Randomized, Controlled, Multicenter, Double-Masked, Parallel, Phase 2b/3 Trial to Evaluate the Safety and Efficacy of TP-03 for the Treatment of *Demodex* Blepharitis (Saturn-1)

Protocol Number: TRS-009

IND Sponsor: Tarsus Pharmaceuticals, Inc.

Funded by: Tarsus Pharmaceuticals, Inc.

[redacted]

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NCT04475432

[redacted]

STATEMENT OF COMPLIANCE

The trial will be carried out in accordance with International Conference on Harmonisation Good Clinical Practice (ICH GCP) and the following:

- United States (US) Code of Federal Regulations (CFR) applicable to clinical studies (45 CFR Part 46, 21 CFR Part 50, 21 CFR Part 56, and 21 CFR Part 312)

Investigators and clinical trial site staff who are responsible for the conduct, management, or oversight of clinical trials have completed Human Subjects Protection and ICH GCP Training.

The protocol, informed consent form(s), recruitment materials, and all participant materials will be submitted to the Institutional Review Board (IRB) for review and approval. Approval of both the protocol and the consent form must be obtained before any participant is enrolled. Any amendment to the protocol will require review and approval by the IRB before the changes are implemented to the study. In addition, all changes to the consent form will be IRB-approved; a determination will be made regarding whether a new consent needs to be obtained from participants who provided consent using a previously approved consent form.

1 PROTOCOL SUMMARY

1.1 SYNOPSIS

Title:	Randomized, Controlled, Multicenter, Double-Masked, Parallel, Phase 2b/3 Trial to Evaluate the Safety and Efficacy of TP-03 for the Treatment of *Demodex* Blepharitis (Saturn-1)
Study Description and Hypotheses:	This Phase 2b/3 study is a randomized, controlled, multicenter, double-masked, parallel trial to compare the safety and efficacy of TP-03 to vehicle control for the treatment of *Demodex* blepharitis. The hypothesis for the study is the proportion of participants cured at Day 43 with treatment by TP-03, lotilaner ophthalmic solution, 0.25%, is greater than the proportion cured by treatment with vehicle.
Test Article:	TP-03, lotilaner ophthalmic solution, 0.25%
Control Article:	Vehicle of TP-03
Study Design:	Prospective, randomized, double-masked, multicenter, two-arm, parallel vehicle-controlled study
Objective:	To demonstrate the safety and efficacy of TP-03, 0.25%, for the treatment of *Demodex* blepharitis
Endpoints:	Primary Endpoint: Proportion of participants cured based on their collarette score of the upper eyelid of the analysis eye at Day 43.

Secondary Endpoints:

- Proportion of participants with their *Demodex* mites eradicated in the analysis eye at Day 43.
- Proportion of participants cured based on a composite of collarette and erythema scores of the upper eyelid of the analysis eye at Day 43.

Safety will be determined by assessing adverse effects related to the active treatment as well as evaluating any changes in visual acuity, intraocular pressure, slit lamp biomicroscopy and dilated ophthalmoscopy findings.

Phase:	2b/3
Number of Participants:	Up to 418 participants
Study Population:	Participants with blepharitis due to *Demodex* infestation defined as having an elevated mite density, collarettes and erythema
Description of Sites:	
Description of Study Treatment:	Participants eligible to be randomized will receive one of the following treatments administered bilaterally BID for 43 days: TP-03, 0.25%, or the TP-03 vehicle ophthalmic solution.
Study Duration:	
Participant Duration:	The study duration for an individual participant is estimated to be approximately weeks for participants enrolled in and weeks for participants enrolled in

Summary of Visit Schedule: Screening, Day 1, Day 8, Day 15, Day 22, Day 43 and Day 57 [redacted]

1.2 SCHEMA

At the Screening visit, potential participants will be evaluated for eligibility. Prior to performing any study specific procedures, potential participants must provide informed consent using the current IRB-approved informed consent form. [redacted]

[redacted]

[redacted] Screening

- Obtain informed consent
- Obtain demographics, medical/ophthalmic history, concomitant medications
- Corrected distance visual acuity (CDVA)
- Slit lamp biomicroscopy
- Collarette grading; erythema assessment
- *Demodex* count
- Urine pregnancy test, as required

Day 1 Initiation of study treatment

- [redacted]
- CDVA [redacted]
- Slit lamp biomicroscopy [redacted]
- Corneal staining
- Intraocular pressure
- [redacted]
- Dilated fundus examination
- [redacted]
- Randomization
- Dispense study drug [redacted]
- [redacted]
- Adverse event review and evaluation

Day 8 [redacted] Follow-up assessments of study endpoints and safety

- Concomitant medication review
- [redacted]
- CDVA
- Slit lamp biomicroscopy

- Collarette grading; erythema assessment
- Corneal staining
- [redacted]
- [redacted]
- Adverse event review and evaluation

Day 15 [redacted] **Follow-up assessments of study endpoints and safety**

- Concomitant medication review
- [redacted]
- CDVA
- Slit lamp biomicroscopy
- Collarette grading; erythema assessment
- Corneal staining
- *Demodex* count
- [redacted]
- [redacted]
- Adverse event review and evaluation

Day 22 [redacted] **Follow-up assessments of study endpoints and safety**

- Concomitant medication review
- [redacted]
- CDVA
- Slit lamp biomicroscopy
- Collarette grading; erythema assessment
- Corneal staining
- *Demodex* count
- [redacted]
- [redacted]
- Adverse event review and evaluation

Day 43 [redacted] **End of treatment assessments**

- Concomitant medication review
- [redacted]
- CDVA
- Slit lamp biomicroscopy
- Collarette grading; erythema assessment
- Corneal staining
- Intraocular pressure
- [redacted]
- *Demodex* count
- Dilated fundus examination
- [redacted]
- [redacted]
- Urine pregnancy test, as required
- Adverse event review and evaluation
- [redacted]
- Study exit [redacted]

Day 57 [redacted] Observational study assessment [redacted]

- Concomitant medication review
- CDVA
- Slit lamp biomicroscopy
- Collarette grading; erythema assessment
- Corneal staining
- Intraocular pressure
- *Demodex* count
- [redacted]
- Adverse event review and evaluation
- [redacted]

1.3 SCHEDULE OF ACTIVITIES (SOA)

[redacted]