Official Title: Study of Testosterone and rHGH in FSHD (STARFiSH): A Proof-of-Concept Study

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CONSENT FORM

Study of Testosterone and rHGH in FSHD (STARFiSH)

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This consent form describes a research study, what you may expect if you decide to take part and important information to help you make your decision. Please read this form carefully.

The study staff will explain this study to you. Please ask questions about anything that is not clear before you agree to participate. You may take this consent form home to think about and discuss with family or friends.

- Being in this study is voluntary – it is your choice.
- If you join this study, you can change your mind and stop at any time.
- If you choose not to take part, your routine medical care will not be changed in any way.
- There are risks from participating and you should understand what these mean to you.

Introduction

You are being asked to take part in this study because you are a man with facioscapulohumeral muscular dystrophy (FSHD).

Purpose of Study

The purpose of this study is to evaluate whether or not a combination of two drugs (recombinant human growth hormone (rHGH) and testosterone) can be safely given to patients with FSHD and possibly improve walking, strength, muscle mass, quality-of-life, and functional ability.

Overview of the Study

This study will include the following:

I. Screening/baseline visit to the University of Rochester Clinical Research Center (CRC). During this visit a series of evaluations will be carried out to determine how you are affected by FSHD. An additional aspect of this visit is you will be started and monitored on the study drugs (testosterone and rHGH).

II. Follow-up visits to the CRC 8 weeks, 16 weeks, 24 weeks, and 36 week after the baseline visit. During these visits some of the same evaluations from the baseline visit will be repeated to determine how your condition has changed over time.

III. Telephone evaluations. You will receive a telephone call every week while you are enrolled in the study, except for the weeks when you come to the CRC for a study visit. The study coordinator will call you to check on any side effects you may be experiencing and to make sure you are taking your study medication as directed.

Testosterone is a naturally occurring androgen that is produced in both men and women. Testosterone promotes protein synthesis and has anabolic effects on both muscle and bone. It is commonly utilized for men with hypogonadism and conditions associated with low or no endogenous testosterone. It is also recommended for men to improve libido and erectile dysfunction. In women, testosterone supplementation has been used for muscle atrophy associated with acquired immune deficiency syndrome, inoperable metastatic breast cancer, low libido, sexual dysfunction, muscle wasting, and as a postmenopausal therapy. The Endocrine Society currently recommends testosterone to: 1) increase muscle strength and lean body mass in patients with HIV; and 2) improve bone mineral densities in patients receiving high dosages of glucocorticoids.

Human Growth Hormone (HGH) is a naturally occurring peptide hormone that is produced in the pituitary gland of men and women. Like testosterone, HGH can stimulate cell growth and regeneration. Patients with low HGH levels experience exercise intolerance, low bone mineral density, changes in body composition, and a worsening cholesterol profile. HGH supplementation can ameliorate these impairments. Recombinant HGH (rHGH) is a synthesized preparation of HGH that has been used to treat children and adults with growth hormone deficiency, as well as those with muscle wasting, Turner syndrome, Prader-Willi syndrome, chronic renal failure, and short stature.

When given together, rHGH and testosterone have been found to safely improve muscle mass, strength, and aerobic capacity in men; however these studies have not been done in patients with FSHD.

These studies included patients with low or low normal hormone levels, which may not be the case for you.

Number of Subjects

We expect to screen up to 30 subjects to enroll approximately 20 subjects in this study at the University of Rochester.

Duration of the Study

Your participation in the study will last 36 weeks. You will receive study medications for 24 of these weeks. You will also be asked to travel to the University of Rochester in Rochester, NY five times. The first visit will require you to stay at the research center for 24 hours. The other four visits will require you to stay for approximately five or six hours.

Description of Study Procedures

If you decide to participate in this study, you will have an initial study visit to determine if you are eligible to participate. All study visits will take place at the University of Rochester Clinical Research Center (CRC).

The initial activities during your first visit will include:

- Review of the study procedures/consent: Upon arrival at the CRC, the information in this consent form will be reviewed with you in detail. You will be provided the opportunity to ask any questions that you have regarding this study.
- Your height, weight, and vital signs will be recorded.
- Standard blood testing. Up to 4 tablespoons of blood will be taken from a vein in your arm. This blood will be used for laboratory testing including: blood counts, blood chemistries, hormone levels, prostate markers, muscle enzymes, and thyroid, kidney, and liver function. You will receive copies of these test results for your personal records. You will be asked to fast prior to this testing. A breakfast will be provided to you immediately after you provide blood testing.
- A urine sample. This sample will be collected to test your kidney function.
- An assessment of your walking. As part of this testing you will complete a 6-minute walk test (6MWT). During this test, you will be asked to walk as far as you can in 6 minutes. You may use a walker, cane, or bracing if needed. Your blood pressure, heart rate, and breathing rate will be recorded before and after this test.
- A brief physical exam will be performed by a neurologist. This exam will include testing of your strength, movement, and muscle function and a review of your medical history and medications. This physician will also listen to your heart and lungs.
- A digital rectal exam will be performed to ensure that you do not have signs of prostate disease. You will also complete a questionnaire about your prostate health.
- An electrocardiogram (ECG/EKG) will per performed to look for evidence of cardiac disease.

Once you have completed the above screening activities, a study physician will review all results to determine if you are eligible for the study. If you are willing to continue in the study, the following procedures will be performed:

1) You will fill out the “FSHDHI” questionnaire. The FSHDHI is a “paper and pencil” survey designed specifically for people with FSHD. The FSHDHI asks questions about 14 separate categories that pertain to your abilities and the challenges you face related to your muscle disease. It takes approximately 20 minutes to complete.

2) You will be asked to complete additional standardized surveys that ask about your overall health, fatigue, sleepiness, depression, and your exercise habits. These “paper and pencil” questionnaires take about 30-40 minutes to complete.

3) You will participate in the FSHD Specific Composite Outcome Measure (FSHD-COM). A clinical evaluator (physical therapist) will ask you to perform different tasks so they can evaluate how your body moves and functions. For example, you will be asked to lift your arms above your shoulders, and get up from a chair. This testing takes about 60 minutes to complete.

4) The clinical evaluator will also test your strength in multiple muscle groups using both manual techniques and a digital force gauge. Testing takes about 60 minutes to complete.

5) The amount of muscle tissue, fat tissue, and bone in your body will be measured using dual energy Xray absorptiometry (DEXA). The DEXA machine will scan over your body while you lie still for about 15 minutes.

6) Your respiratory function will be tested. You will be asked to blow into a tube to measure how much air you can move in one breath.

7) You will have a formal eye exam performed. A doctor will look at the back of your eye using an ophthalmoscope.

8) After lunch and following these procedures you will be administered your first dose of study medication (testosterone). A nurse will instruct you how to administer this medication by an injection. If you do not have the strength to administer the study medication, a designated person such as a family member, caregiver, or friend can also be taught to administer the medication. After your first dose you will have your blood pressure, pulse, and respiratory rate rechecked and you will be asked about any immediate side effects.

9) About an hour later you will receive your first dose of rHGH. As with the testosterone medication, you (or a family member) will be taught how to administer this medication.

10) You will stay on the research center until the next morning. Your first visit will be officially completed after you have had breakfast.

You will take rHGH daily for a total of 24 weeks. You will also receive testosterone once every 2 weeks during this 24 week period. Between the 24 week period and the 36 week period you will not receive either study medication but will remain in the study for clinical monitoring.

You will be given study medication to take home with you following your baseline visit. You will subsequently receive supplies of both rHGH and testosterone at your week 8 and week 16 study visits.

Our study coordinator will contact you every week to answer questions and enquire about any potential effects or side effects you have noticed from the study medications.

You will return to our center at 8 weeks, 16 weeks, 24 weeks, and 36 weeks. During these visits you will receive the same testing that was performed at your first screening/baseline visit. The exception to this is that you will only receive repeat DEXA scans at 16 weeks, 24 weeks, and 36 weeks and will not receive one at 8 weeks. Your follow-up visits will be shorter than your original visit and last approximately 5-6 hours. You will not be required to stay overnight during your return visits.

After your 24 week visit, you will discontinue taking both study medications.

The following information about your study participation will be included in your electronic health record:

- Documentation that you are in this study
- Results of testing from your standard blood and urine samples

Meals during study visits

While you are staying on the Clinical Research Center at the University of Rochester Medical Center (CRC), you will receive a diet that is planned in advance by the CRC dietitian.

Study Medication

You will be asked to the take two study medications as part of this trial. These include testosterone injections every two weeks, and rHGH injections every day.

The study coordinator will review with you instructions about how and when you should take your study medication. It is important that you remember to bring any unused drug with you to your study appointments.

If you begin to have side effects that might be related to the study medication, the study doctor may want to reduce the dose of one or both of the study medications that you are taking or have you stop one or both medications. If you stop taking a medication because of side effects; or, if you no longer want to take the study medication, you can still continue to attend the remainder of your study visits. If you decide to stop taking a study medication and no longer wish to be in the study, we will ask that you return for a final study visit. The procedures at this visit will be the same as those at your first visit.

Tell the study doctor before you take any new medication even if it is prescribed by another doctor for a different medical problem.

Risks of Study Procedures

There are risks when you participate in a research study. The risks of specific tests in the STARFiSH study are listed below.

For some subjects, completing surveys and answering specific questions about how your disease affects your physical functioning and emotional health may cause feelings of distress. We will ask you about depression and thoughts of suicide. We will take safety measures if we believe you may be at risk of suicide, including escorting you to emergency psychiatric care or contacting other emergency services.

Testing your muscle strength and function may cause bruising or temporary muscle soreness. For bedside respiratory testing, subjects may have difficulty breathing or may feel fatigued. To minimize these risks, all study staff are fully trained in testing techniques and they will ask you how you are feeling throughout the course of the visit. You will be asked to report any concerns you have to study staff immediately.

During the DEXA scan, there is no pain, but there could be minor discomfort from lying in the same position for about 15 minutes. The amount of radiation you will be exposed to during the study due to the DEXA scans is relatively small. There is no known

minimum level of radiation exposure that is recognized as being totally free of the risk of causing genetic defects (cellular abnormalities) or cancer. However, the risk associated with the amount of radiation exposure that you will receive from this study is considered to negligible when compared to other everyday risks. Your risk of radiation-related injury may depend on your total lifetime exposure, not just the radiation dose you will be receiving in this study.

Blood draws may cause pain, redness, bruising or infection at the site of the needle stick. Rarely some people feel lightheaded or faint. The study team member may apply numbing cream to the area so that the needle stick won't hurt as much.

An electrocardiogram (ECG/EKG) is a painless test that is performed while you lie still for about 5 minutes. It involves placing electrodes on the chest and arms/legs and recording the electrical activity of your heart. Other than possibly experiencing some minor skin irritation from the electrodes there are no anticipated risks related to completing the electrocardiogram.

A digital (finger) rectal examination (DRE) is done to check for signs of prostate abnormalities. The DRE will also be combined with a blood test (prostate-specific antigen). These two tests are often done together to check for prostate irregularities. During the rectal examination, the doctor gently puts a lubricated, gloved finger of one hand into the rectum. You may feel some discomfort or pain during the DRE. Your doctor must press firmly on the prostate to feel for problems. This pressure may make you feel the need to urinate. The examination may be painful if the prostate gland is swollen or irritated. A small amount of bleeding from the rectum may occur after an examination, especially if hemorrhoids or anal fissures are present. In rare cases, you may feel lightheaded and faint. As a result of the DRE and blood tests completed as part of this study, we may discover a prostate irregularity. You will be told if your results suggest that you are in need of further testing. The study doctor/staff will talk with you about the findings and your options. You may be told to follow up with your regular doctor or other specialists for future care.

Breathing tests may cause you to have difficulty breathing or you may feel fatigued during the test. If you have any of these symptoms, you should tell the study staff immediately.

A funduscopic examination is a study of the back of the eye. The doctor will look through the ophthalmoscope, which is simply a light with extra pieces (such as lenses) that allow the doctor to evaluate for signs of nerve swelling. Other than the light of the ophthalmoscope possibly causing some discomfort, there are no anticipated risks associated with this exam.

Because this study involves collecting personal, identifiable information about you, there is a potential for invasion of privacy or breach in confidentiality. To minimize this risk, we will assign you a study number instead of labeling the information we collect from you with your name [or medical record number]. All of the information we collect will be stored in a secure manner and only study team members will have access to it. 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 Web site will include a summary of the results. You can search this website at any time.

The study team may be notified if you receive other health care services at URMC or its Affiliates (e.g., visit to the emergency room). In addition, the following individuals may know you participated in this research and may see results of testing conducted for this study:

- Staff at the University of Rochester Medical Center and its Affiliates (e.g., Strong Memorial Hospital, Highland Hospital, URMC primary care, specialist physician offices) who have a reason to access your electronic health record.
- Individuals who request a copy of information from your health record for activities such as treatment or payment (e.g., medical insurance companies, worker's compensation).

Risk from Study Medications

Both testosterone and rHGH are both approved therapeutics for use in human populations.

Both testosterone and rHGH may cause side effects. Because everyone can have a different reaction to medications, you may experience some side effects from the study medications. Potential side effects include but are not limited to the below listed items. The most common side effects seen with these two medications are also highlighted in the provided drug inserts.

Risks of Study drugs:

Testosterone

Common

- **Dermatologic:** Acne (up to 8%), rash or discomfort at the injection site
- **Endocrine metabolic:** Increased breast size (1% to 3%)
- **Gastrointestinal:** Oral irritation (9.2%)
- **Neurologic:** Headache (1% to 6%)
- **Reproductive:** Large prostate (11.7%), increased PSA (prostate blood test) (1% to 11.1%)
- **Respiratory:** Inflammation of the nasal and throat passage (3.8% to 8.7%), nasal discharge (3.8% to 7.8%), nose bleed (3.8% to 6.5%), sense of smell altered (5.8%), bronchitis (3.8% to 4.3%), upper respiratory infection (3.8% to 4.3%), sinus infection (3.8%)

Serious

- **Cardiovascular:** Death, cardiovascular events, swelling, myocardial infarction, heart failure
- **Hematologic:** Blood clots (thromboembolic disorder), reduced blood cell counts
- **Hepatic:** Impaired bile flow, liver cancer, inflammation of the liver, liver damage
- **Neurologic:** Stroke, irritability or aggressive behavior, sleep apnea, visual changes, suicidal ideation, depression, carpal tunnel syndrome, potential drug abuse or dependence
- **Reproductive:** Benign enlargement of the prostate (Up to 2%), prostate cancer (up to 1.2%)

- **Respiratory:** Pulmonary embolism (blood clot of the lung)
- **Endocrine:** Weight gain, change in body hair, change in muscle bulk
- **Reproductive:** Male infertility

Other serious side effects, while very rare, may include: anaphylaxis (shock) reactions, congestive heart failure, or other life-threatening cardiovascular events.

While testosterone has not been shown to be a cause of cancer in humans, it is not recommended in patients with an active malignancy. You should not participate in this study if you have any preexisting history of cancer or if you are known to have cancer. In addition, testosterone may be associated with increase cardiovascular events in patients older than 65 and those with preexisting cardiac, kidney, or liver disease. To this end, you will not be eligible to participate in this clinical trial if you are greater than 65 years of age or if you have preexisting cardiac, kidney, or liver disease.

Growth Hormone

Common

- **Cardiovascular:** Swelling (up to 42%)
- **Dermatologic:** Injection site reaction, loss of fat at injection site, acne, psoriasis (patches of abnormal skin)
- **Hematologic:** Elevation in blood cell counts (11% to 12%), Hematoma (blood under the skin) (9%)
- **Musculoskeletal:** Joint pain (up to 27%), Muscle pain (up to 15%)
- **Neurologic:** Carpal tunnel syndrome (24%), Numbness (up to 17.3%), headache (up to 10.9%)
- **Respiratory:** Runny nose (up to 13.5%)
- **Other:** Flu-like symptoms (up to 22.9%), increased breast tissue size

Serious

- **Cardiovascular:** Disorder of cardiovascular system, high blood pressure
- **Endocrine metabolic:** Hypothyroidism (16%), impaired glucose tolerance (6%), diabetes (0.4%)
- **Gastrointestinal:** Inflammation of the pancreas (rare)
- **Immunologic:** Increased immune response to medication
- **Musculoskeletal:** Worsening scoliosis, hip dislocation (slipped upper femoral epiphysis)
- **Neurologic:** Brain tumor, increased intracranial pressure (pressure inside the skull), potential drug abuse or dependence
- **Other:** Worsening of preexisting cancer

While rHGH has not been shown to be a cause of cancer in humans, it is not recommended in patients with an active malignancy. You should not participate in this study if you have any preexisting history of cancer or if you are known to have cancer.

Prior to participation in this study, you will also be provided with the “label” information for both testosterone and rHGH to review with a member of our study team. These “labels” are used to educate patients and physicians who receive and prescribe these medications in the general community. Any question you have about either study medication or their label will be discussed.

The study team will be monitoring for side effects every week and at each study visit. Additionally, we will ask you to contact us if any symptoms occur.

Benefits of Participation
You might not benefit from being in this research study. The potential benefit to you from being in this study might be some improvement in muscle strength.

Alternatives to Participation
You do not have to participate in this study to receive care for your medical problem. Testosterone and rHGH are FDA approved drugs and can be prescribed by your regular neurologist or primary care physician.

New Study Findings
If we discover anything that might make you change your mind about continuing in the study, we will let you know.

Sponsor Support
The University of Rochester is receiving payment from the National Institutes of Health for conducting this research study. Pfizer, Inc is supplying the human growth hormone.

Financial Disclosure Statement
Dr. Heatwole has a copyright for the FSHD-HI that is being used in this study. This instrument could potentially be licensed from a pharmaceutical company at a future date.

Costs
There will be no cost to you to participate in this study. Procedures and tests performed as part of this study will be provided to you for no cost.

Reimbursement for Travel and Lodging
You will be reimbursed for reasonable out of pocket expenses after submission of receipts to the study team. You will only be reimbursed for expenses up to a maximum amount of $500 per visit. Such reimbursed expenses are not taxable. If you require a family member to assist with the administration of either or both medication in this study, you will also be reimbursed for your family member's travel expenses up to $500 for the initial visit only.

Payments
You will be paid $100 per visit for your 8 week, 16 week, 24 week, and 36 week visits (for a total of $400). For this study we use a subject payment system called Advarra Participant Payments. The system allows three ways to provide payment. You can choose: a reloadable debit card; direct deposit; or mailed paper checks. The study team will help you create a subject profile in the system. In order to provide payment, you will need to enter your name and date of birth into your subject profile**.** Depending on which payment method you choose, you may also need to enter your email address and banking information. If you already have an Advarra account (because you are in another study that uses this system), your existing profile will be used to provide payment. See the

‘**Information Sheet for Advarra Participant Payments”** for additional information.

Payment received for participation in research is considered taxable income. If you receive $600.00 or more in a calendar year from the University of Rochester or its affiliates, the University is required to report this information to the Internal Revenue Service (IRS) in a 1099 (Miscellaneous Income) form. If a 1099 is completed, you will be sent a copy of the form. Depending on the amount you are paid in this study, you may be asked to submit a W-9 form, which includes your Social Security Number.

Circumstances for Dismissal

In the event that you experience side effects of treatment or elevated drug levels, you may be asked to reduce or possibly even stop study drug, but you will not be asked to leave the study.

Early Termination

If you decide to stop taking the study drugs for any reason, you will be asked to return to the University of Rochester to complete all evaluations that were performed at your first visit. This is both for your safety and to help us determine how the drugs might be working.

Compensation for Injury

If you are directly injured by the drugs being studied, or by medical procedures needed because of this study, and you receive medical care for the injury, you may need to pay for that care. You will be reimbursed for reasonable and necessary medical costs for such care, but you might not be reimbursed for care covered and paid for by a third party like your health insurance provider, or costs such as required co-payments or deductibles related to that coverage. No other funds have been set aside to pay for such things as lost wages or expenses due to a current underlying illness or condition.

If your research injury is paid for by the University or the sponsor, we will collect your name, date of birth, gender, and Medicare Health Insurance Claim Number or Social Security Number to determine your Medicare status. This information will be used only in accordance with the law. If you are a Medicare beneficiary, information about the study you are in, and any payments made related to your injury, will be reported to the Centers for Medicare & Medicaid Services (CMS), in accordance with CMS requirements. This information will not be used for any other purpose.

Confidentiality of Records and Authorization to Use and Disclose Information for Research Purposes

The University of Rochester makes every effort to keep the information collected from you private. In order to do so, we will assign you a study number instead of labeling the information we collect from you with your name [or medical record number]. All of the information we collect will be stored in a secure manner and only study team members will have access to it.

Sometimes, however, researchers need to share information that may identify you with people that work for the University, regulators or the study sponsor.

If you have never received a copy of the University of Rochester Medical Center (URMC) and Affiliates Notice of Privacy Practices, please ask the investigator for one.

What information may be used and given to others?

The study doctor will get your personal and medical information. For example:

- Research records
- Records about phone calls made as part of this research
- Records about your study visits
- Past and present medical records related to the study
- Results of medical tests

Who may use and give out information about you?

- The study doctor and the study staff
- URMC and Affiliates

Your information may be given to:

- The Department of Health and Human Services
- The University of Rochester
- The National Institute for Arthritis and Musculoskeletal and Skin Diseases (NIAMS)
- Pfizer, Inc
- Advarra Participant Payments
- The U.S. Food and Drug Administration (FDA) may also need to inspect study records at some point during the study or even after it has been completed. In the event that this should occur, every effort will be made to keep identifying information about you private.

Why will this information be used and/or given to others?

- To do the research
- To study the results
- To see if the research was done right

If the results of this study are made public, information that identifies you will not be used.

What if I decide not to give permission to use and give out my health information?

Then you will not be able to be in this research study.

May I review or copy my information?
Yes, but only after the research is over.

How long will this permission be valid?
This permission will last indefinitely.

May I cancel my permission to use and disclose information?
You may cancel your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor. Upon receiving the written notice, the study team will no longer use or disclose your health information and you will not be able to stay in this study. Information that has already been gathered may need to be used and given to others for the validity of the study.

May I withdraw from the study?
If you withdraw your permission to be in the study, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others.

Is my health information protected after it has been given to others?
There is a risk that your information will be given to others without your permission.

Contact Persons
For more information concerning this research or if you feel that your participation has resulted in any research related injury, emotional or physical discomfort, please contact**:** **Chad Heatwole, MD, MS-CI** at (**585) 275-2559**.

Please contact the University of Rochester Research Subjects Review Board at 265 Crittenden Blvd., CU 420628, Suite 1-250 Rochester, NY 14642, Telephone (585) 276-0005 or (877) 449-4441 for the following reasons:

- You wish to talk to someone other than the research staff about your rights as a research subject;
- To voice concerns about the research;
- To provide input concerning the research process;
- In the event the study staff could not be reached.

Voluntary Participation
Taking part in this study is voluntary. You are free not to take part or to withdraw at any time, for whatever reason. No matter what decision you make, there will be no penalty or loss of benefit to which you are entitled. In the event that you do withdraw from this study, the information you have already provided will be kept in a confidential manner.

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SIGNATURE/DATES

After reading and discussing the information in this consent form you should understand:

- Why this study is being done;
- What will happen during the study;
- Any possible risks and benefits to you;
- Other options you may have instead of being in the study;
- How your personal information will be protected;
- What to do if you have problems or questions about this study.

Subject Consent
I have read (or have had read to me) the contents of this consent form and have been encouraged to ask questions. I have received answers to my questions. I agree to participate in this study. I have received (or will receive) a signed copy of this form for my records and future reference.

_____
Subject Name (Printed by Subject)

Signature of Subject | Date

Person Obtaining Consent

I have read this form to the subject and/or the subject has read this form. I will provide the subject with a signed copy of this consent form. An explanation of the research was given and questions from the subject were solicited and answered to the subject's satisfaction. In my judgment, the subject has demonstrated comprehension of the information. I have given the subject adequate opportunity to read the consent before signing.

Name and Title (Print)

Signature of Person Obtaining Consent | Date