An Open-Label Study to Evaluate the Long-Term Safety of Topical Administration of FMX103 for 40 weeks in the Treatment of Moderate to Severe Facial Papulopustular Rosacea (Study FX2016-13)

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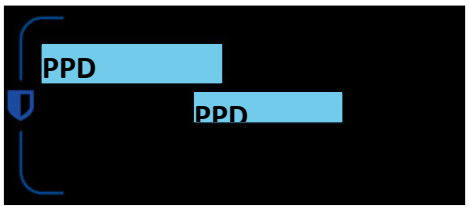
Biostatistician	Print Name: PPD Sign Name: 	14-Jan-2019 | 14:25:19 EST
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1. Overview

This statistical analysis plan (SAP) describes the planned analysis and reporting for Foamix Pharmaceuticals protocol number FX2016-13 (An Open-Label Study to Evaluate the Long-Term Safety of Topical Administration of FMX103 for 40 weeks in the Treatment of Moderate to Severe Facial Papulopustular Rosacea), Version 2 (Amendment 1) dated 22-Jun-2017. 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 Harmonization (ICH) of Technical Requirements for Registration of Pharmaceuticals for Human Use: Guidance on Statistical Principles in Clinical Trials[1]. All work planned and reported for this SAP will follow internationally accepted guidelines, published by the American Statistical Association[2] and the Royal Statistical Society[3], 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.

The statistical plan described hereafter is an *a priori* plan. It will be submitted to file prior to any descriptive analysis of data pertaining to Foamix Pharmaceuticals Study FX2016-13.

Subjects for this open-label extension study were selected according to pre-defined entry criteria from 2 Phase 3, randomized, multicenter, 12-week, double-blind, vehicle-controlled studies. Analyses for those 2 studies, FX2016-11 and FX2016-12, are reported separately.

2. Study Objectives and Endpoints

2.1. Study Objectives

2.1.1. Primary Objective

The primary objective is to show that open-label extended treatment with FMX103 1.5%, for up to an additional 40 weeks, is safe and well tolerated.

2.2. Study Endpoints

2.2.1. Safety Endpoints

The safety endpoints of this study include the following:

- Incidence, severity, and causality of any treatment-emergent adverse events (TEAEs), any serious TEAE, any treatment-related TEAE, and any TEAE leading to study discontinuation.
- Change from baseline in vital signs (at Weeks 4, 10, 16, 22, 28, 34, and 40), laboratory parameters (at Weeks 16 and 40), and physical examinations (at Week 40).

- Assessment of local signs and symptoms, erythema, telangiectasia, burning/stinging, flushing/blushing, dryness/xerosis, itching, peeling/desquamation, and hyperpigmentation.

2.2.2. Efficacy Endpoints

2.2.2.1. Primary Efficacy Endpoint

The primary efficacy endpoints are:

- The absolute change in the inflammatory lesion count at Week 40 compared to Baseline.
- The dichotomized IGA score where success is defined as a 2-step improvement resulting in a 0 (clear) or 1 (almost clear) score at Week 40 compared to Baseline.

2.2.2.2. Secondary Efficacy Endpoint(s)

The secondary efficacy endpoints are:

- The absolute change from Day 0/Baseline in the inflammatory lesion count at Weeks 4, 10, 16, 22, 28 and 34.
- The dichotomized IGA score where success is defined as a 2-step improvement resulting in a 0 (clear) or 1 (almost clear) score at Weeks 4, 10, 16, 22, 28, and 34 compared to Day 0/Baseline.
- The percent change in inflammatory lesion count at Weeks 4, 10, 16, 22, 28, and 34 compared to Day 0/Baseline.
- The Subject Satisfaction Questionnaire administered at Visit 7 (Week 40/Final Visit).

3. Overall Study Design

This is an open-label, multicenter, 40-week extension study to evaluate the long-term safety, tolerability, and efficacy of FMX103 1.5% topical foam in the treatment of subjects with moderate to severe facial papulopustular rosacea. Subjects who complete 1 of 2 double-blind, vehicle-controlled, 12 week, Phase 3 studies (FX2016-11 or FX2016-12) and meet all of the entry criteria will be invited to enroll in the extension study until enrollment goal is met.

Subjects will apply (or have applied) the assigned study drug topically as directed. Treatment will be guided by each subject's clinical response. The Investigator may elect to suspend treatment of some or all facial areas if there is clinical improvement or resolution of the rosacea in those areas. Even if treatment is partially or completely suspended temporarily, the subject will continue in the study and will attend all scheduled clinic visits. If at any time, their rosacea worsens, treatment of the affected areas may be resumed. Subjects will be advised to apply the study drug at approximately the same time each day, preferably about 1 hour before bedtime.

The baseline visit will occur on the same day as the Week 12 visit of either Study FX2016-11 or Study FX2016-12. Subjects will return for in-person visits at Weeks 4, 10, 16, 22, 28, 34, and 40. At the discretion of the clinic staff and for the convenience of subjects or clinic staff, visits can be scheduled to occur 5 days before or after the nominal scheduled date for all visits. A safety telephone call will be made 4 weeks after the Week 40 clinic visit to follow-up on AEs and record any new concomitant medications.

Subjects may be discontinued from the study at any time if their disease becomes refractory or they become intolerant of the product.

3.1. Overall Design

3.2. Sample Size and Power

The planned minimum enrollment is 400 male and female subjects who were previously enrolled in Study FX2016-11 or Study FX2016-12. The sample size is intended to ensure that at least 300 subjects continue to self-administer the study drug as needed for at least 6 months and 100 subjects continue for at least 1 year (ie, combined duration of treatment between the double-blind and open-label studies). The number of subjects at each site will be determined by the rate of recruitment in Studies FX2016-11 and FX2016-12. No statistical rationale for subject number is provided.

3.3. Study Population

The study population will be comprised of healthy male and non-pregnant females, aged ≥18 years who had a clinical diagnosis of moderate-to-severe facial papulopustular rosacea at the start of the previous double-blind study (Study FX2016-11 or Study FX2016-12) and who have completed the previous study to Week 12, did not have a worsening of disease during the study, and are willing and eligible to continue into this 40-week open-label extension study.

3.4. Treatments Administered

All subjects will receive FMX103 1.5% minocycline foam. Treatment will be administered daily for 40 weeks. The description of the study drug kits and treatment is shown in Table 2 of the protocol.

3.5. Method of Assigning Subjects to Treatment Groups

This is an open-label extension study with all subjects assigned to the active treatment.

For analysis purposes, subjects will be categorized depending on the treatment they received in the initial double-blind study. Subjects who received active treatment during the double-blind phase will be in the DB - FMX103 1.5% subgroup and subjects who received Vehicle Foam during the double-blind phase will be in the DB – Vehicle subgroup.

3.6. Blinding and Unblinding

Subjects will not be blinded as part of this study.

3.7. Schedule of Events

A detailed schedule of events for the study is provided in Table 1.

Table 1: Schedule of Study Assessments and Procedures

Assessment or Procedure		Baseline[a]	Visits						Final Visit[b]	Safety Follow-up[c]
Study Visit		(FV of previous DB Study)	1	2	3	4	5	6	7	N/A
Study Week (Week since beginning of previous DB study)		1 (12)	4 (16)	10 (22)	16 (28)	22 (34)	28 (40)	34 (46)	40 (52)	44 (56)
Informed consent		X								
Record subject identification[d]		X								
Inclusion/exclusion criteria		X								
Physical examination (including weight)		X							X	
Blood pressure/heart rate[e]		X	X	X	X	X	X	X	X	
Blood/urine samples for clinical laboratory tests		X			X				X	
Urine pregnancy test[f]		X	X	X	X	X	X	X	X	
Lesion counts		X	X	X	X	X	X	X	X	
Investigator's Global Assessment		X[g]	X	X	X	X	X	X	X	
Subject Satisfaction Questionnaire									X	
Local signs and symptom assessments[h]		X	X	X	X	X	X	X	X	
Concomitant medications		X	X	X	X	X	X	X	X	X
Adverse events		X	X	X	X	X	X	X	X	X
Perform drug accountability			X	X	X	X	X	X	X	
Collect used drug canister(s)			X	X	X	X	X	X	X	
Dispense study drug		X	X	X	X	X	X	X		
Review application instructions		X	X	X	X	X	X	X		
Schedule/confirm next visit or call (for safety follow-up only)		X	X	X	X	X	X	X	X	

DB = double-blind; FV = final visit; N/A = not applicable, no visit

a. Baseline for the study will be conducted at the same time as Visit 5/Week 12 (Final Visit) of Study FX2016-11 or Study FX2016-12. All assessments performed at Visit 5/Week 12 (Final Visit) of Study FX2016-11 or Study FX2016-12 should not be repeated but should be recorded as the same assessments at Baseline for this study.

b. If a subject withdraws from the study prematurely, all evaluations described under Visit 7/Week 40 (Final Visit) should be performed.

c. A safety follow-up telephone call will be made 4 weeks after Visit 7/Week 40 (Final Visit).

d. Previously assigned subject identification from Study FX2016-11 or Study FX2016-12 will be used in this study.

e. Measure blood pressure and heart rate after the subject has been sitting for at least 5 minutes at rest.

f. A urine pregnancy test will be done at the study site at every visit for all subjects of childbearing potential; home pregnancy tests will be dispensed at each visit, if needed, and will be performed at least monthly or whenever there is a suspicion of pregnancy (eg, a missed menstrual period).

g. The subject's Investigator's Global Assessment (IGA) at Visit 5/Week 12 (Final Visit) should not have worsened relative to the subject's IGA at Day 0/Baseline of one of the previous double-blind studies.

h. The severity of each of the following local rosacea signs/symptoms will be measured: erythema, telangiectasia, burning/stinging, flushing/blushing, dryness/xerosis, itching, peeling/desquamation, and hyperpigmentation.

4. Statistical Analysis and Reporting

Statistical analysis will be performed following Premier Research's standard operating procedures.

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 statistical methodology report will detail what software was used for what purposes.

Continuous (quantitative) variable summaries will include the number of subjects (n) with non-missing values, mean, standard deviation (SD), median, minimum, and maximum. Coefficient of variation will also be presented for primary efficacy endpoints.

Categorical (qualitative) variable summaries will include the frequency and percentage of subjects who are in the particular category or each possible value. Missing responses will be enumerated, unless otherwise specified.

The minimum and maximum will be reported with the same degree of precision (ie, 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 (eg, SD) will be reported to 2 degrees of precision more than the observed data.

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

There will be no hypothesis testing performed.

4.2. Interim Analysis and Data Monitoring

No interim analyses are planned.

5. Analysis Populations

The following analysis population is planned for this study:

- **All Treated Population:** The All Treated Population includes all subjects who use the study drug at least once. This population will be used for safety and efficacy analyses.

6. General Issues for Statistical Analysis

6.1. Statistical Definitions and Algorithms

6.1.1. Baseline

For all safety and efficacy analyses, Baseline will be defined as Day 0/Baseline of the initial double-blind study, ie, either Study FX2016-11 or Study FX2016-12. The last observation recorded prior to the first dose of FMX103 1.5% or vehicle foam will be used as the baseline observation for all calculations of the primary and secondary endpoints.

The baseline visit of the extension study which is equal to the Final Visit/Week 12 of the initial double-blind study will also be presented as Baseline (Week 12) in the listings for inflammatory lesion count and IGA.

6.1.2. Adjustments for Covariates

No adjustments will be made for covariates.

6.1.3. Multiple Comparisons

No adjustments will be made for multiple comparisons.

6.1.4. Handling of Dropouts or Missing Data

Any subject who withdraws from the study before the Week 40 visit should undergo all assessments specified for the Week 40/Final visit. For subjects who prematurely discontinue the study, their early termination (ET) visit data will be assigned to the closest visit by study day as described in Section 6.1.5. Missing data will not be imputed. All analyses will be based on observed data.

6.1.5. Analysis Visit Windows

All visit-based variables for this study will be analyzed according to their windowed visits defined by actual study day (see Table 2 below). Scheduled visits will be selected over unscheduled visits.

For those subjects who discontinue early from the study, Table 2 will be used to assign the appropriate analysis visit.

The study day, relative to first dose of study drug during the open-label phase, will be calculated for each scheduled or ET visit and compared to the lower and upper bounds presented in Table 2 to define the visit window used for analyses. The analysis visit windows only apply to those visits that are applicable to the specific assessment. For example, if the scheduled or ET visit falls at Week 4 but a specific assessment was not scheduled at that visit (see Table 1, Schedule of Events) then that assessment will not be used.

The following analysis visit windows will apply:

Table 2: Analysis Visit Windows

Analysis Visit	Analysis Visit Name	Target Day of Planned Visit	Assessment Window (Days)
1	Baseline/Week 12	0	NA – this is the baseline visit of the open-label study
2	Week 4	28	Post-dose ─ 49
3	Week 10	70	50 ─ 91
4	Week 16	112	92 ─ 133
5	Week 22	154	134 ─ 175
6	Week 28	196	176 ─ 217
7	Week 34	238	218 ─ 259
8	Week 40	280	260 ─ 301

If more than 1 visit occurs within a single visit window, then the analysis will use the visit closest to the target day. If 2 visits within the same visit window are equidistant from the target day, then the analysis will use the later visit.

6.1.6. Derived Variables

- Total number of inflammatory lesion count = number of papules + number of pustules + number of nodules in all facial areas (forehead, left and right cheeks, nose, and chin)

- Change from baseline in inflammatory lesion count = (value at baseline) – (post-baseline value)

  Thus, a positive change will reflect a reduction in inflammatory lesion count. Change from baseline will be calculated at the following time points: 4, 10, 16, 22, 28, 34, and 40 weeks.

- Percentage change from baseline inflammatory lesion count =

$$100 \times \frac{value\ at\ baseline - post\ baseline\ value}{value\ at\ baseline}$$

  Thus, a positive percentage change will reflect a reduction in inflammatory lesion count. The percentage change from baseline will be calculated at the following time points: 4, 10, 16, 22, 28, 34, and 40 weeks.

- Coefficient of Variation =

$$100 \times \frac{Standard\ Deviation\ of\ change\ from\ baseline}{Mean\ change\ from\ baseline}$$

for absolute and percent change in inflammatory lesion count.

- TEAE = any AE with an onset date after the first dose date of the open-label extension study and before the last application of study drug plus 3 days having been absent pre-treatment or worsening relative to the pre-treatment state. Adverse events reported at the baseline visit (Week 12 visit of the double-blind phase) will be assigned to the respective double-blind study. For subjects with >3 days of study drug interruption during the 40-week treatment period, the definition of a TEAE will also consider the date of the last dose before study drug interruption. For these subjects, AEs that start >3 days after the last dose before study drug interruption and before the drug is re-administered will not be considered as treatment-emergent.

- Body mass index (kg/m^2) = $\frac{weight\ in\ kilograms}{(height\ in\ meters)^2}$

- Age groups Age group=1 if 18≤ age (full years) ≤40
  Age group=2 if 41≤ age (full years) ≤64
  Age group=3 if 65≤ age (full years)

- Treatment duration (days) =

  Date of last dose of study drug – Date of first dose of study drug + 1 day

- Study drug exposure (days) =

  Treatment duration (days) – Number of days that a subject reported missing a dose – Number of days of drug interruption (as instructed by the investigator, between the date of first and last dose)

- Compliance (%) = 100 x Study drug exposure (days) / Treatment duration (days)

  Study drug compliance will not be calculated for subjects whose date of last study drug application is unknown.

  For subjects who are instructed to discontinue and then restart study drug application during the study, number of days off treatment will be added back into the numerator in the calculation of compliance since they will be considered compliant during that time. For subjects who are missing the date of last study drug application, the last known contact date will be used in the calculation of treatment duration and study drug exposure.

- Treatment duration (days) of FMX103 1.5% =

  Date of last dose of FMX103 1.5% – Date of first dose of FMX103 1.5% + 1 day

  For subjects who received vehicle during study FX2016-11 and FX2016-12, the date for first dose of FMX103 1.5% will occur during the FX2016-13 study

- IGA treatment success = yes if the following conditions are both satisfied:
  - IGA score of 0 or 1
  - at least a 2-grade improvement (decrease) from baseline

  Otherwise, IGA treatment success = no

6.1.7. Data Adjustments/Handling/Conventions

All collected data will be presented in listings. 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.

Adverse events will be coded using the Medical Dictionary for Regulatory Activities (MedDRA), Version 20.0. In general, a TEAE is defined as an AE with an onset date after the first dose of the open-label extension study and before the last application of study drug plus 3 days having been absent pre-treatment or worsening relative to the pre-treatment state. AEs reported at the baseline visit (Week 12 visit of the double-blind phase) will be assigned to the initial double-blind study. For subjects with >3 days of study drug interruption during the 40-week treatment period, the definition of a TEAE will also consider the date of the last dose before study drug interruption. For these subjects, AEs that start >3 days after the last dose before study drug interruption and before the drug is re-administered will not be considered as treatment-emergent.

Any AE that started before the first dose of study drug and worsens in severity or changes from non-serious to serious on or after the first dose date of the open-label phase will also be designated as a TEAE. If an event worsens in severity during the study, the outcome of the lower grade event would be RECOVERED/RESOLVED or RECOVERED/RESOLVED WITH SEQUELAE with an end date (of that grade). A new event is recorded on the AE case report form (CRF) with a start date that matches the end date, and the term recorded includes "Worsened" (eg, "Worsened Headaches"). If an event becomes serious, the date that the event became serious is recorded on the AE CRF as the End Date of that AE and the Start Date of the corresponding SAE.

Any AE or concomitant medication that was ongoing at the end of the double-blind study will be copied into the extension study database with start dates entered as the original start date. Adverse events and concomitant medications that are ongoing at the end of the open-label study will be closed out with a stop date of "ongoing."

A treatment-related AE is any AE with a relationship to the study drug of possible or probable.

Adverse events or medications with missing complete start dates will be classified as treatment emergent or concomitant, as appropriate.

For analysis purposes, an AE that does not have a recorded relationship to the study drug value will be considered as "Probably Related" to the study drug, unless the start date of the AE is before the date of first study drug administration, in which case the event would be considered as "Unlikely Related." If the severity of an AE is missing, the severity will be considered as "Missing."

If partial AE or concomitant medication onset dates occur, the convention for replacing missing dates for the purpose of statistical analysis is as follows: if just day is missing then the day assigned is the first day of the month or the date of first dose (if in the same month), whichever is later; if just month is missing then the month assigned is the month of the first dose, unless that results in a date prior to the first dose in which case the month after the first dose is used; and if both month and day are missing then the month assigned is the month of the first dose and the day assigned is either the first day of the month or the first dose date, whichever is later.

These conventions will be applied only to onset dates with the following precaution related to AE onset dates: if the missing date reflects the date of onset of an AE, the modified date will be constructed to match the first documented date post-drug administration while preserving the order in which the AE was reported in the CRF.

For partial end dates, the convention for replacing missing dates for the purpose of statistical analysis is as follows: if only the day is missing, then the day is assigned the last day of the month; if both day and month are missing, they are assigned the last day of the year (31 Dec).

For subjects who are missing the date of last study drug application, for any reason, the last known contact date will be used in the calculation of treatment duration and study drug exposure. Study drug compliance will not be calculated for those subjects whose date of last study drug application is unknown.

For analysis purposes, repeat laboratory test results will not be used unless the original laboratory value is missing or indicated as invalid, in which case the first non-missing repeat laboratory value will be used for data analysis.

7. Study Subjects and Demographics

All analyses outlined in this section will be performed on the All Treated population.

7.1. Disposition of Patients/Subjects and Withdrawals

The number and percentage of subjects that are included in the All Treated population, completed the study, participated in each double-blind study (FX2016-11 and FX2016-12), and withdrew from the study (overall and by reason for withdrawal), summarized overall and by treatment group (9 month active and 12 month active).

The number and percentage of subjects who were in the safety populations of each double-blind study (FX2016-11 and FX2016-12) and the number and percentage of subjects who continued on to study FX2016-13 will be summarized overall and treatment group. Percentages will be calculated out of the total number of subjects in studies FX2016-11 and FX2016-12 combined.

A by-subject enrollment and disposition listing will be presented for all treated subjects. Subjects who are screen failures will be presented in a separate listing.

7.2. Protocol Violations and Deviations

Protocol deviations will be listed for all treated subjects.

7.3. Demographics and Other Baseline Characteristics

Summary statistics of demographics and baseline characteristics will be summarized overall and by treatment group. The following demographic and baseline variables will be included:

- Age (years)
- Age group in full years (18 to 40 years, 41 to 64 years, ≥ 65 years)
- Sex
- Race
- Ethnicity
- Baseline body weight (kg), height (cm), and body mass index (BMI) (kg/m2)
- Baseline inflammatory lesion count (from Day 0 of the initial double-blind study)
- Baseline IGA score (moderate=3, severe=4)

For continuous variables, the number of non-missing values and the mean, SD, minimum, median, and maximum will be tabulated.

For categorical variables, the counts and proportions of each value will be tabulated. Subjects reporting more than 1 race will be included in a "More than one race" category for purposes of tabulating summary statistics. Past medical histories for all treated subjects will be provided in a by-subject listing.

7.4. Exposure and Compliance

The following parameters of study drug exposure and compliance will be summarized overall and by treatment groups for the FX2016-13 study:

- Treatment duration (days)
- Study drug exposure (days)
- Study drug compliance (%)

For a given day, a subject is considered compliant with treatment if any amount of study drug is applied to the facial area. For subjects who are missing the date of last study drug application, for any reason, the last known contact date will be used in the calculation of treatment duration and study drug exposure. Study drug compliance will not be calculated for those subjects whose date of last study drug application is unknown. For subjects who are instructed to discontinue treatment and then restart study drug during the study, days that the subject was not taking study

drug will be included in treatment duration and exposure and will be considered compliant during that time.

Overall treatment duration (days) of FMX103 1,5% will also be summarized by treatment received during the initial double-blind study as the date of the last dose of FMX103 1.5% minus the date of the first dose of FMX103 1.5% plus one day. For subjects who initially received vehicle, treatment with FMX103 1.5% began during study FX2016-13. The number and percentage of subjects who were exposed to FMX103 1.5% for six months(>168 days) or more and one year or more (>350 days) will be summarized.

8. Efficacy Analysis

All efficacy analyses outlined in this section will be performed on the All Treated population.

8.1. Primary Efficacy Analysis

The primary efficacy analyses are based on the AT population and are as follows:

- Absolute change from baseline in inflammatory lesion count at Week 40
- Dichotomized IGA Success Rate at Week 40

Descriptive summaries will be presented for each of the co-primary endpoints. For change from baseline, the number of non-missing values, mean, SD, coefficient of variation (CV), median, minimum and maximum will be presented. For IGA Success Rate, the number of non-missing values and the frequency and proportion of subjects who achieve treatment success will be summarized. No hypothesis testing will be performed.

In order to evaluate any differences in the co-primary endpoints due to the treatment received in the initial double-blind study, the primary endpoints will be summarized overall and by treatment sequence.

8.2. Secondary Efficacy Analysis

The following secondary efficacy endpoints will be analyzed similarly to the appropriate co-primary efficacy parameters:

- The absolute change from baseline in inflammatory lesion count at Weeks 4, 10, 16, 22, 28, and 34
- The dichotomized IGA Success Rate at Weeks 4, 10, 16, 22, 28 and 34
- The percent change from baseline in inflammatory lesion count at Weeks 4, 10, 16, 22, 28, 34, and 40.
- The Subject Satisfaction Questionnaire (SSQ) at Week 40.

8.3. Subject Satisfaction Questionnaire

Answers to the SSQ will be summarized for Week 40 (or the ET visit) using frequency counts and percentages for the All Treated population. The SSQ will be summarized overall and by treatment group.

9. Safety and Tolerability Analysis

Safety will be evaluated from reported AEs, changes in clinical laboratory values, changes in vital signs, and physical examination results. All safety analyses will be performed on the All Treated Population.

Safety assessments will be summarized using descriptive statistics overall and by treatment group and in individual subject listings.

No statistical tests will be performed for any of the safety assessments.

9.1. Adverse Events

All AE terms will be coded using MedDRA, Version 20.0.

All AEs that occur after enrollment in the extension study but before administration of the study drug will be reported as an AE in the respective double-blind study and recorded as medical history in this study. TEAEs will be defined as any adverse event with an onset date after the first dose date of the open-label extension study and before the last application of study drug plus 3 days having been absent pre-treatment or worsening relative to the pre-treatment state. AEs reported at the baseline visit (Week 12 visit of the double-blind phase) will be assigned to the respective double-blind study. For subjects with >3 days of study drug interruption during the 40-week treatment period, the definition of a TEAE will also consider the date of the last dose before study drug interruption. For these subjects, AEs that start >3 days after the last dose before study drug interruption and before the drug is re-administered will not be considered as treatment-emergent. If relationship to treatment is missing, the event will be summarized conservatively as probably related to study drug unless the start date of the AE is before the first study drug administration, in which case the event would be considered as not related. If severity is missing, the event will be summarized as “missing”. Through the data cleaning process, all attempts will be made to avoid missing values for relationship and severity.

All AEs summarized by system organ class (SOC) and preferred term (PT) will be sorted in order of descending frequency of the SOC and then by descending frequency order (total across treatment groups) of the PT within each SOC.

An overall summary of AEs will be presented for the All Treated population. This summary will include the total number of events, frequency counts, and percentages for:

- Any AEs
- Any TEAEs
- Any SAEs
- Any treatment-related TEAEs

- Any TEAE leading to study discontinuation
- TEAEs resulting in death

Summaries of the incidence of TEAEs and SAEs will be displayed by:

- SOC and PT
- SOC, PT, and maximum severity (mild, moderate, severe)
- SOC, PT, and maximum causality (not related, related) to the study drug

If there are multiple occurrences of the same TEAE within the same subject, each subject will only be counted once for each PT. In the summaries showing severity and relationship to the study drug, the event with the maximum severity or strongest relationship will be reported.

All AEs will be presented in a by-subject listing, detailing the verbatim term given by the Investigator, the PT, SOC, onset date and time, end date and time, severity, outcome, relationship to study drug, action taken with study drug, other action taken, seriousness, and criteria for seriousness. All SAEs will be presented in a separate listing.

9.1.1. Adverse Events Leading to Withdrawal

A summary of incidence rates (frequencies and percentages) of TEAEs leading to withdrawal of study drug (and subsequent permanent discontinuation from the study), by SOC, and preferred term will be presented.

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.

Serious adverse events will be listed and also tabulated by system organ class and preferred term. All SAEs will also be presented by maximum severity and maximum causality.

9.2. Clinical Laboratory Evaluations

Absolute and changes from baseline values will be summarized by treatment group and time point for clinical laboratory (chemistry and hematology) results using descriptive statistics. The number of subjects with clinical laboratory values below, within, or above the normal range will be tabulated for each clinical laboratory test at the Week 40 visit. Shift tables for each clinical laboratory test will cross-tabulate the number of subjects with values below the laboratory reference range (low), values within the laboratory reference range (normal), or above the laboratory range (high) at baseline with the number of subjects with low, normal or high values at the Week 40 visit. Normal ranges and values outside the normal ranges will be identified by the central laboratory. A separate listing of out of normal range laboratory results will be provided for all chemistry, hematology, and urinalysis tests.

A listing of all subjects with treatment-emergent clinically significant abnormal chemistry, hematology, or urinalysis values will be presented for each treatment group. Clinical significance will be based on the Investigator's judgment.

Urinalysis and urine pregnancy test results will be presented in by-subject listings.

9.3. Vital Signs

Descriptive summaries of actual values and changes from baseline will be calculated for supine systolic blood pressure, supine diastolic blood pressure, heart rate, respiratory rate, and oral body temperature.

9.4. Physical Examinations

Shifts from baseline for physical examinations will be presented for the Week 40 visit overall and by treatment group.

Abnormal physical examination findings will be displayed in a by-subject listing.

9.5. Local Signs and Symptoms Assessments

Erythema, telangiectasia, burning/stinging, flushing/blushing, dryness/xerosis, itching, peeling/desquamation, and hyperpigmentation at the sites of study drug application will be assessed at each study visit. All local signs/symptoms with the exception of erythema will be graded on a 0 to 3 scale (0=none; 1=mild; 2=moderate; 3=severe). Erythema will be graded on a 0 to 4 scale (0=clear skin/no signs of erythema; 1=almost clear of erythema, slight redness; 2=mild erythema, definite redness; 3=moderate erythema, marked redness; 4=severe erythema, fiery redness). Itching will be assessed on the same 0 to 3 scale based on the subjects' subjective assessment.

The severity of each assessed local sign/symptom will be summarized using frequency counts and percentages at each visit by treatment group and overall.

9.6. Concomitant Medication

A concomitant medication is any non-protocol specified drug or substance administered during participation in the study, including medications that are ongoing at the time of informed consent. This period of participation is from the time of enrollment in the extension study through the last contact at 4 weeks after the Week 40 clinic visit. Medications that were considered concomitant during the initial double-blind study but were stopped before enrollment in the extension study will be considered prior medications.

Prior and concomitant medications will be summarized descriptively by treatment group and overall using counts and percentages in each Anatomical Therapeutic Chemical (ATC) level 2 group and PT (ie, generic name).

Prior medications will be presented separately from concomitant medications. Medications that started prior to Day 1 of the extension study will be considered prior medications whether or not

they were stopped prior to Day 1. Any medications continuing or starting after Day 1 will be considered to be concomitant. If a medication starts prior to Day 1 and continues after Day 1 it will be considered both prior and concomitant.

- Medications will be coded using the World Health Organization Drug Dictionary Version March 2017.

10. Changes from Planned Analysis

There are no changes from the analyses planned in the protocol.

11. Other Planned Analysis

11.1. Pharmacokinetic Analysis

No pharmacokinetic analysis is planned for this study.

12. References

1. ASA. (2016) Ethical Guidelines for Statistical Practice. Prepared by the Committee on Professional Ethics, April 2016. http://www.amstat.org/about/ethicalguidelines.cfm
2. 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.
3. 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.

13. Tables, Listings, and Figures

All listings, tables, and graphs 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 (ie, listing number where applicable).

13.1. Planned Table Descriptions

The following are planned summary tables for protocol number FX2016-13. The table numbers and page numbers are place holders only and will be determined when the tables are produced.

During the 40-week open-label treatment extension study, subjects who were applying FMX103 1.5% at the end of the respective double-blind study will continue this treatment, while subjects who were administering vehicle will crossover to FMX103 1.5%.

For the table summaries, the 2 treatment groups representing FMX103 1.5% and Vehicle to FMX103 1.5% will be presented as: DB – FMX103 1.5% and DB – Vehicle, respectively.

Table 3: Disposition, Demographic, Prior Medications, and Study Drug Exposure Data Summary Tables

Table Number	Population(s)	Table Title / Summary	Supporting listing
14.1 Disposition, Demographic, Prior Medications, and Study Drug Exposure Data			
Table 14.1.1	All Subjects	Summary of Subject Enrollment and Disposition	16.2.1.1 16.2.1.2 16.2.4.1
Table 14.1.2	All Subjects in Safety populations of FX2016-11 and FX2016-12	Summary of Study Enrollment	16.2.1.1
Table 14.1.3	All-Treated Population	Summary of Demographics and Baseline Characteristics	16.2.4.1 16.2.6.1 16.2.6.2
Table 14.1.4	All-Treated Population	Summary of Prior Medications by ATC Level 2 and Preferred Term	16.2.4.3
Table 14.1.5	All-Treated Population	Summary of Study Drug Exposure	16.2.5.1 16.2.5.2
Table 14.1.6	All-Treated Population	Summary of Overall FMX103 1.5% Treatment Duration (Days) by Treatment	16.2.5.1 16.2.5.2
Table 14.1.7	All-Treated Population	Study Drug Compliance	16.2.5.3

Table 4: Efficacy Data

Table Number	Population(s)	Table Title / Summary	Supporting listing
14.2 Efficacy Data			
Table 14.2.1.1	All-Treated Population	Change from Baseline in Inflammatory Lesion Count	16.2.6.2
Table 14.2.1.2	All-Treated Population	Change from Baseline (Week 12) in Inflammatory Lesion Count	16.2.6.2
Table 14.2.2.1	All-Treated Population	Descriptive Summary of IGA Treatment Success	16.2.6.1
Table 14.2.2.2	All-Treated Population	Descriptive Summary of IGA Treatment Success from Baseline (Week 12)	16.2.6.1
Table 14.2.3	All-Treated Population	Descriptive Summary of Subject Satisfaction Questionnaire	16.2.6.3

Table 5: Safety Data

Table Number	Population(s)	Table Title / Summary	Supporting listing
14.3 Safety Data			
14.3.1 Displays of Adverse Events			
Table 14.3.1.1	All-Treated Population	Summary of All Adverse Events	16.2.7.1
Table 14.3.1.2	All-Treated Population	Treatment-Emergent Adverse Events by System Organ Class and Preferred Term	16.2.7.1
Table 14.3.1.3	All-Treated Population	Treatment-Emergent Adverse Events by Severity, System Organ Class, and Preferred Term	16.2.7.1
Table 14.3.1.4	All-Treated Population	Treatment-Emergent Adverse Events by Relationship to Study Drug, System Organ Class, and Preferred Term	16.2.7.1
14.3.2 Other Serious and Significant Adverse Events			
Table 14.3.2.1	All-Treated Population	Serious Adverse Events by System Organ Class and Preferred Term	16.2.7.2
Table 14.3.2.2	All-Treated Population	Serious Adverse Events by Severity, System Organ Class, and Preferred Term	16.2.7.2
Table 14.3.2.3	All-Treated Population	Serious Adverse Events by Relationship to Study Drug, System Organ Class, and Preferred Term	16.2.7.2
Table 14.3.2.4	All-Treated Population	Adverse Events Leading to Withdrawal from the Study by System Organ Class and Preferred Term	16.2.7.3
Table 14.3.2.5	All-Treated Population	Adverse Events Leading to Withdrawal from the Study by Severity, System Organ Class, and Preferred Term	16.2.7.3
Table 14.3.2.6	All-Treated Population	Adverse Events Leading to Withdrawal from the Study by Relationship to Study Drug, Systemic Organ Class, and Preferred Term	16.2.7.3

Table Number	Population(s)	Table Title / Summary	Supporting listing
14.3.5 Laboratory Data Summary Tables			
Table 14.3.5.1	All-Treated Population	Clinical Chemistry Results	16.2.8.1
Table 14.3.5.2	All-Treated Population	Shift Table of Clinical Chemistry Results	16.2.8.1
Table 14.3.5.3	All-Treated Population	Hematology Results	16.2.8.2
Table 14.3.5.4	All-Treated Population	Shift Tables of Hematology Results	16.2.8.2
14.3.6 Other Safety and Tolerability Summary Tables			
Table 14.3.6.1	All-Treated Population	Shift Table of Physical Examination Results	16.2.9.2
Table 14.3.6.2	All-Treated Population	Vital Sign Results	16.2.9.1
Table 14.3.6.3	All-Treated Population	Concomitant Medications by ATC Level 2 and Preferred Term	16.2.9.3
Table 14.3.6.4	All-Treated Population	Summary of Local Signs and Symptoms Assessments	16.2.9.4

Planned Listing Descriptions

The following are planned data and subject data listings for protocol FX2016-13.

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

In all listings, a blank line will be placed between each subject. Within a data listing, if an item appears line after line (eg, 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.

Table 6: Planned Listings

Data Listing Number	Population	Data Listing Title / Summary
16.2 Subject Data Listings **16.2.1 Subject Discontinuations/Completions**		
Data listing 16.2.1.1	All Treated Subjects	Study Completion Status
Data listing 16.2.1.2	All Treated Subjects	Inclusion and Exclusion Criteria Not Met
16.2.2 Protocol Deviations		
Data listing 16.2.2.1	All Treated Subjects	Protocol Deviations
16.2.3 Subjects Excluded from the Efficacy Analyses		
NA		
16.2.4 Demographic Data and Other Baseline Characteristics		
Data listing 16.2.4.1	All Treated Subjects	Demographic Data
Data listing 16.2.4.2	All Treated Subjects	Medical History
Data listing 16.2.4.3	All Treated Subjects	Prior Medications
16.2.5 Compliance Data		
Data listing 16.2.5.1	All Treated Subjects	Study Drug Accountability

Data Listing Number	Population	Data Listing Title / Summary
Data listing 16.2.5.2	All Treated Subjects	Study Drug Stoppage and Restart
Data listing 16.2.5.3	All Treated Subjects	Study Drug Compliance
16.2.6 Individual Efficacy Response Data		
Data listing 16.2.6.1	All Treated Subjects	IGA Score
Data listing 16.2.6.2	All Treated Subjects	Inflammatory Lesion Count by Facial Area
Data listing 16.2.6.3	All Treated Subjects	Subject Satisfaction Questionnaire (SSQ)
16.2.7 Adverse Event Listings		
Data listing 16.2.7.1	All Treated Subjects	Adverse Events
Data listing 16.2.7.2	All Treated Subjects	Serious Adverse Events
Data listing 16.2.7.3	All Treated Subjects	Adverse Events Leading to Withdrawal
Data listing 16.2.7.4	All Treated Subjects	Deaths
16.2.8 Laboratory Data Listings		
Data listing 16.2.8.1	All Treated Subjects	Clinical Chemistry Results
Data listing 16.2.8.2	All Treated Subjects	Hematology Results
Data listing 16.2.8.3	All Treated Subjects	Urinalysis Results
Data listing 16.2.8.4	All Treated Subjects	Clinically Significant Laboratory Tests for Hematology, Chemistry, and Urinalysis
Data listing 16.2.8.5	All Treated Subjects	Out of Range (Abnormal) Laboratory Tests for Hematology, Chemistry, and Urinalysis
Data listing 16.2.8.6	All Treated Subjects	Pregnancy Test Results
16.2.9 Other Clinical Observations and Measurements		
Data listing 16.2.9.1	All Treated Subjects	Vital Signs

Data Listing Number	Population	Data Listing Title / Summary
Data listing 16.2.9.2	All Treated Subjects	Abnormal Physical Examination Results
Data listing 16.2.9.3	All Treated Subjects	Concomitant Medications
Data listing 16.2.9.4	All Treated Subjects	Local Signs and Symptoms Assessments
Data listing 16.2.9.5	All Treated Subjects	Telephone Contact

13.2. Planned Figure Descriptions

There are no planned figures.

14. Tables, Listings, and Listing Shells

14.1. Standard Layout for all Tables, Listings, and Figures

Table and listing shells are provided in a separate document.

Note that programming notes may be added after each table, listing or figure (TLF) shell if appropriate.

Appendix 1: Premier Research Library of Abbreviations

Abbreviation	Definition
AE	adverse event
AT	All Treated population
ATC	Anatomical Therapeutic Chemical
CRF	case report form
CSR	clinical study report
CV	Coefficient of variation
DB	Double-blind
ET	early termination
IGA	Investigator's Global Assessment
MedDRA	medical dictionary for regulatory activities
PT	preferred term
SAE	serious adverse event
SAP	statistical analysis plan
SAS®	a software system used for data analysis
SD	standard deviation
SOC	system organ class
SSQ	subject satisfaction questionnaire
TEAE	treatment-emergent adverse event

Statistical Analysis

Table and Listing Shells

Sponsor	*Foamix Pharmaceuticals*
Protocol Title:	*An Open-Label Study to Evaluate the Long-Term Safety of Topical Administration of FMX103 for 40 weeks in the Treatment of Moderate to Severe Facial Papulopustular Rosacea (Study FX2016-13)*
Protocol Number:	*FX2016-13*
Premier Research PCN:	*FOAM166108*
Document Version:	*Final Version 1.0*
Document Date:	*08-Jan-2019*

Table and Listing Shells for Foamix FX2016-13

14.1 Disposition, Demographic, Prior Medications and Study Drug Exposure Data Summary Tables

Table 14.1.1
Summary of Subject Enrollment and Disposition
All Subjects

Status	DB - FMX103 1.5%	DB - Vehicle	Overall
All Treated population	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Enrolled from the FX2016-11 study	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Enrolled from the FX2016-12 study	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Completed the study	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Discontinued early	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Reason for discontinuation			
Adverse event	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Abnormal laboratory result	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Lost to follow-up	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Subject request	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Protocol deviation	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Other	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)

Note: Percentages are based on the number of subjects in the All Treated population. DB = Treatment received during double-blind study
The All Treated population is defined all subjects who use the study drug at least once.
Source: Listing 16.2.1.1, 16.2.1.2, 16.2.4.1

Table 14.1.2
Summary of Study Enrollment
All Subjects in Safety populations of FX2016-11 and FX2016-12

Number of Subjects	DB - FMX103 1.5%	DB - Vehicle	Overall
FX2016-11 Safety Population[1]	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
FX2016-12 Safety Population[1]	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
Subjects who continued to FX2016-13[2]	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)

Note: Percentages are based on the total number of subjects in studies FX2016-11 and FX2016-12.

[1]Includes all subjects that were randomized and received at least one application of study medication.

[2]Includes all subjects who enrolled in study FX2016-13.

Table 14.1.3
Summary of Demographics and Baseline Characteristics
All Treated Population

Variable	Sample Characteristic/Category	DB - FMX103 1.5% (N=xxx)	DB - Vehicle (N=xxx)	Overall (N=xxx)
Age [years] [1]	n (# missing)	xxx (xx)	xxx (xx)	xxx (xx)
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x
	Min to Max	xx to xx	xx to xx	xx to xx
Weight [kg]	n (# missing)	xxx (xx)	xxx (xx)	xxx (xx)
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x
	Min to Max	xx to xx	xx to xx	xx to xx
Height [cm] [2]	n (# missing)	xxx (xx)	xxx (xx)	xxx (xx)
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x
	Min to Max	xx to xx	xx to xx	xx to xx
Body Mass Index (BMI) [kg/m^2]	n (# missing)	xxx (xx)	xxx (xx)	xxx (xx)
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x
	Min to Max	xx to xx	xx to xx	xx to xx
Age group [full years] [1]	18 to 40	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	41 to 64	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	≥ 65	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Missing	xx	xx	xx
Sex	Male	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Female	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Missing	xx	xx	xx

Table 14.1.3 (cont'd)

Variable	Sample Characteristic/Category	DB - FMX103 1.5% (N=xxx)	DB - Vehicle (N=xxx)	Overall (N=xxx)
Ethnicity	Hispanic/Latino	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Non-Hispanic/Latino	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Missing	xx	xx	xx
Race	American Indian or Alaska native	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Asian	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Black or African American	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Native Hawaiian or other Pacific Islander	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	White	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	More than one race	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Missing	xx	xx	xx
IGA Score	3	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
	4	xxx (xx.x%)	xxx (xx.x%)	xxx (xx.x%)
	Missing	xx	xx	xx
Inflammatory Lesion Count	n (# missing)	xxx (xx)	xxx (xx)	xxx (xx)
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x
	Min to Max	xx to xx	xx to xx	xx to xx

Note: Percentages exclude missing data. SD = standard deviation. DB = Treatment received during double-blind study. Baseline is defined as the Baseline visit in the initial double-blind study (FX2016-11 or FX2016-12).
[1] Age (years) at the baseline visit.
[2] For subjects who were missing height, weight and/or BMI at baseline, these variables were imputed from the closest other study visit for which it was taken.
Source: Listing 16.2.4.1, 16.2.6.1, 16.2.6.2

Table 14.1.4
Summary of Prior Medications by ATC Level 2 and Preferred Term
All Treated Population

ATC Level 2 Preferred Term [1]	DB - FMX103 1.5% (N=xxx)	DB - Vehicle (N=xxx)	Overall (N=xxx)
Any prior medication	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
ATC level 2 entry 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
PT 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
PT 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
PT 3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
...			
ATC level 2 entry 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
PT 4	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
PT 5	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
PT 6	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
ATC level 2 entry 3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
...	...	...	...
..	..	..	..
.	.	.	.

Note: Percentages are 100*n/N. Subjects were counted only once for each Anatomical Therapeutic Chemical (ATC) or preferred term. Medications that started prior to Day 1 are considered prior whether or not they were stopped prior to Day 1. Medications that were considered concomitant during the initial double-blind study but were stopped before enrollment in the extension study will be considered prior medications. DB = Treatment received during double-blind study
[1] Medications were coded using WHO-DD (Enhanced version March 2017) ATC level 2. Preferred Term is ATC level 5.
Source: Listing 16.2.4.3

Programming Note: Whenever possible, keep all PT within an ATC level on one page. Sort by ATC level and then PT.

Table 14.1.5
Summary of Study Drug Exposure
All Treated Population

Variable	Sample Characteristics	DB - FMX103 1.5% (N=xxx)	DB - Vehicle (N=xxx)	Overall (N=xxx)
Treatment Duration (days) [1]	n (# missing)	xxx (xx)	xxx (xx)	xxx (xx)
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x
	Min to Max	xx to xx	xx to xx	xx to xx
Total Days of Exposure [2]	n (# missing)	xxx (xx)	xxx (xx)	xxx (xx)
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x
	Min to Max	xx to xx	xx to xx	xx to xx

Note: For subjects who are missing the date of last dose, the last known contact date will be used in the calculation of treatment duration and exposure. DB = Treatment received during double-blind study
[1] Treatment duration (days) is defined as the date of last dose of study drug minus the date of first dose of study drug plus 1 day.
[2] Total days of exposure is defined as the difference in treatment duration (days) and the number of days that a subject reported missing a dose (between the date of first and last dose). For subjects who are instructed discontinue and then restart study drug application during the study, the number of days off treatment will also be subtracted exposure.
Source: Listing 16.2.5.1, 16.2.5.2

Table 14.1.6
Summary of Overall FMX103 1.5% Treatment Duration (Days)[1] by Treatment[2]
All Treated Population

Variable	Sample Characteristics	DB - FMX103 1.5% (N=xxx)	DB - Vehicle (N=xxx)	Overall (N=xxx)
Treatment Duration (days) [1]	n (# missing)	xxx (xx)	xxx (xx)	xxx (xx)
	Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
	Median	xx.x	xx.x	xx.x
	Min to Max	xx to xx	xx to xx	xx to xx
Subjects exposed to ≥ 6 months (>168 days)	n (%)	xxx (xx.xx%)	xxx (xx.xx%)	xxx (xx.xx%)
Subjects exposed to ≥ 1 year (>350 days)	n (%)	xxx (xx.xx%)	xxx (xx.xx%)	xxx (xx.xx%)

[1] Treatment duration (days) is defined as the date of last dose of study drug FMX103 1.5% minus the date of first dose of study drug FMX103 1.5% plus 1 day. For subjects who are missing the date of last dose, the last known contact date will be used
[2] Subjects are presented by the treatment received during studies FX2016-11 and FX2016-12. For the vehicle group, treatment of FMX103 1.5% started in study FX2016-13.

Table 14.1.7
Study Drug Compliance
All Treated Population

Statistic	DB - FMX103 1.5% (N=xxx)	DB - Vehicle (N=xxx)	Overall (N=xxx)
n (# missing)	xx (xx)	xx (xx)	xx (xx)
Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
Median	xx.x	xx.x	xx.x
Min to Max	xx.x to xx.x	xx.x to xx.x	xx.x to xx.x

Note: Compliance (%) = 100 x Study drug exposure (days) / Treatment duration days). DB = Treatment received during double-blind study. For subjects who are instructed to discontinue then restart study drug application, the number of days of stoppage will not be removed from the numerator as they will be considered to be compliant during that time. Subjects who are missing last dose dates are not included.
Source: Listing 16.2.5.3

14.2 Efficacy Data

Table 14.2.1.1
Change from Baseline in Inflammatory Lesion Count
All Treated Population

Visit	Variable	Sample Characteristics	DB - FMX103 1.5% (N=xxx)	DB - Vehicle (N=xxx)	Overall (N=xxx)
Baseline [1]	Observed value	n (# missing)	xxx (xx)	xxx (xx)	xxx (xx)
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x
		Min to Max	xx to xx	xx to xx	xx to xx
Baseline (Week 12) [2]	Observed value	n (# missing)	xxx (xx)	xxx (xx)	xxx (xx)
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x
		Min to Max	xx to xx	xx to xx	xx to xx
Week 4	Observed value	n (# missing)	xxx (xx)	xxx (xx)	xxx (xx)
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x
		Min to Max	xx to xx	xx to xx	xx to xx
	Change from Baseline [3]	n (# missing)	xxx (xx)	xxx (xx)	xxx (xx)
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		CV	xx.x	xx.x	xx.x
		Median	xx.x	xx.x	xx.x
		Min to Max	xx to xx	xx to xx	xx to xx
	Percent Change from Baseline [3]	n (# missing)	xxx (xx)	xxx (xx)	xxx (xx)
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		CV	xx.x	xx.x	xx.x
		Median	xx.x	xx.x	xx.x
		Min to Max	xx to xx	xx to xx	xx to xx

Programming Note: Continue for Weeks 10, 16, 22, 28, 34, and 40.

Note: The coefficient of variation (CV) is defined as the standard deviation (SD) divided by the mean times 100. DB = Treatment received during double-blind study.
[1] Baseline is defined as the Baseline visit in the initial double-blind study (FX2016-11 or FX2016-12).

[2] Baseline (Week 12) is defined as the baseline visit of the open-label extension study.
[3] Change from baseline is calculated as the value at baseline minus the post-baseline value. Thus, a positive change will reflect a reduction in lesion count. The same definition is used in the numerator for percent change.
Source: Listing 16.2.6.2

Table 14.2.1.2
Change from Baseline (Week 12)[1] in Inflammatory Lesion Count
All Treated Population

See Table 14.2.1.1

Programming Note: Continue for Weeks 10, 16, 22, 28, 34, and 40. Use Baseline(Week 12) of the open-label extension study as the baseline visit for this table.

Note: The coefficient of variation (CV) is defined as the standard deviation (SD) divided by the mean times 100. DB = Treatment received during double-blind study.
[1] Baseline is defined as the Baseline visit in the open-label extension study (Week 12 of DB study).
[2] Change from baseline is calculated as the value at baseline minus the post-baseline value. Thus, a positive change will reflect a reduction in lesion count. The same definition is used in the numerator for percent change.
Source: Listing 16.2.6.2

Table 14.2.2.1
Descriptive Summary of IGA Treatment Success
All Treated Population

Visit	Score/ Success?	DB - FMX103 1.5% (N=xxx)	DB - Vehicle (N=xxx)	Overall (N=xxx)
Baseline [1]	n (# missing)	xxx (xx)	xxx (xx)	xxx (xx)
	3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	4	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Baseline [2]	n (# missing)	xxx (xx)	xxx (xx)	xxx (xx)
	3	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	4	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Week 4	n (# missing)	xxx (xx)	xxx (xx)	xxx (xx)
	Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Week 10	n (# missing)	xxx (xx)	xxx (xx)	xxx (xx)
	Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Week 16	n (# missing)	xxx (xx)	xxx (xx)	xxx (xx)
	Yes	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	No	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Programming Note: Continue for Weeks 22, 28, 34, and 40.

Note: Percentages are based on the number of subjects with a non-missing value (yes or no) at each visit. IGA treatment success is Yes if the IGA score is either 0 or 1 and there is at least a 2-grade improvement (decrease) from baseline. Otherwise IGA treatment success is No. DB = Treatment received during double-blind study.
[1] Baseline is defined as the Baseline visit in the initial double-blind study (FX2016-11 or FX2016-12).
[2] Baseline (Week 12) is defined as the baseline visit of the open-label extension study.
Source: Listing 16.2.6.1

Table 14.2.2.2
Descriptive Summary of IGA Treatment Success from Baseline (Week 12)[1]
All Treated Population

See Table 14.2.2.1

Programming Note: Continue for Weeks 22, 28, 34, and 40. Use Baseline (Week 12) of the open-label extension study as the baseline visit for this table.

Note: Percentages are based on the number of subjects with a non-missing value (yes or no) at each visit. IGA treatment success is Yes if the IGA score is either 0 or 1 and there is at least a 2-grade improvement (decrease) from baseline. Otherwise IGA treatment success is No. DB = Treatment received during double-blind study.
[1] Baseline is defined as the Baseline visit in the open-label extension study (Week 12 of DB study).
Source: Listing 16.2.6.1

Table 14.2.3
Descriptive Summary of Subject Satisfaction Questionnaire
All Treated Population

Variable	Category	DB - FMX103 1.5% (N=xxx)	DB - Vehicle (N=xxx)	Overall (N=xxx)
Easy to Use	Non-missing response	xx	xx	xx
	1-Very satisfied	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	2-Satisfied	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	3-Somewhat satisfied	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	4-Dissatisfied	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	5-Very dissatisfied	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Missing response	xx	xx	xx
Feels on skin	Non-missing response	xx	xx	xx
	1-Very satisfied	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	2-Satisfied	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	3-Somewhat satisfied	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	4-Dissatisfied	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	5-Very dissatisfied	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Missing response	xx	xx	xx

Programming Note: Continue for 'Odor', 'Color', 'Ease of application', 'Ease fitting into daily routine', 'Compared to Other Products', 'Use with other Rosacea treatments', 'Recommend to Friend', and 'Overall satisfaction'

Recommend to Friend	Non-missing response	xx	xx	xx
	1-Very likely	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	2-Likely	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	3-Somewhat likely	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	4-Unlikely	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	5-Very unlikely	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Missing response	xx	xx	xx

Note: Percentages exclude missing responses. Subject Satisfaction Questionnaire is completed at the Week 40 visit or at the final visit for those subjects that prematurely withdraw from the study. DB = double-blind study.
Source: Listing 16.2.6.3

14.3 Safety Data

14.3.1 Displays of Adverse Events

Table 14.3.1.1
Summary of All Adverse Events
All Treated Population

	DB - FMX103 1.5% (N=xxx)	DB - Vehicle (N=xxx)	Overall (N=xxx)
All Adverse Events (AEs)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Treatment-emergent adverse events (TEAEs) [1]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Serious TEAEs	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Treatment-related TEAEs [2]	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Adverse events leading to study discontinuation	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
TEAEs resulting in death	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Note: Percentages are 100*n/N. Number (%) of subjects with at least 1 AE in the category are presented. Adverse events were coded using MedDRA, Version 20.0.
[1] For subjects who are missing the date of last dose, any AE occurring after the first dose is considered treatment emergent.
[2] Any TEAE reported as possibly related or probably related, or is missing, is considered as related to study drug.
Source: Listing 16.2.7.1

Table 14.3.1.2
Treatment-Emergent Adverse Events by System Organ Class and Preferred Term
All Treated Population

System Organ Class Preferred Term	DB - FMX103 1.5% (N=xxx)	DB - Vehicle (N=xxx)	Overall (N=xxx)
Number of Any event	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
SOC 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
PT 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
PT 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
SOC 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
PT 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
PT 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
...			

Programming Note: Order SOCs by descending number of subjects (total within both treatment groups) and preferred terms within SOC also by descending number of subjects (and for all other tables where AEs are arranged by SOC and PT)

Note: Percentages are 100*n/N. Subjects were counted only once for each System Organ Class and Preferred Term. Adverse events were coded using MedDRA, Version 20.0. For subjects who are missing the date of last dose, any AE occuring after the first dose is considered treatment emergent. AEs are sorted in descending frequency of SOC and PT.
Source: Listing 16.2.7.1

Table 14.3.1.3
Treatment-Emergent Adverse Events by Severity, System Organ Class, and Preferred Term
All Treated Population

System Organ Class Preferred Term Severity	DB - FMX103 1.5% (N=xxx)	DB - Vehicle (N=xxx)	Overall (N=xxx)
Any System Organ Class			
Any Event (Total)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Missing	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
SOC 1			
Any Event (Total)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
PT 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
PT 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
SOC 2			
Any Event (Total)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Severe	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Moderate	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Mild	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
...			
Programming Note: Only include Missing category when SOC or PT has missing values, otherwise just include Severe, Moderate, and Mild			

Note: Percentages are 100*n/N. Subjects were counted only once for each System Organ Class and Preferred Term. Adverse events were coded using MedDRA version 20.0. For subjects who are missing the date of last dose, any AE occurring after the first dose is considered treatment emergent.
Source: Listing 16.2.7.1

Table 14.3.1.4
Treatment-Emergent Adverse Events by Relationship to Study Drug, System Organ Class, and Preferred Term
All Treated Population

System Organ Class Preferred Term Relationship to Study Drug [1]	DB - FMX103 1.5% (N=xxx)	DB - Vehicle (N=xxx)	Overall (N=xxx)
Any System Organ Class			
Any Event (Total)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Related	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Not Related	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
SOC 1			
Any Event (Total)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Related	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Not Related	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
PT 1	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Related	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Not Related	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
PT 2	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Related	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Not Related	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
SOC 2			
Any Event (Total)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Related	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
Not Related	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
...			

Note: Percentages are 100*n/N. Subjects were counted only once for each System Organ Class and Preferred Term. Adverse events were coded using MedDRA version 20.0. For subjects who are missing the date of last dose, any AE occurring after the first dose is considered treatment emergent. Treatment groups are based on treatment received. DB = Treatment received during double-blind study
[1] Any TEAE reported as possibly related or probably related, or is missing, is considered as related to study drug unless the start date is prior to the first date of study drug administration.
Source: Listing 16.2.7.1

14.3.2 Other Serious and Significant Adverse Events

Table 14.3.2.1
Serious Adverse Events by System Organ Class and Preferred Term
All Treated Population

See Table 14.3.1.2

Note: Percentages are 100*n/N. Subjects were counted only once for each System Organ Class and Preferred Term. Adverse events were coded using MedDRA, Version 20.0. Treatment groups are based on treatment received.
Source: Listing 16.2.7.2

Table 14.3.2.2
Serious Adverse Events by Severity, System Organ Class, and Preferred Term
All Treated Population

See Table 14.3.1.3

Note: Percentages are 100*n/N. Subjects were counted only once for each System Organ Class and Preferred Term. Adverse events were coded using MedDRA version 20.0. Treatment groups are based on treatment received.
Source: Listing 16.2.7.2

Table 14.3.2.3
Serious Adverse Events by Relationship to Study Drug, System Organ Class, and Preferred Term
All Treated Population

See Table 14.3.1.4

Note: Percentages are 100*n/N. Subjects were counted only once for each System Organ Class and Preferred Term. Adverse events were coded using MedDRA, Version 20.0. Treatment groups are based on treatment received.
[1] Any AE reported as possibly related or probably related, or is missing, is considered as related to study drug unless the start date is prior to the first date of study drug administration.
Source: Listing 16.2.7.2

Table 14.3.2.4
Adverse Events Leading to Withdrawal from the Study by System Organ Class and Preferred Term
All Treated Population

See Table 14.3.1.2

Note: Percentages are 100*n/N. Subjects were counted only once for each System Organ Class and Preferred Term. Adverse events were coded using MedDRA, Version 20.0. Treatment groups are based on treatment received.
Source: Listing 16.2.7.3

Table 14.3.2.5
Adverse Events Leading to Withdrawal from the Study by Severity, System Organ Class, and Preferred Term
All Treated Population

See Table 14.3.1.3

Note: Percentages are 100*n/N. Subjects were counted only once for each System Organ Class and Preferred Term. Adverse events were coded using MedDRA, Version 20.0. Treatment groups are based on treatment received.
Source: Listing 16.2.7.3

Table 14.3.2.6
Adverse Events Leading to Withdrawal from the Study by Relationship to Study Drug, System Organ Class, and Preferred Term
All Treated Population

See Table 14.3.1.4

Note: Percentages are 100*n/N. Subjects were counted only once for each System Organ Class and Preferred Term. Adverse events were coded using MedDRA, Version 20.0. Treatment groups are based on treatment received.
[1] Any AE reported as possibly related or probably related, or is missing, is considered as related to study drug unless the start date is prior to the first date of study drug administration.
Source: Listing 16.2.7.3

14.3.5 Laboratory Data Summary Tables

Table 14.3.5.1
Clinical Chemistry Results
All Treated Population

Analyte	Visit	Statistic	DB - FMX1O3 1.5% (N=xxx)	DB - Vehicle (N=xxx)	Overall (N=xxx)
Analyte 1 (unit) - Absolute value	Baseline [1]	n (# missing)	xx (xx)	xx (xx)	xx (xx)
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x
		Min to Max	xx.x to xx.x	xx.x to xx.x	xx.x to xx.x
	Week x	n (# missing)	xx (xx)	xx (xx)	xx (xx)
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x
		Min to Max	xx.x to xx.x	xx.x to xx.x	xx.x to xx.x
...					
Analyte 1 (unit) - Change from baseline	Week x	n (# missing)	xx (xx)	xx (xx)	xx (xx)
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x
		Min to Max	xx.x to xx.x	xx.x to xx.x	xx.x to xx.x
...					

Programming Note: Repeat for all applicable visits and all clinical chemistry analytes.

Note: Change from baseline is calculated as the value at the specified visit minus the value recorded at baseline; negative values represent a decrease in laboratory values since baseline. DB = Treatment received during double-blind study
[1] Baseline is defined as the Baseline visit in the initial double-blind study (FX2016-11 or FX2016-12).
Source: Listing 16.2.8.1

Table 14.3.5.2
Shift Table of Clinical Chemistry Results
All Treated Population

Analyte	Treatment	Assessment at Final Visit [2]	Assessment at Baseline [1]				
			Missing N (%)	Low N (%)	Normal N (%)	High N (%)	Total N (%)
Analyte 1 [unit]	DB - FMX103 1.5%	Missing	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)
		Low	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)
		Normal	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)
		High	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)
		Total	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)
	DB - Vehicle	Missing	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)
		Low	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)
		Normal	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)
		High	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)
		Total	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)
	Overall	Missing	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)
		Low	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)
		Normal	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)
		High	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)
		Total	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)	xx (xxx.x%)

...

DB = Treatment received during double-blind study
[1] Baseline is defined as the Baseline visit in the initial double-blind study (FX2016-11 or FX2016-12).
[2] Final Visit is the Week 40 visit for subjects that completed the study or the last post-dose lab assessment for subjects that withdrew from the study early.
Source: Listing 16.2.8.1

Table 14.3.5.3
Hematology Results
All Treated Population

See Table 14.3.5.1

Note: Change from baseline is calculated as the value at the specified visit minus the value recorded at baseline; negative values represent a decrease in laboratory values since baseline.
Source: Listing 16.2.8.2

Table 14.3.5.4
Shift Table of Hematology Results
All Treated Population

See Table 14.3.5.2

Source: Listing 16.2.8.2

14.3.6 Other Safety and Tolerability Summary Tables

Table 14.3.6.1
Shift Table of Physical Examination Results
All Treated Population

			Assessment at Baseline				
Assessment	Treatment	Assessment at Week 40 Visit	Normal N (%)	Abnormal, NCS N (%)	Abnormal, CS N (%)	Not Done N (%)	Total N (%)
General appearence	DB - FMX103 1.5%	Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
		Abnormal, NCS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
		Abnormal, CS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
		Not done	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
		Total	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	DB - Vehicle	Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
		Abnormal, NCS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
		Abnormal, CS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
		Not done	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
		Total	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
	Overall	Normal	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
		Abnormal, NCS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
		Abnormal, CS	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
		Not done	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
		Total	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)

Note: Percentages exclude missing data. NCS = not clinically significant; CS = clinically significant; DB = Treatment received during double-blind study
Source: Listing 16.2.9.2

Table 14.3.6.2
Vital Sign Results
All Treated Population

Variable	Visit	Sample Characteristics	DB - FMX103 1.5% (N=xxx)	DB - Vehicle (N=xxx)	Overall (N=xxx)
Variable1- Absolute value	Baseline[1]	n (# missing)	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x
		Min to Max	xx.x to xx.x	xx.x to xx.x	xx.x to xx.x
	Week x	n (# missing)	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x
		Min to Max	xx.x to xx.x	xx.x to xx.x	xx.x to xx.x
...					
Variable1- Change from baseline	Week x	n (# missing)	xx	xx	xx
		Mean (SD)	xx.x (xx.xx)	xx.x (xx.xx)	xx.x (xx.xx)
		Median	xx.x	xx.x	xx.x
		Min to Max	xx.x to xx.x	xx.x to xx.x	xx.x to xx.x

Programming Note: Repeat for all vital signs variables and all scheduled visits

Note: Change from baseline is calculated as the value at the specified visit minus the value recorded at baseline; negative values represent a decrease from baseline. DB = Treatment received during double-blind study
[1] Baseline is defined as the Baseline visit in the initial double-blind study (FX2016-11 or FX2016-12).
Source: Listing 16.2.9.1

Table 14.3.6.3
Concomitant Medications by ATC Level 2 and Preferred Term
All Treated Population

See Table 14.1.3

Note: Percentages are 100*n/N. Subjects were counted only once for each Anatomical Therapeutic Chemical (ATC) or preferred term. Any medications continuing or starting after Day 1 were considered to be concomitant.
[1] Medications were coded using WHO-DD (Enhanced version March 2017) ATC level 2. Preferred term is ATC level 5.
Source: Listing 16.2.9.3

Table 14.3.6.4
Summary of Local Signs and Symptoms Assessments
All Treated Population

Visit	Sign/Symptom	Category	DB - FMX103 1.5% (N=xxx)	DB - Vehicle (N=xxx)	Overall (N=xxx)
Baseline[1]					
	Erythema	Non-missing response	xx	xx	xx
		0-clear skin/no signs of erythema	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
		1-almost clear of erythema, slight redness	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
		2-mild erythema, definite redness	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
		3-moderate erythema, marked redness	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
		4-severe erythema, fiery redness	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
		Missing response	xx	xx	xx
	Telangiectasia	Non-missing response	xx	xx	xx
		0-None	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
		1-Mild: scattered telangiectasia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
		2-Moderate: numerous telangiectasia	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
		3-Severe: dense telangiectasia forming sprays of vessels	xx (xx.x%)	xx (xx.x%)	xx (xx.x%)
		Missing response	xx	xx	xx

Programming Note: Continue for 'Burning/Stinging', 'Flushing/Blushing', 'Dryness/Xerosis', 'Itching', 'Peeling/Desquamation', 'Hyperpigmentation'. Continue for Baseline (Week 12), Weeks 4, 10, 16, 22, 28, 34 and 40. See protocol Section 10.7.1.1 for categories.

Note: Percentages exclude missing responses. DB = Treatment received during double-blind study.
[1] Baseline is defined as the Baseline visit in the initial double-blind study (FX2016-11 or FX2016-12).
[2] Baseline (Week 12) is defined as the baseline visit of the open-label extension study.
Source: Listing 16.2.9.4

16.2 Subject Data Listings

16.2.1 Subject Discontinuations/Completions

Listing 16.2.1.1
Study Completion Status
All Treated Subjects

Treatment group during DB study:

Subject ID	Completed Study?	Date of Completion or Discontinuation	Reason for Discontinuation	Treatment Start Date	Treatment End Date	AEs at Final Visit? [1]	Date of Last Contact
Xxxxxx	xxxxx	ddmmmyyyy	xxxxx	ddmmmyyyy	ddmmmyyyy	xxxxx	ddmmmyyyy
Xxxxxx	xxxxx	ddmmmyyyy	xxxxx	ddmmmyyyy	ddmmmyyyy	xxxxx	ddmmmyyyy

[1] Indicates if subject presented with any new or ongoing AEs at the final visit. DB = double-blind.

Listing 16.2.1.2
Inclusion and Exclusion Criteria Not Met
All Subjects

Treatment group during DB study: XXXXXXX

Subject ID	Met All Inclusion/Exclusion Criteria?	Inclusion/Exclusion Criteria Number(s) Not Met [1]
XXXXXX	Yes	
XXXXXX	Yes	
XXXXXX	Yes	
XXXXXX	No	XX
XXXXXX	Yes	
XXXXXX	No	XX;XX

DB = double-blind.
[1] XX = XXXXXXXXXXXXXXXXXXXXXXX.
[2] XX = XXXXXXXXXXXXXXXXX; XX = XXXXXXXXXXXXXXXXXXXXXXXXXXXXXXX.

Programming note: *If more than 1 inclusion or exclusion criterion number exists, concatenate with a comma as shown above. Decode any relevant criteria in the footnotes as shown in the example. If no criteria are present for a column, remove the [1] and/or [2] from the column header.*

16.2.2 Protocol Deviations

Listing 16.2.2.1
Protocol Deviations
All Treated Subjects

Treatment group during DB study:

Subject ID	Date of Deviation	Severity Classification	Type	Description	Action Taken	Submitted to IRB?
xxxxxx	ddmmmyyyy	xxxxx	xxxxx	Xxxxx	xxxxx	xxxxx
xxxxxx	ddmmmyyyy	xxxxx	xxxxx	Xxxxx	xxxxx	xxxxx

Note: Missed doses <5 are not listed. DB = double-blind.

16.2.4 Demographic Data and Other Baseline Characteristics

Listing 16.2.4.1
Demographic Data
All Treated Subjects

Treatment group during DB study:

Subject ID	Date of IC	Date of Birth	Age (full years)	Sex	Race	Ethnicity	Child-Bearing Potential?	DB Protocol Subject was Enrolled Previously
xxxxxx	ddmmmyyyy	ddmmmyyyy	xx	x	xxx	xxx	xxx	xxxxx
xxxxxx	ddmmmyyyy	ddmmmyyyy	xx	x	xxx	xxx	xxx	xxxxx

IC = Informed Consent. DB = double-blind.

Listing 16.2.4.2
Medical History
All Treated Subjects

Treatment group during DB study:

Subject ID	Any Medical History?	System Organ Class/ Preferred Term/ Verbatim Term	Start Date	End Date
xxxxxx	xxxxx	xxxxxxxxxxx/ xxxxxxxx/ xxxxxxxxx	ddmmmyyyy	ddmmmyyyy
xxxxxx	xxxxx	xxxxxxxxxxx/ xxxxxxxx/ xxxxxxxxx	ddmmmyyyy	Ongoing

DB = double-blind. *Programming Note: If Medical Condition is Ongoing, then End Date will be "Ongoing".*

Listing 16.2.4.3
Prior Medications
All Treated Subjects

Treatment group during DB study:

Subject ID	Any Medication?	Anatomic Therapeutic Class/ Preferred Term/ Verbatim Term	Start Date	End Date	Indication	Dose (unit) Route/ Frequency
xxxxxx	xxxxx	xxxxxxxxxxx/ xxxxxxxx/ xxxxxxxxx	ddmmmyyyy	ddmmmyyyy	xxxxx	xxx/ xxxxx/ xxxxxxx
xxxxxx	xxxxx	xxxxxxxxx/ xxxxxxxx/ xxxxxxxxxxx	ddmmmyyyy	Ongoing	xxxxx	xxx/ xxxxxxxxx/ xxxxxxxxxx

Note: Medications were coded using WHO-DD (Enhanced version March 2017) ATC level 2. Preferred Term is ATC level 5. DB = double-blind.

Programming Note: If Medication is Ongoing, then End Date will be "Ongoing".

16.2.5 Compliance Data

Listing 16.2.5.1
Study Drug Accountability
All Treated Subjects

Treatment group during DB study:

				Dispensed					Returned			
Subject ID	Visit	Study Drug Dispensed?	Reason Not Dispensed	Date	Kit ID	Canister ID	Study Drug Returned?	Reason Not Returned	Date	Kit ID	Canister ID	Any Doses Missed?/Number
xxxxxx	xxxxx	xxx	xxxx	ddmmmyyyy	xxx	xxxx	xxx	xxxx	ddmmmyyyy	xxx	xxxx	Yes/xx
xxxxxx	xxxxx	xxx	xxxx	ddmmmyyyy	xxx	xxxx	xxx	xxxx	ddmmmyyyy	xxx	xxxx	No

DB = double-blind

Listing 16.2.5.2
Study Drug Stoppage and Restart
All Treated Subjects

Treatment group during DB study:

Subject ID	Visit	Did Investigator Suspend Treatment?	Date Treatment Stopped	Did Subject Restart Treatment at this Visit?	Date Treatment Restarted
xxxxxx	xxxxx	Xxx	xxxx	xxx	xxxx
xxxxxx	xxxxx	Xxx	xxxx	xxx	xxxx

Listing 16.2.5.3
Study Drug Compliance
All Treated Subjects

Treatment group during DB study:

Subject ID	First Dose Date	Last Dose Date	Duration Drug Suspended	Treatment Duration (Days) [1]	Number of Missed Doses	Compliance (%) [2]
xxxxxx	ddmmmyyyy	ddmmmyyyy	Xxx	xxx	xx	xxxx
xxxxxx	ddmmmyyyy	ddmmmyyyy	Xxx	xxx	xx	xxxx

Note: Subjects who are missing last dose dates are not included. DB = double-blind
[1] Treatment duration (days) = Date of last dose of study drug - Date of first dose of study drug + 1 day
[2] Compliance (%) = 100 x Study drug exposure (days) / Treatment duration (days). For subjects who were instructed to stop and restart treatment over the course of the study, they will be considered compliant on those days.

Programming Note: Round compliance to one decimal.

16.2.6 Individual Efficacy Response Data

Listing 16.2.6.1
IGA Score
All Treated Subjects

Treatment group during DB study:

Site ID	Subject ID	Visit	Was Assessment Performed?	Reason Not Performed	Assessor Initials	Date	Time	Study Day	IGA Score	IGA Treatment Success [1]
xxx	xxxxxx	Baseline [2]	xxx	Xxxx	xx	ddmmmyyyy	hh:mm	xx	x	-
		Baseline (Week 12)	xxx	Xxxx	xx	ddmmmyyyy	hh:mm	xx	x	-
		Week 4	xxx	Xxxx	xx	ddmmmyyyy	hh:mm	xx	x	xxx
		Week 10	xxx	Xxxx	xx	ddmmmyyyy	hh:mm	xx	x	xxx
		Week 16	xxx	Xxxx	xx	ddmmmyyyy	hh:mm	xx	x	xxx
		Week 22	xxx	Xxxx	xx	ddmmmyyyy	hh:mm	xx	x	xxx
		Week 28	xxx	Xxxx	xx	ddmmmyyyy	hh:mm	xx	x	xxx
		Week 34	xxx	Xxxx	xx	ddmmmyyyy	hh:mm	xx	x	xxx
		Week 40	xxx	Xxxx	xx	ddmmmyyyy	hh:mm	xx	x	xxx
xxx	xxxxxx	Baseline	xxx	Xxxx	xx	ddmmmyyyy	hh:mm	xx	x	xxx

[1] IGA treatment success is Yes if the IGA score is either 0 or 1 and there is at least a 2-grade improvement (decrease) from baseline. Otherwise IGA treatment success is No. DB = double-blind.
[2] Baseline is defined as the Baseline visit in the initial double-blind study (FX2016-11 or FX2016-12).

Listing 16.2.6.2
Inflammatory Lesion Count by Facial Area
All Treated Subjects

Treatment group during DB study:

Site ID	Subject ID	Visit	Assessor Initials	Date	Time	Study Day	Facial Area	Facial Area Not Assessed?	Reason Not Assessed	Papules	Pustules	Nodules	Total
Xxx	xxxxxx	Baseline [1]	xx	ddmmmyyyy	hh:mm	Xx	Forehead	xxx	xxxxx	xx	xx	xx	xx
							Right cheek	xxx	xxxxx	xx	xx	xx	xx
							Left cheek	xxx	xxxxx	xx	xx	xx	xx
							Nose	xxx	xxxxx	xx	xx	xx	xx
							Chin	xxx	xxxxx	xx	xx	xx	xx
							Total			xx	xx	xx	xx
		Baseline (Week 12)	xx	ddmmmyyyy	hh:mm	xx	Forehead	xxx	xxxxx	xx	xx	xx	xx
		Week 4	xx	ddmmmyyyy	hh:mm	xx	Forehead	xxx	xxxxx	xx	xx	xx	xx
		Week 10	xx	ddmmmyyyy	hh:mm	xx	Forehead	xxx	xxxxx	xx	xx	xx	xx
		Week 16	xx	ddmmmyyyy	hh:mm	xx	Forehead	xxx	xxxxx	xx	xx	xx	xx
		Week 22	xx	ddmmmyyyy	hh:mm	xx	Forehead	xxx	xxxxx	xx	xx	xx	xx
		Week 28	xx	ddmmmyyyy	hh:mm	xx	Forehead	xxx	xxxxx	xx	xx	xx	xx
		Week 34	xx	ddmmmyyyy	hh:mm	xx	Forehead	xxx	xxxxx	xx	xx	xx	xx
		Week 40	xx	ddmmmyyyy	hh:mm	xx	Forehead	xxx	xxxxx	xx	xx	xx	xx
Xxx	xxxxxx	Baseline	xx	ddmmmyyyy	hh:mm	xx	Left cheek	xxx	xxxxx	xx	xx	xx	xx

[1] Baseline is defined as the Baseline visit in the initial double-blind study (FX2016-11 or FX2016-12). DB = double-blind

Listing 16.2.6.3
Subject Satisfaction Questionnaire (SSQ)
All Treated Subjects

Treatment group during DB study:

Subject ID	Date	Study Day	SSQ Performed?	Question/Reason Not Performed	Response
xxxxxx	ddmmmyyyy	xx	xx	How satisfied are you with how easy this product is to use?	xxxxx
				How satisfied are you with how this product feels on you skin after treatment?	xxxxx
				How satisfied are you with the odor of this product after treatment?	xxxxx
				How satisfied are you with the color of this product after treatment?	xxxxx
				How satisfied are you with the ease of application of the product to your skin?	xxxxx
				How satisfied are you with the ease in which this product fits into your daily routine?	xxxxx
				How satisfied are you with this product compared to other products you have previously used for rosacea, such as gels and creams?	xxxxx
				Overall, how likely are you to use this product with other rosacea treatments?	xxxxx
				Overall, how likely are you to recommend this product to a friend?	xxxxx
				Overall, how satisfied are you with this product?	xxxxx
xxxxxx	ddmmmyyyy	xx	xx	How satisfied are you with how easy this product is to use?	xxxxx

Note: SSQ was completed only at the Week 40/Final Visit. DB = double-blind.

16.2.7 Adverse Event Listings

Listing 16.2.7.1
Adverse Events
All Treated Subjects

Treatment group during DB study:

Subject ID	Any AEs?	TEAE?	System Organ Class/ Preferred Term/ Verbatim Term	Start Date	End Date	Was AE Reported as Ongoing in the Core Study?	Severity/ Rel to Study Drug	Outcome/ Study Drug Action Taken	Serious?/ Life-Threat?	Hosp	Disab	Birth Defect?	Med Sig?
xxxxxx	xxx	xx	xxxxx/ xxxxxxx/ xxxxxxxxx	ddmmmyyyy	ddmmmyyyy	xx	xxxx/ xxxxxx	xxxx/ xxxxxxxx	xx/ xx	xx	xxx	xxx	xx
Xxxxxx	xxx	xxx	xxxxx/ xxxxxxx/ xxxxxxxxx	ddmmmyyyy	Ongoing	xx	xxxx/ xxxxxx	xxxx/ xxxxxxx	xx/ xx	xx	xx	xx	xx

Note: Adverse events were coded using MedDRA, Version 20.0. Rel = Relationship; Threat = Threatening; Hosp = Requires Inpatient/Prolonged Hospitalization; Disab = Results in Persistent or Significant Disability or Incapacity; Birth Defect = Congenital Anomaly or Birth Defect; Med Sig = Medically Significant. DB = double-blind.

Programming Note: If AE is Ongoing then report 'Ongoing' for 'End Date'

Listing 16.2.7.2
Serious Adverse Events
All Treated Subjects

Treatment Group:
See Listing 16.2.7.1; Remove ‘Any AEs?’ column

Listing 16.2.7.3
Adverse Events Leading to Withdrawal
All Treated Subjects

Treatment Group:
See Listing 16.2.7.1; Remove ‘Any AEs?’ column

Listing 16.2.7.4
Deaths
All Treated Subjects

Treatment Group:
See Listing 16.2.7.1; Remove ‘Any AEs?’ column

16.2.8 Laboratory Values

Listing 16.2.8.1
Clinical Chemistry Results
All Treated Subjects

Treatment group during DB study:

Subject ID	Lab Test (unit)	Visit	Samples Collected?	Reason Not Collected	Collection Date	Result	Reference Range Low	Reference Range High	Abnormal?	Clinically Significant?
xxxxxx	xxxxx	xxxxx	xxxx	xxxx	ddmmmyyyy	xxxx	xxxx	xxxx	xxxx	xxxx
		xxxxx	xxxx	xxxx	ddmmmyyyy	xxxx	xxxx	xxxx	xxxx	xxxx

DB = double-blind

Listing 16.2.8.2
Hematology Results
All Treated Subjects

Treatment group during DB study:

Subject ID	Lab Test (unit)	Visit	Samples Collected?	Reason Not Collected	Collection Date	Result	Reference Range Low	Reference Range High	Abnormal?	Clinically Significant?
xxxxxx	xxxxx	xxxxx	xxxx	xxxx	ddmmmyyyy	xxxx	xxxx	xxxx	xxxx	xxxx
		xxxxx	xxxx	xxxx	ddmmmyyyy	xxxx	xxxx	xxxx	xxxx	xxxx

Listing 16.2.8.3
Urinalysis Results
All Treated Subjects

Treatment group during DB study:

Subject ID	Lab Test (unit)	Visit	Samples collected?	Reason Not Collected	Collection Date	Result	Reference Range Low	Reference Range High	Abnormal?	Clinically Significant?
xxxxxx	xxxxx	Xxxxx	xxxx	xxxx	ddmmmyyyy	xxxx	xxxx	xxxx	xxxx	xxxx
		Xxxxx	xxxx	xxxx	ddmmmyyyy	xxxx	xxxx	xxxx	xxxx	xxxx

Listing 16.2.8.4
Clinically Significant Laboratory Tests for Hematology, Chemistry, and Urinalysis
All Treated Subjects

Treatment group during DB study:

Subject ID	Visit	Category	Lab Test (unit)	Collection Date	Result	Reference Range Low	Reference Range High	Abnormal?
xxxxxx	xxxxx	xxxx	xxxxx	ddmmmyyyy	xxxx	xxxx	xxxx	xxxx
	xxxxx	xxxx	xxxxx	ddmmmyyyy	xxxx	xxxx	xxxx	xxxx

Listing 16.2.8.5
Out of Range (Abnormal) Laboratory Tests for Hematology, Chemistry, and Urinalysis
All Treated Subjects

Treatment group during DB study:

Subject ID	Visit	Category	Lab Test (unit)	Collection Date	Result	Reference Range Low	Reference Range High	Abnormal?	Clinically Significant?
xxxxxx	xxxxx	Xxxx	xxxxx	ddmmmyyyy	xxxx	xxxx	xxxx	xxxx	xxxx
	xxxxx	Xxxx	xxxxx	ddmmmyyyy	xxxx	xxxx	xxxx	xxxx	xxxx

Listing 16.2.8.6
Pregnancy Test Results
All Treated Subjects

Treatment group during DB study:

Subject ID	Visit	Pregnancy Test Performed?	Reason Not Performed	Collection Date	Result
xxxxxx	xxxxx	xxxx	xxxx	ddmmmyyyy	xxxxx
	xxxxx	xxxx	xxxx	ddmmmyyyy	xxxxx

16.2.9 Other Clinical Observations and Measurements

Listing 16.2.9.1
Vital Signs
All Treated Subjects

Treatment group during DB study:

Subject ID	Visit	Vital Signs Collected?	Collection Date	Height (cm)	Weight (kg)	BMI (kg/m^2)	Heart Rate (beats/min)	Systolic BP (mmHg)	Diastolic BP (mmHg)
Xxxxxx	xxxxx	Xxx	ddmmmyyyy	xxx	xxx	xxx	xxx	xxx	xxx
	xxxxx	Xxx	ddmmmyyyy		xxx		xxx	xxx	xxx

Programming Note: Height and BMI will only be listed for Baseline (Pre-dose) visit.

Listing 16.2.9.2
Abnormal Physical Examination Results
All Treated Subjects

Treatment group during DB study:

Subject ID	Visit	Examination Date	Body System	Result	Abnormal Finding
xxxxxx	xxxxx	ddmmmyyyy	xxxx	xxxx	xxxx
			xxxx	xxxx	xxxx

Listing 16.2.9.3
Concomitant Medications
All Treated Subjects

Treatment group during DB study:

See Listing 16.2.4.3

Note: Medications were coded using WHO-DD (Enhanced version March 2017) ATC level 2. Preferred Term is ATC level 5. DB = double-blind.

Programming Note: If Medication is Ongoing, then End Date will be "Ongoing".

Listing 16.2.9.4
Local Signs and Symptoms Assessments
All Treated Subjects

Treatment group during DB study:

Subject ID	Visit	Date	Assessment Performed?	Study Day	Assessor Initials	Sign/Symptom	Severity [1]
xxxxxx	Xxxx	ddmmmyyyy	xxxxx	xxxxx	xxxxx	Erythema	xxxx
						Telangiectasia	xxxx
						Burning/Stinging	xxxx
						Flushing/Blushing	xxxx
						Dryness/Xerosis	xxxx
						Itching	xxxx
						Peeling/Desquamation	xxxx
						Hyperpigmentation	xxxx
xxxxxx	Xxxx	ddmmmyyyy	xxxxx	xxxxx	xxxxx	Erythema	xxxx

[1] All signs/symptoms, except erythema, are based on a 4-point scale with 0=none, 1=mild, 2=moderate, and 3=severe. Erythema is based on a 5-point scale with 0=clear, 1=almost clear, 2=mild erythema, 3=moderate erythema, and 4=severe erythema.

Listing 16.2.9.5
Telephone Contact
All Treated Subjects

Treatment group during DB study:

Subject ID	Was the subject contacted by phone?	Reason not contacted	Date of Call	Were all adverse events assessed?	Were all concomitant medications assessed?
xxxxxx	ddmmyyyy	xxxxx	ddmmmyyyy	xxx	xxx
	ddmmyyyy	xxxxx	ddmmmyyyy	xxx	xxx
	ddmmyyyy	xxxxx	ddmmmyyyy	xxx	xxx
	ddmmyyyy	xxxxx	ddmmmyyyy	xxx	xxx
xxxxxx	ddmmyyyy	xxxxx	ddmmmyyyy	xxx	xxx