You Are Being Asked to Be in a Research Study

What Is a Research Study?

The main purpose of research studies is to gain knowledge. This knowledge may be used to help others. Research studies are not intended to benefit you directly, though some might.

Do I Have to Do This?

No. Being in this study is entirely your choice. If you decide to join this study, you can change your mind later on and withdraw from the research study.

Taking part in a study is separate from medical care. The decision to join or not join the research study will not affect your status as a patient.

What Is This Document?

This form is an informed consent document. It will describe the study risks, procedures, and any costs to you.

This form is also a HIPAA Authorization document. It will describe how your health information will be used and by whom.

Signing this form indicates you are willing to take part in the study and allow your health information to be used.

What Should I Do Next?

1. Read this form, or have it read to you.
2. Make sure the study doctor or study staff explains the study to you.
3. Ask questions (e.g., time commitment, unfamiliar words, specific procedures, etc.)
4. If there will be medical treatment, know which parts are research and which are standard care.
5. Take time to consider this, and talk about it with your family and friends.

Emory University
Consent to be a Research Subject / HIPAA Authorization

Title: **Functional Resolution of Multi-loci Pathogenic Variants and VUSs in Pompe Disease**

Principal Investigator: **Samya Chakravorty, PhD, (Department of Human Genetics)**

Co-Investigators: **Peng Jin, PhD (Department of Human Genetics)**
Madhuri Hegde, PhD, FACMG (Department of Human Genetics)

Sponsor: **Sanofi Genzyme**

Introduction

You are being asked to volunteer for this research study because either you are affected by Pompe Disease (Glycogen Storage Disease Type II) or Limb Girdle Muscular Dystrophy (LGMD), or you are a volunteer not affected by LGMD or Pompe disease, or a normal healthy volunteer, and your sample will be used as normal control in our project if you decide to provide informed consent.

This form is designed to tell you everything you need to think about before you decide if you want to be a part of the study. **It is entirely your choice. If you decide to take part, you can change your mind later on and withdraw from the research study.** The decision to join or not join the research study will not cause you to lose any medical benefits. If you decide not to take part in this study, your doctor will continue to treat you.

Before making your decision:

- Please carefully read this form or have it read to you
- Please listen to the study doctor or study staff explain the study to you
- Please ask questions about anything that is not clear

You can take a copy of this consent form, to keep. Feel free to take your time thinking about whether you would like to participate. You may wish to discuss your decision with family or friends. Do not sign this consent form unless you have had a chance to ask questions and get answers that make sense to you. By signing this form you will not give up any legal rights.

Description of Research Study

This is a research study aimed to understand the genetic variants of uncertain significance (VUS) and multiple gene contributions in Pompe and limb-girdle muscular dystrophy (LGMD). Individuals clinically diagnosed or suspected to have Pompe or a LGMD subtype where no initial definitive molecular diagnosis could be made are enrolled and further studied to determine the type of disease (either Pompe or a LGMD subtype) using functional studies. This will enhance our Pompe and LGMD disease understanding, available clinical trial recruitment, personalized medicine and clinical care.

What is the purpose of this study?

The purpose of this study is to understand the genetic cause of Pompe disease and LGMD in order to facilitate faster molecular diagnosis. We will be using functional molecular experiments in clinical cases where definitive molecular diagnosis could not be performed due to the finding of genetic variants of uncertain significance (VUS) and cases with

pathogenic genetic mutations in multiple genes. A total of 350 individuals will be recruited for this study and your direct participation in this study will end after you chose to give informed consent or not. In case, if we need more specimens from you, you will be contacted by us to provide further consents to receive more of your samples.

What will I be asked to do?

First, you will review the entire consent form mailed to you. If you have any further questions you may contact the study coordinator or investigator and make sure all your questions are answered. If you decide to participate, you will be asked to sign this consent form and a HIPAA authorization form.

After the consent and HIPAA forms are signed, you will be asked several questions about your specific disease. You will be asked about any treatment you may have had for your disease in the past. You will also be asked your age and your gender. Please answer these questions to the best of your ability. After you have answered, the study investigator or the coordinator or your physician will be able to tell you if you are eligible to participate in this study.

If you are eligible, your already-collected muscle biopsy (with your physician) and/or your peripheral blood in 2 tubes (~ 20 ml) and/or your dried blood spots will be collected by the research group from your physician. If you do not want to give consent, you should not participate in this study. These analyses could include one or all of the following: examine the protein in your biopsy or blood samples and/or isolate and evaluate DNA and RNA from biopsy or whole blood or dried blood spots for the identification and functional validation of DNA variants.

This study is designed to examine the clinical significance of variants (genetic mutations) of uncertain significance (VUS) and understand multi-gene variant contribution to Pompe and LGMD clinical features. This will help in classifying the VUSs, provide definitive diagnosis to a Pompe or LGMD sub-type, numerous clinical trial recruitment, and creation of comprehensive Pompe or LGMD gene networks for discovery of disease biomarkers and new therapies. The observed results will be produced to you as a research report and not as a clinical report. Although your biopsy or blood specimen will be analyzed after you have consented, your direct participation in this study will end once you consent.

The muscle biopsy or blood sample will then be sent to the study PI Dr. Samya Chakravorty and co-Is Dr. Madhuri Hegde and Dr. Peng Jin, Emory University. The Study PI and co-Is will use it to determine the functional significance of VUS and multi-gene variants using functional assays after extracting RNA and protein. The remaining biopsy will be banked for future repeat assays to confirm. In order to protect your privacy, all samples will be assigned an identification code that does not include any of your personal information. Your name, phone number, social security number, etc., will not be on the sample shipped to Emory University.

Who owns my study information and samples?

If you join this study, you will be donating your samples and study information. You will not receive any compensation if your samples or information are used to make a new product. Your sample will be stored in PI's and co-I's laboratory for as long as it is useful. If you withdraw from the study, data and samples that were already collected may be still be used for this study. You may ask the PI or co-I to destroy it at any time. You may request that your sample be destroyed by contacting the study investigator and co-investigator, Dr. Peng Jin or Dr. Madhuri Hegde, at 404-727-1197.

What are the possible risks and discomforts?

You do not have any risk associated since your muscle biopsy is already collected by your physician and stored in their respective facility. The collection of the blood sample for this study is a standard medical procedure. It is considered to be of minimal risk to you. Risks associated with drawing blood from your arm include pain, bruising, and lightheadedness. On rare occasions, you may get an infection. Precautions will be taken to avoid these risks. A second potential risk that might be involved is a breach of confidentiality. The PI will take all measures to avoid this. Precautions will be taken to avoid any risk whatsoever. A secondary potential risk that might be involved is a breach of confidentiality. The PI and co-I will take all measures to avoid this. The information will be stored in a locked

cabinet in the PI and co-Is laboratory accessed by only the PI and co-Is.

We may need to perform genetic testing for confirmatory purposes and to supplement our other assays. If a genetic change is found, most families find this information helpful. This is because it may explain why you or your family member has a particular muscle problem. But, sometimes learning that a person has a genetic change can cause emotional problems or a disruption in family relationships. In order to lessen these risks, we recommend that you discuss any results with your doctors and genetic counselors as they have experience in helping people understand the results and implications of genetic testing.

Some people believe that using DNA in research brings up special concerns about your privacy. For example, it is possible that an employer could try to deny employment, or an insurance company could try to deny insurance if information about a person's DNA were known. For this reason, the research team works hard to keep DNA information private. Your genetic information will not be revealed to any third party without your permission, unless required by law. Dr. Samya Chakravorty and Dr. Peng Jin are experienced scientists and researchers in this respect. Co-I Dr. Madhuri Hegde has spent many years conducting DNA-based research involving thousands of samples. She does not know of any research participant who has been harmed by donating DNA to research. We therefore believe that risks associated with donating DNA are very low.

It is possible that the researchers will learn something new during the study about the risks of being in it. If this happens, they will tell you about it. Then you can decide if you want to continue to be in this study or not. You may be asked to sign a new consent form that includes the new information if you decide to stay in the study.

Genetic Information, Risks and Protections

For the purpose of this study, your genetic information may be produced by the study or future research. We will follow the National Institute of Health (NIH) guidelines on informed consent for genomics research at http://www.genome.gov/27559024.

How is my Genetic Information Protected? What are the Risks?

The Genetic Information Nondiscrimination Act (GINA) is a federal law that generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. This law generally will protect you in the following ways:

- Health insurance companies and group health plans may not request your genetic information that we get from this research.
- Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums.
- Employers with 15 or more employees may not use your genetic information that we get from this research when making a decision to hire, promote, or fire you or when setting the terms of your employment.

Be aware that GINA does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance, and does not apply to employers with less than 15 employees.

In addition to GINA, the State of Georgia has laws that prohibit insurers from using genetic testing information for any non-treatment purpose. However, like GINA, this state law protection has exclusions: life insurance policies, disability income policies, accidental death or dismemberment policies, Medicare supplement policies, long-term care

insurance policies, credit insurance policies, specified disease policies, hospital indemnity policies, blanket accident and sickness policies, franchise policies issued on an insurance policy written as a part of workers' compensation equivalent coverage, or other similar limited accident and sickness policies.

Privilege

In the State of Georgia, in some circumstances your genetic information has may have special legal protections called "privilege." This means that the information cannot be used as evidence in a court. By allowing us to use and disclose your genetic information for this research study along with other information about you that genetic information used in the research may no longer have that legal protection. Other protections described in this form will still apply. There are also other confidentiality protections for research data in general under Georgia state law.

Will I benefit directly from the study?

You will receive no direct medical benefit for participating in this research study. We hope the information gained from this study may help identify Pompe or LGMD subtype, Pompe or LGMD therapy and cure. This study is designed to learn more about the genetic and molecular causes of Pompe disease and related LGMD subtype, suggest physicians on possible patient recruitment to clinical trials and potentially discover new therapeutic targets for Pompe or LGMD sub-types. The study results may be used to help others in the future.

What about results or new findings? The information that is learned from this study will be used to develop an accurate map of gene network for Pompe or specific LGMD subtype, and annotation of the clinical significance of the VUSs. You will not receive any results or money from the development of new tests from participation in this study.

Will I be compensated for my time and effort?

You will not receive any money for the biopsy you will be consenting to donate to us. There will be no extra costs to you or your insurance company for participating in the study.

What are my other options?

Taking part in this study is your choice. You are free to not take part in this study. You may withdraw from the study at any time. Your decision to be or not be in this study will in no way affect your current or future medical treatment. Your respective physician, from whom we will be collecting your muscle biopsy once you consent, will discuss these with you. You do not have to be in this study to be treated for Pompe or LGMD.

How will you protect my private information that you collect in this study?

Whenever possible, a study number, rather than your name, will be used on study records. Your name and other identifying information will not appear when we present or publish the study results.

Study records can be opened by court order. They also may be provided in response to a subpoena or a request for the production of documents.

Storing and Sharing your Information

Your muscle biopsy sample will be stored in the laboratories of PI Dr. Samya Chakravorty and co-Is Dr. Madhuri Hegde and Dr. Peng Jin, Emory University. The research team will use it to determine the functional significance of VUS and multi-gene variants using functional assays after extracting RNA and protein. The remaining biopsy will be banked for future repeat assays to confirm. In order to protect your privacy, all samples will be assigned an identification code that does not include any of your personal information. Your name, phone number, social security number, etc., will not be on the sample shipped to Emory University. Your samples, genomic data and health information will be stored and shared with other researchers without identifying of any of your personal information. The samples and information will be available for any research question, such as research to understand what causes certain diseases, development of

new scientific methods, or the study of where different groups of people may have come from.

Medical Record

If you have been an Emory Healthcare patient before, then you already have an Emory Healthcare medical record. If you have never been an Emory Healthcare patient, you do not have one. An Emory Healthcare medical record will be made for you if an Emory provider or facility gives you any services or procedures for this study.

We will take reasonable steps to keep copies of this form out of Emory Healthcare's medical records system. If we aren't successful in keeping these forms out, despite our efforts, we will take steps to remove them. If they cannot be removed, we will take steps to limit access to them.

Emory Healthcare may create study information about you that can help with your care. For example, the results of study tests or procedures that helps in molecular diagnosis of the disease. These study results will be put in your Emory Healthcare medical record because it may be useful for treating you now and in the future. Anyone who has access to your medical records will be able to have access to all the study information placed there. The confidentiality of the study information in your medical record will be protected by laws like the HIPAA privacy rule. State and federal laws may not protect the research information from disclosure.

The results of some study tests and procedures will be used only for research purposes and will *not* be placed in your medical record. For this study, those items include: novel scientific understanding of the molecular mechanisms of disease, genetics and clinical correlation, and the creation of a comprehensive genetic map of the muscle in neuromuscular diseases, Pompe disease or LGMD in particular. These results will help drive the field in discovering novel therapeutic targets and clinical strategies in general.

Tests and procedures done at non-Emory places may not become part of your Emory medical record. Also, if you decide to be in this study, it is up to you to let your other health providers know.

In Case of Injury

If you get ill or injured from being in the study, Emory will help you get medical treatment. Emory and the sponsor have not, however, set aside any money to pay you or to pay for this medical treatment. The only exception is if it is proven that your injury or illness is directly caused by the negligence of an Emory or sponsor employee. "Negligence" is the failure to follow a standard duty of care.

If you become ill or injured from being in this study, your insurer will be billed for your treatment costs. If you do not have insurance, or if your insurer does not pay, then you will have to pay these costs.

If you believe you have become ill or injured from this research, you should contact Dr. Samya Chakravorty and Dr. Madhuri Hegde and Dr. Peng Jin at telephone number 404-727-1197 or 470-337-2847. You should also let any health care provider who treats you know that you are in a research study.

In this study, you do not have any major risk of injury associated since your muscle biopsy is already collected by your physician. Moreover, there are none to minimal risk in drawing blood or sterile prick for dried blood spots. Precautions will be taken to avoid any risk whatsoever.

Costs

There will be no costs to you for participating in this study. You will not be charged for any of the research activities.

Withdrawal from the Study

You have the right to leave a study at any time without penalty. The researchers also have the right to stop your participation in this study without your consent for any reason, especially if they believe it is in your best interest or if you were to object to any future changes that may be made in the study plan. If you withdraw from the study, data and samples that were already collected may still be used for this study. You may ask the PI or co-I to destroy it at any time. You may request that your sample be destroyed by contacting the study investigator and co-investigator, Dr. Samya Chakravorty or Dr. Madhuri Hegde, at 404-727-1197.

Who should I call if I have questions? If you have any questions about this study contact the study investigator, Dr. Samya Chakravorty at 404-727-1197. If you have any questions about your rights as a participant in this research study, call the Emory University Institutional Review Board at 404-712-9699 or 877-503-9797.

Authorization to Use and Disclose Protected Health Information

The privacy of your health information is important to us. We call your health information that identifies you, your "protected health information" or "PHI." To protect your PHI, we will follow federal and state privacy laws, including the Health Insurance Portability and Accountability Act (HIPAA). We refer to all of these laws in this form as the Privacy Rules. This form explains how we will use your PHI for this study.

Please read this form carefully and if you agree with it, sign it at the end.

PHI That Will Be Used/Disclosed
Your PHI that will be used to include physician records, hospital records, laboratory results.

Purposes for Which Your PHI Will Be Used
If you sign this form, you give us your permission to use your PHI for the conduct and oversight of this research study.

People That Will Use or Disclose Your PHI and Purpose of Use/Disclosure
Different people and groups will use and disclose your PHI. They will do this only in connection with the research study. The following persons or groups may use and/or disclose your PHI:

- The Principal Investigator, Co-Investigator and the research staff.
- The Principal Investigator may use other people and groups to help conduct the study. These people and groups will use your PHI to do this work.
- Sanofi Genzyme is the Sponsor of this Research. The Sponsor(s) may use and disclose your PHI to make sure the research is done correctly. They may also use your PHI to collect and analyze the results of the research. The Sponsor may have other people and groups help conduct, oversee, and analyze the study. These people or groups will use your PHI.
- The following groups may also use and disclose your PHI. They will do this to make sure the research is done correctly and safely. The groups are:
    - the Emory University Institutional Review Board
    - the Emory University Office for Clinical Research
    - the Emory University Office of Research Compliance
    - research monitors and reviewers
    - data and safety monitoring boards

We will use or disclose your PHI when we are required to do so by law. This includes laws that require us to report child abuse or elder abuse. We also will comply with legal requests or orders that require us to disclose your PHI. These include subpoenas or court orders.

Revoking Your Authorization
You do not have to sign this form. Even if you do, at any time later on you may revoke (take back) your permission. If you want to do this, you must write to:

Samya Chakravorty, PhD,
Department of Human Genetics,
Emory University School of Medicine,
615 Michael St, Atlanta, GA-30322
E-mail: samya.chakravorty@emory.edu
Phone: 404-727-1197

After that point, the researchers would not collect any more of your PHI. But they may use or pass along the information you already gave them so they can follow the law, protect your safety, or make sure the research was done properly. If you have any questions about this, please ask.

Other Items You Should Know
If we disclose information to people who do not have to follow the Privacy Rules, your information will no longer be protected by the Privacy Rules. People who do not have to follow the Privacy Rules can use or disclose your information with others without your permission if they are allowed to do so by the laws that cover them. Let us know if you have questions about this.

You do not have to sign this form. If you do not sign, you may not participate in the research study

During the study you will generally not have access to records related to the research study. This is to preserve the integrity of the research. You may have access to these records when the study is complete. These records may include research related PHI your health care providers use to make decisions about your care. If necessary for your care, this information may be available to your doctor before the end of the study.

If identifiers are removed from your PHI, then the remaining information will not be subject to the Privacy Rules. It may be used or disclosed with other people or organizations, and/or for other purposes.

Expiration Date
Your permission to use and disclose your PHI will expire at the end of the research study.

Contacts
If you have any questions regarding the study, you may call Dr. Samya Chakravorty or Dr. Madhuri Hegde at (404) 727-1197. If you have any questions about the study, or your rights as a study subject, you may contact the Emory University Institutional Review Board at 404-712-0720 or 1-877-503-9797, by email at irb@emory.edu.

Authorization
A copy of this form will be given to you.

TO BE FILLED OUT BY SUBJECT ONLY

Please **print** your name, **sign**, and **date** below if you agree to be in the main study. By signing this consent and authorization form, you will not give up any of your legal rights.

_____

Name of Subject

_____

Signature of Subject (18 or older and able to consent) **Date** **Time**

_____

Subject's Signature to consent for DNA extraction and banking: **Date** **Time**

_____

Signature of Legally Authorized Representative with authority for research decisions **Date** **Time**

_____

Authority of Legally Authorized Representative or Relationship to Subject

TO BE FILLED OUT BY STUDY TEAM ONLY

_____

Name of Person Conducting Informed Consent Discussion

_____ _____

Signature of Person Conducting Informed Consent Discussion **Date** **Time**