**INFORMED CONSENT FORM AND**

**AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION**

|  |  |
| --- | --- |
| **Sponsor / Study Title:** | **Eyebiotech Ltd. / “A RANDOMIZED, DOUBLE-MASKED, MULTI-CENTER, 3-ARM PIVOTAL PHASE 2/3 STUDY TO EVALUATE THE EFFICACY AND SAFETY OF INTRAVITREAL EYE103 COMPARED WITH INTRAVITREAL RANIBIZUMAB (0.5MG) IN PARTICIPANTS WITH DIABETIC MACULAR EDEMA”** |
| **Protocol Number:** | **EYE-RES-102** |
| **Principal Investigator:**  **(Study Doctor)** | **John Carlson, MD** |
| **Telephone:** | **909-335-8940 (24 Hour)** |
| **Address:** | **Retina Consultants of Southern Ca**  **1895 Orange Tree Lane**  **Suite 204**  **Redlands, CA 92374** |

**Why are you receiving this information?**

You are being invited to take part in a clinical study because your doctor has diagnosed you with decreased vision due to diabetic macular edema (DME).

DME occurs when the retina, the light-sensitive tissue at the back of your eye, becomes swollen due to damage from diabetes. Your participation in this study is voluntary, meaning that you may or may not choose to take part. You may choose to not participate without penalty or loss of benefits to which you are otherwise entitled and without any effect on your future medical care. Before you decide, it is important that you understand why the study is being done and what it will involve.

This is a study of an investigational drug called EYE103 (also referred to as the “study drug”), which is being developed by Eyebiotech Limited (hereafter referred to as “EyeBio”) for the possible treatment of patients with decreased vision associated with DME. “Investigational” means that the drug is currently being tested and is not approved for sale by the U.S. Food and Drug Administration (FDA).

This document is called an Informed Consent Form (ICF), and the following information describes the study and your role as a possible participant. This document may contain words that you do not understand. Please take your time to review this information carefully. Ask your study doctor any questions you may have so you may decide if you would like to participate. If you wish, you may take home an unsigned copy of this form and discuss it with your family, friends, and/or your primary care physician (PCP) or general practitioner (GP). If you agree to take part, your study doctor will then ask you to sign and date this ICF.

The study doctor will ask you about your health and your family history. This background information about your medical history, along with the results of screening tests, will help the study doctor decide if you will be eligible to continue to the dosing portion of the study.

If you are not able to take part in this study, the study doctor will discuss your treatment options with you and may refer you back to your ophthalmologist (if different than the study doctor), PCP, or GP (if applicable).

## What is the purpose of this clinical study?

The purpose of this study is to determine whether EYE103 is safe and effective for the treatment of DME. EYE103 is designed to decrease fluid leaking and swelling in the retina (the back of your eye) by improving the health of retinal blood vessels. EYE103 has a different way of working compared to the current treatment available and therefore, may have therapeutic effects that add to or are different from standard available treatment.

The available treatment for DME involves eye injections given every month until the swelling in the retina improves. The injections may continue to be given monthly at that point or decreased in frequency to every 2-3 months. These injections work by blocking a substance in the eye called vascular endothelial growth factor (VEGF). To evaluate the effectiveness and safety of EYE103 when administered in participants with DME, EYE103 will be compared to a currently available anti-VEGF treatment for DME known as ranibizumab, also known as Lucentis®.

EYE103 is an investigational drug being studied by EyeBio for the treatment of DME. An investigational drug is one which is being tested but has not yet been approved for treatment by the regulatory authorities, such as the FDA. To date, a total of 28 participants with DME received EYE103 in a completed 2-part research study evaluating EYE103 for the treatment of DME or neovascular age related macular degeneration (NVAMD). The study showed improvements in both vision and retinal thickening and EYE103 was well-tolerated. No study drug-related side effects have been seen to date.

The current study will be conducted at approximately 200 study centers globally in South America, the European Union (EU), the United Kingdom (UK), Australia, Israel, and North America. Approximately 960 participants both men and women are expected to take part in the overall study.

## What procedures are involved?

If you decide to participate in this study, you will be randomly assigned to 1 of 3 study treatment groups by chance, like the flip of a coin, in a 1:1:1 ratio. Each study drug will be given as an intravitreal injection, which is an injection by needle into the back of the eye. You will have an equal chance of receiving:

1. **A low dose of study drug:** 0.5 mg of EYE103 via intravitreal injection
2. **A high dose of study drug:** 0.8 mg of EYE103 via intravitreal injection
3. **Currently available treatment for DME:** 0.5 mg of Lucentis® via intravitreal injection

This study will be double-masked, which means that neither you nor the study doctor and study staff will know whether you are receiving study drug (or which dose) or whether you are receiving Lucentis®.

This study consists of:

* A Screening Period of up to 28 days, during which tests will be performed to determine whether you are eligible for this study.
* A Day 1 randomization visit, during which you are assigned to one of the 3 study treatment groups if you are eligible for the study.
* A Study Treatment Period of 100 weeks, during which you will receive injections of EYE103 or Lucentis® every 4 weeks in the first year (52 weeks) of the study. In Year 2 starting at Week 56, you will receive injections of EYE103 or Lucentis® every 4, 8, or 12 weeks depending on your individual response to the study treatment.
* A Safety Follow-up visit, which is approximately 4 weeks after the end of the Study Treatment Period.

All study drug and Lucentis® injections will be performed on one eye only. This will be called the “study eye.” Your study doctor or other study staff will discuss with you which eye will be the study eye, based on the study requirements.

If you decide to take part in this study, you will be asked to read, sign and date this form before you have any study procedures. There will be several screening examinations, tests and procedures that you will undergo to find out if you are eligible for the study. If you are not familiar with any of these procedures, please ask your study doctor to explain how they are performed. If your screening results indicate that you are eligible to continue in this study, you will be asked to come back to the study site on Day 1 for study dosing. After the Screening Period, you will be in the study for 104 weeks (approximately 2 years). The following assessments will be performed during the study:

## Demographics and Medical History – Performed at Screening visit

## The study doctor will ask questions about you, including your age, gender, and medical history. If you do not object, your study doctor may need to contact and obtain previous medical history or data from your other treating physician(s). This is done for your safety. A full eye history, including any prior eye treatments, will be noted.

## Physical Examination – Performed at Screening visit

## A general physical examination (for example, head, eyes, ears, nose, and throat; heart; lungs; abdomen) will be performed at Screening. After Screening, a focused and more limited physical examination guided by any notable change to your health may be performed at the discretion of the study doctor.

## Vital Signs – Performed at Screening, Day 1, Week 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, 72, 76, 80, 84, 88, 92, 96, 100, and Safety Follow Up (SFU)/Early Withdrawal (EW) visit

## Your pulse rate, blood pressure, and body temperature will be measured at these visits.

## Pregnancy Test – Performed at Screening, Day 1, Week 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, 72, 76, 80, 84, 88, 92, 96, and 100

## If you are a woman capable of becoming pregnant, a serum (blood) sample will be taken for the pregnancy test at the Screening visit, and urine on all subsequent visits. If your urine test is positive, your blood will also be tested to confirm whether you are pregnant.

## Blood Samples for laboratory tests – Performed at Screening, Week 24, 52, and SFU/EW visit

## At these visits, blood samples (about 3 teaspoons or 15 mL per visit) will be collected for routine safety laboratory tests, to check your blood cell counts, protein levels and to check your liver and kidney function.

## Your blood samples will only be used for testing related to this study and will be destroyed after analysis.

## Blood Samples for Anti-Drug Antibodies (ADA) – Performed at Day 1, Week 24, 52, 76 and 100

## Additional blood samples (about 1 teaspoon or 4 mL per visit) will be taken to test for the detection of ADA. This is to understand potential immune responses that may also affect your response to EYE103.

## Your blood samples will only be used for testing related to this study and will be destroyed after analysis.

## Blood Samples for Pharmacokinetic (PK) Testing – Performed at Day 1, Week 24, 52, 76 and 100

## Pharmacokinetics means seeing how the body handles the study drug. It involves taking blood samples at various timepoints to see how much study drug is circulating in your blood. To do this the study site will take additional blood samples (approximately 1 teaspoon or 4 mL per visit) at the Day 1, Week 24, Week 52, Week 76 and Week 100 visits. At these visits, the concentration levels of EYE103 in your blood will be tested to see how your body is processing the study drug.

## Your blood samples will only be used for testing related to this study and will be destroyed after analysis.

## Best Corrected Visual Acuity (BCVA) – Performed at Screening, Day 1, Week 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, 72, 76, 80, 84, 88, 92, 96, 100, and SFU/EW visit

## Your vision will be tested by a trained technician. First, your vision will be corrected with trial lenses, similar to wearing glasses. You will then be asked to read letters or numbers off of a chart placed at varying distances. Your vision will be tested in both eyes at all study visits.

## Biomicroscopy – Performed at Screening, Day 1, Week 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, 72, 76, 80, 84, 88, 92, 96, 100, and SFU/EW visit

## In this exam the study doctor will use a slit-lamp to examine your eye closely to check for any abnormalities.

## This exam will be completed via a slit-lamp in both eyes at Screening, Day 1, Week 24, Week 52, Week 76, and SFU/EW visit. Only the study eye will be tested at all other visits.

## Fundoscopy – Performed at Screening, Day 1, Week 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, 72, 76, 80, 84, 88, 92, 96, 100, and SFU/EW visit

## This exam will use a magnifying lens and a light to check the fundus (the back and inside) of your eye. Your pupils will be dilated with eye drops so the study doctor can easily see to the back of the eye.

## This exam will be completed in both eyes at Screening, Day 1, Week 24, Week 52, Week 76, and SFU/EW visit. Only the study eye will be examined at all other visits.

## Intraocular Pressure (IOP) – Performed at Screening, Day 1, Week 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, 72, 76, 80, 84, 88, 92, 96, 100, and SFU/EW visit

## Eye pressure will be measured using a tonometer, a device that briefly touches the surface of your numbed eye to measure the pressure inside.

## This exam will be completed in both eyes at Screening, Day 1, Week 24, Week 52, Week 76, and SFU/EW visit. Only the study eye will be tested at all other visits.

## After every injection there will be a vision check and eye pressure will be measured for the study eye. You will be asked to stay in the study site for approximately a half hour after each injection to confirm that you are tolerating the injection well. If you are doing well after the injection, you may be able to leave sooner, or the study doctor may ask you to stay longer if needed.

## Spectral Domain Optical Coherence Tomography (SD-OCT) – Performed at Screening, Day 1, Week 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, 72, 76, 80, 84, 88, 92, 96, 100, and SFU/EW visit

## SD-OCT uses invisible light rays to take a picture of the back of your eyes and is done to measure the thickness of your retina.

## SD-OCT will be completed in both eyes at Screening, Day 1, Week 24, Week 52, Week 76, and SFU/EW visit. Only the study eye will be tested at all other visits.

## Optical Coherence Tomography Angiography (OCT-A), if available – Performed at Screening, Day 1, Week 4, 8, 12, 16, 20, 24, 28, 32, 36, 40, 44, 48, 52, 56, 60, 64, 68, 72, 76, 80, 84, 88, 92, 96, 100, and SFU/EW visit

## OCT-A uses invisible light rays to measure the blood flow through the blood vessels in the back of your eye. This test is only performed at some study sites that have the special equipment; please check with your study doctor to see whether this test is being performed.

## OCT-A should be completed in both eyes at Screening, Day 1, Week 24, Week 52, Week 76, and SFU/EW visit. Only the study eye will be tested at all other visits.

## 

## Color Fundus Photography (CFP) – Performed at Screening, Week 12, 24, 36, 52, 76, 88, and SFU/EW visit

## CFP uses a special camera to take color photos of the back of your eye. This is conducted in both eyes at Screening, Week 24, Week 52, Week 76 and SFU/EW visit. Only the study eye will be tested at all other visits.

## Fluorescein Angiography (FA) – Performed at Screening, Week 12, 24, 52, 76, and SFU/EW visit

## This test involves first injecting a dye into a vein in your arm and then taking photos of the back of your eye. These photos help to get a better look at the blood vessels and other structures in the back of the eye. The FA is conducted in both eyes at all applicable visits.

## What is expected from you?

When deciding whether to participate, consider if you are able and willing to do the following:

* Keep your study appointments.
* Tell your study doctor or study staff about any side effects, doctor visits, or hospitalizations that you may have.
* Tell your study doctor or study staff if you experience pain or discomfort during any of the procedures required by this study.
* While participating in this study, you are not allowed to take certain treatments that may affect your study eye. You must tell your study doctor before taking any new medication during the study. This is to protect you from possible harm that may result from combining medications.
* While participating in this study, you should not take part in any other research project.
* Ask questions as you think of them.
* Tell your study doctor or study staff if you change your mind about staying in the study.

## What will happen at the end of the study or if you stop your participation early?

Week 104 will be the final visit of the study. After the study drug is stopped, your study doctor will discuss your future options with you and may refer you back to your ophthalmologist (if different than the study doctor), PCP or GP (if applicable).

## If you have withdrawn from the study before its conclusion, your study doctor may ask you to complete an Early Withdrawal visit. If you fail to return for final assessments, one of the study staff may contact you by phone for a follow-up. This is done to have complete data about your health and safety at the end of the study. If you leave the study, there will be no penalty, and you will not lose any benefits you are entitled to. Leaving the study will not affect the quality of the health care you are given.

## The study doctor may stop study drug or end your participation in this study for any of the following reasons:

## An unwanted side effect, known as an adverse event

## If you request to stop participating in the study

## If you don’t attend visits

## If you become pregnant (if applicable)

## The study doctor will tell you the reason why you should stop being in the study. Also, the Sponsor may stop the study at any time for safety, regulatory, legal, or other reasons aligned with good clinical practice (GCP).

## If you have experienced any side effects, you may be followed up until it is resolved. If the event is not resolved, you may be followed up for an additional 3 months or longer if necessary.

## BENEFITS AND RISKS

## Are there any possible benefits of being in the study?

Taking part in this study may or may not help to treat your DME. If the study drug is effective, your DME may be reduced in its severity, meaning that the risk of developing sight-threatening complications of DME could be lower for you. Additionally, if you do develop the sight-threatening complications of DME, receiving EYE103 may help improve your vision or reduce the severity of those complications. It is possible that you may not personally benefit from your participation in this study. However, by taking part, you will provide new information that may benefit other people in the future.

## What are the potential risks and discomforts?

You may have side effects from the drugs or procedures used in this study. Side effects can vary from mild to very serious and may vary from person to person. Everyone taking part in the study will be watched carefully for any side effects.

Possible risks from receiving the study treatment, EYE103:

* EYE103 may not improve your DME or your vision. The damage to the back of your eye and your ability to see due to your diabetes may get worse. Previous large studies of eye injections that use an anti-VEGF treatment for DME have suggested approximately 5 to 10% of participants may be expected to lose 15 or more letters (3 lines on the visual acuity chart) over time, regardless of the specific intravitreal anti-VEGF agent used.
* It is possible that EYE103 might not improve your DME or your vision, and that a different treatment, such as anti-VEGF treatment, would improve your DME or your vision, or that such alternative therapy would be more efficacious.
* EYE103 may have a risk of eye inflammation as do other eye injections but this is not known at this time.

Sometimes people have allergic reactions to drugs. If you have had an allergic reaction in the past, you must tell your study doctor. Some things that happen during an allergic reaction that could be a sign or symptom of a life-threatening allergic reaction (anaphylaxis) are:

* Severe eye inflammation, with eye pain, sensitivity to light, or redness
* Rash
* Fast pulse
* Sweating
* Feeling of dread
* Swelling around the eyes and mouth
* Swelling of the throat
* Wheezing
* Having a hard time breathing
* Sudden drop in blood pressure (making you feel dizzy or lightheaded)
* Inability to breathe without assistance

You should get medical help and contact the study doctor or study staff if you have any of these or any other side effects during the study.

The study drug might have other side effects, including serious ones, which are not known at this time. If new information is discovered that might change your decision to stay in the study, you will be told about it and asked to sign an updated consent.

Eye injections can cause other eye problems. Some side effects of intravitreal injections observed in more than 10% (more than 10 of 100) of participants, include the following:

* Eye inflammation – the inside of your eye can become irritated and inflamed due to the injection procedure or due to the study drug.
* Bleeding under the skin of the eye – the white part of your eye might turn bright red. This is from a small amount of bleeding on the surface of your eye and due to the eye injection procedure. It will not change how well you see and will usually clear up in about a week.
* Eye irritation and pain – your eye may feel irritated or painful and make a lot of tears for a few hours.
* Cataracts – clouding of the eye’s lens.

Other side effects observed in less than 10% (less than 10 in 100) of participants include the following:

* Vitreous detachment (separation of the gel like substance in the middle of the eye from the retina – light-sensitive tissue at the back part of the eye).
* Increased eye pressure.
* Feeling that something is in your eye.
* Floaters (spots in your vision) – you might see small specks or floaters. Many people already have floaters. These new floaters may go away in a few days, or you may stop noticing them.
* Damage to the retina – the retina can become torn or detached due to the eye injection. If you see a curtain over your vision or part of your vision becomes missing, you should let your study doctor know right away.
* Damage to the cornea or other structures of the eye.
* Bleeding within the eye.
* An infection inside the eye. This happens rarely with any injection inside the eye but can be serious.

Some of these complications are rare, yet may lead to severe, permanent loss of vision. Therefore, it is very important that you be aware of any symptoms that might indicate one of these complications and that you report new symptoms to your study doctor right away. If your study doctor is not available for any reason, you should contact another eye doctor in the office immediately or seek emergency medical attention. These symptoms to be aware of include:

* Eye pain or increased discomfort
* Worsening eye redness
* Blurred or decreased vision
* Increased sensitivity to light
* Increased number of floaters (shadows/spots that float through your field of vision)

Blood Tests:

When a sample of your blood is taken, you may experience some temporary discomfort, bruising, swelling, and/or, in rare circumstances, infection at the needle site. You may feel dizzy, or you may feel faint. There is also a small risk of nerve damage at the place where the needle is inserted, which can be permanent in rare cases.

Eye Examination:

For the eye examination, your pupils will be dilated using eye drops. Dilation of the pupil may cause light sensitivity and slight blurring of vision for up to 4 hours after the examination. Wearing sunglasses for several hours after dilation can help reduce the discomfort of light sensitivity. Driving may be difficult, and it is better to have someone take you home. On the day of the visit, you should refrain from driving and operating machinery.

Fluorescein Angiogram:

After the yellow dye (fluorescein) is injected into a vein in your arm or hand, your skin may turn yellow for several hours. The yellow color will disappear as your kidneys remove the dye from your body. Because the dye passes through your kidneys, your urine will turn dark orange for up to 24 hours after the procedure. You may have an upset stomach during the procedure, but this usually lasts only a few seconds. If the dye leaks out of your vein during the injection, some of the skin around the injection site may feel uncomfortable or become yellow. The discomfort usually lasts a few minutes, and the yellow color goes away in a few days.

Also, injection of the fluorescein dye may cause pain at the site of the injection and carry a risk of bleeding, bruising, and/or infection at the puncture site.

An allergic reaction to fluorescein is rare. If this does happen, you may have a rash or experience itching of your skin. A severe allergic reaction occurs very rarely (fewer than 1 in 1 million people) and may involve breathing and/or heart rhythm problems, which can be life-threatening. The study doctor will monitor you closely after the dye is injected and you may need to stay at the study site for a little while afterwards to check that you are okay.

Spectral Domain Optical Coherence Tomography (SD-OCT) Imaging

Taking images and photographs of your eyes may cause temporary discomfort from bright lights and holding your eye wide open.

## Are there any reproductive risks?

Women:

It is not known if EYE103 may affect an unborn child or nursing infant. For this reason, if you are pregnant, breast-feeding or planning to become pregnant, you may not participate in this study. If you are capable of becoming pregnant, and are having sex with a man, you must use an acceptable method of birth control (see below) during the entire study and for 30 days after the last study drug injection. During the study, if you think that you might be pregnant, you should tell your study doctor right away, as your participation in the study must be stopped. Data and information about your pregnancy and delivery may be collected.

Men:

It is not known if EYE103 may affect your sperm or an unborn child. For this reason, you must use an acceptable method of birth control (see below) throughout the entire study. You should not donate sperm or father a child during the study or within 30 days following the last dose of study drug. It is important that you tell the study doctor immediately if your partner becomes pregnant during the study. Your partner may be asked to sign a separate ICF for the collection of data about the pregnancy and the outcome of the pregnancy, if required by country regulations.

Birth Control Methods for Men and Women:

Birth control methods with a failure rate of less than 1% (less than 1 in 100 people) per year are considered acceptable for this study and include the following:

* Bilateral tubal ligation (surgically sterilized)
* Oral contraceptives (when properly used)
* Contraceptive patch
* Long-acting injectable contraceptive (hormonal implants)
* Vasectomy (male sterilization)
* Intrauterine device
* Sexual abstinence (if in accordance with your normal lifestyle)

Men must use a condom with their female partner, and it is suggested the female partner also use one of the contraceptive methods detailed above.

Birth control methods that have a failure rate of 1% or more are not acceptable and include a cap, diaphragm, or sponge with spermicide, or a male or female condom with or without spermicide. You must discuss with the study doctor the type of birth control method that you use, and the study doctor must approve that method before you can enter the study.

## Are there any alternative treatments?

Your study doctor will explain the risks and benefits of other treatments before you decide if you want to take part in the study. If you decide not to participate in this study, you may receive the standard treatment(s) for DME recommended by your doctors, which may include treatment of your underlying diabetes, eye injections, and/or laser treatments for your eye. You may also choose to not use any treatment for your DME.

## Whom to contact about this study

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study such as:

* Whom to contact in the case of a research-related injury or illness;
* Payment or compensation for being in the study, if any;
* Your responsibilities as a research participant;
* Eligibility to participate in the study;
* The study doctor’s or study site’s decision to withdraw you from participation;
* Results of tests and/or procedures;

**Please contact the study doctor at the telephone number listed on the first page of this consent document.**

If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research participants. If you have any questions about your rights as a research participant, contact:

* By **mail**:

Study Subject Adviser

Advarra IRB

6100 Merriweather Dr., Suite 600

Columbia, MD 21044

* or call **toll free**:    877-992-4724
* or by **email**:          [adviser@advarra.com](mailto:adviser@advarra.com)

Please reference the following number when contacting the Study Subject Adviser: Pro00080625.

## Are there any costs if you decide to participate?

The study drugs will be made available to you at no charge, and you will not be required to pay for any study procedures. You or your insurance company may be billed for any standard medical care that is not required for the study.

## Is there a payment if you decide to participate?

You may be reimbursed for reasonable, out-of-pocket expenses you incur related to travel in connection with your study visits, such as parking, mileage reimbursement, or transportation fees. You will be reimbursed after you submit your travel receipts to the study staff.

You will also be paid $100 per visit completed for your participation in this study. You will be paid following each completed visit.

Reimbursement for out-of-pocket expenses and compensation for completed study visits **may be** provided through a third-party vendor, Greenphire, and will require you to provide personal data such as your name, address, contact details and bank details. The vendor will not store your personal data for a longer period than is required for the purpose of compensation or for compliance with applicable laws. Your data will not be used for any other purpose or disclosed to a third party or the sponsor for another purpose.

Transportation services may be provided through a third-party vendor, which may require you to provide personal data such as your name, address, and contact details. The vendor will not store your personal data for a longer period than is required for the purpose of transportation. Your data will not be used for any other purpose or disclosed to a third-party or the sponsor for another purpose.

If you have any questions regarding your compensation for participation, please contact the study staff.

## Will you receive compensation if you are injured as a result of the study?

If you are physically injured because of your participation in this study, treatment for the physical injury will be made available through the study doctor and study site.

If you are physically injured as a direct result of taking the study drug(s) or from procedures done solely for the purpose of this study, the Sponsor will pay for those medical expenses necessary to treat your physical injury that are not covered by your medical insurance or any other third-party coverage.

To pay medical expenses, the Sponsor will need to know some information about you like your name, date of birth, and Medicare Beneficiary Identifier (MBI). This is because the Sponsor has to check to see if you receive Medicare and if you do, report the payment it makes to Medicare.

You are not waiving any legal rights by signing and dating this form, accepting medical care or accepting payment for medical expenses.

## Will the study doctor and study staff receive any payment?

The study doctor listed on page 1 of this document receives payment from EyeBio, who is the Sponsor of this study.

**What will happen to your data?**

This study may be performed only by collecting and using your medical information and other personal data. As with all studies and research activities, there is a chance that confidentiality could be compromised; however, we will take reasonable steps designed to protect the confidentiality of your study records. For example, we will take steps designed to ensure that such records are not disclosed to third parties, except as necessary to conduct or support this study, to comply with applicable laws and as otherwise described in this document. In most cases, with respect to information shared beyond the study site, only a number will be used to identify you. You will not be personally identified in any reports or publications that may result from this study. Because of the research goals of this study, however, your study records cannot be kept completely confidential.

The study staff, the Sponsor, and its agents will need to review the medical information and other personal data collected from you for use in this study in order to accurately record information for this study. In addition, in order to review the study findings, the US Food and Drug Administration (FDA) and other regulatory agencies may review your medical records and other personal data. The following sections provide a specific description of how your information will be used and disclosed if you participate in this study. By signing this ICF, you are authorizing such access. If you do not sign this form to authorize access, you will not be able to participate in this study.

The medical information and other personal data that will be collected from or about you if you participate in the study includes the following:

* Information obtained from procedures to determine your eligibility to participate in the study, including a routine medical history, vital signs, blood and urine tests, visual acuity, eye examinations, OCT, fundus photography, and fluorescein angiography.
* Information that is created or collected from you during your participation in the study, including the results of the tests included in the previous bullet point and any other procedures performed during the study.
* Information contained in your medical records that is related to your medical history and treatment.

The medical information may contain, for example, your name, address, telephone number, social security number, health plan number, study number, date of birth, dates of various medical procedures, and other personal data.

Participants located in the UK/EEA should refer to the **PRIVACY NOTICE FOR UK/EEA CLINICAL TRIAL PARTICIPANTS** for further information on the processing of their personal data.

## Will information about this study be publicly available?

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

This Web site only shows data in English, but you can request information from the study staff at any time and have access to data that are publicly available.

After this study is over, a brief report of the overall results will be prepared for the general public. The study results may also be shared with scientific journals and the scientific community. Whenever the results of the study are shared or published, your identity will remain private.

# Statement of Consent

* I have read and understand the statements in this informed consent form.
* I have had the opportunity to ask questions, and I am satisfied with the answers given to me.
* I understand that this study may only be performed by collecting and using my health data and other personal data. Therefore, by signing this informed consent form, I specifically give permission for my data to be checked, transferred, and processed as follows:
* The authorized representatives of the Eyebiotech Limited (EyeBio), the Advarra IRB, and inspectors for regulatory authorities may review my health data and other personal data by directly accessing my health records.
* Study data, including my coded health data and other personal data, may be used and shared for legitimate study and scientific purposes.
* I agree to take part in this study of my own free will.
* I understand that I will receive a copy of this signed and dated written informed consent form.
* I agree to my primary physician or family doctor (general practitioner) being informed that I am taking part in this study.

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Printed Name of Participant, in full**

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Signature of Participant Date**

* I have presented the study and answered the participant’s questions.
* I will give the participant a copy of this signed and dated informed consent form.

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Printed Name of Person Obtaining Consent (Study Doctor/Delegate), in full**

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Signature of Person Obtaining Consent Date**

**WITNESS SIGNATURE FOR SUBJECTS WHO CANNOT READ (if applicable)**

The study subject has indicated that he/she is unable to read. The consent document has been read to the subject by a member of the study staff, discussed with the subject by a member of the study staff, and the subject has been given an opportunity to ask questions of the study staff.

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Printed Name of Impartial Witness**

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Signature of Impartial Witness Date**

**AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION**

If you decide to be in this study, the study doctor and study staff will use and share health data about you to conduct the study. Health data may include:

* Your name.
* Address.
* Phone number.
* Date of birth.
* Medical history.
* Information from your study visits, including all test results.

Health data may come from your study records or from existing records kept by your doctor or other health care workers.

For this study, the study staff may share health data about you with authorized users. Authorized users may include:

* Representatives of EyeBio.
* Representatives of TFS Health Science (Clinical Research Organization).
* Representatives of Advarra IRB (an Institutional Review Board that reviews this study).
* The Food and Drug Administration (FDA) and other US federal and state agencies.
* Government agencies to whom certain diseases (like HIV, hepatitis, and STDs) must be reported.
* Governmental agencies of other countries.
* Outside individuals and companies, such as laboratories and data storage companies, that work with the researchers and Sponsor and need to access your information to conduct this study.
* Other research doctors and medical centers participating in this study, if applicable.
* A data safety monitoring board which oversees this study, if applicable.

Your health data will be used to conduct and oversee the research, including for instance:

* To see if EYE103 works and is safe.
* For other research activities related to EYE103.

Once your health data has been shared with authorized users, it may no longer be protected by federal privacy law and could possibly be used or disclosed in ways other than those listed here.

Your permission to use and share health data about you will end in 50 years unless you revoke it (take it back) sooner.

You may revoke (take back) your permission to use and share health data about you at any time by writing to the study doctor at the address listed on the first page of this form. If you do this, you will not be able to stay in this study. No new health data that identifies you will be gathered after your written request is received. However, health data about you that has already been gathered may still be used and given to others as described in this form.

Your right to access your health data in the study records will be suspended during the study to keep from changing the study results. When the study is over, you can access your study health data.

If you decide not to sign and date this form, you will not be able to take part in the study.

**STATEMENT of authorization**

I have read this form, and its contents were explained. My questions have been answered. I voluntarily agree to allow study staff to collect, use and share my health data as specified in this form. I will receive a signed and dated copy of this form for my records. I am not giving up any of my legal rights by signing and dating this form.

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Printed Name of Participant, in full**

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Signature of Participant Date**

**WITNESS SIGNATURE FOR SUBJECTS WHO CANNOT READ (if applicable)**

The study subject has indicated that he/she is unable to read. The consent document has been read to the subject by a member of the study staff, discussed with the subject by a member of the study staff, and the subject has been given an opportunity to ask questions of the study staff.

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Printed Name of Impartial Witness**

\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_\_

**Signature of Impartial Witness Date**

*[European notice]*

**EYEBIOTECH LIMITED.**

## PRIVACY NOTICE FOR UK/EEA CLINICAL TRIAL PARTICIPANTS

**Sponsor name:** EYEBIOTECH LIMITED

**Sponsor address:** International Building, 71 Kingsway, London, WC2B 6ST, United Kingdom

EYEBIOTECH LIMITED (referred to as “**EyeBio**”, “**we**”, “**us**” or “**our**”) respects your privacy and is committed to protecting your personal data. In this Privacy Notice, we describe how your personal data will be collected, used and shared in connection with the study referenced above, if you decide to participate in the study. This Privacy Notice is intended to meet our obligations of transparency under the General Data Protection Regulation (GDPR) 2016/679 (“**EU GDPR**”) and the GDPR as it forms part of UK law (“**UK GDPR**”) (together, “**GDPR**”).

***Who is responsible for the handling of my personal data?***

EyeBio is a clinical-stage ophthalmology biotech company engaged in discovering, developing and commercializing a new generation of therapies for eye diseases.

EyeBio is the ‘controller’ (under the GDPR) of your personal data processed in connection with the study. This means that EyeBio is responsible for the handling of your personal data (including the processing carried out by the study team in the conduct of the study as described in more detail below).

***What types of personal data will be processed in connection with the study?***

* Name
* Date of Birth
* Address
* Email
* Phone Number
* Medical History

The personal data processed about you in connection with the study is as set out above, under **‘AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION’.**

*Who collects your data?*

The personal data detailed above will be collected from you by the study doctor and/or study staff at the site at which the study is carried out.

*Use of key-coded data*

The study staff will, where possible, remove your identification information, and apply a participant key-coded ID number to your study-specific data before sharing it with EyeBio and/or any third parties (see below for more information on data sharing).

The ‘code list’ or ‘reference table’, which links this key-coded ID number back to you and your Identification Information is then stored separately from the study-specific data (e.g., by study doctor and/or study staff and not by EyeBio).

However, there are circumstances where this code list may be used and EyeBio (including its representatives, partners and service providers) auditors and regulatory authorities may link study-specific data back directly to you and your identification information and may have access to other relevant documents maintained by the study doctor. This may happen, for example, if this is necessary to verify that the study is proceeding in accordance with the study plan, to comply with applicable legal requirements and/or in certain other limited circumstances (e.g., in the event of an adverse reaction or side effect requiring such identification).

***What information will EyeBio, study doctor and/or study staff share and for what purposes?***

EyeBio, study doctor and/or study staff may share your personal data as described in the **‘AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION’.**

Where your personal data is shared outside the study site, your identity will be protected in accordance with accepted industry standards and applicable laws.

The study doctor, the study staff, and EyeBio (and representatives, partners and service providers who work with them) will use and disclose your personal data as described above:

* to conduct the study;
* to check that the information collected for the study is correct;
* to make sure the study is carried out in accordance with applicable legal requirements and guidelines;
* for adverse event reporting;
* to get approval for EyeBio’s study drug or products;
* for research related to the study and to engage in other research or develop or conduct other studies; and
* for any other purposes described in this ICF.

***What are the legal bases relied upon by EyeBio for the processing carried out?***

EyeBio must have a legal basis under the GDPR for its processing of your personal data. The legal bases relied upon by EyeBio for its processing of your personal data are as follows:

|  | **Processing activities required to comply with law:** | **Processing activities related to research:** |
| --- | --- | --- |
| **Relevant purposes for processing:** | * + To make sure the study is carried out in accordance with applicable legal requirements and guidelines   + For adverse event reporting   + To get approval for EyeBio’s study drug or products   + Relevant data sharing described above (e.g., with research ethics boards, with regulatory authorities and for adverse event reporting etc.) | * + To conduct the study   + To check that the information collected for the study is correct   + For research related to the study and to engage in other research or develop or conduct other studies   + Relevant data sharing described above (e.g., with licensees, collaborators, and/or partners of EyeBio etc.) |
| **Legal basis:** | Compliance with legal obligations, including those that pertain to quality and safety standards for medicinal products – Article 6(1)(c) of the GDPR | Pursuit of legitimate interests in carrying out scientific research in relation to the study and associated research pertaining to the data collected therein – Article 6(1)(f) of the GDPR |
| **Condition for processing special category personal data (e.g., your health-related data, genetic information, and ethnicity data):** | Necessity for reasons of public interest in the area of public health, such as ensuring high standards of quality and safety of healthcare and of medicinal products – Article 9(2)(i) of the GDPR | * Depending on the context:   + necessity for reasons of public interest in the area of public health, such as ensuring high standards of quality and safety of healthcare and of medicinal products – Article 9(2)(i) of the GDPR; or   + necessity for scientific research purposes – Article 9(2)(j) of the GDPR. |

***Where will my personal data be maintained?***

Personal data about your participation in the study may be recorded in your medical records at the study site. Personal data may be shared as described above in the “*What information will EyeBio, study doctor and/or study staff share and for what purposes?”* section.

If applicable, your personal data may be transferred by your study doctor to information servers managed by EyeBio’s third party service providers supporting the study, located outside of (including in the United Kingdom or in the European Economic Area and/or back to the United States. This may include countries in respect of which the relevant supervisory authority has not issued an ‘adequacy decision’. A country that has not received an ‘adequacy decision’ is a country that has not been deemed to provide an adequate level of protection for your data for the purposes of the GDPR. However, in these cases we will take measures to protect your personal data, which may include:

* Specific ‘appropriate safeguards’, which are designed to ensure that your personal data is protected – for example, we may enter into the relevant form of the so-called ‘Standard Contractual Clauses’ or any equivalent replacement that is issued or approved from time to time by the relevant supervisory authority or government; or
* In certain limited circumstances, EyeBio may rely on an exception, or ‘derogation’, which permits us to transfer your data to such country despite the absence of an ‘adequacy decision’ or ‘appropriate safeguards’ – for example, reliance on your explicit consent to that transfer or reliance on the fact that the transfer is necessary for important reasons of public interest in the area of public health.

***How will my information be protected?***

EyeBio takes reasonable measures that are designed to protect your personal data from unauthorized access and use in accordance with the GDPR.

***What happens if I withdraw from the study?***

If you decide to participate in the study, you have the right to withdraw from the study at any time (by contacting the study doctor using the contact details set out in the “*How do I submit privacy questions or concerns*?” section below). If you choose to withdraw from the study, it will not affect your ability to receive standard medical care.

If you withdraw from the study, the personal data collected in connection with the study, including personal data collected during any follow-up visits after your withdrawal from treatment, cannot be deleted and will remain part of the study. This is necessary (i) to preserve the value and integrity of the research; (ii) to follow up on safety events that might have happened while you were part of the study; and (iii) to comply with applicable law, including requirements for obtaining drug authorization.

No new personal data will be collected without your permission, except to follow up on safety events that might have happened while you were part of the study or as otherwise described in this Privacy Notice.

***What rights do I have in relation to my personal data?***

In certain circumstances, you may be able to exercise the following data privacy rights with regard to your data that is processed by EyeBio:

* **Request access to your data**. This enables you to receive a copy of the data EyeBio holds about you and to check that EyeBio is processing it lawfully.
* **Request correction of your data**. This enables you to correct any incomplete or inaccurate information EyeBio holds about you.
* **Request erasure of your data**. This enables you to ask EyeBio to delete or remove data where there is no good reason for EyeBio to continue processing it. You also have the right to ask EyeBio to delete or remove your data where you have exercised your right to object to processing. However, please note that this right will not be available where any relevant processing is necessary for reasons of public interest in the area of public health, such as ensuring high standards of quality and safety of healthcare and of medicinal products.
* **Object to processing of your data**. This right exists where EyeBio is relying on pursuit of a legitimate interest as the legal basis for its processing, and there is something about your particular situation which makes you want to object to processing on this ground. However, please note that, EyeBio may reject your objection where it can demonstrate compelling legitimate grounds for continuing the processing, which override your interests, rights and freedoms and/or the processing is required for the establishment, exercise or defense of legal claims.
* **Request the restriction of processing of your data**. This enables you to ask EyeBio to suspend its processing of your data (e.g., if you want EyeBio to establish its accuracy or the reason for processing it).
* **Request the transfer of your data**. This enables you to ask EyeBio, in certain circumstances, to provide to you, or a third party you have chosen, your data in a structured, commonly-used, and machine-readable format.
* **Withdraw consent**. You may withdraw your consent to EyeBio’s processing of your data. However, please note that this right only exists in relation to those processing operations that EyeBio is carrying out in reliance on your consent – which, as noted in *“What are the legal bases relied upon by EyeBio for the processing carried out?”* above, will often not apply.

As noted above, EyeBio may hold some or all of your data in a form that does not identify you (e.g., associated only with a participant key-coded ID number). This means that we may not be able to identify you and your data without some further information. Where this is the case, we may ask you for further information to enable us to be able to identify you and your data. We cannot act on your requests if we cannot identify you and your data.

You should direct your inquiries and requests to the study doctor using the contact details set out in the “*How do I submit privacy questions or concerns*?” section below. EyeBio will assist the study doctor as necessary.

***How long will my information be retained?***

Your personal data will be retained as necessary to comply with applicable laws, for the purposes of future research and as otherwise stated in this ICF.

***How do I submit privacy questions or concerns?***

If you have questions about how your personal data is handled in connection with the study, or if you wish to exercise your rights under the GDPR, please refer to the contact details under ‘Whom to contact about this study’.

If your concern cannot be resolved by the study doctor, you may submit a complaint to the data protection regulator in the UK/EEA.

* *For participants in the EEU* – the contact information for the data protection regulator in your place of residence can be found here: <https://edpb.europa.eu/about-edpb/board/members_en>
* *For participants in the UK* – the contact information for the UK data protection regulator can be found here: <https://ico.org.uk/make-a-complaint/>