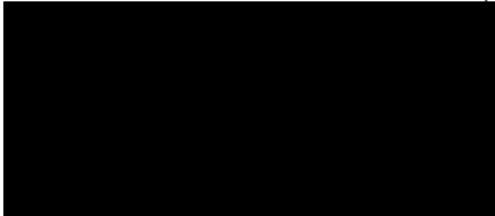


Sponsor *Arcutis Biotherapeutics, Inc.*
Protocol Title: *A Phase 3, Multicenter, Open-Label Extension Study of the Long-Term Safety of ARQ-151 Cream 0.3% in Subjects with Chronic Plaque Psoriasis*
Protocol Number: *ARQ-151-306*
Premier Research PCN: *ARCU9904*
IND Number: *135681*
Document Version: *Final 3.0*
Document Date: *08NOV2023*

Approvals

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Document History

Version	Date	Description
V1.0	21Jan2021	Initial version.
V2.0	29Jun2022	On the basis of the need to describe the results of this study for pediatric population (age 2-11-year-old), the statistical analysis plan was amended in the following ways: 1. The definition of Pediatric Safety (PEDSAF) was added under analysis populations, Section 5. 2. Schedule visits for subject from ARQ-151-215 study were added to the analysis visits windows, Section 6.1.5. 3. One method for classifying BMI for subjects less than 18-year-old was added to Section 6.17. The method for calculating BMI categories for adults (age>18 years old) is not proper for pediatric and adolescents' population, since BMI categories for pediatric and adolescents' population are calculated based on the BMI percentile. 4. Children's Depression Inventory 2 (CDI-2) scores calculation was updated for cases with missing items, Section 6.1.7. 5. Subset of tables for pediatric population (age 2 to 11-year-old) were added to sections 13.1.1, 13.1.2, and 13.1.3.
V3.0	07Nov2023	Protocol Amendment 2 extended enrolment to add approximately 50 pediatric subjects, specifically subjects 2–11 years of age. The following changes were made in preparation for the analysis after the final database lock and study closure: 1. Added reference to protocol amendment 2 to Section 1. 2. Updated schedule of events in Section 3.7 to indicate that laboratory assessments were removed in protocol amendment 2. 3. Section 11: Added details regarding subgroup analyses for subjects <18 years old. 4. Section 13: Added tables for subgroup analyses described in Section 11.

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LIST OF ABBREVIATIONS

Abbreviation	Definition
AE	adverse event
ATC	anatomic therapeutic chemical
BMI	body mass index
BSA	body surface area
CDI-2	children depression inventory, second edition
CDISC	clinical data interchange standards consortium
CRF	case report form
CS	clinically significant
CSR	clinical study report
CSSRS	columbia-suicide severity rating scale
DBP	diastolic blood pressure
eCRF	electronic case report form
EDC	Electronic data capture
EMA	European medicines agency
ERT	Electronic reporting toll
FDA	food and drug administration
HR	heart rate
ICH	international conference for harmonisation
IGA	investigator global assessment
I-IGA	Intertriginous IGA

Abbreviation	Definition
I-IGA-SAF-P	I-IGA safety population
I-IGA-SAF-S	I-IGA safety population
IP	investigational product
MedDRA	medical dictionary for regulatory activities
mPASI	modified psoriasis area and severity index
N	number
NA	not applicable
NCS	Not clinically significant
OLE	Open label extension
PASI	psoriasis area and severity index
PD	protocol deviation
PE	physical examination
PHQ-A	patient health questionnaire depression scale
PHQ-8	modified PHQ-9 for adolescents
PI	principal investigator
PRU4-SAF-P	Pruritus Safety Population Primary
PRU4-SAF-S	Pruritus Safety Population Sensitivity
PT	preferred term
QD	once daily ("quaque die")
SAE	serious adverse event
SAF	safety population

Abbreviation	Definition
SAP	statistical analysis plan
SAS®	a software system used for data analysis
SBP	systolic blood pressure
SD	standard deviation
SOC	system organ class
TEAE	treatment-emergent adverse event
WHO-DDE	world health organization drug dictionary enhanced
WHODrug	world health organization drug dictionary
WI-NRS	worst itch – numeric rating score

1. Overview

This statistical analysis plan (SAP) describes the planned analysis and reporting for Arcutis Biotherapeutics, Inc. protocol number ARQ-151-306 (*A Phase 3, Multicenter, Open-Label Extension Study of the Long-Term Safety of Roflumilast Cream 0.3% in Subjects with Chronic Plaque Psoriasis*), final version dated 27-Nov-2019, including Protocol Amendment 1 dated 18-May-2020 and Protocol Amendment 2 dated 25-Oct-2022. Reference materials for this statistical plan include the protocol and the accompanying sample data collection documents. Operational aspects related to collection and timing of planned clinical assessments are not repeated in this SAP unless relevant to the planned analysis.

The structure and content of this SAP provides sufficient detail to meet the requirements identified by the Food and Drug Administration (FDA), European Medicines Agency (EMA), and International Conference on Harmonisation (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use: Guidance on Statistical Principles in Clinical Trials¹. All work planned and reported for this SAP will follow internationally accepted guidelines, published by the American Statistical Association² and the Royal Statistical Society³, for statistical practice.

The planned analyses identified in this SAP may be included in clinical study reports (CSRs), regulatory submissions, or future manuscripts. Also, post-hoc exploratory analyses not necessarily identified in this SAP may be performed to further examine study data. Any post-hoc or unplanned, exploratory analysis performed will be clearly identified as such in the final CSR.

2. Study Objectives and Endpoints

2.1. Study Objectives

2.1.1. Primary Objective

The primary objective of this study is to assess long-term safety in a multicenter, open-label, single-arm, 24-week study in subjects treated with ARQ-151 Cream 0.3%.

2.2. Study Endpoints

2.2.1. Primary Endpoints

The primary endpoint of this study is analysis of safety monitored through application site assessments in the clinic using the method of Berger and Bowman, clinical laboratory testing (laboratory assessments have been removed by protocol amendment 2), Patient Health Questionnaire depression scale (PHQ-8), Modified PHQ-9 for Adolescents (PHQ-A) or Children Depression Inventory, Second Edition (CDI-2) parent report (Children's Depressive Index-2 for children 6 to 11 years old), Columbia-Suicide Severity Rating Scale (C-SSRS) and adverse events (AEs). Two primary endpoint analyses are planned:

- Occurrence of Treatment-emergent Adverse Events (TEAE)
- Occurrence of Serious Adverse Events (SAE)

2.2.2. Secondary Endpoints

The secondary endpoints are related to efficacy and include:

- Achievement of an Investigator Global Assessment (IGA) of 'clear' or 'almost clear'
- In subjects who achieve a 'clear' IGA, Intertriginous IGA (I-IGA) and Psoriasis Area and Severity Index (PASI) scores and stop treatment to all lesions, time to re-starting investigational product (duration of response)
- Achievement of a 50% reduction in PASI over time
- Achievement of a 75% reduction in PASI over time
- Achievement of a 90% reduction in PASI over time
- Achievement of a 100% reduction in PASI over time
- Achievement of an I-IGA of 'clear' or 'almost clear' over time
- Change in Worst Itch – Numeric Rating Score (WI-NRS) over time

3. Overall Study Design and Plan

3.1. Overall Design

This is an open-label, single-arm, long-term safety study of ARQ-151 Cream 0.3% in subjects with chronic plaque psoriasis involving between 0 and 25% Body Surface Area (BSA). For Cohort 1, eligible subjects will enroll into the long-term safety study on the same day as the last visit of a prior ARQ-151 cream study. Cohort 2 will be ARQ-151 naïve 2 to 17-year-old subjects. Study medication will be applied by the subjects/caregivers topically once daily (QD) for 24 weeks at home. Protocol Amendment 2 restricted enrollment to roflumilast naïve 2 to 11-year-old subjects.

3.2. Sample Size and Power

Up to approximately 330 subjects will be enrolled at up to approximately 100 clinical study sites in the United States, Canada, and Dominican Republic. This sample size provides a sufficient population size to evaluate the long-term safety of ARQ-151 Cream 0.3% over 24 weeks of treatment, and in the combination with other studies provides the development program with sufficient numbers of subjects to meet ICH exposure goals.

3.3. Study Population

Males and females ages 2 years and older with chronic plaque psoriasis.

Cohort 1 will include subjects who successfully completed a prior ARQ-151 cream study in psoriasis, i.e., ARQ-151-301/302 (Group 1) and ARQ-151-107/215/216 (Group 2).

Cohort 2 (Group 3) will include subjects who are naïve to treatment with ARQ-151 cream with a clinical diagnosis of psoriasis vulgaris of at least 3 months' duration, with psoriasis vulgaris on the face, extremities, trunk, and/or intertriginous areas involving 2% to 25% of BSA (excluding the scalp, palms, and soles), and with an IGA of at least Mild ('2') at Day 1.

3.4. Treatments Administered

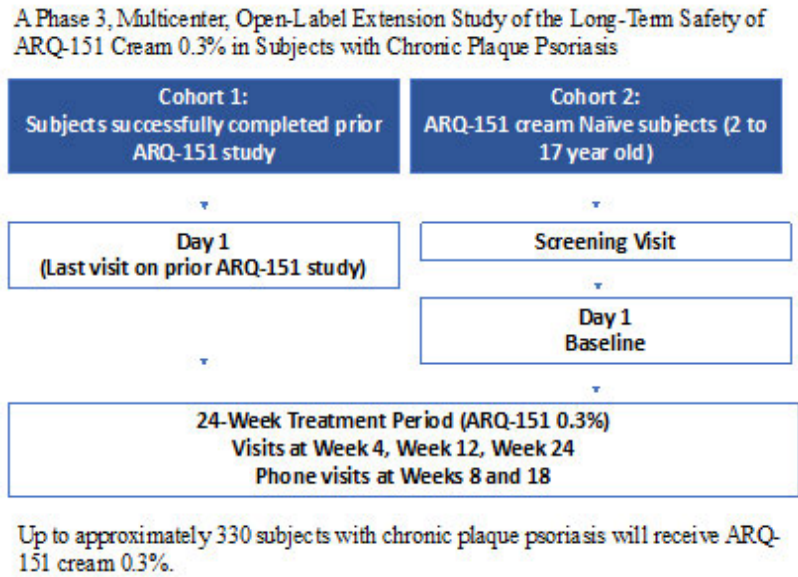
All subjects will be treated with ARQ-151 Cream 0.3% with the number of kits dispensed to a subject based on the BSA involvement of psoriasis.



3.5. Blinding and Unblinding

This is an open-label study and no blinding is planned.

3.6. Study Schema



3.7. Schedule of Events

A detailed schedule of events for the study is provided in [Table 1](#).

Table 1: Schedule of Events

Study Procedure	Washout ^k (Cohort 2)	Day 1	Wk 4	Wk 8	Wk 12	Wk 18	Wk 24/ET
Visit	Screening	Completion of ARQ-151 Study	1	Phone Visit	2	Phone Visit	3
Visit Window	-35 days	or Baseline for Naïve (Cohort 2)	+/- 3 days	+/- 5 days	+/- 5 days	+/- 5 days	+/- 7 days
Informed consent/assent	X ⁱ	X ⁱ					
Physical examination ^a		X ^h					X
I/E criteria	X	X					
Hematology, Serum Chemistries, and Urine Analysis	X	X ^h	X ^l		X ^l		X ^l
Vital signs, height, weight ^b		X ^h	X		X		X
IGA ^c , I-IGA ^c , PASI/mPASI ^c , BSA ^c	X	X ^h	X		X		X
C-SSRS (≥12 years), PHQ-8 (adults), PHQ-A (adolescents), CDI-2 (6-11 years old)	X	X ^h	X		X		X
WI-NRS ^j	X	X ^h	X		X		X
Urine pregnancy test ^d		X ^h	X		X		X
Local Tolerability Assessment ^e		X ^h	X		X		X
Dispense study medication kit ^f		X	X		X		
Dispense/review diary		X	X		X		X
Weigh study medication		X	X		X		X
Adverse event assessment ^g	X	X	X	X	X	X	X
Concomitant medications	X	X	X	X	X	X	X

^a Limited physical examination: skin, lungs, and heart only

^b Height will be collected at Day 1 and Week 24/ET. Weight will be collected at all study visits. Subject to void prior to weight being taken. Remove any jackets, outerwear and shoes. Remove any objects of significant weight (i.e. cell phones, wallet, key chains). A 5% weight loss should be reported to the medical monitor on Page 1.

^c IGA (based on whole body involvement) will be a 5-point scale ranging from clear (0) to severe (4). **IGA should be completed prior to other physician assessments and by the same Evaluator at each study visit.** Total BSA affected by psoriasis will be determined by the subject's hand method, where the subject's hand (including fingers) surface area is assumed to equal 1% of the BSA. PASI/mPASI will be determined by standard methods. NOTE: while palms and soles will be treated with investigational product (IP), they are not counted towards IGA, PASI/mPASI, or BSA assessments.

Intertriginous area involvement will be recorded using the same IGA scale but evaluating intertriginous areas ONLY and NOT whole body involvement. **This 'intertriginous area IGA' should be done AFTER the 'standard whole body IGA' (primary endpoint).**

mPASI will be collected for Cohort 1 subjects only if collected in previous ARQ-151 cream study (i.e., only if subject has a baseline value from a prior study)

^d A urine pregnancy test will be administered to all females of child-bearing potential. A negative result is required for continued participation in the study, and results must be available prior to dispensing of investigational product at each visit.

- ^e Local tolerability will be assessed by the clinic using the method of Berger and Bowman. **Reactions at the site of investigational product application, which may occur post-Baseline, should be differentiated from the preexisting inflammation associated with the subject's Psoriasis.**
- ^f Kits will be dispensed based on %BSA affected. Each IP tube should be weighed and recorded at every visit. See IP Handling Manual for details.
- ^g Any emergent AEs will be followed in the clinic for up to one month at the Investigator's discretion until resolved or otherwise judged as clinically stable.
- ^h This data will be obtained from completion visit of prior ARQ-151 cream study and used as the Day 1 data for this long-term safety study (ARQ-151-306).
- ⁱ For Cohort 1, the consent will be signed after completion visit of prior ARQ-151 cream study. Cohort 2 will sign consent prior to any study-related procedures at the Screening Visit.
- ^j The WI-NRS will be collected from all subjects; subjects 8 years and older will self-report, and caregivers will report if subjects are younger than 8 years.
- ^k See Table 2 in the Clinical Protocol for washout requirements.
- ^l These assessments were removed in Protocol Amendment 2

4. Statistical Analysis and Reporting

4.1. Introduction

Data processing, tabulation of descriptive statistics, calculation of inferential statistics, and graphical representations will be performed primarily using SAS (release 9.4 or higher). If the use of other software is warranted, the final CSR will detail what software was used for what purposes.

Continuous (quantitative) variable summaries will include the number of subjects (n) with no missing values, mean, standard deviation (SD), median, Q1, Q3, minimum, and maximum.

Categorical (qualitative) variable summaries will include the frequency and percentage of subjects who are in the particular category or each possible value. In general, the denominator for the percentage calculation will be based upon the total number of subjects in the study population for the relevant group, unless otherwise specified.

The minimum and maximum will be reported with the same degree of precision (i.e., the same number of decimal places) as the observed data. Measures of location (mean and median) will be reported to 1 degree of precision more than the observed data and measures of spread (SD) will be reported to 2 degrees of precision more than the observed data, unless otherwise specified.

Percentages will be presented to 1 decimal place, unless otherwise specified.

ARQ-151 cream 0.3% will be described as “Roflumilast cream 0.3%” throughout the tables, figures, and listings.

4.2. Interim Analysis and Data Monitoring

Interim analyses were performed to support the initial NDA for roflumilast for the treatment of plaque psoriasis and the subsequent 120-day safety update report.

5. Analysis Populations

The following analysis populations are planned for this study:

- **Safety Population (SAF):** The Safety Population includes all subjects who are enrolled and received at least 1 confirmed dose of Roflumilast Cream 0.3% in this extension study.
- **Pruritus Safety Population Primary (PRU4-SAF-P):** The PRU4 population is a subset of the safety population and includes subjects with WI-NRS pruritus score ≥ 4 at Baseline (primary). This population will be used for the analysis of achievement of a 4-point reduction in WI-NRS pruritus score as compared to Baseline (primary).
- **Pruritus Safety Population Sensitivity (PRU4-SAF-S):** The PRU4 population is a subset of the safety population and includes subjects with WI-NRS pruritus score ≥ 4 at Baseline (sensitivity). This population will be used for the analysis of achievement of a 4-point reduction in WI-NRS pruritus score as compared to Baseline (sensitivity).

- **I-IGA Safety Population (I-IGA-SAF-P):** The I-IGA-SAF population is a subset of the SAF population and includes subjects with intertriginous area involvement, and with severity of the intertriginous lesions at least ‘mild’ ($I-IGA \geq 2$) at Baseline (primary).
- **I-IGA Safety Population (I-IGA-SAF-S):** The I-IGA-SAF population is a subset of the SAF population and includes subjects with intertriginous area involvement, and with severity of the intertriginous lesions at least ‘mild’ ($I-IGA \geq 2$) at Baseline (sensitivity).

6. General Issues for Statistical Analysis

6.1. Statistical Definitions and Algorithms

6.1.1. Baseline

For subjects in Cohort 1 (ARQ-151 301/302 or ARQ-151 107/215/216), the baseline value for safety and efficacy parameters will be defined as the last observation prior to the first dose of Roflumilast Cream 0.3% in either the ARQ-151 parent study or this study (Primary Baseline). Sensitivity analyses of efficacy will be performed where the baseline value for subjects in Cohort 1 is defined as the last observation prior to the first dose of Roflumilast Cream 0.3% cream in this study (Sensitivity Baseline). If subjects choose to enroll in this study, study procedures will not be repeated; study sites will carry over the information from the prior ARQ-151 cream study to the Day 1 visit for this study.

For subjects in Cohort 2, baseline values for efficacy and safety will be defined as the last observation recorded prior to the first dose of Roflumilast Cream 0.3% in this study. Baseline values will most commonly be from Day 1. Cohort 2 will have the same definition of baseline for Primary and Sensitivity Baseline.

For C-SSRS assessment baseline is defined as the most severe ideation and behavior reported in the past 6 months prior to the first dose of investigational product (IP).

6.1.2. Adjustments for Covariates

No adjustments for covariates are planned for this study.

6.1.3. Multiple Comparisons

No inferential statistical analyses are planned for this study.

6.1.4. Handling of Dropouts or Missing Data

Missing data will remain missing and will not be imputed.

6.1.5. Analysis Visit Windows

Subject participation for Cohort 1 involves a minimum of 3 clinic visits at Week 4, Week 12, and Week 24, and 2 phone visits at Weeks 8 and 18. Cohort 2 will also include a Screening



Visit. The anticipated maximum duration of subject participation is about 24 weeks. The procedures performed during the study are as described in Schedule of Events (Section 3.7).

The final study visit will occur approximately at the end of Week 24 of overall involvement in the study. The procedures performed during this visit are as described in Schedule of Events for the Week 24 Visit (Section 3.7). A 7-day scheduling leeway period is allowed for this visit.

If a subject is withdrawn or wishes to exit the study, a termination visit will be scheduled. This visit should include the procedures and assessments that would be performed at the final study visit (End of Study visit).

Visits will be analyzed as scheduled (Section 3.7). Unscheduled, early termination visits, and/or repeated measurements will only be included if a scheduled measurement is not available, and the early termination or unscheduled/repeated measurement falls within the analysis visit windows as presented below:

Table 2: Analysis Windows for Efficacy and Safety Assessments

	Primary Baseline for cohort 1 - Roflumilast		Primary Baseline for cohort 1 - Placebo & cohort 2 + Sensitivity Baseline	
Scheduled Visit	Target Study Day	Window (Days)	Target Study Day	Window (Days)
ARQ-151-301/302/215 Week 2	15	2 to 22	n.a.	n.a.
ARQ-151-107 Week 2	15	2 to 18	n.a.	n.a.
ARQ-151-107 Week 3	22	19 to 25	n.a.	n.a.
ARQ-151-301/302/215 Week 4	29	23 to 35	n.a.	n.a.
ARQ-151-107 Week 4	29	26 to 32	n.a.	n.a.
ARQ-151-107 Week 5	36	33 to 39	n.a.	n.a.
ARQ-151-301/302 Week 6	43	36 to 50	n.a.	n.a.
ARQ-151-301/302 Week 8	57	51 to 61	n.a.	n.a.
Week 4 OLE				
ARQ-151-215	57	43 to 85	29	15 to 57
ARQ-151-301/302	85	71 to 113		
ARQ-151-306	29	15 to 57	29	15 to 57
Week 12 OLE				

ARQ-151-215	113	86 to 239	85	58 to 127
ARQ-151-301/302	141	114 to 183		
ARQ-151-306	85	58 to 127		
Week 24 OLE				
ARQ-151-215	197	≥ 240	169	≥ 128
ARQ-151-301/302	225	≥ 184		
ARQ-151-306	168	≥ 128		

Data collected at early termination and unscheduled visits prior to Study Day 15 will not be analyzed, with the exception of those identified as baseline values.

Unscheduled/repeated measurements will be listed.

6.1.6. Pooling of Sites

The clinical study will be conducted under a common protocol for each investigational site with the intention of pooling the data for analysis. Every effort will be made to promote consistency in study execution at each investigational site.

6.1.7. Derived Variables

- **Study day** is calculated as:
 - observation date – first dose date + 1 if record is collected on or after first dose date
 - observation date – first dose date if record is collected prior to first dose date.
- **IGA Success** = IGA of ‘Clear’ or ‘Almost Clear’ plus at least a 2-point improvement from baseline.
- **I-IGA Success** = I-IGA of ‘Clear’ or ‘Almost Clear’ plus at least a 2-grade improvement from baseline.
- **PASI** = $(0.1 \times [E_h + T_h + S_h] \times A_h) + (0.2 \times [E_a + T_a + S_a] \times A_a) + (0.3 \times [E_t + T_t + S_t] \times A_t) + (0.4 \times [E_l + T_l + S_l] \times A_l)$
 where *E*, *T*, and *S* are erythema, thickness, and scaling, respectively, scored on a scale of 0 to 4, *A* is estimated area of skin involved, graded on a scale of 0 to 6, and *h*, *a*, *t*, and *l* are head, arms, trunk, and legs, respectively (range for total score 0 to 72). If any of the component scores are missing, the PASI cannot be calculated.
- **Modified PASI (mPASI)** = same as PASI, except that for subjects with <10% of any particular involved anatomic area, the mPASI will be calculated using the actual percentage of the anatomical area involved rather than the 0 to 6 estimated area score (e.g. 0.1 for 1%, 0.2 for 2%, 0.3 for 3%, ... 0.9 for 9%).

- **PASI-50 (mPASI-50)** = achievement of a 50% reduction in PASI (mPASI) from baseline.
- **PASI-75 (mPASI-75)** = achievement of a 75% reduction in PASI (mPASI) from baseline.
- **PASI-90 (mPASI-90)** = achievement of a 90% reduction in PASI (mPASI) from baseline.
- **PASI-100 (mPASI-100)** = achievement of a 100% reduction in PASI (mPASI) from baseline.
- **Duration of IGA/I-IGA Success** = time from the first observation of IGA Success to the last time a subject's disease response meets the criteria for IGA Success. The duration of IGA Success for subjects who end treatment in IGA Success will be censored at the last disease assessment date. Only the first duration of IGA/I-IGA success will be analyzed.
 - Duration of IGA Success = last date when subject meets IGA success (before re-starting treatment) - first date when subject achieve IGA success + 1
- **Duration of IGA/I-IGA Clear / Almost Clear** (time to re-starting IP) = the time from the first date when subjects achieve a 'Clear' or 'Almost Clear' IGA score until date of re-starting IP. Subjects who end treatment with 'Clear' and 'Almost Clear' score will be censored at the last disease assessment date. Only the first duration of IGA/I-IGA clear / almost clear will be analyzed.
 - Duration of Clear / Almost Clear = date of re-starting IP (end of 'Clear' or 'Almost Clear' score period) – first date when subject achieved 'Clear' or 'Almost Clear' IGA score +1
- **Treatment-free interval** (time to re-starting IP) = the time from the first date when subjects achieve disease clearance until date of re-starting IP. Subjects who end treatment with 'Clear' score will be censored at the last disease assessment date.
 - Treatment free interval = date of re-starting IP (end of 'Clear' score period) – first date when subject achieve disease clearance +1
- **CDI-2 total score** = a sum of the 17 questions (individual questions scored as much or most of the time=3, often=2, some of the time=1, Not at all=0; range for score 0 to 51). All CDI-2 raw scores can be prorated using the following formula, rounding to the nearest whole number:
 - Prorated score = (Obtained raw score for scale) * (Total # of items on scale/subscale) / Total # items on scale/subscale with responses

- CDI-2 emotional problem scale is a sum of 9 questions (Q1, Q3-6, Q8, Q10-12). If more than 1 item is missing the score should not be calculated. If 1 item is missing the score is calculated as (sum of answered items*9)/number of answered items (=8).
- CDI-2 functional problem scale is a sum of 8 questions (Q2, Q7, Q9, Q13-17). If more than 1 item is missing the score should not be calculated. If 1 item is missing the score is calculated as (sum of answered items*8)/number of answered items (=7).
- CDI-2 total score is a sum of 17 questions. If more than 2 items are missing the score should not be calculated. If 1 item is missing the score is calculated as (sum of answered items*17)/number of answered items (=16). If 2 items are missing the score is calculated as (sum of answered items*17)/number of answered items (=15).
- **PHQ-8** = sum of the 8 questions (individual questions scored as Not at all=0, Several days=1, More than half the days=2, and Nearly every day=3, (range for score 0 to 24). If more than 1 item is missing the score should not be calculated. If 1 item is missing the score is calculated as (sum of answered items*8)/number of answered items.
- **PHQ-A** = sum of the 8 questions (individual questions scored as Not at all=0, Several days=1, More than half the days=2, and Nearly every day=3, (range for score 0 to 24). If more then 1 item is missing the score should not be calculated. If 1 items are missing the score is calculated as (sum of answered items*8)/number of answered items.
- **BSA (body surface area)** = sum of coverage areas of head, limbs, upper limbs and trunk/genitalia.
- **Change from baseline** = value at current time point – value at Baseline.
- **% Change from baseline** = [(value at current time point – value at Baseline) / Baseline] * 100%
- **TEAE** = any AE with an onset date/time after the first application of IP through study completion.
- **C-SSRS suicidal ideation** = A “yes” answer at any time during treatment to any one of the five suicidal ideation questions (Categories 1-5: Wish to be Dead; Nonspecific Active Suicidal Thoughts; Active Suicidal Ideation with Any Methods (No Plan) without Intent to Act; Active Suicidal Ideation with Some Intent to Act, without Specific Plan; Active Suicidal Ideation with Specific Plan and Intent).
- **C-SSRS suicidal behavior** = A “yes” answer at any time during treatment to any one of the five suicidal behavior questions (Categories 6-10: Preparatory Acts or Behavior,

Aborted Attempt, Interrupted Attempt, Actual Attempt (nonfatal), Completed Suicide).

- **C-SSRS suicidal ideation or behavior** = A “yes” answer at any time during treatment to any one of the ten suicidal ideation and behavior questions (Categories 1-10) on the C-SSRS.

Compliance = number of applications divided by the expected number of IP applications for each subject. Number of expected study treatment applications will be calculated as the sum of number of IP applications and number of doses missed. Compliance will be calculated using drug accountability data over the entire treatment period for each subject, up to treatment completion or discontinuation.

- **Number of expected IP applications** = last treatment or missed dose date - first treatment date + 1.
- **Number of IP applications** = number of expected IP applications – number of days with missed IP applications as collected in the CRF. Missed IP applications will not be taken into consideration in determining number of IP applications if the reason for missing dose is per investigator confirmation of clear.
- **Number of Days on IP** = last treatment date – first treatment date + 1.
- **Total Weight of IP Applied (g)** = dispensed tube weight – returned tube weight.
- **Average Daily Weight of IP Applied (g/day)** = total weight of IP applied/number of days on IP.
- **Body Mass Index (BMI) (kg/m²)** = (weight in kg)/[(height in cm/100)²]. Baseline height will be used to derive BMI.
- **BMI categories (Pediatrics and Adolescents Age <18):**
After BMI is calculated using the same formula above for children, it is expressed as a percentile obtained using data files and instructions provided by the CDC (https://www.cdc.gov/growthcharts/percentile_data_files.htm).
 - Underweight: BMI less than 5th percentile
 - Normal weight: BMI ranging from 5th percentile to 84th percentile
 - Overweight: BMI ranging from 85th percentile to 94th percentile
 - Obesity: BMI at or greater than the 95th percentile
- **BMI Categories (Adults Age ≥18)**
 - Underweight = BMI < 18.5
 - Normal = 18.5 ≤ BMI ≤ 24.9
 - Overweight = 25.0 ≤ BMI ≤ 29.9
 - Obese = BMI ≥ 30.0
- **Age categories:**
 - Pediatrics = Age 2 – 11

- Adolescents = Age 12 – 17
- Adults = Age ≥ 18
- **Duration of PASI-50** = time from the first observation of a 50% reduction in the PASI from baseline to the last time a subject's PASI score is at least 50% less than baseline. The duration of PASI-50 for subjects who end treatment with PASI score at least 50% less than baseline will be censored at the last disease assessment date.
 - Duration of PASI-50 = last date when subject has PASI-50 - first date when subject achieve PASI-50 +1
- **Duration of PASI-75** = analogously to duration of PASI-50
- **Disease Clearance** = IGA and mPASI scores of 0 (post-baseline)
- **Disease Recurrence** = any instance where IGA is ≥ 2 and mPASI is greater than 0 (among subjects who stop therapy due to disease clearance)
- **Disease Control** = IGA score of 0 or 1 (among subjects who restart therapy after having stopped therapy due to disease clearance)
- **Time to disease recurrence** (among subjects who stop therapy due to disease clearance) = time to disease recurrence is defined as the time from the last dose of ARQ-151 to the first observation of IGA is ≥ 2 and mPASI is greater than 0. The time to disease recurrence among subjects with clearance at the end of the study observation period will be censored at the last observed disease assessment.
 - Time to disease recurrence = date when first observation of disease recurrence - first date when subject achieve disease clearance (date of last dose) +1
- **Time to disease control** (among subjects who restart therapy after having stopped therapy due to disease clearance) = time to disease control is the time from the re-start of therapy to the first reported IGA score of 0 or 1.
 - Time to disease control = date of first observation of an IGA score of 0 or 1 (among subjects who restart therapy after having stopped therapy due to disease clearance) - date of re-start of therapy after disease clearance +1
- **Worst Itch – Numeric Rating Score (WI-NRS) 4-point reduction** = achievement of a 4-point reduction in WI-NRS pruritus score compared to baseline, calculated only for subjects with a pruritus score of ≥ 4 at baseline.

6.1.8. Data Adjustments/Handling/Conventions

All collected data will be presented in listings or clinical data interchange standards consortium (CDISC) datasets. Data not subject to analysis according to this plan will not appear in any tables or graphs but will be included only in the data listings or CDISC datasets.



In the event that data from a questionnaire for a particular visit is present in both the electronic data capture (EDC) database and the electronic reporting tool (ERT) database, the values present in the ERT database will be used for all analyses. If a questionnaire for a visit is only present in the ERT database, then the ERT values will be used, and similarly if only present in the EDC database then the EDC values will be used.

For laboratory values that are $< X$ ($X = \text{a number}$), $\leq X$, $> X$ or $\geq X$ then X will be used in the analysis.

For partial AE and medication start dates:

- If the year is unknown, then do not impute the date but assign a missing value.
- If the year is known, but the month or month and day is unknown, then:
 - If the year matches the year of first dose date and the end date (if present) is after first dose date, then impute as the month and day of the first dose date.
 - Otherwise, assign 01 January.
- If the year and month are known, but the day is unknown, then:
 - If the month and year match the month and year of the first dose date, then impute as the day of the first dose date.
 - Otherwise, assign 01.

For partial AE and medication end dates:

- If the year is unknown, then do not impute the date but assign as missing value.
- If the year is known, but the month or month and day is unknown, then:
 - If the year matches the year of the last date of the study (date of last contact if subject lost to follow-up; date of completion or early termination otherwise), then impute as the month and day of the last date of the study.
 - Otherwise, assign 31 December.
- If the year and month are known, but the day is unknown, then:
 - If the month and year match the month and year of the last date of the study, then impute as the day of the last date of the study.
 - Otherwise, assign the last day of the month.

6.1.9. Special Handling for COVID-19

The impact of COVID-19 on this clinical trial and participants will be assessed by including in summaries/listings relevant information as captured on the electronic case report form (eCRF). Information collected will include the following:

- Any visit disruption caused by COVID-19

- Early termination due to COVID-19
- Weight loss due to complications associated with COVID-19
- Local tolerability assessment and WI-NRS disruption caused by COVID-19
- Study drug interruption (missed dose) due to COVID-19
- Delay in any assessment caused by COVID-19
- Protocol deviation (PD) due to COVID-19

7. Study Subjects and Demographics

7.1. Disposition of Subjects and Withdrawals

Disposition will be summarized for all subjects enrolled by group within each cohort i.e., Cohort 1 (Group 1 = previous treatment group [ARQ-151-301/302 Roflumilast Cream 0.3%, ARQ-151-301/302 Vehicle and Total], Group 2 = ARQ-151 107/215/216), Cohort 2 (Group 3), and overall.

Disposition will include tabulations of the number of subjects enrolled into each cohort group, the number of subjects who received treatment, number of subjects completing the study, tabulated reasons for discontinuation from the study overall and due to COVID-19 disruption, and number of subjects in SAF.

Disposition for all subjects will be listed.

7.2. Protocol Violations and Deviations

The number of subjects with important PDs and/or eligibility deviations will be summarized by cohort group and overall, including PD COVID-19 related and COVID-19 infections.

All subjects' PDs and eligibility criteria will be listed.

7.3. Demographics and Other Baseline Characteristics

Summary statistics for subjects' demographics (age, age groups [2- 11, 12 – 17 and ≥ 18 years old], gender, childbearing potential [female subjects only], ethnicity, race, height, weight, BMI and BMI categories and for subjects' baseline characteristics (BSA [percent BSA covered with plaque psoriasis], IGA, I-IGA, PASI, mPASI, and WI-NRS) will be presented by cohort group and overall.

Baseline characteristics will be presented for both primary and sensitivity baselines.

For the continuous variables, the number of nonmissing values and the mean, SD, minimum, median, and maximum will be tabulated. For the categorical variables, the counts and proportions of each value will be tabulated. For ordinal variables, such as the IGA descriptive statistics, as well as frequency counts of each level of the ordinal variable, will be presented.

All subjects' demographics and baseline characteristics will be listed.

The number and percent of subjects reporting various medical histories, grouped by Medical Dictionary for regulatory activities (MedDRA) system organ class (SOC) and preferred term (PT) (coded using MedDRA v23.0), will be tabulated by cohort group, and overall.



Medical history for all subjects will be listed.

7.4. Exposure and Compliance

The number of IP applications by each subject based on diary data will be summarized using descriptive statistics appropriate for continuous variables.

The amount of IP used by each subject based on tube weight will be summarized descriptively by cohort and overall using continuous methods. Total amount of study drug will be calculated as the difference between tube weights at dispensation and return.

A subject will be considered compliant with the dosing regimen if the subject applies at least 80% of the expected applications during the IP application period and does not miss more than 3 consecutive doses. The number and percent of subjects that missed more than 3 consecutive doses will be tabulated by cohort group and overall.

IP application compliance will be calculated based on number of applications divided by the expected number of IP applications for each subject. Compliance will be summarized descriptively by cohort group and overall using the following categories:

- >100%
- $\geq 80\%$ - $\leq 100\%$
- <80%

Drug exposure and compliance will be presented using primary and sensitivity baselines.

Drug exposure and compliance will be listed for all subjects.

8. Efficacy Analysis

This study is open label without a comparator group; therefore, is not intended to assess efficacy, but IGA, I-IGA, and PASI/mPASI are included to determine the need for treatment and subsequent re-treatment after treatment course in parent study or ARQ-151-306. Certain efficacy data and endpoints will, however, be summarized.

For the continuous variables, the number of nonmissing values and the mean, SD, minimum, median and maximum will be tabulated by cohort group, overall and visit and similarly, categorical variables will have the counts and proportions of each value will be tabulated by cohort group, overall and visit.

For efficacy summaries 2 baselines will be used (primary and sensitivity) as defined in Section 6.1.1.

All efficacy summaries will be presented by group within each cohort i.e., Cohort 1 (Group 1 = previous treatment group [ARQ-151-301/302 Roflumilast Cream 0.3%, ARQ-151-301/302 Vehicle and Total], Group 2 = ARQ-151-107/215/216), Cohort 2 (Group 3), and overall, unless otherwise stated. Efficacy tabulation and sensitivity efficacy tabulation baselines will be included in summaries.

Efficacy variables will not be imputed.



8.1. IGA / I-IGA

The IGA is an ordinal scale with 5 severity grades reported only in integers:

Score	Description
0	Clear: No erythema, no scaling (hypo-hyperpigmentation can be present)
1	Almost clear: Residual slight erythema and/or trace amounts of scaling
2	Mild: Pink to red color and/or slight scaling
3	Moderate: Distinct redness and/or clearly visible scaling
4	Severe: Severe erythema (intense, fiery red) and/or severe scaling (coarse, thick scales with flaking onto clothes or skin)

The efficacy endpoint for this study is success in IGA disease severity, defined as an IGA of ‘Clear’ or ‘Almost Clear’ plus 2-grade improvement.

IGA and I-IGA (subjects with intertriginous involvement) scores, changes and percent changes from baseline will be summarized using descriptive statistics by cohort group and overall at Baseline visit of parent study (ARQ-151-301/302) [Primary Baseline], Baseline visit of this extension study [sensitivity Baseline] and every scheduled visit through end of study (Day 1, Weeks 4, 12, and 24) including visits from parent studies ARQ-151-301/302. The I-IGA will be tabulated in a similar way to IGA at each scheduled visit using the I-IGA-SAF-P or I-IGA-SAF-S populations accordingly.

The number and percentage of subjects who achieve IGA clear/almost clear (i.e., IGA of ‘Clear’ or ‘Almost Clear’) will be tabulated at each scheduled visit by cohort group and overall. In addition, IGA success (i.e., IGA of ‘Clear’ or ‘Almost Clear’ plus 2-grade improvement from Baseline [only relevant for Primary Baseline]) also will be tabulated. I-IGA success and I-IGA clear/almost clear will be summarized in a similar way as IGA success and clear/almost clear.

In addition, shift from baselines (primary and OLE) in IGA score to the last reported IGA score on the study will be summarized.

8.2. PASI / mPASI

PASI/mPASI combines the assessment of the severity of lesions and the area affected into a single score in the range 0 (no disease) to 72 (maximal disease). PASI / mPASI scores will be derived as described in Section 6.1.7.

PASI/mPASI scores, changes and percent changes from baseline (primary and OLE) and the proportion of 50%, 75%, 90% and 100% reductions in PASI/mPASI scores will be summarized in a similar way as IGA at each scheduled visit (Day 1, Weeks 4, 12, and 24) by cohort group and overall.

8.3. Duration and Time to

Duration of IGA Clear / Almost Clear

Duration of Clear / Almost Clear is defined as the time from the first observation of IGA 'Clear' or 'Almost Clear' until date of re-starting IP will be summarized. Number (%) of subjects with IGA Clear / Almost Clear will be summarized as well.

- The number of days between the end date of initial treatment (when subject achieve 'Clear' or 'Almost Clear' status) until date of re-starting treatment (if applicable) or the last disease assessment date in this study +1. Subjects with continual clearance will be censored at their last disease assessment date.

The median time (number of days) for IGA 'Clear' or 'Almost Clear' will be analyzed using the Kaplan–Meier method and will be accompanied with a plot, where event is defined as restarting treatment after achieving 'Clear' or 'Almost Clear' status. Subjects who discontinue study without relapse or restarting treatment will be considered censored in the Kaplan–Meier analyses.

Duration of IGA Clear / Almost Clear will be summarized using primary baseline and will be presented by cohort group and overall.

Treatment Free Interval

Time to restarting study drug (treatment free interval) defined as time when subject achieves disease clearance and stop treatment to all lesions, will be calculated and summarized in the same manner as Duration of 'Clear' or 'Almost Clear'. The number (%) of subjects who responded and stopped treatment will be presented as well.

Duration of IGA/I-IGA Success

Duration of IGA/I-IGA Success is defined as the time from the first observation of IGA/I-IGA Success to the last time a subject's disease response meets the criteria for IGA/I-IGA Success. The duration of IGA/I-IGA Success for subjects who end treatment in IGA/I-IGA Success will be censored at the last assessment date. This will be calculated and summarized in the same manner as Duration of 'Clear' or 'Almost Clear'. The number (%) of subjects who have IGA/I-IGA Success will be presented as well.

Duration of PASI-50 and Duration of PASI-75

Duration of PASI-50 or PASI-75 is defined as the time from the first observation of a 50% reduction (or 75% reduction) in the PASI from baseline to the last time a subject's PASI score is at least 50% (or 75%) less than baseline. The duration of PASI-50 or PASI-75 for subjects who end treatment with PASI score at least 50% (or 75%) less than baseline will be censored at the last assessment date. This will be calculated and summarized in the same manner as Duration of 'Clear' or 'Almost Clear'. The number (%) of subjects who achieved PASI-50 and PASI-75 will be presented as well.

Time to Disease Recurrence

Time to disease recurrence (among subjects who stop therapy due to disease clearance) is defined as the time from the last dose of ARQ-151 to the first observation of an IGA is ≥ 2 and mPASI is greater than 0. The time to disease recurrence among subjects with clearance at the end of the study observation period will be censored at the last observed disease assessment. This will be calculated and summarized in the same manner as Duration of 'Clear' or 'Almost Clear'. The number (%) of subjects who stop therapy during the study due to disease clearance,

and number (%) of subjects with disease recurrence among subjects who stop therapy due to disease clearance will be presented as well.

Time to Disease Control

Time to disease control (among subjects who restart therapy after having stopped therapy due to disease clearance) is the time from the re-start of therapy to the first reported IGA score of 0 or 1. The time to disease control among subjects who restart therapy at the end of the study observation period will be censored at the last observed disease assessment. This will be calculated and summarized in the same manner as Duration of 'Clear' or 'Almost Clear'. The number (%) of subjects with disease control among subjects who restart therapy after having stopped therapy due to disease clearance will be presented as well.

8.4. Worst Itch Numerical Rating Scale (WI-NRS)

The WI-NRS is a simple, single item to assess the patient-reported severity of this symptom at its highest intensity during the previous 24-hour period. The WI-NRS will be determined by asking the subject's assessment of worst itch over the past 24 hours. The scale is from '0 to 10' ("no itch" to "worst imaginable itch").

Observed, change, and percent change from baseline (primary and OLE; limited to subjects with a non-zero baseline score) scores in WI-NRS itch severity will be summarized descriptively by cohort group and overall, at each scheduled visit (Day 1, Weeks 4, 12, and 24). In addition, categorical summaries (number and percentage of subjects) in each category will be summarized.

In subjects with WI-NRS pruritus score ≥ 4 at baseline (primary and OLE), achievement of a 4-point reduction in WI-NRS pruritus score at each scheduled visit (Day 1, Weeks 4, 12, and 24) will be summarized.

In subjects with WI-NRS pruritus score ≥ 4 at baseline (primary and OLE), achievement of a 4-point reduction in WI-NRS pruritus score and WI-NRS score of 0 or 1 at each scheduled visit (Day 1, Weeks 4, 12, and 24) will be summarized.

WI-NRS results will be listed for all subjects.

8.5. Body Surface Area (BSA)

The BSA affected by psoriasis will be determined by the subject's hand method, where the subject's hand (including fingers) surface area is assumed to equal 1% of BSA.

BSA (%) observed, changes, and percent changes from baseline (primary and OLE) will be summarized using descriptive statistics by cohort group and overall at Baseline Visit of parent study and every scheduled visit through end of study (Day 1, Weeks 4, 12, and 24).



9. Safety and Tolerability Analysis

Safety will be evaluated from reported AEs, local tolerability assessments, changes in clinical laboratory values, changes in vital signs, C-SSRS, and PHQ-8/PHQ-A results.

Baseline will be used as defined in Section 6.1.1.

All safety summaries will be presented by each cohort.

9.1. Adverse Events

All AEs, TEAEs, and SAEs will be coded using the MedDRA dictionary v. 23.0.

A TEAE is defined as an AE that started after application of IP at the Baseline Visit in this extension study, or in parent study through study completion. A treatment-related AE is any AE with a relationship to the study drug of unlikely, possibly, probably, or likely. TEAEs will be summarized from primary safety and sensitivity baselines.

An overall summary of TEAEs will be provided by cohort and overall; this summary will present number and percent of subjects who reported at least 1 TEAE (including number of TEAEs, TEAEs by maximum severity, and TEAEs by greatest relationship), at least 1 SAE (including number of SAEs), who discontinued the study due to a TEAE, or who had a TEAE resulting in death.

The number and percent of subjects reporting treatment-emergent AEs and SAEs, grouped by MedDRA SOC and PT, will be tabulated by severity or greatest relationship to study IP, cohort group and overall. In the case of multiple occurrences of the same TEAE within the same subject, each subject will only be counted once for each PT. In addition, a summary table by age groups (pediatrics, adolescents, and adults) will be presented.

In the summaries showing severity and relationship to study medication the event with the maximum severity (mild < moderate < severe) or strongest relationship (not related < unlikely < possibly < probably < likely) will be reported. If a particular event is missing the severity and/or relationship, then the strongest possible severity or relationship will be assumed for analysis (severity = severe, relationship = likely).

In the AE data listings, all AEs will be displayed. AEs that are treatment-emergent will be flagged. The event onset will also be shown relative (in number of days) to date of first application.

9.1.1. Adverse Events Leading to Withdrawal

A summary of incidence rates (frequencies and percentages) of TEAEs leading to withdrawal of study drug, by cohort group, SOC, and PT will be prepared. In addition, a similar table for related TEAEs will be provided.

A data listing of AEs leading to withdrawal of study drug will also be provided, displaying details of the event(s) captured on the CRF.



9.1.2. Deaths and Serious Adverse Events

Any deaths that occur during the study will be listed.

SAE will be listed and tabulated by SOC and PT and presented by cohort group and overall, as well as by relationship to IP and maximum severity.

9.2. Local Tolerance Assessments

The investigator's assessment of the application site reaction will be summarized by cohort group and overall at each scheduled visit (Day 1, Weeks 4, 12, and 24) using categorical methods for dermal response and other effects (number and percentage of subject with each score), and continuous methods for dermal response (mean, SD, median, minimum, and maximum). Sensitivity baseline will be used for this summary.

The investigator's assessment will be listed for all subjects.

9.3. Clinical Laboratory Evaluations

Laboratory test results will be summarized descriptively by cohort group at each scheduled visit as both observed values, changes, and percent changes from baseline.

The number of subjects with clinical laboratory values below, within, or above the normal range by time point and in relation to baseline will be tabulated for each clinical laboratory analyte by cohort group (shift table).

Primary baseline will be used for this summary.

All clinical laboratory results will be listed. Abnormal results will be flagged.

9.4. Vital Signs

Descriptive summaries of observed values, changes, and percent changes from baseline will be calculated for body weight, systolic blood pressure (SBP), diastolic blood pressure (DBP), heart rate (HR), respiratory rate, height, and BMI and oral body temperature by cohort group at each scheduled visit. Listings will include subject-reported reason for weight loss (intentional, unintentional).

Shift tables by cohort group will summarize the number of subjects who gain or lose $\geq 5\%$ of their baseline body weight during the course of the study, as well as subjects who gain or lose $\geq 10\%$ of their baseline body weight over the course of the study. In addition, a similar table by age groups (pediatrics, adolescents, and adults) will be presented.

The incidence of shifts from baseline to last, highest, and lowest BMI category will be presented in shift tables.

Shift tables for weight and BMI will also be summarized by intentional and unintentional weight loss (defined from question on vital sign eCRF).



Weight and other vital signs summaries will use primary baseline.

Vital signs, including weight loss, will be listed for all subjects.

9.5. Patient Health Questionnaire depression scale (PHQ-8) and Modified Patient Health Questionnaire depression scale for Adolescents (PHQ-A)

PHQ-8 will be completed by adult subjects and modified PHQ-A is filled by adolescent subjects of age 12-17 years inclusive. Data for PHQ-8 and Modified PHQ-A will be classified using each subject's total score at a time point into a category based on the following scoring system:

- None – Minimal depression (0 to 4)
- Mild depression (5 to 9)
- Moderate depression (10 to 14)
- Moderately severe depression (15 to 19)
- Severe depression (20 to 24)

The number and percentage of subjects in each category will be summarized by cohort group and overall, at each scheduled visit (Day 1, Weeks 4, 12, and 24). Additionally, shift tables showing the category of severity at each scheduled visit by cohort group will be presented. Sensitivity baseline will be used for this summary.

9.6. Columbia-Suicide Severity Rating Scale (C-SSRS)

The C-SSRS is a questionnaire that prospectively assesses Suicidal Ideation and Suicidal Behavior. At the Screening study visit, "Screening" version of the C-SSRS will be used for Cohort 2 only. This version assesses Suicidal Ideation and Suicidal Behavior during the subject's lifetime and during the past 6 months. For the Screening Visit, "lifetime" experience of the subject with Suicidal Ideation and Suicidal Behavior will be summarized. After Baseline Visit, the "Since Last Visit" version will be used.

Suicidality data collected on the C-SSRS will be listed for all subjects. Tables will include results from the Suicidal Ideation and Suicidal Behavior sections of the C-SSRS. Frequencies and percentages of subjects with a response of "Yes" at any point on the Suicidal Ideation and Suicidal Behavior items will be summarized by cohort group at each scheduled visit (Day 1, Week 4, 12, 24).

All C-SSRS data will be listed.

9.7. Children's Depression Inventory 2 (CDI-2)

The CDI-2 assessment will be performed only for subjects 6-11 years old (inclusive). The CDI-2 quantifies depressive symptomatology using reports from children/adolescents, teachers, and parents or caregivers. CDI-2 emotional problem scale is a sum of 9 questions, and CDI-2 function problem is a sum of 8 questions, as defined in Section [6.1.7](#).



Descriptive summaries for each scale will be presented by cohort group and overall at each scheduled visit (Baseline, Day 1, Weeks 4, 12, and 24).

Sensitivity baseline will be used for this summary.

9.8. Prior and Concomitant Medication

Prior and concomitant medications will be summarized descriptively by cohort group and overall using counts and percentages.

Prior medications will be presented separately from concomitant medications. Medications that started prior to the first application of study drug will be considered prior medications whether or not they were stopped prior to the first application of study drug. Any medications continuing or starting post the first application of study drug will be considered to be concomitant. If a medication starts prior to the first application of study drug and continues after the first application of study drug it will be considered both prior and concomitant. This will include only medications in this extension study (ARQ-151-306). Sensitivity baseline is used.

Medications will be coded using World Health Organization drug dictionary (WhoDrug) Global B3, vSep2019. All prior and concomitant medication will be listed.

9.9. Physical Examination

The number and percentage of subjects with normal and abnormal findings in the physical examination (PE) will be displayed by cohort group and overall at each study visit (Day 1 and Week 24).

PE data will be presented in listing.

10. Changes from Planned Analysis

All the exploratory endpoints have been added in the SAP, but they were not specified in the protocol.

11. Other Planned Analysis

Subgroup analyses will be performed to focus on results in subjects <18, including the following subgroups:

1. Age 2 to 5
2. Age 6 to 11
3. Age 2 to 11
4. Age 12 to 17
5. Age 2 to 17

For previous analyses, subjects were assigned to analysis groups using the first study in which the subject participated, ie ARQ-151-301 or -302 (Group 1), ARQ-151-107 or -215 (Group 2), or ARQ-151-306 (Group 3). The subgroup analyses will include subjects in analysis groups



by age alone. Data summaries that will be produced for the age subgroups are identified in Section 13.

12. References

1. US Federal Register. (1998) International Conference on Harmonization; Guidance on Statistical Principles for Clinical Trials. Department of Health and Human Services: Food and Drug Administration [Docket No. 97D-0174]. Federal Register Volume 63, Number 179, pages 49583-49598. September 16, 1998.
2. ASA. (2016) Ethical Guidelines for Statistical Practice. Prepared by the Committee on Professional Ethics, April 2016. <http://www.amstat.org/about/ethicalguidelines.cfm>
3. RSS. (2014) The Royal Statistical Society: Code of Conduct, 2014. <http://www.rss.org.uk/Images/PDF/join-us/RSS-Code-of-Conduct-2014.pdf>.



13. Tables, Listings, and Figures

All tables, listings, and figures will have a header showing the sponsor company name and protocol and a footer showing the version of SAS, the file name and path, and the source of the data (case report form [CRF] page or listing number).

13.1. Planned Table and Descriptions

The following are planned summary tables for protocol number ARQ-151-306. The table numbers and page numbers are place holders only and will be determined when the tables are produced.

13.1.1. Demographic Data

Number	Population	Title
Table 14.1.1.1	All Enrolled	Summary of Subject Disposition: Cohort 1
Table 14.1.1.2	All Enrolled	Summary of Subject Disposition: All Enrolled
Table 14.1.1.3	All Enrolled Subjects with Age <18	Summary of Subject Disposition: All Enrolled Subjects with Age <18
Table 14.1.2.1	Safety	Summary of Demographics: Cohort 1
Table 14.1.2.2	Safety	Summary of Demographics: Overall
Table 14.1.2.3	Safety with Age <18	Summary of Demographics: Safety Population with Age <18
Table 14.1.2.4 ^a	Safety	Summary of Sensitivity Baseline Characteristics: Cohort 1
Table 14.1.2.5 ^a	Safety	Summary of Primary Baseline Characteristics: Cohort 1
Table 14.1.2.6 ^a	Safety	Summary of Sensitivity Baseline Characteristics: Overall
Table 14.1.2.7	Safety with Age <18	Summary of Primary Baseline Characteristics: Safety Population with Age <18
Table 14.1.3.1	Safety	Medical History: Cohort 1
Table 14.1.3.2	Safety	Medical History: Overall
Table 14.1.3.3	Safety with Age <18	Medical History: Safety Population with Age <18
Table 14.1.4.1	Safety	Summary of Protocol Deviations: Cohort 1
Table 14.1.4.2	Safety	Summary of Protocol Deviations: Overall
Table 14.1.4.3	Safety with Age <18	Summary of Protocol Deviations: Safety Population with Age <18
Table 14.1.5.1	Safety	Summary of Prior Medications by ATC Class Level 4 and Preferred Term (Sensitivity Baseline): Cohort 1
Table 14.1.5.2	Safety	Summary of Prior Medications by ATC Class Level 4 and Preferred Term (Sensitivity Baseline): Overall
Table 14.1.6.1	Safety	Summary of Study Drug Exposure and Compliance (Primary Baseline): Cohort 1
Table 14.1.6.2	Safety	Summary of Study Drug Exposure and Compliance (Primary Baseline): Overall
Table 14.1.6.3	Safety	Summary of Study Drug Exposure and Compliance (Sensitivity Safety Baseline): Cohort 1
Table 14.1.6.4	Safety	Summary of Study Drug Exposure and Compliance (Sensitivity Safety Baseline): Overall

Number	Population	Title
Table 14.1.6.5	Safety with Age <18	Summary of Study Drug Exposure and Compliance: Safety Population with Age <18

^a Only the table number was revised relative to previous analyses.

13.1.2. Efficacy Data

Number	Population	Title
Table 14.2.1.1.1	Safety	Summary, Change, and Percent Change from Primary Baseline in Investigator Global Assessment (IGA) Grades by Study Visit: Cohort 1
Table 14.2.1.1.2	Safety	Summary, Change, and Percent Change from Primary Baseline in Investigator Global Assessment (IGA) Grades by Study Visit: Overall
Table 14.2.1.1.3	Safety	Summary, Change, and Percent Change from Sensitivity Baseline in Investigator Global Assessment (IGA) Grades by Study Visit: Cohort 1
Table 14.2.1.1.4	Safety	Summary, Change, and Percent Change from Sensitivity Baseline in Investigator Global Assessment (IGA) Grades by Study Visit: Overall
Table 14.2.1.1.5	Safety with Age <18	Summary, Change, and Percent Change from Primary Baseline in Investigator Global Assessment (IGA) Grades by Study Visit: Safety Population with Age <18
Table 14.2.1.2.1	I-IGA Safety (Primary)	Summary, Change, and Percent Change from Primary Baseline in Intertriginous Investigator Global Assessment (I-IGA) Grades by Study Visit: Cohort 1
Table 14.2.1.2.2	I-IGA Safety (Primary)	Summary, Change, and Percent Change from Primary Baseline in Intertriginous Investigator Global Assessment (I-IGA) Grades by Study Visit: Overall
Table 14.2.1.2.3	I-IGA Safety (Sensitivity)	Summary, Change, and Percent Change from Sensitivity Baseline in Intertriginous Investigator Global Assessment (I-IGA) Grades by Study Visit: Cohort 1
Table 14.2.1.2.4	I-IGA Safety (Sensitivity)	Summary, Change, and Percent Change from Sensitivity Baseline in Intertriginous Investigator Global Assessment (I-IGA) Grades by Study Visit: Overall
Table 14.2.1.3.1	Safety	Summary of Investigator Global Assessment (IGA) Grades by Study Visit (Primary Baseline): Cohort 1
Table 14.2.1.3.2	Safety	Summary of Investigator Global Assessment (IGA) Grades by Study Visit (Primary Baseline): Overall
Table 14.2.1.3.3	Safety	Summary of Investigator Global Assessment (IGA) Grades by Study Visit (Sensitivity Baseline): Cohort 1
Table 14.2.1.3.4	Safety	Summary of Investigator Global Assessment (IGA) Grades by Study Visit (Sensitivity Baseline): Overall
Table 14.2.1.3.5	Safety with Age <18	Summary of Investigator Global Assessment (IGA) Grades by Study Visit (Primary Baseline): Safety Population with Age <18

Number	Population	Title
Table 14.2.1.3.6 ^a	I-IGA Safety (Primary)	Summary of Intertriginous Investigator Global Assessment (I-IGA) Grades by Study Visit (Primary Baseline): Cohort 1
Table 14.2.1.3.7 ^a	I-IGA Safety (Primary)	Summary of Intertriginous Investigator Global Assessment (I-IGA) Grades by Study Visit (Primary Baseline): Overall
Table 14.2.1.3.8 ^a	I-IGA Safety (Sensitivity)	Summary of Intertriginous Investigator Global Assessment (I-IGA) Grades by Study Visit (Sensitivity Baseline): Cohort 1
Table 14.2.1.3.9 ^a	I-IGA Safety (Sensitivity)	Summary of Intertriginous Investigator Global Assessment (I-IGA) Grades by Study Visit (Sensitivity Baseline): Overall
Table 14.2.1.4.1	Safety	Shift from Primary Baseline in Investigator Global Assessment (IGA) Grades to the Last Reported IGA Score: Cohort 1
Table 14.2.1.4.2	Safety	Shift from Sensitivity Baseline in Investigator Global Assessment (IGA) Grades to the Last Reported IGA Score: Cohort 1
Table 14.2.1.4.3	Safety	Shift from Primary Baseline in Investigator Global Assessment (IGA) Grades to the Last Reported IGA Score: Overall
Table 14.2.1.4.4	Safety	Shift from Sensitivity Baseline in Investigator Global Assessment (IGA) Grades to the Last Reported IGA Score: Overall
Table 14.2.1.4.5	Safety with Age <18	Shift from Primary Baseline in Investigator Global Assessment (IGA) Grades to the Last Reported IGA Score: Safety Population with Age <18
Table 14.2.2.1.1	Safety	Summary and Change from Primary Baseline in Psoriasis Area and Severity Index (PASI) by Study Visit: Cohort 1
Table 14.2.2.1.2	Safety	Summary, Change, and Percent Change from Primary Baseline in Modified Psoriasis Area and Severity Index (mPASI) by Study Visit: Cohort 1
Table 14.2.2.1.3	Safety	Summary, Change, and Percent Change from Primary Baseline in Psoriasis Area and Severity Index (PASI) by Study Visit: Overall
Table 14.2.2.1.4	Safety	Summary, Change, and Percent Change from Primary Baseline in Modified Psoriasis Area and Severity Index (mPASI) by Study Visit: Overall
Table 14.2.2.1.5	Safety	Summary, Change, and Percent Change from Sensitivity Baseline in Psoriasis Area and Severity Index (PASI) by Study Visit: Cohort 1
Table 14.2.2.1.6	Safety	Summary, Change, and Percent Change from Sensitivity Baseline in Modified Psoriasis Area and Severity Index (mPASI) by Study Visit: Cohort 1
Table 14.2.2.1.7	Safety	Summary, Change, and Percent Change from Sensitivity Baseline in Psoriasis Area and Severity Index (PASI) by Study Visit: Overall
Table 14.2.2.1.8	Safety	Summary, Change, and Percent Change from Sensitivity Baseline in Modified Psoriasis Area and Severity Index (mPASI) by Study Visit: Overall

Number	Population	Title
Table 14.2.2.1.9	Safety with Age <18	Summary, Change, and Percent Change from Primary Baseline in Psoriasis Area and Severity Index (PASI) by Study Visit: Safety Population with Age <18
Table 14.2.2.1.10	Safety with Age <18	Summary, Change, and Percent Change from Primary Baseline in Modified Psoriasis Area and Severity Index (mPASI) by Study Visit: Safety Population with Age <18
Table 14.2.3.1.1	Safety	Summary of Duration of Treatment-Free Interval and Clear / Almost Clear (Primary Baseline): Cohort 1
Table 14.2.3.1.2	Safety	Summary of Duration of Treatment-Free Interval and Clear / Almost Clear (Primary Baseline) Overall
Table 14.2.3.2.1	Safety	Summary of Duration of IGA Success (Primary Baseline): Cohort 1
Table 14.2.3.2.2	Safety	Summary of Duration of IGA Success (Primary Baseline): Overall
Table 14.2.3.3.1	Safety	Summary of Duration of PASI-50 and PASI-75 (Primary Baseline): Cohort 1
Table 14.2.3.3.2	Safety	Summary of Duration of PASI-50 and PASI-75 (Primary Baseline): Overall
Table 14.2.3.4.1	Safety	Summary of Disease Recurrence and Disease Control (Primary Baseline): Cohort 1
Table 14.2.3.4.2	Safety	Summary of Disease Recurrence and Disease Control (Primary Baseline): Overall
Table 14.2.4.1.1 ^a	Safety	Summary, Change, and Percent Change from Primary Baseline in Worst Itch – Numeric Rating Scale (WI-NRS) Pruritus Score by Study Visit: Cohort 1
Table 14.2.4.1.2 ^a	Safety	Summary, Change, and Percent Change from Primary Baseline in Worst Itch – Numeric Rating Scale (WI-NRS) Pruritus Score by Study Visit: Overall
Table 14.2.4.1.3	Safety with Age <18	Summary, Change, and Percent Change from Primary Baseline in Worst Itch – Numeric Rating Scale (WI-NRS) Pruritus Score by Study Visit: Safety Population with Age <18
Table 14.2.4.1.4 ^a	Safety	Summary, Change, and Percent Change from Sensitivity Baseline in Worst Itch – Numeric Rating Scale (WI-NRS) Pruritus Score by Study Visit: Cohort 1
Table 14.2.4.1.5 ^a	Safety	Summary, Change, and Percent Change from Sensitivity Baseline in Worst Itch – Numeric Rating Scale (WI-NRS) Pruritus Score by Study Visit: Overall
Table 14.2.4.2.1	Pruritus Safety (Primary)	Worst-Itch- Numeric rating Scale (WI-NRS) Pruritus Score Success by Study Visit: Cohort 1
Table 14.2.4.2.2	Pruritus Safety (Primary)	Worst-Itch- Numeric rating Scale (WI-NRS) Pruritus Score Success by Study Visit: Overall

Number	Population	Title
Table 14.2.4.2.3	Safety with Age <18	Worst-Itch- Numeric rating Scale (WI-NRS) Pruritus Score Success by Study Visit: Safety Population with Age <18
Table 14.2.4.2.4 ^a	Pruritus Safety (Sensitivity)	Worst-Itch- Numeric rating Scale (WI-NRS) Pruritus Score Success by Study Visit: Cohort 1
Table 14.2.4.2.5 ^a	Pruritus Safety (Sensitivity)	Worst-Itch- Numeric rating Scale (WI-NRS) Pruritus Score Success by Study Visit: Overall
Table 14.2.4.3.1 ^a	Pruritus Safety (Primary)	Worst-Itch- Numeric rating Scale (WI-NRS) Pruritus Score Success (0 or 1) by Study Visit: Cohort 1
Table 14.2.4.3.2 ^a	Pruritus Safety (Primary)	Worst-Itch- Numeric rating Scale (WI-NRS) Pruritus Score Success (0 or 1) by Study Visit: Overall
Table 14.2.4.3.3	Safety with Age <18 (Primary)	Worst-Itch- Numeric rating Scale (WI-NRS) Pruritus Score Success (0 or 1) by Study Visit: Safety Population with Age <18
Table 14.2.4.3.4 ^a	Pruritus Safety (Sensitivity)	Worst-Itch- Numeric rating Scale (WI-NRS) Pruritus Score Success (0 or 1) by Study Visit: Cohort 1
Table 14.2.4.3.5 ^a	Pruritus Safety (Sensitivity)	Worst-Itch- Numeric rating Scale (WI-NRS) Pruritus Score Success (0 or 1) by Study Visit: Overall
Table 14.2.5.1	Safety	Summary, Change, and Percent Change from Primary Baseline in Percentage Body Surface Area (BSA) affected by psoriasis by Study Visit: Cohort 1
Table 14.2.5.2	Safety	Summary, Change, and Percent Change from Primary Baseline in Percentage Body Surface Area (BSA) affected by psoriasis by Study Visit: Overall
Table 14.2.5.3	Safety	Summary, Change, and Percent Change from Sensitivity Baseline in Percentage Body Surface Area (BSA) affected by psoriasis by Study Visit: Cohort 1
Table 14.2.5.4	Safety	Summary, Change, and Percent Change from Sensitivity Baseline in Percentage Body Surface Area (BSA) affected by psoriasis by Study Visit: Overall
Table 14.2.5.5	Safety with Age <18	Summary, Change, and Percent Change from Primary Baseline in Percentage Body Surface Area (BSA) Affected by Psoriasis by Study Visit: Safety Population with Age <18

^a Only the table number was revised relative to previous analyses.

13.1.3. Safety Data

Number	Population	Title
Table 14.3.1.1.1.1	Safety	Summary of Treatment Emergent Adverse Events (Primary): Cohort 1
Table 14.3.1.1.1.2	Safety	Summary of Treatment Emergent Adverse Events (Sensitivity): Cohort 1

Number	Population	Title
Table 14.3.1.1.2.1	Safety	Summary of Treatment Emergent Adverse Events (Primary): Overall
Table 14.3.1.1.2.2	Safety	Summary of Treatment Emergent Adverse Events (Sensitivity): Overall
Table 14.3.1.2.1.1	Safety	Incidence of Treatment Emergent Adverse Events by System Organ Class and Preferred Term (Primary): Cohort 1
Table 14.3.1.2.1.2	Safety	Incidence of Treatment Emergent Adverse Events by System Organ Class and Preferred Term (Sensitivity): Cohort 1
Table 14.3.1.2.2.1	Safety	Incidence of Treatment Emergent Adverse Events by System Organ Class and Preferred Term (Primary): Overall
Table 14.3.1.2.2.2	Safety	Incidence of Treatment Emergent Adverse Events by System Organ Class and Preferred Term (Sensitivity): Overall
Table 14.3.1.2.2.3	Safety with Age <18	Incidence of Treatment Emergent Adverse Events by System Organ Class and Preferred Term (Sensitivity): Safety Population with Age <18
Table 14.3.1.2.3.1	Safety	Incidence of Treatment Emergent Adverse Events by System Organ Class, Preferred Term and by Age Group (Primary)
Table 14.3.1.2.3.2	Safety	Incidence of Treatment Emergent Adverse Events by System Organ Class, Preferred Term and by Age Group (Sensitivity)
Table 14.3.1.3.1.1	Safety	Incidence of Treatment Emergent Adverse Events by System Organ Class, Preferred Term, and Maximum Severity (Primary): Cohort 1
Table 14.3.1.3.1.2	Safety	Incidence of Treatment Emergent Adverse Events by System Organ Class, Preferred Term, and Maximum Severity (Sensitivity): Cohort 1
Table 14.3.1.3.2.1	Safety	Incidence of Treatment Emergent Adverse Events by System Organ Class, Preferred Term, and Maximum Severity (Primary): Overall
Table 14.3.1.3.2.2	Safety	Incidence of Treatment Emergent Adverse Events by System Organ Class, Preferred Term, and Maximum Severity (Sensitivity): Overall
Table 14.3.1.3.2.3	Safety with Age <18	Incidence of Treatment Emergent Adverse Events by System Organ Class, Preferred Term, and Maximum Severity (Sensitivity): Safety Population with Age <18
Table 14.3.1.4.1.1	Safety	Incidence of Treatment Emergent Adverse Events by System Organ Class, Preferred Term, and Relationship to Study Drug (Primary): Cohort 1
Table 14.3.1.4.1.2	Safety	Incidence of Treatment Emergent Adverse Events by System Organ Class, Preferred Term, and Relationship to Study Drug (Sensitivity): Cohort 1
Table 14.3.1.4.2.1	Safety	Incidence of Treatment Emergent Adverse Events by System Organ Class, Preferred Term, and Relationship to Study Drug (Primary): Overall

Number	Population	Title
Table 14.3.1.4.2.2	Safety	Incidence of Treatment Emergent Adverse Events by System Organ Class, Preferred Term, and Relationship to Study Drug (Sensitivity): Overall
Table 14.3.1.4.2.3	Safety with Age <18	Incidence of Treatment Emergent Adverse Events by System Organ Class, Preferred Term, and Relationship to Study Drug (Sensitivity): Safety Population with Age <18
Table 14.3.1.5.1.1	Safety	Incidence of Treatment Emergent Adverse Events Leading to Study Drug Discontinuation by System Organ Class and Preferred Term (Primary): Cohort 1
Table 14.3.1.5.1.2	Safety	Incidence of Treatment Emergent Adverse Events Leading to Study Drug Discontinuation by System Organ Class and Preferred Term (Sensitivity): Cohort 1
Table 14.3.1.5.2.1	Safety	Incidence of Treatment Emergent Adverse Events Leading to Study Drug Discontinuation by System Organ Class and Preferred Term (Primary): Overall
Table 14.3.1.5.2.2	Safety	Incidence of Treatment Emergent Adverse Events Leading to Study Drug Discontinuation by System Organ Class and Preferred Term (Sensitivity): Overall
Table 14.3.1.5.2.3	Safety with Age <18	Incidence of Treatment Emergent Adverse Events Leading to Study Drug Discontinuation by System Organ Class and Preferred Term (Sensitivity): Safety Population with Age <18
Table 14.3.1.5.3.1	Safety	Incidence of Related Treatment Emergent Adverse Events Leading to Study Drug Discontinuation by System Organ Class and Preferred Term (Primary): Cohort 1
Table 14.3.1.5.3.2	Safety	Incidence of Related Treatment Emergent Adverse Events Leading to Study Drug Discontinuation by System Organ Class and Preferred Term (Sensitivity): Cohort 1
Table 14.3.1.5.4.1	Safety	Incidence of Related Treatment Emergent Adverse Events Leading to Study Drug Discontinuation by System Organ Class and Preferred Term (Primary): Overall
Table 14.3.1.5.4.2	Safety	Incidence of Related Treatment Emergent Adverse Events Leading to Study Drug Discontinuation by System Organ Class and Preferred Term (Sensitivity): Overall
Table 14.3.1.5.4.3	Safety with Age <18	Incidence of Related Treatment Emergent Adverse Events Leading to Study Drug Discontinuation by System Organ Class and Preferred Term (Sensitivity): Safety Population with Age <18
Table 14.3.2.1.1.1	Safety	Incidence of Serious Adverse Events by System Organ Class and Preferred Term (Primary): Cohort 1
Table 14.3.2.1.1.2	Safety	Incidence of Serious Adverse Events by System Organ Class and Preferred Term (Sensitivity): Cohort 1

Number	Population	Title
Table 14.3.2.1.2.1	Safety	Incidence of Serious Adverse Events by System Organ Class and Preferred Term (Primary): Overall
Table 14.3.2.1.2.2	Safety	Incidence of Serious Adverse Events by System Organ Class and Preferred Term (Sensitivity): Overall
Table 14.3.2.1.2.3	Safety with Age <18	Incidence of Serious Adverse Events by System Organ Class and Preferred Term (Sensitivity): Safety Population with Age <18
Table 14.3.2.2.1.1	Safety	Incidence of Serious Adverse Events by System Organ Class, Preferred Term, and Maximum Severity (Primary): Cohort 1
Table 14.3.2.2.1.2	Safety	Incidence of Serious Adverse Events by System Organ Class, Preferred Term, and Maximum Severity (Sensitivity): Cohort 1
Table 14.3.2.2.2.1	Safety	Incidence of Serious Adverse Events by System Organ Class, Preferred Term, and Maximum Severity (Primary): Overall
Table 14.3.2.2.2.2	Safety	Incidence of Serious Adverse Events by System Organ Class, Preferred Term, and Maximum Severity (Sensitivity): Overall
Table 14.3.2.3.1.1	Safety	Incidence of Serious Adverse Events by System Organ Class, Preferred Term, and Relationship to Study Drug (Primary): Cohort 1
Table 14.3.2.3.1.2	Safety	Incidence of Serious Adverse Events by System Organ Class, Preferred Term, and Relationship to Study Drug (Sensitivity): Cohort 1
Table 14.3.2.3.2.1	Safety	Incidence of Serious Emergent Adverse Events by System Organ Class, Preferred Term, and Relationship to Study Drug (Primary): Overall
Table 14.3.2.3.2.2	Safety	Incidence of Serious Emergent Adverse Events by System Organ Class, Preferred Term, and Relationship to Study Drug (Sensitivity): Overall
Table 14.3.2.4.1.1	All Enrolled	Adverse Events Leading to Study Drug Discontinuation (Primary)
Table 14.3.2.4.1.2	All Enrolled	Adverse Events Leading to Study Drug Discontinuation (Sensitivity)
Table 14.3.2.5.1.1	All Enrolled	Serious Adverse Events (Primary)
Table 14.3.2.5.1.2	All Enrolled	Serious Adverse Events (Sensitivity)
Table 14.3.2.6.1.1	All Enrolled	Adverse Events Resulted in Deaths (Primary)
Table 14.3.2.6.1.2	All Enrolled	Adverse Events Resulted in Deaths (Sensitivity)
Table 14.3.3.1.1	Safety	Summary of Investigator Local Tolerability Assessment (Dermal Response) by Study Visit (Sensitivity Baseline): Cohort 1
Table 14.3.3.1.2	Safety	Summary of Investigator Local Tolerability Assessment (Dermal Response) by Study Visit (Sensitivity Baseline): Overall
Table 14.3.3.1.3	Safety with Age <18	Summary of Investigator Local Tolerability Assessment (Dermal Response) by Study Visit (Sensitivity Baseline): Safety Population with Age <18

Number	Population	Title
Table 14.3.3.2.1	Safety	Summary of Investigator Local Tolerability Assessment (Dermal Response) by Study Visit Sensitivity Baseline (Categorical Results): Cohort 1
Table 14.3.3.2.2	Safety	Summary of Investigator Local Tolerability Assessment (Dermal Response) by Study Visit (Sensitivity Baseline) Categorical Results: Overall
Table 14.3.3.2.3	Safety with Age <18	Summary of Investigator Local Tolerability Assessment (Dermal Response) by Study Visit (Sensitivity Baseline) Categorical Results: Safety Population with Age <18
Table 14.3.3.3.1	Safety	Summary of Investigator Local Tolerability Assessment (Other Effects) by Study Visit (Sensitivity Baseline) Categorical Results: Cohort 1
Table 14.3.3.3.2	Safety	Summary of Investigator Local Tolerability Assessment (Other Effects) by Study Visit Sensitivity Baseline (Categorical Results): Overall
Table 14.3.3.3.3	Safety with Age <18	Summary of Investigator Local Tolerability Assessment (Other Effects) by Study Visit Sensitivity Baseline (Categorical Results): Safety Population with Age <18
Table 14.3.4.1.1	Safety	Summary of Clinical Chemistry Laboratory Results by Study Visit (Primary Baseline): Cohort 1
Table 14.3.4.1.2	Safety	Summary of Clinical Chemistry Laboratory Results by Study Visit (Primary Baseline): Overall
Table 14.3.4.1.3	Safety	Shift from Primary Baseline in Clinical Chemistry Laboratory Results by Study Visit Cohort 1
Table 14.3.4.1.4	Safety	Shift from Primary Baseline in Clinical Chemistry Laboratory Results by Study Visit Overall
Table 14.3.4.1.5	Safety with Age <18	Summary of Clinical Chemistry Laboratory Results by Study Visit (Primary Baseline): Safety Population with Age <18
Table 14.3.4.1.6	Safety with Age <18	Shift from Primary Baseline in Clinical Chemistry Laboratory Results by Study Visit: Safety Population with Age <18
Table 14.3.5.1.1	Safety	Summary of Hematology Laboratory Results by Study Visit (Primary Baseline): Cohort 1
Table 14.3.5.1.2	Safety	Summary of Hematology Laboratory Results by Study Visit (Primary Baseline): Overall
Table 14.3.5.1.3	Safety	Shift from Primary Baseline in Hematology Laboratory Results by Study Visit Cohort 1
Table 14.3.5.1.4	Safety	Shift from Primary Baseline in Hematology Laboratory Results by Study Visit Overall
Table 14.3.5.1.5	Safety with Age <18	Summary of Hematology Laboratory Results by Study Visit (Primary Baseline): Safety Population with Age <18

Number	Population	Title
Table 14.3.5.1.6	Safety with Age <18	Shift from Primary Baseline in Hematology Laboratory Results by Study Visit: Safety Population with Age <18
Table 14.3.6.1.1	Safety	Summary of Quantitative Urinalysis Laboratory Results by Study Visit (Primary Baseline): Cohort 1
Table 14.3.6.1.2	Safety	Summary of Quantitative Urinalysis Laboratory Results by Study Visit (Primary Baseline): Overall
Table 14.3.6.1.3	Safety	Shift from Primary Baseline in Quantitative Urinalysis Laboratory Results by Study Visit Cohort 1
Table 14.3.6.1.4	Safety	Shift from Primary Baseline in Quantitative Urinalysis Laboratory Results by Study Visit Overall
Table 14.3.6.1.5	Safety	Summary of Qualitative Urinalysis Laboratory Results by Study Visit (Primary Baseline): Cohort 1
Table 14.3.6.1.6	Safety	Summary of Qualitative Urinalysis Laboratory Results by Study Visit (Primary Baseline): Overall
Table 14.3.6.1.7	Safety with Age <18	Summary of Quantitative Urinalysis Laboratory Results by Study Visit (Primary Baseline): Safety Population with Age <18
Table 14.3.6.1.8	Safety with Age <18	Shift from Primary Baseline in Quantitative Urinalysis Laboratory Results by Study Visit: Safety Population with Age <18
Table 14.3.6.1.7	Safety with Age <18	Summary of Qualitative Urinalysis Laboratory Results by Study Visit (Primary Baseline): Safety Population with Age <18
Table 14.3.7.1.1	Safety	Summary of Vital Signs by Study Visit (Primary Baseline): Cohort 1
Table 14.3.7.1.2	Safety	Summary of Vital Signs by Study Visit (Primary Baseline): Overall
Table 14.3.7.1.3	Safety with Age <18	Summary of Vital Signs by Study Visit (Primary Baseline): Safety Population with Age <18
Table 14.3.7.2.1 ^a	Safety	Shift from Primary Baseline in Weight by Study Visit: Cohort 1
Table 14.3.7.2.2 ^a	Safety	Shift from Primary Baseline in Weight by Study Visit: Overall
Table 14.3.7.2.3	Safety with Age <18	Shift from Primary Baseline in Weight by Study Visit: Safety Population with Age <18
Table 14.3.7.2.4 ^a	Safety	Shift from Primary Baseline in Weight by Age Group and Study Visit
Table 14.3.7.2.5 ^a	Safety	Shift from Primary Safety Baseline in Weight by Study Visit and by Intentional/Non-intentional Weight Loss: Cohort 1
Table 14.3.7.2.6 ^a	Safety	Shift from Primary Safety Baseline in Weight by Study Visit and by Intentional/Non-intentional Weight Loss: Overall
Table 14.3.7.2.7	Safety with Age <18	Shift from Primary Safety Baseline in Weight by Study Visit and by Intentional/Non-intentional Weight Loss: Safety Population with Age <18
Table 14.3.7.3.1 ^a	Safety	Shift from Primary Baseline in BMI by Study Visit: Cohort 1
Table 14.3.7.3.2 ^a	Safety	Shift from Primary Baseline in BMI by Study Visit: Overall

Number	Population	Title
Table 14.3.7.3.3	Safety with Age <18	Shift from Primary Baseline in BMI by Study Visit: Safety Population with Age <18
Table 14.3.7.3.4 ^a	Safety	Shift from Primary Baseline in BMI by Study Visit and by Intentional/Non-intentional Weight Loss: Cohort 1
Table 14.3.7.3.5 ^a	Safety	Shift from Primary Baseline in BMI by Study Visit and by intentional/Non-intentional Weight Loss: Overall
Table 14.3.7.3.6	Safety with Age <18	Shift from Primary Baseline in BMI by Study Visit and by intentional/Non-intentional Weight Loss: Safety Population with Age <18
Table 14.3.8.1.1	Safety	Summary of Patient Health Questionnaire Depression Scale Assessments (PHQ-8) by Study Visit (Sensitivity Baseline): Cohort 1
Table 14.3.8.1.2	Safety	Summary of Patient Health Questionnaire Depression Scale Assessments (PHQ-8) by Study Visit (Sensitivity Baseline): Overall
Table 14.3.8.1.3	Safety	Shift from Sensitivity Baseline in Patient Health Questionnaire Depression Scale Assessments (PHQ-8) by Study Visit: Cohort 1
Table 14.3.8.1.4	Safety	Shift from Sensitivity Baseline in Patient Health Questionnaire Depression Scale Assessments (PHQ-8) by Study Visit: Overall
Table 14.3.9.1.1	Safety	Summary of Modified Patient Health Questionnaire Depression Scale Assessments (PHQ-A) by Study Visit (Sensitivity Baseline): Cohort 1 - Adolescent
Table 14.3.9.1.2	Safety	Summary of Modified Patient Health Questionnaire Depression Scale Assessments (PHQ-A) by Study Visit (Sensitivity Baseline): Overall - Adolescent
Table 14.3.9.1.3	Safety	Shift from Sensitivity Baseline in Modified Patient Health Questionnaire Depression Scale Assessments (PHQ-A) by Study Visit: Cohort 1
Table 14.3.9.1.4	Safety	Shift from Sensitivity Baseline in Modified Patient Health Questionnaire Depression Scale Assessments (PHQ-A) by Study Visit: Overall
Table 14.3.10.1	Safety	Summary of Columbia-Suicide Severity Rating Scale (C-SSRS) Suicidal Ideation and Suicidal Behaviour by Study Visit (Sensitivity Baseline): Cohort 1
Table 14.3.10.2	Safety	Summary of Columbia-Suicide Severity Rating Scale (C-SSRS) Suicidal Ideation and Suicidal Behaviour by Study Visit (Sensitivity Baseline): Overall
Table 14.3.11.1	Safety	Summary of Children's Depression Inventory 2 (CDI-2) by Study Visit (Sensitivity Baseline): Cohort 1
Table 14.3.11.2	Safety	Summary of Children's Depression Inventory 2 (CDI-2) for subjects 6-11 years old (parent report) by Study Visit (Sensitivity Baseline): Overall

Number	Population	Title
Table 14.3.12.1	Safety	Summary of Concomitant Medications by ATC Class Level 4 and Preferred Term: Cohort 1
Table 14.3.12.2	Safety	Summary of Concomitant Medications by ATC Class Level 4 and Preferred Term: Overall
Table 14.3.12.3	Safety with Age <18	Summary of Concomitant Medications by ATC Class Level 4 and Preferred Term: Safety Population with Age <18
Table 14.3.13.1	Safety	Summary of Physical Examination by Study Visit: Cohort 1
Table 14.3.13.2	Safety	Summary of Physical Examination by Study Visit: Overall
Table 14.3.13.3	Safety with Age <18	Summary of Physical Examination by Study Visit: Safety Population with Age <18

^a Only the table number was revised relative to previous analyses.

13.2. Figures Descriptions

The following are planned figures for protocol number ARQ-151-306. The figure numbers and page numbers are place holders only and will be determined when the figures are produced.

Number	Population	Title
Figure 14.2.3.3.1	Safety	Kaplan-Meier Plot of Treatment-Free Interval (Days)
Figure 14.2.3.3.2	Safety	Kaplan-Meier Plot of IGA Success (Days)

13.3. Planned Listing Descriptions

The following are planned data and patient/subject data listings for protocol number ARQ-151-306.

In general, one listing will be produced per CRF domain. All listings will be sorted by cohort, site, and subject number. All calculated variables will be included in the listings.

In all listings a blank line will be placed between each subject. Within a data listing, if an item appears line after line (e.g., repetition of subject number), then only the first occurrence will be displayed.

In data listings, the information for one subject will be kept on one page if at all possible, rather than splitting a subject's information across pages.

13.3.1. Subjects Data Listings

Number	Population	Title
Listing 16.2.1.1	All Enrolled	Subject Disposition
Listing 16.2.1.2	All Enrolled	Study Visits

Number	Population	Title
Listing 16.2.2.1	All Enrolled	Inclusion and Exclusion Criteria
Listing 16.2.2.2.1	All Enrolled	All Protocol Deviations
Listing 16.2.2.2.2	All Enrolled	Major Protocol Deviations
Listing 16.2.3	All Enrolled	Analysis Populations
Listing 16.2.4.1	All Enrolled	Demographics and Baseline Characteristics
Listing 16.2.4.2	All Enrolled	Medical History
Listing 16.2.4.3	All Enrolled	Prior and Concomitant Medications
Listing 16.2.5.1	All Enrolled	Study Drug Application at the Study Site
Listing 16.2.5.2	All Enrolled	Tubes
Listing 16.2.5.3	All Enrolled	Diary Dispensation
Listing 16.2.5.4	All Enrolled	Study Drug Interruption
Listing 16.2.5.5	All Enrolled	Drug Exposure and Compliance
Listing 16.2.6.1.1	All Enrolled	Investigator Global Assessment (IGA)
Listing 16.2.6.1.2	All Enrolled	Intertriginous Investigator Global Assessment (I-IGA)
Listing 16.2.6.2.1	All Enrolled	Psoriasis Area and Severity Index (PASI)
Listing 16.2.6.2.2	All Enrolled	Modified Psoriasis Area and Severity Index (mPASI)
Listing 16.2.6.3	All Enrolled	Worst Itch Numerical Rating Scale (WI-NRS)
Listing 16.2.6.4	All Enrolled	Body Surface Area (BSA)
Listing 16.2.7.1	All Enrolled	Adverse Events
Listing 16.2.8.1	All Enrolled	Investigator Local Tolerability Assessments
Listing 16.2.9.1	All Enrolled	Clinical Laboratory Data: Clinical Chemistry
Listing 16.2.9.2	All Enrolled	Clinical Laboratory Data: Hematology
Listing 16.2.9.3	All Enrolled	Clinical Laboratory Data: Urinalysis
Listing 16.2.9.4	All Enrolled	Clinical Laboratory Data: Serum and Urine Pregnancy Test
Listing 16.2.10.1	All Enrolled	Vital Signs
Listing 16.2.10.2	All Enrolled	Vital Signs - Weight
Listing 16.2.11.1	All Enrolled	Patient Health Questionnaire (PHQ-8)
Listing 16.2.11.2	All Enrolled	Modified Patient Health Questionnaire (Modified PHQ-A) Adolescent subjects
Listing 16.2.12	All Enrolled	Columbia-Suicide Severity Rating Scale (C-SSRS)
Listing 16.2.13	All Enrolled	Children's Depression Inventory 2 (CDI-2)
Listing 16.2.14	All Enrolled	Physical Examination

