If you are using Epic for this study, fax a copy of the signed consent form to 410-367-7382.

Patient I.D. plate

RESEARCH PARTICIPANT INFORMED CONSENT AND PRIVACY AUTHORIZATION FORM

Protocol Title: A Phase 1b/2, Open-Label, Multiple Ascending Dose Study to Evaluate the Safety, Tolerability, Efficacy Pharmacokinetics and Pharmacodynamics of PF-06252616 in Ambulatory Participants with LGMD2I

Application No.: IRB00089732

Sponsor: Hugo W. Moser Research Institute, Kennedy Krieger
Financial support for this study is provided by Pfizer, Inc.

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1. What you should know about this study:

- You are being asked to join a research study. This consent form explains the research study and your part in it. Please read it carefully and take as much time as you need. Ask your study doctor or the study team to explain any words or information that you do not understand.
- You are a volunteer. If you join the study, you can change your mind later. There will be no penalty or loss of benefits if you decide to quit the study.
- During the study, we will tell you if we learn any new information that might affect whether you wish to continue to participate.
- If we think your participation in this study may affect your clinical care, information about your study participation will be included in your medical record, which is used throughout Johns Hopkins. Doctors outside of Johns Hopkins may not have access to this information. You can ask the research team to send this information to any of your doctors.
- When Johns Hopkins is used in this consent form, it includes The Johns Hopkins University, The Johns Hopkins Hospital, Johns Hopkins Bayview Medical Center, Howard County General Hospital, Johns Hopkins Community Physicians, Suburban Hospital, Sibley Memorial Hospital and All Children's Hospital.
- Biospecimens will be collected in this study. Biospecimens may include any of the following: blood, tissue, saliva, urine, bone marrow, cells, etc. Most biospecimens contain DNA, which is the genetic code for each person.
- 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.

- If you would like to review the information for this study, or a summary of the results, ask the study team doctor for the ClinicalTrials.gov study registration number.
- During this study, you will not have access to certain medical information and test results collected for study purposes. If an emergency occurs while you are in the study, medical information needed for your treatment can be made available to your study physician and other physicians who treat you. When the study is completed, all the information in your medical record will be available to you.

2. Why is this research being done?

This research is being done to test the safety and effects of the investigational drug PF-06252616 in people with limb girdle muscular dystrophy 2I (LGMD2I). This research study will look at how the body of an individual with LGMD2I responds to PF06252616 by looking at drug levels in the blood, seeing how fast the drug levels rise and fall, and what effects they have on the body function. This is known as the pharmacokinetics (PK) and pharmacodynamics (PD) of a drug. We want to find out what effects, good or bad, PF-06252616 has on people with LGMD2I. We also want to find out the effects of different doses of this drug in LGMD2I patients: 5 mg/kg, 20 mg/kg, and 40 mg/kg.

PF-06252616 is an investigational drug produced by the pharmaceutical company, Pfizer, Inc. The word "investigational" means that PF-06252616 is not approved for marketing by the Food and Drug Administration (FDA). The FDA is allowing the use of PF-06252616 in this study.

PF-06252616 is an engineered protein, called a monoclonal antibody, which was designed to bind to and inhibit a naturally occurring protein called myostatin. Monoclonal antibodies are usually produced by the body's immune system to identify and fight foreign objects in your body, but can be made in the lab to target specific proteins that are affecting normal function.

PF-06252616 was made to target a protein called myostatin that is normally produced by the body to keep the muscles from growing too large. If PF-06252616 is able to bind to myostatin, it may prevent it from limiting the size of the muscles and may provide improved function.

Adults with LGMD2I who are ambulatory (able to walk) may join the study.

How many people will be in this study?
About 20 people are expected to take part in this study at Johns Hopkins.

3. What will happen if you join this study?

If you agree to be in this study, we will ask you to do the following things.

Study Overview
Participation will include a screening period that can last up to 2 weeks where you may have 1 to 2 study visits. The screening period is the time when you will be evaluated to see if you qualify medically for the study. If you qualify, there is 16-week lead-in period before the first dose is given and then a study drug regimen period. There will be a follow-up period when you will no longer receive study drug, but you will come back to the clinic at 4 and 16 weeks after your last dose of study drug in the study regimen period so that your study doctor can test your health. After completing the follow-up period, you will be asked if you would like to continue receiving the study drug in the extension period. The length of each study visit varies depending on the tests performed in addition to the infusion.

All participants will receive the study drug. There is no placebo (an inactive material that does not contain any active study drug). The study drug is PF-06252616.

The doses being tested are 5 mg/kg, 20mg/kg, and 40mg/kg of your body weight. PF-06252616 is a liquid that will be given to you as an intravenous (IV) infusion that will take about 2 hours to administer. It will be given every 28 days. IV infusion means you will have a needle in a vein in your arm and the study drug will slowly drip into your vein.

The study will include 3 study groups or "cohorts." About 20 eligible subjects will be consecutively assigned to 1 of 3 cohorts. The doses of PF-06252616 will start at a very low dose in the first group of participants that was found to be safe in previous testing. If the dose is well tolerated, the dose will be increased in the next group of participants. Participants will be entered sequentially into each dosing group until that group is complete.

If you are eligible and assigned to one of the 3 cohorts, you will be followed for an initial 16-week "lead-in period" before the first dose of the study drug to determine any changes in the progression of disease since screening.

Cohort 1 (number of participants= 4):
- Lead-in period (16 weeks)
- Study Drug Regimen A: PF-06252616, 5 mg/kg (32 weeks)
- Study Drug Regimen B: PF-06252616, 40 mg/kg (32 weeks)
- Follow-up period (16 weeks)
- Extension period: PF-06252616, 40 mg/kg (28 weeks)

Cohort 2 (number of participants=8):
- Lead-in period (16 weeks)
- Study Drug Regimen: PF-06252616 20 mg/kg (32 weeks)
- Follow-up period (16 weeks)
- Extension period: PF-06252616, 40 mg/kg (40 weeks)

Cohort 3 (number of participants=8):
- Lead-in period (16 weeks)
- Study Drug Regimen: PF-06252616 40 mg/kg (32 weeks)
- Follow-up period (16 weeks)
- Extension period: PF-06252616, 40 mg/kg (24 weeks)

The study will begin with 4 subjects being enrolled into Cohort 1. If you are assigned to Cohort 1, following the lead-in period, you will receive the study drug dose of 5 mg/kg (lowest dose) for a total of 32 weeks (8 doses). If you are assigned to Cohort 2, following the lead-in period, you will receive the mid dose level of 20 mg/kg once safety has been confirmed with subjects in Cohort 1 who have received the study drug for 16 weeks (4 doses). If you are assigned to Cohorts 1 and 3, you will receive the study drug at the highest dose level (40 mg/kg) once safety has been confirmed with subjects in Cohort 2 who have received the study drug for 16 weeks (4 doses).

Each dose level will be evaluated for 32 weeks (8 doses each). If you are assigned to Cohort 1, you will receive 2 dose levels (5 mg/kg every 28 days for 8 doses followed by 40 mg/kg every 28 days for 8 doses) and your total study drug administration time will be 64 weeks, although the total time may be longer if there is a pause to collect safety information before starting the 40 mg/kg dose.

If you completed the follow-up period and would like to continue receiving the study drug in the extension period, you will be receiving 40mg/kg every 28 days. If you belong to Cohort 1, you will receive the drug for additional 28 weeks. If you belong in Cohort 2, you will receive the drug for additional 40 weeks. If you belong in Cohort 3, you will receive the drug for additional 24 weeks.

STUDY SCHEDULE

Cohort 1

	Screen	Lead-In	Study Drug Regimen								Follow-up		Early Withdrawal
Visit	1	2	A (5 mg/kg) 3	4	5	6	7	8	9	10	19	20	
			B (40 mg/kg) 11	12	13	14	15	16	17	18			
Informed Consent	X												
Medical History	X												
Physical Examination	X	X	X			X					X	X	X
Pregnancy Test	X	X	X	X	X	X	X	X	X	X	X	X	X
Diary Cards	X	X	X	X	X	X	X	X	X	X	X	X	X
Height		X											
Weight	X	X	X	X	X	X	X	X	X	X	X	X	X
Vital Signs	X	X	X	X	X	X	X	X	X	X	X	X	X
12- lead ECG	X		X			X					X	X	X
Echocardiogram	X										X	X	X
Laboratory tests	X	X	X	X	X	X	X	X	X	X	X	X	X
Stool Sample	X		X	X	X	X	X	X	X	X	X	X	X
C-SSRS	X	X	X	X	X	X	X	X	X	X	X	X	X
MRI-Liver	X		X			X					X	X	X
MRI-Muscle		X	X								X	X	X
DXA Whole Body		X	X								X	X	X
DXA Spine and Hip			X								X	X	X
Functional Assessments		X	X[1]				X				X	X	X
Surveys			X								X	X	X
Study Drug Regimen			X	X	X	X	X	X	X	X			
Needle muscle biopsy		X	X								X	X	X
Blood sample for Immunogenicity			X								X	X	X
Blood sample for PD			X		X		X		X		X	X	X
Blood sample for PK			X		X		X		X		X	X	X
Blood sample for Biomarkers		X					X			X			

Cohort 2 and 3

	Screen	Lead-in	Study Drug Regimen								Follow-up	Early Withdrawal	
Visit	1	2	3	4	5	6	7	8	9	10	11	12	
Informed Consent	X												
Medical	X												

	Screen	Lead-in	Study Drug Regimen								Follow-up	Early Withdrawal	
Visit	**1**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	
History													
Physical Examination	X	X	X			X					X	X	X
Pregnancy Test	X	X	X	X	X	X	X	X	X	X	X	X	X
Diary Cards	X	X	X	X	X	X	X	X	X	X	X	X	X
Height		X											
Weight	X	X	X	X	X	X	X	X	X	X	X	X	X
Vital Signs	X	X	X	X	X	X	X	X	X	X	X	X	X
12- lead ECG	X		X			X					X	X	X
Echocardiogram	X										X	X	
Laboratory tests	X	X	X	X	X	X	X	X	X	X	X	X	X
Stool sample	X		X	X	X	X	X	X	X	X	X	X	X
C-SSRS	X	X	X	X	X	X	X	X	X	X	X	X	X
MRI-Liver	X					X					X	X	X
MRI-Muscle		X	X								X	X	X
DXA Whole Body		X	X								X	X	X
DXA Spine and Hip			X								X	X	X
Functional Assessments		X	X[1]				X				X	X	X
Surveys			X								X	X	X
Study Drug Regimen			X	X	X	X	X	X	X	X			
Needle muscle biopsy		X	X								X	X	X
Blood sample for Immunogenicity			X								X	X	X
Blood sample for PD			X		X		X		X		X	X	X
Blood sample for PK			X		X		X		X		X	X	X
Blood sample for Biomarkers		X					X			X			

[1]This test will be performed twice during Visit 3 before the first dose is given

Study Schedule for Extension

Cohort 1

Cohort 1 Extension Period (40mg/kg)	Study Drug Regimen							Follow-up	Early Withdrawal
Visit Number (Study Day Visit Window)	**21 (±3)**	**22 (±3)**	**23 (±3)**	**24 (±3)**	**25 (±3)**	**26 (±3)**	**27 (±3)**	**Telephone Follow-up 30±3 days after final dosing visit**	
Physical Examination				X			X		X
Pregnancy Test	X	X	X	X	X	X	X		X
Diary Cards	X	X	X	X	X	X	X		X
Contraception Review	X	X	X	X	X	X	X		X
Height							X		
Weight	X	X	X	X	X	X	X		
Vital Signs				X			X		X
12- lead ECG							X		X
Echocardiogram							X		X
Clinical Laboratory Tests				X			X		X
Serum Ferritin, Serum Iron, Transferrin Saturation, TIBC				X			X		X

Cohort 1 Extension Period (40mg/kg)	**Study Drug Regimen**							**Follow-up**	**Early Withdrawal**
Visit Number (Study Day Visit Window)	**21 (±3)**	**22 (±3)**	**23 (±3)**	**24 (±3)**	**25 (±3)**	**26 (±3)**	**27 (±3)**	**Telephone Follow-up 30± 3 days after final dosing visit**	
Hormone Testing (LH, FSH, estrogen)							X		X
GLDH				X			X		X
PK, PD, Immunogenicity, Biomarkers							X		X
Fecal Occult Blood				X			X		X
C-SSRS				X			X		X
Questionnaires (InQol, SF-36)							X		X
MRI-Liver							X		X
DXA Spine and Hip							X		X
Muscle Strength (MMT, dynamometry)				X			X		X
4SC; 10-meter walk/run; 2MWT ; Timed up-and-go				X			X		X
PUL				X			X		X
Respiratory Function (FVC, FEV1, MIP/MEP)				X			X		X
Study Drug Administration	X	X	X	X	X	X	X		
Adverse event monitoring	X	X	X	X	X	X	X	X	X
Infusion site reaction monitoring	X	X	X	X	X	X	X		X
Concomitant medications	X	X	X	X	X	X	X	X	X

Cohort 2

Cohort 2 Extension (40mg/kg)	**Study Drug Regimen**										**Follow-up**	**Early Termination**
Visit Number (Study Day Visit Window)	**13 (±3)**	**14 (±3)**	**15 (±3)**	**16 (±3)**	**17 (±3)**	**18 (±3)**	**19 (±3)**	**20 (±3)**	**21 (±3)**	**22 (±3)**	**Telephone Follow-up 30± 3 days after final dosing visit**	
Physical Examination				X			X			X		X
Pregnancy Test	X	X	X	X	X	X	X	X	X	X		X
Diary Cards	X	X	X	X	X	X	X	X	X	X		X
Contraception Review	X	X	X	X	X	X	X	X	X	X		X
Height										X		X
Weight	X	X	X	X	X	X	X	X	X	X		X
Vital Signs				X			X			X		X
12- lead ECG							X			X		X
Echocardiogram										X		X
Clinical Laboratory Tests				X			X			X		X
Serum Ferritin, Iron, Transferrin Saturation, TIBC				X			X			X		X
Hormone Testing (LH, FSH, estrogen)										X		X
GLDH				X			X			X		X
PK/ PD/ Immunogenicity/Biomarkers										X		X
Fecal Occult Blood				X			X			X		X
C-SSRS				X			X			X		X
Questionnaires: InQol, SF-36										X		X

Cohort 2 Extension (40mg/kg)	Study Drug Regimen										Follow-up	Early Termination
Visit Number (Study Day Visit Window)	13 (±3)	14 (±3)	15 (±3)	16 (±3)	17 (±3)	18 (±3)	19 (±3)	20 (±3)	21 (±3)	22 (±3)	Telephone Follow-up 30± 3 days after final dosing visit	
MRI-Liver										X		X
DXA Spine and Hip										X		X
Muscle Strength (MMT, dynamometry)				X			X			X		X
4SC; 10-meter walk/run; 2MWT; Timed up-and-go				X			X			X		X
PUL				X			X			X		X
Respiratory Function (FVC, FEV1, MIP/MEP)				X			X			X		X
Study Drug Administration	X	X	X	X	X	X	X	X	X	X		
Adverse event monitoring	X	X	X	X	X	X	X	X	X	X	X	X
Infusion site reaction	X	X	X	X	X	X	X	X	X	X		X
Concomitant medications	X	X	X	X	X	X	X	X	X	X	X	X

Cohort 3

Cohort 3 Extension (40mg/kg)	Study Drug Regimen						Follow-up	Early Withdrawal
Visit Number (Study Day Visit Window)	13 (±3)	14 (±3)	15 (±3)	16 (±3)	17 (±3)	18 (±3)	Telephone Follow-up 30± 3 days after final dosing visit	
Physical Examination			X			X		X
Pregnancy Test	X	X	X	X	X	X		X
Diary Cards	X	X	X	X	X	X		X
Contraception Review	X	X	X	X	X	X		X
Height						X		X
Weight	X	X	X	X	X	X		X
Vital Signs			X			X		X
12- lead ECG						X		X
Echocardiogram			X			X		X
Clinical Laboratory Tests			X			X		X
Serum Ferritin, Serum Iron, Transferrin Saturation, TIBC			X			X		X
Hormone Testing (LH, FSH, estrogen)						X		X
GLDH			X			X		X
PK/PD/Immunogenicity/Biomarkers						X		X
Fecal Occult Blood			X			X		X
C-SSRS			X			X		X
Questionnaires: InQol, SF-36						X		X
MRI-Liver						X		X
DXA Spine and Hip						X		X
Muscle Strength (MMT, dynamometry)			X			X		X
4SC; 10-meter walk/run; 2MWT; Timed up-and-go			X		X	X		X
PUL			X		X	X		X
Respiratory Function (FVC, FEV1, MIP/MEP)			X			X		X
Study Drug Administration	X	X	X	X	X	X		
Adverse event monitoring	X	X	X	X	X	X	X	X
Infusion site reaction	X	X	X	X	X	X		X
Concomitant medications	X	X	X	X	X	X	X	X

About the Study Procedures

You will have tests done to see if you qualify to be in the study, to check your health, and to follow the effects of the study drug during the study. These tests are done as part of research. Your study doctor will tell you the exact dates and times of your visits. The schedule of which tests will be performed at which visit is shown above. Below is a description of the tests and procedures that will be done during the study:

1. Informed consent: You will be asked to read, understand and sign this informed consent form before being involved with any study procedures.

2. Demography/Medical history: You will be asked about your race, ethnicity, health and any medications you are taking or have previously taken at the Screening visit.

3. Physical exam: This is an overall exam of your body. A complete physical exam will be done as shown on the study schedule. Your height will be measured during the lead-in visit only. Your weight will be measured every study visit.

4. Vital signs: Your blood pressure, temperature, heart rate and breathing rate (vital signs) will be checked. Vital signs will be done at every visit and twice on the visits where you receive study drug, both before and after you receive the study drug.

5. Blood samples for health and safety: Blood will be taken from you to check your health and the safety of the drug at all study visits except the lead-in visit. About 1 tablespoon of blood will be collected from a vein in your arm.

6. Urine samples: Urine will be collected to check your kidney function and the safety of the drug at all study visits except the lead-in visit.

7. Pregnancy tests and contraception: If you are a female who is capable of having children, you will have a urine pregnancy test at all study visits. You will not be able to participate in this study if you are pregnant, and if you become pregnant during the study, the study drug will be discontinued.

If you are a female participant, you will be given a diary booklet to write down the first day of your monthly menstrual period. We will review the diary at each study visit.

If you are a male or female participant, you must agree to use a protocol-permitted birth control method consistently and correctly throughout this study. We will review your method of contraception at each visit.

8. Fecal occult Blood: You will give a bowel movement (stool) sample using a kit that will be provided to you. The sample will be given at all study visits except the Lead-in visit and may be collected at home. Sample collected at home will be sent via mail at room temperature.

9. Blood samples for pharmacodynamics (PD) and immunogenicity: You will have blood samples taken from a vein in your arm, about 1 ½ tablespoon, to test for the possible effects of the study drug on your body and your muscles (this is called pharmacodynamics) and to test for possible effects of the study drug in your immune system (immunogenicity) as indicated in the study schedule.

10. Study drug blood measurements (pharmacokinetics - PK): You will have blood samples taken throughout the study to measure how much of the study drug is in your body over a period of time. About ½ teaspoon of blood will be collected from a vein in your arm during each visit.

11. **Electrocardiogram (heart tracing)**: This test measures the electrical activity of your heart and will be performed as shown on the study schedule.

12. **Echocardiogram** (sound wave test of the heart) will be performed as shown in the study schedule to help determine if there are any heart problems that might make it unsafe for you to be in the Study.

13. **Columbia Suicide Severity Rating Scale (CSSRS)**: During all study visits, you will be asked questions pertaining to behaviors or ideas that may indicate that you are going to harm or hurt yourself.

    If there are concerns that you may harm or hurt yourself, you will be referred to a mental health care provider.

14. **Questionnaires**: You will be asked to complete the following questionnaires at the visits shown in the study schedule to the best of your ability, making every effort to answer all questions.

    - Individualized neuromuscular quality of life questionnaire (INQoL): It measures how your disease affects your daily routine.
    - Short Form Health Survey-36: This questionnaire will help better understand your general health and any problems related to your muscle condition.

15. **Imaging Assessments:** You will have the following imaging tests that can see inside your body at the visits shown in the study schedule:
    - Magnetic Resonance Imaging (MRI) of liver
    - MRI of skeletal muscle: This will include a whole body MRI and a thigh

    MRI scans create images of the body using a magnet and radio waves. While the procedure is much like a CT scan, there is no radiation involved in an MRI exam. The MRI exam will take about 30 minutes (liver) and about 2 hours (muscle). Prior to the exam, you will be asked to complete a standard questionnaire. The purpose of this questionnaire is to ensure that you are able to safely enter the MRI area.

    Since the MRI machine uses a strong magnet that will attract other metals, you may not take part in this study if you have a pacemaker, an implanted defibrillator, or certain other implanted electronic or metallic devices, shrapnel, or other metal.

    If you have a history of metal in your head or eyes, you will need an x-ray exam of your skull in order to find out if the MRI exam is safe for you.

    To start your MRI test, you will lie on a padded table. A soft padded coil will be placed at the area where the pictures will be taken. The table on which you are lying will be moved to the center of an MRI magnet, which looks like a long narrow tube. Even though the tube is open, some people feel confined (claustrophobic) in small places. If this bothers you, please notify the MRI staff.

    You may end your participation in this study at any time by telling the MRI staff. When MRI pictures are taken, radio-signals and magnetic fields are used. When this happens, it is normal for the MRI machine to make loud, banging, and clicking noises. You will be asked to wear earplugs or headphones for your comfort during the test. A soft padded coil will be placed at the position where the pictures will be taken.

During the exam, the MRI staff is able to see and hear you. You will be able to hear the MRI staff. The MRI staff will be talking to you throughout his MRI exam and may issue simple instructions regarding holding your breath, maintaining position, etc. You will generally be requested to lie perfectly still throughout the exam.

The MRI of the skeletal muscle may take about 2 hours for scanning and positioning. Because of the length of time inside the scanner, you may become anxious about the procedure or it may be difficult for you to keep still. You may ask your study doctor for a medicine (lorazepam) that will calm you during the MRI scan.

Incidental Findings:
The MRI, DXA scan, and echocardiogram you are having as part of this research study will be reviewed by a qualified person just as it would be if you were having these imaging procedures done as part of your routine medical care. There is a possibility that while reviewing your MRI, DXA, or echocardiogram we may see an abnormality that we did not expect to see in this study. This is what is called an "incidental finding." We will let you know if we see such an incidental finding.

Depending on the type of incidental finding, we may contact you by mail or by phone. In the case of a potential serious emergency, someone may go to your home. A qualified person (usually a member of the research team) will talk to you if there is an incidental finding. You do not have an option to decline information about an incidental finding.

If you want, we will give information about this incidental finding to your primary doctor or we will refer you to an appropriate doctor for further evaluation.

An incidental finding may cause you to feel anxious. Since an incidental finding will be part of your medical record, it may affect your current or future life or health insurance coverage. This risk will vary depending on the type of insurance plan involved.

The costs for any care that will be needed to diagnose or treat an incidental finding would not be paid for by this research study. These costs would be your responsibility.

- Dual-energy X-ray absorptiometry (DXA): This will measure your bone density and also measure your fat and lean body mass. In order to get an accurate measurement, you should not eat anything two hours before the scan. You will be asked to lie still on a table for about 30 minutes.
- DXA of the whole body will be obtained during the Lead-in visit, Visits 3, 11, 19, and 20 if you are in cohort 1 and during the Lead-in visit, Visits 3, 11, and 12 if you are in Cohorts 2 and 3.
- DXA of the spine and hip will be obtained during Visits 3, 11, 19, and 20 if you are in Cohort 1, and during Visits 3, 11, and 12 if you are in Cohorts 2 and 3.
- DXA will also be performed if you leave the study early.

16. **Functional Assessments:** The following tests of function will be performed the visits as shown in the study schedule:

- Lung function- this test will see how much air you can blow out of your lungs after taking a very deep breath.
- Muscle Strength Test - this test will measure how strong the muscles of your legs, arms and shoulders are.

- Timed function tests will include the following:
  a. Timed up and go- a timed test to measure how fast you stand up from sitting position, walk to the line on the floor, turn around, walk back to the chair and sit down.
  b. 10 meter run -a timed test to measure how fast you can walk or run 10 meters. You choose how fast you want to safely walk or run.
  c. 2-minute walk distance- measures the distance you can walk quickly in 2 minutes. We will ask you to walk as far as you can for two minutes.
  d. 4-step climb/descend- a timed test that measures how fast you can go up and down 4 stairs.
- Performance of Upper Limb (PUL) – test of the movement of your arms and hands

17. **Needle Muscle Biopsy:** A needle muscle biopsy will be performed on the visits shown in the study schedule: You will be asked to lie on an exam table and one of your lower legs will be shaved and cleaned. The skin over the area to be biopsied from your leg (tibialis anterior muscle) will be numbed by injecting a local anesthetic (1% lidocaine with 1:100,000 epinephrine). A small incision less than 1 cm will be made in your skin. A small piece of muscle tissue (about 30 mg), less than the tip of an eraser, will be removed with a 14 gauge needle (the size of an intravenous needle). A piece of the muscle biopsy will be sent to Pfizer Inc. for analysis. We will put a bandage on your lower leg and you will be able to get up and use your leg normally immediately after the needle muscle biopsy.

18. **Concomitant Medications:** At each study visit, starting on the Lead-in visit, you will be asked about changes in your health and/or medications. A list of your past and current medications, vitamins, and dietary supplements will be recorded and reviewed for any changes since the last study visit.

19. **Adverse Event Monitoring**: At each study visit, starting on the Lead-in visit, you will be asked questions about any changes in your health while taking part in the research study.

Request to collect and store biospecimens for future research

As part of this research study, we would like to ask you to let us store your biospecimens and health information for future research. This research could include other diseases.

The study doctor can provide you with additional information if you have questions. Also, further information about our use of your biospecimens can be found in this consent document under the heading *What happens to Data and Biospecimens that are collected in the study?*

Will you allow us to store the biospecimens we collect for this study for use in future research*?*

YES ☐ _____
Signature of Participant

NO ☐ _____
Signature of Participant

How long will you be in the study?

You will be in this study for about 128 weeks if you are in Cohort 1, about 108 weeks if you are in Cohort 2, and about 92 weeks if you are in Cohort 3.

4. What are the risks or discomforts of the study?

PF-06252616:

Any research has some risks, which may include things that could make you sick, make you feel uncomfortable, or harm you. You might experience negative effects related to the study drug while participating in the study. All individuals taking part in the study will be watched carefully for any negative effects; however, the study team does not know all the effects that the study drug may have on you. The study team may give you medicines to help reduce negative effects. These effects may be mild or serious. In some cases, these effects might be long lasting, or permanent, and may even be life threatening.

Often, the amount of study drug to be tested in humans is at a dose level about 10 times below the dose tested in animals where there appeared to be no side effects. However, the amount of drug that will be tested in this study is only about 2 times below this dose in animals. This is because the study drug is being tested in LGMD2I, which is a severe disabling condition and there are no other current treatments or cures. The negative events that are the most likely to happen to you if you take part in this study are listed below.

The possible risks and side effects associated with the study drug, PF-06252616, are based on a clinical study tested in a small number of healthy adult volunteers and also on testing the study drug in animals (monkeys and rats).

In the healthy adult volunteer study, most subjects received single doses and a small group received as many as 3 doses of PF-06252616 over 4 weeks. These doses were smaller than the moderate and highest doses in this study. Fewer than 10 adults have received the 20 and 40 mg doses. Based on the results from the clinical study, there were no side effects that seemed to be related to PF-06252616.

In animal studies, the following side effects were noted:

- Liver damage including fibrosis (scar tissue) and necrosis (liver tissue death) were seen when male animals were given PF-06252616 at high doses. In female animals, liver damage was seen at all dose levels of PF-06252616. Liver damage was caused by a buildup of iron in liver. At the end of dosing animals did not recover from the liver damage. Low levels of iron in the blood may not be harmful and may be able to be treated before they become harmful to other organs such as the liver.
- It is believed that the liver damage seen as a side effect in animals is caused by increased liver iron which can be tested for by blood tests and a MRI scan. Iron increases in the liver to dangerous levels that might cause liver damage should be prevented by these measures. You will be closely monitored throughout the study for any side effects or signs of toxicity.

- You will have blood tests during the study to monitor the level of iron in your blood. Imaging tests will also be done to look for iron buildup in your liver. If the blood tests are very high or do not come back to a proper range or if the imaging tests are abnormal, the study doctor may decide it is not safe for you to continue in the study.

- Stomach ulceration (sore or opening in the stomach lining) and bleeding were found in rats that were given study drug at high doses, which will not be tested in clinical trials. Animals recovered from these findings when dosing was stopped. Because other drugs that you are taking could also cause stomach irritation or bleeding, both blood and bowel movement tests will be done in this study to monitor for this side effect.

Other potential side effects:

- Other investigational (still being tested) drugs with similarities to PF-06252616 have been given to people some of whom experienced side effects including nose bleeds and skin rashes.
- It is unknown whether PF-06252616 can affect the ability to have children.

This drug once injected can remain in the body for several weeks or months.

Clinical and animal studies do not always predict the side effects people may experience. This drug is investigational, so not all of its side effects are known. There may be rare and unknown side effects, including reactions that may be life threatening.

Other Risks: Other reported side effects in humans included headache, fatigue, upper respiratory tract infection and muscle spasms.

Since PF-06252616 is investigational when taken alone or in combination with other medications, there may be other risks that are unknown. All drugs have a potential risk of an allergic reaction, which if not treated promptly, could become life threatening. You should get medical help and contact the study doctor right away if you think you have any of the following symptoms of a serious allergic reaction: trouble breathing, or swelling of the face, mouth, lips, gums, tongue or neck. Other allergic reactions may include rash, hives, or blisters.

If you experience an allergic reaction during the time the study drug is given, the drip (infusion) will be stopped and you will be given medication for an allergic reaction.

It is important that you report all symptoms and side effects that you experience as soon as they occur, whether or not you think they are.

Intravenous (IV) Catheter**:** The study drug will be given to you by an IV catheter and the study drug will slowly drip into your vein (2 hours). The IV catheters may cause pain, bruising, clotting, bleeding, leakage of drug solution, and possibly infection at the catheter site. You may receive some medication (cream) on your skin to help numb the area before the needle is placed.

Blood collection: A blood draw may cause faintness, inflammation of the vein, pain, bruising, or bleeding at the site of puncture. You may receive some medication (cream) on your skin to help numb the area before the needle is placed. The total amount of blood that will be taken from you during the entire study will be about 468 mL (about2 cups or 32 tablespoons) if you are in Cohort 1 or about 283 ml (about 1 cup or 19 tablespoons).

Urine and stool collection: You may experience discomfort during collection of urine or stool.

ECG: You may experience discomfort when the stickers that record the heart rhythm are removed. There may be signs of skin irritation or redness.

Echocardiogram: You may feel a slight pressure on your chest from the transducer. You may experience skin irritation and a rash from the gel that is used during the study.

DXA and X-ray**:** This research study includes exposure to radiation from x-rays or gamma rays. This radiation exposure is for research purposes only and is not part of your medical care. X-rays and gamma rays can damage cells, but at low doses, the body is usually able to repair these cells.

The radiation exposure (DXA scans and possible skull x-ray) that you will get in this research study is 0.015 rem (a rem is a unit of absorbed radiation). This is less than the 0.3 rem that the average person in the United States gets each year from natural sources like the sun, outer space, air, food, and soil. The risk from the radiation exposure in this research study is very small.

The radiation exposure described here is what you will get from this research study only. It does not include any exposure you may have received or will receive from other medical tests outside of this study that are a part of your medical care. If you have questions about the total amount of radiation you will be receiving, you should ask your doctor.

Fasting**:** Fasting could cause dizziness, headache, stomach discomfort or fainting.

MRI**:** The effects of magnetic fields in an MRI scanner have been extensively studied. While no significant risks have been found from the use of MRI scans, you may be bothered by the MRI machine noise and by feelings of being closed in (claustrophobia). You will be asked to wear earplugs or earphones while in the magnet. You will not be able to take part in this study if you have any of the following because of risks from an MRI: an artificial heart valve, pacemaker, metal plate, pin or other metallic objects in your body (including gun shot or shrapnel). You may also become anxious from lying in a tight space without moving. The MRI scan does not expose you to x-ray radiation.

Lorazepam (Ativan): Drowsiness, dizziness, loss of coordination, headache, nausea, blurred vision, constipation, heartburn, or change in appetite may occur. Serious side effects may be unlikely because of the low dose given for the procedure. These side effects include, mental/mood changes (such as hallucinations, depression, thoughts of suicide), slurred speech or difficulty talking, vision changes, unusual weakness, trouble walking, memory problems, signs of infection (such as fever, persistent sore throat), trouble breathing (especially during sleep)

Needle muscle biopsy: During the needle muscle biopsy, you might feel some pain or discomfort. Pain medication may be given to you during this procedure. You might have some minimal bleeding and mild bruising around the site after the procedure. There is risk of infection, nerve damage, and hematoma formation from muscle biopsy. A hematoma is a collection of blood underneath the skin. If a hematoma occurs, an additional surgery to evacuate the blood may be necessary. The risk of infection, nerve damage and hematoma formation from needle muscle biopsy is less than 1% (less than 1 in 100).

Functional Assessments: You might feel some mild discomfort and/or become tired and be unable to do some of the tests that are asked of you. During the lung function testing, you may experience dizziness or lightheadedness during and after the test. You can stop any of the tests at any time for any reason.

Scales/Questionnaires**:** The scale or questionnaires may contain questions that are sensitive in nature. You may refuse to answer any question that makes you feel uncomfortable. If you have concerns after completing the questionnaire, you should contact your study doctor. You may get tired or bored when we are asking you questions or you are completing questionnaires. You do not have to answer any question you do not want to answer.

Review of Diary and Contraception methods: You may experience discomfort and feel embarrassed when answering questions about your monthly menstrual period or methods of contraception.

Time Commitment: The research study involves multiple study visits. You may miss some time at work and with family. We realize that participation in this study is a significant time commitment; therefore we will do our best to schedule at your convenience.

Confidentiality: There is the risk that information about you may become known to people outside this study. We will try to minimize the chance of this happening by removing all personal identifiers from any blood samples collected. Samples will be labeled with a code and the key to the code will be kept in a password-protected computer at Johns Hopkins that will only be accessible to the Principal Investigator and study key personnel. The samples will be stored at a facility chosen by the Sponsor.

You may find that these tests and visits are inconvenient and require special effort. In addition, some tests may be uncomfortable.

There may be side effects and discomforts that are not yet known.

5. Are there risks related to pregnancy?

The effects of PF-06252616 on sperm, a pregnancy, or a nursing child are not known. If you are physically able to have children and are sexually active, you must use birth control consistently and correctly throughout this entire study.

There are no known risks from MRI imaging without contrast during pregnancy. There may be risk from the lorazepam. There may be risks that are currently unknown.

The study doctor will discuss with you the allowed methods of birth control during this research study and will help you select birth control that is appropriate for you. The study doctor will instruct you in consistent and correct use of your selected birth control method and review at each visit your use of birth control.

- Female monkeys developed problems in the reproductive organs (blocked development of follicles in the ovaries) and atrophy (weakening) in the lining of cervix and vagina.
- At this time, it is unknown whether PF-06252616 can cause harm to the embryo/fetus when given to pregnant women. PF-06252616 should not be given to women who can have children who are not using a highly effective method of contraception.
- It is also unknown whether PF-06252616 is passed into human milk. Therefore, PF-06252616 should not be given to women who are nursing a baby.

Pregnancy Follow Up

Birth control methods, even when used consistently and correctly, are not perfect. If you become pregnant or father a child or want to stop the required birth control during the study, you should tell the study doctor immediately. You may be withdrawn from the study if you discontinue birth control, become pregnant or father a child.

Please also tell the doctor who will be taking care of you during the pregnancy that you took part in this study. The study doctor will ask if you, or your partner, or the pregnancy doctor is willing to provide updates on the progress of the pregnancy and its outcome.

This research may hurt an embryo or fetus in ways we do not currently know.

6. Are there benefits to being in the study?

There may or may not be a direct benefit to you from being in this study. However, there is no guarantee that you will benefit in any way.

Information from this study may help other people with LGMD2I in the future.

7. What are your options if you do not want to be in the study?

If you decide not to join this study, other options are available. You do not have to join this study to get treatment. Other treatment options may include physical therapy if appropriate as determined by your physician.

The study doctor will discuss with you the risks and benefits of the alternative treatments.
You do not have to join this study. If you do not join, your care at Kennedy Krieger and Johns Hopkins will not be affected.

8. Will it cost you anything to be in this study?

There will be no charge to you for your participation in this study. The study drug, study-related procedures, and study visits will be provided at no charge to you or your insurance company. Medications that you are already taking at the start of the study will not be provided or paid for.

You will need to continue to obtain any such medications as you usually do.

You will receive a separate Insurance and Research Participant Financial Responsibility Information Sheet (Sheet).

This Sheet will give you the following information:

- The procedures, tests, drugs or devices that are part of this research and that will be paid for by the study (no cost to you).
- The procedures, tests, drugs or devices that will be billed to you and/or your health insurer. If you have health insurance, you will be responsible for any co-pays or deductibles not covered by your insurance.

9. Will you be paid if you join this study?

You will not receive any payment for taking part in this study. Reasonable travel expenses (including mileage, airfare, hotel, ground transportation, and meals) will be covered for you for all required visits to the study site.

10. Can you leave the study early?

Taking part in this research study is up to you. You may choose not to take part. You can change your mind and withdraw (drop out) later. There will be no penalty, and you won't lose any benefits you receive now or have a right to receive.

We will tell you if we learn new information that could change your mind about your taking part or continuing in this research study. If you want to drop out, you should tell us. We will make sure you can end the study in the safest way. We will also talk to you about follow-up care, if needed.

You have the right to take back (revoke) your Authorization at any time by writing to the study doctor, Dr. Kathryn Wagner. If you revoke your Authorization, the study team will not collect any new health information about you. However, they can continue to use and disclose any already collected information if that is necessary for the reliability (the scientific value) of the study. The investigator and Pfizer, Inc. can also still keep and use any information that it has already received. In addition, during and after your participation in the study your study doctor will be required to report to Pfizer, Inc. information related to any serious adverse effect that you may experience due to your participation in the study. If you revoke your Authorization, you can no longer continue to participate in the study.

11. Why might we take you out of the study early?

You may be taken out of the study if:

- Staying in the study would be harmful.
- You need treatment not allowed in the study.
- You fail to follow instructions.
- You become pregnant.
- The study is cancelled.
- There may be other reasons to take you out of the study that we do not know at this time.

If you are taken out of the study early, Johns Hopkins may use or give out your health information that it has already collected if the information is needed for this study or any follow-up activities**.**

To help you leave the study safely, the study doctor may ask you to participate in more tests.

If you withdraw or are removed from the study, any remaining biological samples (for example, blood or urine samples) that have been collected from you can be destroyed by making a written request to the study doctor. However, any information already received from your samples will be kept to maintain the value of the study.

12. How will your privacy be protected?

We have rules to protect information about you. Federal and state laws and the federal medical Privacy Rule also protect your privacy. By signing this form you provide your permission, called your "authorization," for the use and disclosure of information protected by the Privacy Rule.

The research team working on the study will collect information about you. This includes things learned from the procedures described in this consent form. They may also collect other information including your name, address, date of birth, and information from your medical records (which may include information about HIV status, drug, alcohol or STD treatment, genetic test results, or mental health treatment).

The research team will know your identity and that you are in the research study. Other people at Johns Hopkins, particularly your doctors, may also see or give out your information. We make this information available to your doctors for your safety.

People outside of Johns Hopkins may need to see or receive your information for this study. Examples include government agencies (such as the Food and Drug Administration), safety monitors, other sites in the study and companies that sponsor the study.

If you are in a cancer study that receives federal funding, the National Cancer Institute (NCI) now requires that we report identifiable information (such as, zip code) about your participation. You may contact the NCI if you have questions about how this information is used.

We cannot do this study without your authorization to use and give out your information. You do not have to give us this authorization. If you do not, then you may not join this study.

We will use and disclose your information only as described in this form and in our Notice of Privacy Practices; however, people outside Johns Hopkins who receive your information may not be covered by this promise or by the federal Privacy Rule. We try to make sure that everyone who needs to see your information keeps it confidential–but we cannot guarantee that your information will not be re-disclosed.

The use and disclosure of your information has no time limit. You may revoke (cancel) your permission to use and disclose your information at any time by notifying the Principal Investigator of this study by phone or in writing. If you contact the Principal Investigator by phone, you must follow-up with a written request that includes the study number and your contact information. The Principal Investigator's name, address, phone and fax information are on page one of this consent form.

If you do cancel your authorization to use and disclose your information, your part in this study will end and no further information about you will be collected. Your revocation (cancellation) would not affect information already collected in the study, or information we disclosed before you wrote to the Principal Investigator to cancel your authorization.

13. Will the study require any of your other health care providers to share your health information with the researchers of this study?

As a part of this study, the researchers may ask to see your health care records from your other health care providers. You will be asked to give us a list of other health care providers that you use.

PRIMARY CARE PHYSICIAN / SPECIALIST NOTIFICATION OPTION: Please indicate below whether you want us to notify your primary care physician or your specialist of your participation in this study.

_____ Yes, I want the study doctor to inform my primary care physician/specialist of my participation in this study.

_____ No, I do not want the study doctor to inform my primary care physician/specialist of my participation in this study.

_____ I do not have a primary care physician/specialist.

14. What treatment costs will be paid if you are injured in this study?

Johns Hopkins does not have a program to pay you if you are hurt or have other bad results from being in the study. However, medical care at Johns Hopkins is open to you as it is to all sick or injured people.

The costs for any treatment or hospital care you receive as the result of a study-related injury that are not covered by a health insurer will be billed to you.

By signing this form you will not give up any rights you have to seek compensation for injury.

13. What other things should you know about this research study?

a. What is the Institutional Review Board (IRB) and how does it protect you?

The Johns Hopkins Medicine IRB is made up of:

- Doctors
- Nurses
- Ethicists
- Non-scientists
- and people from the local community.

The IRB reviews human research studies. It protects the rights and welfare of the people taking part in those studies. You may contact the IRB if you have questions about your rights as a participant or if you think you have not been treated fairly. The IRB office number is 410-955-3008. You may also call this number for other questions, concerns or complaints about the research.

When the Johns Hopkins School of Medicine Institutional Review Board (IRB) reviews a study at another site, that site (institution) is solely responsible for the safe conduct of the study and for following the protocol approved by the Johns Hopkins IRB.

If you are a participant at Kennedy Krieger Institute, you may contact Karen Cox, Vice President and Research Administrator at 443-923-9302.

b. What do you do if you have questions about the study?
Call the principal investigator, Dr. Kathryn Wagner at 443-923-9525. If you wish, you may contact the principal investigator by letter or by fax. The address and fax number are on page one of this consent form. If you cannot reach the principal investigator or wish to talk to someone else, call the IRB office at 410-955-3008.

If you are taking part at Kennedy Krieger Institute, call Dr. Kathryn Wagner at 443-923-9525.

c. What should you do if you are injured or ill as a result of being in this study?
If you think you are injured or ill because of this study, call Dr. Kathryn Wagner at 443-923-9525 during regular office hours.

If you have an urgent medical problem related to taking part in this Study, call Dr. Kathryn Wagner at 443-923-9525 during regular office hours and at 410-245-9314 after hours and on weekends.

d. What happens to Data and Biospecimens that are collected in the study?
Johns Hopkins and our research partners work to understand and cure diseases. The biospecimens and/or data you provide are important to this effort.

If you join this study, you should understand that you will not own your biospecimens or data, and should researchers use them to create a new product or idea, you will not benefit financially.

With appropriate protections for privacy, Johns Hopkins may share your biospecimens and information with our research sponsors and partners.

Pfizer, Inc. may use information resulting from the study to develop products or processes from which they may make a profit. There are no plans to pay you or provide you with any products developed from this research. Pfizer, Inc. will own all products or processes that are developed using information from the study.

14. What does your signature on this consent form mean?

Your signature on this form means that: You understand the information given to you in this form, you accept the provisions in the form and you agree to join the study. You will not give up any legal rights by signing this consent form.

WE WILL GIVE YOU A COPY OF THIS SIGNED AND DATED CONSENT FORM

Signature of Participant	(Print Name)	Date/Time

Signature of Person Obtaining Consent	(Print Name)	Date/Time

I have received the separate Insurance and Research Participant Financial Responsibility Information Sheet.

Signature of Participant, LAR or Parent/Guardian	(Print Name)	Date/Time

NOTE: A COPY OF THE SIGNED, DATED CONSENT FORM MUST BE KEPT BY THE PRINCIPAL INVESTIGATOR; A COPY MUST BE GIVEN TO THE PARTICIPANT; IF YOU ARE USING EPIC FOR THIS STUDY A COPY MUST BE FAXED TO 410-367-7382; IF YOU ARE NOT USING EPIC A COPY MUST BE PLACED IN THE PARTICIPANT'S MEDICAL RECORD (UNLESS NO MEDICAL RECORD EXISTS OR WILL BE CREATED).

ONLY CONSENT FORMS THAT INCLUDE THE JOHNS HOPKINS MEDICINE LOGO CAN BE USED TO OBTAIN THE CONSENT OF RESEARCH PARTICIPANTS.

DOCUMENTATION OF PHYSICIAN/MID-LEVEL PROVIDER CONSENT

My signature below indicates that I have discussed the risks, benefits, and alternatives, answered any questions, and believe the participant is able to make an informed choice to join the study.

Signature of Physician/Mid-Level Provider	(Print Name)	Date/Time

Signature of Participant	(Print Name)	Date/Time

NOTE: A COPY OF THE SIGNED, DATED CONSENT FORM MUST BE KEPT BY THE PRINCIPAL INVESTIGATOR; A COPY MUST BE GIVEN TO THE PARTICIPANT; IF YOU ARE USING EPIC FOR THIS STUDY A COPY MUST BE FAXED TO 410-367-7382; IF YOU ARE NOT USING EPIC A COPY MUST BE PLACED IN THE PARTICIPANT'S MEDICAL RECORD (UNLESS NO MEDICAL RECORD EXISTS OR WILL BE CREATED).

ONLY CONSENT FORMS THAT INCLUDE THE JOHNS HOPKINS MEDICINE LOGO CAN BE USED TO OBTAIN THE CONSENT OF RESEARCH PARTICIPANTS.