

**Sponsor**

Novartis Pharmaceuticals

Generic Drug Name

SAF312

Trial Indication(s)

Post-operative corneal induced chronic pain (CICP) following Photorefractive Keratectomy (PRK) or Laser-assisted in Situ Keratomileusis (LASIK) surgeries

Protocol Number

CSAF312B12201

Protocol Title

A 12-week parallel group, randomized, placebo-controlled, double-blinded, multi-center study to evaluate efficacy and safety of 2 concentrations of SAF312 eye drops (5 mg/ml and 15 mg/ml) used twice-daily in the treatment of post-operative corneal induced chronic pain (CICP) following Photorefractive Keratectomy (PRK) or Laser-assisted in Situ Keratomileusis (LASIK) surgeries

Clinical Trial Phase

Phase 2

Phase of Drug Development

Phase II

Study Start/End Dates

Study Start Date: April 21, 2021 (Actual)
Primary Completion Date: June 07, 2023 (Actual)
Study Completion Date: June 08, 2023 (Actual)

Reason for Termination (If applicable)

None

Study Design/Methodology

This was a Phase II randomized, double-masked, multi-center, parallel group, placebo-controlled study to evaluate the safety and efficacy of SAF312, 5 mg/mL and 15 mg/mL eye drops versus Placebo used twice-daily in both eyes for 12 weeks. The study consisted of a 12-week observation period starting from Screening Visit (Visit 1) until the Baseline/Randomization Visit (Visit 2). Subjects who met eligibility criteria at Visit 2 were randomized to one of the three treatment arms (SAF312 5 mg/mL, SAF312 15 mg/mL, Placebo) in a 1:1:1 ratio. Subjects who qualified for randomization had visits every 2 weeks for the first 4 weeks, and then monthly visits for the remainder of the 12-week treatment period.

Centers

28 centers in 3 countries: United States(24), Japan(2), United Kingdom(2)

Objectives:

This study was designed to demonstrate the safety and efficacy of two dose concentrations of SAF312 eye drops (5 mg/mL and 15 mg/mL) in subjects with corneal induced chronic pain (CICP) persisting at least for 4 months after refractive or cataract surgery, and chronicity of pain confirmed during the 3 month observation period. The primary

objective was to demonstrate the efficacy of at least 1 of 2 concentrations of SAF312 (5 mg/mL or 15 mg/mL) with superiority to Placebo in reducing ocular pain severity.

The secondary objectives were to evaluate additional efficacy of 2 concentrations of SAF312 vs. Placebo; to demonstrate SAF312 does not induce negative effects to the ocular surface after prolonged TRPV1 inhibition; and to evaluate the safety of 2 concentrations of SAF312 (0.5 and 1.5%).

Test Product (s), Dose(s), and Mode(s) of Administration

SAF312 5 mg/mL (0.5%) or 15 mg/mL (1.5%) eye drops, suspension, twice a day (b.i.d.) or SAF312 Placebo eye drops, suspension, b.i.d.

Statistical Methods

The Full Analysis Set (FAS) included all subjects to whom study treatment was assigned by randomization. The Safety Set (SAF) included all subjects who received at least one dose of study treatment.

Analysis of primary endpoint: The primary objective of the study was to demonstrate the efficacy of at least 1 of 2 concentrations of SAF312 (5 mg/mL or 15 mg/mL) with superiority to Placebo in reducing ocular pain severity. The primary estimand was defined as follows for signs and symptoms:

- The target population was subjects with Corneal Induced Chronic Pain (CICP) persisting at least 4 months after refractive surgery or cataract surgery, and chronicity of pain confirmed during the 3-month observation period, who met the inclusion and exclusion criteria.
- The primary endpoint was the change from baseline in ocular pain severity VAS at Week 12. The score was derived by averaging the 7 daily measurements of each week.
- The treatment of interest was SAF312 arms versus Placebo, had subjects not needed rescue or prohibited medications and behaved like other subjects who did not take them, had they not discontinued treatment and behaved like other subjects who did not discontinue treatment.

Analysis of secondary endpoints: Analysis of the secondary endpoints included the following:

- Change from baseline in pain severity visual analogue scale (VAS) at Day 7 and Day 14.
- Change from baseline to Week 12 in pain frequency VAS.
- Change from baseline in Ocular Pain Assessment Scale (OPAS) subscale quality of life at Week 12.
- Change from baseline to Week 12 in ocular surface parameters (corneal staining score, conjunctival staining score, Schirmer score, conjunctival redness score).

Study Population: Key Inclusion/Exclusion Criteria

Key Inclusion Criteria:

- Subjects who have undergone refractive surgery (i.e., PRK, LASIK, LASEK, RK, or SMILE) in both eyes or cataract surgery in both eyes, with or without refractive enhancement in one or both eyes, ≥ 4 months prior to Screening Visit and experiencing persistent ocular surface pain since the surgery, and have been seen by an ophthalmologist or optometrist at least once with complaint of continued ocular pain since surgery.
- Subjects who demonstrate a $\geq 60\%$ reduction in ocular pain within 5 minutes after instillation of a single topical ocular anesthetic drop at Screening Visit.

At Baseline

- Subjects with an average pain severity VAS score of ≥ 30 mm based on Daily eDiary for the last 7 days prior to Baseline Visit.
- Subjects who have reported pain severity > 10 mm based on Daily eDiary for $> 50\%$ of the days of the observational period (Screening)

Key Exclusion Criteria:

- Use of nerve growth factor eye drops within 14 days of the Screening Visit
- Seasonal allergic conjunctivitis, or other acute or seasonal ocular diagnosis that are active at the time of Screening or would be active during the course of the study.

- Any history of ocular herpes simplex virus or herpes zoster virus infection, or other severe ocular conditions such as graft versus host disease, Stevens-Johnson syndrome or sarcoidosis.
- Presence of any ocular infection (bacterial, viral, or fungal) within 30 days prior to Screening.
- Chronic topical ocular medications (ie. cyclosporine, lifitegrast) initiated <6 months prior to Screening Visit, or any anticipated change during the study.
- Use of ocular or nasal corticosteroids within 30 days of Screening Visit.
- Use of neuromodulatory medications (eg, gabapentin, pregabalin) or opioid use for non-ocular pain within 30 days of Screening Visit.
- Chronic medications (both over the counter and prescription) that have not been stable for at least 30 days prior to Screening Visit, or any anticipated change in the chronic medication regimen.
- Subjects requiring hospitalization within 6 months prior to screening for severe psychiatric disorders (e.g. psychosis, schizophrenia, mania, depression) or major psychiatric illness.

Participant Flow Table

Overall Study

	SAF312 15 mg/mL	SAF312 5 mg/mL	SAF312 Placebo	Total
Arm/Group Description	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily	
Started	50	49	51	150
Completed	46	45	47	138
Not Completed	4	4	4	12
Adverse Event	1	1	1	3
Physician Decision	0	2	0	2

Protocol Violation	1	0	1	2
Withdrawal by Subject	2	1	2	5

Baseline Characteristics

	SAF312 15 mg/mL	SAF312 5 mg/mL	SAF312 Placebo	Total
Arm/Group Description	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily	
Number of Participants [units: participants]	50	49	51	150
Baseline Analysis Population Description				
Age Continuous (units: years) Analysis Population Type: Participants Mean \pm Standard Deviation				
	61.0 \pm 15.56	60.4 \pm 15.12	56.8 \pm 17.15	59.4 \pm 15.99
Sex: Female, Male (units: Participants) Analysis Population Type: Participants Count of Participants (Not Applicable)				
Female	35	34	40	109
Male	15	15	11	41
Race (NIH/OMB) (units: Participants) Analysis Population Type: Participants Count of Participants (Not Applicable)				
American Indian or Alaska Native	0	0	0	0
Asian	7	7	9	23

Native Hawaiian or Other Pacific Islander	1	0	0	1
Black or African American	6	5	4	15
White	35	37	38	110
More than one race	1	0	0	1
Unknown or Not Reported	0	0	0	0
Ethnicity (NIH/OMB) (units: Participants) Analysis Population Type: Participants Count of Participants (Not Applicable)				
Hispanic or Latino	3	0	3	6
Not Hispanic or Latino	47	49	48	144
Unknown or Not Reported	0	0	0	0

Primary Outcome Result(s)

Change from baseline at Week 12 in Ocular Pain Severity Visual Analog Scale (VAS)

Description	The pain severity Visual Analogue Scale (VAS) was completed by the subject using an electronic diary. A vertical mark was placed on the horizontal scoring line (anchored with 'No Pain' on the left and 'Very Severe' pain on the right) to score the severity of ocular pain over the past 24 hours, with a range from 0 (min) to 100 (max). Higher scores indicate higher pain severity. A negative change from baseline is a positive outcome.
Time Frame	Baseline, Week 12
Analysis Population Description	Full Analysis Set - all treated patients

SAF312 15 mg/mL
SAF312 5mg/mL
SAF312 Placebo

Arm/Group Description	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily
Number of Participants Analyzed [units: participants]	50	49	51
Change from baseline at Week 12 in Ocular Pain Severity Visual Analog Scale (VAS) (units: Scores on a scale)	Least Squares Mean ± Standard Error	Least Squares Mean ± Standard Error	Least Squares Mean ± Standard Error
	-23.7 ± 3.70	-21.7 ± 3.71	-25.3 ± 3.51

Statistical Analysis

Groups	SAF312 15 mg/mL, SAF312 Placebo	
Type of Statistical Test	Superiority	
P Value	0.930	Reporting the adjusted p-value derived based on Dunett procedure.
Method	Mixed Models Analysis	mixed-model repeated measures (MMRM) analysis
Other Least Square (LS) mean difference	1.6	
Standard Error of the mean	5.10	
95 % Confidence Interval 2-Sided	-8.5 to 11.7	

Statistical Analysis

Groups	SAF312 5mg/mL, SAF312 Placebo	
Type of Statistical Test	Superiority	
P Value	0.699	Reporting the adjusted p-value derived based on Dunett procedure.

Method	Mixed Models Analysis	mixed-model repeated measures (MMRM) analysis
Other Least Square (LS) mean difference	3.7	
Standard Error of the mean	5.11	
95 % Confidence Interval 2-Sided	-6.4 to 13.8	

Secondary Outcome Result(s)

Ocular Pain Severity Visual Analog Scale (VAS): summary statistics of change from baseline at Day 7 and Day 14

Description	The pain severity Visual Analogue Scale (VAS) was completed by the subject using an electronic diary. A vertical mark was placed on the horizontal scoring line (anchored with 'No Pain' on the left and 'Very Severe' pain on the right) to score the severity of ocular pain over the past 24 hours, with a range from 0 (min) to 100 (max). Higher scores indicate higher pain severity. A negative change from baseline is a positive outcome.
Time Frame	Baseline, Days 7 and 14
Analysis Population Description	Participants in the Full Analysis Set with an available value for the outcome measure at baseline and at each timepoint.

	SAF312 15 mg/mL	SAF312 5mg/mL	SAF312 Placebo
Arm/Group Description	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily
Number of Participants Analyzed [units: participants]	45	44	44

**Ocular Pain Severity Visual Analog Scale (VAS):
summary statistics of change from baseline at Day 7
and Day 14**

(units: Scores on a scale)

	Mean ± Standard Deviation	Mean ± Standard Deviation	Mean ± Standard Deviation
Day 7 (n=45,44,43)	-10.89 ± 18.373	-11.45 ± 20.661	-17.40 ± 21.558
Day 14 (n=45,37,44)	-12.20 ± 21.484	-14.89 ± 25.790	-21.00 ± 21.624

Ocular Pain Frequency Visual Analog Scale (VAS): summary statistics of weekly mean change from baseline to Week 12

Description The pain frequency Visual Analogue Scale (VAS) was completed by the subject using an electronic diary. A vertical mark was placed on the horizontal scoring line (anchored with 'No Pain' on the left and 'Very Frequent' pain on the right) to score the frequency of ocular pain over the past 24 hours, with a range from 0 (min) to 100 (max). Higher scores indicate higher pain frequency. A negative change from baseline is a positive outcome.

Time Frame Baseline, Weeks 1 to 12

Analysis Population Description Participants in the Full Analysis Set with an available value for the outcome measure at baseline and at each timepoint.

	SAF312 15 mg/mL	SAF312 5mg/mL	SAF312 Placebo
Arm/Group Description	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily
Number of Participants Analyzed [units: participants]	50	49	50
Ocular Pain Frequency Visual Analog Scale (VAS): summary statistics of weekly mean change from baseline to Week 12 (units: Scores on a scale)	Mean ± Standard Deviation	Mean ± Standard Deviation	Mean ± Standard Deviation
Week 1	-10.22 ± 16.404	-9.96 ± 15.464	-12.45 ± 15.484
Week 2 (n=49,48,50)	-14.38 ± 21.073	-12.68 ± 20.344	-18.80 ± 20.489
Week 3 (n=49,47,49)	-17.35 ± 21.332	-14.75 ± 23.314	-22.45 ± 22.980

Week 4 (n=49,46,48)	-19.06 ± 23.070	-12.75 ± 24.076	-24.07 ± 25.230
Week 5 (n=49,46,48)	-20.34 ± 24.524	-14.31 ± 23.711	-26.18 ± 22.404
Week 6 (n=48,47,48)	-19.84 ± 25.511	-15.60 ± 23.332	-23.88 ± 25.433
Week 7 (n=47,47,48)	-22.84 ± 25.774	-17.60 ± 24.715	-25.09 ± 24.489
Week 8 (n=47,45,48)	-23.25 ± 26.009	-17.40 ± 23.636	-24.69 ± 26.072
Week 9 (n=46,44,48)	-24.30 ± 25.650	-18.01 ± 25.040	-24.92 ± 25.648
Week 10 (n=46,44,47)	-25.16 ± 25.381	-18.44 ± 24.387	-25.72 ± 26.428
Week 11 (n=46,45,47)	-26.62 ± 26.057	-21.68 ± 24.754	-25.66 ± 28.343
Week 12 (n=46,43,47)	-26.24 ± 25.322	-20.38 ± 24.296	-26.98 ± 25.977

Ocular Pain Assessment Scale (OPAS) Subscale Quality of Life: summary statistics of change from baseline to Week 12

Description	Each question in the Ocular Pain Assessment Survey (OPAS) quality of life subscale was scored by the subject on a line marked from 0 (not at all) to 10 (completely) that described how much pain interfered with or affected a particular activity (max score= 10/question). A higher score suggests a higher impact by pain on a particular activity. A negative change from baseline is a positive outcome. There are 7 questions in total regarding Quality of Life. The average score of the 7 Quality of Life questions is reported (mean (SD)).
Time Frame	Baseline, Weeks 2, 4, 8, 12
Analysis Population Description	Participants in the Full Analysis Set with an available value for the outcome measure at baseline and at each timepoint.

	SAF312 15 mg/mL	SAF312 5mg/mL	SAF312 Placebo
Arm/Group Description	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily
Number of Participants Analyzed [units: participants]	48	46	49
Ocular Pain Assessment Scale (OPAS) Subscale Quality of Life: summary statistics of change from	Mean ± Standard Deviation	Mean ± Standard Deviation	Mean ± Standard Deviation

baseline to Week 12
(units: Scores on a scale)

Week 2 (n=48,46,46)	-1.39 ± 1.839	-0.99 ± 2.027	-1.52 ± 1.704
Week 4 (n=46,46,49)	-1.68 ± 2.360	-1.39 ± 2.040	-2.00 ± 2.138
Week 8 (n=47,45,45)	-1.61 ± 2.428	-1.30 ± 2.103	-1.82 ± 1.805
Week 12 (n=45,45,45)	-2.20 ± 2.317	-1.79 ± 2.225	-2.06 ± 2.284

Ocular surface parameters: summary statistics of change from baseline by week - Conjunctival Redness - Nasal (oculus dexter (OD) = Right Eye)

Description	Conjunctival redness in each of two regions (nasal and temporal) was graded on a scale from 0 to 5 using the McMonnies conjunctival redness photographic scale (max score=5/region). Higher scores suggest higher degrees of redness (worsening). A negative change from baseline is a positive outcome.
Time Frame	Baseline, Weeks 2, 4, 8, 12
Analysis Population Description	Participants in the Full Analysis Set with an available value for the outcome measure at baseline and at each timepoint.

	SAF312 15 mg/mL	SAF312 5mg/mL	SAF312 Placebo
Arm/Group Description	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily
Number of Participants Analyzed [units: participants]	47	45	46
Ocular surface parameters: summary statistics of change from baseline by week - Conjunctival Redness - Nasal (oculus dexter (OD) = Right Eye) (units: Scores on a scale)	Mean ± Standard Deviation	Mean ± Standard Deviation	Mean ± Standard Deviation
Week 2 (n=47,44,43)	-0.1 ± 0.75	-0.0 ± 0.43	-0.1 ± 0.65
Week 4 (n=44,45,46)	-0.2 ± 0.77	-0.0 ± 0.67	0.0 ± 0.52
Week 8 (n=45,43,42)	-0.2 ± 0.72	-0.1 ± 0.68	-0.2 ± 0.62

Week 12 (n=44,43,44)

-0.2 ± 0.70

-0.0 ± 0.75

-0.1 ± 0.76

Ocular surface parameters: summary statistics of change from baseline by week - Conjunctival Redness - Nasal (oculus sinister (OS) = Left Eye)

Description	Conjunctival redness in each of two regions (nasal and temporal) was graded on a scale from 0 to 5 using the McMonnies conjunctival redness photographic scale (max score=5/region). Higher scores suggest higher degrees of redness (worsening). A negative change from baseline is a positive outcome.
Time Frame	Baseline, Weeks 2, 4, 8, 12
Analysis Population Description	Participants in the Full Analysis Set with an available value for the outcome measure at baseline and at each timepoint.

	SAF312 15 mg/mL	SAF312 5mg/mL	SAF312 Placebo
Arm/Group Description	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily
Number of Participants Analyzed [units: participants]	47	45	46
Ocular surface parameters: summary statistics of change from baseline by week - Conjunctival Redness - Nasal (oculus sinister (OS) = Left Eye) (units: Scores on a scale)	Mean ± Standard Deviation	Mean ± Standard Deviation	Mean ± Standard Deviation
Week 2 (n=47,44,43)	-0.2 ± 0.67	-0.1 ± 0.45	-0.2 ± 0.61
Week 4 (N=44,45,46)	-0.3 ± 0.78	0.0 ± 0.67	-0.1 ± 0.41
Week 8 (n=45,43,42)	-0.2 ± 0.70	-0.2 ± 0.73	-0.2 ± 0.61
Week 12 (n=44,43,44)	-0.2 ± 0.68	-0.1 ± 0.59	-0.2 ± 0.83

Ocular surface parameters: summary statistics of change from baseline by week - Conjunctival Redness - Temporal (oculus dexter (OD) = Right Eye)

Description	The pain severity Visual Analogue Scale (VAS) was completed by the subject using an electronic diary. A vertical mark was placed on the horizontal scoring line (anchored with 'No Pain' on the left and 'Very Severe' pain on the right) to score the severity of ocular pain over the past 24 hours, with a range from 0 (min) to 100 (max). Higher scores indicate higher pain severity. A negative change from baseline is a positive outcome. A negative change from baseline is a positive outcome.
Time Frame	Baseline, Weeks 2, 4, 8, 12
Analysis Population Description	Participants in the Full Analysis Set with an available value for the outcome measure at baseline and at each timepoint.

	SAF312 15 mg/mL	SAF312 5mg/mL	SAF312 Placebo
Arm/Group Description	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily
Number of Participants Analyzed [units: participants]	47	45	46
Ocular surface parameters: summary statistics of change from baseline by week - Conjunctival Redness - Temporal (oculus dexter (OD) = Right Eye) (units: Scores on a scale)	Mean ± Standard Deviation	Mean ± Standard Deviation	Mean ± Standard Deviation
Week 2 (n=47,44,43)	-0.2 ± 0.72	0.1 ± 0.55	-0.1 ± 0.68
Week 4 (n=44,45,46)	-0.3 ± 0.83	0.0 ± 0.71	-0.1 ± 0.57
Week 8 (n=45,43,42)	-0.2 ± 0.84	-0.1 ± 0.80	-0.2 ± 0.76
Week 12 (n=44,43,44)	-0.3 ± 0.78	-0.1 ± 0.73	-0.3 ± 0.99

Ocular surface parameters: summary statistics of change from baseline by week - Conjunctival Redness - Temporal (oculus sinister (OS) = Left Eye)

Description	Conjunctival redness in each of two regions (nasal and temporal) was graded on a scale from 0 to 5 using the McMonnies conjunctival redness photographic scale (max score=5/region). Higher scores suggest higher degrees of redness (worsening). A negative change from baseline is a positive outcome.
Time Frame	Baseline, Weeks 2, 4, 8, 12
Analysis Population Description	Participants in the Full Analysis Set with an available value for the outcome measure at baseline and at each timepoint.

	SAF312 15 mg/mL	SAF312 5mg/mL	SAF312 Placebo
Arm/Group Description	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily
Number of Participants Analyzed [units: participants]	47	45	46
Ocular surface parameters: summary statistics of change from baseline by week - Conjunctival Redness - Temporal (oculus sinister (OS) = Left Eye) (units: Scores on a scale)	Mean ± Standard Deviation	Mean ± Standard Deviation	Mean ± Standard Deviation
Week 2 (n=47,44,43)	-0.2 ± 0.74	0.0 ± 0.53	-0.1 ± 0.72
Week 4 (n=44,45,46)	-0.4 ± 0.81	0.1 ± 0.61	0.1 ± 0.57
Week 8 (n=45,43,42)	-0.2 ± 0.67	-0.1 ± 0.70	-0.1 ± 0.69
Week 12 (n=44,43,44)	-0.3 ± 0.71	-0.1 ± 0.63	-0.2 ± 0.90

Ocular surface parameters: summary statistics of change from baseline by week - Conjunctival Staining (oculus dexter (OD) = Right Eye)

Description	The degree of lissamine conjunctival staining in two regions (temporal and nasal) was graded on a scale from 0 to 4 (max score = 8/eye). Higher scores suggest higher degrees of corneal staining (worsening). A negative change from baseline is a positive outcome.
Time Frame	Baseline, Weeks 2, 4, 8, 12

Analysis Population Description
Participants in the Full Analysis Set with an available value for the outcome measure at baseline and at each timepoint.

	SAF312 15 mg/mL	SAF312 5mg/mL	SAF312 Placebo
Arm/Group Description	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily
Number of Participants Analyzed [units: participants]	47	45	46
Ocular surface parameters: summary statistics of change from baseline by week - Conjunctival Staining (oculus dexter (OD) = Right Eye) (units: Scores on a scale)	Mean ± Standard Deviation	Mean ± Standard Deviation	Mean ± Standard Deviation
Week 2 (n=47,44,43)	0.1 ± 0.99	-0.0 ± 1.23	-0.1 ± 1.06
Week 4 (n=44,45,46)	0.0 ± 1.27	0.2 ± 1.62	-0.2 ± 1.23
Week 8 (n=45,42,42)	-0.2 ± 1.00	0.0 ± 1.06	0.3 ± 1.27
Week 12 (n=44,43,44)	0.1 ± 1.39	-0.1 ± 1.24	0.0 ± 1.54

Ocular surface parameters: summary statistics of change from baseline by week - Conjunctival Staining (oculus sinister (OS) = Left Eye)

Description The degree of lissamine conjunctival staining in two regions (temporal and nasal) was graded on a scale from 0 to 4 (max score = 8/eye). Higher scores suggest higher degrees of corneal staining (worsening). A negative change from baseline is a positive outcome.

Time Frame Baseline, Weeks 2, 4, 8, 12

Analysis Population Description Participants in the Full Analysis Set with an available value for the outcome measure at baseline and at each timepoint.

SAF312 15 mg/mL

SAF312 5mg/mL

SAF312 Placebo

Arm/Group Description	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily
Number of Participants Analyzed [units: participants]	47	45	46
Ocular surface parameters: summary statistics of change from baseline by week - Conjunctival Staining (oculus sinister (OS) = Left Eye) (units: Scores on a scale)	Mean ± Standard Deviation	Mean ± Standard Deviation	Mean ± Standard Deviation
Week 2 (n=47,44,43)	0.0 ± 0.99	-0.1 ± 1.51	-0.2 ± 1.41
Week 4 (n=44,45,46)	-0.1 ± 1.20	0.1 ± 1.47	-0.1 ± 1.41
Week 8 (n=45,42,42)	-0.2 ± 1.01	-0.3 ± 1.32	0.1 ± 1.46
Week 12 (n=44,43,44)	-0.1 ± 1.25	-0.1 ± 1.16	-0.1 ± 1.25

Ocular surface parameters: summary statistics of change from baseline by week - Corneal Staining (oculus dexter (OD) = Right Eye)

Description	The degree of corneal fluorescein staining in each of five regions (superior, inferior, nasal, temporal, and central) was graded on a scale from 0 to 4 (max score=20/eye). Higher scores suggest higher degrees of corneal staining (worsening). A negative change from baseline is a positive outcome.
Time Frame	Baseline, Weeks 2, 4, 8, 12
Analysis Population Description	Participants in the Full Analysis Set with an available value for the outcome measure at baseline and at each timepoint.

	SAF312 15 mg/mL	SAF312 5mg/mL	SAF312 Placebo
Arm/Group Description	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily
Number of Participants Analyzed [units: participants]	49	47	49

Ocular surface parameters: summary statistics of change from baseline by week - Corneal Staining (oculus dexter (OD) = Right Eye)
(units: Scores on a scale)

	Mean ± Standard Deviation	Mean ± Standard Deviation	Mean ± Standard Deviation
Week 2 (n=49,46,46)	-0.6 ± 2.02	-0.7 ± 1.73	-0.7 ± 2.76
Week 4 (n=46,47,49)	-0.8 ± 2.84	-0.1 ± 2.47	-0.9 ± 2.32
Week 8 (n=47,45,45)	-0.9 ± 2.93	-0.6 ± 2.09	-0.8 ± 2.40
Week 12 (n=46,45,47)	-0.7 ± 3.10	-0.1 ± 1.95	-1.5 ± 2.78

Ocular surface parameters: summary statistics of change from baseline by week - Corneal Staining (oculus sinister (OS) = Left Eye)

Description	The degree of corneal fluorescein staining in each of five regions (superior, inferior, nasal, temporal, and central) was graded on a scale from 0 to 4 (max score=20/eye). Higher scores suggest higher degrees of corneal staining (worsening). A negative change from baseline is a positive outcome.
Time Frame	Baseline, Weeks 2, 4, 8, 12
Analysis Population Description	Participants in the Full Analysis Set with an available value for the outcome measure at baseline and at each timepoint.

	SAF312 15 mg/mL	SAF312 5mg/mL	SAF312 Placebo
Arm/Group Description	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily
Number of Participants Analyzed [units: participants]	49	47	49
Ocular surface parameters: summary statistics of change from baseline by week - Corneal Staining (oculus sinister (OS) = Left Eye) (units: Scores on a scale)	Mean ± Standard Deviation	Mean ± Standard Deviation	Mean ± Standard Deviation
Week 2 (n=49,46,46)	-0.5 ± 2.48	-0.7 ± 2.55	-1.0 ± 2.82

Week 4 (n=46,47,49)	-0.7 ± 2.67	-0.6 ± 2.62	-0.6 ± 2.51
Week 8 (n=47,45,45)	-1.2 ± 3.51	-0.8 ± 2.46	-0.9 ± 2.85
Week 12 (n=46,45,47)	-0.9 ± 3.33	-0.5 ± 2.19	-1.5 ± 3.14

Ocular surface parameters: summary statistics of change from baseline by week of tear production - Schirmer Test (mm) (oculus dexter (OD) = Right Eye)

Description	The Schirmer's test was performed without anesthetic. Tear secretion was measured in millimeters based on the length of strip wetted by tears (max score =35 mm/eye). Lower values indicate lower relative amounts of tear secretion (worsening). A negative change from baseline is a positive outcome.
Time Frame	Baseline, Weeks 2, 4, 8, 12
Analysis Population Description	Participants in the Full Analysis Set with an available value for the outcome measure at baseline and at each timepoint.

	SAF312 15 mg/mL	SAF312 5mg/mL	SAF312 Placebo
Arm/Group Description	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily
Number of Participants Analyzed [units: participants]	49	47	49
Ocular surface parameters: summary statistics of change from baseline by week of tear production - Schirmer Test (mm) (oculus dexter (OD) = Right Eye) (units: mm)	Mean ± Standard Deviation	Mean ± Standard Deviation	Mean ± Standard Deviation
Week 2 (n=49,45,46)	-1.1 ± 8.38	-0.3 ± 8.62	-0.3 ± 7.67
Week 4 (n=46,47,49)	-0.3 ± 7.45	-1.4 ± 7.85	0.1 ± 7.40
Week 8 (n=47,43,45)	0.0 ± 8.04	-1.7 ± 9.89	-1.4 ± 8.45
Week 12 (n=46,45,47)	-0.7 ± 7.79	-0.9 ± 7.02	0.9 ± 7.77

Ocular surface parameters: summary statistics of change from baseline by week of tear production - Schirmer Test (mm) (oculus sinister (OS) = Left Eye)

Description	The Schirmer's test was performed without anesthetic. Tear secretion was measured in millimeters based on the length of strip wetted by tears (max score =35 mm/eye). Lower values indicate lower relative amounts of tear secretion (worsening). A negative change from baseline is a positive outcome.
Time Frame	Baseline, Weeks 2, 4, 8, 12
Analysis Population Description	Participants in the Full Analysis Set with an available value for the outcome measure at baseline and at each timepoint.

	SAF312 15 mg/mL	SAF312 5mg/mL	SAF312 Placebo
Arm/Group Description	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily
Number of Participants Analyzed [units: participants]	49	47	49
Ocular surface parameters: summary statistics of change from baseline by week of tear production - Schirmer Test (mm) (oculus sinister (OS) = Left Eye) (units: mm)	Mean ± Standard Deviation	Mean ± Standard Deviation	Mean ± Standard Deviation
Week 2 (n=49,45,46)	-0.7 ± 8.98	-1.5 ± 7.81	0.6 ± 4.82
Week 4 (n=46,47,49)	0.7 ± 7.52	-2.1 ± 7.78	1.4 ± 7.59
Week 8 (n=47,43,45)	0.2 ± 8.30	-1.1 ± 8.71	-0.7 ± 6.92
Week 12 (n=46,45,47)	0.1 ± 9.51	-2.2 ± 8.60	1.1 ± 7.88

Number of participants with treatment emergent adverse events

Description	An adverse event (AE) is any untoward medical occurrence (e.g. any unfavorable and unintended sign [including abnormal laboratory findings], symptom or disease) in a clinical investigation participant after providing written informed consent for participation in the study.
Time Frame	Adverse events were reported from first dose of study treatment until end of study treatment plus 30 days post treatment, up to a maximum timeframe of 119 days (approximately 4 months).

Analysis
Population
Description

Safety set

	SAF312 15 mg/mL	SAF312 5mg/mL	SAF312 Placebo
Arm/Group Description	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily
Number of Participants Analyzed [units: participants]	50	49	51
Number of participants with treatment emergent adverse events (units: Participants)	Count of Participants (Not Applicable)	Count of Participants (Not Applicable)	Count of Participants (Not Applicable)
Any adverse events	21 (42%)	12 (24.49%)	18 (35.29%)
-Any ocular adverse events	11 (22%)	10 (20.41%)	10 (19.61%)
-Any non-ocular adverse events	13 (26%)	4 (8.16%)	13 (25.49%)
Any serious adverse events	0 (%)	0 (%)	1 (1.96%)
-Any ocular serious adverse events	0 (%)	0 (%)	0 (%)
-Any non-ocular serious adverse events	0 (%)	0 (%)	1 (1.96%)
Any study drug related adverse events	5 (10%)	5 (10.2%)	2 (3.92%)
-Any study drug related ocular adverse events	5 (10%)	5 (10.2%)	2 (3.92%)
-Any study drug related non-ocular adverse events	0 (%)	1 (2.04%)	0 (%)
Any adverse events leading to study drug discontinuation	1 (2%)	1 (2.04%)	1 (1.96%)

-Any ocular adverse events leading to study drug discontinuation	0 (%)	1 (2.04%)	0 (%)
-Any non-ocular adverse events leading to study drug discontinuation	1 (2%)	1 (2.04%)	1 (1.96%)
Any study drug related serious adverse events	0 (%)	0 (%)	0 (%)
-Any study drug related ocular serious adverse events	0 (%)	0 (%)	0 (%)
-Any study drug related non-ocular serious adverse events	0 (%)	0 (%)	0 (%)
Death	0 (%)	0 (%)	0 (%)

Ocular treatment emergent adverse events, by primary system organ class (SOC) and preferred term (PT)

Description	An adverse event (AE) is any untoward medical occurrence (e.g. any unfavorable and unintended sign [including abnormal laboratory findings], symptom or disease) in a clinical investigation participant after providing written informed consent for participation in the study. MedDRA Version 26.0 was used for the reporting of adverse events.
Time Frame	Adverse events were reported from first dose of study treatment until end of study treatment plus 30 days post treatment, up to a maximum timeframe of 119 days (approximately 4 months).
Analysis Population Description	Safety set

	SAF312 15 mg/mL	SAF312 5mg/mL	SAF312 Placebo
Arm/Group Description	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily
Number of Participants Analyzed [units: participants]	50	49	51

Ocular treatment emergent adverse events, by primary system organ class (SOC) and preferred term (PT) (units: Participants)	Count of Participants (Not Applicable)	Count of Participants (Not Applicable)	Count of Participants (Not Applicable)
Number of subjects with at least one event	11 (22%)	10 (20.41%)	10 (19.61%)
SOC: Eye disorders	10 (20%)	8 (16.33%)	10 (19.61%)
-Eye pain	3 (6%)	0 (%)	2 (3.92%)
-Dry eye	2 (4%)	2 (4.08%)	0 (%)
-Eye pruritus	2 (4%)	1 (2.04%)	0 (%)
-Dry age-related macular degeneration	1 (2%)	0 (%)	0 (%)
-Eye discharge	1 (2%)	2 (4.08%)	1 (1.96%)
-Eye irritation	1 (2%)	1 (2.04%)	1 (1.96%)
-Vision blurred	1 (2%)	1 (2.04%)	1 (1.96%)
-Vitreous detachment	1 (2%)	0 (%)	0 (%)
-Blepharitis	0 (%)	0 (%)	1 (1.96%)
-Chalazion	0 (%)	0 (%)	2 (3.92%)
-Conjunctival papillae	0 (%)	1 (2.04%)	0 (%)
-Corneal oedema	0 (%)	0 (%)	1 (1.96%)
-Erythema of eyelid	0 (%)	3 (6.12%)	0 (%)

-Lacrimation increased	0 (%)	1 (2.04%)	0 (%)
-Ocular hyperaemia	0 (%)	2 (4.08%)	1 (1.96%)
-Optic nerve cupping	0 (%)	0 (%)	1 (1.96%)
-Swelling of eyelid	0 (%)	1 (2.04%)	0 (%)
SOC: General disorders and administration site conditions	0 (%)	4 (8.16%)	0 (%)
-Instillation site irritation	0 (%)	2 (4.08%)	0 (%)
-Instillation site pruritus	0 (%)	1 (2.04%)	0 (%)
-Therapy responder	0 (%)	1 (2.04%)	0 (%)
SOC: Immune system disorders	0 (%)	1 (2.04%)	0 (%)
-Drug hypersensitivity	0 (%)	1 (2.04%)	0 (%)
SOC: Infections and infestations	2 (4%)	0 (%)	0 (%)
-Hordeolum	2 (4%)	0 (%)	0 (%)
SOC: Injury, poisoning and procedural complications	0 (%)	0 (%)	1 (1.96%)
-Corneal abrasion	0 (%)	0 (%)	1 (1.96%)
-Foreign body in eye	0 (%)	0 (%)	1 (1.96%)

Summary of non-ocular treatment emergent adverse events

Description	An adverse event (AE) is any untoward medical occurrence (e.g. any unfavorable and unintended sign [including abnormal laboratory findings], symptom or disease) in a clinical investigation participant after providing written informed consent for participation in the study.
Time Frame	Adverse events were reported from first dose of study treatment until end of study treatment plus 30 days post treatment, up to a maximum timeframe of 119 days (approximately 4 months).
Analysis Population Description	Safety set

	SAF312 15 mg/mL	SAF312 5mg/mL	SAF312 Placebo
Arm/Group Description	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily
Number of Participants Analyzed [units: participants]	50	49	51
Summary of non-ocular treatment emergent adverse events (units: Participants)	Count of Participants (Not Applicable)	Count of Participants (Not Applicable)	Count of Participants (Not Applicable)
Number of subjects with at least one event	13 (26%)	4 (8.16%)	13 (25.49%)

Safety Results

Time Frame	Adverse events are reported from first dose of study treatment until end of study treatment plus 30 days post treatment, up to a maximum timeframe of 119 days (approximately 4 months).
Source Vocabulary for Table Default	MedDRA (26.0)

Collection
Approach for Table Systematic Assessment
Default

All-Cause Mortality

	SAF312 15 mg/mL N = 50	SAF312 5 mg/mL N = 49	SAF312 Placebo N = 51	Total N = 150
Arm/Group Description	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily	Total
Total Number Affected	0	0	0	0
Total Number At Risk	50	49	51	150

Serious Adverse Events

Time Frame	Adverse events are reported from first dose of study treatment until end of study treatment plus 30 days post treatment, up to a maximum timeframe of 119 days (approximately 4 months).
Source Vocabulary for Table Default	MedDRA (26.0)
Collection Approach for Table Systematic Assessment Default	

SAF312 15 mg/mL N = 50	SAF312 5 mg/mL N = 49	SAF312 Placebo N = 51	Total N = 150
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Arm/Group Description	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily	Total
Total # Affected by any Serious Adverse Event	0	0	1	1
Total # at Risk by any Serious Adverse Event	50	49	51	150
Injury, poisoning and procedural complications				
Spinal compression fracture	0 (0.00%)	0 (0.00%)	1 (1.96%)	1 (0.67%)

Other (Not Including Serious) Adverse Events

Time Frame	Adverse events are reported from first dose of study treatment until end of study treatment plus 30 days post treatment, up to a maximum timeframe of 119 days (approximately 4 months).
Source Vocabulary for Table Default	MedDRA (26.0)
Collection Approach for Table Default	Systematic Assessment

Frequent Event Reporting Threshold 0%

SAF312 15 mg/mL
N = 50

SAF312 5 mg/mL
N = 49

SAF312 Placebo
N = 51

Total
N = 150

Arm/Group Description	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily	Randomized to a 1:1:1 topical eye drops, twice daily	Total
Total # Affected by any Other Adverse Event	21	12	18	51
Total # at Risk by any Other Adverse Event	50	49	51	150
Eye disorders				
Blepharitis	0 (0.00%)	0 (0.00%)	1 (1.96%)	1 (0.67%)
Chalazion	0 (0.00%)	0 (0.00%)	2 (3.92%)	2 (1.33%)
Conjunctival papillae	0 (0.00%)	1 (2.04%)	0 (0.00%)	1 (0.67%)
Corneal oedema	0 (0.00%)	0 (0.00%)	1 (1.96%)	1 (0.67%)
Dry age-related macular degeneration	1 (2.00%)	0 (0.00%)	0 (0.00%)	1 (0.67%)
Dry eye	2 (4.00%)	2 (4.08%)	0 (0.00%)	4 (2.67%)
Erythema of eyelid	0 (0.00%)	3 (6.12%)	0 (0.00%)	3 (2.00%)
Eye discharge	1 (2.00%)	2 (4.08%)	1 (1.96%)	4 (2.67%)
Eye irritation	1 (2.00%)	1 (2.04%)	1 (1.96%)	3 (2.00%)
Eye pain	3 (6.00%)	0 (0.00%)	2 (3.92%)	5 (3.33%)
Eye pruritus	2 (4.00%)	1 (2.04%)	0 (0.00%)	3 (2.00%)
Lacrimation increased	0 (0.00%)	1 (2.04%)	0 (0.00%)	1 (0.67%)
Ocular hyperaemia	0 (0.00%)	2 (4.08%)	1 (1.96%)	3 (2.00%)
Optic nerve cupping	0 (0.00%)	0 (0.00%)	1 (1.96%)	1 (0.67%)
Swelling of eyelid	0 (0.00%)	1 (2.04%)	0 (0.00%)	1 (0.67%)
Vision blurred	1 (2.00%)	1 (2.04%)	1 (1.96%)	3 (2.00%)
Vitreous detachment	1 (2.00%)	0 (0.00%)	0 (0.00%)	1 (0.67%)
Gastrointestinal disorders				
Nausea	1 (2.00%)	0 (0.00%)	0 (0.00%)	1 (0.67%)

Vomiting	1 (2.00%)	0 (0.00%)	0 (0.00%)	1 (0.67%)
General disorders and administration site conditions				
Instillation site irritation	0 (0.00%)	2 (4.08%)	0 (0.00%)	2 (1.33%)
Instillation site pruritus	0 (0.00%)	1 (2.04%)	0 (0.00%)	1 (0.67%)
Medical device site irritation	0 (0.00%)	0 (0.00%)	1 (1.96%)	1 (0.67%)
Non-cardiac chest pain	1 (2.00%)	0 (0.00%)	0 (0.00%)	1 (0.67%)
Therapy responder	0 (0.00%)	1 (2.04%)	0 (0.00%)	1 (0.67%)
Immune system disorders				
Drug hypersensitivity	0 (0.00%)	1 (2.04%)	0 (0.00%)	1 (0.67%)
Infections and infestations				
COVID-19	2 (4.00%)	1 (2.04%)	3 (5.88%)	6 (4.00%)
Ear infection	1 (2.00%)	0 (0.00%)	0 (0.00%)	1 (0.67%)
Herpes virus infection	1 (2.00%)	0 (0.00%)	0 (0.00%)	1 (0.67%)
Herpes zoster	1 (2.00%)	0 (0.00%)	0 (0.00%)	1 (0.67%)
Hordeolum	2 (4.00%)	0 (0.00%)	0 (0.00%)	2 (1.33%)
Laryngitis	1 (2.00%)	0 (0.00%)	0 (0.00%)	1 (0.67%)
Nasopharyngitis	0 (0.00%)	0 (0.00%)	2 (3.92%)	2 (1.33%)
Pharyngitis streptococcal	0 (0.00%)	0 (0.00%)	1 (1.96%)	1 (0.67%)
Sinusitis	3 (6.00%)	0 (0.00%)	0 (0.00%)	3 (2.00%)
Upper respiratory tract infection	1 (2.00%)	0 (0.00%)	0 (0.00%)	1 (0.67%)
Urinary tract infection	1 (2.00%)	0 (0.00%)	0 (0.00%)	1 (0.67%)
Injury, poisoning and procedural complications				
Buttock injury	0 (0.00%)	0 (0.00%)	1 (1.96%)	1 (0.67%)

Corneal abrasion	0 (0.00%)	0 (0.00%)	1 (1.96%)	1 (0.67%)
Fall	0 (0.00%)	0 (0.00%)	1 (1.96%)	1 (0.67%)
Foreign body in eye	0 (0.00%)	0 (0.00%)	1 (1.96%)	1 (0.67%)
Joint injury	0 (0.00%)	0 (0.00%)	1 (1.96%)	1 (0.67%)
Skin laceration	0 (0.00%)	0 (0.00%)	1 (1.96%)	1 (0.67%)
Musculoskeletal and connective tissue disorders				
Arthralgia	1 (2.00%)	0 (0.00%)	0 (0.00%)	1 (0.67%)
Back pain	0 (0.00%)	0 (0.00%)	1 (1.96%)	1 (0.67%)
Exostosis	0 (0.00%)	0 (0.00%)	1 (1.96%)	1 (0.67%)
Osteoarthritis	0 (0.00%)	0 (0.00%)	1 (1.96%)	1 (0.67%)
Neoplasms benign, malignant and unspecified (incl cysts and polyps)				
Sarcoma	0 (0.00%)	1 (2.04%)	0 (0.00%)	1 (0.67%)
Nervous system disorders				
Dizziness	1 (2.00%)	0 (0.00%)	1 (1.96%)	2 (1.33%)
Headache	1 (2.00%)	0 (0.00%)	0 (0.00%)	1 (0.67%)
Respiratory, thoracic and mediastinal disorders				
Oropharyngeal pain	0 (0.00%)	0 (0.00%)	1 (1.96%)	1 (0.67%)
Rhinorrhoea	1 (2.00%)	0 (0.00%)	0 (0.00%)	1 (0.67%)
Skin and subcutaneous tissue disorders				
Dermatitis contact	0 (0.00%)	1 (2.04%)	0 (0.00%)	1 (0.67%)
Diabetic bullosis	1 (2.00%)	0 (0.00%)	0 (0.00%)	1 (0.67%)
Pruritus	0 (0.00%)	1 (2.04%)	1 (1.96%)	2 (1.33%)
Rash	0 (0.00%)	1 (2.04%)	0 (0.00%)	1 (0.67%)

Vascular disorders

Hot flush	0 (0.00%)	0 (0.00%)	1 (1.96%)	1 (0.67%)
Hypertension	1 (2.00%)	0 (0.00%)	0 (0.00%)	1 (0.67%)

Other Relevant Findings

None

Conclusion:

The primary endpoint was change from baseline to Week 12 in weekly mean pain severity Visual Analog Scale. The Least Squares Mean treatment difference between SAF312 15 mg/mL and Placebo was 1.6 with 95% CI (-8.5, 11.7) $p = 0.930$. The Least Squares Mean treatment difference between SAF312 5 mg/mL and Placebo was 3.7 with 95% CI (-6.4, 13.8) $p = 0.699$. Treatment from either active arm or placebo resulted in a reduction in weekly mean pain severity, but no statistically significant or clinically meaningful differences were observed.

These results indicate there was no significant difference in change from baseline to Week 12 on weekly mean pain severity between subjects treated with SAF312 and those with Placebo; therefore, the primary objective was not met. No safety issues were identified.

Date of Clinical Trial Report

28 Nov 2023