CLOUDBREAK THERAPEUTICS

Protocol-short

A Phase 2 multicenter, double-masked, randomized, vehicle-controlled, parallel study to evaluate the safety, efficacy and pharmacokinetics of CBT-008 ophthalmic solution in patients with Meibomian Gland Dysfunction associated Dry Eye Disease (MGD-DED)

Protocol Number:	**CBT-CS102**
ClinicalTrials.gov Identifier	**NCT04884243**
Name of Investigational Product:	**CBT-006 Ophthalmic Solution**
Governing IRB/IEC:	**Sterling IRB**
Sponsor:	**Cloudbreak Therapeutics, LLC** **15615 Alton Parkway, Suite 450** **Irvine, CA 92618, USA**
Emergency Phone Numbers:	**1-949-678-9752**
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Date: **February 10, 2023**

Study Number: CBT-CS102

Name of Sponsor: Cloudbreak Therapeutics

Name of Finished Product: Ophthalmic Solution of CBT-006

Name of Active Ingredient: CBT-006

Title of Study: A Phase 2 multicenter, double-masked, randomized, vehicle-controlled, parallel study to evaluate the safety, efficacy and pharmacokinetics of CBT-006 ophthalmic solution in patients with Meibomian Gland Dysfunction associated Dry Eye Disease (MGD-DED)

Study Period:

Study Initiation Date (First Subject Enrolled): 21 July 2021

Study Completion Date (Last Subject Completed): 24 September 2022

Phase of Development: Phase 2

Objectives:

To evaluate the safety and effect of CBT-006 ophthalmic solution dosed in both eyes topically TID for 3 months in patients with MGD-DED

Methodology:

Strategy:

- Evaluate the ocular and systemic safety profiles of CBT-006 ophthalmic solution in patients with MGD-DED
- Assess whether CBT-006 is efficacious in improving the symptoms.
- Assess whether CBT-006 is efficacious in improving the signs.

Plan:

A multicenter, double-masked, randomized, vehicle-controlled and parallel study is designed with 3 months TID repeat ocular dosing of vehicle, lower and higher concentration of CBT-006. Ophthalmic and physical examinations will be performed at screening, day 1 and weeks 2, 4, 8, 12.

Number of Subjects: 90

Diagnosis and Main Criteria for Eligibility:

Major Inclusion Criteria

- Diagnosed with MGD in both eyes and meet the following:
    a. ODS ≥ 2
    b. VAS score between 35-90% for at least 1 of the 7 categories
    c. Total Cornea staining grade ≥ 3
    d. Total meibum quality score (MQS) between 6-17 from the sum of the 6 lower eyelid central glands in at least one lower eyelid
    e. FTBUT ≤ 5 s
    f. Schirmer I Test (anaesthetized) ≥ 5 mm after 5 minutes in study eye
    g. BCVA LogMAR $\geq +0.7$ in each eye.

- Willing to withhold the use of artificial tears and eye lubricants during the treatment phase.
- ≥ 18 years old
- Able to provide written informed consent and comply with study assessments for the full duration of the study.

Major Exclusion Criteria

- Uncontrolled systemic disease in the opinion of the Investigator
- Active allergy, infection, or ocular surface inflammatory disease unrelated to MGD
- History of ocular herpes disease in either eye
- Ocular surgery history within 6 months
- Patients taking eye lubricants must stop after Day 1 visit
- Use of topical treatment of the eye/eyelid with antibiotics, NSAIDS, or vasoconstrictors to treat MGD or DED within 14 days of screening; steroids, cyclosporin A or lifitegrast within 28 days of screening
- Current or anticipated use of other topical ophthalmic medications. Patients must have discontinued use of ophthalmic medications for at least 2 weeks prior to the screening visit, the use of artificial tears is allowed.
- Anticipated wearing of contact lenses during any portion of the study. Patients, who wear soft contact lenses should discontinue wearing them at least 3 days prior to screening visit. Patients wearing rigid gas permeable or hard contact lenses should discontinue wearing them at least 3 weeks prior to screening visit
- Active rosacea involving the eyelids within 60 days of Screening
- Current enrollment in an investigational drug or device study or participation in such a study within 30 days prior to entry into this study
- Any condition or situation which may put the patient at significant risk, may confound the study results, or may interfere significantly with the patient's participation in the study
- Female patients who are pregnant, nursing, or planning a pregnancy during the study

Test Product, Dose and Mode of Administration, Batch Number: CBT-006 ophthalmic solution of vehicle, lower and higher concentration dosed in both eyes topically TID.

Reference Therapy, Dose and Mode of Administration, Batch Number: Not applicable.

Duration of Treatment: 3 months of continuous ocular dosing

Study Measurements:

Safety (Primary):

- Ocular: ocular symptoms, visual acuity, intraocular pressure, biomicroscopy, ophthalmoscopy

  Systemic: vital signs, pregnancy test, and adverse event reporting

Efficacy (Co-Primary):

- Comparison between drug-treated and vehicle-treated groups on change of mean ODS at Week 12 from Day 1 baseline (questionnaire);
- Comparison between drug-treated and vehicle-treated groups on change of mean cornea staining grade at Week 12 from Day 1 baseline (By site PI);

Efficacy (Secondary):

Comparison between drug-treated and vehicle-treated groups on change of mean ODS at Weeks 2, 4, 8 from Day 1 baseline (questionnaire);

Comparison between drug-treated and vehicle-treated groups on change of mean VAS at Weeks 2, 4, 8, 12 from Day 1 baseline (questionnaire);

Comparison between drug-treated and vehicle-treated groups on change of mean cornea staining grade at Weeks 2, 4, 8 from Day 1 baseline (By site PI);

Comparison between drug-treated and vehicle-treated groups on change at Weeks 2, 4, 8, 12 from Day 1 baseline.

Statistical Methods: One database lock is planned for the study. The final analysis will be performed after study completion.

In general, continuous data will be summarized with descriptive statistics (number of patients, mean, standard deviation, median, minimum and maximum) and will be analyzed using analysis of variance (ANOVA) or covariance (ANCOVA) techniques with contrasts for between-group comparisons, and paired t-tests for within-group analyses. Categorical variables will be summarized by sample size (N), frequency count and percent, and analyzed using Pearson's chi-square test or Fisher's exact test. Ordinal variables will be analyzed using the ordinal regression model with contrasts for between-group comparisons and the signed-rank test for within-treatment comparisons. Two between-group comparisons are planned: CBT-006 lower concentration vs vehicle and CBT-006 higher concentration vs vehicle. All hypothesis testing will be performed with a significance level of 5%, 2-sided, without adjustment for multiple comparisons.

Duration of Study Follow-Up: None

Schedule of Events

Study Procedures	Visit 1 Screening	Visit 2 Day 1[a]	Visit 3 Week 2	Visit 4 Week 4	Visit 5 Week 8	Visit 6 Week 12
Informed Consent/Authorization	X					
Subject ID Assignment	X					
Demographics	X					
Medical / Ocular History	X					
Concomitant Medications/Concurrent Procedures	X	X	X	X	X	X
Vital Sign measurements (blood pressure, heart rate, body temperature)	X	X	X	X	X	X
Pregnancy test, if applicable	X	X	X	X	X	X
[redacted]						
Ophthalmoscopy (dilated)	X					X
Query for Serious Medical Events/Adverse Events	X	X	X	X	X	X
Randomization		X				
Inclusion/Exclusion Criteria	X	X				
Study Medication		Dispense		Dispense+ Collect	Dispense+ Collect	Collect
Exit						X

a All measurements at baseline Day 1 are prior to the instillation of first dose.