Study Title: Dornase Alfa for ARDS in Patients with SARS-CoV-2

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CONSENT FORM AND HIPAA AUTHORIZATION FOR PARTICIPATION IN A RESEARCH STUDY

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PROJECT IRB #: 2022206

STUDY TITLE: INHALED DORNASE ALFA FOR TREATMENT OF ARDS IN PATIENTS WITH SARS-COV-2

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.

If you are reading this as the person legally authorized to consent on the participant's behalf, "you" refers to the participant.

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 **Zach Holliday, MD**. The people working with **Zach Holliday, MD** on this study are called the study team.

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 there is evidence that using inhaled dornase alfa may improve respiratory outcomes in patients with SARS-CoV-2 respiratory failure. We hope to learn if this intervention will indeed improve outcomes and if so, by what cellular mechanism.
- We invite you to take part in this study because you have been effected by SARS-CoV-2 related respiratory failure.
- About 5-10 people will take part in this study at the University of Missouri.
- If you take part in this study, you will have blood tests and flexible bronchoscopy with sampling. You will also receive dornase alfa as an inhaled medication. We will explain these procedures in this form.
- If you join this study, you will not have to stop your condition treatment for as long as you are in the study.
- The total amount of time you could be in this study is about **3 months.**
- 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 SARS-CoV-2 related respiratory failure. **There is no guarantee that taking part in this research will result in any improvement in your condition.**
- The specimens we take from you for this study may be used to develop new products that the sponsor would sell. You will not receive any money from these sales.
- As with any research study, there are risks that we know about and there may be some we don't 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 dornase alfa (also called the study drug in this form), is effective at improving respiratory symptoms in people with SARS-CoV-2.

Dornase alfa is approved by the U.S. Food and Drug Administration (FDA) for use in patients with respiratory disease such as cystic fibrosis but is not approved in patients with SARS Co-V 2. Dornase alfa may help patients recover more quickly t we won't know until we do more research studies.

We don't know if this study will help you. Your condition may get better, but it could stay the same or even get worse. We hope the information we get from this study will help us to develop better treatment for SARS C0-V 2 in the future.

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.
- Blood Tests: We will take about 5 teaspoons of blood from a vein in your arm for some tests.
- 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.

If the results of these tests show that you can be in the study, you will start in the study **the next day.** 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.

Study Tests and Procedures

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

- Prior to starting therapy, you will undergo blood sampling and flexible bronchoscopy with bronchoalveolar lavage which will already be a part of your routine care.
- After baseline samples have been obtained you will receive inhaled dornase alfa 2.5 mg twice daily for 3 days (6 doses).
- After all doses have been completed, follow up blood sampling and flexible bronchoscopy with bronchoalveolar lavage will be obtained to determine the effects of therapy; these sampling studies may or may not be a part of your routine care. We will use excess blood not used in clinical testing at each time point so no additional blood sampling will be required. The amount of bronchoalveolar lavage fluid to be collected per time point (2 sampling time points) will be 10-20 cc. All procedures and blood draws will be performed in the medical intensive care unit in your room. The follow up (72 hours after starting therapy) flexible bronchoscopy is an optional procedure. You do not have to agree to the 72-hour bronchoalveolar lavage, if performed not as part of your clinic care, to take part in this study. At the end of this consent form, we will ask you if we can keep your samples and store them for future testing. No further samples will be obtained after hospitalization.

Collection of the follow up 72-hour bronchoalveolar lavage are optional to be apart of the study and are not required for participation. These samples though will be helpful in determining if the drug has a meaningful effect.

We will keep the information and samples we collect from you for this study to use in future research/to share with other investigators to use in future studies without asking for your consent again. Information that could identify you will be removed from your research data/samples so no one will know that it/they belong to you. Agreeing to future use of information and samples is optional and is not required to be a part of the study.

Your samples may be used by the investigator to develop new treatments that may be sold commercially for profit. You will not share in these profits.

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 90 days.
You will take the inhaled dornase alfa for at least 3 days.
After the drug is finished, we want to keep in touch with you to follow your health over time. We will call you monthly for 3 months and ask about symptoms.

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. Early termination will have no effect on your clinical care and will only consist of not receiving additional doses of the drug.

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
- Your condition gets worse
- 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 is a risk that you may get a drug that does not help your condition or makes it worse. 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.

Dornase alfa 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. You may receive other drugs to make side effects less severe and uncomfortable. Complications of some of the side effects listed below may lead to life-threatening events such as anaphylactic reaction.

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. Investigator's telephone number is 573-884-2696. For more information about risks and side effects, ask the investigator or contact Zach Holliday at 573-884-2696

- **Dornase alfa risks:** In other studies, the side effects that other people have experienced so far with dornase alfa are: rash, temporary voice change, or very rarely, anaphylactic reaction to the drug.
- **Blood testing risks**: Taking blood from you may cause some discomfort from the needle stick, bruising, or very rarely, infection.
- **Procedural risks**: Performed flexible bronchoscopy with bronchoalveolar lavage has a small risk of airway trauma, fever, infection, or very rarely, pneumothorax.
- **Unknown risks**: The experimental drug in this study may have side effects that no one knows about yet. The study team will tell you if they learn anything that might make you change your mind about being in the study.

ARE THERE BENEFITS TO TAKING PART IN THE STUDY?

We don't know if this study will help you. Your condition may get better, but it could stay the same or even get worse. We hope the drug will improve the respiratory status of those on mechanical ventilation related to SARS-CoV-2 and reduce the number of days on mechanical ventilation, days in the hospital and mortality. We hope that this study will help us to learn more about SARS-CoV-2 pneumonia and respiratory failure/ARDS, and to develop new treatments for respiratory failure/ARDS related to SARS-CoV-2 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. If you do not want to join this study, your doctor will discuss other choices with you.

Your other choices include:

- There is no known effective treatment for your condition, but there are cares deemed standard of care for your condition
- Joining another research study
- The drug offered on this study may also be available to you without being in this study
- Not joining this study and continuing your regular medical care

The study doctor can discuss the possible benefits and risks of the other options available to you.

WHAT ABOUT PRIVACY AND CONFIDENTIALITY?

The study team needs to access/collect/use some of your health/personal information. This information comes from questions we ask you, forms you fill out, and/or 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
- ☐ Address
- ☐ Dates related to you
- ☒ Telephone number(s)
- ☐ Fax Number
- ☐ Email Address
- ☐ Social Security Number
- ☒ Medical Record Number
- ☐ Health Plan Beneficiary Number
- ☐ Account Numbers
- ☐ Certificate or License Numbers
- ☐ Any vehicle or device serial number
- ☐ Web Address (URL)
- ☐ Internet Protocol (IP) Address(es)
- ☐ Biometric Identifiers (finger/voice print)
- ☐ Photographic images
- ☐ Any other characteristic that could identify you

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

- ☒ Radiology Images
- ☒ Discharge Summaries

☒Radiology Reports
☒EKG Recordings/Reports
☒Progress Notes
☒History and Physical Exams
☒Operative Reports
☒Pathology Reports
☒Laboratory Reports
☐Photographs/Video Recordings
☐Health Care Billing or Financial Records
☐Consultations
☒Medications
☐Emergency Medicine Reports
☐Dental Records
☒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)
☐Other:

Certain sensitive information about you can only be released if you give your specific permission. This includes information such alcohol or drug abuse, HIV/AIDS testing, and mental health records. We will ask you to indicate your permission to release this information at the end of this consent form. This is your specific permission for release of this information. Federal rules do not allow any use of the information to criminally investigate or prosecute any alcohol or drug abuse. Federal rules do not allow any use of the information to criminally investigate or prosecute any alcohol or drug abuse.

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 2 years after completion of the study unless you cancel your permission.

You can cancel your permission at any time by writing to:
Investigator's Name: Zach Holliday
Institution: University of Missouri
Department: Internal Medicine
Address: 1 Hospital Dr., Columbia, MO, 65212

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. We may also record your research information, including the results of tests and procedures, in your medical record. The

medical information produced by this study will become part of your hospital medical record, and people allowed to look at your medical records may see this research information.

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.

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
- The FDA
- Other government or inspection agencies

If the study investigator is not your regular doctor, he/she must ask your permission before contacting your regular doctor for your health history.

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

ARE THERE ANY COSTS TO BEING IN THE STUDY?

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

The study will pay for all research tests and performed flexible bronchoscopy with fluid analysis that is not part of your routine clinical care.
You and/or your health plan/insurance will be billed for all other tests and procedures you need for your routine health care while you are in this study.

Some health plans/insurance companies will not pay for these costs for people who are in research studies. Check with your health plan/insurance company to find out what they will pay for. If you have any questions about which tests/procedures will be billed to you and/or your health plan/insurance, please ask us.

WILL I BE PAID FOR TAKING PART IN THIS STUDY?

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

Possible Commercial Products

All tissue and body fluid samples are important to this research study. Your samples will be owned by University of Missouri. These people may make products from this study that can be sold. If they sell these products, you will not receive any money.

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/she 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.

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. Holliday at 573-884-2696.

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.

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.

SIGNATURE OF STUDY PARTICIPANT

My initials below indicate my choice about the optional tests in this study:

I agree to the optional flexible bronchoscopy with bronchoalveolar lavage

Yes _____ No _____

My initials below indicate my choice about using my data/samples for future research:

My data/samples may be stored and used for future research.

Yes _____ No _____

My initials below indicate my permission to release the sensitive information listed below:

____I agree to the release of information about drug and alcohol abuse, diagnosis or treatment.

____I agree to the release of HIV/AIDS testing information.

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**

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**

IF THE PARTICIPANT IS DECISIONALLY IMPAIRED, THE LEGALLY AUTHORIZED REPRESENTATIVE (LAR) SHOULD READ AND SIGN BELOW:

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 this participant taking part in this research study. I have been told that they can stop participating at any time.

Signature of legally authorized representative	

Relationship of LAR to Participant	**Date**

Signature of Witness	**Date**

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

MO Rev Stat 431.064: Experimental treatment, tests, and drugs, consent to administer by third party — life-threatening emergencies, consent by whom. —
1. When an adult person, because of a medical condition, is treated by a teaching hospital for a medical school accredited by the American Osteopathic Association or the American Medical Association and such person is incapable of giving informed consent for an experimental treatment, test or drug, then such treatment, test or drug may proceed upon obtaining consent of a legal guardian, attorney-in-fact, or a family member in the following order of priority:
(1) Spouse unless the patient has no spouse, or is separated, or the spouse is physically or mentally incapable of giving consent, or the spouse's whereabouts is unknown or the spouse is overseas;
(2) Adult child;
(3) Parent;
(4) Brother or sister;
(5) Relative by blood or marriage.

2. Nothing in this section shall authorize such legal guardian, attorney-in-fact, or family member to consent to treatment in contravention to such incapacitated person's expressed permission regarding such treatment.

(L. 1993 H.B. 564 § 33, A.L. 2003 S.B. 431, A.L. 2006 H.B. 1601 merged with S.B. 765)