Informed Consent Form

Official title：	**A Phase 2, Multicenter, Randomized, Double-Blind, Placebo-Controlled Study Evaluating the Efficacy and Safety of HBM9036 Ophthalmic Solution 0.25% versus Placebo in Subjects with Moderate to Severe Dry Eye**
NCT number:	**NCT04092907**
Document date	**9 January 2019**

HARBOUR BIOMED	Informed Consent Form	Test Site Number:
Protocol Number and Revision: 9036.1/1.2	Informed Consent Form Version 1.2	Subject Number:

Informed Consent Form

Study title: A phase II, multi-center, randomized, double-blind, placebo-controlled study to evaluate the efficacy and safety of HBM9036 (HL036) Eye Drops (0.25%) compared with placebo in the treatment of patients with moderate and severe dry eye

Name of Sponsor: Hebo Pharmaceutical

(Guangzhou) Co., Ltd.

Investigator/Study Doctor:

Name and address of study site:

Daytime contact number:

24-hour emergency telephone number:

This consent form is for use by subjects who are capable or incapable of agreeing to participate in this trial. In this informed consent form, "you" refers to subjects who participate in the trial. If you are the legally acceptable representative, please remember that "you" refers to the subject of the trial.

You are being asked to take part in this trial because you may have dry eye.

It is important that you read this consent form carefully, which contains important information that will help you decide whether or not you want to take part in this trial. Your study doctor will explain the details of the trial and the possible risks and benefits of your participation in the trial during an interview. Any unclear question can be asked at any time.

After reading and discussing this consent form, you will be informed that:

- Why this test is performed;
- What happens during the trial;
- Any benefits you may receive;
- Possible risks to you;
- What other choices do you have besides being in this trial;
- What will happen to your personal information/health information during and after the trial, and what privacy rights you have;

- Any costs that you may incur in this trial;
- What you can do if you have questions or concerns about the trial.

Your participation in this trial is entirely voluntary (your choice). Given that there may be differences between the care received by participating in the trial and the care provided by a doctor outside of the trial, you may propose to discontinue your participation at any time if you participate in the trial. You have the right not to sign this consent form. If you do not sign, you cannot take part in this trial. If you decide to take part in this trial, please sign and date the end of this form.

Test objective

The purpose of this trial is to compare the efficacy and safety of HBM9036 (HL036) eye drops and placebo in the treatment of dry eye.

The test drug used in this trial, HBM9036 (HL036) eye drops, has not been approved by the National Medical Products Administration (NMPA) for the treatment of any disease, therefore, its use in this trial is considered investigational. This trial has been approved by China Food and Drug Administration, with the approval letter number of 2018L03036.

The trial will be conducted in China with an expected total number of participants including screen failures of approximately 200 and is expected to be randomized 100 subjects.

Test Description

If you are eligible to take part in this trial and sign this informed consent form, you will be screened for a 14 ± 2-day lead-in period during which you will receive placebo. The placebo does not contain any active pharmaceutical ingredients: sodium chloride (tonicity modifier), citric acid monohydrate (buffer), sodium hydroxide solution and hydrochloric acid 1% (both for pH adjustment), and sterile water for injection as a solvent. If you are still eligible to participate in this trial after the lead-in period, you will be scheduled for a treatment period of approximately 56 days. A total of 6 visits to the study site occurred during the run-in and treatment periods.

During this period, you will be randomly assigned to receive the study drug HBM9036 (HL036) eye drops or placebo. You will have a 50% chance of getting into one of the following treatment groups:

A 0.25% HBM9036 (HL036) Eye Drops

B Placebo group

This is a double-blind trial, which means that neither you nor the study doctor will know which drug you are taking. The purpose of randomization is to give each subject an equal opportunity to receive a treatment and to ensure that the information obtained is compared as reliably as possible. If the study doctor believes it is necessary for safety reasons to know, the investigator can quickly obtain information about the use of the drug.

Test Flow

<u>Prior to test initiation</u>

Before the first screening visit, you will first need to read and sign this informed consent form before starting the trial.

To make sure you are eligible to take part in this trial, you will be asked some questions to check that you meet the conditions.

The results of the tests and/or questions at the screening visit will help our trial team decide if you can continue with the trial. If these tests show that you are eligible to take part in the trial, you will be able to continue taking part. If you do not meet the eligibility criteria, you will not be able to continue the trial. Do not go to another trial site for screening for this trial.

Visit 1 (Day -13 ± 2):

before entering the dry

eye room

- A study staff member will ask you about your medical history and whether you are taking or taking any medications. Then, you will have tests done to make sure that you are in good health and can take part in the study.
- Basic personal information, medical history, medication history
- Inclusion/Exclusion Criteria
- Pregnancy test (If you are a woman who is still able to have children, the study staff will ask you to provide a urine sample for a pregnancy test.)
- Complete a Subject Questionnaire: You will be asked to complete a questionnaire and assess dry eye symptoms.
- Ophthalmic Examination Assessments: The study doctor will ask you to have an eye examination, including a visual acuity test. The eyes were examined for general health and redness of the eye and eyelids. The study doctor will put a yellow (fluorescein) test strip in your eye to see if the eye is dry
  (Lucifer Yellow) to determine the rate of tear break-up (Tear
  Break-up Time (TFBUT)).
- Adverse events were interrogated and recorded.

Screening Challenge (dry eye chamber 1)

- Subjects who meet the criteria for all of the above evaluations (Prechamber Dry Eye 1) will undergo further screening evaluations in the dry eye room. Subjects will be exposed to the dry eye chamber for 90 ± 5 minutes. A self-assessment score (ODS) for ocular discomfort evaluated by the Ora Calibra ® Ocular Discomfort Scale will be obtained prior to, during, and after exposure to dry eye chamber. ODS was collected at t = 0 during dry eye chamber exposure and then every 5 minutes for a period of 90 ± 5 minutes.

After leaving dry eye room

- Complete subject questionnaires
- Ocular Examination Assessments
- Schirmer test: The study doctor will place a small piece of special paper in the corner of your eye to measure the amount of tears in both eyes within 5 minutes.
- Intraocular pressure: Eye drops will be used on your eyes to paralyze the eyes, and then the study doctor will measure the pressure in the eyes by touching the eyes with an instrument.
- Fundus color photography: The study doctor will look at the results of the fundus photography to check the health of the eye.
- Review of Partial Inclusion/Exclusion Criteria
- Review of your health and any changes you may have while taking your medications.
- Interrogate and record adverse events
- Dispensing and Management of Study Drug and Diary: If you are eligible, you will be dispensed a subject diary and a run-in drop kit to take home. You are reminded to apply the appropriate amount of the Run-in Drops to each eye on the evening of Visit 1. You will be reminded to use the Lead-in Eye Drops 2 times a day (morning and evening), one drop for both left and right eyes before Visit 2. You will need to assess dry eye symptoms in the diary provided twice a day before using the Run-in Eye Drops until the next visit. In the Dosing section of the Daily Diary, record whether you used the Run-in Eye Drops each time. You should start using the Run-in Eye Drops the evening of Visit 1.
- Visit 2 Scheduled: Visit 2 was scheduled at the end of Visit 1. On the morning of Visit 2, you will be asked to rate dry eye symptoms in a diary. Note, however, that since the study doctor must evaluate your eyes first, you will be instructed not to use the Run-in Eye Drops in the morning of Visit 2.

Visit 2 (Baseline Visit, Day 1)

A study staff member will ask you about your medical history and symptoms related to dry eye. Then, you will have some tests done to make sure you are in good health and ready to take part in the trial.

Pre-Dry Room Procedures

- Site staff will confirm that you did not take the run-in drop in the morning before your visit
- Run-in Drops and Diary Collection: Study personnel will collect used and unused run-in drops, packaging materials, and diaries
- Collect adverse events and medication updates since last visit: study staff will ask follow-up questions about health or medication changes
- Complete subject questionnaires
- Eye examination assessment including visual acuity test
- Review of

Inclusion/Exclusion
Criteria Screening
Challenge Requalification
(Dry Room 2)

- Subjects will be exposed to the dry eye chamber for 90 ± 5 minutes. A self-assessment score (ODS) for ocular discomfort will be obtained immediately before, during, and after exposure to the dry eye chamber. ODS was collected at t = 0 during dry eye chamber exposure and then every 5 minutes for a period of 90 ± 5 minutes.

Post Dry Room Procedures

- Complete subject questionnaires
- Ocular Examination Assessments
- Schirmer's tear test
- Adverse Event Query
- Review of inclusion/exclusion criteria
- Randomization and Study Drug Instillation: If eligible, you will instill (place) one drop of study drug into each eye under the supervision of a trained study technician.
- Ophthalmic Solution Comfort Assessment
- Dispensing and Management of Study Drug and Diary: If you are eligible, you will be dispensed a subject diary and study drug kit to take home. Of these, the amount of study drug is enough for you to take before the V4 visit. You should start filling before instillation of study drug on the evening of Visit 2

Write subject diary. You are reminded to take the study drug ophthalmic solution twice a day (one drop in the morning and one drop in the right eye) until your next visit. In the Administration section of the Daily Diary, record whether you used the study eye drops each time. You will also need to assess dry eye symptoms in the morning and evening before taking the study drug before the next visit.

- Visit 3 Scheduling: Visit 3 will be scheduled for you one week later. On the morning of Visit 3, you will be asked to rate dry eye symptoms in a diary. Note, however, that since the study doctor must evaluate your eyes first, you will be instructed not to instill the study medication in the morning of Visit 3.

Visit 3 (Day 8 ± 1)

- Site staff must confirm you did not take any study drug in the morning before the study visit
- Study Drug and Log Collection: Study Drug Log/Collection of Used Study Drug and Packaging Materials
- Collect AEs and medication updates since last visit
- Complete subject questionnaires
- Eye examination assessment including visual acuity test
- Instillation of study medication at the site
- Monitor for adverse events
- Dispensing and Management of Study Drug and Diary: You will be given a new subject diary to take home. You should start completing the subject diary before instillation of the study drug on the evening of Visit 3. You will be reminded to take the study drug ophthalmic solution 2 times a day (morning and evening), one drop for both eyes until your next visit. In the Administration section of the Daily Diary, record whether you used the study eye drops each time. You will also need to assess dry eye symptoms in the morning and evening before taking the study drug before the next visit.
- Visit 4 appointment: Visit 4 will be scheduled for you one week later. In the morning of Visit 4, you will be asked to assess dry eye symptoms in a diary. Note, however, that since the study doctor must evaluate the condition of the eye first, you will be instructed not to instill the study drug on the morning of Visit 4.

Visit 4 (Day 15 ± 2 days)

- Site staff must confirm you did not take any study drug in the morning before the study visit
- Study Drug and Log Collection: Study Drug Log/Collection of Used Study Drug and Packaging Materials
- Collect AEs and medication updates since last visit
- Complete subject questionnaires
- Eye examination assessment including visual acuity test
- Schirmer's tear test
- Dispensing and Management of Study Medication and Diary: You will be dispensed a new subject diary and re-dispensed the study medication box you used at Visit 4 to take home. You should start completing the subject diary prior to instillation of study drug on the evening of Visit 4. You will be reminded to take the study drug ophthalmic solution 2 times a day (morning and evening), one drop for both eyes until your next visit. In the Administration section of the Daily Diary, record whether you used the study eye drops each time. You will also need to assess dry eye symptoms in the morning and evening before taking the study drug before the next visit.
- Visit 5 Scheduled: Visit 5 will be scheduled for you two weeks later. In the morning of Visit 5, you will be asked to rate the dry eye symptoms in the diary. Note, however,

that since the study doctor must evaluate the condition of the eye first, you will be instructed not to instill the study medication in the morning of Visit 5.

Visit 5 (Day 29 ± 2)

Entered Dry Eye Room

- Site staff will confirm that you did not take the study drug drops in the morning before your visit.
- Study Drug and Log Collection: Study Drug Log/Collection of Used Study Drug and Packaging Materials
- Collect AEs and medication updates since last visit
- Complete subject questionnaires
- Eye exam assessment,

including visual acuity testing
in the dry eye room

- Subjects will use a dry eye chamber for 90 ± 5 minutes. A self-assessment score (ODS) for ocular discomfort will be obtained immediately before, during, and after dry eye room use. ODS was collected at t = 0 during dry eye chamber use and then every 5 minutes for 90 ± 5 minutes.

After leaving dry eye room

- Complete subject questionnaires
- Ocular Examination Assessments
- Schirmer's tear test
- Adverse Event Query
- Dispensing and Management of Study Drug and Diary: You will be dispensed a new subject diary and re-dispensed with the study drug kit for use at Visit 5 to take home. You should start completing the subject diary prior to instillation of study drug on the evening of Visit 5. You will be reminded to take the study drug ophthalmic solution 2 times a day (morning and evening), one drop for both eyes until your next visit. In the Administration section of the Daily Diary, record whether you used the study eye drops each time. You will also need to assess dry eye symptoms in the morning and evening before taking the study drug before the next visit.
- Visit 6 is scheduled: Visit 6 will be scheduled for you 4 weeks later. On the morning of Visit 6, you will be asked to rate the dry eye symptoms in the diary. Note, however, that since the study doctor must evaluate the condition of the eye first, you will be instructed not to instill the study drug on the morning of Visit 6.

Visit 6 (Day 57 ± 3)

Entered Dry Eye Room

- Site staff will confirm that you did not take the study drug drops in the morning before your visit.
- Study drug and diary collection: Study personnel will retrieve the study drug, packaging materials, and diary.
- Monitoring Adverse Events and Medication Updates
- Complete subject questionnaires
- Eye examination assessment including visual acuity test
- Pregnancy test (If you are a woman who is still able to have children, the study staff will ask you to provide a urine sample for a pregnancy test.) In the dry eye room
- Subjects will use a dry eye chamber for 90 ± 5 minutes. A self-assessment score (ODS) for ocular discomfort will be obtained immediately before, during, and after dry eye room use. ODS was collected at t = 0 during dry eye chamber use and then every 5 minutes for 90 ± 5 minutes.

After leaving dry eye room

- Complete subject questionnaires
- Ocular Examination Assessments
- Schirmer's tear test
- Intraocular pressure
- Fundus color photography
- Adverse Event Query
- Study termination

In Appendix A of this document, you will see a detailed overview and schedule of all visits, which lists the test tests and procedures scheduled for each visit. The study doctor or trial staff will read this Appendix A with you.

In Appendix B of this document you can see a more detailed description of the different tests and procedures including the associated risks. The study doctor or trial staff will read this Appendix B with you.

(Early) Termination Visit

You will have an "End of Treatment" visit after you have completed the entire trial period or if you decide to stop taking trial drug. You will not receive any further treatment with the study drug. At this visit, the study doctor will discuss your further treatment and any medications you need.

* Unless otherwise specified, each procedure will be performed as described in the previous visit.

- Monitoring Adverse Events
- Medication Update
- Study Drug and Diary Collection
- Urine pregnancy test (for women of childbearing potential)
- Complete subject questionnaires

- Eye examination assessment including visual acuity test
- Intraocular pressure
- Fundus color photography

Unscheduled Visit

In the event of an adverse event, an unscheduled visit may be required. In addition, the study doctor may schedule other unscheduled visits as needed for safety reasons. Depending on the reason for the unscheduled visit, the following may occur:

- You may be asked about any changes in your health, medical history and medications since the last visit
- The study doctor may do eye exams, including visual acuity tests
- Intraocular pressure
- Color examination of fundus
- Urine pregnancy test (for women of childbearing potential)
- Any other evaluations that may be required to check your safety.

What you need to cooperate with

- To ensure your safety during this study, you must tell the trial doctor about your health history truthfully. If you have already been treated by another doctor, it is important that you tell the trial staff about the treatment you have received and what has happened.
- You need to follow the trial instructions and procedures given by the trial staff and perform the trial visits at all scheduled times.
- You will be asked to enter the dry eye room for 90 minutes and complete the questionnaire assessment. The Dry Eye Room is a conditioning room consisting of two containers: a clinical container and an HVAC secondary container. The clinical shipping container measures approximately 12.1m long x 2.4m wide x 2.9m high and weighs approximately 15,000
  kg. Containers are isolated from the environment to minimize external influences on their humidity, and have ventilation ducts to allow airflow to pass through
  HVAC secondary container. Inside the clinical container there are 4 chairs, 12 fans, 1 television and a headlight. There is a door and a staircase at the entrance to the clinical container and an emergency exit on the other side. The clinical container also has an electrical console that controls the humidity and temperature of the HVAC secondary container and lighting inside the clinical container. The exterior of the clinical container has a connecting device to allow air access
  HVAC facilitates container handling. The HVAC auxiliary container is approximately 12.1m long x 2.4m wide x 2.9m high and weighs approximately 20,000 kg. Inside the container, there are 2 identical HVAC units, each with 1 air conditioning unit, 1 dehumidification unit
  Wheel and 1 air heater. The dry eye room is like a room with standardized environmental conditions in which the humidity (≤ 10% relative humidity), temperature (comfortable, room temperature), airflow (constant, no disturbance), lighting conditions (sufficient to illuminate the room without light sensitivity), and visual operation (watching TV) are regulated. Dry eye rooms represent situations you encounter every day (e.g., forced hot air heating, air travel, computer use) and standardize these external influences.
- You need to take the study drug as instructed by the study staff. You must remember to bring all empty bottles and packing materials to each trial visit and explain them if

there is any loss or absence of trial medication.

- If you experience any adverse events or feel unwell, you will need to call even if you do not know if it has any relationship with this trial
  /Inform the study doctor.
- You need to tell the study doctor about all prescription and non-prescription drugs, herbal preparations and food supplements you are taking/taking or plan to take/take. There may be foods that you should avoid during the trial and your study doctor will review this information with you.

Potential benefits

You may or may not benefit from participating in this trial. You can obtain your health information from different tests that have been done. If you have dry eye, then this may improve, stay the same, or be worse. In addition, your participation may provide new information that may benefit other patients and provide the medical and scientific communities with information about the treatment of patients with dry eye.

RISKS AND/OR DISCOMFORTS

There are risks involved in participating in any trial. You may also experience adverse events while taking the study drug. Some of these adverse events can be treated. Some adverse events may go away after you stop taking the study drug. Some adverse events may be mild, but others may persist longer or be permanent. Some adverse events may be life-threatening or fatal.

As with other medications, allergic reactions may occur with this trial drug. Allergic reactions can be mild or severe and may even lead to death. Call the study doctor right away if you think you have an allergic reaction.

Test Drug < HBM9036 (HL036) Eye Drops >

Possible adverse events with the use of the investigational product, HBM9036 (HL036) Ophthalmic Solution, include conjunctival hyperemia and possibly rare eye itching, dryness, burning sensation, tearing, irritation, or pain.

Since this drug is under investigation, all adverse events are currently unknown.

If you have any adverse event, you must tell the study doctor or study staff in detail about all the conditions. If you do not tell the truth about an adverse event, continued participation may be bad for you.

In the appendix, you will find a more detailed description of the risks associated with adverse events of the investigational drug, and the study doctor or trial staff will discuss the contents in the appendix with you.

Placebo Risks

If you receive placebo, you will not be able to receive HBM9036 (HL036) Eye Drops and your condition may get worse, stay the same, or improve. If you feel that your symptoms are getting worse, depending on the severity of your symptoms, you may contact your study doctor or go to the emergency room immediately for medical care.

Possible risks and adverse events of stopping existing treatment (if any):

If you stop taking your existing medicine, you may experience discomfort or adverse events. We recommend that you consult with your doctor about any potential adverse events.

Risks of trial procedures:

In the appendix, you will find a more detailed description of the risks associated with the trial procedures, and the study doctor or trial staff will discuss the contents in the appendix with you.

Unforeseen Risks:

There may be other risks from participating in this trial that are not known at this time.

If you have any questions about the risks of the trial, please ask your study doctor Raw.

You will be closely observed for adverse events. You may experience any signs of drug toxicity or other damage

Be stopped from participating in this trial. You must tell the study doctor or trial staff all the details. If you fail to tell the truth about the adverse events, your continued participation in the trial may be detrimental to you.

If you experience any adverse event, you need to inform your study doctor or trial staff immediately, whether or not you think it is related to or caused by the trial drug.

Other treatment options

In addition to participating in this clinical trial, you have other options which may include:

- Receiving other treatment options, such as eye drops, ointments, or surgery.
- Participation in another trial.
- No treatment for dry eye.
- Comfort Care. This type of treatment may help reduce pain, fatigue, appetite problems, and other symptoms and discomforts caused by dry eye. It does not treat dry eye directly, but relieves symptoms.

Please tell the study doctor your choice before you decide if you want to take part in this trial.

New information about the trial

During the trial, you will be informed in a timely manner of changes in trial procedures, newly identified adverse events or significant findings that may affect your health or willingness to participate. You may be asked to sign a new informed consent form to say that you have been informed of new information about the trial.

Information about contraception

Female trial subjects

If you are pregnant or breastfeeding, you cannot take part in this trial. If you are pregnant, pregnant, or breastfeeding, taking part in this trial could result in risks to yourself and/or your child/unborn child that are not currently known. For women who are able to become pregnant, a pregnancy test will be required before, during, or at the end of this trial, unless you are not likely to become pregnant due to surgery (hysterectomy with removal of the uterus), tubal ligation (ligation of the tubal), oophorectomy (removal of the ovary), or menopause.

If you are a woman who is sexually active, you must agree to use an acceptable form of birth control during this trial. Acceptable methods of birth control include:

- Hormonal method:
  - Birth control drug
  - Implantable contraceptives
  - Injectable contraceptives (Depo-Provera)
  - Transdermal contraceptives (patch)
- Mechanical – combined spermicide barrier method:
  - Spermicide and barrier (condom or diaphragm) Intrauterine device (IUD) Surgical sterilization of sexual partner (vasectomy)

For women who are not sexually active, abstinence is an adequate method of contraception; however, if you are sexually active during the trial, you must agree to use adequate contraception as described above for the remainder of the trial;

If you become pregnant or think you may be pregnant during the trial, be sure to tell the study doctor immediately. In this case, the study doctor will discuss the appropriate options with you. If you become pregnant during the trial, your participation in the trial will be stopped immediately. The study doctor may ask you questions about the pregnancy and the baby, and we will contact you regularly to learn about your pregnancy.

Male Trial Subjects

The effect of participating in this test on sperm is unknown. If you decide to take part in this trial, you will also be required to use birth control during the trial.

Termination of participation in the trial

You may choose to stop taking the study drug or withdraw completely from the study at any time. Your decision will not result in any penalty or prejudice to your rights. Leaving the trial will not affect your future medical care.

It is important that you tell the study doctor if you are thinking about stopping or have decided to stop so that your study doctor can assess the risks of stopping trial drug. In some cases, there may be risks associated with an abrupt stop of the trial drug that will be explained to you by the study doctor.

The following lists three possible scenarios that could stop your participation in the trial. Your study doctor will discuss these with you.

- **You can stop taking the study drug but agree to continue participation and/or continue to be contacted**

If you decide to stop taking the trial drug, you may continue to attend trial visits. If the trial staff can call or someone you choose

You will be contacted (e.g., by your family doctor, friend, or relative) and asked about your general health. Alternatively, you are asked to allow the trial staff to collect this information from your medical records until the end of the trial. This information is of great scientific value for the correct interpretation of the results of the trial. You have the right to refuse such regular contact. Your decision will not affect your future medical care.

- **You can completely stop trial drug and trial participation and withdraw your consent**

You have the right to withdraw your consent at any time. If you decide to stop taking the trial drug and participating in the trial, you should complete the final assessments as soon as possible, e.g., physical examination, laboratory tests, etc. This is important for your safety and health. In addition, you need to return all unused study drug and used study drug packages. No further information about you will be entered into the trial database after the final assessment.

All data and samples already collected up to the time you withdraw your consent, including any data collected at your final assessment, will still be used. These data will be included in the analysis and results of the trial for the purpose of scientific research. Results will be shared with others as necessary to ensure the quality and integrity of the trial and/or trial oversight. Once you have withdrawn consent, you will not be able to continue in the trial.

- **Your study doctor may decide that you need to stop the trial**

Your study doctor may decide to stop your trial drug or participation in the trial even if he/she does not obtain your consent if he/she judges it is in your best health interest to stop the trial. Some reasons why this might happen are listed below:

- Your symptoms worsen or do not improve, and there is a more appropriate alternative.
- The test was found to be unsafe/invalid.
- You cannot take the trial drug/participate in the trial as instructed.
- The sponsor or regulatory agency cancels the trial.
- Or for other unforeseen reasons, it is necessary

to stop your participation in the trial. If you are removed from the trial, the study doctor will explain to you why you were removed.

Confidentiality/Privacy and Data Sharing

Use of your personally identifiable information

If you decide to participate in this trial, to confirm your identity and to verify that you have not been treated with the study drug or device in another clinical trial within 30 days or 5 half-lives, whichever is longer, before this trial, we will need to log into the information system to look up your ID card and keep a copy of your ID card.

Parts of your personal information that directly identify you (e.g., your name and address) will remain at the trial site and will be accessible by the study doctor and the trial staff he/she assists. By signing this consent form, you give the study doctor permission to share your personal health information with all authorized users. Including the following personnel:

- Inspection at the trial site by the sponsor or representative of the sponsor (e.g., a monitor employed by the sponsor through a facilitator),
- An ethical review board that conducts ethical review of this trial, and/or
- National Medical Products Administration (NMPA) that approves the use of drugs.

These individuals checked at the trial site that the trial was conducted correctly. They are bound by a duty of confidentiality.

Use of coded data

Your personally identifiable information and health information collected for the purpose of the study will be labeled with a unique code. This code will be used in place of your name and other information that can easily identify you. Only the trial site will have access to the correspondence between your personal information and the coded data. This correspondence will not be provided to the sponsor; only your coded data will be sent to the sponsor. The Sponsor will take measures to protect the confidentiality and security of your coded data and your privacy in accordance with current laws.

The Sponsor and other members of Platinum Pharmaceutical and those working with them (such as their colleagues, partners, trial partners, agents, licensees and designees, and their affiliates and agents, as well as other individuals and organizations) may use your coded data and use it for the following purposes:

- The data will be stored electronically and analyzed to understand the testing and the

results of the testing.

- Share data with regulatory agencies that approve the use of drugs, such as the National Medical Products Administration (NMPA).
- Data will be shared with the Ethics Review Committee to check that the trial is working properly.
- Use these data to improve the quality of this and other clinical trials.

Your coded data will be kept by the sponsor for at least five years after the investigational drug is approved for marketing, and the investigator should keep the clinical trial data for at least five years after the termination of the clinical trial.

If your coded data are used by scientists, other companies, or medical researchers at academic institutions to facilitate data analysis/comparison with other data to further understand:

- Use of the investigational drug in this trial/in other therapeutic areas.
- The design, implementation and analysis of this type of clinical trial in the future.

During this process, we will make sure that your coded data will be anonymized.

Right to Access and Revise Information

You may request relevant archival records of your participation at any time. You also have the right to request correction of incorrect data. To maintain the integrity of the trial, you may not have access to all data until the end of the trial.

Clinical Trial Websites and Publications

The information of this trial may be available through the drug clinical trial registration and information publicity platform of the Center for Drug Evaluation, CFDA http://www.chinadrugtrials.org.cn/ Query. This Web site will not include information that can identify you. At most, the website content will include a summary of the results. You may visit this website at any time.

Information obtained from this trial may be presented at meetings or published in medical journals. The information contained in the meeting or journal will not include your name or other information that can easily be traced back to you.

Fee

There will be no additional cost to you for participating in this trial. All trial procedures including laboratory work, tests, doctor visits, and trial drugs/devices will be paid for by the Sponsor and provided to you free of charge and will not be billed to you or your insurance company.

If you complete all scheduled visits according to the protocol, you will receive 6,000 RMB as allowance for visits required by the trial, such as meal, transportation costs, lost labor costs, etc. If you do not complete the whole trial, you will receive corresponding fees according to the completed visit according to the actual situation: upon completion of Visit 1, you will receive a subsidy of 200 RMB; upon completion of Visit 2, you will receive a subsidy of 400 RMB; upon completion of Visit 3, you will receive a subsidy of 600 RMB; upon completion of Visit 4, you will receive a subsidy of 800 RMB; upon completion of Visit 5, you will receive a subsidy of 1,000 RMB; upon completion of Visit 6, you will receive a subsidy of 3,000 RMB. The above fees will be paid to your bank card by bank transfer. The sponsor is the owner of the test results. If tests using your samples and/or data are commercialized or otherwise valuable, such products and discoveries will be owned, patented, licensed, or otherwise developed for commercial distribution by the Sponsor, other researchers, or companies. If this occurs, you will not receive any financial benefits or other proprietary benefits from any commercialized products or discoveries that may result from these trials.

Injury/Insurance

If you experience any discomfort or injury during the study, please inform your study doctor immediately so that you can receive appropriate treatment in a timely manner. In accordance with the relevant provisions of Good Clinical Practice, the sponsor has purchased insurance for the subjects participating in the clinical trial.

If the subject suffers trial-related injury during the trial, the sponsor will assume corresponding insurance liability, and provide relevant treatment cost and corresponding economic compensation to the subject according to laws.

The amount and availability of compensation may vary depending on the circumstances involved and their limitations. And Platinum Pharmaceutical shall only provide such insurance if:

- You take the study drug in strict accordance with the instructions of the study staff;
- These physical injuries are not caused artificially;
- You have informed your study doctor in a timely manner;
- You have followed the medical advice of your study doctor;
- Direct damage to the body is not the result of the natural progression of the disease or

its complications.

Bill of Rights of Trial Subjects

As a subject in this trial, you have the following rights:

- Understand the nature and purpose of this trial.
- Know the procedures used in this trial and any medicines or devices that will be used.
- Be aware of any anticipated adverse events, discomforts, or risks associated with participation in this trial.
- Understand any benefits that may be gained from this trial.
- Be aware of any medical treatment available if problems arise with this trial.
- Have the opportunity to ask any questions about this trial or procedure.
- Have the opportunity to independently decide whether or not to participate in this trial, and can withdraw from the trial at any time after knowing that they agree to participate in this trial. You may withdraw from the trial at any time without penalty.
- Obtain a copy of the signed and dated informed consent form.

Emergency Contact/Ethics Contact

If you have any questions, concerns or complaints about this trial, or to report a trial-related injury, please contact the study doctor on page 1 of this consent form. You have the right to be informed by the above study doctor of your condition and the effect of the study drug on you at any time and as needed.

In case of emergency, contact the trial doctor:

If you cannot reach anyone by the number above and you need immediate medical care (life threatening), go to the nearest emergency room.

If you have any questions, concerns or complaints about your rights as a trial subject, or would like information or comments, you may contact the Ethics Committee for this trial:

Appendix A: Visit Schedule

Items indicated in boxes marked with an X will be performed at each visit. These procedures

are described in Appendix B.

Procedure	Visit 1 Day -13 ± 2 days		Visit 2 Day 1		Visit 3 8th ± 1 day	Visit 4 15th ± 2 days	Visit 5 Day 29 ± 2		Visit 6 Day 57 ± 3		EOT[4]	FU[2]
	Dry Eye Preroom	Postdry room	Dry Eye Preroom	Postdry room	No dry eye Chamber	No dry eye Chamber	Dry Eye Preroom	Postdry room	Dry Eye Preroom	Postdry room		
Informed Consent	X											
Medical/medication history and demographics	X											
Update of medical/medication history			X		X	X	X		X			
Placebo Run-in Dispensing		X										
Placebo Run-in Recovery			X									
Randomization				X								
Study Drug Dispensing				X		X		X				
Study drug instillation				X	X							
Study Drug Recovery					X	X	X		X		X	
Log Distribution		X		X	X	X		X				
Log Recycle			X		X	X	X		X		X	
Inclusion and exclusion criteria review	X	X	X	X								
Adverse Event Collection	X	X	X	X	X	X	X	X	X	X	X	X
Urine pregnancy test	X1								X1		X1	
Assessment of eye drop tolerance				X								
Ora Calibra ® Ocular Discomfort Scale	X	X	X	X	X	X	X	X	X	X		
Ora Calibra ® Eye Discomfort and 4 symptom questionnaire	X	X	X	X	X	X	X	X	X	X		
VAS discomfort scale	X	X	X	X	X	X	X	X	X	X		
OSDI © questionnaire	X		X		X	X	X		X			
Visual acuity (ETDRS)	X		X		X	X	X		X		X	
Slit Lamp Biomicroscopy	X	X	X	X	X	X	X	X	X	X	X	

Conjunctival redness	X	X	X	X	X	X	X	X	X	X		
TFBUT	X	X	X	X	X	X	X	X	X	X		
Fluorescein staining	X	X	X	X		X	X	X	X	X		
Dry Eye Room Use	X		X				X		X			
Discomfort Scores During Dry Eye Room Use	X		X				X		X			
Schirmer's test		X		X		X		X		X		
Intraocular pressure		X								X	X	
Fundus color photography3		X								X	X	
Withdrawal of Subjects from the Study										X		

EOT: End of treatment
1: For women of childbearing potential, see definitions.

2:7 telephone follow-up to collect safety information.
3: If retinopathy is found or the optic disc and macula cannot be clearly photographed at the same time, indirect ophthalmoscopy or pre-examination should be performed under dilated conditions.
4: Examinations for which the subject withdrew prematurely

Appendix B: Description of Test Procedures and Risks

The trial doctor or trial staff will discuss with you the trial procedures and the risks associated with you. Please ask any questions you have. In addition to the listed risks, there is always the possibility of occurrence of risks that are not known at this time.

Procedure	Description	Risk
Intraocular pressure (IOP)	Intraocular pressure (IOP) was measured by the examiner using a non-contact tonometer	Intraocular pressure testing may cause mild eye discomfort
Fundus color photography	Used for examination of vitreous body, retina, macula, choroid and optic nerve	It may not be possible to obtain clear and complete photographs to observe the fundus, which requires further pupil dilation examination; pupil dilation can lead to pupil dilation at a certain time, causing discomfort such as photophobia
Slit Lamp Biomicroscopy	Can be used for diagnostic observation on cornea, conjunctiva, anterior chamber, iris, lens and eyelid	Very slight discomfort to eye during observation due to slit lamp brightness
Fluorescein staining	Used for diagnostic examination on the damage or ulcer of corneal and conjunctival epithelium	Possible slight discomfort to eye during examination
Schirmer's test	Diagnostic examination of tear volume to diagnose the severity of dry eye	Possible slight discomfort to eye during examination
TFBUT	Diagnostic examination of tear film stability	Possible slight discomfort to eye during examination
Urine test	Use to see if you are pregnant	Only urine needs to be collected after you urinate normally, so there should be no discomfort or known risk

Dry eye room	In a controlled adverse environment	You may experience some discomfort like dry skin, dry nose due to the warm, dry air. You may experience eye irritation such as dryness, redness, or itching. If you have any questions, please tell the study staff.

Subject Informed Consent Statement

I have read this informed consent form and fully understand its contents, as well as the possible benefits and risks of the trial. I voluntarily agree to be part of this trial after having had enough time to think about it, for the purposes and conditions described above. I agree that the trial team will store, process and use the information described above

My biological samples and personal data. I have been given the opportunity to ask questions about the trial and all of my questions have been answered to my satisfaction. I will receive a copy of this signed and dated consent form for my files. I do not give up any legal rights by signing this consent form.

Printed Name of Subject	Signature of Subject	DATE

For subjects unable to read and/or illiterate

Printed Name of Impartial Witness	Signature of Impartial Witness	DATE

☐ N/A (Please check this box if signature of impartial witness is not required. If the subject or the subject's legally acceptable representative is illiterate, the signature of an impartial witness is required.)

❖ **The subject/impartial witness must personally date the signature.**

Investigator's Statement:

I guarantee that I have explained the nature and purpose of this trial, the terms and conditions under which participation in the trial should be conducted, and the benefits and risks that may be associated with participation in the trial to the person named above. I have answered the questions raised by the trial subject and the trial subject will receive a copy of this signed informed consent document.

I acknowledge that I am responsible for the care and maintenance of the health of the trial subject named above, for the respect of the subject's rights and wishes, and for the conduct of the trial in accordance with applicable Good Clinical Practice and regulations.

Printed Name of Investigator	Investigator's Signature	DATE