Official Title: A Phase 2, Efficacy and Safety Study of Ruxolitinib Cream in Participants with Facial and/or Neck Atopic Dermatitis Involvement

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Statistical Analysis Plan

INCB 18424-215

A Phase 2, Efficacy and Safety Study of Ruxolitinib Cream in Participants with Facial and/or Neck Atopic Dermatitis Involvement

Product:	**Ruxolitinib**
IND Number:	[redacted]
EudraCT Number:	**2021-000489-14**
Sponsor:	**Incyte Corporation** **1801 Augustine Cut-Off** **Wilmington, DE 19803** **United States**
Protocol Version:	**Protocol Amendment 02 dated 04 AUG 2022**
CRF Approval Date:	**15 MAR 2022**
SAP Version:	**Original**
SAP Author:	[redacted] **Biostatistician**
Date of Plan:	**26 SEP 2023**

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

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LIST OF ABBREVIATIONS

Abbreviation	Term
AD	atopic dermatitis
AE	adverse event
ASR	application site reaction
BID	twice daily
BMI	body mass index
BSA	body surface area
CI	confidence interval
CMH	Cochran-Mantel-Haenszel
CRF	case report form
CTCAE	Common Terminology Criteria for Adverse Events
DBVC	double-blind vehicle-controlled
EASI	Eczema Area and Severity Index
EASI75	≥ 75% improvement in EASI score
FAS	full analysis set
eCRF	electronic case report form
IGA	Investigator's Global Assessment
IGA-TS	Investigator's Global Assessment Treatment Success
MedDRA	Medical Dictionary for Regulatory Activities
NRI	nonresponder imputation
NRS	numerical rating scale
OL	open-label
[redacted]	[redacted]
PT	preferred term
rux	ruxolitinib
SAP	Statistical Analysis Plan
SOC	system organ class
TEAE	treatment-emergent adverse event
VC	vehicle-controlled
WHO	World Health Organization

1. INTRODUCTION

INCB 18424-215 is a decentralized, randomized, DBVC study with a 4-week, OL period in adolescent and adult participants with AD (including AD on the face and/or neck) eligible for topical therapy.

This study will be conducted through a single, stand-alone, virtual site in the US. All study visits will be conducted in the participant's home with the assistance of a mobile healthcare provider and investigator or designee present through telemedicine (telephone and/or video visits).

Participants will be randomized 2:1 to blinded treatment with ruxolitinib 1.5% cream BID or vehicle cream BID with stratification by the participant's face and/or neck IGA score (IGA 2 or 3) at screening. Participants with a face and/or neck IGA score of 2 at screening will constitute approximately 25% of the overall study population.

Two Phase 3 pivotal studies (INCB 18424-303 and INCB 18424-304) demonstrated that ruxolitinib 1.5% cream BID was statistically and significantly superior to vehicle cream after 8 weeks of treatment, reaching the primary endpoint, IGA-TS, with a score of 0 or 1 with ≥ 2-grade improvement from baseline, as well as key secondary endpoints. Key secondary endpoints included a 75% improvement in the EASI and at least a 4-point improvement in Itch NRS (Papp et al 2020). The ruxolitinib 1.5% cream was consistently more efficacious than the ruxolitinib 0.75% cream; however, the safety and tolerability profiles of both regimens were comparable and nondifferentiating.

The purpose of this study is to further investigate and confirm the efficacy and safety of ruxolitinib 1.5% cream when applied to affected areas on the face and neck.

The purpose of this SAP is to provide details of the statistical analyses that have been outlined in the INCB 18424-215 Protocol. The Department of Biostatistics at Incyte or designee will execute the scope of this plan.

2. STUDY INFORMATION, OBJECTIVES, AND ENDPOINTS

2.1. Protocol and Case Report Form Version

This SAP is based on INCB 18424-215 Protocol Amendment 2 dated 04 AUG 2022 and CRFs approved 15 MAR 2022. Unless superseded by an amendment, this SAP will be effective for all subsequent Protocol amendments and eCRF versions.

2.2. Objectives and Endpoints

Table 1 presents the objectives and endpoints.

Table 1: Objectives and Endpoints

Objectives	Endpoints
Primary	
To establish the efficacy of ruxolitinib cream in participants with AD on the face and/or neck.	Proportion of participants who achieve an EASI75 of the head and neck region at Week 4.
Secondary	
To further assess efficacy of ruxolitinib cream for the treatment of AD on the face, neck, and other body areas.	Proportion of participants who achieve an EASI75 of the head and neck region at Weeks 2 and 8. Proportion of participants who achieve an overall EASI75 at Weeks 2, 4, and 8.
To assess the safety and tolerability of ruxolitinib in participants with AD on the face and/or neck.	The type, frequency, and severity of AEs, including the evaluation of vital signs.
[redacted]	

3. STUDY DESIGN

This is a decentralized, randomized, DBVC study with a 4-week, OL period in adolescent and adult participants with AD (including AD on the face and/or neck) eligible for topical therapy. This study will be conducted through a single, stand-alone, virtual site in the US. All study visits will be conducted in the participant's home with the assistance of a mobile healthcare provider and investigator or designee present through telemedicine (telephone and/or video visits).

During the 4-week DBVC period, participants will apply ruxolitinib 1.5% cream BID, or vehicle cream BID, to all areas identified for treatment at the baseline visit; this treatment will be followed by participants even if the AD begins to improve and the lesions decrease in size.

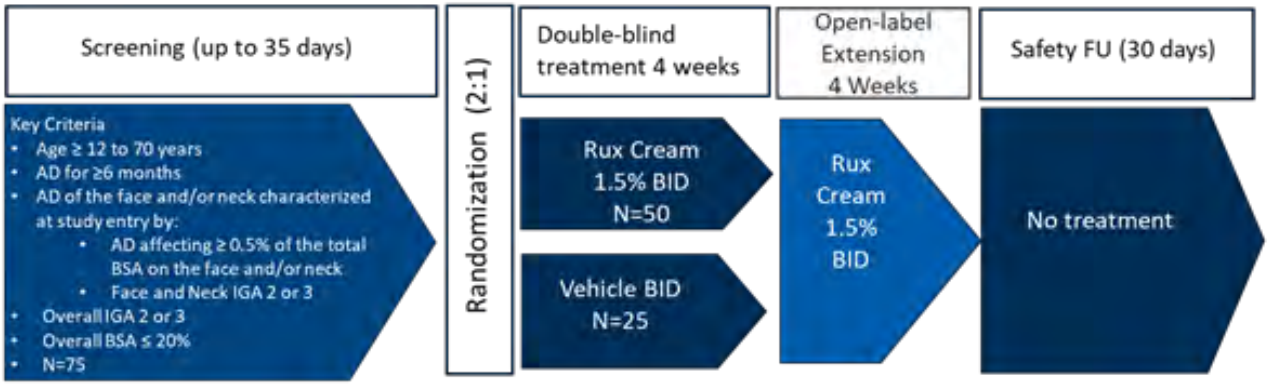
Mobile healthcare providers will take comprehensive photographs. The investigator will use these photos to assess the AD-affected areas for the Week 4 clinician-reported assessments. The participants who complete the study with no safety concerns through Week 4 will then continue into the 4-week, OL period, where individuals will apply ruxolitinib cream 1.5% BID only to affected areas.

The cumulative duration of this study will be approximately 17 weeks as follows: up to 35 days in the screening period; 4 weeks in the DBVC period; 4 weeks in the OL period; and 30 days (+ 3, as needed) for follow-up after the last application of the study drug.

At Week 4, efficacy (the primary endpoint of the study) will be evaluated as the proportion of participants who achieve an EASI75 of the head and neck region. Additional efficacy assessments and patient-reported outcomes will be conducted.

Figure 1 presents the study design schema.

Figure 1: Study Design Schema



3.1. Randomization

In the DBVC period, the Interactive Response Technology system will assign approximately 75 participants in a 2:1 ratio to ruxolitinib 1.5% cream BID and vehicle cream BID, respectively. Additionally, participants will be stratified by face and/or neck IGA score (2 or 3) at screening. Participants with a face and/or neck IGA score of 2 at screening will constitute approximately 25% of the overall study population.

3.2. Control of Type I Error

For the primary analysis, the overall 2-sided Type I error of 0.05 will be used.

3.3. Sample Size Considerations

Approximately 75 participants will be randomized 2:1 (ie, ruxolitinib 1.5% cream BID to vehicle cream BID, respectively). The sample size calculation is based on the Fisher's exact test for the primary efficacy endpoint. Based on the results from the 2 pivotal studies, INCB 18424-303 and -304, the response rate of EASI75 at Week 4 on the head and neck is assumed to be 55% for the active arm of ruxolitinib 1.5% cream BID versus 15% for vehicle cream BID. Using a 2-sided alpha of 0.05, the sample size will have a > 90% power to detect a difference between the ruxolitinib 1.5% cream BID versus vehicle cream BID. In addition, to provide adequate power for efficacy variables, the sample size is determined to provide a large database for safety evaluation.

4. DATA HANDLING DEFINITIONS AND CONVENTIONS

4.1. Scheduled Study Evaluations and Study Periods

4.1.1. Day 1

Day 1 is the date that the first application of ruxolitinib cream or vehicle cream is administered to the participants in the specific period.

4.1.2. Study Day

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

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

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

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

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

4.1.3. Baseline Value

Baseline is the last nonmissing measurement obtained before or on the day of first application of ruxolitinib cream or vehicle cream. For safety analyses, participants who cross-over treatment in OL period, baseline is the last nonmissing measurement obtained before or on the first administration of study treatment in OL period.

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

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

4.1.4. Handling of Missing and Incomplete Data

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

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

4.2. Variable Definitions

4.2.1. Body Mass Index

Body mass index will be calculated as follows:

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

4.2.2. Prior and Concomitant Medication

Prior medication is defined as any nonstudy medication started before the first application of study treatment.

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

- Before the date of first application of study treatment and is ongoing throughout the study or ends on/after the date of first application of study treatment.
- On/after the date of first application of study treatment and is ongoing or ends during the course of study treatment.

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

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

5. STATISTICAL METHODOLOGY

5.1. General Methodology

Unless otherwise noted, SAS® software (SAS Institute Inc, Cary, NC; v9.1) will be used for the generation of all tables, graphs, and statistical analyses. Descriptive summaries for continuous variables will include, but not be limited to the number of observations, mean, standard deviation, median, minimum, maximum, first quartile, third quartile, and 95% CI. Descriptive summaries for categorical variables will include the number and percentage of participants in each category.

5.2. Treatment Groups

This is a randomized, DBVC study followed by an OL period. Data will be summarized based on the treatment (ruxolitinib 1.5% cream BID or vehicle cream BID) that the participant actually applied (ie, FAS).

During the DBVC period, the treatment groups will be ruxolitinib 1.5% cream BID and vehicle cream BID. The treatment groups for the OL period will be ruxolitinib 1.5% cream BID to ruxolitinib 1.5% cream BID, and vehicle cream BID to ruxolitinib 1.5% cream BID.

5.3. Analysis Populations

5.3.1. Full Analysis Set

The FAS will include all participants who are randomized and applied the study drug at least once. Treatment groups for this population will be determined according to the actual treatment the participant applied on Day 1 regardless of assigned study treatment.

The FAS population will be used for the summary of demographics, baseline characteristics, and participant disposition, and analyses of all efficacy and safety data.

5.3.2. Open-Label Evaluable Population

The OL-evaluable population will include all participants who applied ruxolitinib cream at least once during the OL period.

All analyses for the OL period will be conducted with the OL-evaluable population.

6. BASELINE, EXPOSURE, AND DISPOSITION

Appendix A provides a list of planned tables, figures, and listings. Sample data displays are included in a separate document.

6.1. Demographics, Baseline Characteristics, and Disease History

6.1.1. Demographics and Baseline Characteristics

The following demographics and baseline characteristics will be summarized for the FAS population in the DBVC period: age, sex, race, ethnicity, weight, height, and BMI.

6.1.2. Baseline Disease Characteristics

The following baseline disease characteristics will be summarized for the FAS population in the DBVC period:

- Time since first onset of AD
- Prior history of asthma (no/yes)
- Prior allergies (no/yes) and type of allergy
- History of contact dermatitis (no/yes)
- Common complications of AD
- Prior treatments for AD
- Time since onset of current flare of AD
- Prior therapy for AD given in the past 30 days (no/yes)
- Total % BSA involvement in current AD episode
- Total % BSA involving face and/or neck in the current episode
- Facial and/or neck involvement during the past episodes/flares (no/yes)
- Number of AD episodes/flares over the last 12 months
- Average duration of episodes/flares
- IGA score (2/3) at screening
- Baseline IGA score (2/3)
- Baseline facial and/or neck IGA (2/3)
- Baseline EASI score
- Baseline face and/or neck EASI score
- Baseline Itch NRS score

6.1.3. Disease History

Not applicable.

6.1.4. Medical History

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

6.2. Disposition of Participant

The number and percentage of participants who were randomized, who were treated, who completed the period, who discontinued study treatment with a primary reason for discontinuation, and who withdrew from the study with a primary reason for withdrawal will be summarized for the FAS population in the DBVC period.

The number and percentage of participants who were treated, who completed the period, who discontinued study treatment with a primary reason for discontinuation, and who withdrew from the study with a primary reason for withdrawal will be summarized for the OL-evaluable population in the OL period.

6.3. Protocol Deviations

Protocol deviations recorded on the eCRF will be summarized and listed for the FAS and OL-evaluable populations.

6.4. Exposure

For participants in the FAS and OL-evaluable population, descriptive statistics will be provided. That is, by treatment group for duration of treatment, average daily weight of study drug, and total weight of study drug. Duration of treatment with ruxolitinib cream or vehicle cream is defined as the number of days from Day 1 to the last record of ruxolitinib cream or vehicle cream application in the specific period.

6.5. Study Drug Compliance

For participants in the FAS population, the overall compliance (%) for the application of ruxolitinib cream or vehicle cream during the DBVC period will be calculated as follows:

> Overall application compliance (%) = 100 × [total number of nonmissing applications] / [total number of intended applications],

where the total number of nonmissing applications is the total number of applications that the participant actually applied during the study and the total number of intended applications is the number of planned applications minus the number of interrupted applications.

6.6. Prior and Concomitant Medication

Prior medications and concomitant medications will be coded using the WHO Drug Dictionary. The number and percentage of participants in the FAS population during the DBVC period will be summarized by WHO drug class and WHO drug term for each prior and concomitant medication.

For participants in the OL period, only concomitant medications will be summarized. Prior medications for AD will be summarized by treatment group, as well as listed for the FAS population.

7. EFFICACY

Appendix A provides a list of planned tables, figures, and listings. Sample data displays are included in a separate document.

7.1. General Considerations

For all continuous variables, both the actual value and change and/or percentage change from baseline (if available) will be analyzed.

All by-visit analyses will include the follow-up period, if the data are available.

7.2. Efficacy Hypothesis

Not applicable.

7.3. Analysis of the Primary Efficacy Parameters

Digital photographs will be used to evaluate clinician-reported outcome assessments (eg, EASI, [redacted] and BSA).

7.3.1. Primary Efficacy Measure

7.3.1.1. Eczema Area and Severity Index Score

Atopic dermatitis will be assessed using the EASI scoring system, which is a validated scoring system that grades the physical signs of AD to provide a measure of AD severity (ranging from 0 to 72). The EASI scoring system examines 4 regions of the body (head/neck, upper limbs, trunk, and lower limbs) and weights them. Each of the 4 body regions is assessed separately for erythema (E), induration/papulation/edema (I), excoriations (Ex), and lichenification (L) for an average degree of severity of each sign in each region.

The disease severity strata for the EASI are as follows: 0 = clear; 0.1 to 1.0 = almost clear; 1.1 to 7.0 = mild; 7.1 to 21.0 = moderate; 21.1 to 50.0 = severe; 50.1 to 72.0 = very severe. Specifically for head and neck region, EASI score ranges from 0 to 7.2.

The categorical variable EASI75 of the head and neck region will be equal to 1, if the percentage improvement from baseline of the EASI score is ≥ 75% or greater and will be equal to 0 for percentage improvement of less than 75% for the head and neck region.

Additionally, the categorical variable EASI75 for the entire body (ie, overall) will be equal to 1 if the percentage improvement from baseline of the EASI score is ≥ 75% or greater, and equal to 0 for percentage improvement of less than 75% for the entire body.

7.3.2. Primary Efficacy Analyses

The primary endpoint is the proportion of participants who achieve EASI75 of the head and neck region at Week 4. The primary analysis will be based on the FAS population in the DBVC period. The primary alternative hypothesis (superiority of ruxolitinib 1.5% cream BID compared with vehicle cream BID) will be tested at a 2-sided $\alpha = 0.05$ level using the CMH test stratified by the stratification factor (ie, the participant's face and/or neck IGA score at screening).

Odds ratio in response rates (ruxolitinib cream vs vehicle) at Week 4 will be computed and provided, as well as the p-values. The difference in proportion of participants who achieve an EASI75 score of the head and neck region (ruxolitinib cream vs vehicle) at Week 4 will also be computed. The 95% CI for the difference will be computed based on a large-sample normal approximation with continuity correction. The p-value and stratum-adjusted EASI75 response rate difference with 95% CI will be provided.

All nonresponders during the DBVC period, as well as all participants who discontinue study treatment at any time before Week 4, or withdraw from the study for any reason, will be defined as nonresponders for the NRI analysis.

7.3.3. Subgroup Analyses for Primary Endpoint

Not applicable.

7.3.4. Sensitivity and Supportive Analyses for Primary Endpoint

Not applicable.

7.4. Analysis of Secondary Efficacy Parameters

All secondary efficacy variables will be summarized using descriptive statistics.

For categorical measurements, summary statistics will include sample size, frequency, and percentages.

[redacted]

7.5.1.2. Investigator's Global Assessment

The IGA is an overall eczema severity rating on a 0 to 4 scale that will be used during treatment period visits to assess a participant's face and/or neck. The grades for the IGA are shown in Table 2.

Table 2: Investigator's Global Assessment

Grade	Severity	Status
0	Clear	No erythema or induration/papulation, no oozing/crusting; there may be minor residual discoloration.
1	Almost clear	There may be trace faint pink erythema, with almost no induration/papulation, and no oozing/crusting.
2	Mild	There may be faint pink erythema, with mild induration/papulation and no oozing/crusting.
3	Moderate	There may be pink-red erythema with moderate induration/papulation and there may be some oozing/crusting.
4	Severe	There may be deep or bright red erythema with severe induration/papulation and with oozing/crusting.

Source: Food and Drug Administration 2012.

The IGA-TS is defined as an IGA score of 0 or 1 with ≥ 2 grade improvement from baseline for both overall and the face and/or neck region.

[redacted]

8. SAFETY AND TOLERABILITY

Appendix A provides a list of planned tables figures, and listings. Sample data displays are included in a separate document.

8.1. General Considerations

The analyses in this section will be provided for the FAS and OL-evaluable populations in the DBVC and OL periods. Summary tables may be replaced with listings when appropriate. For instance, an AE frequency table may be replaced with a listing if it only contains a few unique PTs reported on relatively few participants.

Unless otherwise stated, table summaries will be limited to AEs occurring within 30 days of the last application of study drug or the first application in the OL period (if available) of the study, whichever is earlier.

8.2. Adverse Events

8.2.1. Adverse Event Definitions

A TEAE is any AE either reported for the first time or worsening of a pre-existing event after first application of the study drug. Analysis of AEs (as discussed below) will be limited to TEAEs, but data listings will include all AEs regardless of their timing in relation to study drug administration.

Adverse events will be tabulated by MedDRA PT and SOC. Severity of AEs will be graded using the National Cancer Institute CTCAE v5 (Grades 1 to 5). The CTCAE reporting guidelines and grading details are available on the Cancer Therapy Evaluation Program website.

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

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

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

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

Application site reaction is an AE that occurs at the site of drug application. A summary of ASRs will be provided.

8.2.2. Adverse Event Summaries

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

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

The following summaries will be produced by MedDRA term (if 2 or fewer participants appear in a table, a listing may be appropriate):

- Summary of TEAEs by SOC and PT
- Summary of TEAEs by PT in decreasing order of frequency
- Summary of ASRs by PT in decreasing order of frequency
- Summary of Grade 3 or higher AEs by SOC and PT
- Summary of Grade 3 or higher AEs by PT in decreasing order of frequency
- Summary of serious TEAEs by SOC and PT
- Summary of serious TEAEs by PT in decreasing order of frequency
- Summary of treatment-related TEAEs by SOC and PT
- Summary of treatment-related TEAEs by PT in decreasing order of frequency
- Summary of Grade 3 or higher treatment-related TEAEs by SOC and PT
- Summary of treatment-related serious TEAEs by SOC and PT
- Summary of TEAEs with a fatal outcome by SOC and PT
- Summary of TEAEs leading to dose interruption of study drug by SOC and PT
- Summary of TEAEs leading to discontinuation of study drug by SOC and PT

8.3. Clinical Laboratory Tests

8.3.1. Laboratory Value Definitions

All laboratory assessments will be performed using a central laboratory, except for urine pregnancy tests (as applicable). Laboratory values will be summarized descriptively, as well as listed, for the FAS population at screening; non-numeric test values will be tabulated when necessary.

8.4. Vital Signs

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

Criteria for clinically notable vital sign abnormalities will be defined in Table 3, Table 4, and Table 5. The abnormal values for participants exhibiting clinically notable vital sign abnormalities will be listed along with their assigned treatment group. Alert vital signs are defined as an absolute value outside the defined range and percentage change > 25%. The abnormal values for participants exhibiting alert vital sign abnormalities will be listed.

Table 3: Criteria for Clinically Notable Vital Sign Abnormalities for 12 to 15 Years

Parameter	High Threshold	Low Threshold
Systolic blood pressure	> 131 mmHg	< 110 mmHg
Diastolic blood pressure	> 83 mmHg	< 64 mmHg
Pulse	> 100 bpm	< 60 bpm
Temperature	> 38.0ºC	< 35.5ºC
Respiratory rate	> 20 breaths/min	< 8 breaths/min

Table 4: Criteria for Clinically Notable Vital Sign Abnormalities for 16 to 17 Years

Parameter	High Threshold	Low Threshold
Systolic blood pressure	> 120 mmHg	< 90 mmHg
Diastolic blood pressure	> 85 mmHg	< 50 mmHg
Pulse	> 100 bpm	< 45 bpm
Temperature	> 38.0ºC	< 35.5ºC
Respiratory rate	> 20 breaths/min	< 8 breaths/min

Table 5: Criteria for Clinically Notable Vital Sign Abnormalities for ≥ 18 Years

Parameter	High Threshold	Low Threshold
Systolic blood pressure	> 155 mmHg	< 85 mmHg
Diastolic blood pressure	> 100 mmHg	< 40 mmHg
Pulse	> 100 bpm	< 45 bpm
Temperature	> 38ºC	< 35.5ºC
Respiratory rate	> 20 breaths/min	< 8 breaths/min

9. PLANNED ANALYSES

No formal interim analysis is planned for this study.

10. CHANGES AND MODIFICATIONS TO THE ANALYSIS PLAN

All versions of the SAP are listed in Table 6.

Table 6: Statistical Analysis Plan Versions

SAP Version	Date
Original	26 SEP 2023

[redacted]

10.2. Changes to the Statistical Analysis Plan

Not applicable.

11. REFERENCES

Charman C, Venn A, and Williams H. The patient-oriented eczema measure: development and initial validation of a new tool for measuring atopic eczema severity from the patients' perspective. Arch Dermatol 2004;140:1513-1519.

Food and Drug Administration. Draft Guidance on Pimecrolimus. 2012.

Papp K, Szepietowski J, Kircik L, et al. Efficacy and safety of ruxolitinib cream for the treatment of atopic dermatitis: results from two phase 3, randomized, double-blind studies. Second Annual Revolutionizing Atopic Dermatitis Conference; 2020. Chicago, IL.

APPENDIX A. PLANNED TABLES AND FIGURES

This appendix provides a list of the planned tables, figures, and listing for the Clinical Study Report. Shells are provided in a separate document for tables that are not in the most current Standard Safety Tables v1.13.

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

Tables

Table No.	Title	Population	Standard
Baseline and Demographic Characteristics			
1.1 Disposition			
1.1.1	Analysis Populations	FAS	X
1.1.2.1	Summary of Participant Disposition in the Double-Blind Vehicle-Controlled Period	FAS	X
1.1.2.2	Summary of Participant Disposition in the Open-Label Period	OL-Evaluable	X
1.2 Demography			
1.2.1	Summary of Demographics	FAS	X
1.3 Baseline Characteristics			
1.3.1	Summary of Baseline Disease Characteristics	FAS	X
1.4 Prior Medication and Concomitant Medication			
1.4.1	Summary of Prior Medications	FAS	X
1.4.2	Summary of Prior Medications for Atopic Dermatitis	FAS	X
1.4.3.1	Summary of Concomitant Medications for Double-Blind Vehicle-Controlled Period	FAS	X
1.4.3.2	Summary of Concomitant Medications in the Open-Label Period	OL-Evaluable	X
1.5 Others			
1.5.1	Summary of General Medical History	FAS	X
1.5.2	Summary of Protocol Deviations During Double-Blind Vehicle-Controlled Period	FAS	X
1.5.3	Summary of Protocol Deviations During Open-Label Period	OL-Evaluable	X
Efficacy			
2.1 EASI			
2.1.1	Summary and Analysis of Participants Who Achieved EASI75 of the Head and Neck Region During the Treatment Period	FAS	
2.1.3	Summary and Analysis of Participants Who Achieved an Overall EASI75 During the Treatment Period	FAS	
[redacted]			

[redacted]

Exposure and Safety			
3.1 Study Drug Exposure			
3.1.1.1	Summary of Exposure in the Double-Blind Vehicle-Controlled Period	FAS	X
3.1.1.2	Summary of Exposure in the Open-Label Period	OL-Evaluable	X
3.1.1.3	Summary of Exposure During the Treatment Period	FAS	X
3.1.2.1	Summary of Study Drug Compliance in the Double-Blind Vehicle-Controlled Period	FAS	
3.2 Adverse Events			
3.2.1.1	Overall Summary of Treatment-Emergent Adverse Events in the Double-Blind Vehicle-Controlled Period	FAS	X
3.2.1.2	Overall Summary of Treatment-Emergent Adverse Events in the Open-Label Period	OL-Evaluable	X
3.2.1.3	Overall Summary of Treatment-Emergent Adverse Events During the Treatment Period	FAS	X
3.2.2.1	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term in the Double-Blind Vehicle-Controlled Period	FAS	X
3.2.2.2	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term in the Open-Label Period	OL-Evaluable	X
3.2.2.3	Summary of Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term During the Treatment Period	FAS	X
3.2.3.1	Summary of Application Site Reactions by MedDRA Preferred Term in Decreasing Order of Frequency in the Double-Blind Vehicle-Controlled Period	FAS	X
3.2.3.2	Summary of Application Site Reactions by MedDRA Preferred Term in Decreasing Order of Frequency in the Open-Label Period	OL-Evaluable	X
3.2.3.3	Summary of Application Site Reactions by MedDRA Preferred Term in Decreasing Order of Frequency During the Treatment Period	FAS	X
3.2.4.1	Summary of Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency in the Double-Blind Vehicle-Controlled Period	FAS	X
3.2.4.2	Summary of Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency in the Open-Label Period	OL-Evaluable	X
3.2.4.3	Summary of Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency During the Treatment Period	FAS	X
3.2.5.1	Summary of Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term in the Double-Blind Vehicle-Controlled Period	FAS	
3.2.5.2	Summary of Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term in the Open-Label Period	OL-Evaluable	

Table No.	Title	Population	Standard
3.2.5.3	Summary of Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term During the Treatment Period	FAS	
3.2.6.1	Summary of Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency in the Double-Blind Vehicle-Controlled Period	FAS	X
3.2.6.2	Summary of Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing order of Frequency in the Open-Label Period	OL-Evaluable	X
3.2.6.3	Summary of Grade 3 or Higher Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing order of Frequency During the Treatment Period	FAS	X
3.2.7.1	Summary of Serious Treatment-Emergent Adverse Events By MedDRA System Organ Class and Preferred Term in the Double-Blind Vehicle-Controlled Period	FAS	X
3.2.7.2	Summary of Serious Treatment-Emergent Adverse Events By MedDRA System Organ Class and Preferred Term in the Open-Label Period	OL-Evaluable	X
3.2.7.3	Summary of Serious Treatment-Emergent Adverse Events By MedDRA System Organ Class and Preferred Term During the Treatment Period	FAS	X
3.2.8.1	Summary of Serious Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing order of Frequency in the Double-Blind Vehicle-Controlled Period	FAS	X
3.2.8.2	Summary of Serious Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing order of Frequency in the Open-Label Period	OL-Evaluable	X
3.2.8.3	Summary of Serious Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing order of Frequency During the Treatment Period	FAS	X
3.2.9.1	Summary of Treatment-Related Treatment-Emergent Adverse Events By MedDRA System Organ Class and Preferred Term in the Double-Blind Vehicle-Controlled Period	FAS	X
3.2.9.2	Summary of Treatment-Related Treatment-Emergent Adverse Events By MedDRA System Organ Class and Preferred Term in the Open-Label Period	OL-Evaluable	X
3.2.9.3	Summary of Treatment-Related Treatment-Emergent Adverse Events By MedDRA System Organ Class and Preferred Term During the Treatment Period	FAS	X
3.2.10.1	Summary of Treatment-Related Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency in the Double-Blind Vehicle-Controlled Period	FAS	X
3.2.10.2	Summary of Treatment-Related Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency in the Open-Label Period	OL-Evaluable	X
3.2.10.3	Summary of Treatment-Related Treatment-Emergent Adverse Events by MedDRA Preferred Term in Decreasing Order of Frequency During the Treatment Period	FAS	X
3.2.11.1	Summary of Grade 3 or Higher Treatment-Related Treatment-Emergent Adverse Events By MedDRA System Organ	FAS	X

Table No.	Title	Population	Standard
	Class and Preferred Term in the Double-Blind Vehicle-Controlled Period		
3.2.11.2	Summary of Grade 3 or Higher Treatment-Related Treatment-Emergent Adverse Events By MedDRA System Organ Class and Preferred Term in the Open-Label Period	OL-Evaluable	X
3.2.11.3	Summary of Grade 3 or Higher Treatment-Related Treatment-Emergent Adverse Events By MedDRA System Organ Class and Preferred Term During the Treatment Period	FAS	X
3.2.12.1	Summary of Treatment-Related Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term in the Double-Blind Vehicle-Controlled Period	FAS	
3.2.12.2	Summary of Treatment-Related Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term in the Open-Label Period	OL-Evaluable	
3.2.12.3	Summary of Treatment-Related Serious Treatment-Emergent Adverse Events by MedDRA System Organ Class and Preferred Term During the Treatment Period	FAS	
3.2.13.1	Summary of Treatment-Emergent Adverse Events With a Fatal Outcome by MedDRA System Organ Class and Preferred Term in the Double-Blind Vehicle-Controlled Period	FAS	
3.2.13.2	Summary of Treatment-Emergent Adverse Events With a Fatal Outcome by MedDRA System Organ Class and Preferred Term in the Open-Label Period	OL-Evaluable	
3.2.13.3	Summary of Treatment-Emergent Adverse Events With a Fatal Outcome by MedDRA System Organ Class and Preferred Term During the Treatment Period	FAS	
3.2.14.1	Summary of Treatment-Emergent Adverse Events Leading to Dose Interruption by MedDRA System Organ Class and Preferred Term in the Double-Blind Vehicle-Controlled Period	FAS	
3.2.14.2	Summary of Treatment-Emergent Adverse Events Leading to Dose Interruption by MedDRA System Organ Class and Preferred Term in the Open-Label Period	OL-Evaluable	
3.2.14.3	Summary of Treatment-Emergent Adverse Events Leading to Dose Interruption by MedDRA System Organ Class and Preferred Term During the Treatment Period	FAS	
3.2.15.1	Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug by MedDRA System Organ Class and Preferred Term in the Double-Blind Vehicle-Controlled Period	FAS	X
3.2.15.2	Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug by MedDRA System Organ Class and Preferred Term in the Open-Label Period	OL-Evaluable	X
3.2.15.3	Summary of Treatment-Emergent Adverse Events Leading to Discontinuation of Study Drug by MedDRA System Organ Class and Preferred Term During the Treatment Period	FAS	X
3.3 Laboratory			
3.3.1.1	Summary of Laboratory Values at Screening	FAS	X
3.4 Vital Signs			
3.4.1.1	Summary of Systolic Blood Pressure in the Double-Blind Vehicle-Controlled Period	FAS	X
3.4.1.2	Summary of Systolic Blood Pressure in the Open-Label Period	OL-Evaluable	X

Table No.	Title	Population	Standard
3.4.2.1	Summary of Diastolic Blood Pressure in the Double-Blind Vehicle-Controlled Period	FAS	X
3.4.2.2	Summary of Diastolic Blood Pressure in the Open-Label Period	OL-Evaluable	X
3.4.3.1	Summary of Pulse in the Double-Blind Vehicle-Controlled Period	FAS	X
3.4.3.2	Summary of Pulse Pressure in the Open-Label Period	OL-Evaluable	X
3.4.4.1	Summary of Respiratory Rate in the Double-Blind Vehicle-Controlled Period	FAS	X
3.4.4.2	Summary of Respiratory Rate in Open-Label Period	OL-Evaluable	X
3.4.5.1	Summary of Body Temperature in the Double-Blind Vehicle-Controlled Period	FAS	X
3.4.5.2	Summary of Body Temperature in the Open-Label Period	OL-Evaluable	X

Figures

Figure No.	Title	Population
4.1.1	Proportion of Participants Who Achieved EASI75 of the Head and Neck Region During the Treatment Period	FAS
4.1.3	Proportion of Participants Who Achieved an Overall EASI75 During the Treatment Period	FAS
[redacted]		

Listings

Listing No.	Title
2.1.1	Participant Enrollment and Disposition Status
2.1.2	Participant Inclusion and Exclusion Criteria Violations
2.2	Protocol Deviations
2.3	Analysis Population
2.4.1	Demographic Characteristics
2.4.2	Baseline Disease Characteristics
2.4.3	Prior and Concomitant Medications
2.4.4	Prior Medications for Atopic Dermatitis
2.4.5	Medical History
2.5	Study Drug Exposure and Compliance

Listing No.	Title
Efficacy	
2.6.1	Head and/or Neck EASI Score
2.6.2	Total EASI Score
2.6.3	Itch NRS Score
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
Adverse Events	
2.7.1	Adverse Events
2.7.2	Adverse Events Leading to Drug Discontinuation
2.7.3	Serious Adverse Events
2.7.4	Treatment-Related Adverse Events
2.7.5	Adverse Events With a Fatal Outcome
2.7.6	Adverse Events Leading to Interruption of Study Drug
2.7.8	Adverse Events with Grade 3 or Higher
Laboratory Data	
2.8.1	Clinical Laboratory Values – Hematology
2.8.2	Clinical Laboratory Values – Serum Chemistry
2.8.3	Abnormal Clinical Laboratory Values – Hematology
2.8.4	Abnormal Clinical Laboratory Values – Serum Chemistry
Vital Signs	
2.9.1	Vital Signs
2.9.2	Abnormal Vital Sign Values
2.9.3	Alert Vital Sign Values