Consent of an Adult to Be in a Research Study

In this form "you" means a person 18 years of age or older who is being asked to volunteer to participate in this study.

Participant's Name_____

Medical Record # _____

What is the purpose of this form?

This form will provide you with information about this research study. You do not have to be in the study if you do not want to. You should have all your questions answered before you agree to be in this study.

Please read this form carefully. If you want to be in the study, you will need to sign this form. You will be given a copy of this form.

Who is funding this study?

This study is being funded by Flexion Therapeutics.

Key Information About This Research Study

Principal Investigator:	Brian Werner, MD 545 Ray C. Hunt Drive Charlottesville, VA 22903
Sponsor:	Flexion Therapeutics

You are being asked to take part in a research study. You do not have to take part in this study. You should only agree to take part in this study after reading this consent form and discussing it with the study team. You may also discuss this with your family, friends, health care providers or others before you make a decision.

What problem is this study trying to solve?

This study is trying to find out if Zilretta FX006 (triamcinolone acetonide) extended release injection is effective at decreasing shoulder pain and increasing function in patients with adhesive capsulitis.

You are being asked to take part in this study because your doctor has determined that you have adhesive capsulitis, and that you may benefit from a steroid injection.

Why would you want to take part in this study?
You might like to take part in this study because your shoulder may feel better after the injection, and allow you to do more things with your shoulder.

Why would you NOT want to take part in this study?
You might not want to take part in this study because it requires extra study visits, and requires you to complete questionnaires when you come back to see your doctor. This injection is also not yet approved by the FDA to be used in the shoulder.

What will I have to do if I take part in this study?
Full details of all the procedures are found later in this form.

If you take part in this study you will:

- Have an injection of FX006 (an unapproved drug) in your shoulder
- Follow up with your doctor several times over the next year
- Answer questionnaires about how you are feeling during your visits
- If diabetic, you will have you blood glucose checked 4-6 hours after your injection

What is the difference between being in this study and getting usual care?
If you choose not to take part in this study,

- You will not receive a FX006 injection, but rather a different kind of steroid injection
- You will not have to follow up with your doctor after your injection
- If diabetic, you will not have to have your blood glucose checked 4-6 hours after your injection
- You will not have to answer questionnaires when you have visits with your doctor

This is a research study about FX006, an experimental drug that has not been proven to be safe or helpful in the shoulder joint. This drug is not approved by the U.S. Food and Drug Administration (FDA) for use in the shoulder, but is approved in the knee joint. So far, the drug has been given to 687 people with orthopeadic injuries.

What other treatments may I receive if I decide to not take part in this study?
The following alternative treatments are available to you if you decide not take part in this study:

- Physical therapy
- Get a different type of steroid injection

- Have surgery to break up adhesions in your shoulder

Your participation in this study will require 5 or 6 study visits over 1 year. Each visit will last about 1 hour.

What will happen if you are in the study?

SCREENING (visit will last about 1 hour)

Visit 1

If you agree to participate, you will sign this consent form before any study related procedures take place. Before you can start in the study, there will be a screening period. You will have tests and procedures during this time to make sure you are eligible and it is safe for you to participate. These include the following:

- Shoulder exam including range of motion, tenderness, strength, and stability measures
- An x-ray of your shoulder as part of your standard of care
- Ask you how much pain you're having in your shoulder
- Ask you questions about your medical and surgical history and to complete the following questionnaires:
    - ASES activities of daily living- this measures your ability to carry out activities of daily living
    - Visual Analog Scale- to measure how much pain you are in
    - VR-12 Health Survey- this is done to measure how much your health has impacted your usual activities
    - PROMIS- this is done to measure the level of your physical function

If these tests show you are eligible, you will return to the clinic to begin study treatment, or you may start study treatment the same day.

STUDY TREATMENT

Visit 2 (this visit will last 1 hour)

In this study, you will have a medication injected into your shoulder. The medicine that is being injected is called Zilretta FX006, which is a steroid. This medicine is approved by the FDA for use in the knee, when treating osteoarthritis. In this study, we are using it in the shoulder to treat adhesive capsulitis.

Your injection is part of your standard of care treatment, but the medication in the injection is being used for research purposes only. The injection is done under ultrasound guidance. This is part of your standard of care for getting an injection in your shoulder.

If you are diabetic, you will check your blood glucose 4-6 hours after your shoulder injection and report it to a member of the study.

FOLLOW UP (1, 3, 6, and 12 months after injection):

Visits 3-6 (these visits will last 30 minutes)
If you choose to participate in this study, you will follow up with the study team 4 times after your injection. You will come back 1 month, 3 months, 6 months, and 1 year after your shoulder injection. During these visits, you will be asked about any changes in your health. We will ask you whether you have had any other injections in your shoulder at each visit. You will also be asked to answer questionnaires and have a shoulder exam. These visits will occur in the clinical research unit, at 560 Ray C. Hunt Drive, with a member of the study team.

All of the procedures done at your follow up visits are being done for research purposes.

During this study, you will be asked to fill out some questionnaires. These questionnaires ask about:

- how you are feeling
- how you shoulder is feeling
- your activity level
- your emotions
- how much pain you are in

These questionnaires will take about 15 minutes to complete.

During the research, if we learn you are having thoughts about suicide or hurting yourself or others, the research staff will ask you more questions about your thoughts. Based on your response, the staff may provide you with help to get treatment. This may include: working with you to contact your doctor or therapist, referral to a therapist to discuss your thoughts, contact a trusted family member, significant other or clergy or work with you on a plan that may include getting you to a hospital for safety and treatment.

Study Schedule

	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Visit 6
Visit Designation	Baseline	Injection	1 Month	3 Months	6 Months	12 Months
Informed Consent	X					
Review of Inclusion/Exclusion	X					
Review of Medical History	X					
Shoulder Exam and Evaluation	X		X	X	X	X
Injection (Zilretta FX006)		X				
Blood Glucose Measurement		X*				
Questionnaires	X		X	X	X	X

*blood glucose is measured 4-6 hours after the injection in diabetic patients only

END OF STUDY:

Once you have completed your 12 month visit, you will be done participating in the research study.

What are your responsibilities in the study?

You have certain responsibilities to help ensure your safety.

These responsibilities are listed below:

- You must come to each study visit.
- You must be completely truthful about your health history.
- Follow all instructions given.
- You should tell the study doctor or study staff about any changes in your health or the way you feel.
- Answer all of the study-related questions completely.

If you want to know about the results before the study is done:

During the study your study leader will let you know of any test results that may be important to your health. In addition, as the research moves forward, your study leader will keep you informed of any new findings that may be important for your health or may help you decide if you want to continue in the study. The final results of the research will not be known until all the information from everyone is combined and reviewed. At that time you can ask for more information about the study results.

What are the risks of being in this study?

The risks of this injection for use in the shoulder are still unknown. This product has not yet been approved by the FDA for use in the shoulder. The risks listed below are based off of the risks that are associated with use of this injection in the knee, which is FDA approved.

Risks and side effects related to the Zilretta FX006 injection:
Zilretta may alter the bodys response to infection. Should you develop signs of infection seek medical attention and inform your health provider that you received a long-lasting steroid injection.

Likely

- Injection site pain
- Bruising at the injection site
- Sinusitis
- cough

Less Likely

- Swelling in injection area
- Headache

Rare but serious

- Allergic reaction to the medicine (Zilretta FX006)- this could be a rash, hives, or more serious body reaction, that could potentially be life threatening

Risks from Completing Questionnaires
Some of the questions asked may be upsetting, or you may feel uncomfortable answering them. If you do not wish to answer a question, you may skip it and to the next question.

Other unexpected risks:
You may have side effects that we do not expect or know to watch for now. Call the study leader if you have any symptoms or problems.

Could you be helped by being in this study?

You may or may not benefit from being in this study. Possible benefits include an increase in your shoulder function and your shoulder feeling better. In addition, information researchers get from this study may help others in the future.

What are your other choices if you do not join this study?

You do not have to be in this study to be treated for your illness or condition. You can get the usual treatment even if you choose not to be in this study. The usual treatment would include:

- A corticosteroid injection in your shoulder that is not Zilretta FX006
- You will not have to complete questionnaires at your clinic visits

If you are an employee of UVa your job will not be affected if you decide not to participate in this study. If you are a student at UVa, your grades will not be affected if you decide not to participate in this study.

Will you be paid for being in this study?

You will be paid $200 ($50 for each completed follow up visit) for finishing this study by check in the mail.

You should get your payment about 2-4 weeks after each visit. The income may be reported to the IRS as income.

If you do not finish the study, you will be paid $50 for each visit you have finished.

If you owe money to any Virginia state agency, the state can use the money you earn in this study to pay those debts. These state agencies include the UVa Medical Center, VCU Medical Center or a college or university. The money may be withheld to pay back debt for such things as unpaid medical bills, taxes, fines, child support. Even if this happens, the money you earn may be reported to the IRS as taxable income.

Will being in this study cost you any money?

The following procedures/tests, which are being done for research purposes, will be provided at no cost to you or your health insurance: questionnaires, blood glucose test (if diabetic), and any visits done in the clinical research unit (1 month, 3 month, 6 month, and 12 month). The drug used in this study is being provided at no cost to you. If any of the post-injection visits occur in the UVA Sports Medicine clinic with a doctor or PA, it will be billed to you/your insurance.
You and/or your insurance company must pay for any tests or care given beyond what is required in this study. In addition, you and/or your health insurance may also have to pay for other drugs or treatments that are given to help you control any side effects. You will have to pay for any costs not covered by your health plan. You may be responsible for any co-payments or deductibles. You may wish to ask your insurance company for an estimate of what these costs might be or if pre-approval is required.

You will be responsible for the cost of travel to come to any study visit and for any parking costs.

What if you are hurt in this study?

You do not give up any legal rights, such as seeking compensation for injury, by signing this form. If you feel you have been injured as a result of this study you may contact the Principal Investigator or the IRB (phone numbers are located near the end of this form). If you are hurt as a result of being in this study, there are no plans to pay you for medical expenses, lost wages, disability, or discomfort. The charges for any medical treatment you receive will be billed to your insurance. You will be responsible for any amount your insurance does not cover.

What happens if you leave the study early?

You can change your mind about being in the study any time. You can agree to be in the study now and change your mind later. If you decide to stop, please tell us right away. You do not have to be in this study to get services you can normally get at the University of Virginia.

Even if you do not change your mind, the study leader can take you out of the study. Some of the reasons for doing so may include

a) Your study physician is concerned about your health
b) The side effects of the treatment are too dangerous for you
c) New information shows the treatment will not work or is not safe for you
d) You do not follow your doctor's instructions

If you decide to stop being in the study, we will ask you to contact the research team, and let them know that you no longer wish to participate.

Any data collected about you up until the time you leave the study must be kept in order to determine the results of the study.

How will your personal information be shared?

The UVa researchers are asking for your permission to gather, use and share information about you for this study. If you decide not to give your permission, you cannot be in this study, but you can continue to receive regular medical care at UVA.

If you sign this form, we may collect any or all of the following information about you:

- Personal information such as name, address and date of birth
- Social Security number ONLY IF you are being paid to be in this study
- Your health information if required for this study. This may include a review of your medical records and test results from before, during and after the study from any of your doctors or health care providers. This may include mental health care records, substance abuse records, and/or HIV/AIDS records.

Who will see your private information?

- The researchers to make sure they can conduct the study the right way, observe the effects of the study and understand its results
- People or groups that oversee the study to make sure it is done correctly
- The sponsor(s) of this study, and the people or groups it hires to help perform or review this research

- Insurance companies or other organizations that may need the information in order to pay your medical bills or other costs of your participation in the study
- Tax reporting offices (if you are paid for being in the study)
- People who evaluate study results, which can include sponsors and other companies that make the drug or device being studied, researchers at other sites conducting the same study, and government agencies that provide oversight such as the Food and Drug Administration (FDA) if the study is regulated by the FDA.
- If you tell us that someone is hurting you, or that you might hurt yourself or someone else, the law may require us to let people in authority know so they can protect you and others.

Information about you and/or samples from you may be given to other researchers outside of the University of Virginia after all identifiers such as name, address, phone number have been removed.

Some of the people outside of UVa who will see your information may not have to follow the same privacy laws that we follow. They may release your information to others, and it may no longer be protected by those laws.

The information collected from you might be published in a medical journal. This would be done in a way that protects your privacy. No one will be able to find out from the article that you were in the study.

Information obtained from you during this study will not be used in future research.

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.

What if you sign the form but then decide you don't want your private information shared?

You can change your mind at any time. Your permission does not end unless you cancel it. To cancel it, please send a letter to the researchers listed on this form or complete the "Leaving the Study Early" part of this form and return it to the researchers. Then you will no longer be in the study. The researchers will still use information about you that was collected before you ended your participation.

A copy of this consent form will be put in your medical record. (This is not the same as the record of this research study.) This means that everyone who is allowed to see your medical records will be able to find out that you are in this study. This is done so your regular doctors

will know what you receive as part of this study. If you have other health problems during the study, they will be able to treat you properly.

Please contact the Principal Investigator listed earlier in this form to:

- Obtain more information about the study
- Ask a question about the study procedures or treatments
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished
- Express a concern about the study

Principal Investigator: Brian Werner, MD
545 Ray C. Hunt Dr., Charlottesville VA, 22903
Telephone: 434-243-0265

What if you have a concern about this study?

You may also report a concern about this study or ask questions about your rights as a research subject by contacting the Institutional Review Board listed below.

University of Virginia Institutional Review Board for Health Sciences Research
PO Box 800483, Charlottesville, Virginia 22908
Telephone: 434-924-9634

When you call or write about a concern, please give as much information as you can. Include the name of the study leader, the IRB-HSR Number (at the top of this form), and details about the problem. This will help officials look into your concern. When reporting a concern, you do not have to give your name.

Signatures

What does your signature mean?

Before you sign this form, please ask questions about any part of this study that is not clear to you. Your signature below means that you have received this information and all your questions have been answered. If you sign the form it means that you agree to join the study.

You will receive a copy of this signed document.

Consent From Adult

_____	_____	_____
PARTICIPANT (SIGNATURE)	PARTICIPANT (PRINT)	DATE

To be completed by participant if 18 years of age or older.

Person Obtaining Consent

By signing below you confirm that you have fully explained this study to the potential subject, allowed them time to read the consent or have the consent read to them, and have answered all their questions.

_____	_____	_____
PERSON OBTAINING CONSENT (SIGNATURE)	PERSON OBTAINING CONSENT (PRINT)	DATE

Signature of Impartial Witness

If this consent form is read to the subject because the subject is blind or illiterate, an impartial witness not affiliated with the research or study doctor must be present for the consenting process and sign the following statement. The subject may place an X on the Participant Signature line above.

I agree the information in this informed consent form was presented orally in my presence to the **identified individual(s)** who has had the opportunity to ask any questions he/she had about the study. I also agree that the **identified individual(s)** freely gave their informed consent to participate in this trial.

Please indicate with check box the identified individual(s):

☐ Subject

_____	_____	_____
IMPARTIAL WITNESS (SIGNATURE)	IMPARTIAL WITNESS (PRINT)	DATE

Notification of My Health Care Provider

Your health care provider will be notified of your participation in this study.

Leaving the Study Early

Signatures should be obtained in this section if the subject decides to leave the study early.

If you leave the study early the study leader will keep the data collected about you up until the time you leave the study to help determine the results of the study.

Check one option below:

____ I am withdrawing my consent from the intervention or treatment part of this study but agree to continue to have follow up information about me collected by the study team.
The follow up information will be collected by:

- Obtaining information from my medical records

____ I am withdrawing my consent for this study. No additional information may be collected about me including follow up information from my medical records.

Consent From Adult

_____	_____	_____
PARTICIPANT (SIGNATURE)	PARTICIPANT (PRINT)	DATE

To be completed by participant if 18 years of age or older.

Person Obtaining Consent

By signing below you confirm that you have fully explained the implications of withdrawing from the study to the subject and have answered all their questions.

_____	_____	_____
PERSON OBTAINING CONSENT (SIGNATURE)	PERSON OBTAINING CONSENT (PRINT)	DATE