CONSENT FORM AND HIPAA AUTHORIZATION FOR PARTICIPATION IN A RESEARCH STUDY

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PROJECT IRB #: 2038203

STUDY TITLE: ROLE OF NEURAMINIDASE ACTIVITY ON ENDOTHELIAL DYSFUNCTION IN TYPE 2 DIABETES

We invite you to take part in this research study. This consent form tells you why we are doing the study, what will happen if you join the study, and other important information about the study.

Please take as much time as you need to read this consent form. You can discuss it with your family, friends, or personal doctor. If there is anything you do not understand, please ask us to explain. Then you can decide if you want to take part in the study or not.

The Principal Investigator (also called the study doctor) is **Dr. Luis Martinez-Lemus, PhD**. The people working with **Dr. Martinez-Lemus** on this study are called the study team.
National Institutes of Health (called the sponsor in this form) is paying for this study.

WHAT SHOULD I KNOW BEFORE I DECIDE WHETHER TO TAKE PART IN THIS STUDY?

- Research studies help us to learn new things and test new ideas about treating certain conditions/diseases.
- Taking part in a research study is voluntary. You decide if you want to take part, and you can stop taking part at any time. Your regular medical care at the University of Missouri Hospitals and Clinics will not be affected now or in the future if you decide you do not want to be in this study.
- We are doing this study because we want to learn more about whether the medicine zanamivir can benefit the cardiovascular health of people with type 2 diabetes. We hope to learn if zanamivir can help restore endothelial function in individuals with type 2 diabetes. Zanamivir is a Food and Drug Administration (FDA) approved medication for the treatment of influenza virus. Zanamivir is being used in an off-label manner for this research study.
- We invite you to take part in this study because you have the diagnosis of type 2 diabetes.
- About 20 people will take part in this study at the University of Missouri.
- If you take part in this study, you will come to the University of Missouri Clinical Research Center for three separate study visits. You will have blood tests, questionnaires, vascular ultrasound measurements, and a noninvasive Glycocheck test performed. We will explain these procedures in this form.
- If you join this study, you will not have to stop your diabetes treatment for as long as you are in the study.
- The total amount of time you could be in this study is about **1 month**.

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- Taking part in this study may or may not make your health better. We hope that the information we learn from this study will help in the future treatment of people with type 2 diabetes. **There is no guarantee that taking part in this research will result in any improvement in your condition.**
- As with any research study, there are risks that we know about and there may be some we do not know about. We will explain these risks in this form.
- We will only include you in this study if you give us your permission first by signing this consent form.

WHY ARE THE RESEARCHERS DOING THIS STUDY?

In this study, we want to find out if a drug called zanamivir (also called the study drug in this form) improves endothelial function (blood vessel function) in patients with type 2 diabetes.

WHAT WILL HAPPEN IF I TAKE PART IN THIS STUDY?

Screening Tests

If you decide to join this study, you will sign this form and then you will have some screening tests to see if you qualify to be in the study. These are the screening tests:

- Medical Chart Review: The study doctors will review your medical chart.
- Pregnancy Tests: The drug used in this study may affect unborn babies. For this reason, pregnant women cannot take part in this study. If you are a female who can become pregnant (you have had your first period and have not reached menopause), we will do a urine pregnancy test to make sure you are not pregnant.
- Practice use of the Glycocheck study equipment

If the results of these tests show that you can be in the study, you will start in the study within the next 3 weeks. If you do not qualify to be in the study, the study doctor will discuss other options with you and/or refer you back to your regular doctor.

Research Study Treatment

The treatment will include taking the study drug for five days. We will check with everyone via phone regularly after the initiation of treatment to ensure compliance and to inquiry about potential side effects.

Study Tests and Procedures

If you take part in this study, you will have the following tests and procedures:

After signing the consent form, medical information will be obtained by the study team, including DOB, gender, ethnic/racial category, height, body weight (history of body weight gain or loss), waist circumference, vitals (including: heart rate, respirations, temperature, and blood pressure), and a medical history questionnaire.

You will be asked to fast for eight or more hours and hold any medications that you take the morning of each of the assessment (pre and post) study visits.

At each of the assessment visits, vitals and a fasting blood draw will be taken to test for biochemistries. You will also undergo measurements including Glycocheck and brachial artery flow-mediated dilation (FMD) at each of your assessment visits. You can find a description of these procedures in this form.

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The information and/or samples we collect from you for this study will not be used or shared with other investigators for future research studies. This applies even if we remove all information that could identify you from the data and samples.

Study Medication
The study medication, zanamivir, is an oral inhalation medication that is dispensed from a disk inhaler. You will be instructed to take 10mg of the study medication via inhalation, twice daily for five consecutive days. The medication may have side effects that include allergic reactions, sinusitis, dizziness, fever and/or chills, and joint pain and/or inflammation. You should not take this medication if you have COPD or asthma. The study medication should not be used until two weeks following administration of live attenuated influenza vaccine if applicable, and you will be advised not to receive the live attenuated influenza vaccine until 48 hours following stopping treatment with zanamivir. The medication should not be administered to anyone with a history of allergic reaction to milk proteins. The study staff will inquire about your food and/or medication allergies prior to administering the medication. Zanamivir can also cause bronchospasm (irritation of your airways that results in wheezing and/or coughing), allergic reaction, and neuropsychiatric events (agitation, depression, sleeping problems, suicidal thoughts and actions, etc.). You will be monitored by the study physician and study safety officer while receiving treatment. The use of zanamivir in this study is off-label.

Brachial artery FMD
A blood pressure cuff will be inflated on your forearm for up to five minutes. During this time, your arm may get numb due to decreased blood flow. An ultrasound image/video of your upper arm will be taken before, during, and after the inflation of the blood pressure cuff. This is a measurement of vascular function. There are no risks associated with this procedure. When assessing FMD, the blood pressure cuff will squeeze your arm tightly; however, any discomfort will be alleviated as soon as the pressure in the cuff is released. We will complete this test twice per study visit.

Glycocheck
A small, light-emitting probe will be placed under your tongue. The probe allows researchers to assess the integrity of your blood vessels. This procedure can take up to 1 hour to perform and can cause discomfort. There are no risks associated with this test.

Blood drawing/venipuncture
We will take a blood sample from a vein in your arm using a needle at each of the four assessment visits that you complete. Each sample will be about 20mL or four teaspoons. We will take a total of about 40mL or two to three tablespoons of blood for the whole study (over the course of 1 month). Taking blood from you may cause some discomfort from the needle stick, dizziness, bruising, or very rarely, infection.

We will tell you if we learn information from these procedures that may be important for you to know. It is possible that this will mean you need more testing or treatment for a new or existing medical condition. You and/or your health plan/insurance will be responsible for the costs of this extra testing and/or treatment.

HOW LONG WILL I BE IN THE STUDY?
You will be in this study for about month. The study screening visit will take about 1 hour to complete. If you are eligible to participate in the study intervention, you will be scheduled within

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3 weeks to participate in the pre-assessment. The pre-assessment visit will last about 3 hours. Following pre-assessment, you will take the study medication for 5 days. After your final dose of study medication, you will have a final, post-assessment visit that will last about 3 hours.

CAN I STOP BEING IN THE STUDY?

You can stop being in the study at any time without giving a reason. If you stop being in the study, your regular medical care will not change. Leaving the study will not affect your future medical care at the University of Missouri.

There is no penalty to you if you do not join the study or if you leave it early. You will not lose any benefits you are entitled to if you leave the study.

If you decide to stop participating in the study, you should discuss your decision with the study doctor. **If you decide to stop participating in the study, just let us know.**

The study doctor may decide to take you off this study at any time, even if you want to stay in the study. The study doctor will tell you the reason why you need to stop being in the study. These reasons may be:

- If it is in your best medical interest
- You do not follow the study rules
- The whole study is stopped
- New information becomes available about the study drug

If necessary, the study doctor will arrange for you to continue your medical care with your regular doctor.

WHAT HEALTH RISKS OR PROBLEMS CAN I EXPECT FROM THE STUDY?

There are risks to taking part in any research study. There may also be problems (also called side effects) we do not know about yet. If we learn about new important risks and side effects, we will tell you. We will tell you about any new information we learn that may affect your decision to continue taking part in the study.

Drugs can affect people in different ways. Not everyone gets the same side effects. Side effects may be mild or very serious. Many go away soon after you stop taking the drug. Some side effects can last a long time or never go away.
We will closely watch everyone in the study for side effects. You need to tell the study doctor immediately if you have any problems, side effects, or changes in your health. Dr. Luis Martinez-Lemus's telephone number is (573) 882-3244. For more information about risks and side effects, ask the investigator or contact Dr. Camila Manrique at (573) 529-1141.

WHAT OTHER RISKS ARE THERE?

Other procedures and drugs that are part of this study might also involve some risks:

Reproductive Risks

- **Risks to women who could become pregnant:**
  The drug in this study might affect a baby, before or after it is born. We do not know if the drug can harm a baby, and so we do not want anyone who might be pregnant to be in the study.

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You should not become pregnant or breastfeed a baby while taking part in this study and for four weeks after finishing treatment. You must use effective birth control while you are in the study.

You must tell the study doctor right away if you think you are pregnant. We will ask you to take a pregnancy test to be sure you are not pregnant at the start of the study and again before starting the second arm of the study.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

We do not know if this study will help you. Your condition may get better, but it could stay the same or even get worse. We hope that this study will help us to learn more about endothelial dysfunction in type 2 diabetics, and to develop new treatments for vascular disease in the future.

WHAT OTHER CHOICES DO I HAVE?

You do not have to take part in this study. You are free to say yes or no.

WHAT ABOUT PRIVACY AND CONFIDENTIALITY?

The study team needs to use some of your health/personal information. This information comes from questions we ask you, forms you fill out, and your medical record. One risk of taking part in a research study is that more people will handle your personal health information. We are committed to respecting your privacy and to keeping your personal information confidential. The study team will make every effort to protect your information and keep it confidential to the extent allowed by law. However, it is possible that an unauthorized person will see it.
State and federal privacy laws (HIPAA) protect the use and release of your health information. If you decide to take part in this study, you also give us your permission to use your private health information, including the health information in your medical records and information that can identify you.

You have the right to refuse to give us your permission for us to use your health information. However, doing so would mean that you could not take part in this study.

The following identifiers will be obtained from your health records:

- ☒ Name
- ☒ Dates related to you
- ☐ Fax Number
- ☒ Social Security Number
- ☐ Health Plan Beneficiary Number
- ☐ Certificate or License Numbers
- ☐ Web Address (URL)
- ☐ Biometric Identifiers (finger/voice print)
- ☐ Any other characteristic that could identify you
- ☒ Address
- ☒ Telephone number(s)
- ☒ Email Address
- ☒ Medical Record Number
- ☐ Account Numbers
- ☐ Any vehicle or device serial number
- ☐ Internet Protocol (IP) Address(es)
- ☐ Photographic images

The following is the type of protected health information that will be used in the study:

- ☐ Radiology Images
- ☐ Radiology Reports
- ☐ EKG Recordings/Reports
- ☐ Progress Notes
- ☒ History and Physical Exams
- ☐ Operative Reports
- ☐ Discharge Summaries
- ☐ Health Care Billing or Financial Records
- ☐ Consultations
- ☒ Medications
- ☐ Emergency Medicine Reports
- ☐ Dental Records

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☐ Pathology Reports
☒ Laboratory Reports
☐ Photographs/Video Recordings
☒ Demographics (age, race, etc.)
☐ Questionnaires, Surveys, Diaries
☐ Audio Recordings
☒ Social Security Number (This is only collected for billing/payment purposes and will not be shared with the study sponsor)

We may share any of this information with the following:

- Authorized members and staff of the University of Missouri Institutional Review Board (IRB).
- Laboratories and other individuals and organizations that may need to see your health information in connection with this study.
- Study monitors and auditors who make sure that the study is being done properly.
- Government agencies and public health authorities, such as the Food and Drug Administration (FDA), the Department of Health and Human Services (DHHS), and the Office for Human Research Protections (OHRP)

Any research information shared with outside entities will not contain your name, address, telephone or social security number, or any other personal identifier unless it is necessary for review or required by law.
The people who get your health information may not be required by Federal privacy laws (such as the HIPAA Privacy Rule) to protect it. Some of those people may be able to share your information with others without your separate permission.

Your permission for us to use and/or release your information will last until the end of the study unless you cancel your permission.

You can cancel your permission at any time by writing to:

Dr. Luis Martinez-Lemus, PhD
University of Missouri
Dalton Cardiovascular Research Center
134 Research Park Dr
Columbia, MO 65203

The information we have already collected may still be used for this research study, but we will not collect anymore information after we receive your letter.

You will not be allowed to access your protected health information that is obtained or created during this research project until the end of the study.

If you have not already received a copy of the University of Missouri Healthcare Privacy Notice, you may request one. If you have any questions or concerns about your privacy rights, you may contact the Privacy Officer at 573-882-9054.

We will scan a copy of this consent form into your medical record.

Information that does not become part of your medical record will be stored in the investigator's electronic/computer or paper files. Computer files are protected with a password and the computer is in a locked office that only study team members can open. Paper files are kept in a locked drawer in a locked office that only study team members can open.

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Your records will be given a code number and will not contain your name or other information that could identify you. The code number that connects your name to your information will be kept in a separate, secure location. Information that may identify you may not be given to anyone who is not working on this study without your written consent, or if required by law.

The people who may use and/or release your research information include:

- Those working on the study team at the University of Missouri
- The members of the University of Missouri Institutional Review Board (IRB)
- Those who check on research activities to make sure it is being done correctly and safely
- Other government or inspection agencies

We may present the results of this study in public talks or written articles, but we will not use information that can identify you.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by University of Missouri which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

ARE THERE ANY COSTS TO BEING IN THE STUDY?

The study will pay for all research tests and procedures. You and/or your health plan/insurance will not be billed for tests and procedures that are done in this research study.

There is no cost to you for taking part in this study.

WILL I BE PAID FOR TAKING PART IN THIS STUDY?

The total amount that you could receive is $600. You will be paid $50 after completion of screening, $250 after completion of the pre-assessment visit, and $350 after the post-assessment visit (after completion of the study). Thus, a total compensation of $600 will be provided as study events are completed.
If you decide to leave the study early, you will still receive a payment for each visit you completed.

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We will need your social security number in order to pay you. Any payment may need to be reported as income on your tax return. If you are not a resident/citizen (non-resident alien) of the United States, you will need to work with the MU Nonresident Tax Specialist at 573-882-5509.

WHAT HAPPENS IF I AM INJURED DURING THE STUDY?

It is not the policy of the University of Missouri to compensate human subjects in the event the research results in injury. The University of Missouri, in fulfilling its public responsibility, has provided medical, professional and general liability insurance coverage for any injury in the event such injury is caused by the negligence of the University of Missouri, its faculty and staff.
The University of Missouri also will provide, within the limitations of the laws of the State of Missouri, facilities and medical attention to subjects who suffer injuries while participating in the research projects of the University of Missouri.

In the event you have suffered injury as the result of participation in this research program, you are to contact the Risk Management Officer, telephone number (573) 882-1181, at the Health Sciences Center, who can review the matter and provide further information.
This statement is not to be construed as an admission of liability.

WHAT ARE MY RIGHTS AS A STUDY PARTICIPANT?

Taking part in this study is voluntary. You do not have to take part. Your present or future medical care will not be affected if you decide not to take part.

If you do decide to take part, you can change your mind and drop out of the study at any time. This will not affect your current or future care at the University of Missouri Hospitals and Clinics. There is no penalty for leaving the study and you will not lose any benefits that you are entitled to receive.

If the study investigator decides to take you off the study, he will explain the reasons and help arrange for your continued care by your own doctor, if needed.

We will tell you about any new information discovered during this study that might affect your health, welfare, or change your mind about taking part.
A Data Safety and Monitoring Board, an independent group of experts, will review the data collected during this study. We will tell you about any new information discovered during this study that might affect your health, welfare, or change your mind about taking part.

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Where Can I Get More Information About This Study?

A description of this clinical trial will be available on 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.

Who Can Answer My Questions About The Study?

If you have more questions about this study at any time, you can call Dr. Luis Martinez-Lemus at (573) 882-3244.

You may also contact the University of Missouri Institutional Review Board (IRB) if you:

- Have any questions about your rights as a study participant;
- Want to report any problems or complaints; or
- Feel under any pressure to take part or stay in this study.

The IRB is a group of people who review research studies to make sure the rights of participants are protected. Their phone number is 573-882-3181. There email is muresearchirb@missouri.edu.

If you want to talk privately about your rights or any issues related to your participation in this study, you can contact University of Missouri Research Participant Advocacy by calling 888-280-5002 (a free call), or emailing MUResearchRPA@missouri.edu.

We will give you a copy of this consent form. Please keep it where you can find it easily. It will help you to remember what we discussed today.

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SIGNATURE OF STUDY PARTICIPANT

Consent to Participate in Research

By signing my name below, I confirm the following:

- I have read/had read to me this entire consent form.
- All of my questions were answered to my satisfaction.
- The study's purpose, procedures, risks and possible benefits were explained to me.
- I voluntarily agree to take part in this research study. I have been told that I can stop at any time.

Subject's Signature	**Date**

Signature of Witness (if applicable)*	**Date**

**A witness is required when a participant is competent to provide consent but is blind, or cannot read or write.*

SIGNATURE OF PERSON AUTHORIZED TO OBTAIN CONSENT*

I have explained the purpose of the research, the study procedures (identifying those that are investigational), the possible risks and discomforts and potential benefits of the study, and have answered questions regarding the study to the best of my ability.

Signature of Person Authorized to Obtain Consent	**Date**

**This signature is required for FDA regulated research and/or research that involves any medical procedure or surgical treatment.*

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