Informed Consent

A Prospective, Multi-Center, Randomized, Triple-Blinded, Placebo-Controlled study of IL-1RA Treatment in Patients with Acute ACL Tear and Painful Effusions

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A Prospective, Single-Center, Randomized, Triple-Blinded, Placebo-Controlled study of IL-1RA Treatment in Patients with Acute ACL Tear and Painful Effusions

Note: References to "you" in this document may refer to <u>you</u> or <u>your child</u>

WHY ARE YOU BEING INVITED TO TAKE PART IN THIS RESEARCH?

You are being invited to take part in a research study about Kineret®. You are being invited to take part in this research study because you are between the ages of 14-40, are active and have been diagnosed with an anterior cruciate ligament (ACL) tear.

Kineret® was chosen because it is a well tolerated drug and has been used to treat Rheumatoid Arthritis (RA) and post-surgical persistent knee effusions (joint swelling) as well as knee stiffness. Although Kineret® is approved by the US Food and Drug Administration (FDA) for the treatment of RA and Neonatal-Onset Multisystem Inflammatory Disease, it is not currently approved by the FDA for use in treating ACL injury. Therefore, the use of Kineret® in this study is investigational.

If you volunteer to take part in this study, you will be one of about 40 people to do so at the University of Kentucky.

WHO IS DOING THE STUDY?

The person in charge of this study is Cale Jacobs, PhD of University of Kentucky, Department of Orthopaedic Surgery and Sports Medicine. There may be other people on the research team assisting at different times during the study.

WHAT IS THE PURPOSE OF THIS STUDY?

Injury to the knee during sports participation often involves partial or full detachment of the anterior cruciate ligament (abbreviated as ACL). ACL tears cause pain, swelling and inflammation. While the swelling and inflammation usually goes away in time, individuals with ACL injuries may experience pain and notice knee instability (knee slipping, etc.). Often surgery can repair or replace the ACL within the joint, allowing individuals the ability to walk or run again pain free or participate in sports. Unfortunately, osteoarthritis of the knee, which also causes pain and swelling, can occur in that same knee 10-20 years later for reasons which are not well understood.

In this research study, we want to study how Kineret impacts initial pre-operative pain and to see if the use of Kineret does decrease the risk of developing arthritis in individuals with ACL injuries by treating them within 28 days after their injury.

This research study is designed to allow health care professionals and researchers to answer many questions about the reasons why ACL injury leads to knee pain and disability and osteoarthritis. The purpose of this research is to gather information on how effective Kineret® is in alleviating knee pain following ACL rupture.

The results of this study will be shared with Arthritis Foundation, the company providing Kineret®, Swedish Orphan Biovitrium (Sobi), the Food and Drug Administration and other federal agencies, if required, the University of Kentucky Center for Clinical and Translational Science, Duke University, the Cleveland Clinic Foundation, the University of California, San Francisco and Bluegrass Research Consultants.

ARE THERE REASONS WHY YOU SHOULD NOT TAKE PART IN THIS STUDY?

You should not take part in this study if:

- You are younger than 14 and older than 40
- You are unable to provide informed consent
- You have had prior surgery to your currently-injured knee
- You have received corticosteroid injections into the injured knee within three months of enrollment into this study
- You are allergic to Kineret®
- You have received any live vaccines such as smallpox, MMR (measles, mumps and rubella), flu, polio, typhoid, chicken pox, yellow fever, herpes zoster 1 week prior to Visit 1, or are scheduled to receive a "live" vaccine within 1 week after study injection.
- You have an infection (or signs/symptoms of an infection ie: fever), including infections of the skin, a history of infections that keep coming back or other problems that can increase your risk for infections
- You are pregnant or planning to become pregnant
- You are breastfeeding or plan to breastfeed
- You have been diagnosed with hepatitis B or tuberculosis
- You have a disease that weakens your immune system such as diabetes, cancer, HIV or AIDS
- You have an underlying inflammatory disease (i.e. Rheumatoid Arthritis, Psoriatic Arthritis, etc.)
- You are currently taking Kineret®, humira, enbrel or any other immune suppressive drugs for inflammatory disease
- You have a history of bleeding disorders or are taking any blood thinning medications, aspirin or other medications affecting blood clotting
- You are allergic to latex or tape
- You have had a reaction to any local or general anesthesia
- You have received any investigational drug within 4 weeks of study Visit 1

WHERE IS THE STUDY GOING TO TAKE PLACE AND HOW LONG WILL IT LAST?

The research procedures will be conducted at the UK Medical Center. You need to come to the UK Healthcare at Turfland located at 2195 Harrodsburg Road in Lexington, KY. You will be asked to come to this location six times during the study. Each of those visits will take about 30 minutes. On the day of your surgery will need to come to the Center for Advanced Surgery at the University Of Kentucky Medical Center in Pavilion H. You will have three visits to campus to complete the research MRI scans, 40 Whitney Hendrickson Bldg at 740 Rose St in Lexington, KY (Visit 1, 5 & 6). All exams and questionnaires will be administered during the otherwise necessary routine visits for any participant who has suffered an ACL tear. No additional visit is necessary. The total amount of time you will be asked to volunteer for this study is about 3 1/2 hours, over the next 2 years.

WHAT WILL YOU BE ASKED TO DO?

A Summary of Study Procedures can be found as an attachment to this document. More detailed information about some of the procedures is shown below.

All participants with sports related ACL injuries enrolled in this study will be seen and may elect to undergo surgery, if necessary. Note: Surgery is not part of this protocol. Should you be enrolled into the study and choose not to undergo ACL reconstruction (surgery), you will receive treatment according to this protocol.

You will undergo knee aspirations (draining of fluid from the knee). The first one is performed at Visit 1 and is considered standard of care for your injury. The next two (1 each at Visits 2 and 3) are required for the study. Should a subject be enrolled into the study and choose not to undergo ACL reconstruction aspiration at time of surgery (Visit 2) will be omitted.

At Visit 1: you may have a large effusion that requires aspiration. This will be done as part of your normal routine care.

At Visit 2: you may have to undergo a study required aspiration depending on the amount of fluid in the knee.

At Visit 3: should you elect to undergo ACL reconstruction surgery, you will undergo a study required knee aspiration. Should you elect not to undergo ACL reconstruction surgery, you will not undergo the knee aspiration.

During a knee aspiration, the study doctor will remove fluid from the space around your knee using a needle and syringe. This is usually performed under a local anesthetic to either relieve swelling or to obtain fluid for analysis to diagnose a joint disorder and/or problem. Knee aspirations after ACL tear with a painful effusion are a common orthopaedic practice and standard of care in our institution. Thus they are not considered additional interventions with regard to this study unless you have no fluid in the knee.

During each aspiration procedure: Generally, a joint aspiration procedure follows this process:

1. You will be positioned so that the study doctor can easily reach the joint that is to be aspirated.
2. The skin over the joint aspiration site will be cleansed with an antiseptic solution.
3. If a local anesthetic is used, you will feel a needle stick when the anesthetic is injected. This may cause a brief stinging sensation.
4. The study doctor will insert the needle through the skin into the joint. You may feel some discomfort or pressure.
5. The study doctor will remove the fluid by drawing it into a syringe that is attached to the needle.
6. At Visit 1, the study medication (Kineret®/or saline) will be injected through the same needle. No medication will be injected in your knee at Visits 2 or 3.
7. The needle will be removed and a sterile bandage or dressing will be applied.
8. The fluid sample will be sent to a laboratory for examination.

After the aspiration procedure: Once you are home, it is important for you to keep the joint aspiration site clean and dry. Leave the bandage in place for as long as instructed by your study doctor. The aspiration site may be tender or sore for a few days after the joint aspiration procedure. Take a pain reliever for soreness as recommended by your study doctor. Be sure to take only recommended medications.

Notify the study doctor to report any of the following:

- Fever
- Redness, swelling, bleeding, or other drainage from the aspiration site
- Increased pain around the aspiration site

Randomization: Once it has been determined that you meet the entry requirements of the study you will be randomized, like drawing from a hat, into one of two groups. Both groups will receive knee injections with either Kineret® or a saline placebo. The saline placebo will contain no active medication. Neither you, or the study doctor, or the staff will know what treatment group you are assigned to. However, if you have a medical emergency you study doctor will be able to find out what treatment group you have been assigned to. If this is happens, you will removed from the study.

- **Group 1** will receive an injection of Anakinra (Kineret®, IL-1ra; 150mg) 1-28 days after ACL injury.
- **Group 2** will receive an injection of saline placebo 1-28 days after ACL injury.

X-rays: All subjects would have undergone a routine clinical x-ray analysis at prior to Visit 1.

MRI: All subjects will undergo initial MRI examination to confirm ACL injury at Visit 1 and subsequent MRIs will be performed at Visits 5 and 6.

Visit 1 Screening (1-28 days following injury)

- Obtain informed consent and assent if necessary of potential subjects
- Review medical history to determine eligibility based on inclusion/exclusion criteria.
- MRI scheduled
- Review medications history to determine eligibility based on inclusion/exclusion criteria.
- Perform medical examinations and collect vital signs as needed to determine eligibility based on inclusion/exclusion criteria. All subjects must have a clinical exam that is consistent with an ACL tear.
- Height and weight will be recorded
- Collection of urine and blood for laboratory testing. Women of child bearing potential will be given a urine pregnancy test. Test must be negative in order to enroll into the study. Parents/Legal Guardians of minor females: Your child will have a pregnancy test to see if they are eligible to be in the study. The results will not be disclosed to anyone other than your child, except in the case of a risk to health or welfare.

- Subjects will have the following assessments: range of motion, knee instability (Lachman's test) and standardized weight bearing x-rays. At this time the subjects will also be asked to fill in a standard questionnaire covering the KOOS, IKDC, VR-12, and a Likert pain scale.

Following the review of above assessment results and a review of inclusion/exclusion criteria, subjects will be randomized into 1 of 2 groups. Following randomization, subjects will undergo a knee aspiration and will receive their first dose study medication.

Visit 2 (day of surgery or 4-6 weeks post injury)

- Medical history
- Medication history
- ROM will be performed
- Knee aspiration (in the operating room under anesthesia. This will be omitted if you do not have surgery)
- KOOS, IKDC, VR-12, and a Likert pain scale administered prior to surgery
- Biomarkers (urine and serum) pre-operatively
- Review AEs and SAEs

Visit 3 (4-14 days after Visit 2)

- Knee aspiration (if clinical indicated)
- Biomarkers (urine and serum)
- Review for AE's and SAE's
- ROM will be performed

Visit 4 (6 months after Visit 2)

- Patient reported outcomes (PROs) administered
- KOOS, IKDC, VR-12, and a Likert pain scale administered
- ROM will be performed
- Review of AEs and SAEs

Visit 5 (12 months after Visit 2)

- MRI
- Patient reported outcomes (PROs) administered
- KOOS, IKDC, VR-12, and a Likert pain scale administered
- Biomarkers (serum and urine only)
- Review of AEs and SAEs

- ROM will be performed

Visit 6 (24 months after Visit 2)

- MRI
- Patient reported outcomes (PROs) administered
- KOOS, IKDC, VR-12, and a Likert pain scale administered
- Biomarkers (urine and serum)
- Review of AEs and SAEs
- ROM will be performed

The total amount of blood we will ask you to give is approximately 6 teaspoons.

The blood and fluid samples we collect from you during the study will NOT UNDERGO GENETIC TESTING. Your samples will be analyzed and stored at a University of Kentucky research laboratory. Your samples will be tested for special markers of cartilage breakdown and will remain property of the University of Kentucky indefinitely or until they are completely used. You may request that your samples be destroyed at any time. Please inform your study doctor if you wish to have your study samples destroyed.

Some of the fluid we collect will be sent to a research laboratory at Duke University where it will be tested for biomarkers. A biomarker is a test that can be used to measure health, or the progress of disease or the effects of treatment. Your sample will be kept indefinitely or until they are completely used.

The results we obtain from your analyzed samples are important only for research, not for helping to care for you. For this reason, these results will not be released to you or your family. Should future discoveries with these samples identify a clinically important problem that requires treatment, you will be told of this.

Your samples will be labeled with a barcode, but your name will not be provided. Your identity will remain confidential. All samples will be stored by barcode and no identifying information will be included with them. Your biomarker data will be stored in a locked file, and in a computer with restricted access. Any information that could be used to potentially identify you in the computer will be stored in a separate file and encrypted. Only the Principal Investigator and their research assistants will have access to the original research data.

Data from your biomarker tests will not be revealed to family members, insurance companies, employers, or other individuals or organizations. Any information gained from this research will be reported in anonymous summary form. No information regarding the biomarker research will be entered into your regular medical record. Although future research that uses your samples may lead to the development of new products, you will not receive any payments for these new products.
All links with your identity will be removed from the sample. You may request that your samples be destroyed at any time. Please inform your study doctor if you wish to have your study samples destroyed.

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

Kineret® may cause serious side effects, including:

• **Serious Infections. There is a very low risk that** Kineret® may lower your ability to fight infections. During your treatment with Kineret, call your healthcare provider right away if you:

- ✓ get an infection
- ✓ have any sign of an infection including a fever or chills
- ✓ have any open sores on your body

Do not receive "live" vaccines such as smallpox, MMR (measles, mumps and rubella), flu, polio, typhoid, chicken pox, yellow fever, herpes zoster, within 30 days of study entry without first talking to your study doctor.

- **Allergic reactions.** Get emergency help right away if you have any of these symptoms of a severe allergic reaction as an allergic reactions such as these may lead to death.
  - ✓ swelling of your face, lips, mouth or tongue
  - ✓ trouble breathing
  - ✓ wheezing
  - ✓ severe itching
  - ✓ skin rash, redness, or swelling outside of the injection site area
  - ✓ dizziness or fainting
  - ✓ fast heartbeat or pounding in your chest (tachycardia)
  - ✓ sweating

The most common side effects of Kineret include injection site reaction. Most injection site reactions are mild, happen early during treatment, and last about 14 to 28 days. The symptoms of injection site skin reactions may include:

- ✓ redness
- ✓ swelling
- ✓ bruising
- ✓ itching
- ✓ stinging

Reproductive Risks: It is not known whether receiving Kineret® is harmful to an unborn child. Pregnancy after administration of Kineret® may involve risks to the mother and her baby. Therefore, female who are capable of having a child, must use effective contraceptive methods. These methods must be used from the time of screening until Visit 2 during which any remaining medication will be washed out of the joint during the surgery. If you do not elect to have surgery (Visit 2) contraception methods will be documented until the end of the study. Examples of effective birth control are: hormonal contraceptives (the pill, implant, transdermal patch, or injection), barrier methods (condom with spermicide, diaphragm with spermicide), IUD, or a male partner had a vasectomy.

Lactating women: It is not known whether Kineret® is excreted in human milk. Because many drugs are excreted in human milk, you will not be allowed to participate in the study if you are breastfeeding.

Local Anesthetic: You may feel a brief stinging as the anesthetic is being injected. Along with its needed effects, a medicine may cause some unwanted effects. Although not all of these side effects may occur, if they do occur they may need medical attention.

While you are in the hospital or your study medical doctor's office, you will be carefully followed for any signs of allergic reaction. However, some effects may not be noticed until later. ***Check with your doctor immediately*, or call 911 if any of the following side effects occur:**

- breathing problems
- chest pain
- convulsions (seizures)
- dizziness
- fever
- headache
- itching
- nausea and/or vomiting
- raised red swellings on the skin, lips, tongue, or in the throat
- rapid heart rate
- skin rash

Risks associated with knee joint aspirations: As with any surgical procedure, complications can occur. Some possible complications may include, but are not limited to, the following:

- Fever
- Pain or discomfort at the aspiration site
- Bruising at the aspiration site
- Redness, swelling, bleeding or other drainage from the aspiration site
- Infection at the aspiration site

Blood draws: There is a risk of local pain, soreness, bleeding, bruising and swelling, as well as lightheadedness, dizziness and rarely, fainting and/or a local infection.

There is always a chance that any medical treatment can harm you, and the investigational treatment in this study is no different. In addition to the risks listed above, you may experience a previously unknown risk or side effect.

WILL YOU BENEFIT FROM TAKING PART IN THIS STUDY?

We cannot and do not guarantee that you will receive any benefit from taking part in this study. Your willingness to take part may, however, increase knowledge regarding the treatment of ACL injury and help future subjects. Previous studies using the study medication (Kineret®) in the knee joint after ACL injury or stiffness have resulted in pain relief for the patient and you may benefit from this effect.

You will have physical examinations and laboratory tests provided to you at no cost. Your study doctor will share with you any findings on these tests that indicate a potential problem.

DO YOU HAVE TO TAKE PART IN THE STUDY?

If you decide to take part in the study, it should be because you really want to volunteer. You will not lose any benefits or rights you would normally have if you choose not to volunteer. You can stop at any time during the study and still keep the benefits and rights you had before volunteering. If you decide not to take part in this study, your decision will have no effect on the quality of medical care you receive.

IF YOU DON'T WANT TO TAKE PART IN THE STUDY, ARE THERE OTHER CHOICES?

If you do not want to take part in the study, you have the choice to undergo our standard treatment for ACL injuries. Standard of care treatment includes the aspiration of painful knee effusions (fluid in your knee), pre-surgical rehabilitation, reconstruction of the ACL ligament, and subsequent physical therapy.

WHAT WILL IT COST YOU TO PARTICIPATE?

You and/or your insurance company, Medicare or Medicaid will be responsible for the costs of all care and treatment you receive during this study that you would normally receive for your condition. These are costs that are considered medically reasonable and necessary and will be part of the care you receive if you do not take part in this study. These costs include the following:

- Knee aspiration done at Visit 1 (if necessary)
- Range of Motion at all study visits
- X-Ray (if necessary)

The University of Kentucky may not be allowed to bill your insurance company, Medicare or Medicaid for the medical procedures done strictly for research. The following will be provided at no cost to you: the injection of Kineret®, the second knee aspiration and potentially the third knee aspiration, questionnaires and three MRIs.

WHO WILL SEE THE INFORMATION THAT YOU GIVE?

We will make every effort to keep private all research records that identify you to the extent allowed by law.

Your information will be combined with information from other people taking part in the study. When we write about the study to share it with other researchers, we will write about the combined information we have gathered. You will not be personally identified in these written materials. We may publish the results of this study; however, we will keep your name and other identifying information private.

In order to process your study payments, we will need to collect your social security number. You do not have to give us this number however, refusing to provide us with your social security number may result in your not receiving study payment. You can refuse to provide us your social security and still be enrolled into the study.

We will make every effort to prevent anyone who is not on the research team from knowing that you gave us information, or what that information is.

The study information collected from your participation in the study may be entered into a secure computer system. The study doctor is committed to maintaining the privacy of every study subject and any personal information submitted and follows the principles of the Health Insurance Portability and Accountability Act (HIPAA) of 1996. All data are stored at a secure site behind a firewall, which monitors and protects against unauthorized access.

Your charts and any other items containing confidential items will be stored in a safe place overnight and not left on the desk. Charts will not be left in an area where others might have access to them.

You should know, however, that there are some circumstances in which we may have to show your information to other people. For example, the law may require us to show your information to a court or to tell authorities if you report information about a child being abused or if you pose a danger to yourself or someone else.

Officials of the University of Kentucky, the Arthritis Foundation, Sobi, members of an independent Data Safety Monitor Board, the Center for Clinical and Translational Science, Bluegrass Research Consultants and researchers at Duke University, the Cleveland Clinic Foundation, and University of California San Francisco (UCSF), may look at or copy pertinent portions of records that identify you.

If you withdraw from the study or are withdrawn, data collected to that point will be kept.

CAN YOUR TAKING PART IN THE STUDY END EARLY?

If you decide to take part in the study you still have the right to decide at any time that you no longer want to continue. You will not be treated differently if you decide to stop taking part in the study. The individuals conducting the study may need to withdraw you from the study and the study medication will no longer be provided free of charge. This may occur if you are not able to follow the directions they give you, if they find that your being in the study is more risk than benefit to you, or if the agency funding the study decides to stop the study early for a variety of scientific reasons.

ARE YOU PARTICIPATING OR CAN YOU PARTICIPATE IN ANOTHER RESEARCH STUDY AT THE SAME TIME AS PARTICIPATING IN THIS ONE?

You may not take part in this study if you are currently involved in another research study. It is important to let the investigator/your doctor know if you are in another research study. You should also discuss with the investigator before you agree to participate in another research study while you are enrolled in this study.

WHAT HAPPENS IF YOU GET HURT OR SICK DURING THE STUDY?

If you believe you are hurt or if you get sick because of something that is due to the study, you should call Dr. Austin Stone at (859) 218-3065 immediately. If you are become hurt or sick after normal business hours or on the weekend or holiday, please call (859) 323-5321 and ask to speak to the orthopedic resident on call. Dr. Stone will determine what type of treatment, if any, that is best for you at that time.

It is important for you to understand that the University of Kentucky have funds set aside to pay for the cost of any care or treatment that might be necessary because you get hurt or sick while taking part in this study. Also, the University of Kentucky will not pay for any wages you may lose if you are harmed by this study.

Therefore, these costs will be your responsibility.

You do not give up your legal rights by signing this form.

WILL YOU RECEIVE ANY REWARDS FOR TAKING PART IN THIS STUDY?

You will receive up to $150.00 for taking part in this study. You will receive $50.00 for each MRI you complete (Visits 1, 5 and 6). Payment will be in the form of a check which will be mailed approximately four to six weeks following the study visit. If the participant is your child the compensation will be mailed to your child.

If you leave the study early, or if we have to take you out of the study, you will be paid only for the visits you have completed.

If you earn $600.00 or more by participating in any research, it is potentially reportable for tax purposes.

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS, CONCERNS, OR COMPLAINTS?

Before you decide whether to accept this invitation to take part in the study, please ask any questions that might come to mind now. Later, if you have questions, suggestions, concerns, or complaints about the study, you can contact the investigator, Dr. Stone at (859) 218-3065. If you have any questions about your rights as a volunteer in this research, contact the staff in the Office of Research Integrity at the University of Kentucky between the business hours of 8am and 5pm EST, Mon-Fri at 859-257-9428 or toll free at 1-866-400-9428. We will give you a signed copy of this consent form to take with you.

WHAT IF NEW INFORMATION IS LEARNED DURING THE STUDY THAT MIGHT AFFECT YOUR DECISION TO PARTICIPATE?

If the researcher learns of new information in regards to this study, and it might change your willingness to stay in this study, the information will be provided to you. You may be asked to sign a new informed consent form if the information is provided to you after you have joined the study.

POTENTIAL FUTURE USE

Contacting Research Subjects for Future Studies

Do you give your permission to be contacted in the future by Cale Jacobs, PhD or his research staff regarding your willingness to participate in future research studies about how to prevent, detect, or treat ACL tears and painful effusions?

☐ **Yes** ☐ **No** _____**Initials**

WHAT ELSE DO YOU NEED TO KNOW?

The sponsor of the study is Dr. Austin Stone, MD, The Arthritis Foundation is providing financial support for this study. Swedish Orphan Biovitrium (Sobi) is providing Kineret®.

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

The sample(s) (blood or fluids) that you are giving might be used in studies that lead to new products for research, diagnosis or treatment. These products might have some commercial value. There are no plans to provide financial compensation to you should this occur.

AUTHORIZATION TO USE OR DISCLOSE YOUR IDENTIFIABLE HEALTH INFORMATION

The privacy law, HIPAA (Health Insurance Portability and Accountability Act), requires researchers to protect your health information. This form describes how researchers may use your information. Please read it carefully.

Your health information that may be accessed, used and/or released includes:

- Demographic information [Name, initials, gender, race, age, study number, mailing address, home phone number, social security number, and Medicare ID number (if applicable)
- Dates including date of birth, hospital admissions/discharges, study visits
- Results of physical exams, x-rays, blood tests, urinalysis, MRIs and other diagnostic and medical procedures related to this study
- Questionnaire answers
- Medical and medication
- Pregnancy test results

The Researchers may use and share your health information with:

- The University of Kentucky's Institutional Review Board/Office of Research Integrity.
- Law enforcement agencies when required by law.
- UK Hospital or University of Kentucky representatives if applicable.
- UK Center for Clinical and Translational Science (CCTS)
- Austin Stone, MD
- Arthritis Foundation
- Swedish Orphan Biovitrium (Sobi)
- Duke University
- University of California San Francisco (UCSF)
- Cleveland Clinic Foundation
- Bluegrass Research Consultants
- FDA

The researchers agree to only share your health information with the people listed in this document. Should your health information be released to anyone that is not regulated by the privacy law, your health information may be shared with others without your permission; however, the use of your health information would still be regulated by applicable federal and state laws.

You may not be allowed to participate in the research study if you do not sign this form. If you decide not to sign the form, it will not affect your:

- **Current or future healthcare at the University of Kentucky**
- **Current or future payments to the University of Kentucky**
- **Ability to enroll in any health plans (if applicable)**

- **Eligibility for benefits (if applicable)**

After signing the form, you can change your mind and NOT let the researcher(s) collect or release your health information (revoke the Authorization). If you revoke the authorization:

You will send a written letter to: Cale Jacobs, PhD to inform him of your decision.

University of Kentucky Medical Center
Dept. of Orthopaedic Surgery and Sports Medicine
Kentucky Clinic Room K401
740 S. Limestone Street
Lexington, KY 40536

You understand that you will not be allowed to review the information collected for this research study until after the study is completed. When the study is over, you will have the right to access the information.

The use and sharing of your information has no time limit.

If you have not already received a copy of the Privacy Notice, you may request one. If you have any questions about your privacy rights, you should contact the University of Kentucky's Privacy Officer between the business hours of 8am and 5pm EST, Mon-Fri at: (859) 323-1184.

You are the subject or are authorized to act on behalf of the subject. You have read this information, and you will receive a copy of this form after it is signed.

_____ _____
Signature of research subject (*if applicable:*) Date

_____ _____
Printed name of research subject

_____ _____
Name of [authorized] person obtaining informed consent/HIPAA authorization Date

_____
Signature of Principal Investigator or Sub/Co-Investigator

Below is a Visit Table that describes for you what will happen at each study visit. Those tests being performed for the research study are noted as **R** and will be performed at no cost to you. Those tests and procedures being performed as part of our standard of care are noted as **NR** and their cost will be charged to either you or your insurance provider.

Visit Table

Procedures	Screening (Visit 1)		Visit 2[e]	Visit 3	Visit 4	Visit 5	End of Study Visit 6
Time point	1-28 days post injury		Surgery day or 4-6 weeks post injury	4-14 day after Visit 2	6 months after Visit 2	12 months after Visit 2	24 months after Visit 2
Informed Consent	**R**						
Demographics	**R**						
Medical history	**R**		**R**	**R**	**R**	**R**	**R**
Randomization	**R**						
Administer Investigational Product	**R**						
Concurrent meds	**R**		**R**	**R**	**R**	**R**	**R**
Physical Exam	**R**						
Range of Motion	**NR**		**NR**	**NR**	**NR**	**NR**	**NR**
Vital signs	**R**						
Height	**R**						
Weight	**R**						
Questionnaires	**R**		**R**		**R**	**R**	**R**
Knee Aspiration	**NR**		**R**[a]	**R**[h]			
Biomarkers	**R**		**R**	**R**		**R**[d]	**R**[d]
Safety Lab Tests[b]	**R**						
Urine pregnancy tests[c]	**R**						
Adverse event evaluation	**R**		**R**	**R**	**R**	**R**	**R**
X-Ray[f]	**NR**						
MRI[g]	**R**					**R**	**R**

a: Should a subject be enrolled into the study and choose not to undergo ACL reconstruction aspiration at time of surgery will be omitted.
b: Albumin, alkaline phosphatase, total bilirubin, bicarbonate, BUN, calcium, chloride, creatinine, glucose, LDH, phosphorus, potassium, total protein, SGOT [AST], SGPT [ALT], sodium.
c: Urine pregnancy test (women of childbearing potential).
d: Serum and urine only
e. Should a subject be enrolled into the study and choose not to undergo ACL reconstruction, subject will receive treatment according to this protocol.
f. All subjects must have standardized MTP-2 weight bearing x-ray. Documentation of closed growth plates at screening will be noted in the routine SOC x-ray
g. All subjects enrolled will have an MRI performed regardless if surgery is to be scheduled or not. However, randomization can be performed prior to MRI as the MRI examination is not necessary or required to diagnose the ACL tear.
h. We will only perform the aspiration at Visit 3 if participants had elected to have surgery performed, and if they have fluid on their knee.