MASTER INFORMED CONSENT FORM AND AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

Sponsor / Study Title:	**F. Hoffmann-La Roche Ltd / "A PHASE III, MULTICENTER, RANDOMIZED, DOUBLE-MASKED, SHAM-CONTROLLED STUDY TO INVESTIGATE THE EFFICACY, SAFETY, PHARMACOKINETICS, AND PHARMACODYNAMICS OF RO7200220 ADMINISTERED INTRAVITREALLY IN PATIENTS WITH UVEITIC MACULAR EDEMA"**
Protocol Number:	**GR44278**
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Section 1: Study Overview

1.1 INTRODUCTION

- You are being asked to take part in this research study (also known as a clinical trial) because you have been diagnosed with inflammation inside your eye (uveitis) and have developed inflammation−related fluid swelling in a delicate layer at the back of the eye called the retina. This build-up of fluid in the retina is called uveitic macular edema (UME), sometimes also called retinal swelling or cystoid edema. UME can cause reduced vision. This study is testing a drug called RO7200220. RO7200220 is a treatment to control inflammation and remove the fluid that has built-up within the retina to help your vision.

- All individuals will be considered for this clinical trial, regardless of race, ethnicity, sexual orientation, gender identity, sex, veteran status, or disability status.

- F. Hoffmann-La Roche Ltd (hereafter referred to as Roche) is the sponsor of this study and is paying the study site to cover the costs of this study.

- This consent form tells you what will happen if you take part. It also tells you about the possible benefits and risks of being in the study.

- Taking part in this study is your choice. Please read the information carefully and feel free to ask questions. It may be helpful for you to discuss this information with your family and friends.

- Instead of taking part in this study, you may choose to
  - Get treatment for your UME without being in this study
  - Join a different study
  - Get no treatment
- Talk to your study doctor about all of your choices, and the risks and benefits of each choice. If you choose not to take part, you will not lose the regular care you receive from your doctors.
- If you decide to take part, you will be asked to sign this consent form. You will be given a copy of your signed consent form.

1.2 What is the purpose of this study?

The purpose of this study is to assess the effects, good or bad, of RO7200220 treatment for participants with UME compared to a control treatment called a "sham", in which no active study treatment will be given. Sham treatment will be compared to RO7200220 treatment to test how good RO7200220 is for treating UME and helping your vision.

In this study, you will receive either RO7200220 as a 0.25-mg injection into the eye OR RO7200220 as a 1.0-mg injection into the eye OR a sham procedure. The sham procedure feels like a real drug injection but does not involve a needle being inserted into the eye, and nothing is injected into the eye.

The main current treatment for UME is with steroids given as eye drops, tablets, or injections inside or around the eye. Steroids can cause side-effects, including increased eye pressure. If untreated eye pressure can cause damage to the nerve that connects the eye to the brain, this is known as glaucoma and results in vision loss. Other side effects of steroids can include clouding of the lens in the eye (this is called cataract), and health problems outside of the eye (such as high blood pressure, diabetes, and an increased likelihood of getting infections). RO7200220 is not a steroid treatment and has been developed to avoid these problems.

During uveitis, and some other conditions, certain inflammatory proteins are made by the body, including one called interleukin-6 (IL-6). This can cause inflammation and damage to your eye (including UME), and you can feel pain, light sensitivity, and blurred vision.

The study treatment, RO7200220, blocks IL-6 protein inside the eye to help reduce inflammation and treat your UME and help your vision. RO7200220 has been specifically designed for injection inside the eye and is not a steroid drug so it should not cause the same side effects as steroids.

About 225 participants will take part in this study world-wide.

RO7200220 is an experimental drug, which means health authorities (for example, the U.S. Food and Drug Administration [FDA] and European Medicines Agency [EMA]) have not approved RO7200220 for the treatment of UME or any other indications.

1.3 What will happen if I participate?

This study has four parts:

1. Screening (to see if you are eligible for the study)
2. Part 1: Monthly study treatment (Weeks 1−12; no study treatment given at Week 16)
3. Part 2: As needed study treatment (Weeks 20−48)
4. Follow-up (to check on you after study treatment is finished) (Week 52)

Screening Phase

If you agree to participate in this study, the study doctor will first need to check if you can be in the study. This process is called "screening."

The following activities will occur during the screening phase of the study:

- Discussion of this study and review and signing of this Informed Consent Form.

  You will be asked to read this Informed Consent Form or, if you are unable to read, it will be read to you. If you agree to take part in this study, you will sign this Informed Consent Form before any study-related procedures are performed.

- Tests or procedures (see Section 2.2 STUDY PROCEDURES AND POTENTIAL RISKS) to check if you might benefit from the study treatment and to make sure that there are no eye or general health reasons that could make the study treatment unsuitable for you.

  Some of these tests or procedures may be part of your regular eye and general medical care and may be done even if you do not take part in the study. This may include vision checks, eye examinations, eye pressure checks, and pictures of the back of your eyes. If you have had some of the tests or procedures recently, they may not need to be repeated.

After the screening period, if you are willing to participate and can be in the study, we call this being "eligible", you will be able to begin study treatment. If you are not eligible to join the study, you will continue usual care with your study doctor. It may be possible for you to be re-screened at a later date.

The purpose of re-screening is to re-assess whether you can participate in the study. This will be discussed with your study doctor. During the study, you will be given RO7200220 in one eye only. This eye will be called the "study eye." If you have UME in both eyes, your study doctor will decide which eye will be given this study treatment. We call your other eye the "non-study eye" as you will not be given study treatment in that eye. (See Section 1.3 below for more information about treatment for your non-study eye).

Study Treatment Phase

If you join the study, you will be placed into one of three study treatment groups (Group A, B or C). If you are in Group A or B, you will receive RO7200220 at one of two different doses. If you are in Group C, you will receive a sham procedure. The sham group will not receive any RO7200220.

You will have an equal chance of being in any one of the three groups. Your group will be randomly chosen by a computer program and not by you, your study doctor, or any of the study staff. This means that 2 out of 3 participants will receive RO7200220, and 1 out of 3 participants will receive sham treatment.

If you were taking tablets or receiving injections for uveitis or other conditions before joining the study your study doctor will review these medications and check whether you will be able continue to take these medications while participating in the study. Most standard types of tablets and injection treatments for uveitis can be continued during the study, provided the treatment has been stable for a while and was not prescribed at a dose higher than is permitted in the study. This includes eye drops, such as steroid eye drops, in the study eye and the non-study eye; tablet medications used for uveitis (steroid or immunosuppression); and injected medications (such as adalimumab). You may also continue medications for non-uveitis conditions. Your study doctor will tell you about any medications that you cannot take while receiving study treatment and you should therefore still be able to have your usual treatment alongside the study treatment you are given.

During the study, if your study doctor recommends additional new medications or increases the dose of tablets or injections that you are already taking, you will be able to have these medications and your study doctor will discuss with you whether you can continue in the study as, certain medications cannot be used alongside the study treatment (See Section 1.6).

Part 1 Study Treatment (Day 1 through Week 12; No Study Treatment Given at Week 16)

In Part 1, depending on your group, you will be given the following study treatment in the study eye every 4 weeks from Day 1 to Week 12, meaning you will be given 4 study treatments:

- Group A will be given RO7200220 (1.0 mg dose)
- Group B will be given RO7200220 (0.25 mg dose)
- Group C will be given a "sham procedure" and will not receive any study treatment with RO7200220

You will continue to be in the same group during your entire study participation, and your study doctor cannot switch you between groups. Neither you, your study doctor, or the study staff will know which group you are in. This is known as "masking to study treatment."

Only the pharmacist or trained specialist preparing your medication and the doctor who performs the injection or sham procedure will know which study treatment you are receiving. Your study doctor can find out which study treatment you are receiving if your safety is at risk.

After Week 12, the next study visit is at Week 16. At the Week 16 visit, you will undergo several study assessments, but no study treatment will be given.

Part 2 As Needed Study Treatment (Weeks 20−48)

In Part 2, you will have planned study visits every 4 weeks for the rest of your participation in the study:

- Assessments will be performed at every study visit and RO720220 or sham will be given as needed. At some visits you may not need study treatment.
- RO7200220 or sham can be given at any scheduled study visit if your study doctor decides that you need further study treatment. RO7200220 or sham can be given every 4 weeks or less frequently, depending on how your UME in the study eye is responding
- You will stay on the same study treatment that you received in Part 1, and you will remain on this study treatment until Week 48. For example, if you are in Group A, you will continue to have 1.0 mg RO7200220 as needed, and if you are in Group C you will have sham treatment as needed.

Follow Up (Final Study Visit at Week 52)

You will have a final study assessment at Week 52, and then you will continue your usual care with your doctor.

Sham Treatment

During the study, neither you nor your study doctor will know if you are receiving study drug or sham treatment. For the safety of all participants in the study, the study includes close monitoring and regular follow-up visits. As described above, you will be able to continue medications you were taking when you entered the study, so all participants in the study, including those on sham treatment, will continue to receive ongoing treatment for uveitis.

For all participants during the study (including those on sham treatment): if your UME does not improve or if it worsens, your study doctor can recommend a different treatment, with non-study medications that are standard for your condition. This is called rescue treatment and is described below. This ensures that appropriate treatment for UME is not delayed if you are receiving sham treatment.

Health Concerns and Unscheduled Safety Visits

- Contact the study site if you have any health-related concerns including if you have any new eye symptoms including pain, light sensitivity, redness, or reduced vision.

- If necessary, you will be asked to return to the clinic for an unscheduled safety assessment visit. Unscheduled visits can take place at any time during the study if recommended by your study doctor. The tests done at this visit will be determined by your study doctor (for example vision testing, eye pressure measurement, or ocular imaging may be performed). The study site will provide you with details for how to contact them.

Summary of Study Schedule

Study visits will be approximately every 4 weeks from the start of the study until the end of the study at Week 52, and overall, you will have about 15 clinic study visits.

Visits may last from a few hours up to half a day. The length of the visit will vary according to the assessments needed and according to whether any study treatment is scheduled or recommended by your study doctor.

The study procedures are described in detail in Section 2.2 STUDY PROCEDURES AND POTENTIAL RISKS. Some procedures will be the same as your regular care for UME, and some procedures will be just for this study.

Study Eye Rescue Treatment

During the study, your condition will be closely monitored to evaluate if there is improvement, no change, or a worsening. If your UME or uveitis is not improving or worsens, your study doctor may recommend that you to have a different treatment for the study eye instead of the study treatment (this is called a "rescue treatment"). Your study doctor may recommend rescue treatment if they think you require a different treatment to prevent loss of vision. Rescue treatment is available to all participants.

Rescue treatment is treatment for uveitis that is normally used for uveitis and UME care (and is not sham or RO7200220 treatment). Rescue treatment is used to ensure that appropriate treatment for uveitis and UME is not delayed if you are receiving sham treatment. The type of treatment and how it is given to you will be decided by your study doctor. The treatment may involve medications given directly to the eye, such as drops or injections and/or systemic medications such as tablets or injections. The medication may be an increased dose of a medication you are already taking or an additional treatment. Rescue treatment can be given anytime from Week 4 onwards at any planned or unscheduled visit. If you are given rescue treatment, you will not be given any further study treatment. However, please continue your study visits, and complete all other scheduled assessments.

Early Discontinuation of Study Drug/Study Treatment

You may stop study treatment during the course of the study for various reasons . For example, your study doctor may recommend that you have a different treatment for your condition or may find that your condition has not improved or has worsened during the study, or you may choose to stop study treatment.. However, you can still continue to be followed up in the study. Continuing in the study is completely up to you. You will be asked to continue to attend planned study visits and to complete all other scheduled assessments. If you choose to remain in the study, your study doctor will discuss this with you and will continue your ongoing care with standard treatments (not RO7200220 or sham) that are used to treat uveitis and UME and that they think are best for you. This may be treatment with eye drops or injections for the study eye and/or medications given as tablets or injections.

If you withdraw from the study treatment early, and decide not to continue in the study, you will be asked to complete an early termination visit no sooner than 4 weeks after your last study treatment. At this early termination visit, you will have the same tests and procedures that are done at the final study treatment visit. You will then continue your usual care (non-study treatment) with your study doctor. Further information about stopping study participation is in Section 1.10.

Non−Study Eye Treatment

During the study, you may need treatment for uveitis, UME, or other non-uveitis conditions in the non-study eye recommended by your study doctor. For treatment of uveitis, you will be able to continue with eye drops, such as steroid drops. You may also continue eye drops for any other conditions, such as high eye pressure. During the study, you may receive steroid drops, including drops at higher doses if you have a flare up, and eye steroid injection or steroid implant treatments needed for uveitis or UME, if recommended by your study doctor. You will also be able to undergo any procedures needed in the non-study eye. If this treatment is approved by the regulatory agency in your country and you do not have financial coverage for it, the Sponsor may cover the cost of the treatment. Financial coverage only applies while you remain in this study.

1.4 Are there any benefits?

Your health may or may not improve in this study, but the information that is learned may help other people who have a similar medical condition in the future.

1.5 Are there any risks?

You may have side effects from the drug or procedures used in this study, as described in Sections 2.1 STUDY TREATMENT RISKS and 2.2 STUDY PROCEDURES AND POTENTIAL RISKS. Side effects can be mild to severe, and they can vary from person to person. Talk to your study doctor right away if you have any of the following during the study:

- Symptoms that are new or have worsened
- Changes in your prescribed or over-the-counter medications (including herbal therapies)
- Visits to the doctor or hospital, including urgent care or emergency room visits

There may be a risk in exposing an unborn child to study drug, and all risks are not known at this time. Pregnant participants must take precautions to avoid exposing an unborn child to study drug, as described in Section 1.6 ARE THERE ANY SPECIAL REQUIREMENTS?. If you are pregnant, become pregnant, or are currently breastfeeding, you cannot take part in this study.

1.6 Are there any special requirements?

While participating in this study, there are certain requirements, as listed below:

- You should not join another research study.

  Studies for minerals and vitamins for the eye may be allowed with your study doctor's permission.
- For women of childbearing age: If you can become pregnant, you must use a reliable birth control method (with a failure rate of less than 1% per year).during the study and for at least 4 weeks after your final dose of RO7200220. Talk with your study doctor about what method may be best for you. You must not donate eggs during this same period. Tell your study doctor right away if you get pregnant during this period. If you get pregnant, the study doctor will want to follow up with you on the outcome of the pregnancy and will ask for your permission to collect information on the baby.

- It is important that you attend all your study appointments and complete all the scheduled study assessments and study treatments.
- If you cannot attend a study appointment, please contact the study personnel (for example, the study doctor or study staff) as soon as possible.
- Inform study personnel about any symptoms, changes in medications, doctor's or nurse's appointments, or hospital admissions that you may have had since your last visit.
- Inform your other doctors that you are taking part in this study.
    - Certain medications should not be started or used during this study as they may affect your eyes and vision, and they may make it hard to interpret the true effect and safety of RO7200220. For example, you cannot be given much higher doses of steroid tablet medications, much higher doses of steroid eye drops, or have steroid injections in the study eye, while you are still having the study treatment. Your study doctor will talk to you about these medications and can check a detailed list of medications you cannot take during the study.
    - During the study, if your doctor recommends that you need additional treatment for treatment of uveitis, in either eye, you will be able to have these medications, and your study doctor will discuss with you if you can continue with study treatment or if you need to discontinue study treatment. Additional treatment may include new medications or an increased dose of drops, tablets, or injections that you are already taking.
    - You should talk to your study doctor before starting any medications, vitamins, or other supplements (including vaccines, topical medications, or herbal remedies), even if they don't need a prescription. Examples of medications you cannot take while you are having the study treatment include, but are not limited to any other study or investigational medicines:
        - Any new medications that can suppress your immune system or any increases in the dose of this type of medication if you already take one or more of these
        - Any non-study injections inside or around the eye
        - Any drugs that are associated with eye side-effects and could affect your vision
        - Any laser eye treatments

Note: You may continue to take stable doses of medicines that are prescribed to you, including treatments for uveitis and any other health conditions and problems, including long-term eye drops and tablets

1.7 Will I be paid to participate?

You will be paid $120 for each visit that you complete, including unscheduled visits. You will be paid following each completed visit.

You will be reimbursed for your reasonable costs (for example, transportation, parking) to travel from your home to the study site.

Information from this study, including information from research on your samples, may lead to discoveries, inventions, or development of commercial products. You and your family will not receive any benefits or payment if this happens.

1.8 Will it cost me anything?

While participating in this study, you will not have to pay for drugs or procedures that are required only for this study and are not part of your regular medical care. You or your health plan will have to pay for medicines and clinic, hospital, and doctors' services that are part of your regular medical care. Some health plans will not pay for medications or procedures for people participating in research studies. Your study doctor can find out what your health plan will pay for.

1.9 What happens if I am injured?

If you get injured because you took part in this study, contact your study doctor as soon as possible at telephone number listed on the first page of this consent document. Your study doctor will explain your options and tell you where to get treatment.

Roche will pay for reasonable costs of immediate care for any physical injury that results from the study drug or your participation in the study but only if all of the following are true:

- Roche and the study doctor agree that your injury resulted from the study drug or your participation in the study and not from a preexisting medical condition
- The costs are not paid for by your medical insurance
- Your injury was not because you or the study staff did not follow instructions

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 will not receive any other kind of payment.

If you get injured in this study, you will not lose any of your legal rights to seek payment by signing this form.

1.10 Can I stop being in the study?

Your decision to participate in this study is voluntary. You may choose to not participate or you can leave this study at any time without penalty or loss of benefits to which you are otherwise entitled to. Tell your study doctor if you are thinking about stopping, and your study doctor will tell you how to stop safely. If you leave this study, you will not lose access to any of your regular care. However, please note that the FDA requires that any information collected up to the point of your withdrawal cannot be removed from the study.

If there are important new findings or changes in this study that may affect your health or willingness to continue, your study doctor will let you know as soon as possible.

You may be required to stop participating in the study, even if you wish to continue. Below are some of the reasons why you may be asked to stop:

- Your safety would be at risk if you continued
- You were unable to or did not follow study instructions or procedures
- You need medical care that is not allowed by this study
- This study has been stopped by Roche or a health authority

When your participation ends, no new information will be collected about you with two exceptions: 1) if you experience a side effect after the study that is believed to be related to RO7200220, the study doctor may report the side effect to Roche, and 2) any laboratory samples collected prior to stopping may still be tested, unless you specifically ask for your samples to be destroyed. However, Roche will still be able to use information that was collected prior to stopping, including information from samples that were tested prior to stopping.

Section 2: Study Details

2.1 Study Treatment Risks

Risks Associated with RO7200220

RO7200220 has had limited testing in humans. The known side effects of this drug, as well as potential side effects based on human and laboratory studies or knowledge of similar drugs, are listed below. There may be side effects that are not known at this time.

As of 2 March 2023, a total of 36 participants with UME or diabetes related macular edema (DME), have received RO7200220 eye injection treatment in other studies, including some participants with DME who received eye injection treatment with a combination of RO7200220 with another approved drug called ranibizumab (a different drug type to RO7200220).

Data from these ongoing studies supported further evaluation of RO7200220 for treatment of UME in the current study.

Risks Associated with Drug Administration into the Eye

The most common side-effects of study treatment are those caused by the injection procedure itself. These include temporary eye discomfort, bleeding beneath the membrane that covers the white of the eye (sub-conjunctival bleeding), temporary changes in vision including blurring or spots in the vision. A complete list of known side-effects is shown below:

Known Side Effects	
● Eye pain or discomfort ● Redness of the eye ● Dry or gritty sensation ● Eye swelling ● Clouding of the eye lens (cataract) ● Sensitivity to light (photophobia) ● Bleeding within the white surface part of the eye (sub-conjunctival hemorrhage) ● Bleeding inside the eye (vitreous hemorrhage)	● Reduced vision ● Floaters or spots in the vision ● Raised eye pressure ● Inflammation inside the eye ● Infection inside the eye or around the eye. ● Damage to the retina (the light-sensitive layer at the back of the eye) ● Separation of the retina from the underlying tissue (retinal detachment)

Risks Associated with Sham Procedure

The sham procedure involves putting anesthetic eye drops (pain killer) and antiseptic solution on the surface of the eye and eyelids, and then pressing the blunt end of a syringe (without a needle) against the white part of the eye. The procedure feels the same as a real injection, but does not involve a needle, and nothing is injected into the eye.

Known Side Effects	
● Eye pain or discomfort ● Redness of the eye ● Bleeding within the white surface part of the eye (sub-conjunctival hemorrhage) ● Dry or gritty sensation	● Eye swelling ● Reduced vision, floaters, or spots in the vision ● Sensitivity to light

Other Potential Risks

Some people develop increased pressure within the eye when a medication is injected into the eye. If you have a history of high eye pressure, you may be at more risk for this. Therefore, if you have a history of high eye pressure, this must be well controlled for you to participate in this study.

You may experience temporary visual problems following eye drops, eye examinations or after the injection. You are advised to wear sunglasses, and you should not drive or use machinery until your visual function has recovered sufficiently. You may need to bring a caregiver with you to the clinic who can help you return home after you have completed all the study visit assessments.

Reactions of the Immune System

Although rare, some people receiving injections of medications into their eye have developed inflammation inside the eye, ranging from mild to severe episodes. There is a possibility that you may develop inflammation after RO7200220 injection and this could cause reduced vision. Some people develop antibodies against drugs and it is possible that you may develop these against RO7200220. Antibodies against a drug may sometimes cause inflammation or reduce the drug's effect. Blood samples will be taken during the study to look for such antibodies.

2.2 Study Procedures and Potential Risks

Procedures with associated risks are listed below. The study doctor will provide more detailed information about the risks and their frequency. Participation in the study may also involve unanticipated risks.

Procedures with Associated Risks		
Procedure	Approximate Timing	Potential Risks
Injection into the eye	● Day 1, Weeks, 4, 8, and 12 ● As needed, at your study doctor's discretion from Week 20 onwards	See Section 2.1 STUDY TREATMENT RISKS
Blood sample (about 0.5−1 tablespoon at each visit)	● Screening ● Days 1 and 8, Weeks 4, 16, 20, 28, and 40 ● Week 52 or early termination visit ● Unscheduled safety visit, if needed	Drawing blood can cause pain, bruising, or infection where the needle is inserted. Some people experience dizziness, fainting, or upset stomach when their blood is drawn.
Fluorescein angiography photographs (pictures of the back of your eye enhanced by a special dye to look at uveitis and UME related leakage in the retina)	● Screening or Day 1 (preferred, if possible) ● Week 16 ● Week 52 or early termination visit ● Unscheduled safety visit, if needed	The test requires an injection of a dye into a vein in your arm using a small plastic tube (removed after the test). This may cause some discomfort at the insertion site, and the injection of the dye could cause redness and swelling at the injection site. It is possible that the vein or the skin around the site could be damaged. Side effects of the dye include nausea and vomiting, feeling faint and occasionally allergic reactions. The dye may also stain your skin and urine a yellow color, although this will only last for about a day.
Eye drops	● Screening ● Every study visit ● Unscheduled safety visit, if needed	You may experience blurred vision for a short period of time after the eye drops, which are used to dilate your pupil(s) for the various eye tests.
Eye cleaning/anti-infection procedure	● Every study treatment visit	The study doctor will use an antiseptic to clean and sterilize the surface of the eye and eyelids before the injection to protect against infection. You may experience temporary discomfort, blurred vision, redness, or irritation of the eye following this.

Procedures with Associated Risks		
Procedure	Approximate Timing	Potential Risks
Anti-microbial eye drops	● Based on your study doctor's judgment	Your study doctor may put some antibiotic eye drops into your eye before and/or after the injection. This may cause some irritation, itching, swelling or redness of the eye. You may be instructed by your study doctor to self-administer antimicrobial eye drops prior to your study treatment visit as well as following your study treatment.
Anesthetic procedure for the study eye	● Every study treatment visit	Your study doctor will numb (anesthetize) your study eye for comfort before the injection. The anesthetic may be administered as eye drops alone or in combination with an injection to the tissues surrounding the eye. You may experience blurred vision, pain or discomfort, or stinging in your eye, tearing and redness, light sensitivity for a period after the anesthetic is administered.
A sedation or general anesthetic procedure	● If required, every study treatment visit	In addition to an anesthetic for your eye, your study doctor and anesthetic doctor may suggest other medication to either make you feel relaxed during your injection procedure. This is completely optional, and most participants do not require it. This medication may make you sleepy (called sedation) or put you fully to sleep (general anesthetic). The risks and benefits of this medication must be discussed with you, your study doctor, and the anesthetic doctor, if applicable.

Non-invasive procedures with minimal risks are listed below.

Non-Invasive Procedures with Minimal Risks	
Procedure	Approximate Timing
Review of medical history, including medications	● Screening
Recording of demographic information, such as age, sex, race/ethnicity	● Screening

Completion of an interviewer-administered questionnaire to collect information on how UME affects your vision and everyday activities	● Day 1 and Week 16 ● Week 52 or early termination visit
Vital signs: temperature, pulse rate, blood pressure, and breathing rate	● Screening ● Day 1 ● Week 52 or early termination visit ● Unscheduled safety visit, if needed
Physical examination	● Screening ● Week 52 or early termination visit
Height and weight measurements	● Screening ● Week 52 or early termination visit
Finger-counting vision test	● Every study treatment visit ● Unscheduled safety visit, if needed
Review changes in your health or medications	● Every study visit ● Unscheduled safety visit
Urine sample	● Screening ● Early termination visit
Urine pregnancy test (if you can become pregnant); will be confirmed by the serum (blood) pregnancy test if urine test is positive	● Screening ● Every study visit (prior to study treatment, when applicable)
Vision testing (reading letters on an eye chart to test the sharpness of your vision) in both eyes	● Screening ● Every study visit ● Unscheduled safety visit, if needed
Non-Invasive Procedures with Minimal Risks	
Procedure	Approximate Timing
Optical coherence tomography (OCT): special scan pictures taken of your eye[s] to assess thickness of your retina and presence of UME	● Screening ● Every study visit ● Unscheduled safety visit, if needed
Color fundus photos: Photographic examination of the inside of your eye[s]	● Screening ● Weeks 16 ● Week 52 or early termination visit ● Unscheduled safety visit, if needed
Measurement to determine the pressure within your eye[s]	● Screening ● Every study visit ● Unscheduled safety visit, if needed
Slit-lamp eye examination, to check for inflammation and any related conditions within your eye	● Screening ● Every study visit ● Unscheduled safety visit, if needed

Eye examination using a light and a headset worn by a doctor to examine the inside of the eye (called indirect ophthalmoscopy)	• Screening • Every study visit • Unscheduled safety visit, if needed
Corneal endothelial cell count picture to evaluate the health of the front window of the eye (cornea)	• Screening or Day 1 (preferred, if possible) • Week 24 • Week 52 or early termination visit

2.3 Access to Study Drug after Completing the Study

You will be eligible to receive the Roche study drug (RO7200220) for free after you complete the study if all of the following are true:

- You have a sight-threatening or severe medical condition and require continued Roche study drug treatment for your well-being
- There are no appropriate alternative treatments available to you
- You and your study doctor meet any legal or regulatory requirements that apply

You will not be eligible to receive the Roche study drug (RO7200220) after you complete the study if any of the following are true:

- The Roche study drug is available in your country and is reasonably accessible to you (for example, it is covered by your insurance or would not create a financial burden for you)
- Roche has discontinued development of the study drug, or information suggests that the study drug is not effective for UME
- Roche has safety concerns about the study drug as a treatment for UME
- Provision of the Roche study drug is not permitted under the laws and regulations of your country

2.4 Use and Handling of Laboratory Samples

Sample Use

Blood and urine samples will be collected as part of this study. Samples will be collected for reasons such as the following:

• Check your health through standard laboratory tests • Find out if you are pregnant • Check how quickly your blood clots • Check for an infection with syphilis, a bacterial infection usually spread by sexual contact • Measure cholesterol and other lipids (fats) • Measure the amount of study drug present in your blood	• Find out if your body is making antibodies against the study drug • Perform additional analyses related to processing of study drug, your biological response to study drug, or development of antibodies to study drug (if needed) • Measure the amount of IL-6 in your blood

● Measure C-reactive protein, a marker of inflammation in the body	● Find out how variations in protein markers in your body (such as inflammation-related proteins) affect your disease or your response to study drug ● Develop tests or tools that help with detecting, understanding your disease, or the study drug

Sample Storage

Samples will be securely stored for a defined period (as described below) and will then be destroyed.

Samples will be stored for up to 5 years after the final study results have been reported.

2.5 Protection, Use, and Sharing of Information

During this study, health and personal information ("information") about you will be collected. This section describes the protection, use, and sharing of your information, which consists of the following:

- Information in your medical record, which is held by study site
- Information (including imaging data) that is collected or produced during this study ("study data"), which is held by the study site, Roche, Roche affiliates, and Roche's representatives (people and companies who work for Roche)

    "Study data" include screening information from all participants, even participants who are not eligible for or decide not to take part in the study.

Your privacy is very important, and Roche uses many safeguards to protect your privacy, in accordance with applicable data privacy laws and laws related to the conduct of clinical trials.

Your study data and samples will be labeled with a participant identification (ID) number that is unique to you and not related to or derived from information that identifies you (such as your name or any other personally identifying information). Roche, Roche affiliates, and Roche's representatives will only have access to study data and samples labeled with a participant ID number, except when accessing your medical record under certain circumstances, as described below:

Your information (including your medical record, which contains personal information that can identify you) may need to be reviewed to make sure the study is being done properly or to check the quality of the information. This information will be kept private. The following people and groups of people may review this information:

- Authorized individuals (such as study monitors and auditors) representing Roche and Roche's collaborators and licensees (people and companies who partner with Roche)
- The Institutional Review Board or Ethics Committee (people responsible for protecting the rights and safety of people who take part in research studies)
- Regulatory authorities (government agencies involved in keeping research safe for people) like the U.S. Food and Drug Administration.

Roche, Roche affiliates, and Roche's collaborators and licensees may use study data labeled with your participant ID number. Your study data may also be shared with independent researchers or government agencies, but only after personal information that can identify you has been removed. Your study data may be combined with other people's data and/or linked to other data collected from you. Your study data may be used to help better understand why people get diseases and how to best prevent, diagnose, and treat diseases, and to develop and provide access to new medicines, medical devices, and health care solutions.

Your information will not be given to your insurance company or employer, unless required by law. If the results from this study are published in a medical journal or presented at a scientific meeting, you will not be identified.

Information from this study will be retained by the study site for 15 years after the end of the study or for the length of time required by applicable laws, whichever is longer. In addition, Roche will retain the study data for 25 years after the final study results have been reported or for the length of time required by applicable laws, whichever is longer.

Syphilis is a reportable disease where you live. If you test positive for this disease, the law requires your study doctor to report your name to the

appropriate authority. Please ask your study doctor for details if you have concerns about this report.

If a participant is eligible for Medicare, federal law requires Roche to inform the Centers for Medicare & Medicaid Services (the agency responsible for the Medicare program) when Roche is going to pay for a participant's injury. Roche may need to share personal information, such as your name, date of birth, sex, and Medicare ID number (if you have one), with the Centers for Medicare & Medicaid Services.

If you sign this authorization, you give permission to the study site to use and/or share your "health information," which includes all information about you that has been and will be collected by the study site (including imaging data) and information in your study site medical record. Your health information may be used or shared for the purposes of this research study and for research related to UME or retinal diseases, common pathways (links) among diseases, the use of experimental drugs in disease therapy, and/or the development of tests or tools that help with detecting or understanding UME. You do not have to sign this authorization, but if you do not, you cannot take part in this research study.

Your health information may be used by and/or shared with Roche, Roche affiliates, Roche's collaborators and licensees, the Institutional Review Board or Ethics Committee, and regulatory authorities. Your health information and samples may be analyzed in any country worldwide. Those persons who receive your health information may not be required by federal privacy laws to protect it and may share your health information with others without your permission, if permitted by laws that apply to them.

You have the right to see and get a copy of your medical records kept by the study site that are related to the study. However, by signing this consent form, you agree that you generally will not be able to review or receive some of your records related to the study until after the entire study has been completed. This is to protect the scientific integrity of the study.

Your permission to use and share your health information does not have an expiration date. In California and any other state that requires an expiration date, the Authorization will expire 50 years after you sign this authorization document.

You may change your mind and take back your authorization at any time. If you take back your consent, no new health information will be collected about you. However, Roche will still be able to use and share any health information about you that has already been collected during this study. To take back your authorization, you must do so in writing by contacting your study doctor (see Section 2.7 WHOM TO CONTACT ABOUT THIS 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 this form.

Participant's name (print)	
Participant's signature	Date
Witness name [a] (print)	
Witness signature [a]	Date

[a] If the study doctor or Institutional Review Board or Ethics Committee deems a witness signature is necessary (as per International Council for Harmonisation [ICH] Guidelines, Good Clinical Practice [E6], 4.8.9, or local regulations).

2.6 Study Results

Results from exploratory biomarker tests will not be shared with you or your doctor, unless required by law, and will not be part of your medical record.

A clinical study report containing the results of this trial may be made available to anyone who requests a copy. Before this report is provided, additional steps will be taken to protect your information from being linked to you.

An easy to understand summary of the results of this study will be available at https://forpatients.roche.com/. Your study doctor may inform you about the availability of the summary for this study. Once the summary is available, you can view it by entering the study number (GR44278) in the search bar. This summary will not contain any information that could lead to the identification of you or any other study participants.

A description of this clinical trial will be available at 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.

2.7 WHOM TO CONTACT ABOUT THIS STUDY

During the study, if you experience any medical problems, suffer a research-related injury or illness, 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

Please reference the following number when contacting the Study Subject Adviser: Pro00066480.

2.8 OTHER RESEARCH STUDIES

Roche may inform your study doctor about other Roche research studies that might be of interest to you, taking into consideration your medical records and/or information collected as part of this study. If allowed by local laws, your study doctor may contact you in the future to see if you would like to learn more about taking part in a new research study. Taking part in a new research study would be entirely voluntary.

Signature

I confirm that I have read this consent form, or it has been read to me. I understand the information presented and have had my questions answered. I understand that I will be given a copy of all pages of this form after it has been signed and dated. I agree to take part in this research study as described above.

Participant's name (print)

Participant's signature | Date

I, the undersigned, have fully explained this informed consent to the participant named above.

Name of person conducting informed consent discussion (print)

Signature of person conducting informed consent discussion | Date

Witness name [a] (print)

Witness signature [a] | Date

[a] If the study doctor or Institutional Review Board or Ethics Committee deems a witness signature is necessary (as per ICH Guidelines, Good Clinical Practice [E6], 4.8.9, or local regulations).