Day 505)	Week 84 (Day 589)	Week 96 (Day 673)			
	Year 3	Week 108 (Day 757)	Week 120 (Day 841)	Week 132 (Day 925)	Week 144 (Day 1,009)			
	Year 4	Week 156 (Day 1,093)	Week 168 (Day 1,177)	Week 180 (Day 1,261)	Week 192 Day (1,345)			
	Year 5	Week 204 (Day 1,429)	Week 216 (Day 1,513)	Week 228 (Day 1,597)	Week 240 (Day 1,681)			
	Year 6	Week 252 (Day 1,765)	Week 264 (Day 1,849)	Week 276 (Day 1,933)	Week 288 (Day 2,017)/ EOT			
Visit Window (± n days)		14	14	14	14		3	
[redacted]								
Endoscopy and Endoscopic Biopsies								
Endoscopy (colonoscopy/sigmoidoscopy) [f]					X			Section 9.1.1 (Endoscopies and Biopsies)
[redacted]								
Additional Efficacy Assessments								
[redacted]								

Table 2-7: Long-term Procedural Outline (IM011077) - Ulcerative Colitis

Procedure		Q1	Q2	Q3	Q4	ET	Final Safety Visit (28 days after EOT or ET)	Notes
	Year 2	Week 60 (Day 421)	Week 72 (Day 505)	Week 84 (Day 589)	Week 96 (Day 673)			
	Year 3	Week 108 (Day 757)	Week 120 (Day 841)	Week 132 (Day 925)	Week 144 (Day 1,009)			
	Year 4	Week 156 (Day 1,093)	Week 168 (Day 1,177)	Week 180 (Day 1,261)	Week 192 Day (1,345)			
	Year 5	Week 204 (Day 1,429)	Week 216 (Day 1,513)	Week 228 (Day 1,597)	Week 240 (Day 1,681)			
	Year 6	Week 252 (Day 1,765)	Week 264 (Day 1,849)	Week 276 (Day 1,933)	Week 288 (Day 2,017)/ EOT			
Visit Window (± n days)		14	14	14	14		3	
[redacted]								
Health-Outcomes Assessments								
[redacted]								

Table 2-7: Long-term Procedural Outline (IM011077) - Ulcerative Colitis

Procedure		Q1	Q2	Q3	Q4	ET	Final Safety Visit (28 days after EOT or ET)	Notes
	Year 2	Week 60 (Day 421)	Week 72 (Day 505)	Week 84 (Day 589)	Week 96 (Day 673)			
	Year 3	Week 108 (Day 757)	Week 120 (Day 841)	Week 132 (Day 925)	Week 144 (Day 1,009)			
	Year 4	Week 156 (Day 1,093)	Week 168 (Day 1,177)	Week 180 (Day 1,261)	Week 192 Day (1,345)			
	Year 5	Week 204 (Day 1,429)	Week 216 (Day 1,513)	Week 228 (Day 1,597)	Week 240 (Day 1,681)			
	Year 6	Week 252 (Day 1,765)	Week 264 (Day 1,849)	Week 276 (Day 1,933)	Week 288 (Day 2,017)/ EOT			
Visit Window (± n days)		14	14	14	14		3	
Safety Assessments (in addition to the above)								
SAE Assessment		X	X	X	X		X	Section 9.2 (AEs); Appendix 3
AE Assessment		X	X	X	X		X	Section 9.2 (AEs); Appendix 3
Study Treatment								
Dispense Study Treatment		X	X	X	X [h]			deucravacitinib
Clinic Study Treatment Administration		X	X	X	X			Section 9.5 (Pharmacokinetics)
Review Study Treatment Compliance		X	X	X	X			Section 7.6 (Treatment Compliance)

Abbreviations: AE = adverse event; [redacted] ECG = electrocardiogram; [redacted] EOT = end of treatment; ET = early termination; [redacted] IP = Investigational Product; n = number; [redacted] Q = Quarter; [redacted] SAE = serious adverse event; [redacted] TB = tuberculosis; [redacted] WOCBP = women of childbearing potential.

[a] Required only if ECG at ET is abnormal.

[redacted]

[redacted]

[d] Serum pregnancy test can be performed as an alternative to urine pregnancy test, based on the clinical judgment of the investigator. A serum pregnancy test should be performed prior to study treatment administration in WOCBP where a urine pregnancy test does not adequately exclude a clinical suspicion of pregnancy.

[redacted]

[f] The endoscopy should be done within a 14-day window of the scheduled visit.

[redacted]

[h] Study treatment will not be dispensed at an EOT or ET visit.

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

3 INTRODUCTION

Inflammatory bowel diseases (IBDs), including Crohn's disease (CD) and ulcerative colitis (UC), are chronic, remitting, and relapsing inflammatory disorders of the gastrointestinal (GI) tract. Both diseases are associated with significant morbidity, impact on quality of life, and healthcare expenditures with increasing incidence throughout the world. The etiology of IBD is multifactorial and includes a dysregulated mucosal immune response against commensal nonpathogenic bacteria of the colon, resulting in bowel inflammation.[1,2]

Despite the differences in pathology, the clinical presentation of CD and UC may be similar, with patients suffering from diarrhea, rectal bleeding (RB), weight loss, and abdominal pain.[3,4,5] Extra-intestinal manifestations such as uveitis, arthritis, ankylosing spondylitis, or primary sclerosing cholangitis may also be seen in conjunction with either CD or UC.[6]

The overall goal of treatment for patients with active IBD is to induce and maintain remission as well as to induce and maintain mucosal healing.[7,8,9] Treatment consists of anti-inflammatory and immunomodulatory therapies that are chosen to maximize efficacy while minimizing toxicity. Despite advances in available therapies, there remains a substantial unmet need for novel effective and safe treatments for patients with moderate to severe IBD.

3.1 Study Rationale

IM011077 is an open-label, long-term extension study designed to evaluate the long-term safety and efficacy of deucravacitinib 6 mg twice daily (BID) in participants who have previously been enrolled in a Phase 2 deucravacitinib study for moderate to severe CD (Study IM011023) or moderate to severe UC (Studies IM011024 and IM011127). The objectives and endpoints for this study are listed in Section 4. The approach to analyzing study data are discussed in Section 10.

[redacted]

3.2 Background

Tyrosine kinase 2 (TYK2) is an intracellular signaling kinase that mediates cytokine-driven immune and proinflammatory signaling pathways that are critical in the cycle of chronic inflammation central to a number of immune-mediated diseases.[10] TYK2-dependent pathways and the cytokine networks they modulate have been implicated in the pathophysiology of multiple immune-mediated diseases, including CD, UC, psoriasis, psoriatic arthritis, systemic lupus erythematosus (SLE), and spondyloarthropathies.[11,12]

Deucravacitinib is an orally administered selective TYK2 inhibitor with a unique mechanism of action with the potential to treat a wide spectrum of immune-mediated diseases.[11,12]

[redacted]

[redacted]

Inhibition of TYK2 is expected to provide therapeutic benefit for patients with CD and UC for multiple reasons: 1) IL-12 and IL-23 have been implicated in the pathogenesis of these diseases[13,14,15]; 2) ustekinumab, a biologic targeting IL-12/IL-23p40, has been approved for the treatment of CD[16] and UC[17] (other biologic agents that target IL-23p19 are in clinical development and have shown promising results in CD and UC[18,19,20]); and 3) deucravacitinib has shown positive results in psoriasis and psoriatic arthritis, IL-23-mediated diseases, in recent Phase 2 and Phase 3 studies.[21,22]

[redacted]

Three Phase 2 clinical studies are ongoing to determine the safety and efficacy of deucravacitinib in CD and UC:

- Study IM011023 is a multicenter, Phase 2, randomized, double-blind, placebo-controlled clinical study designed to assess the safety and efficacy of oral deucravacitinib 6 mg BID and 3 mg BID compared with placebo in participants with moderate to severe CD.
- Study IM011024 is a multicenter, Phase 2, randomized, double-blind, placebo-controlled clinical study designed to assess the safety and efficacy of oral deucravacitinib 6 mg BID compared with placebo in participants with moderate to severe UC.
- Study IM011127 is multicenter, Phase 2, randomized, double-blind, placebo-controlled clinical study designed to assess the safety and efficacy of oral deucravacitinib 12 mg BID and 6 mg BID compared with placebo in participants with moderate to severe UC.

Studies IM011023 and IM011024 include a double-blind placebo-control period of 52 weeks followed by a 52-week open-label extension (OLE) period. Study IM011127 includes a 12-week double-blind control period followed by a 40-week OLE period. Deucravacitinib is dosed at 6 mg BID in all parent study OLE periods.

3.2.1 Nonclinical Toxicology

A comprehensive battery of nonclinical toxicology studies were completed in compliance with the International Council for Harmonisation guidelines and good laboratory practice regulations to fully assess the toxicologic profile of deucravacitinib. Key findings are briefly summarized below, and the additional toxicology results are listed in the Investigator's Brochure (IB).[24]

- Deucravacitinib was tolerated at all doses in rats (≤ 75 mg/kg for 1 month; ≤ 15 mg/kg for 3 months; and ≤ 50 mg/kg for 6 months [≤ 106× area under the concentration-time curve

(AUC) multiple]). [redacted] All changes were reversible except for the decreased food consumption body weight and spleen weights, and nonadverse increased incidence of macrophage aggregation in the lung. [redacted]

- In repeat-dose (≤ 3 months) oral toxicity studies in monkeys, deucravacitinib was tolerated at all doses (≤ 5 mg/kg). In the 9-month monkey toxicity study with a 2-month recovery, the main findings at all doses (≥ 1 mg/kg, ≥ 3× AUC multiple) included generally dose-dependent and various skin changes (swollen, dry, lesion, flaking, papule, red, white, scab) throughout the body, [redacted]
- Deucravacitinib was not genotoxic or phototoxic, was not a human skin or ocular irritant, was not a sensitizer in a mouse local lymph node assays, and was well tolerated at all doses in the single-dose oral studies in rats, dogs, and monkeys.
- Deucravacitinib was not carcinogenic in rasH2 transgenic mice when dosed orally at doses ≤ 60 mg/kg (≤ 80× AUC multiple) or in rats at doses ≤ 15 mg/kg (≤ 22× AUC multiple).
- There was no evidence of teratogenicity or effects on embryo-fetal development in pregnant rats (≤ 75 mg/kg; ≤ 115× AUC multiple) and rabbits (≤ 10 mg/kg; ≤ 39×/8× total/free-fraction AUC multiples).

In summary, the totality of the nonclinical toxicity assessments demonstrate that deucravacitinib has an acceptable dose-related nonclinical safety profile with findings that are fully reversible or trending toward recovery, clinically monitorable, and manageable.

3.2.2 Early Clinical Experience

The clinical data available to date supporting the safety of deucravacitinib are from 12 completed Phase 1 studies of deucravacitinib in healthy volunteers (Studies IM011002, IM011015, IM011016, IM011019, IM011025, IM011031, IM011039, IM011045, IM011048, IM011067, IM011068, and IM011071), and completed Phase 2 (Study IM011011) and Phase 3 (Study IM011046) studies in adult participants with moderate to severe plaque psoriasis.

The following deucravacitinib studies are currently ongoing: Phase 2 studies in CD (Study IM011023), UC (Studies IM011024 and IM011127), SLE (Studies IM011021 and IM011074), lupus nephritis (Study IM011073), and psoriatic arthritis (Study IM011084); and Phase 3 studies

in psoriasis (Studies, IM011047, IM011065, IM011066, and IM011075), studying dose regimens up to deucravacitinib 6 mg BID or 12 mg once daily (QD) orally (PO).

In the Phase 1 trials of deucravacitinib, acneiform skin reactions, including folliculitis lesions, have been observed. The reactions appear to be dose related, [redacted] All of the reactions have been mild or moderate, nonserious, and reversible and have rarely led to discontinuation of study treatment. There have been no signs or symptoms of circulatory or respiratory impairment and no suggestions of a systemic hypersensitivity reaction. The acneiform skin reactions requiring treatment have been well managed with topical treatment such as benzoyl peroxide cream, clindamycin solution, chlorhexidine ointment, salicylic acid ointment, or retinoid gel. The mechanism(s) behind the acneiform dermatitis is not currently known. Other than these skin findings, there have not been other significant adverse events (AEs) that have been consistently observed with deucravacitinib.

Deucravacitinib was shown to be effective in Phase 2 studies of moderate to severe plaque psoriasis (IM011011) and psoriatic arthritis (IM011084), both diseases considered to be IL-23-mediated diseases.[25] The most common AEs reported in the overall study population in Study IM011011 were nasopharyngitis, upper respiratory tract infection, headache, diarrhea, and nausea. Overall, the majority of the AEs were mild or moderate in intensity. An increased occurrence of mild to moderate acne was observed in the deucravacitinib treatment groups compared with placebo and were manageable with topical medications as needed and did not result in discontinuation. Treatment was also generally well-tolerated in the Phase 2 psoriatic arthritis study, and the safety and laboratory parameter profile of deucravacitinib was consistent with that observed in the Phase 2 psoriasis study.

Deucravacitinib was generally well-tolerated across all studies, and no safety issues have been identified to limit the investigation of deucravacitinib in further clinical studies.

A detailed description of the chemistry, pharmacology, efficacy, and safety of deucravacitinib is provided in the IB.[24]

3.2.2.1 Deucravacitinib Dose Regimen Studies

Several studies of deucravacitinib have been conducted using single- or multiple-dose regimens of deucravacitinib 6 mg BID PO or higher. These studies demonstrated that deucravacitinib has a favorable pharmacokinetic (PK) profile characterized by consistent oral absorption, dose-related increase in exposure, no evident time dependency, and no clinically significant food effect. [redacted] Drug-drug interaction (DDI) studies showed no impact on exposure to rosuvastatin and did not meaningfully alter the exposures to methotrexate, mycophenolate mofetil, and oral contraceptives like ethinyl estradiol and norethindrone. Finally, in a study evaluating the cardio dynamic effects of deucravacitinib, no clinically relevant effect on heart rate or on electrocardiogram (ECG) parameters was observed.

3.3 Benefit/Risk Assessment

Multiple lines of evidence suggest that inhibition of TYK2 signaling by deucravacitinib may be beneficial in patients with active CD or UC.

Deucravacitinib is being developed as an oral treatment for CD, UC, psoriasis, psoriatic arthritis, SLE, and lupus nephritis. Based on its mechanism of action as an inhibitor of TYK2-mediated signaling pathways downstream of well-characterized pharmaceutical targets for the treatment of CD and UC, [redacted] it is anticipated that participants with IBD may benefit from treatment with deucravacitinib.

[redacted]

The eligibility criteria, efficacy assessments, [redacted] for this study are aligned with Studies IM011023, IM011024 [redacted]

[redacted] Close safety monitoring for this study, which is designed to expedite the detection of treatment-emergent AEs (TEAEs), is described in Section 9.4.

Deucravacitinib is an immunomodulatory Investigational Product (IP) and a potential immunosuppressant. The inclusion (Section 6.1) and exclusion (Section 6.2) criteria have been designed to minimize the risk for serious infections and malignancies. The study has been designed with study visits that allow for close monitoring of study participants' safety throughout the duration of the study, and additional data collection will be triggered if any AEs of interest (AEIs) are observed in this study.

In addition to comprehensive monitoring of safety with oversight by the investigators, Medical Monitors from BMS, and the BMS Safety Physician, the safety of participants will also be monitored by an independent Data Monitoring Committee (DMC). Furthermore, all participants may remain on permitted background standard-of-care (SOC) therapy.

The global coronavirus disease 2019 (COVID-19) pandemic has been identified as a potential risk to clinical trial participants in general, and it may particularly affect individuals with underlying chronic diseases. [redacted]

[redacted] The individual benefit-risk considerations regarding COVID-19 infection remains the responsibility of the investigator. Testing to exclude COVID-19 infection prior to enrollment and to inform decisions about subject care during the study should follow local standard practice and requirements. Study treatment must be interrupted in the context of clinical suspicion for COVID-19, or a positive diagnostic test for SARS-CoV-2 (Section 8.1.1), and requires recovery of a COVID-19 infection, [redacted] In order to facilitate reporting of COVID-19 events that occur during the study, all AEs and serious AEs (SAEs) related to SARS-CoV-2 or COVID-19 must be reported from the time of consent (Section 9.2.1). In addition, such AEs or SAEs will trigger additional data collection through specialized electronic case report form (eCRF) pages, which will allow the Sponsor to further evaluate these events (Section 9.2.8).

Participants in IBD clinical trials may experience an increase in disease activity (ie, disease exacerbation or a "flare") during their participation. This protocol contains detailed criteria for treatment failure (Section 5.1.4) and detailed discontinuation criteria (Section 8) to assist investigators in the recognition and management of treatment failure within the study. SOC rescue therapy can be initiated at any time, at the investigator's discretion (Section 5.1.4).

At the maximum concentrations expected in this study (in portal vein or systemic circulation, as appropriate), the potential for DDIs involving cytochrome P450 (CYP450) enzymes and most transporters is low. Deucravacitinib has low turnover in in vitro metabolism studies, and several enzymes are involved in its metabolism. Deucravacitinib is not an inhibitor or inducer of CYP450 enzymes at the expected clinical concentrations. Therefore, the potential for DDIs resulting from deucravacitinib–induced CYP450 inhibition or induction is low.

DDI studies have also shown that although deucravacitinib is a substrate of the efflux transporters breast cancer resistance protein (BCRP) and permeability glycoprotein, and hepatic uptake transporter OCT1, there is low impact on the exposures of potential concomitant medications that are BCRP substrates, such as rosuvastatin. Additionally, data from a study evaluating the impact of deucravacitinib in women taking oral contraceptives found no impact on exposure of ethinyl estradiol or norethindrone. These studies are detailed in the IB.[24]

The reproductive toxicology studies for deucravacitinib are complete; these are detailed in the IB.[24] Briefly, deucravacitinib is not genotoxic. Deucravacitinib was neither teratogenic nor fetotoxic, and it had no effect on female or male rat reproductive parameters (mating, fertility, and sperm morphology) in reproductive and developmental toxicity studies in rats and/or rabbits. These findings support the contraception requirements for this study.[26]

[redacted] Early detection of common TEAEs observed in previous studies and the minimum of 40 weeks of prior exposure to deucravacitinib in

the parent studies suggest that this study can be performed safely with appropriate precautions in place. In addition, multiple early-phase studies that characterize the safety profile of deucravacitinib are now complete, including a thorough QT/QTc study, multiple DDI studies, and reproductive toxicology studies. Taken together, the benefit-risk profile supports exploration of the long-term efficacy, tolerability, [redacted] of deucravacitinib 6 mg BID PO in this study.

More detailed information about the known and expected benefits and risks and reasonably anticipated AEs of deucravacitinib may be found in the IB.[24]

4 OBJECTIVES AND ENDPOINTS

Table 4-1: Objectives and Endpoints - Crohn's Disease

Objective	Endpoint[a]
Primary	
• To assess the safety and tolerability of long-term use of deucravacitinib in participants with moderate to severe CD.	• Number and proportion of participants experiencing AEs, SAEs, AEs leading to study discontinuation, and AEIs. • Number and proportion of participants experiencing abnormalities in laboratory testing, ECG, and vital sign parameters over time. • Changes from Day 1 for laboratory testing, ECG, and vital signs.
Exploratory	
[redacted]	

Table 4-1: Objectives and Endpoints - Crohn's Disease

Objective	Endpoint[a]
[redacted]	

Abbreviations: AE = adverse event; AEI = adverse event of interest; CD = Crohn's disease; ECG = electrocardiogram; [redacted] SAE = serious adverse event;

[a] See Section 10.4.1.1 for the definition of baseline for efficacy assessments.

Table 4-2: Objectives and Endpoints - Ulcerative Colitis

Objective	Endpoint [a]
Primary	
• To assess the safety and tolerability of long-term use of deucravacitinib in participants with moderate to severe UC.	• Number and proportion of participants experiencing AEs, SAEs, AEs leading to study discontinuation, and AEIs. • Number and proportion of participants experiencing abnormalities in laboratory testing, ECG, and vital sign parameters over time. • Changes from baseline for laboratory testing, ECG, and vital signs.
Exploratory	
[redacted]	

Table 4-2: Objectives and Endpoints - Ulcerative Colitis

Objective	Endpoint [a]
[redacted]	

Abbreviations: AE = adverse event; AEI = adverse event of interest; ECG = electrocardiogram; [redacted] SAE = serious adverse event; [redacted] UC = ulcerative colitis; [redacted]

[a] See Section 10.4.1.1 for the definition of baseline for efficacy assessments.

Table 4-3: Selected Endpoint Definitions

Endpoint	Definition
[redacted]	

Table 4-3: Selected Endpoint Definitions

Endpoint	Definition
[redacted]	

Table 4-3: Selected Endpoint Definitions

Endpoint	Definition
[redacted]	

5 STUDY DESIGN

5.1 Overall Design

This is an open label, multi-center study to evaluate the long-term safety and tolerability of deucravacitinib in participants with moderate to severe CD or moderate to severe UC who have completed one of the applicable parent studies (IM011023, IM011024, or IM011127), are likely to safely derive a clinical benefit from ongoing treatment with deucravacitinib, and are willing and able to participate. Participants will receive deucravacitinib 6 mg BID PO in a tablet formulation.

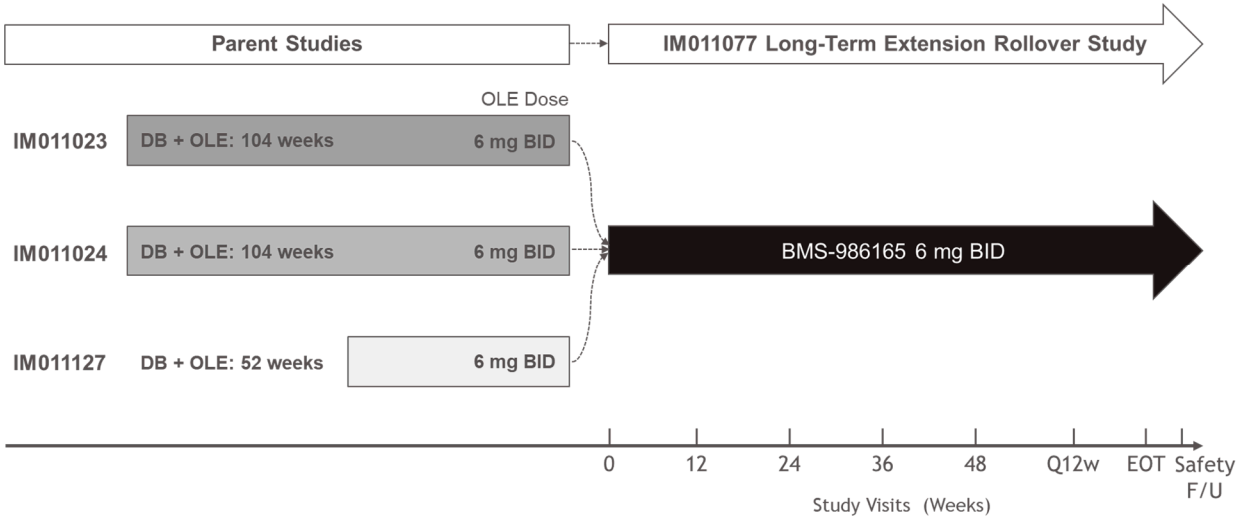
The duration of the study is approximately 296 weeks (2,072 days) as follows:

- Qualification and enrollment: up to 28 days (Section 5.1.2 [Treatment Period])

- Open-label study period: 288 weeks (2,017 days)
- Post-treatment follow-up period: 4 weeks (28 days; Section 5.1.3 [Follow-up Period])

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

Figure 5.1-1: Study Design Schematic



Abbreviations: BID = twice daily; BMS-986165 = deucravacitinib; DB = double-blind; EOT = end of treatment; F/U = follow-up; OLE = open-label extension; Q12W = every 12 weeks.

Physical exams, clinical laboratory evaluations, and other assessments, including the collection of blood [redacted] for [redacted] PK analysis, will be done at select visits during the study. Participants will be closely monitored for AEs throughout the study.

Blood samples will be collected prior to study treatment administration for PK analysis. Unscheduled visits will be allowed throughout the study period as needed for additional safety monitoring.

Throughout the study, participants who permanently discontinue study treatment prior to Week 288 are expected to be followed for protocol-specified follow-up procedures at the Final Safety Visit (4 weeks after the last dose of IP).

Blood samples will be collected prior to study treatment administration for PK analysis.

5.1.1 Qualification and Enrollment into Study

At the end of treatment visit for the parent IBD study (ie, Studies IM011023, IM011024, and IM011127), the end of treatment procedures will be performed per protocol. Participants who successfully complete the protocol-required treatment period with an acceptable safety profile, are in clinical response or clinical remission, *and* who have no worsening on endoscopy by Simple Endoscopic Score for CD (SES-CD) [redacted] or Mayo endoscopic subscore (Appendix 13) from the parent study baseline (as assessed by local read) may be eligible to participate in Study

IM011077. The end of treatment visit for the parent IBD study will also be the baseline visit (Day 1) of Study IM011077.

Prior to enrollment into Study IM011077, the investigator will evaluate whether the participants remain qualified for continued long-term participation based on the inclusion and exclusion criteria listed in Section 6 (Study Population).

Participants entering Study IM011077 will not be expected to complete the [redacted] safety follow-up period of the parent study and are expected to transition into Study IM011077 from the end of treatment visit of the parent study. If same-day transition does not occur between the parent study end of treatment and Day 1 of Study IM011077, participants must enter the study within [redacted] (see below for exceptions) of the end of treatment visit of the parent study. The end of treatment assessments should be repeated as indicated in Section 2 (Schedule of Activities). The only exception to this [redacted] is when the delay is due to clinical or regulatory issues (eg, resolution or treatment for an otherwise exclusionary AE, clinical laboratory value, or delayed Institutional Review Board [IRB]/Independent Ethics Committee [IEC] approval), investigators must discuss a participant's continued participation with the BMS Medical Monitor/designee prior to enrolling the participant.

Relevant laboratory and endoscopy data, along with clinical and patient-reported outcome (PRO) assessments from the end of treatment visit in the parent study will constitute the baseline measures for Study IM011077 (see Section 10.4.1.1 [Definition of Baseline] for a full description of how baseline will be derived for efficacy parameters). Depending on the timing of when a participant enters Study IM011077 (ie, visit window), these procedures may or may not be repeated at the Day 1 visit as indicated in Section 2 (Schedule of Activities). The data from this visit will be entered into both the parent study and Study IM011077 databases (eg, eCRFs). Any assessments specific to Study IM011077 must be performed after the informed consent and prior to dispensation of study treatment.

5.1.2 Treatment Period

At the Day 1 study visit, participants who have met the eligibility criteria for this study will be assigned a unique study identification number (Section 7.2 [Method of Treatment Assignment]) and study treatment will be dispensed. On Day 1, after the informed consent is obtained, study treatment should be taken at the site from Study IM011077.

Prior to each scheduled visit, the participant [redacted] should be reviewed to ensure [redacted] stool frequency (SF) and RB data [redacted] for participants with UC. Prior to each scheduled visit at which Mayo scores are to be calculated, study personnel should ascertain whether an adequate number of days [redacted] have been made. If adequate [redacted] have not been made, the site should contact the participant to reschedule the visit (within the allowed [redacted]) to allow time for a sufficient number [redacted] for endpoint assessments, and the participant should be counseled about proper study procedures.

[redacted] It is recommended that the endoscopy be done as close as possible to the relevant visit.

If a colonoscopy is performed at the end of treatment visit of the parent study, colonoscopy will be the preferred endoscopic procedure for subsequent endoscopies within the study. This approach will facilitate comparison between the individual colonic segments assessed at the Day 1 visit and subsequent assessments.

Discontinuation criteria are detailed in Section 8. Participants who temporarily discontinue study treatment will remain in the study and continue to participate in study procedures (Section 8.1.1).

Participants who permanently discontinue study treatment will complete an early termination (ET) visit and must enter the 4-week post-treatment follow-up period and complete the final safety visit.

5.1.3 Follow-up Period

Participants who complete the treatment period (ie, Week 288) or permanently discontinue study treatment at any time during the study (Section 8) will enter a 4-week post-treatment follow-up period and complete the final safety visit.

5.1.4 Treatment Failure

For the purpose of this study, treatment failure will be defined as:

1) Requirement for [redacted] over the course of a participant's time on study due to increased CD or UC activity, [redacted]

2) Requirement for an alternative, efficacious therapy for CD or UC (eg, initiation of biologics, prednisone (or equivalent) [redacted] daily).

   OR

3) Participants with CD with a loss of response at [redacted] with loss of response defined as:

   [redacted]

   OR

4) Participants with UC with disease worsening at [redacted] apart, with a worsening of clinical disease activity defined as:

[redacted]

5) Participants requiring a [redacted] symptoms.

5.1.5 Data Monitoring Committee and Other External Committees

An external, independent DMC will provide oversight on the safety of trial participants within this study. The DMC will regularly review accumulating data from this study and advise the Sponsor regarding the continuing safety of trial participants, as well as the continuing validity and scientific merit of the trial.

Data summaries and listings will be provided to the DMC to facilitate their safety assessment at regularly scheduled meetings and on an ad hoc basis if needed. The DMC will also be provided with suspected, unexpected serious adverse reaction (SUSAR) reports relating to deucravacitinib and recommendations from other DMCs supporting the deucravacitinib clinical development program.

Regular DMC safety reviews will include all AEs, SAEs, and AEIs. Based on their review of safety data, the DMC will make recommendations regarding the appropriateness of continuing the study, with or without study modifications, or stopping the study. The DMC may request select efficacy data from the blinded parent studies for benefit-risk assessment and study continuation.

Additional details on the DMC's processes and procedures will be outlined in the DMC Charter.

5.2 Number of Participants

Approximately 300 participants are expected to rollover from the parent studies into Study IM011077. All participants must have completed 1 of the parent studies (Studies IM011023, IM011024, or IM011127) and must meet all eligibility criteria as specified in Section 6.1 (Inclusion Criteria) and Section 6.2 (Exclusion Criteria).

5.3 End-of-Study Definition

The start of the trial is defined as the first visit for the first participant enrolled. End of trial is defined as the last scheduled procedure shown in Section 2 (Schedule of Activities). Study completion is defined as the final date on which data were or are expected to be collected. [redacted]

5.4 Scientific Rationale for Study Design

This is an open-label, multicenter study to evaluate the long-term safety and efficacy of deucravacitinib 6 mg BID in participants with moderate to severe UC and moderate to severe CD.

Deucravacitinib acts by inhibiting TYK2, a protein involved in IL-12 and IL-23 signaling, in addition to Type I IFN signaling. Deucravacitinib allosterically inhibits the kinase activity of TYK2 by binding to the regulatory pseudokinase JH2 domain, which prevents receptor-stimulated activation of TYK2.[12,27] The TYK2 locus is associated with IBD in genome-wide association studies.[28] Carriage of a naturally occurring variant in TYK2 is associated with a reduced risk of IBD.[23,29] [redacted]

[redacted]

The IL-12/IL-23 axis has been implicated in the pathogenesis of IBD in humans,[14] as described in Section 3.2 (Background). These data from antibodies under development[13,19,20] and the commercial availability of ustekinumab[16,17,30] provide proof of concept that IL-23 inhibition (either alone or together with IL-12 inhibition) is likely to be therapeutically beneficial in patients with active CD or UC. Providing an opportunity for participants who are likely to derive benefit from long-term dosing with deucravacitinib to continue into this study will allow further evaluation of the long-term safety and efficacy in this patient population.

As a long-term safety and efficacy study, the intent is to assess both the safety and tolerability of long-term exposure to deucravacitinib and the maintenance of clinical response and other efficacy endpoints seen in the parent studies. This study will estimate the effect of deucravacitinib on efficacy using standard CD and UC efficacy instruments to determine eligibility and assess efficacy (Section 9.1).[31,32,33] Disease activity eligibility criteria are clearly defined in Sections 6.1 and 6.2. [redacted] This approach is intended to maximize the efficacy data acquired in this study. Design elements in the current study, namely inclusion/exclusion criteria and safety and efficacy assessments, are based on the design of the phase 2 parent studies. This is designed to facilitate both separate and integrated analyses of exposure/clinical response and exposure[redacted] response, which may inform the selection of a deucravacitinib regimen to be evaluated in an adequately powered Phase 3 clinical trial program.

Section 3.3 contains an additional discussion on the benefit-risk profile of this study.

Justification of the dose levels used in this study is discussed in Section 5.5.

The rationale for the study's sample size is discussed in Section 10.1.

5.5 Justification for Dose

The recommended 6-mg BID dose is based on the current understanding of the PK/PD relationship for deucravacitinib. [redacted] Additional assessments based on competitor IL-12 and IL-23 antibodies also support higher and more frequent dosing to provide robust efficacy. The recommended dose is based on implementation of appropriate safety margins and is within the range of doses tested in the first-in-human study, Phase 2 psoriasis and other indications, and is also within margins based on comparisons of systemic exposure and body surface area.

The following points were considered for dose selection:

1) The data from preclinical studies of deucravacitinib that showed an exposure-response relationship between deucravacitinib PK, target engagement assays, and efficacy indicators of interest in animal models of IBD.
2) CD, UC, and psoriasis are all highly dependent upon the IL-17/IL-23 pathway.[35] Thus, the observed efficacy and dose response observed in psoriasis are assumed to be informative for dose selection in CD and UC. [redacted] Additionally, other IL-12/IL-23 inhibitor antibodies (ustekinumab and risankizumab) have also demonstrated that higher dose and more frequent dosing is required for IBD relative to the dosing in psoriasis. The preclinical data and competitive data support a higher dose (6 mg/day) and more frequent dosing (BID dosing) of deucravacitinib in IBD patients.
3) The PK properties and target engagement assessment in healthy volunteers were also used to inform the dose selection. [redacted]
4) All participants entering this study (Study IM011077) from the parent studies will have received deucravacitinib at 6 mg BID for a minimum of [redacted] weeks (Study IM011127) up to [redacted] weeks (Studies IM011023 and IM011024) prior to entering. With eligibility dependent on participants' demonstration of clinical response at the end of the parent study with an acceptable safety profile, continuing participants at this dose for the long-term extension would be appropriate.

6 STUDY POPULATION

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

6.1 Inclusion Criteria

1) Signed Written Informed Consent

a) Participants must be willing to participate in Study IM011077 and must have the ability to sign the informed consent form.

b) Willing and able to complete all study specific procedures and visits.

2) Type of Participant and Target Disease Characteristics

a) Previously completed OLE treatment in 1 of the parent CD or UC studies;

b) Be in clinical response or clinical remission at Week 104 of Study IM011023 or Study IM011024, or Week 52 of Study IM011127;

i) Evidence of clinical response or clinical remission (compared with baseline in the parent study) as defined by CDAI (refer to Table 4-3 [redacted]) or modified Mayo score (refer to Table 4-3 and Appendix 13);

AND

ii) No worsening of endoscopy (by SES-CD [refer to [redacted] or Mayo endoscopic subscore [refer to Appendix 13]) from the parent study baseline (as assessed by local read).

3) Age and Reproductive Status

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

- The investigator shall evaluate the effectiveness of the contraceptive method in relationship to the first dose of study intervention.
- Local laws and regulations may require the use of alternative and/or additional contraception methods.

a) Female Participants

i) Females, age 18 or local age of majority and older at the time of enrollment.

ii) Women who are not of childbearing potential are exempt from contraceptive requirements.

iii) Women participants must have documented proof that they are not of childbearing potential.

iv) WOCBP must have a negative highly sensitive urine pregnancy test (minimum sensitivity 25 IU/L or equivalent units of human chorionic gonadotropin) within 24 hours prior to the start of study treatment.

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

v) For additional requirements for pregnancy testing during and after study intervention, see Section 2 (Schedule of Activities).

vi) The investigator is responsible for review of medical history, menstrual history, and recent sexual activity to decrease the risk for inclusion of a woman with an early undetected pregnancy.

vii) WOCBP must agree to follow instructions for method(s) of contraception defined in Appendix 4 and as described below and included in the ICF.

viii) WOCBP are permitted to use hormonal contraception methods as described in Appendix 4.

ix) A female participant is eligible to participate if she is not pregnant or breastfeeding and at least one of the following conditions applies:

(1) Is not a WOCBP,

OR

(2) Is a WOCBP and using a contraceptive method(s) as described in Appendix 4, during the treatment period (at a minimum until after the last dose of study treatment).

b) Male Participants

i) Males, age 18 or local age of majority and older at the time of enrollment.

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

6.2 Exclusion Criteria

1) Medical Conditions

a) Women who are pregnant or breastfeeding.

b) Not applicable per Global Protocol Amendment 01.

2) Gastrointestinal Exclusion Criteria

a) Current colonic adenomas or dysplasia diagnosed at the endoscopy performed at the end of treatment visit of the parent study or past confirmed colonic dysplasia in the parent study that has not been eradicated.

A participant with adenomatous polyps may be eligible if the polyps have been completely removed (documented) and the participant is free of polyps at enrollment (Day 1).

A participant with mucosal dysplasia may be eligible if the dysplasia has been completely removed/resected/eradicated (as applicable, documented), and the participant is free of dysplasia at enrollment (Day 1). This should be discussed with the BMS Medical Monitor/designee prior to enrollment.

Participants must be current with surveillance for dysplasia and screening for colorectal cancer (based on local guidelines).

3) Immune and Infectious Disease Exclusion Criteria

a) Known serious infection, defined as any infection requiring hospitalization or treatment with parenteral (intramuscular [IM] or IV) antimicrobial agents (eg, antibiotics, antiviral, antifungal, or antiparasitic agents) within [redacted] of the first dose of study treatment.

Antibiotics used to cover a procedure such as endoscopy would not exclude the participant. Prophylactic antibiotic use should be discussed with the BMS Medical Monitor/designee.

Additionally, in the case of prior SARS-CoV-2 infection, symptoms must have resolved and, based on investigator assessment in consultation with the BMS Medical Monitor/designee, there are no sequelae that would place the participant at a higher risk by receiving investigational treatment.

b) Not applicable per Global Protocol Amendment 01.

4) Prior/Concomitant Therapy

Prohibited concomitant medications are further detailed in Section 7.7.1. Participants must also comply with the protocol requirements for restricted concomitant medications in Section 7.7.2 and permitted medications in Section 7.7.3.

a) Have received any of the following therapies since the first dose of study treatment in the parent study or before Day 1 in Study IM011077:
   i) Treatment with an immunomodulatory or biologic agent for the treatment of IBD.
   ii) Treatment with an investigational agent other than deucravacitinib.
   iii) Treatment with D-penicillamine, leflunomide, thalidomide, S1P inhibitors (eg, ozanimod, fingolimod, and etrasimod), or JAK inhibitors (eg, tofacitinib, upadacitinib, and filgotinib).

b) Are currently receiving or require initiation of any of the following therapies:
   i) Treatment with corticosteroids at a dose that exceeds the prednisone equivalent of [redacted] for adrenal insufficiency.
   ii) Treatment with immunomodulatory agents (eg, azathioprine, 6-mercaptopurine, or methotrexate).

c) Treatment with a live vaccine or live attenuated vaccine within [redacted] prior to Visit 1 of this trial.

   Not applicable per Global Protocol Amendment 01.

   Not applicable per Global Protocol Amendment 01.

   Not applicable per Global Protocol Amendment 01.

d) Not applicable per Global Protocol Amendment 01.

e) Prophylactic antibiotic use should be discussed with the BMS Medical Monitor/designee.

5) Physical and Laboratory Test Findings

a) Evidence of active or latent tuberculosis (TB; see Section 9.4.6)

   Participants diagnosed with latent TB infection (LTBI) in the parent study are eligible to continue in this study if (1) there are no current signs or symptoms of active TB, (2) the participant has received adequate documented treatment for LTBI within 5 years of screening in the parent study.

b) Evidence of active hepatitis B virus (HBV) infection as defined in [redacted]

c) Not applicable per Global Protocol Amendment 01.

d) Not applicable per Global Protocol Amendment 01.

e) Clinically significant abnormalities in laboratory testing at the second to last visit in the parent study or most current result available prior to Day 1 including (but not limited to):

   i) Hematology:

   (1) Hemoglobin level [redacted] g/dL
   (2) White blood cell (WBC) count [redacted] $\times 10^9$/L ($< 3000/mm^3$)
   (3) Lymphocyte count [redacted] $\times 10^9$/L ($< 750/mm^3$)
   (4) Neutrophil count [redacted] $\times 10^9$/L ($< 1000/mm^3$)
   (5) Platelet count [redacted] $\times 10^9$/L ($< 100,000/mm^3$)

ii) Renal Function:

(1) Serum creatinine > 2 × upper limit of normal (ULN) or renal impairment based on an estimated glomerular filtration rate < 45 mL/min/1.73 m^2 (calculated using the Modification of Diet in Renal Disease equation)

iii) Liver-related Blood Tests and Liver Function:

(1) Serum alanine aminotransferase (ALT) > 2 × ULN

(2) Serum aspartate aminotransferase (AST) > 2 × ULN

(3) Serum total bilirubin > 1.5 × ULN

Participants with total bilirubin > 1.5 × ULN who have a confirmed diagnosis of Gilbert's syndrome are not excluded from this study but must be discussed with the BMS Medical Monitor/designee.

(4) Alkaline phosphatase (ALP) > 1.5 × ULN

f) Any other findings on physical examination, vital signs, or clinical laboratory testing that, in the opinion of the investigator, may place the participant at an unacceptable risk for participation in this study.

6) Allergies and Adverse Drug Reaction

a) History of any significant drug allergy (eg, anaphylaxis) or significant adverse drug reaction (eg, hepatotoxicity).

7) Other Exclusion Criteria

a) Participants with cancer screening or surveillance that is suspicious for malignancy, or where the possibility of malignancy cannot be reasonably excluded after additional clinical, laboratory, or other diagnostic evaluations. Participants with non-melanoma skin cancer are not excluded.

b) Class III or IV congestive heart failure, as classified by the New York Heart Association (NYHA) Functional Classification or any recent onset of heart failure resulting in NYHA Class III/IV symptoms.

c) Acute coronary syndrome (eg, myocardial infarction, unstable angina pectoris) and/or any history of significant cerebrovascular disease (eg, stroke, cerebral hemorrhage, transient ischemic attack) within 24 weeks before enrollment.

d) Known history of hereditary galactose intolerance, total lactase deficiency, or glucose-galactose malabsorption.

e) Prisoners or participants who are involuntarily incarcerated. (Note: Under certain specific circumstances and only in countries where local regulations permit, a person who has been imprisoned may be included or permitted to continue as a participant. Strict conditions apply, and Bristol-Myers Squibb approval is required.

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

6.2.1 Enrollment Criteria

Participants must meet the following criteria at the enrollment visit on Day 1 in order to be eligible to be enrolled into Study IM011077 and to receive the first dose of deucravacitinib on this study:

1) The participant continues to meet the **inclusion criteria**, listed in Section 6.1.
2) The participant continues to not meet any of the e**xclusion criteria**, listed in Section 6.2.
3) The participant has discontinued any **prohibited treatments** (Section 7.7.1).

6.3 Lifestyle Restrictions

Participants are required to fast for a minimum of [redacted] before the enrollment visit (Day 1), [redacted] because fasting lipid panel and glucose samples will be obtained at these visits.

6.3.1 Meals and Dietary Restrictions

Study treatment may be taken without regard to meals.

6.3.2 Tobacco and e-Cigarettes

Smoking can have an influence on the severity of IBD disease symptoms. Consequently, use of tobacco products will be assessed at each study visit. Use of a nicotine patch or other nicotine supplements should be recorded as concomitant medication.

6.3.3 Activity

No activity restrictions are required.

6.4 Enrollment Failures

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

7 TREATMENT

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

Study treatment includes both Investigational [Medicinal] Product (IP/IMP) and Non-investigational [Medicinal] Product (Non-IP/Non-IMP) and can consist of the following:

- IP
  - Deucravacitinib

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

Other medications used as support or escape medication for preventative, diagnostic, or therapeutic reasons, as components of the SOC for a given diagnosis, may be considered as Non-IP.

Table 7-1: Study Treatments for Study IM011077

Product Description/ Class and Dosage Form	Potency	IP/Non-IP	Blinded or Open Label	Packaging/ Appearance	Storage Conditions (per label)
Deucravacitinib (BMS-986165) oral tablet	6 mg	IP	Open label	Bottles containing [redacted] tablets	Store at 15°-25°C in a tightly closed container and protected from light

Abbreviation: IP = Investigational Product.

7.1 Treatments Administered

Participants will take deucravacitinib 6 mg BID by taking 1 tablet in the morning and 1 tablet in the evening. Study treatment will be supplied in bottles containing [redacted] tablets. Bottles are to be stored at 15°C to 25°C in a tightly closed container and protected from light.

The selection and timing of dose for each participant is as follows:

Table 7.1-1: Selection and Timing of Dose

Study Treatment	Unit Dose Strength(s)/Dosage level(s)	Dosage Formulation Frequency of Administration	Route of Administration
6 mg BID Deucravacitinib (BMS-986165)	6 mg	1 active tablet in the morning; 1 active tablet in the evening	Oral

Abbreviation: BID = twice daily.

Deucravacitinib can be administered with or without food, and there are no precautions or restrictions to the administration of antacids with deucravacitinib.

7.2 Method of Treatment Assignment

All participants will be assigned to treatment using an Interactive Response Technology (IRT). Before the study is initiated, each user will receive login information and directions on how to access the IRT.

At the time of the first visit in Study IM011077, immediately after informed consent is obtained and before any study-related procedures are performed, the investigative site will access the enrollment option of the IRT system for assignment of a participant number for all participants into the open-dose panel. Enrolled participants, including those not dosed, will be assigned sequential participant numbers starting with [redacted] The participant identification number (PID) will be comprised of a 4-digit site number and 5-digit participant number. For example, the first participant enrolled at site number 1 will have a PID of [redacted]. The participant number will not be used for any other participant. For continuity purposes, the participant number from the parent study will be recorded for each participant enrolled in IM011077.

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

7.3 Blinding

This is a nonrandomized, open-label study; blinding procedures are not applicable.

7.4 Dosage Modification

There is no provision for dose modification of study treatment. Dose modification of study treatment may be allowed for safety reasons or if recommended by the independent DMC. Such cases will be discussed with the BMS Medical Monitor/designee prior to any study treatment modification.

Modification of permitted CD or UC treatments or dose regimens is allowed for safety reasons, or if a participant experiences an AE attributable to that treatment. Participants should continue to take their assigned treatment even if their clinical condition worsens (ie, they experience disease exacerbation or a "flare"), unless any of the criteria in Section 8.1 (Discontinuation Criteria) are met. If a participant's clinical condition worsens to the extent that rescue therapy (other than permitted therapy) is required, based on the investigator's judgment, the participant must discontinue study treatment in favor of appropriate alternative available treatment.

If treatment is interrupted for a participant due to an AE, study treatment can be restarted in consultation with the BMS Medical Monitor/designee if the AE is not serious and assessed as not related to study treatment.

7.5 Preparation/Handling/Storage/Accountability

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

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

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

Please refer to the current version of the IB for complete storage and handling information.

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

7.5.1 Retained Samples for Bioavailability/Bioequivalence/Biocomparability

Not applicable.

7.6 Treatment Compliance

Study treatment compliance will be monitored as indicated in Section 2 (Schedule of Activities) using standard drug accountability procedures (comparing the number of [redacted] returned to number dispensed, considering the expected regimen and any reported missed doses). Drug accountability will be reviewed by the investigative site staff at each visit to confirm treatment compliance. Site staff will discuss any discrepancies with the participant and remind the participant of the importance of compliance with the assigned regimen.

7.7 Concomitant Therapy

All medications taken from within [redacted] before the first dose of study treatment until [redacted] after the last dose of study treatment or last visit (whichever comes later) must be recorded on the appropriate eCRF.

Other than existing treatment for CD or UC (with restrictions as described in the eligibility criteria (Section 6 [Study Population]), concomitant medications (prescription, over-the-counter [OTC], or herbal) should be administered during the study only if they are prescribed for treatment of specific medical reasons separate from CD or UC.

7.7.1 Prohibited Treatments

Prohibited prior and current concomitant medications are summarized in Table 7.7.1-1. Medications taken within [redacted] prior to study treatment administration must be recorded on the eCRF.

Table 7.7.1-1: Summary of Prohibited Concomitant Medications

Prohibited Treatments	
Medication/Formulation	**Notes**
Corticosteroids: Prednisone [redacted] or budesonide MMX [redacted], for the treatment of CD or UC.	[redacted]
Corticosteroids: A course of IV or IM corticosteroids (> 24 hours in duration) or more than 1 discrete exposure to IV or IM	IV or IM corticosteroids are prohibited prior to Day 1 and during the study treatment period.

Table 7.7.1-1: Summary of Prohibited Concomitant Medications

Prohibited Treatments	
Medication/Formulation	**Notes**
corticosteroids (< 24 hours in duration) required to treat CD or UC.	
Immunomodulatory drugs	Prohibited during study
Biologic drugs for IBD	Prohibited during study
Live vaccines	Prohibited from the parent study EOT visit, during the study, or within the [redacted] after the last dose.a
Apheresis	Prohibited from parent study EOT visit and during the study.
Investigational agents (other than deucravacitinib)	Prohibited from the parent study EOT visit and during the study.
Traditional Chinese medicines, herbal medicines, or herbal supplements	Prohibited from the parent study EOT visit and during the study; only exceptions are: medicines/supplements that were previously approved by the BMS Medical Monitor/designee in the parent study or a new exception that has been cleared by the BMS Medical Monitor/designee.

Abbreviations: BMS = Bristol-Myers Squibb; CD = Crohn's disease; EOT = end of treatment; IBD = inflammatory bowel disease; IM = intramuscular; IV = intravenous; mg = milligram; MMX = Multi-Matrix System; [redacted] UC = ulcerative colitis.

[a] Heat-killed (or otherwise inactivated) or protein or subunit vaccines such as influenza and pneumococcal vaccines may be received at any time during the study. [redacted]

7.7.2 Restricted Concomitant Medications

Restricted concomitant medications are summarized in Table 7.7.2-1. Restricted medications taken within [redacted] prior to study treatment administration must be recorded on the eCRF.

Table 7.7.2-1: Summary of Restricted Concomitant Medications

Restricted Treatments	
Medication/Formulation	**Notes**
Corticosteroid Rescue Therapy (Section 7.7.4) **Systemic corticosteroids required to treat CD or UC**	[redacted]

Table 7.7.2-1: Summary of Restricted Concomitant Medications

Restricted Treatments	
Medication/Formulation	**Notes**
Corticosteroids: Topical, inhaled, intra-articular or intrabursal, to treat non-IBD medical conditions	Allowed but must be discussed with the BMS Medical Monitor/designee.
Corticosteroids: Systemic corticosteroids [redacted] to treat non-IBD medical conditions	Allowed but must be discussed with the BMS Medical Monitor/designee to determine if the intercurrent illness affects the safety of the participant or if the corticosteroid treatment is likely to confound efficacy assessment.
Nonsteroidal anti-inflammatory drugs	May be used on an as needed basis during the study, but use is not recommended, as NSAIDs may be associated with GI toxicity, including mucosal injury.

Abbreviations: BMS = Bristol-Myers Squibb; CD = Crohn's disease; GI = gastrointestinal; IBD = inflammatory bowel disease; NSAID = nonsteroidal anti-inflammatory drug; UC = ulcerative colitis.

7.7.3 Permitted Medications

Use of concomitant rectally administered corticosteroids and 5-aminosalicylic acid (5-ASA) are permitted throughout the study.

Use of concomitant oral 5-ASA is permitted per the country label or institutional practice. Dose modification of 5-ASA is allowed during the study if this is required to optimize therapy and for participant safety reasons, such as if a participant experiences an AE attributable to 5-ASA. The rationale for dose modification must be documented in source documents. The AE or SAE eCRF must be completed, if applicable.

Oral corticosteroids for adrenal insufficiency are allowed at a maximum dose of prednisone [redacted] or equivalent. Probiotics are allowed with no restrictions on use. Participants will continue their existing IBD treatment(s) during the study, provided the treatment complies with the eligibility criteria (see Sections 6.1 [Inclusion Criteria] and 6.2 [Exclusion Criteria] and Table 7.7.1-1 and Table 7.7.2-1).

7.7.4 Disease Exacerbation, Corticosteroid Rescue Therapy, and Tapering

7.7.4.1 Disease Exacerbation

Participants who are experiencing symptoms of possible disease exacerbation (loss of response for CD or disease worsening for UC as defined in Table 4-1 and Table 4-2) should be evaluated as deemed appropriate by the investigator in order to determine whether corticosteroid rescue therapy may be appropriate. Participants who are seen by the investigator due to disease exacerbation should undergo the following assessments:

- Symptom-directed physical examination including vital signs
- Assessment of disease activity

- [redacted] complete blood count, and additional laboratory assessments, as indicated
- Stool sample for culture, ova, and parasite evaluation, and *Clostridioides. difficile* assay
- [redacted]
- Endoscopy may be considered and performed

Upon confirmation of loss of response or disease worsening, corticosteroid rescue therapy or alternative efficacious therapy for IBD may be initiated. If the participant still meets the criteria for loss of response or disease worsening [redacted] after first presenting with symptoms and despite treatment, he/she should be identified as a treatment failure, be discontinued from study treatment (Sections 5.1.4 and 8.1), and enter the post-treatment follow-up period (Section 5.1.3).

If an alternative, efficacious therapy for IBD is determined to be the appropriate course of action, the participant will be identified as a treatment failure and must be discontinued from study treatment (Sections 5.1.4 and 8.1).

Corticosteroid rescue therapy and the subsequent tapering is described in detail in Section 7.7.4.2.

7.7.4.2 Corticosteroid Rescue Therapy and Tapering

[redacted] Failure to taper the corticosteroid dose to 0 mg daily [redacted] of initiation will be considered treatment failure, and participants must discontinue from the study, unless the participants require glucocorticoid treatment for adrenal insufficiency. Participants who remain on corticosteroids to treat adrenal insufficiency must be discussed with the BMS Medical Monitor/designee to continue the study. Rescue therapy with medications other than oral corticosteroids, including immunosuppressants or biologics for IBD, are not permitted.

Oral corticosteroid rescue therapy [redacted] may be used [redacted] in response to an increase in CD or UC disease activity at the investigator's discretion (refer to [redacted]. The oral corticosteroid should be tapered upon demonstrated disease improvement per investigator judgement. The recommended corticosteroid taper is as follows:

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

[redacted]

7.8 Treatment After the End of the Study

At the conclusion of the study, participants who continue to demonstrate clinical benefit will be eligible to receive BMS-supplied study treatment. Study treatment will be provided via an extension of the study, a rollover study requiring approval by the responsible Health Authority and IEC, or through another mechanism at the discretion of BMS.

BMS reserves the right to terminate access to BMS-supplied study treatment if any of the following occur: 1) the study is terminated due to safety concerns; 2) the development of deucravacitinib is terminated for other reasons, including, but not limited to, lack of efficacy and/or not meeting the study objectives; or 3) the participant can obtain medication from a government-sponsored or private health program. In all cases, BMS will follow local regulations.

8 DISCONTINUATION CRITERIA

8.1 Discontinuation From Study Treatment

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

- Participant's request to stop study treatment. Participants who request to discontinue study treatment will remain in the study and must continue to be followed for protocol-specified follow-up procedures. The only exception to this is when a participant specifically withdraws consent for any further contact with him/her or persons previously authorized by participant to provide this information.
- Participant meets any of the criteria for treatment failure defined in Section 5.1.4 (Treatment Failure), [redacted].
- Any clinical AE, laboratory abnormality, or intercurrent illness which, in the opinion of the investigator, indicates that continued participation in the study is not in the best interest of the participant.
- Participant who develops a significant infection during the study defined as any infection (viral, bacterial, and fungal) considered by the investigator to be related to IP [redacted]
- Any drug-related rash or hypersensitivity reaction (eg, anaphylaxis, angioedema, urticaria, Stevens-Johnson syndrome, [redacted]
- Pregnancy, [redacted]
- Participant meets any of the following criteria for liver-related laboratory abnormalities. If these abnormalities are identified, repeat testing should occur within 48 to 72 hours and these results should be discussed with the BMS Medical Monitor/designee. Additional

recommendations on the recognition and investigation of potential drug-induced liver injury (DILI) are given in Section 9.2.7 (Potential Drug-induced Liver Injury).

  - ALT or AST > 8 × ULN on a single occasion
  - ALT or AST > 5 × ULN for more than 2 weeks
  - ALT or AST > 3 × ULN and total bilirubin > 2 × ULN or international normalized ratio (INR) > 1.5
  - ALT or AST > 3 × ULN with the appearance of fatigue, nausea, vomiting, right upper quadrant pain or tenderness, fever, rash, and/or eosinophilia (> 5%)

- Participant meets 1 of the following criteria for laboratory abnormalities in 2 sequential laboratory measurements taken 3 to 5 days apart:
  - Hemoglobin < 7.0 g/dL [redacted]
  - WBC count < 1.5 × 109/L (< 1,500/mm3)
  - Absolute lymphocyte count < 0.5 × 109/L (< 500/mm3)
  - Absolute neutrophil count < 0.75 × 109/L (< 750/mm3)
  - Platelet count < 75 × 109/L (< 75,000/mm3)
  - An increase in serum creatinine > 50% over the IM011077 study baseline (Day 1) values and an absolute increase in serum creatinine > 0.5 mg/dL (> 44.2 µmol/L)
  - Creatine kinase elevations > 10 × ULN, unless the causality is known not to be medically serious (eg, exercise induced)
- Inability or failure to comply with protocol requirements.
- Termination of the study by BMS
- Loss of ability to freely provide consent through imprisonment or involuntarily incarceration for treatment of either a psychiatric or physical (eg, infectious disease) illness. (Note: Under specific circumstances and only in countries where local regulations permit, a participant who has been imprisoned may be permitted to continue as a participant. Strict conditions apply and BMS approval is required.)

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

All participants who discontinue study treatment should comply with protocol specified follow-up procedures as outlined in Section 2 (Schedule of Activities). The only exception to this requirement is when a participant withdraws consent for all study procedures, including post-treatment study

follow-up, or loses the ability to consent freely (ie, is imprisoned or involuntarily incarcerated for the treatment of either a psychiatric or physical illness).

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

8.1.1 Temporary Discontinuation From Study Treatment

If treatment is interrupted for a participant due to an AE, study treatment may be restarted in consultation with the BMS Medical Monitor/designee if the AE is not serious and is assessed as not related to study treatment (see Section 7.4 [Dosage Modification]).

Study treatment must be interrupted for participants who test positive for SARS-CoV-2 until recovery [redacted].

8.1.2 Post Study Treatment Study Follow-up

Participants who discontinue study treatment will continue to be followed for 28 days post-last dose of study treatment, or longer, as required, and in line with Section 9.2.3 (Follow-up of AEs and SAEs).

8.2 Discontinuation From the Study

Participants who request to discontinue study treatment (Section 8.1 [Discontinuation From Study Treatment]) will remain in the study and must continue to be followed for protocol-specified follow-up procedures. The only exception to this is when a participant specifically withdraws consent for any further contact with him/her or persons previously authorized by participant to provide this information.

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

8.3 Lost to Follow-up

- All reasonable efforts must be made to locate participants to determine and report their ongoing status. This includes follow-up with persons authorized by the participant.

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

8.4 Replacement of Participants

Participant replacement is not permitted.

8.5 Study Discontinuation

A DMC will provide oversight of the safety of trial participants as outlined in Section 5.1.5 of the protocol and in the DMC Charter.

The DMC will periodically review safety data and make recommendations regarding the appropriateness of continuing the study, with or without study modifications, or stopping the study.

BMS reserves the right to terminate access to BMS-supplied study treatment if any of the following occur: a) the study is terminated due to safety concerns; b) the development of deucravacitinib is terminated for other reasons, including, but not limited to, lack of efficacy and/or not meeting the study objectives; c) the participant can obtain medication from a government-sponsored or private health program. In all cases BMS will follow local regulations.

9 STUDY ASSESSMENTS AND PROCEDURES

- Study procedures and timing are summarized in the Section 2 (Schedule of Activities).
- Protocol waivers or exemptions are not allowed.
- All immediate safety concerns must be discussed with the Sponsor immediately upon occurrence or awareness to determine if the participant should continue or discontinue treatment.
- Adherence to the study design requirements, including those specified in the Schedule of Activities, is essential and required for study conduct.
- All Day 1 evaluations must be completed and reviewed to confirm that potential participants meet all eligibility criteria before first dose of deucravacitinib is provided on Study IM011077 as described in Section 2 (Schedule of Activities).

- Procedures conducted as part of the participant's routine clinical management (eg, blood count) and obtained before signing of informed consent may be utilized for enrollment or baseline purposes provided the procedure meets the protocol-defined criteria and has been performed within the timeframe defined in Section 2 (Schedule of Activities).
- Procedures not specified in the protocol that are part of standard care may be performed if they do not interfere with study procedures. Any data arising from such procedures are not to be reported in the eCRF.
- The study data includes all the information collected as a result of the study, including participant demographics, disease characteristics (eg, Montreal classification), clinical information, blood tests, [redacted] endoscopic videos, intestinal biopsies obtained during endoscopy, and other tests listed in Section 2 (Schedule of Activities). Study data collected during this study will be used to help us understand how deucravacitinib works in people with IBD, and related health conditions. The study data may also be used to help us understand the biology of IBD and related health conditions, how study tests perform in people with IBD, and for other relevant health research relating to deucravacitinib or these health conditions.

9.1 Efficacy Assessments

Every effort must be made to ensure that the same evaluator(s) complete the assessment for each participant. If the evaluator(s) is unable to complete the evaluation, then a qualified individual with overlapping experience may perform the evaluation. Documentation of who performed the evaluation is to be recorded in source documents. Assessments are to be performed at approximately the same time of day throughout the duration of the study.

9.1.1 Endoscopies and Endoscopic Biopsies

Endoscopies and endoscopic biopsies will be submitted to an imaging core lab. Image acquisition guidelines and the submission process will be outlined in the Study IM011077 Image Review Charters to be provided by the core lab.

Endoscopy: Endoscopy (colonoscopy or flexible sigmoidoscopy, as appropriate for the disease indication) will be performed [redacted] as indicated in Section 2 (Schedule of Activities). Endoscopy should be performed at the ET visit if this occurs [redacted] after the last endoscopy, and, if clinically indicated, at unscheduled visits. [redacted]

When possible, and if clinically acceptable, the same type of endoscopy should be performed at specified time points indicated in Section 2 (Schedule of Activities). The video recording of each

procedure will be reviewed by a central reader, or readers, in order to determine the SES-CD and a global index of severity for participants with CD, and the modified Mayo endoscopic (ES) subscore (refer to Appendix 13), [redacted]

Additional details on the standardization of equipment, video recordings, endoscopic assessment, and scoring will be provided in the Endoscopy Image Review Charter.

[redacted]

Endoscopic biopsies: [redacted]

Additional details on the standardization of sample processing, histopathologic assessment, and scoring will be provided in the Histopathology Image Review Charter.

[redacted]

9.1.3 Capturing Data to Assess Disease Activity

Data will be captured using Medidata Rave electronic data capture (EDC) [redacted].

The Physician's Global Assessment (PGA; see Mayo score in Section 9.1.4 [Disease Activity Indices]) for participants with UC, and [redacted] (see Section 9.9 [Health Economics or Medical Resource Utilization and Health Economics]) for all participants

will be captured by the investigator or designee using the Medidata Rave EDC system at the timepoints indicated in Section 2 (Schedule of Activities).

[redacted]

9.1.4 Disease Activity Indices

9.1.4.1 Crohn's Disease

The following instruments will be used to assess disease activity and health-related quality of life during the study as indicated in Section 2 (Schedule of Activities). Selected endpoints that use these indices are defined in Section 4 (Objectives and Endpoints) and described in detail in [redacted]:

CDAI[19,38,39] **and PRO2**[40]: The CDAI and PRO2 scores will be calculated [redacted]

- Prior to each scheduled visit at which CDAI and PRO2 are to be calculated, determine whether an adequate number [redacted] have been made. Should the participant miss [redacted] prior to a study visit, the investigator should assess if the visit should be rescheduled to ensure that an adequate number [redacted] for efficacy assessment are recorded.
- **SES-CD**[41]: [redacted]

Histologic Disease Activity Instruments

Histologic disease activity instruments include:

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

Endoscopic biopsy samples will be obtained from each of the 5 ileocolonic segments (rectum, descending colon/sigmoid, transverse colon, ascending colon, and ileum) on the days indicated in Section 2 (Schedules of Activities). [redacted] Further details on the biopsy collection and processing for this histological assessment will be provided to the site in the Study Reference Manual.

9.1.4.2 Ulcerative Colitis

The following instruments will be used to assess disease activity and health-related quality of life during the study as indicated in Section 2 (Schedule of Activities). Selected endpoints that use these indices are defined in Section 4 (Objectives and Endpoints) and described in detail in Appendix 13 (Mayo):

Total Mayo score: The total Mayo score is a composite disease activity index that comprises 4 subscores: SF, RB, and ES subscores and a PGA subscore.[3] Consistent with regulatory draft guidance, the ES subscore scale has been modified so that friability is no longer included in the definition of an ES subscore = 1.[31,45] Each subscore is scored on a 4-point scale, ranging from 0 to 3, leading to a maximum total score of 12. Higher scores indicate more severe disease. The total Mayo score will be used in endpoint assessment.

Modified Mayo score: The modified Mayo score is a composite of the following total Mayo score subscores: SF, RB, and ES.[31] Friability is not included in the definition of an ES subscore = 1, and the PGA is not included in the calculation of the modified Mayo score.[31,32,45] The maximum total score of the modified Mayo score is 9. The modified Mayo score calculated during the parent study

end of treatment visit may be used to assess eligibility at Day 1. The modified Mayo score will be used in endpoint assessment.

Details regarding the recording of the individual Mayo score components and the calculation of the total Mayo score and modified Mayo score are provided in Appendix 13, whereas timing of assessments are detailed in Section 2 (Schedule of Activities). Briefly, the investigator records the IM011077 study baseline SF at the Day 1 visit, and the PGA at each study visit, [redacted]. The ES subscore will be determined by a central reader. The central reader will also determine a global severity score. The investigator will also record a ES subscore and global severity score, which will be used for post hoc analyses.

[redacted] If a participant is unable to collect an adequate number [redacted] prior to starting bowel preparation for his/her endoscopy, the collection window may be extended [redacted]

Partial Mayo Score: The partial Mayo score is a composite of the following total Mayo score subscores: SF, RB, and PGA.[46] The partial Mayo score may be determined at the timepoints indicated in Section 2 (Schedule of Activities).

Symptomatic Mayo Score: The symptomatic Mayo score is a composite of the total Mayo score SF and RB subscores. It may be calculated at various timepoints and will be used in endpoint assessment.

[redacted]

Additional details on endoscopy image acquisition, image quality control, and central reading for the assessment of Mayo ES subscore [redacted] will be provided in the Endoscopy Image Review Charter.

[redacted]

Geboes Score and RHI[43,49]: The Geboes score and the RHI are instruments used to assess the histological appearance of the mucosa in UC.[49] The Geboes score evaluates 6 histological features (termed Grades), each of which are scored on ordinal scales. The RHI uses the weighted scores from 4 Grades of the Geboes score to derive a score that ranges from 0 to 33, where higher scores indicate a greater degree of histological disease activity. Both Geboes scores[50,51] and the RHI[52] have been used to characterize histological activity in UC.

For determination of the Geboes score and the RHI, biopsies for histological assessment will be obtained as indicated in Section 2 (Schedule of Activities) and evaluated by a central reader. Further details on the biopsy collection and processing for this histological assessment will be provided in the Histopathology Image Review Charter.

The Geboes and RHI assessments will be carried out by the central vendor, who will be responsible for reading and scoring all endoscopies and biopsies.

[redacted]

[redacted]

9.1.6 Laboratory Assessments

The following laboratory tests will be performed according to Section 2 (Schedule of Activities) to gather more information about CD and UC activity: [redacted]

Stool culture, ova, and parasite evaluation, and *Clostridioides difficile* toxin testing are recommended in order to exclude infectious causes of disease exacerbation, as deemed appropriate by the investigator.

9.2 Adverse Events

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

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

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

Contacts for SAE reporting specified in Appendix 3.

9.2.1 Time Period and Frequency for Collecting AE and SAE Information

Sections 5.6.1 and 5.6.2 in the IB represent the Reference Safety Information to determine expectedness of SAEs for expedited reporting.

All AEs (SAEs and nonserious AEs) for this study will be collected from the time the participant signs the informed consent form until the Final Safety Visit (ie, 28 days after EOT or ET) at the timepoints specified in Section 2 (Schedule of Activities). All AEs reported during the parent study that have either resolved or are ongoing [redacted] after the PSEOT visit will be recorded as Medical History in Study IM011077. AEs that are ongoing from the parent study and worsen after the participant signs the informed consent form will be reported as new AEs in Study IM011077.

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

- Medical occurrences that begin before the start of study treatment but after obtaining informed consent will be recorded on the appropriate section of the eCRF module.

- All SAEs will be recorded and reported to Sponsor or designee within 24 hours, as indicated in Appendix 3.
- The investigator will submit any updated SAE data to the Sponsor or designee within 24 hours of updated information being available.

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

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

9.2.2 Method of Detecting AEs and SAEs

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

9.2.3 Follow-up of AEs and SAEs

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

After the initial AE/SAE report, the investigator is required to proactively follow each participant at subsequent visits/contacts. All SAEs, nonserious AEs of special interest (as defined in Section 9.2) and SARS-CoV-2-related AEs will be followed until resolution, until the condition stabilizes, until the event is otherwise explained, or until the participant is lost to follow-up (as defined in Section 8.3).

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

9.2.4 Regulatory Reporting Requirements for SAEs

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

Sponsor or designee will be reporting AEs to regulatory authorities and IECs according to local applicable laws, including European Directive 2001/20/EC and Food and Drug Administration Code of Federal Regulations 21 CFR Parts 312 and 320. A SUSAR is a subset of SAEs and will be reported to the appropriate regulatory authorities and investigators following local and global guidelines and requirements.

9.2.5 Pregnancy

In the event a participant becomes pregnant during the trial, the study treatment must be discontinued immediately. If the participant becomes pregnant during the study period until the end of study, the investigator must immediately notify the BMS Medical Monitor/designee of this event and complete and forward a Pregnancy Surveillance Form to BMS Designee within 24 hours of awareness of the event and in accordance with SAE reporting procedures described in Appendix 3.

Protocol-required procedures for study discontinuation and follow-up must be performed on the participant.

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

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

9.2.6 Laboratory Test Result Abnormalities

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

- Any laboratory test result that is clinically significant or meets the definition of an SAE
- Any laboratory test result abnormality that required the participant to have study treatment discontinued or interrupted
- Any laboratory test result abnormality that required the participant to receive specific corrective therapy

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

9.2.7 Potential Drug-induced Liver Injury

Clinical chemistry and coagulation tests will be assessed as indicated in Section 2 (Schedule of Activities). Participants with abnormal liver blood tests should be further assessed to determine if

these meet the criteria for discontinuation of the study treatment (see Section 8.1 [Discontinuation From Study Treatment]) or the criteria for potential DILI.

Potential DILI is defined as:

1) Aminotransferase (ALT or AST) elevation > 3 × ULN,

   AND

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

   AND

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

Identification of a clinically significant elevation(s) in liver-related chemistry or coagulation tests (including those defined in Section 8.1 [Discontinuation From Study Treatment], or meeting the definition for potential DILI) should be followed by repeat testing of ALT, AST, total bilirubin, ALP, and INR within 48 to 72 hours to: (1) confirm the abnormalities, and (2) determine if they are increasing or decreasing.

Investigators must consult with the BMS Medical Monitor/designee immediately if a participant meets the laboratory criteria for potential DILI.

Investigators should consider gathering additional clinical information and laboratory and imaging tests to seek other possible causes of the observed liver blood test abnormalities, including (but not limited to) acute viral hepatitis, alcoholic and autoimmune hepatitis, biliary obstruction (small and large duct), cardiovascular causes (eg, ischemic hepatitis), nonalcoholic steatohepatitis, and the effect of concomitant treatments.

A review of all concomitant medications should include herbal medicines, dietary supplements, nonprescription OTC medications, including acetaminophen/paracetamol, and occupational exposure to chemical agents.

Wherever possible, timely confirmation of initial liver-related laboratory abnormalities should occur prior to the reporting of a potential DILI event. All occurrences of potential DILI, meeting the defined criteria must be reported as SAEs (see Section 9.2 [Adverse Events] and Appendix 3 for reporting details). All participants with clinically significant abnormalities in liver-related blood tests, or potential DILI, must be followed until all abnormalities return to normal or to the IM011077 study baseline state.

9.2.8 Adverse Events of Interest

All AEs and SAEs that arise in the study will be reported and investigated. However, because of the characteristics of the disease under study, and deucravacitinib in particular, some AEs are

considered AEIs. AEIs may be serious or nonserious. Such events may require further investigation to better characterize and understand them.

In the deucravacitinib clinical development program, certain skin-related AEs (eg, acne), infection AEs, and creatine kinase elevation have been identified as potential AEIs. However, there has been no definitive assessment on the causal relationship between these events and treatment with deucravacitinib.

In addition, given that immunosuppression is consistent with the mechanism of action of deucravacitinib, malignancies are considered to be an important potential risk of therapy with deucravacitinib and will be monitored as AEIs. Malignancies were not identified as adverse findings in nonclinical studies or in clinical studies of deucravacitinib.

Additional information on AEIs will be collected in this study. Reporting of an AE or SAE that includes a Preferred Term that is linked to an AEI will trigger specialized eCRF pages to collect additional information related to characterization, social/family history, risk factors, signs/symptoms, diagnostics, and treatments. Additional information may also be requested to aid in the evaluation of these AEIs.

9.2.9 Other Safety Considerations

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

9.3 Overdose

[redacted]

In the event of an overdose the investigator/treating physician should:

1) Contact the BMS Medical Monitor/designee immediately.
2) Closely monitor the participant for AEs/SAEs and laboratory abnormalities until deucravacitinib can no longer be detected systemically [redacted]
3) Document the quantity of the excess dose as well as the duration of the overdosing in the eCRF.

Decisions regarding study treatment interruptions or modifications will be made by the investigator in consultation with the BMS Medical Monitor/designee based on the clinical evaluation of the participant.

9.4 Safety

Planned time points for all safety assessments are listed in Section 2 (Schedule of Activities). All urgent safety concerns must be discussed with the Sponsor immediately upon occurrence or awareness to determine if the participant should continue or discontinue study treatment.

Safety evaluations that will be performed in addition to AE monitoring are physical examinations (Section 9.4.2), vital signs (Section 9.4.3), ECGs (Section 9.4.4), laboratory tests (Section 9.4.5), TB screening (Section 9.4.6), and concomitant medication use (Section 7.7).

9.4.1 Preventative Care

Investigators are encouraged to ensure that participants are up-to-date with preventative care for IBD, based on local standard of care. This may include:

- Non-live vaccinations
  - Non-live vaccinations can be administered during the study (including SARS-CoV-2 messenger ribonucleic acid (mRNA) vaccines). The efficacy and safety of vaccines in participants receiving deucravacitinib have not been studied.
- Periodic surveillance for IBD associated colonic dysplasia or screening for colorectal carcinoma, based on local standard of care.
  - Biopsies collected for suspected colonic dysplasia should follow site-specific process for screening for colorectal carcinoma.
- Additional preventative care outlined in research society guidance (eg, American College of Gastroenterology guide).[55]

9.4.2 Physical Examinations

Schedules for physical examinations are provided in the Section 2 (Schedule of Activities). Complete physical examinations should be performed by a medical doctor or someone who is authorized to perform the examinations by training and performs this task under the supervision of the investigator. Key aspects of the examination should evaluate important body systems, including skin, as clinically indicated. Every effort should be made to ensure the same evaluator will complete the examination for each participant at all visits throughout the study. Documentation of who performed the examination is to be recorded in source notes.

Significant findings should be recorded as AEs on the AE eCRF. AEs that are continuing from the parent study will be captured in both parent study and Study IM011077 databases.

Schedules for targeted physical examinations are provided in Section 2 (Schedule of Activities). The targeted physical examination will include (at a minimum) an abdominal examination, skin examination, and an examination of body systems with previously noted abnormalities and/or those body systems associated with any new complaints from the participant.

9.4.3 Vital Signs

Vital signs including body weight, body temperature, and seated blood pressure and heart rate will be obtained as indicated in Section 2 (Schedule of Activities) and recorded in the relevant eCRF. Seated blood pressure and heart rate should be measured after the participant has been resting quietly for at least 5 minutes. The Day 1 height measurement should not be collected. This height measurement should be carried over from the parent study screening visit and entered into Study IM011077 database (eg, eCRF).

9.4.4 Electrocardiograms

ECGs will be performed as indicated in Section 2 (Schedule of Activities). ECGs will be read locally. Clinically significant ECG findings will be recorded in the relevant eCRF and should be discussed with the BMS Medical Monitor/designee. Any clinically significant ECG findings should be recorded on the appropriate AE page of the eCRF.

9.4.5 Clinical Safety Laboratory Assessments

Investigators must document their review of each laboratory safety report.

A central or local laboratory (where allowed by local laws, regulations, and guidance) will perform safety laboratory assessments (as indicated in operational documents; except urine pregnancy tests, which may be performed in clinic, as per local SOC) and provide reference ranges and laboratory reports.

Any laboratory test result that the investigator considers clinically relevant for safety is to be recorded on the appropriate AE eCRF.

The timing of laboratory assessments is indicated in Section 2 (Schedule of Activities).

The laboratory parameters to be assessed for clinical safety throughout the study are listed in Table 9.4.5-1.

Table 9.4.5-1: Summary of Laboratory Parameters Used to Assess Clinical Safety

Hematology	
Hemoglobin Hematocrit Iron Ferritin Total iron-binding capacity (TIBC) Total leukocyte count, including absolute neutrophil count (ANC) and absolute lymphocyte count	Platelet count Red blood cell (RBC) count Complete blood count (CBC) differential (manual separate smear preferred; automatic differential acceptable when manual is not available); must include MCV, MCHC, MCH
Chemistry	
Aspartate aminotransferase (AST) Alanine aminotransferase (ALT) Gamma glutamyltransferase (GGT) Total bilirubin Direct bilirubin Alkaline phosphatase (ALP) Lactate dehydrogenase (LDH) Creatinine Blood urea nitrogen (BUN) Uric acid Total protein Albumin Sodium	Potassium Chloride Calcium Phosphorus Magnesium Creatine kinase Performed after ≥ 10-hour fast at annual visits (Weeks 48, 96, 144, 192, 240, and 288): Fasting lipid panel (total cholesterol, high-density lipoprotein cholesterol, low-density lipoprotein cholesterol, and triglycerides) Fasting glucose
Coagulation	
Prothrombin time (PT) International normalized ratio (INR)	Either partial thromboplastin time or activated partial thromboplastin time (aPTT)

Table 9.4.5-1: Summary of Laboratory Parameters Used to Assess Clinical Safety

Urinalysis	
Protein Glucose Blood Leukocyte esterase Specific gravity pH	Microscopic examination of the sediment if blood, protein, or leukocyte esterase are positive on the dipstick • Spot urine will be assessed for urine protein and urine creatinine
Other Analyses	
[redacted] • Follicle-stimulating hormone: to confirm postmenopausal status in females (refer to Appendix 4) • Urine and/or serum pregnancy testing (β-hCG): performed for WOCBP	
Stool Tests (to be performed when deemed appropriate by investigator)	
• Stool culture: culture for potentially pathogenic enteric bacteria, including (but not limited to) *Salmonella*, *Shigella*, *Campylobacter,* and enterohemorrhagic *Escherichia coli*. Testing for additional enteric pathogens, including bacteria, protozoa, ova, and parasites, may be performed based on the investigator's clinical judgment. • Stool for *Clostridioides* (formerly *Clostridium*) *difficile* testing: stool for *C. difficile* Toxin A and B test (EIA) and GDH antigen test (EIA), with reflex to NAAT (*C. difficile* polymerase chain reaction) if either positive.	

Abbreviations: [redacted] β-hCG = beta-human chorionic gonadotropin; [redacted] EIA = enzyme-linked immunosorbent assay; GDH = glutamate dehydrogenase; [redacted] MCH = mean corpuscular hemoglobin; MCHC = mean corpuscular hemoglobin concentration; MCV = mean corpuscular volume; NAAT = nucleic acid amplification test; WOCBP = women of childbearing potential.

9.4.6 Tuberculosis Screening

In order to be eligible for the study, a participant must not have symptoms or signs of active TB, as judged by the investigator.

Evidence of active or latent TB includes:

- History of active TB prior to the Day 1 visit of this study (IM011077); or
- Signs or symptoms of active TB as judged by the investigator; or
- A chest x-ray obtained anytime within [redacted] prior to Day 1 of this study, with documentation, and evidence of current active or old active pulmonary TB; or
- [redacted]
- [redacted]

Prior to receiving the first dose of study treatment in this study and approximately every year, participants should be assessed using the Tuberculosis Risk Assessment Tool (refer to Appendix 5). [redacted]

A participant with a negative QuantiFERON or T-Spot test may be eligible to participate in the study provided he/she does not have any clinical or radiologic evidence supporting a diagnosis of active TB or LTBI.

A participant with an indeterminate QuantiFERON test or a borderline T-Spot test must have a retest before he/she is eligible to participate in the study. If the second result is again indeterminate or borderline, the participant will be excluded from the study. If the second result is negative, the participant may be eligible provided there is no clinical or radiologic suspicion of active TB or LTBI.

[redacted]

A participant diagnosed with LTBI at the end of treatment visit of the parent study should be referred to an appropriate specialist for consideration for prophylactic treatment for LTBI, per local guidelines. [redacted]

9.4.7 Imaging Safety Assessment

Please refer to Section 9.4.1 for periodic surveillance (including study-related endoscopy) for IBD associated colonic dysplasia or screening for colorectal carcinoma.

9.5 Pharmacokinetics

The PK of deucravacitinib and metabolites (if applicable) will be derived from plasma concentration vs time data. The trough observed plasma concentration (Ctrough) will be summarized as part of the PK parameters summary.

The plasma samples will be analyzed for deucravacitinib and metabolites (if applicable) by a validated liquid chromatography tandem mass spectrometry assay. In addition, plasma samples will be archived for potential analysis of other analytes, if the need arises and to the extent possible. Detailed instructions for the PK blood collection, labeling, processing, storage, and shipping will be provided to the site in the Laboratory Manual.

The sampling schedule for the assessment of PK and PD is provided in Table 9.5-1.

Table 9.5-1: Pharmacokinetic Sampling Schedule for All Participants (Study IM011077)

Study Day of Sample Collection Visit window (± 14 days)	Event	Time Relative to Deucravacitinib Dose [a] (hr:min)	Deucravacitinib PK Plasma Sample
Day 1	Predose [b]	00:00	X
Day 169 (Year 1, Week 24)	Predose [c]	00:00	X
Day 337 (Year 1, Week 48)	Predose [c]	00:00	X
Day 505 (Year 2, Week 72)	Predose [c]	00:00	X
Day 673 (Year 2, Week 96)	Predose [c]	00:00	X
Day 841 (Year 3, Week 120)	Predose [c]	00:00	X
Day 1009 (Year 3, Week 144)	Predose [c]	00:00	X
Day 1177 (Year 4, Week 168)	Predose [c]	00:00	X
Day 1345 (Year 4, Week 192)	Predose [c]	00:00	X
Day 1513 (Year 5, Week 216)	Predose [c]	00:00	X
Day 1681 (Year 5, Week 240)	Predose [c]	00:00	X
Day 1849 (Year 6, Week 264)	Predose [c]	00:00	X
Day 2017 (Year 6, Week 288)	Predose [c]	00:00	X
End of Treatment/Early Termination			X

Abbreviations: hr = hour; min = minute; PK = pharmacokinetic.

[a] PK sample is expected to be collected as close to the planned time as operationally feasible and always records the exact PK collection date and time.

[b] The Day 1 pre-dose sample must be drawn before the morning dose of study treatment on the visit date. The post-PK dose of study treatment should be taken at the site from Study IM011077.

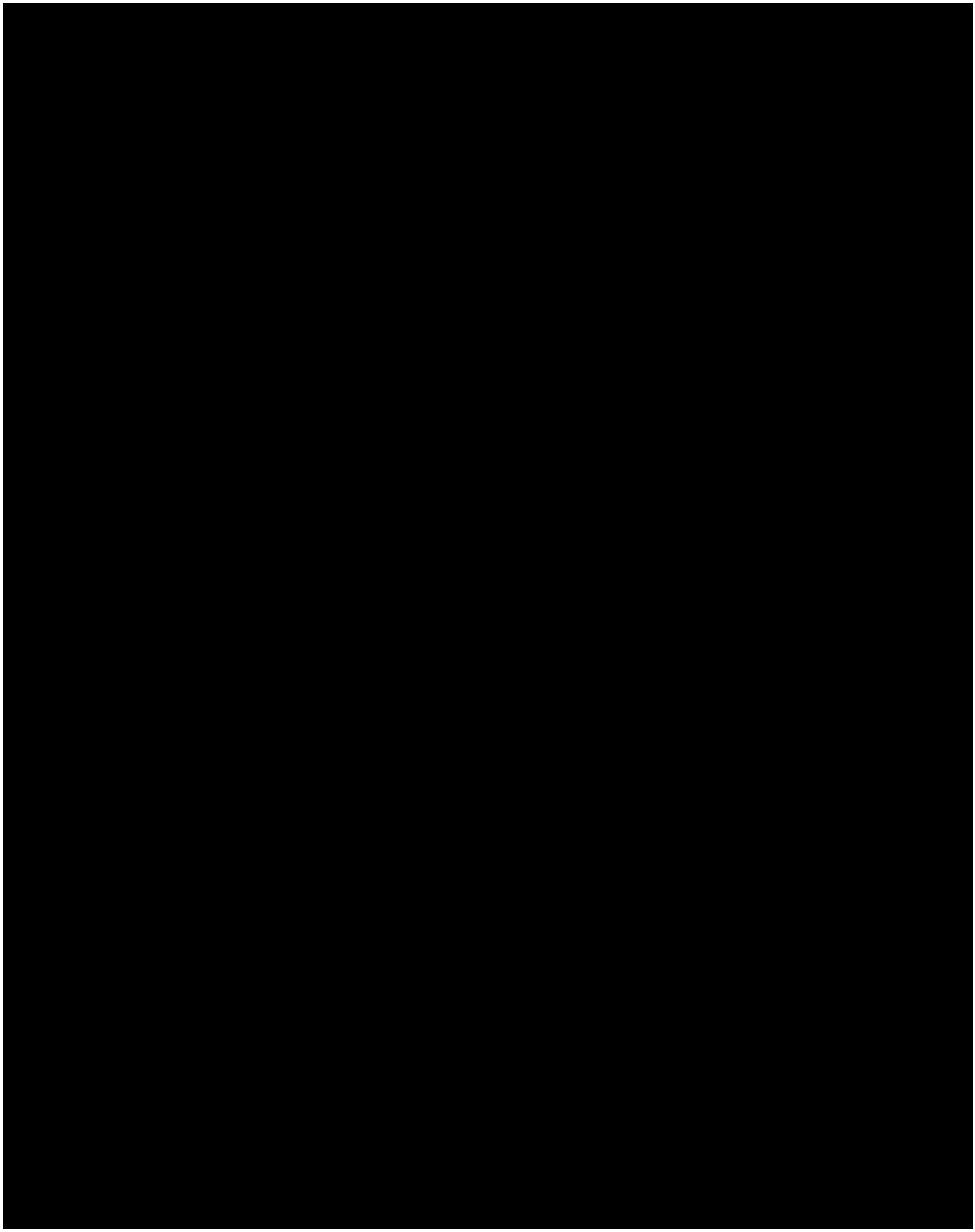
[c] Pre-dose samples must be drawn before the morning dose of study treatment on the visit day; at these visits, study treatment will be taken at the site.

[redacted]

9.7 Pharmacogenomics

Not applicable.

[redacted]



[redacted]

[redacted]

9.9 Health Economics OR Medical Resource Utilization and Health Economics

Medical resource utilization and health economics data associated with medical encounters (disease-related healthcare utilization) will be collected in the eCRF by the investigator and study-site personnel for all participants throughout the study. This instrument provides questions/prompts representative of the data to be collected through eCRF [redacted] Protocol-mandated procedures, tests, and encounters are excluded. [redacted]

9.10 Electronic Informed Consent

Where applicable according to regional, local, and institutional regulations, sites may opt to use electronic informed consent (eConsent). eConsent uses digital technology to provide interactive tools for obtaining informed consent. IRBs/IECs should review the content of any multimedia components prior to launch of the digital platform as part of the informed consent review process.

Participants will be provided with a printed copy of the eConsent. In some cases, depending on local regulations, the multimedia components may be delivered electronically, whereas signatures will be collected on paper. Paper informed consent forms will be available in the event the regulations do not allow the use of eConsent and to allow both options for participants and sites.

10 STATISTICAL CONSIDERATIONS

10.1 Sample Size Determination

Because this uncontrolled, open-label, long-term extension study is for observational purposes only, no formal calculations of sample size and power determination will be made. All qualified participants who complete the final treatment visit from an applicable parent study will be eligible to participate. Approximately 300 participants are expected to roll over into this study from the parent studies.

10.2 Populations for Analyses

For purposes of analysis, the following populations are defined:

Population	Description
Enrolled Population	All participants who sign informed consent for entry into Study IM011077.
As-treated	All enrolled participants who took at least 1 dose of study treatment in Study IM011077.
Biomarker Population	All participants who receive at least 1 dose of study treatment in Study IM011077 and have at least 1 post-treatment biomarker measurement.
PK Population	All participants who receive at least 1 dose of study treatment in Study IM011077 and have any available concentration-time data.

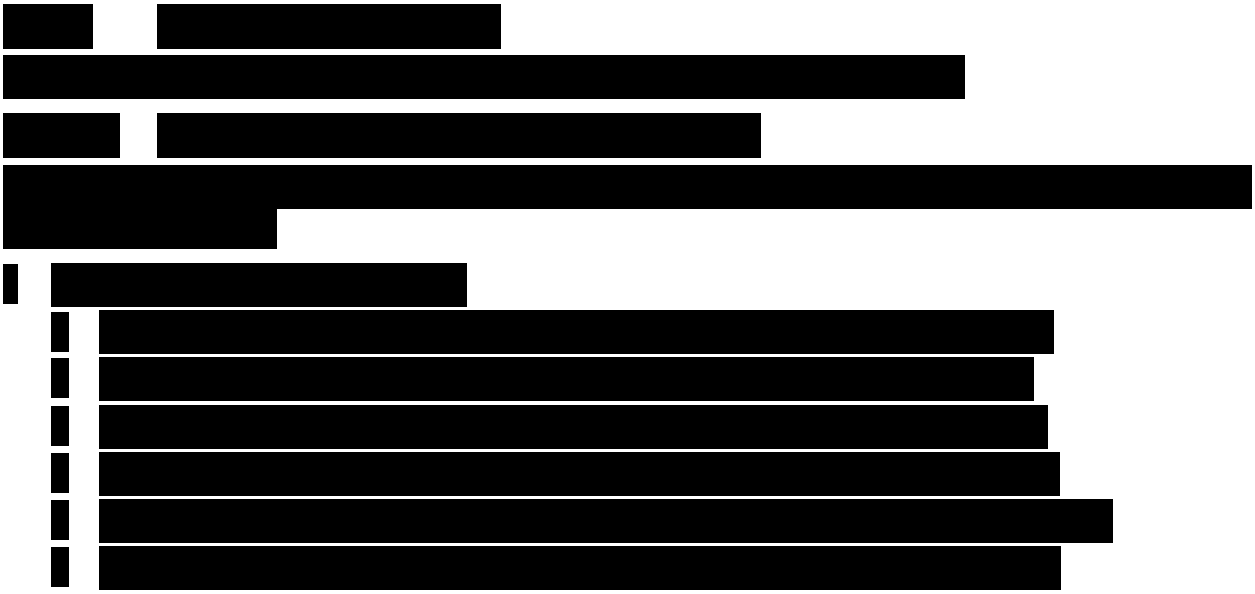
Abbreviation: PK = pharmacokinetic.

10.3 Endpoints

10.3.1 Primary Endpoints

The primary objective of this study is to assess the safety and tolerability of long-term use of deucravacitinib in participants with moderate to severe CD or moderate to severe UC. To support this objective, the following endpoints will be assessed:

- Number and proportion of participants experiencing AEs, SAEs, AEs leading to study discontinuation, and AEIs.
- Number and proportion of participants experiencing abnormalities in laboratory testing, ECG, and vital sign parameters over time.
- Changes from IM011077 study baseline for laboratory testing, ECG, and vital signs.



[redacted]

10.4 Statistical Analyses

10.4.1 Efficacy Analyses

Because this study is for observational purposes, no statistical tests for treatment comparisons will be conducted. Categorical data will be summarized as frequency counts and percentages. Continuous data will be summarized using number of participants (n), mean, standard deviation (SD), median, minimum, and maximum unless otherwise specified. Efficacy variables will be summarized for all visits in which the variable is assessed. Complete details of the planned analyses will be documented in the SAP and finalized before database lock. Summaries will be provided for the As-treated population. Participants will be summarized according to the treatment they received in their parent trial.

10.4.1.1 Definition of Baseline

Baseline data are defined as:

- The **parent study baseline** is the baseline efficacy assessment performed in Study IM011023, IM011024, or IM011127 during the enrollment period or the Day 1 visit, as applicable.
- The **IM011077 study baseline** is the last measurement collected on or prior to the date of the first dose in Study IM011077. Relevant laboratory data, along with clinical and PRO assessments from the end of treatment visit in IM011023, IM011024, or IM011127, may constitute the baseline measures for IM011077. These procedures need not be repeated at the baseline visit in IM011077. Any assessments specific to IM011077 will be performed prior to assignment of IM011077 study treatment.

[redacted]

10.4.2 Safety Analyses

Safety data will be analyzed for AEs, SAEs, laboratory analytes, and vital signs. Safety will be summarized using the As-treated population. Participants will be summarized according to the treatment they received in their parent trial, as well as by indication and overall. Categorical data will be summarized as frequency counts and percentages. Continuous data will be summarized using n, mean, SD, median, minimum, and maximum unless otherwise specified.

10.4.2.1 Adverse Events

AEs for this study will be collected from the time the participant signs the informed consent form until the Final Safety Visit (ie, 28 days after EOT or ET) at the timepoints specified in Section 2 (Schedule of Activities). AEs that are ongoing from parent studies that worsen after the participant signs the informed consent form will be reported as new AEs in Study IM011077. AEs reported during parent studies that have either resolved or are ongoing [redacted] from the parent study end of treatment visit will be recorded as Medical History in Study IM011077.

TEAEs are events that occur after the administration of the first dose of study treatment in Study IM011077. AEs that were ongoing during the parent study and worsen once study treatment is initiated in this study will also be considered treatment emergent. All AEs will be coded using the Medical Dictionary for Regulatory Activities (MedDRA) and presented by System Organ Class and Preferred Term. Serious AEs and deaths, AEs leading to study treatment discontinuation, AEs by maximum severity, and AEs by relationship will also be summarized by the MedDRA System Organ Class and Preferred Term. All TEAEs will also be summarized by Preferred Term sorted by decreasing frequency.

10.4.2.2 Vital Signs and Physical Examinations

Vital signs will be summarized as raw, change from IM011077 study baseline, and change from maximum post-baseline value. Incidence of abnormal physical examination findings will also be summarized.

10.4.2.3 Clinical Laboratory Tests

Laboratory analytes will be summarized as raw, change from IM011077 study baseline, and change from maximum post-baseline value. Incidence of abnormal, high, or low values will be summarized. Shift tables will also be provided.

10.4.3 Other Analyses

Other analysis summaries will be presented as defined in the SAP.

10.4.3.1 Demographics and Baseline Data

Demographics and baseline data obtained during the screening visit of the parent study will be summarized for participants entering Study IM011077 and will be summarized by randomized treatment (on the parent studies) for each applicable analysis population. Categorical data will be summarized as frequency counts and percentages. Continuous data will be summarized using n, mean, SD, median, minimum, and maximum, unless otherwise specified.

10.4.3.2 Prior and Concomitant Medications

Prior and concomitant medications, categorized by medication group and subgroup according to the World Health Organization Drug Dictionary, will be summarized by treatment for the As-treated population. Medications with an end date prior to the first dose of study treatment in Study IM011077 will be considered prior medications.

10.4.3.3 Pharmacokinetics

Ctrough will be summarized by dose and timepoint for the PK population. If warranted, analysis of PK and exposure-response relationships of deucravacitinib will be conducted using a population approach as appropriate and reported separately from the Clinical Study Report.

[redacted]

10.4.4 Interim Analyses

Interim analyses may be performed, and, if planned, the SAP will further describe those planned interim analyses.

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12 APPENDICES

APPENDIX 1 ABBREVIATIONS AND TRADEMARKS

Term	Definition
5-ASA	5-aminosalicylic acid
AE	adverse event
AEI	adverse event of interest
ALP	alkaline phosphatase
ALT	alanine aminotransferase
[redacted]	
AST	aspartate aminotransferase
AUC	area under the concentration-time curve
AT	aminotransferase
β-HCG	beta-human chorionic gonadotrophin
BID	twice daily
BMS	Bristol-Myers Squibb
BMS-986165	deucravacitinib
BCRP	breast cancer resistance protein
[redacted]	
CD	Crohn's disease
CDAI	Crohn's Disease Activity Index
CFR	Code of Federal Regulations
[redacted]	
CONSORT	Consolidated Standards of Reporting Trials
COVID-19	coronavirus disease 2019
Ctrough	trough observed plasma concentration
CYP450	cytochrome P450
DB	double-blind
DDI	drug-drug interaction
DILI	drug-induced liver injury
DMC	Data Monitoring Committee
[redacted]	

Term	Definition
ECG	electrocardiogram
[redacted]	
eConsent	electronic informed consent
eCRF	electronic case report form
EDC	electronic data capture
eGFR	estimated glomerular filtration rate
EIA	enzyme-linked immunosorbent assay
EOT	end of treatment
ES	endoscopic
ET	early termination
FSH	follicle-stimulating hormone
F/U	follow-up
GDH	glutamate dehydrogenase
GI	gastrointestinal
[redacted]	
HBV	hepatitis B virus
[redacted]	
hr	hour
[redacted]	
IB	Investigator's Brochure
IBD	inflammatory bowel disease
[redacted]	
IEC	Independent Ethics Committee
IFN	interferon
[redacted]	

Term	Definition
[redacted]	
IL	interleukin
IM	intramuscular
IMP	Investigational Medicinal Product
INR	international normalized ratio
IP	Investigational Product
IRB	Institutional Review Board
IRT	Interactive Response Technology
IV	intravenous
JAK	Janus kinase
[redacted]	
LTBI	latent tuberculosis infection
MCH	mean corpuscular hemoglobin
MCHC	mean corpuscular hemoglobin concentration
MCV	mean corpuscular volume
MedDRA	Medical Dictionary for Regulatory Activities
min	minute
MMX	Multi-Matrix System
mRNA	messenger ribonucleic acid
N	number of participants or observations
NAAT	nucleic acid amplification test
[redacted]	
NOAEL	no-observed-adverse-effect level
NSAID	nonsteroidal anti-inflammatory drug
NYHA	New York Heart Association
OLE	open-label extension
OTC	over-the-counter
PD	pharmacodynamic
[redacted]	

Term	Definition
PGA	Physician Global Assessment
PID	participant identification number
PK	pharmacokinetic
PO	orally
PRO	patient-reported outcome
PRO2	patient-reported outcome based on the stool frequency and abdominal pain components of the CDAI
PSEOT	parent study end of treatment
Q	quarter
Q12W	every 12 weeks
QD	once daily
RB	rectal bleeding
RBC	red blood cell
RHI	Robarts Histopathology Index
RNA	ribonucleic acid
[redacted]	
SAE	serious adverse event
SAP	Statistical Analysis Plan
SARS-CoV-2	severe acute respiratory syndrome coronavirus 2
SD	standard deviation
SES-CD	Simple Endoscopic Score for Crohn's Disease
SF	stool frequency
[redacted]	
SLE	systemic lupus erythematosus
SOC	standard of care
SUSAR	suspected, unexpected serious adverse reaction
TB	tuberculosis
[redacted]	
TEAE	treatment-emergent adverse event
TIBC	total iron binding capacity

Term	Definition
TNF	tumor necrosis factor
TYK2	tyrosine kinase 2
UC	ulcerative colitis
[redacted]	
ULN	upper limit of normal
US	United States
WBC	white blood cell
WOCBP	women of childbearing potential

APPENDIX 2 STUDY GOVERNANCE CONSIDERATIONS

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

REGULATORY AND ETHICAL CONSIDERATIONS

GOOD CLINICAL PRACTICE

This study will be conducted in accordance with:

- Consensus ethical principles derived from international guidelines including the Declaration of Helsinki and Council for International Organizations of Medical Sciences (CIOMS) International Ethical Guidelines Good Clinical Practice (GCP),
- as defined by the International Council on Harmonisation (ICH)
- in accordance with the ethical principles underlying European Union Directive 2001/20/EC
- United States Code of Federal Regulations, Title 21, Part 50 (21CFR50)
- applicable local requirements.

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

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

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

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

INSTITUTIONAL REVIEW BOARD/INDEPENDENT ETHICS COMMITTEE

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

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

COMPLIANCE WITH THE PROTOCOL AND PROTOCOL REVISIONS

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

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

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

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

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

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

FINANCIAL DISCLOSURE

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

INFORMED CONSENT PROCESS

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

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

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

Investigators must:

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

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

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

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

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

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

SOURCE DOCUMENTS

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

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

STUDY TREATMENT RECORDS

Records for study treatments (whether supplied by BMS, its vendors, or the site) must substantiate study treatment integrity and traceability from receipt, preparation, administration, and through destruction or return. Records must be made available for review at the request of BMS/designee or a Health Authority.

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

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

CASE REPORT FORMS

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

For sites using the Sponsor or designee electronic data capture tool, electronic CRFs will be prepared for all data collection fields except for fields specific to SAEs and pregnancy, which will be reported on the electronic SAE form and Pregnancy Surveillance form, respectively. If electronic SAE form is not available, a paper SAE form can be used. Spaces may be left blank only in those circumstances permitted by study-specific CRF completion guidelines provided by Sponsor or designee.

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

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

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

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

MONITORING

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

Representatives of BMS must be allowed to visit all study site locations periodically to assess the data quality and study integrity. On site they will review study records and directly compare them with source documents, discuss the conduct of the study with the investigator, and verify that the

facilities remain acceptable. Certain CRF pages and/or electronic files may serve as the source documents:

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

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

RECORDS RETENTION

The investigator (or head of the study site in Japan) must retain all study records and source documents for the maximum period required by applicable regulations and guidelines, or institution procedures, or for the period specified by BMS or designee, whichever is longer. The investigator (or head of the study site in Japan) must contact BMS prior to destroying any records associated with the study.

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

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

RETURN OF STUDY TREATMENT

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

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

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

- On-site disposal practices must not expose humans to risks from the drug.
- On-site disposal practices and procedures are in agreement with applicable laws and regulations, including any special requirements for controlled or hazardous substances.
- Written procedures for on-site disposal are available and followed. The procedures must be filed with the site's SOPs and a copy provided to BMS upon request.
- Records are maintained that allow for traceability of each container, including the date disposed of, quantity disposed, and identification of the person disposing the containers. The method of disposal, ie, incinerator, licensed sanitary landfill, or licensed waste disposal vendor must be documented.
- Accountability and disposal records are complete, up-to-date, and available for the Monitor to review throughout the clinical trial period.

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

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

CLINICAL STUDY REPORT

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

For each CSR related to this protocol, the signatory investigator will fulfill at least one of the following criteria:

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

SCIENTIFIC PUBLICATIONS

The data collected during this study are confidential and proprietary to Sponsor or designee. Any publications or abstracts arising from this study must adhere to the publication requirements set forth in the clinical trial agreement (CTAg) governing [Study site or Investigator] participation in the study. These requirements include, but are not limited to, submitting proposed publications to

Sponsor or designee at the earliest practicable time prior to submission or presentation and otherwise within the time period set forth in the CTAg.

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

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

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

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

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

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

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

ADVERSE EVENTS

Adverse Event Definition:

An Adverse Event (AE) is defined as any new untoward medical occurrence or worsening of a preexisting medical condition in a clinical investigation participant administered study treatment and that does not necessarily have a causal relationship with this treatment.

An AE can therefore be any unfavorable and unintended sign (such as an abnormal laboratory finding), symptom, or disease temporally associated with the use of study treatment, whether or not considered related to the study treatment.

Events Meeting the AE Definition

- Any abnormal laboratory test results (hematology, clinical chemistry, or urinalysis) or results from other safety assessments (eg, ECG, radiological scans, vital signs measurements), including those that worsen from baseline, considered clinically significant in the medical and scientific judgment of the investigator. Note that abnormal lab tests or other safety assessments should only be reported as AEs if the final diagnosis is not available. Once the final diagnosis is known, the reported term should be updated to be the diagnosis.
- Exacerbation of a chronic or intermittent pre-existing condition including either an increase in frequency and/or intensity of the condition.
- New conditions detected or diagnosed after study intervention administration even though it may have been present before the start of the study.
- Signs, symptoms, or the clinical sequelae of a suspected drug-drug interaction.
- Signs, symptoms, or the clinical sequelae of a suspected overdose of either study intervention or a concomitant medication. Overdose, as a verbatim term (as reported by the investigator), should not be reported as an AE/SAE unless it is an intentional overdose taken with possible suicidal/self-harming intent. Such overdoses should be reported regardless of sequelae and should specify "intentional overdose" as the verbatim term

Events NOT Meeting the AE Definition

- Medical or surgical procedure (eg, endoscopy, appendectomy): the condition that leads to the procedure is the AE.
- Situations in which an untoward medical occurrence did not occur (social and/or convenience admission to a hospital).

DEFINITION OF SAE

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

SERIOUS ADVERSE EVENTS

Serious Adverse Event (SAE) is defined as any untoward medical occurrence that, at any dose:
Results in death
Is life-threatening (defined as an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe)
Requires inpatient hospitalization or causes prolongation of existing hospitalization (see NOTE below) NOTE: The following hospitalizations are not considered SAEs in BMS clinical studies: • a visit to the emergency room or other hospital department < 24 hours, that does not result in admission (unless considered an important medical or life-threatening event) • elective surgery, planned prior to signing consent • admissions as per protocol for a planned medical/surgical procedure • routine health assessment requiring admission for baseline/trending of health status (e.g., routine colonoscopy) • medical/surgical admission other than to remedy ill health and planned prior to entry into the study. Appropriate documentation is required in these cases • admission encountered for another life circumstance that carries no bearing on health status and requires no medical/surgical intervention (e.g., lack of housing, economic inadequacy, caregiver respite, family circumstances, administrative reason) • admission for administration of anticancer therapy in the absence of any other SAEs (applies to oncology protocols)
Results in persistent or significant disability/incapacity
Is a congenital anomaly/birth defect
Is an important medical event (defined as a medical event(s) that may not be immediately life-threatening or result in death or hospitalization but, based upon appropriate medical and scientific judgment, may jeopardize the participant or may require intervention [e.g., medical, surgical] to prevent one of the other serious outcomes listed in the definition above.) Examples of such events include, but are not limited to, intensive treatment in an emergency room or at home for allergic bronchospasm; blood dyscrasias or convulsions that do not result in hospitalization.) Potential drug induced liver injury (DILI) is also considered an important medical event. (See Section 9.2.7 for the definition of potential DILI.)

Pregnancy and potential drug induced liver injury (DILI) must follow the same transmission timing and processes to BMS as used for SAEs (see section 9.2.5 for reporting pregnancies).

EVALUATING AES AND SAES

Assessment of Intensity

The intensity of AEs is determined by a physician and will use the following levels:

- Mild: An event that is easily tolerated by the subject, causing minimal discomfort and not interfering with everyday activities.
- Moderate: An event that causes sufficient discomfort and interferes with normal everyday activities.
- Severe: An event that prevents normal everyday activities. An AE that is assessed as severe should not be confused with an SAE. Severe is a category utilized for rating the intensity of an event; both AEs and SAEs can be assessed as severe.

Assessment of Causality

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

Follow-up of AEs and SAEs

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

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

All SAEs must be followed to resolution or stabilization.

REPORTING OF SAES TO SPONSOR OR DESIGNEE

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

SAE Email Address: Refer to Contact Information list.

SAE Facsimile Number: Refer to Contact Information list.

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

APPENDIX 4 WOMEN OF CHILDBEARING POTENTIAL DEFINITIONS AND METHODS OF CONTRACEPTION

DEFINITIONS

Woman of Childbearing Potential (WOCBP)

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

Women in the following categories are not considered WOCBP

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

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

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

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

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

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

End of Relevant Systemic Exposure

- End of relevant systemic exposure is the time point where the IMP or any active major metabolites has decreased to a concentration that is no longer considered to be relevant for human teratogenicity or fetotoxicity. This should be evaluated in context of safety margins

from the no-observed adverse effect level (NOAEL) or the time required for 5 half-lives of the IMP to pass.

METHODS OF CONTRACEPTION

For WOCBP, one of the "highly effective" or "less than highly effective" methods of contraception listed below should be commenced at least 30 days prior to initiation of study therapy and should be continued until at a minimum after the last dose of the study treatment.

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

Highly Effective Contraceptive Methods That Are <u>User Dependent</u> *Failure rate of <1% per year when used consistently and correctly.*[a]
• Combined (estrogen- and progestogen-containing) hormonal contraception associated with inhibition of ovulation and/or implantation (This method of contraception can only be used by WOCBP participants in studies where hormonal contraception is permitted by the study protocol)[b] – oral (birth control pills) – intravaginal (vaginal birth control suppositories, rings, creams, gels) – transdermal • Combined (estrogen-and progestogen-containing) hormonal contraception must begin at least 30 days prior to initiation of study therapy
• Progestogen-only hormonal contraception associated with inhibition of ovulation (This method of contraception can only be used by WOCBP participants in studies where hormonal contraception is permitted by the study protocol)[b] – oral – injectable • Progestogen-only hormonal contraception must begin at least 30 days prior to initiation of study therapy
Highly Effective Methods That Are User Independent
• Implantable progestogen-only hormonal contraception associated with inhibition of ovulation and/or implantation (This method of contraception can only be used by WOCBP participants in studies where hormonal contraception is permitted by the study protocol)[b] • Intrauterine device (IUD) • Intrauterine hormone-releasing system (IUS) (This method of contraception can only be used by WOCBP participants in studies where hormonal contraception is permitted by the study protocol)[b,c] • Bilateral tubal occlusion
• Vasectomized partner • Having a vasectomized partner is a highly effective contraception method provided that the partner is the sole male sexual partner of the WOCBP and the absence of sperm has been confirmed. If not, an additional highly effective method of contraception should be used.

- Sexual abstinence

  Sexual abstinence is considered a highly effective method only if defined as refraining from heterosexual intercourse during the entire period of risk associated with the study treatment. The reliability of sexual abstinence needs to be evaluated in relation to the duration of the study and the preferred and usual lifestyle of the participant.

- Continuous abstinence must begin at least 30 days prior to initiation of study therapy.
- It is not necessary to use any other method of contraception when complete abstinence is elected.
- WOCBP participants who choose complete abstinence must continue to have pregnancy tests, as specified in Section 2 (Schedule of Activities).
- Acceptable alternate methods of highly effective contraception must be discussed in the event that the WOCBP participants chooses to forego complete abstinence.
- Periodic abstinence (including but not limited to calendar, symptothermal, post-ovulation methods), withdrawal (coitus interruptus), spermicides only, and lactational amenorrhoea method (LAM) are not acceptable methods of contraception for this study.

NOTES:

[a] Typical use failure rates may differ from those when used consistently and correctly. Use should be consistent with local regulations regarding the use of contraceptive methods for participants participating in clinical studies.

[b] Hormonal contraception may be susceptible to interaction with the study treatment, which may reduce the efficacy of the contraceptive method. Hormonal contraception is permissible only when there is sufficient evidence that the IMP and other study medications will not alter hormonal exposures such that contraception would be ineffective or result in increased exposures that could be potentially hazardous. In this case, alternative methods of contraception should be utilized.

[c] Intrauterine hormone releasing systems are acceptable methods of contraception in the absence of definitive drug interaction studies when hormone exposures from intrauterine devices do not alter contraception effectiveness.

Less Than Highly Effective Contraceptive Methods That Are User Dependent

Failure rate of >1% per year when used consistently and correctly.

- Male or female condom with or without spermicide. Male and female condoms cannot be used simultaneously
- Diaphragm with spermicide
- Cervical cap with spermicide
- Vaginal Sponge with spermicide
- Progestogen-only oral hormonal contraception, where inhibition of ovulation is not the primary mechanism of action (This method of contraception cannot be used by WOCBP participants in studies where hormonal contraception is prohibited)

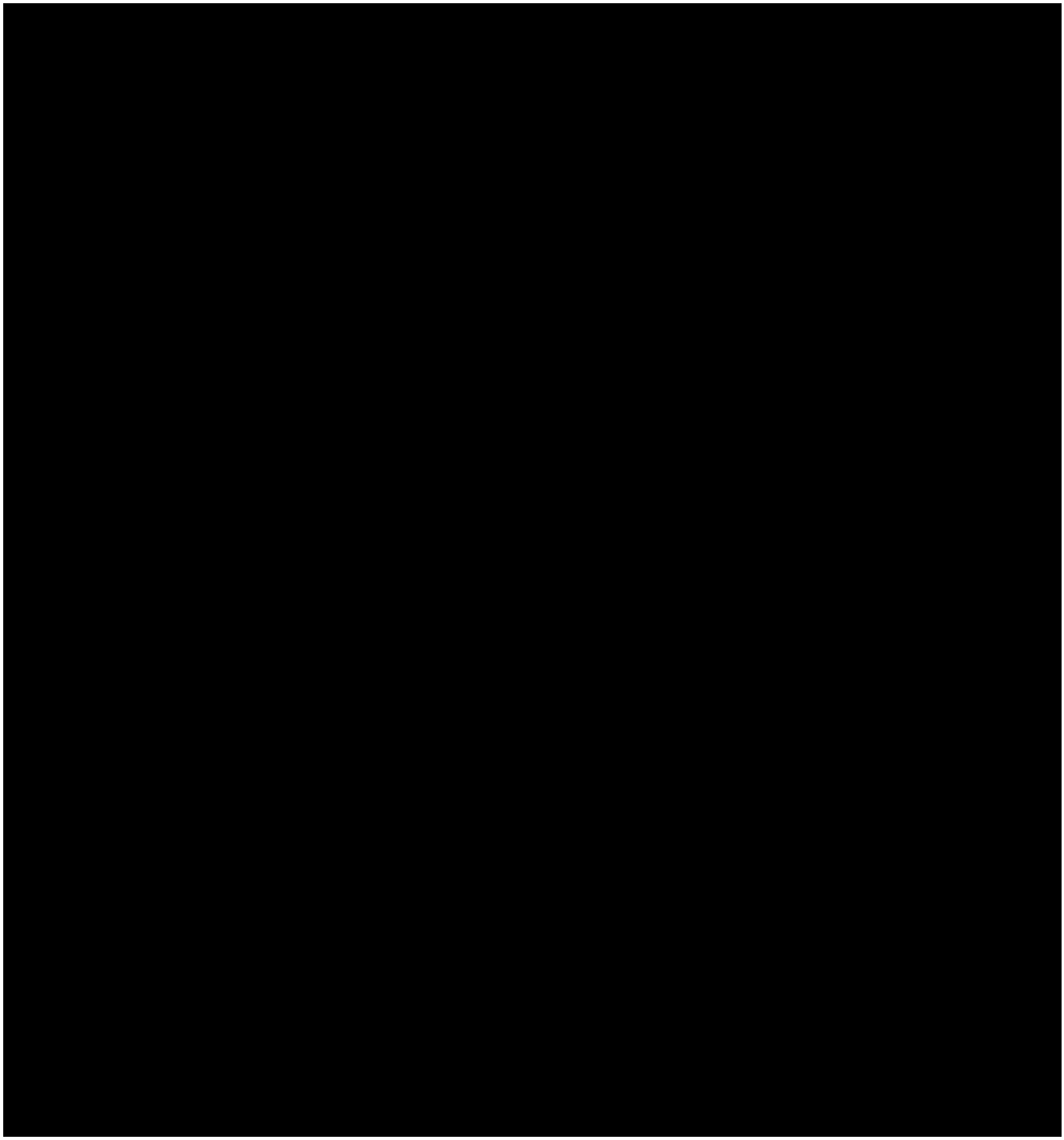
Unacceptable Methods of Contraception

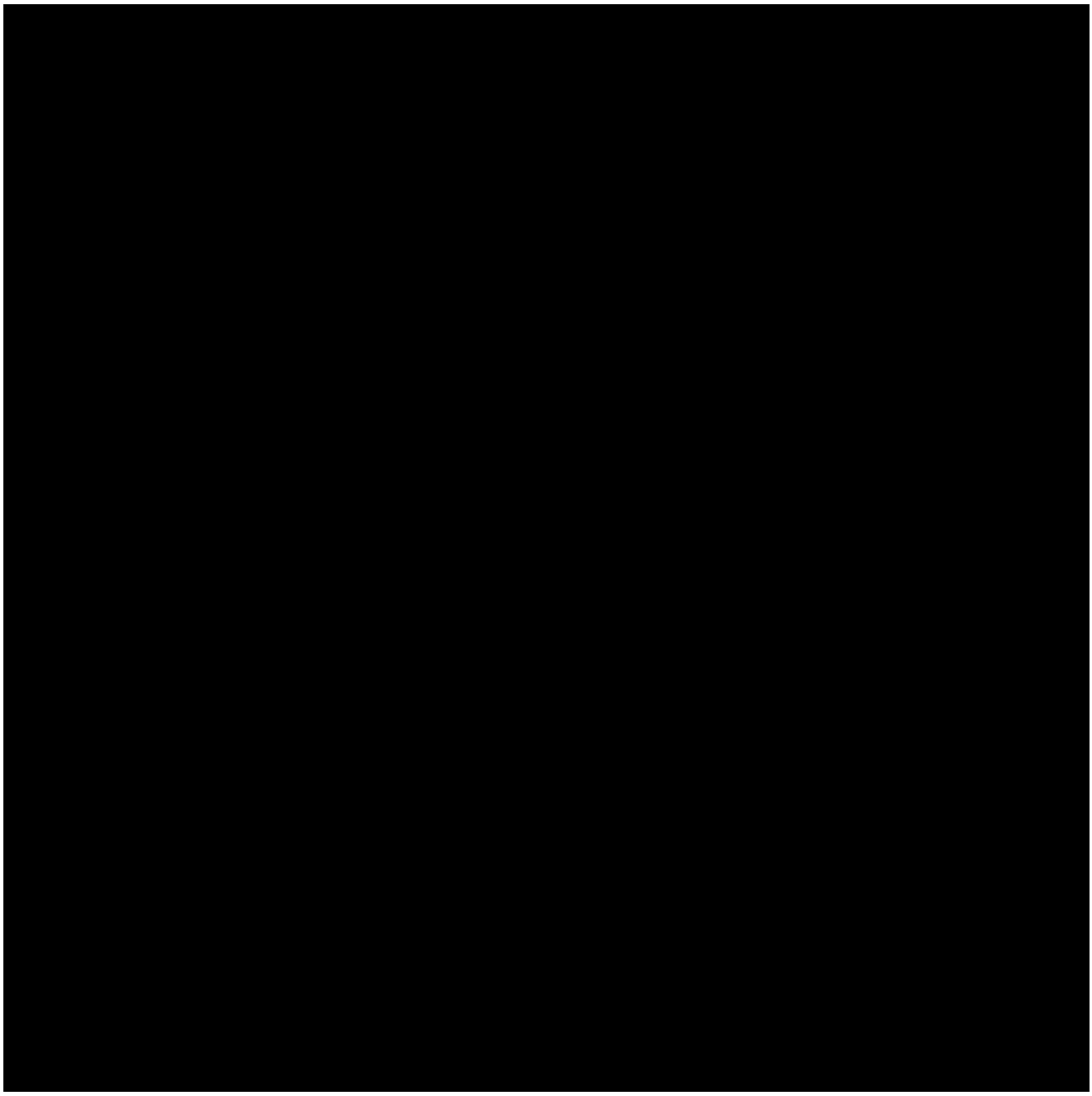
- Periodic abstinence (calendar, symptothermal, post-ovulation methods)
- Withdrawal(coitus interruptus)
- Spermicide only
- Lactation amenorrhea method (LAM)

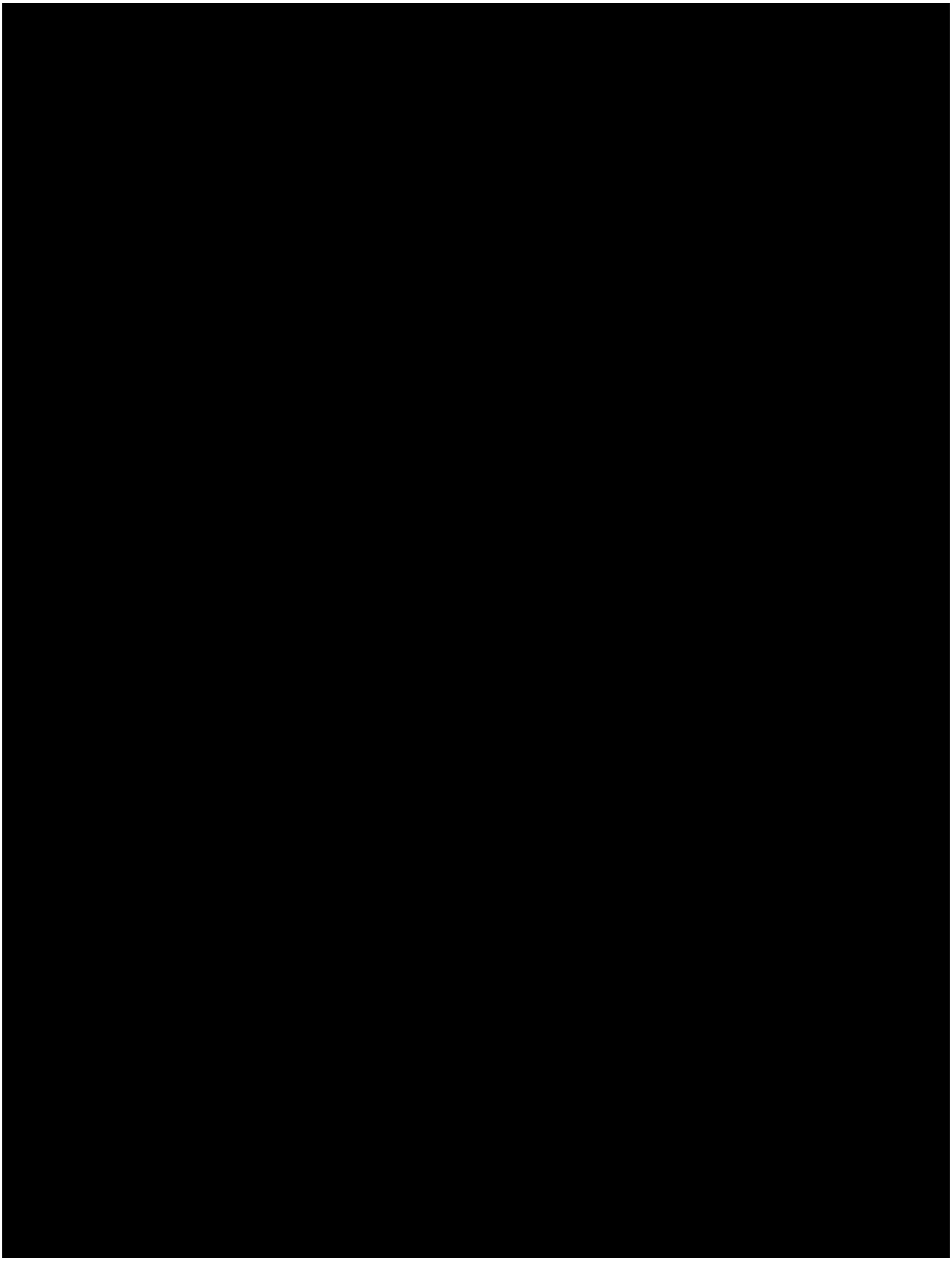
COLLECTION OF PREGNANCY INFORMATION

Guidance for collection of Pregnancy Information and outcome of pregnancy on the Pregnancy Surveillance Form is provided in Section 9.2.5 and the Appendix for Adverse Events and Serious Adverse Events Definitions and procedures for Evaluating, Follow-up and Reporting.

APPENDIX 5 TUBERCULOSIS RISK ASSESSMENT TOOL







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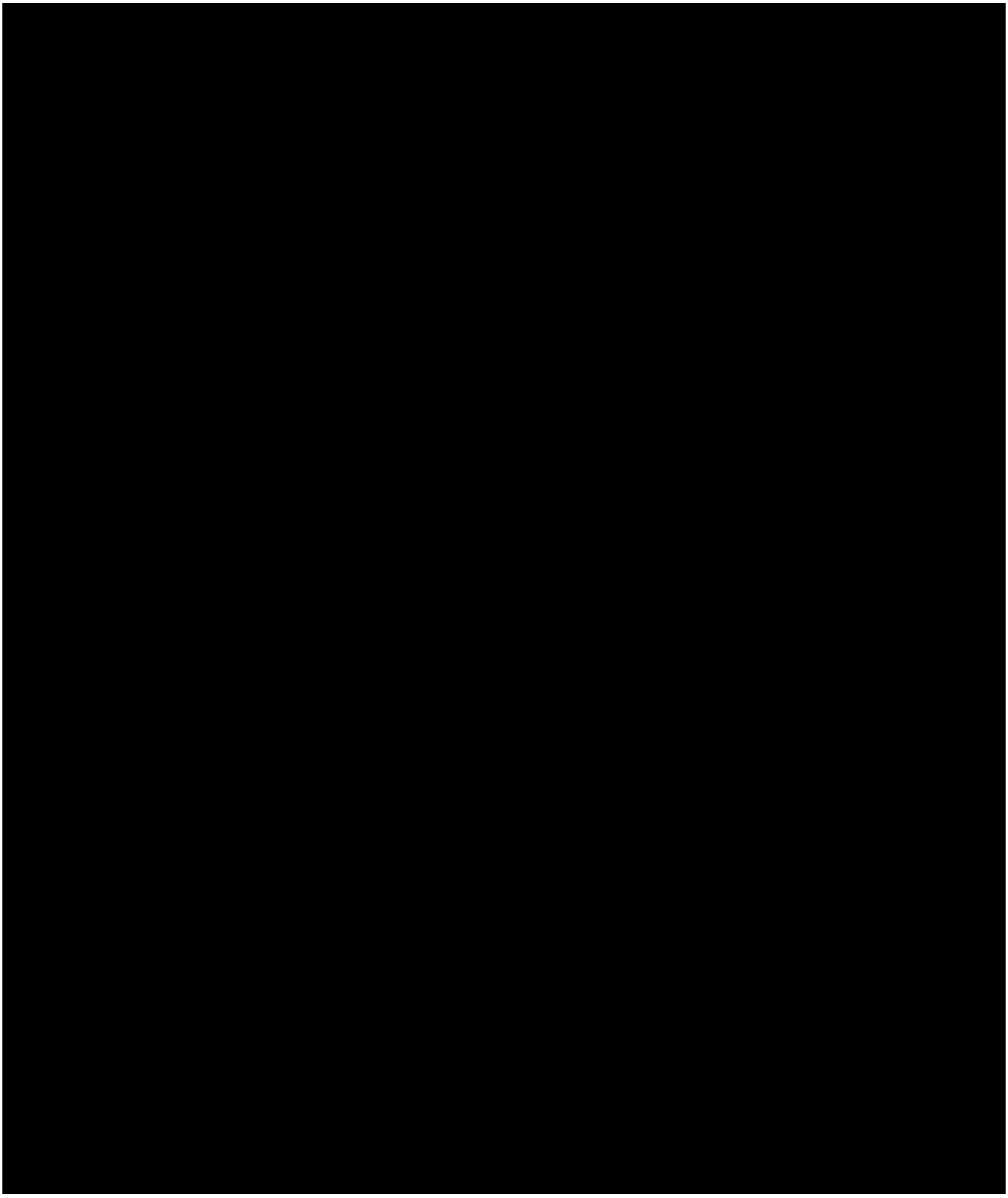

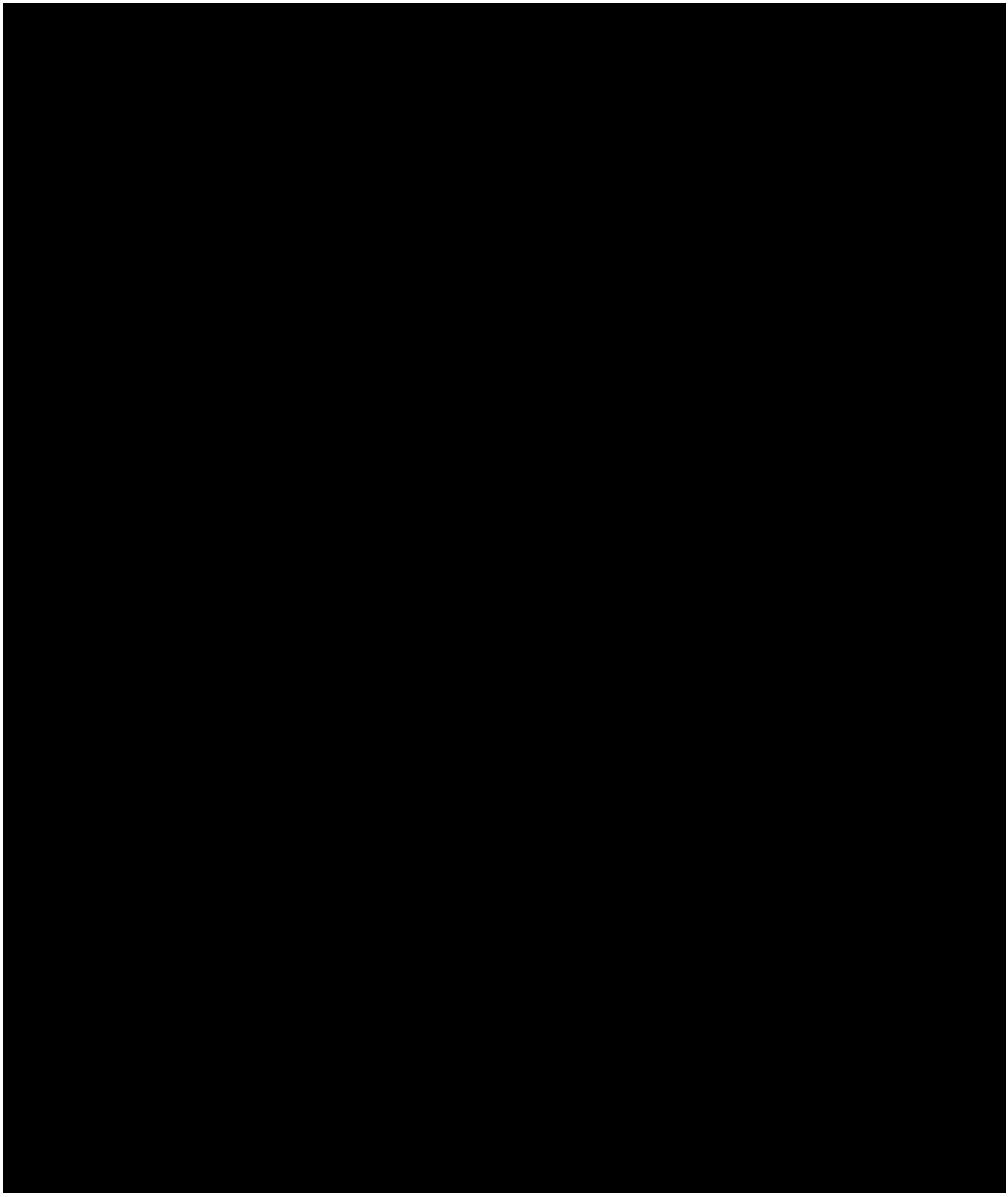

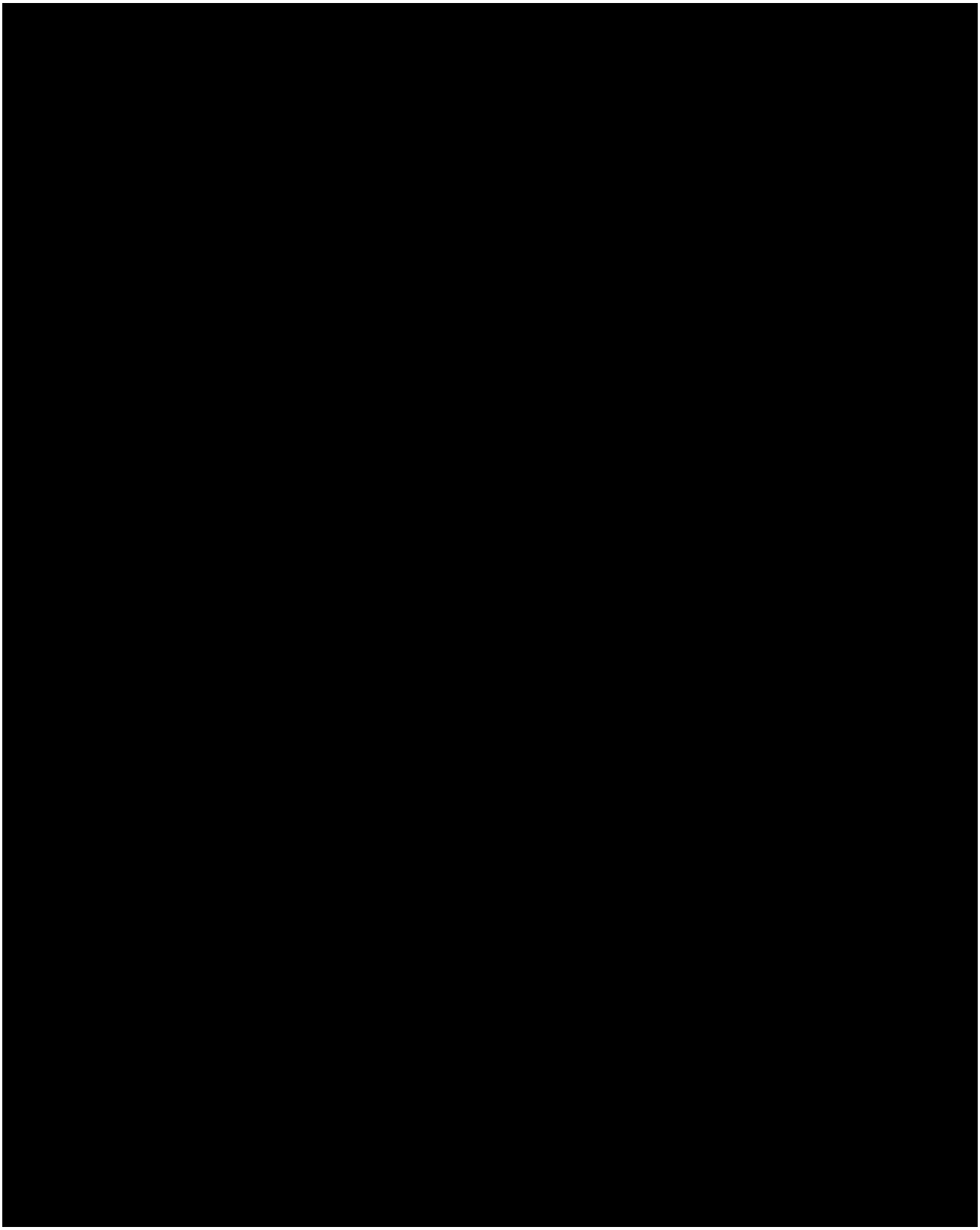

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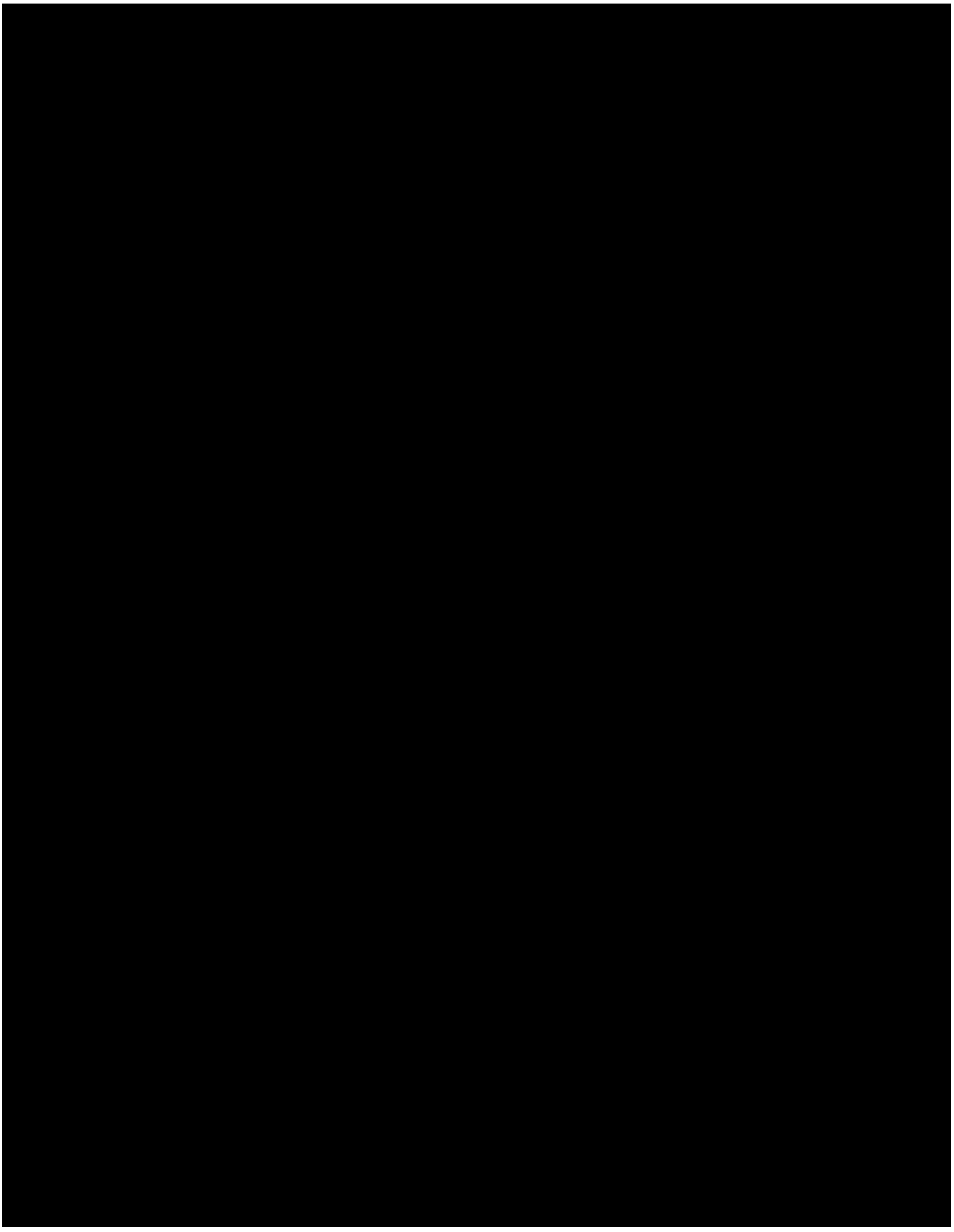

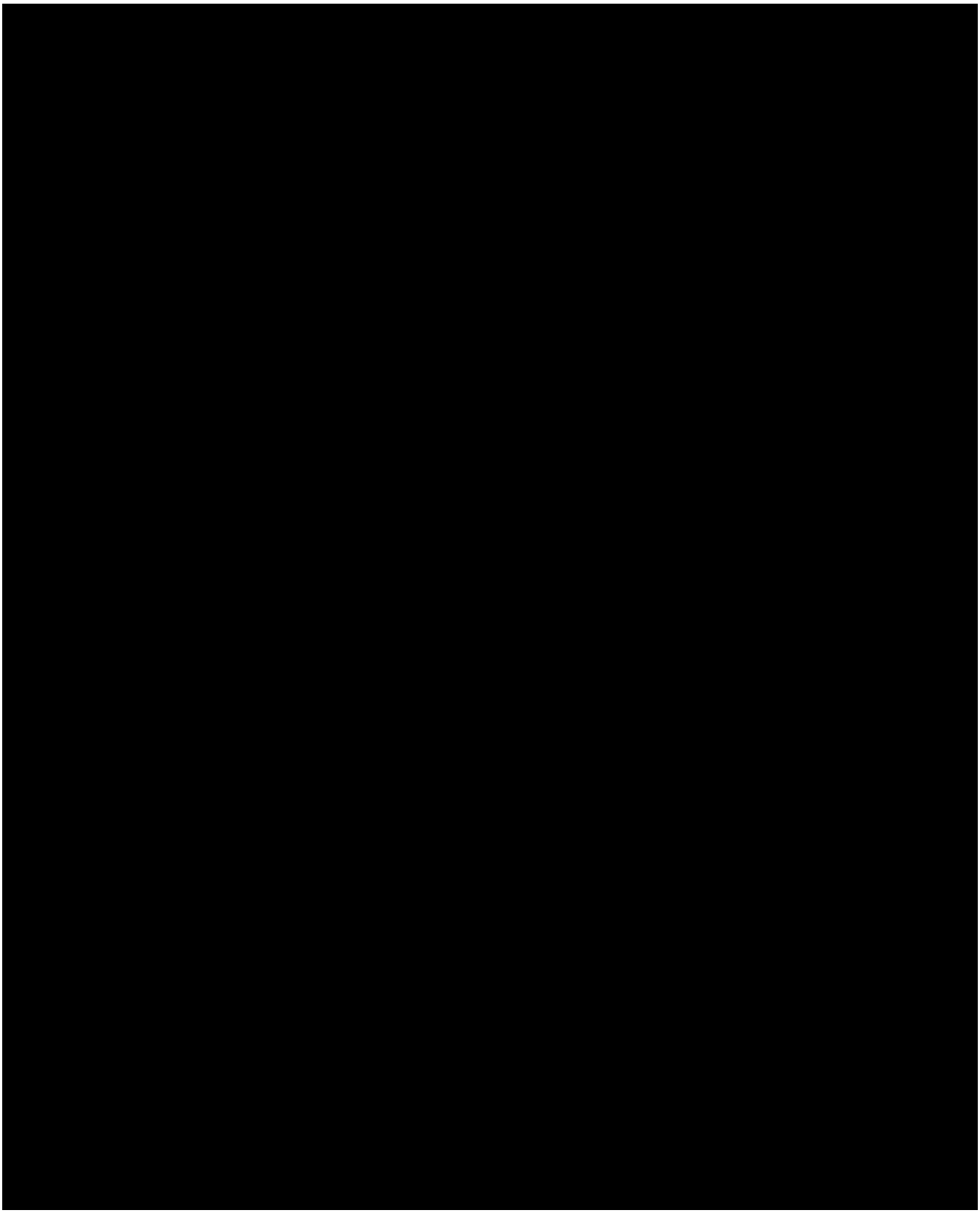

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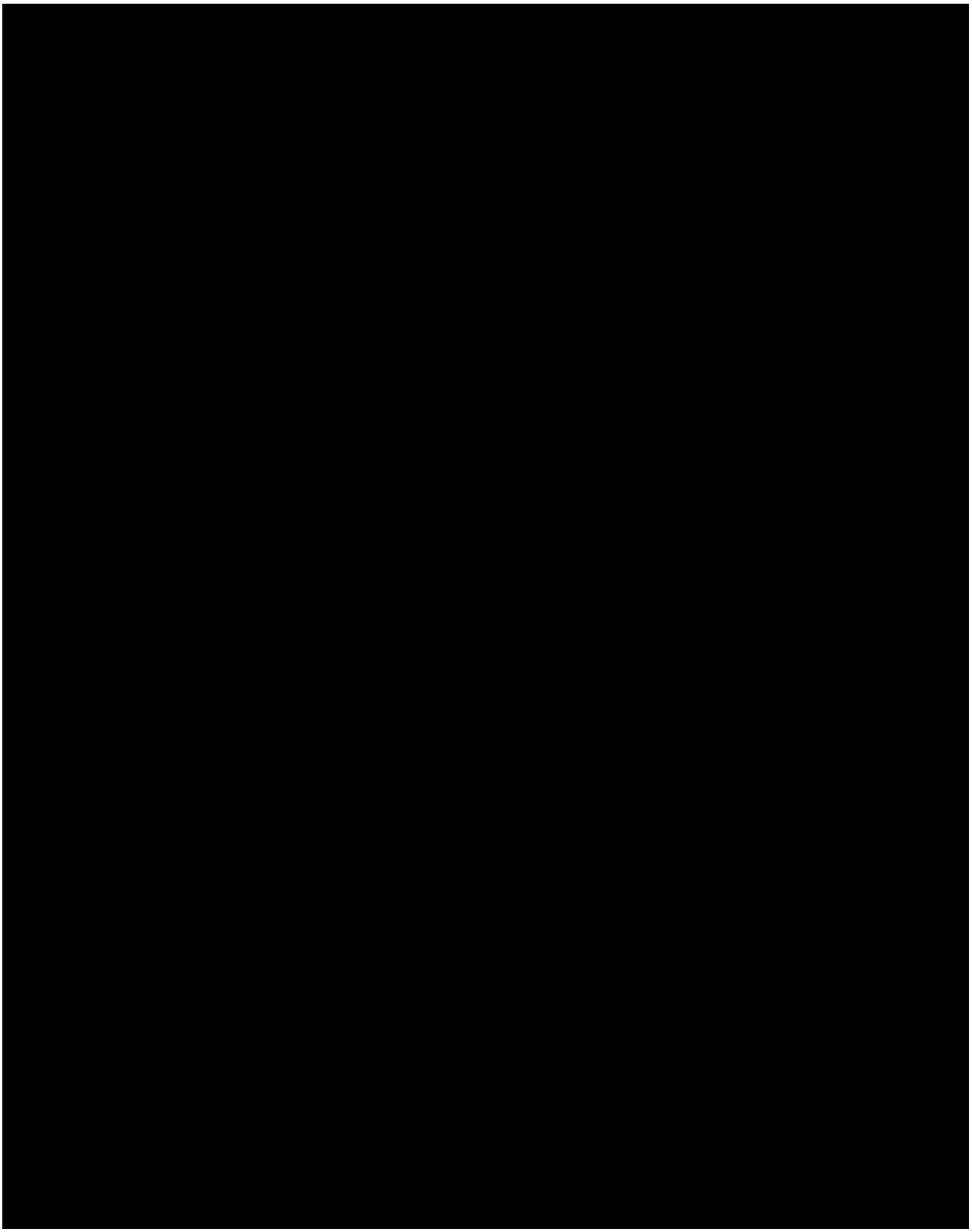

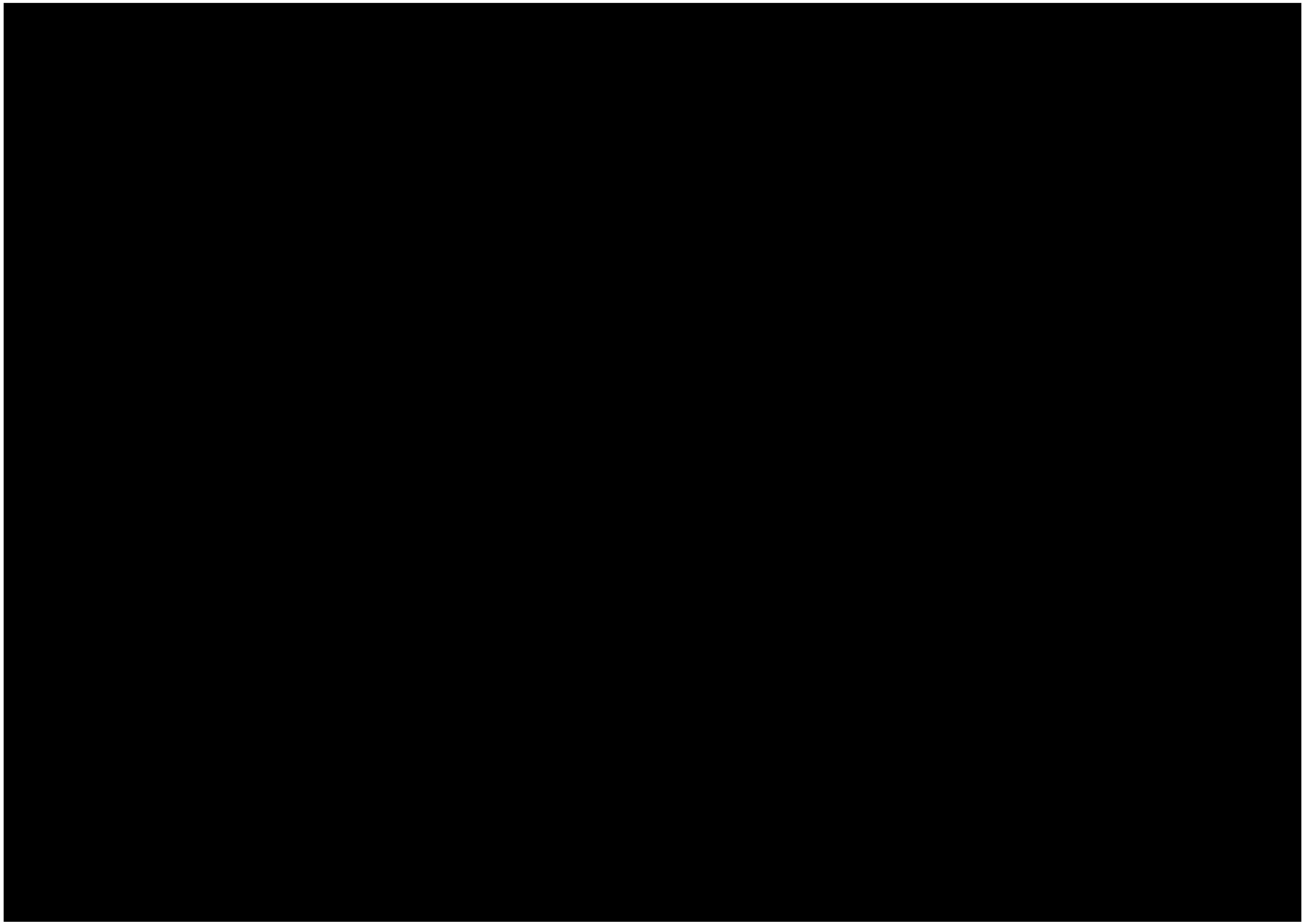

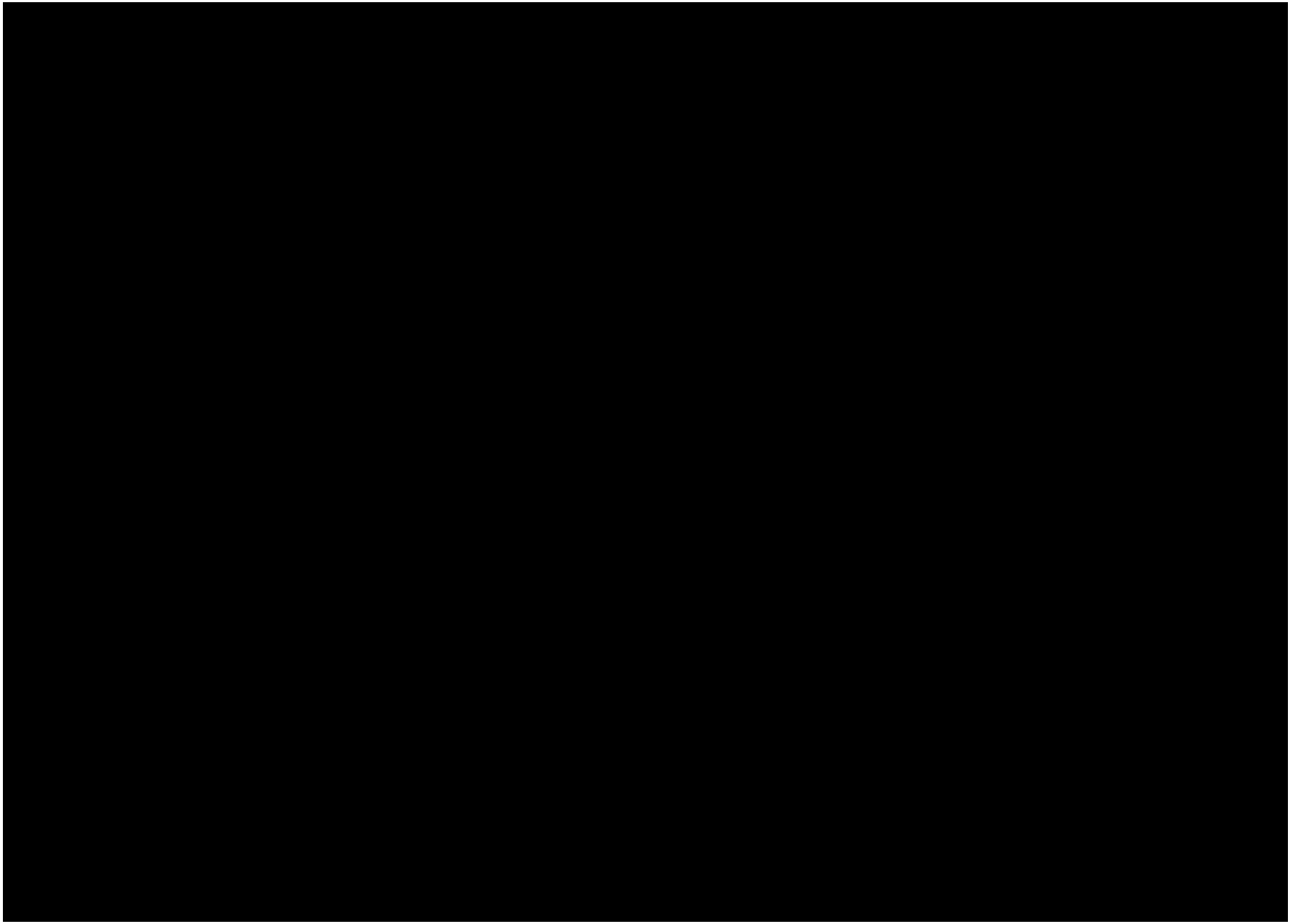

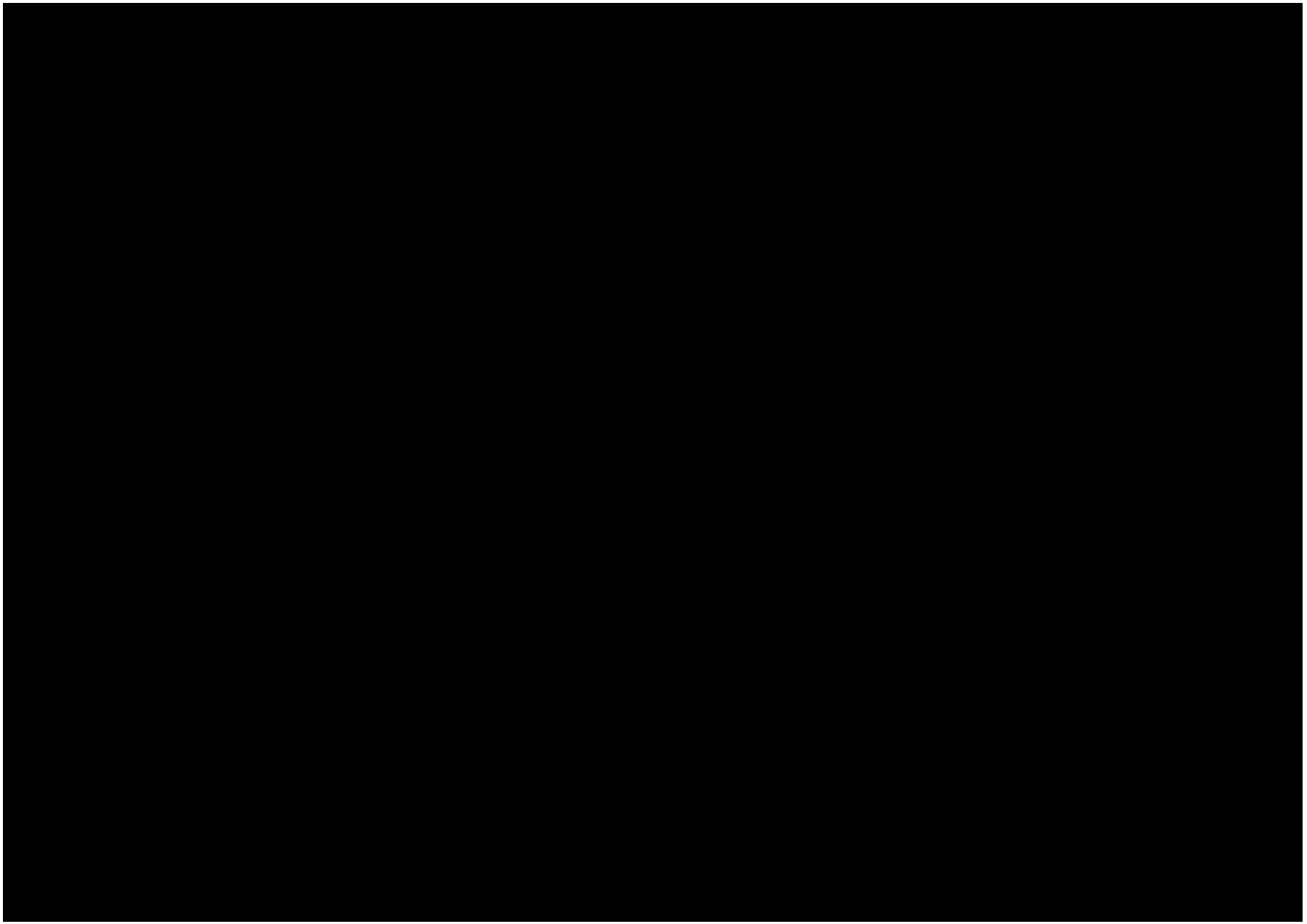

APPENDIX 13 MAYO SCORE: COMPONENT SUBSCORES [redacted]

The Mayo score is a composite instrument designed to assess ulcerative colitis (UC) disease activity. It includes patient-reported outcomes (PROs), an objective assessment of disease activity by endoscopy, and a Physician's Global Assessment (PGA). The Mayo score was first proposed by Schroeder et al.[1] Scherl et al[2] proposed that the Mayo score should be modified by removing "mild friability" from the definition of an endoscopic (ES) subscore = 1. This was supported by draft guidance from the US Food and Drug Administration (FDA) that states the presence of friability is not consistent with the concept of "clinical remission" (lines 249-251).[3] Because the PGA is neither a PRO nor an objective assessment of disease activity, and the concept that it purports to measure is not distinct from the other components of the modified Mayo score, use of the PGA as a component of the modified Mayo score is no longer recommended by US[3] or European regulatory authorities.[4]

Consequently, disease activity assessments for inclusion and efficacy assessment will use the 9-point modified Mayo score (ie, excluding PGA). The PGA will continue to be captured as part of this study to facilitate the calculation of the total Mayo score, which will allow these data to be compared with previous clinical trials. Table 1 outlines the components and scoring used to calculate the modified and total Mayo scores.

Table 1: Components of the Modified and Total Mayo Scores

Stool Frequency (SF)[a]	
0	Normal number of stools for this patient
1	1 to 2 stools/day more than normal
2	3 to 4 stools/day more than normal
3	> 4 stools/day more than normal
Rectal Bleeding (RB)[b]	
0	None
1	Streaks of blood with stool less than half the time
2	Obvious blood with stool most of the time
3	Blood alone passed
Findings of flexible proctosigmoidoscopy (endoscopy used to determine endoscopic [ES] subscore)	
0	Normal or inactive disease
1	Mild disease (erythema, decreased vascular pattern)[c]
2	Moderate disease (marked erythema, absent vascular pattern, friability, erosions)
3	Severe disease (spontaneous bleeding ulceration)
Physician's Global Assessment (PGA) of Disease Activity (not included in the 9-point modified Mayo score)	
0	Normal

Table 1: Components of the Modified and Total Mayo Scores

1	Mild disease
2	Moderate disease
3	Severe disease

[a] Each subject serves as his or her own control to establish the degree of abnormality of the stool frequency.

[b] The daily bleeding score represents the most severe bleeding of the day.

[c] The original description of the Mayo score included "mild friability" in an ES subscore = 1. The modified Mayo score removed friability from an ES subscore = 0.

Adapted from: Schroeder KW, Tremaine WJ, Ilstrup DM. Coated oral 5-aminosalicylic acid therapy for mildly to moderately active ulcerative colitis. a randomized study. New Engl J Med 1987;317:1625-29.

MAYO SCORES: DEFINITIONS

Two different versions of the Mayo score will be used as efficacy endpoints:

Modified Mayo Score: The modified Mayo score is a **9-point scale**; a score of 5 to 9 points (inclusive), which is required for randomization, denotes moderate-to-severe disease (by protocol definition). The modified Mayo score is an adaptation of the total Mayo score (defined below) that excludes the PGA subscore.

The modified Mayo score incorporates the following 3 components:

- Stool frequency (SF) subscore (0 to 3)
- Rectal bleeding (RB) subscore (0 to 3)
- Endoscopic (ES) subscore (0 to 3)

Total Mayo Score: The original total Mayo score incorporates all 4 components of UC severity listed in Table 1; each component subscore ranges from 0 to 3. The total Mayo score is a **12-point scale** in which a higher score equals more severe disease. The modified and total Mayo scores will be calculated using component subscores entered into the electronic case report form (eCRF).

MAYO SCORES: SF AND RB COMPONENT SUBSCORES

SF and RB data will be [redacted] calculated [redacted].

Stool Frequency and Rectal Bleeding Subscores

[redacted]

[redacted]

The following will be considered invalid data and excluded from SF and RB subscore calculations:

- [redacted]
- [redacted]

NOTE: Formal calculation of SF and RB subscores [redacted] will be calculated and used to represent SF and RB subscores in Mayo score determination; averages will be rounded up and down at the 0.5 cutoff.

For the pre-endoscopy screening visit (ie, prior to the availability of [redacted] data) from the parent study:

[redacted]

This **baseline SF** from the parent study is used as the reference for subsequent SF subscores in Study IM011077.

For the endoscopy screening visit:

The endoscopy obtained for the last visit on the parent study (IM011023, IM011024, or IM011127) will be used as the first endoscopy for Study IM011077. The following information should be used in the context of the parent study or when, for any reason, an endoscopy is being obtained prior to the first dose of deucravacitinib on Study IM011077: Best practice is to complete the other screening investigations first and check results to ensure that a subject continues to be potentially eligible for the study prior to commencing bowel preparation for the endoscopy. When the

endoscopy is scheduled, SF and RB data [redacted] from the [redacted] **the bowel preparation day** for the endoscopy will be evaluated to ensure eligibility is maintained.

Following endoscopy, the ES subscore will be received via email from the central reader (Robarts Clinical Trials). This centrally read screening ES subscore will be entered into the eCRF, in addition to the SF and RB subscores, and the modified Mayo score calculated to determine subject eligibility.

For subsequent study visits at which Mayo scores are calculated:

For the annual visits, endoscopy timing should be reviewed prior to the visit to ensure adequate [redacted] are available for SF and RB subscore determination. The averages [redacted] **prior to the bowel preparation day** for the endoscopy will be used.

If adequate entries have not been made, the site should contact the subject to reschedule the visit, and the subject should be counseled about proper study procedures. Following endoscopy, ES subscores will be emailed from the central vendor as noted above and entered into the eCRF together with the SF and RB subscores to calculate the modified Mayo score for a given visit.

Missing Data:

Assessments with fewer [redacted] **prior to the bowel preparation day** for endoscopy are considered missing data and will not count toward assessment of disease activity during the screening period or for endpoint assessment.

[redacted]

[redacted]

ES Subscore

ES subscores will be provided via email by the independent central endoscopy vendor (Alimentiv) for all eligibility and efficacy assessments, at all timepoints. The endoscopy procedure from screening (central read) will be used to determine the **baseline** (Week 0 [Day 1]) ES subscore component of the Mayo score. The ES subscores of the Mayo score will be modified [redacted].

Local assessment of the endoscopy will be utilized to derive the ES component of the Mayo score; this is used for determination eligibility. The central read of the endoscopy will be used for efficacy analysis at all timepoints.

Physician's Global Assessment

The investigator will directly provide the PGA at every required visit.

Physician's Global Assessment (PGA)[a]	
0	Normal
1	Mild disease
2	Moderate disease
3	Severe disease

[a] The PGA is not included in the modified Mayo score. It is included as a stand-alone assessment and as part of the total Mayo score.

REFERENCES:

1 Schroeder KW, Tremaine WJ, Ilstrup DM. Coated Oral 5-aminosalicylic Acid Therapy for Mildly to Moderately Active Ulcerative Colitis. A Randomized Study. N Engl J Med 1987;317(26):1625-9.

2 Scherl EJ, Pruitt R, Gordon GL, et al. Safety and Efficacy of a New 3.3 g b.i.d. Tablet Formulation in Patients with Mild-to-moderately-active Ulcerative Colitis: A Multicenter, Randomized, Double-blind, Placebo-controlled Study. Am J Gastroenterol 2009;104(6):1452-9.

3 US Department of Health and Human Services. Ulcerative colitis: clinical trial endpoints. Draft guidance for industry. Available from: https://www.fda.gov/files/drugs/published/Ulcerative-Colitis--Clinical-Trial-Endpoints-Guidance-for-Industry.pdf. Published August 2016. Accessed 2020 Nov 12.

4 European Medicines Agency, Committee for Medicinal Products for Human Use (CHMP). Guideline on the Development of New Medicinal Products for the Treatment of Ulcerative Colitis. Available from: https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-development-new-medicinal-products-treatment-ulcerative-colitis-revision-1_en.pdf. Published 2018 June 28. Accessed 2020 Nov 12.