Clinical Study Protocol

Protocol Title:

A Double-Blinded, Parallel, Vehicle-Controlled Phase 2 Study of SHJ002 Sterile Ophthalmic Solution in Participants with Dry Eye Disease

Protocol Number: SHJ002-DED2203

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Investigational Product: SHJ002 Sterile Ophthalmic Solution

Brief Title:

A study to investigate the efficacy and safety of SHJ002 sterile ophthalmic solution compared with vehicle in participants aged 18 years or older with dry eye disease.

Study Phase: Phase 2

Sponsor Name: Dreamhawk Vision Biotech Australia Pty Ltd.

Legal Registered Address:

[redacted]

Regulatory Agency Identifier Number(s): NCT05486728

Confidentiality Statement

Protocol Amendment

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1. Synopsis

Protocol Title: A Double-Blinded, Parallel, Vehicle-Controlled Phase 2 Study of SHJ002 Sterile Ophthalmic Solution in Participants with Dry Eye Disease

Brief Title: A study to investigate the efficacy and safety of SHJ002 sterile ophthalmic solution compared with vehicle in participants aged 18 years or older with dry eye disease.

Regulatory Agency Identifier Number(s): NCT05486728

Name of Sponsor: Dreamhawk Vision Biotech Australia Pty Ltd

Investigational Product:
Name: SHJ002 Sterile Ophthalmic Solution

Active Ingredient: SHJ002

Indication: Treatment of signs and symptoms of Dry Eye Disease (DED)

Dose and Administration: SHJ002 Sterile Ophthalmic Solution 0.25%, and vehicle solution, BID, both eyes

Protocol Number: SHJ002-DED2203

Primary Objective: To evaluate the efficacy of SHJ002 ophthalmic solution in improving corneal fluorescein staining scores in participants with Dry Eye Disease (DED).

Secondary Objectives: To assess changes in patient-reported symptom scores using the SANDE and VAS instruments.

Design: Multicenter, double-blinded, randomized, vehicle-controlled, parallel-group Phase 2 trial

Participants: Adults ≥18 years old with signs and symptoms of DED in both eyes for ≥6 months

Randomization: 1:1 ratio to SHJ002 or vehicle group

Treatment: One drop per eye, twice daily (BID) for 84 days

Sites: Australia, Thailand, Taiwan

2. Introduction

2.1 Rationale:

The purpose of this study is to investigate the efficacy and safety of SHJ002 sterile ophthalmic solution compared to the vehicle in participants with DED.

2.2 Background

Dry eye disease (DED) is a multifactorial disease of the tears and ocular surface that results in symptoms of discomfort, visual disturbance, and tear film instability with potential damage to the ocular surface. It is accompanied by increased osmolarity of the tear film and inflammation of the ocular surface (Nelson, 2017).

Jones et al., 2017 summaries a host of treatments for DED. These include surgical intervention for lid or other anatomical pathologies, and punctal plugs to treat DED. Other publications highlight thermal pulsation systems, intense pulsed light and meibomian gland probing, some with seemingly long-lasting effects. However, for the most part, treatment of ocular surface disease requires daily or more frequent treatment with tear products (typically over-the-counter) or one of the five U.S. approved pharmacotherapeutic agents. Ocular surface disease is typically a lifetime disease and requires a vigilant patient and eye care professional to treat the disease, both initially and chronically (Novack 2020).

The investigational drug product SHJ002 is a sterile ophthalmic solution, which was originally developed to control myopia progression in pediatric participants. The first-in-human (FIH) Phase-1 study (Study number: SHJ002-CS201) was conducted in a single-center as an open-label, intra-subject, dose-escalation trial in healthy participants aged 10-15 years old. In this FIH study, there was a Stage 1 for dose escalation and a Stage 2 for the highest tolerable dose from the Stage 1 group. A total of 12 participants were enrolled in the Phase-1 study. There were no clinically significant abnormalities or changes in terms of all ophthalmologic evaluations observed during study period. All the participants had completed the study with full compliance without skipping any dosing. There was only one non-study-medication-related treatment emergent adverse events (TEAE). This was punctate keratitis in the non-treated eye that was observed during the study period, and this event was transient and spontaneously resolved before the end of this study.

3. Objectives and Endpoints

The primary objective of this study is to assess the efficacy of SHJ002 sterile ophthalmic solution relative to vehicle

3.1 Primary Endpoint:

- Change from Baseline to Day 84 in Total Corneal Fluorescein Staining (NEI Scale, score range 0–15; higher scores indicate more severe staining)

3.2 Secondary Endpoints:

- Change from Baseline to Day 84 in SANDE score (0–100 scale, higher = worse symptoms)
- Change from Baseline to Day 84 in VAS eye dryness score (0–100 mm, higher = worse discomfort)

4. Study Design

This is a multi-center, double-blinded, randomized, vehicle-controlled, parallel-group trial in adult participants with signs and symptoms of Dry Eye Disease.

Participants who meet the eligibility criteria at Screening will be randomized to receive the treatment with 0.25% SHJ002 ophthalmic solution or vehicle in a 1:1 ratio. SHJ002 ophthalmic solution or vehicle will be administered to each eye twice daily (BID), for 84 days

This study consists of three periods: a Screening Period of up to 14 days to assess a participant's eligibility, a 1-day Baseline/ randomization period (Day 1) followed by a treatment period of up to 84 days.

Screening Period begins once the participant has provided written informed consent to participate in the study (Visit 1). During this period, participants will be dispensed with the run-in medication (vehicle) for 14 days, along with self-administration instructions. The run-in medication will be administered as the investigational medicinal product (IMP), BID each day. Eligible participants will be thereafter administered with the study treatment (SHJ002), or vehicle bilaterally BID for 12 weeks.

5. Study Population

5.1 Inclusion Criteria:

- Male or female participants 18 years of age or older inclusive, at the time of signing the informed consent.
- Diagnosis of bilateral DED ≥6 months
- Negative pregnancy test for women of childbearing potential

5.2 Exclusion Criteria:

- Significant ocular surface disease other than DED
- Recent ocular surgery or procedures
- Concurrent use of conflicting topical/systemic therapies

5.3. Lifestyle Considerations

Alcohol and/or drug abuse that, in the opinion of the Investigator, may interfere with study compliance, outcome measures, safety parameters, and the general medical conditions of the participant; hence, alcohol and drug abuse should refrain within 12 months prior to Visit 1/Screening.

5.3.1. Meals and Dietary Restrictions

Not applicable

5.3.2. Caffeine, Alcohol, and Tobacco

Not applicable

5.3.3. Activity

Participants will abstain from strenuous exercise for 48 hours before each blood collection for clinical laboratory tests (Screening and Visit 6). Participants may undertake in light recreational activities during studies (e.g., watching television, reading).

5.3.4. Other Restrictions

Not applicable.

5.4. Screen Failures

A screen failure occurs when a participant who has consented to participate in the clinical study is not subsequently assigned to study intervention/entered in the study. A minimal set of screen failure information is required to ensure transparent reporting of screen failure participants to meet the CONSORT publishing requirements and to respond to queries from regulatory authorities. Minimal information includes demography, screen failure details, eligibility criteria, and any SAE. Individuals who do not meet the criteria for participation in this study (screen failure) may be rescreened. Rescreened participant should be assigned a new participant number for every screening/rescreening event.

5.5. Criteria for Temporarily Delaying

Not applicable

6. Study Intervention

Study interventions are all pre-specified, investigational, and non-investigational medicinal products, intended to be administered to the study participants during the study conduct.

6.1 Study Intervention(s) Administered

Participants will be randomly assigned to:

- 0.25% SHJ002 Sterile Ophthalmic Solution
- Vehicle Sterile Ophthalmic Solution without active pharmaceutical ingredient (API)

6.1.1. Study Drug

SHJ002 Sterile Ophthalmic Solution is formulated as a sterile, preservative-free solution at pH 7.0 for topical ophthalmic administration.

6.1.2. Vehicle

The vehicle used in this trial is an artificial tear solution manufactured by the sponsor that mimics the osmolality and natural pH of human tears.

6.2. Preparation, Handling, Storage, and Accountability

The Drug Product is supplied in a single use LDPE vial. Drug products are stored at 2~8°C under ambient humidity until dispensation to participant. Participant may keep drug product either refrigerated (2~8°C) or at room temperature (25±2°C).

IMP kit shipment records will be verified, and accountability performed by comparing the shipment inventory sheet to the actual quantity received at the site. In addition, receipt of IMP

will be confirmed by the study monitor. Accurate records of receipt and disposition of the IMP must be maintained by the Investigator or his/her designee.

At the end of the study and after the monitor has verified kit accountability, all IMP (used or unused) is to be returned to the Sponsor or destroyed at the site and documented per the site's standard process.

6.3. Assignment to Study Intervention

Participants will be randomized in a 1:1 ratio to 0.25% SHJ002 or vehicle in parallel groups.

7. Discontinuation of Study Intervention and Participant Discontinuation/Withdrawal

7.1. Discontinuation of Study Intervention

In rare instances, it may be necessary for a participant to permanently discontinue the study intervention. If the study intervention is permanently discontinued, the participant should, if at all possible, remain in the study to be evaluated. See the SoA for data to be collected at the time of discontinuation of study intervention and follow-up and for any further evaluations that need to be completed.

7.2. Participant Discontinuation/Withdrawal from the Study

A participant may withdraw from the study at any time at the participant's own request for any reason (or without providing any reason).

A participant may be withdrawn at any time at the discretion of the investigator for safety, behavioral, or compliance reasons.

At the time of discontinuing from the study, if possible, an early discontinuation visit should be conducted. Data to be collected at the time of study discontinuation and follow-up and for any further evaluations that need to be completed.

The participant will be permanently discontinued from the study intervention and the study at that time.

If the participant withdraws consent for disclosure of future information, the sponsor may retain and continue to use any data collected before such a withdrawal of consent.

If a participant withdraws from the study, the participant may request destruction of any samples taken and not tested, and the investigator must document this in the site study records.

7.3. Lost to Follow up

A participant will be considered lost to follow-up if the participant repeatedly fails to return for scheduled visits and is unable to be contacted by the study site.

8. Study Assessment and Procedure

8.1 Visit 1

- Obtain written informed consent
- Review Inclusion/exclusion criteria
- Demographics

- Medical and ocular history
- Concomitant medication review
- AE assessment
- SANDE
- Refraction
- BCVA (logMAR)
- Non-invasive lipid layer assessment
- Non-invasive tear break up time (NIBUT)
- Slit lamp biomicroscopy and external eye exam + photography for conjunctival hyperemia
- CFS + photography
- Unanesthetized Schirmer's test
- Intraocular pressure
- Dilated fundoscopy (indirect)
- Urine pregnancy (women of child-bearing potential only)
- Vital signs
- Physical examination
- Clinical laboratory tests

8.2 Visit 2

- Review inclusion/exclusion criteria
- Concomitant medication review
- AE assessment
- SANDE
- Visual Analogue Scale (VAS)
- IP comfort assessment
- BCVA (logMAR)
- Non-invasive lipid layer assessment
- Non-invasive tear break up time (NIBUT)
- Slit lamp biomicroscopy and external eye exam + photography for conjunctival hyperemia
- CFS + photography
- Randomization
- Vital signs

8.3 Visit 3

- Concomitant medication review
- AE assessment
- SANDE
- Visual Analogue Scale (VAS)
- IP comfort assessment
- BCVA (logMAR)
- Non-invasive lipid layer assessment
- Non-invasive tear break up time (NIBUT)
- Slit lamp biomicroscopy/external eye exam + photography for conjunctival hyperemia
- CFS + photography
- Vital signs
- IP return for accountability

8.4 Visit 4

- Concomitant medication review
- AE assessment
- SANDE
- Visual Analogue Scale (VAS)
- IP comfort assessment
- BCVA (logMAR)
- Non-invasive lipid layer assessment
- Non-invasive tear break up time (NIBUT)
- Slit lamp biomicroscopy and external eye exam + photography for conjunctival hyperemia
- CFS + photography
- Urine pregnancy test (women of child-bearing potential only)
- Vital signs

8.5 Visit 5

- Concomitant medication review
- AE assessment
- SANDE
- Visual Analogue Scale (VAS)
- IP comfort assessment
- BCVA (logMAR)
- Non-invasive lipid layer assessment
- Non-invasive tear break up time (NIBUT)
- Slit lamp biomicroscopy and external eye exam + photography for conjunctival hyperemia
- CFS + photography
- Urine pregnancy test (women of child-bearing potential only)
- Vital signs

8.6 Visit 6

- Concomitant medication review
- AE assessment
- SANDE
- Visual Analogue Scale (VAS)
- IP comfort assessment
- BCVA (logMAR)
- Non-invasive lipid layer assessment
- Non-invasive tear break up time (NIBUT)
- Slit lamp biomicroscopy and external eye exam + photography for conjunctival hyperemia
- CFS + photography
- Intraocular pressure
- Dilated fundoscopy (indirect)
- Urine pregnancy test (women of child-bearing potential only)
- IP return for accountability
- Vital signs
- Clinical laboratory tests

9. Statistical Analysis Overview

9.1 Primary Efficacy Analysis

Mixed Model for Repeated Measures (MMRM) for change in NEI tCFS score, with baseline, treatment, visit, and treatment-by-visit interaction as covariates.

9.2 Reporting

Results include LS means, standard error, 95% CI, between-group comparisons with p-values.

9.3 Handling of Missing Data

Assumed to be Missing at Random (MAR); no imputation needed due to full data availability.