CEDARS-SINAI MEDICAL CENTER

CONSENT FORM FOR RESEARCH

Title: LOW-DOSE TENECTEPLASE IN COVID-19 PATIENTS WITH ACUTE PULMONARY EMBOLISM: A RANDOMIZED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL

STUDY SUPPORT PROVIDED BY:	GENETECH, INC.
PRINCIPAL INVESTIGATOR:	VICTOR TAPSON, MD
STUDY PHONE NUMBER AT CSMC:	919-971-6441
AFTER HOURS CONTACT (24 HOURS):	310-423-5000 (ASK FOR THE PULMONOLOGIST ON CALL)

This research study is sponsored by Genentech, Inc. Genentech, Inc. only reimburses Cedars-Sinai Medical Center for the costs associated with running the study; Genentech, Inc. is not providing additional compensation to Cedars Sinai Medical Center or the Principal Investigator for their participation in the study.

1. WHAT IS THE PURPOSE OF THIS RESEARCH STUDY?

We are doing this study to examine the safety and effectiveness of adding a low dose of tenecteplase (TNK), a thrombolytic drug (clot buster), to standard therapy for patients with COVID-19 who have a blood clot. We want to know if and how much a patient's heart rate and blood pressure can be improved after treatment with tenecteplase (TNK), as compared to the standard of care anticoagulant (blood thinning) therapy alone. TNK is a thrombolytic drug which means the drug is designed to dissolve dangerous clots in blood vessels to improve the blood flow and prevent damage to tissue and organs. The standard of care therapy for pulmonary embolism is either heparin or enoxaparin which are anticoagulants. Anticoagulants are commonly referred to as blood thinners. They are used to prevent and reduce the clotting of blood.

You are being asked to take part in this research study because you have a diagnosis of COVID-19 and a blood clot in one or both of your pulmonary arteries (large blood vessels in your chest) that is interfering with blood flow through your heart and lungs.

The study will enroll up to 45 people in total.

This research study is designed to test the investigational use of tenecteplase (TNK). This drug is approved by the U.S. Food and Drug Administration (FDA) for breaking down blood clots found in the heart. However, it is not approved by the FDA for breaking down clots found in the lung at the low dose of the drug being administered in this study.

2. WHAT WILL HAPPEN DURING THE STUDY?

This section provides a general overview of what will happen during your participation in this study. Information included below should be considered along with the flowchart of procedures attached as an Appendix.

The flowchart shows a timeline for research-related or standard of care procedures that are involved in your participation in this study. **Research-related procedures** are those performed solely for the research. They would not be performed if you did not take part in the study. **Standard of care (routine)** procedures would be performed both as part of this study and if you do not participate in this study.

A table describing common medical procedures done solely for the purposes of monitoring and assessing your condition during this study is attached as an Appendix to the end of this consent form. Standard of care procedures that will be repeated or done at greater frequency are listed in the flow chart Appendix.

Overview of study:

- Your doctor will review your medical record, lab results and other test results to determine if you are able to participate in this study.
- An echocardiogram will be performed once to confirm your eligibility, and once more about 24 hours (give or take 6 hours) after bolus completion (if you proceed with study participation). A bolus is the very quick administration of drugs directly into your bloodstream using intravenous (IV) lines.
- You will be randomized to one of two treatment groups. See below for more detailed explanation.
- You will either receive TNK bolus along with standard of care or receive placebo bolus along with standard of care.
- Your vital signs (temperature, respiratory rate, heart rate, blood pressure, and oxygen saturation level) and medical records data will be collected immediately prior to the bolus, within 15 minutes after the bolus, 60 minutes after the bolus, about 24 hours (give or take 6 hours) after bolus completion, and each day of your hospital stay.
- You will also be assessed for adverse events, including bleeding complications, during your hospitalization and if any occur, the information will be recorded in the study record.
- A blood draw to collect biomarkers may be performed before your drug bolus, and 10 minutes, 24 hours after study treatment administration, throughout your hospitalization, and possibly 14/30 days after receiving study treatment.

This is a randomized, double-blind, placebo-controlled research study.

- "**Randomized**" means that you will be assigned to a study group by chance. You will be randomized into one of two study groups, and will have a one in three chance of being placed in the placebo group (Group 1) and a two in three chance of being placed in the intervention group (Group 2).
- "**Double-Blind**" means neither you nor the researchers will know what group you are assigned to.
- "**Placebo-Controlled**" means the study will compare the effects (good or bad) of tenecteplase (TNK) against the effects of a placebo (an inactive substance, such as, saline) on the condition being studied in this research.

This study has 2 study groups:

- Group 1 will get the usual anticoagulation therapy drug (heparin or enoxaparin) to treat pulmonary embolism plus a placebo injection, that will not have any active medication.
- Group 2 will get the usual anticoagulation therapy drug (heparin or enoxaparin) to treat pulmonary embolism, plus the study drug (TNK).

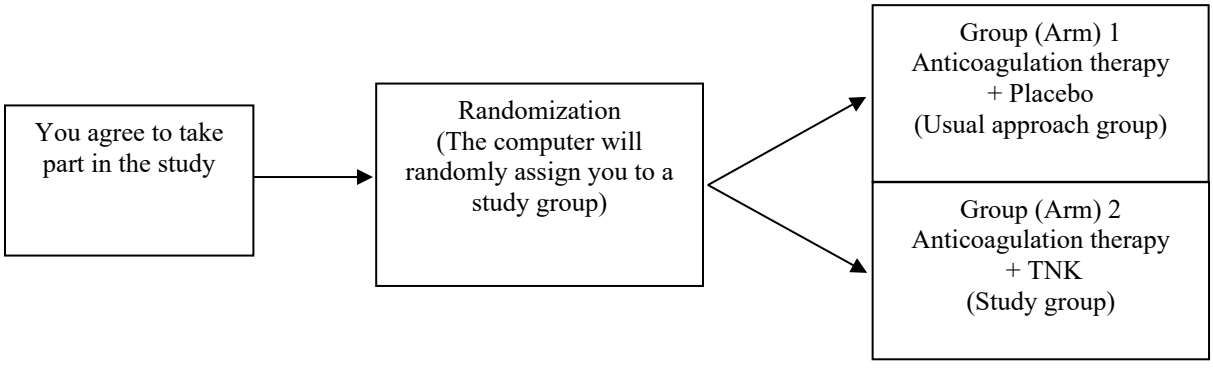
A computer will randomly assign you to a study group. This is done because no one knows if the results experienced by the participants in one study group are better, the same, or worse than the results experienced by participants in the other. Once you are put in one group, you cannot switch to another group. Neither you nor your doctor can choose the group in which you will be placed.

Either of these different approaches could help your condition but could also cause side effects. This study will allow the researchers to learn whether the different approaches are better, the same, or worse than the current standard of care.

In order to properly follow the study's protocol (research plan), all participants will receive treatments and procedures that have been pre-determined by the protocol. In effect, the protocol describes which medications or procedures you will receive, rather than those decisions being made by your personal doctor or based on your preference. There may be options available outside of this study that you will not be able to receive while participating in this study.

Another purpose of this study is for researchers to learn if a biomarker test is helpful in understanding the process of how COVID-19 pneumonia changes over time. A biomarker is a biological molecule found in blood, other body fluids, or tissues that may be a sign of a condition or disease. An extra tube of blood will be drawn for the biomarker test, once at your baseline visit and once at your first follow-up visit 14 days after hospital discharge. The biomarker test will not be used to make decisions about eligibility or treatment assignment. The researchers do not know if using the biomarker test is better, the same, or worse than if you were enrolled in this study without using the biomarker test.

Another way to find out what will happen to you during the study is to read the chart below. Start reading at the left side and read across to the right, following the lines and arrows.



If you are assigned to the control group, you will be followed as you receive the care generally followed for individuals with your condition. Standard (routine) care for controls will involve IV infusion of heparin or injection of enoxaparin.

How long will you be in the study?
We think you will be in this study for about 40 days. The total time includes every day that you are still hospitalized and follow-up after you are discharged. After you are discharged from the hospital, we would like you to visit the office/clinic (in-person or via phone/telemedicine) 2 times at Day 14 and Day 30.

3. WHAT ARE THE POSSIBLE RISKS?

Risks of common medical procedures performed solely for research purposes are described in a table attached to the end of this consent form as an Appendix. Side effects and risks of standard of care procedures are not described in this consent form.

This section describes the possible risks and/or discomforts we anticipate you could experience that are related to the study procedures.

Unknown Risks
There may be other side effects or risks that we cannot predict. Many side effects may go away shortly after the study medication or procedure is stopped. However, in some cases they can be serious, long-lasting, permanent, and/or fatal.

> In the list below, "**Serious**," refers to those side effects that may require hospitalization, may be irreversible, long-term, life-threatening or fatal.

Risks of heparin

Likely, Some May Be Serious (*Occurs in greater than 20% and up to 100 % of people***)**
- None

Less Likely, Some May Be Serious (*Occurs in >3% - 20 % of people)*
- Bleeding in various parts of the body
- Allergic reaction such as itching or hives, swelling in your face or hands, swelling or tingling in your mouth or throat, chest tightness, trouble breathing
- Decreased platelet count
- Abnormal blood clotting

Rare AND Serious (*Occurs in 3% or less of people* ***and*** *may require hospitalization or may be irreversible, long-term, life-threatening or fatal***)**
- Major bleeding

Heparin-induced Thrombocytopenia (HIT) is an immune system reaction from heparin which may cause a decrease of platelet counts and blood clots. HIT may occur up to several weeks after heparin therapy completion. You will not be enrolled in this study if you have a known history of HIT.

Risks of enoxaparin

Likely, Some May Be Serious (*Occurs in greater than 20% and up to 100% of people***)**

- None

Less Likely, Some May Be Serious (*Occurs in >3% - 20% of people)*
- Bleeding in various parts of the body
- Allergic reaction such as itching or hives, swelling in your face or hands, swelling or tingling in your mouth or throat, chest tightness, trouble breathing

Rare AND Serious (*Occurs in 3% or less of people* ***and*** *may require hospitalization or may be irreversible, long-term, life-threatening or fatal***)**
- Decreased platelet count, which may cause abnormal blood clotting
- Major bleeding

In addition to the risks summarized above, the FDA has issued the following warning for enoxaparin:

FDA Blackbox warning: Spinal/Epidural Hematoma
Epidural or spinal hematomas may occur in patients who are anticoagulated with low molecular weight heparins (LMWH) or heparinoids and are receiving neuraxial anesthesia or undergoing spinal puncture. These hematomas may result in long-term or permanent paralysis. Consider these risks when scheduling patients for spinal procedures. Factors that can increase the risk of developing epidural or spinal hematomas in these patients include:
• Use of indwelling epidural catheters
• Concomitant use of other drugs that affect hemostasis, such as non-steroidal anti-inflammatory drugs (NSAIDs), platelet inhibitors, other anticoagulants
• A history of traumatic or repeated epidural or spinal punctures
• A history of spinal deformity or spinal surgery.
Monitor patients frequently for signs and symptoms of neurological impairment. If neurological compromise is noted, urgent treatment is necessary. Consider the benefits and risks before neuraxial intervention in patients anticoagulated or to be anticoagulated for thromboprophylaxis.

Risks of tenecteplase

Likely, Some May Be Serious (*Occurs in greater than 20% and up to 100% of people***)**
- Minor bleeding in parts of the body other than the brain

Less Likely, Some May Be Serious (*Occurs in >3% - 20% of people)*
- Major bleeding in parts of the body other than the brain
- Minor bruising

Rare AND Serious (*Occurs in 3% or less of people* ***and*** *may require hospitalization or may be irreversible, long-term, life-threatening or fatal***)**
- Stroke and brain bleeds
- Major bleeding in the urinary tract, the gut tract, and/or at the site of catheter puncture
- Cholesterol embolization syndrome, which includes features such as gangrene in toes and fingers, heart attack, and acute kidney failure. This condition is also associated with other thrombolytic therapies and with invasive vascular procedures, such as vascular surgery and cardiac catheterization

- Allergic reaction such as itching or hives, swelling in your face or hands, swelling or tingling in your mouth or throat, chest tightness, trouble breathing

Reproductive and Lactation Risks
Taking part in this research study can affect an unborn baby. Therefore, you should not become pregnant or father a baby while on this study. If you or your partner is capable of becoming pregnant you will need to use birth control. Check with the researcher about approved birth control methods to use while participating in this study.

Women should not breastfeed a baby while on this study.

Collection of Pregnancy Outcomes
If you become pregnant during the study, or if you are a male subject whose female partner becomes pregnant, we will collect information on the outcome of the pregnancy including spontaneous or voluntary termination, details of the birth, and the presence or absence of any birth defects, abnormalities, or complications, and the health status of your child. By signing this consent, you are agreeing to have this information about you and your child collected from your medical records in the rare case that you or your female partner become pregnant during your participation in this research study, however, you are always free to withdraw your consent to participate in any research procedure.

Study Design Risks
Participation in a double-blind study means that you may not be able to participate in other, similar trials since unblinding would generally only occur for emergent, life-threatening situations. We might not be able to tell you if you received the study drug or placebo in a situation where you would like to qualify for another research study. Because you may not know the study group to which you were assigned, in the future should you wish to participate in a different study that requires knowing what drug you received in this study, you may not be eligible to participate in the different study.

Follow-up Visit for Discontinuing Participants
While you are free to discontinue your participation at any time, we encourage you to complete a Final Study Visit. During this visit, we will conduct tests to collect safety data, and discuss any information that may be important to share with your treating physician.

4. ARE THERE BENEFITS IN TAKING PART IN THE STUDY?

If you agree to take part in this research study, there may or may not be direct medical benefit to you. The possible benefit of taking part in the research study is that your medical status, as measured by your heart rate and blood pressure, may improve with a low dose, clot-busting medication when given alongside your standard of care treatment for your condition. However, no benefit is guaranteed. It is possible that your condition may remain unchanged or even get worse.

We hope the information learned from this research study will benefit other individuals who have COVID-19 and pulmonary embolism in the future by helping us to learn whether or not tenecteplase can help improve recovery.

5. WILL I BE INFORMED OF RESEARCH RESULTS?

The imaging procedure(s) in this study are for research purposes only. However, the techniques used are the same as those used in standard clinical imaging procedures. The imaging results may be shared with you and may be placed in your Cedars-Sinai medical record.

Some of the research tests done in this study follow standard clinical procedures and are performed in certified clinical labs. These test results may be shared with you and may be placed in your Cedars-Sinai medical record. Other research tests done in this study are for research purposes only and are performed in a research only lab where the results are not intended for clinical use. These research-only results will not be shared with you or included in your Cedars-Sinai medical record.

Unanticipated Incidental Findings
If, unexpectedly, we find that results of your research procedures could suggest important medical information and we determine there is something you or your doctors can do in response to this finding, we will contact you using the last contact information provided by you. If necessary, we may recommend additional clinical testing to confirm the research finding. The cost of any additional testing and any related treatment will be your responsibility.

6. WHY WOULD MY PARTICIPATION BE STOPPED?

Your participation in this study may be stopped at any time by the researcher or the sponsor without your consent for any reason, including:

- The study is stopped or suspended;
- Funding for the study is reduced, stopped or withdrawn;
- If it is in your best interest;
- You do not consent to continue in the study after being told of changes in the research that may affect you;
- You do not follow the study procedures;
- The incidence or severity of adverse events in this or other studies indicates a potential health hazard to patients;
- Patient enrollment is unsatisfactory.

You may choose (or you may be required) to withdraw from certain parts of the study, but invited to continue with other parts. For example, you might stop taking a study drug, but continue with follow-up visits or allow us to continue to collect data from your medical records. Separate written consent will be requested if your continued participation will involve procedures not described in this consent form. If you withdraw from the study, the data collected to the point of withdrawal remains part of the study database and may not be removed.

7. ARE THERE ANY OTHER OPTIONS?

Your participation is voluntary, so you have the right to decline to participate or to withdraw from this research study at any time without any penalty or loss of benefits to which you would be entitled outside of the study. Choosing not to participate will not affect the care you receive at Cedars-Sinai Health System.

If you decide not to take part in this study, you have other choices. For example:

- you may choose to be treated following the usual clinical approach, which is receiving heparin IV infusions or enoxaparin injections.
- you may choose to take part in a different study at CSMC or elsewhere, if one is available
- you could decide not to be treated.
- you may choose to pursue supportive or palliative care for your condition. Such care is focused on reducing suffering and improving the quality of life of individuals with chronic or life-threatening illnesses. The primary intent of palliative care is not to cure a disease or to prolong life. Palliative therapy is focused primarily on managing symptoms.

The researcher will discuss these options and their risks and benefits with you.

8. WILL MY INFORMATION BE KEPT CONFIDENTIAL?

We will do our best to make sure that the personal information collected as part of this study is kept private. However, we cannot guarantee total privacy. A copy of your research consent and authorization forms may be filed in your electronic medical record at CSMC. Your personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other identifiable personal information will not be used. Organizations that may look at and/or copy your medical records for research oversight, quality assurance, and data analysis include: accrediting agencies, government and regulatory groups (such as Food and Drug Administration (FDA), Office for Human Research Protections (OHRP), etc.), safety monitors, companies that sponsor the study, and authorized representatives of the sponsor.

Attached to this consent form is an "Authorization Form" that outlines with whom your information may be shared for the purposes of this research and under what circumstances.

We might share your information and/or research samples collected in this study with other researchers at Cedars-Sinai, other academic institutions, or third party commercial entities for future research without additional informed consent from you. Information that identifies you will be removed and will not be shared with other researchers or anyone outside of Cedars-Sinai.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Website will not include information that can identify you. At most, the Website will include a summary of the results. You can search this Website at any time.

9. WHAT IF I BECOME ILL OR INJURED BECAUSE OF TAKING PART IN THIS STUDY?

Contact your study doctor at once if you feel that you are ill or have been injured because of taking part in this study. If it is a medical emergency, call 911 or go to an emergency room. Promptly notify your study doctor of your situation at the phone number listed on page 1 of this consent form.

Who pays for my research related illness or injury?

Cedars-Sinai has no plans to pay for costs associated with the treatment of research-related injury or illness. We will make every effort to seek reimbursement from your health plan. However, you will be responsible for any deductibles and co-payments required under your health plan and for any claims ultimately denied by your health plan. Financial assistance may be available under Cedars-Sinai's Charity Care Policy and Procedure. If you feel that you have had a research-related injury and need financial assistance, please contact the IRB Office at 310-423-3783. You do not waive any of your legal rights by signing this form.

10. FINANCIAL CONSIDERATIONS

Costs of Participation

Please review the attached Appendix flowchart for a listing of items, drugs and services that will be billed to you and/or your insurance and those that will be covered by the study sponsor.

Only items, drugs and services that are reasonable and necessary for your medical care throughout the study will be billed to your insurance. You remain responsible for all deductibles, co-pays, and balances under your health benefit plan. If your insurance company does not pay, you will be billed for those charges. You should check with your health benefit plan if you have questions or concerns about your insurance coverage.

Compensation for Participating

You will be paid $50 for each research study visit. The total amount you will receive if you complete the whole study is $100. If you do not complete the entire research study, you will only be paid for those visits and procedures you do complete.

You may be required to complete a W-9 Form in order to receive payment. The W-9 Form will be maintained by our accounting department at Cedars-Sinai. Although any amount of payment may be reportable (check with a tax professional if you have questions about your obligations), if total payment by Cedars-Sinai is $600 or more in a calendar year, a 1099 Form will be filed with the IRS in accordance with federal tax law.

If you are a Cedars-Sinai employee, you should provide your employee identification number to the research team so that your payment can be appropriately processed through Payroll. For your own protection and to comply with tax laws, your payment for participation will be reported to the IRS together with other compensation you receive from Cedars-Sinai.

Financial Interest in the Research

The PI and institution have no potential financial conflict of interest with respect to this study.

11. WHAT IF I HAVE QUESTIONS OR PROBLEMS?

Please contact the investigator listed on the first page of this form for questions or concerns about the research.

If you have questions, problems, or concerns that you want to discuss with someone who is not associated with this study, or want to offer suggestions or feedback, please contact:

Cedars-Sinai Human Research Protection Program (HRPP)
Phone: (310) 423-3783
Email: ResearchConcerns@cshs.org

The Cedars-Sinai HRPP has been established to protect the rights and welfare of research participants. You may also contact the Cedars-Sinai HRPP if you want to offer input or obtain information regarding the study.

12. CONSENT PROVISIONS

If you sign this form below, it means that:
(1) You have taken the time to carefully read and understand the information presented in this informed consent form; you should discuss it with others, and if appropriate seek a second opinion to make an informed decision;
(2) The information concerning the research study and its involved procedures has been fully explained to you and your questions have been answered to your satisfaction;
(3) You have received and understand all of the information you desire regarding your participation in the research study;
(4) You have considered the potential risks, any anticipated benefits and alternatives (and their relative risks and benefits) of participation;
(5) You are voluntarily agreeing to participate in this research study;
(6) You understand that by consenting to participate in the research you are not giving up any of your legal rights;
(7) You understand that you have the right to be informed of significant new findings related to this research study which may affect your willingness to continue participating in this study; and
(8) You have been provided with a copy of the "Experimental Subject's Bill of Rights", if applicable to this research study, and have been provided with an opportunity to ask questions regarding the Bill of Rights.

We will give you a copy of this signed and dated consent form and the Experimental Subject's Bill of Rights.

SIGNATURE PAGE

Consent Form for Research and Authorization for Use and Disclosure of Identifiable Health Information (Research)

SIGNATURE BY THE PARTICIPANT OR LEGAL REPRESENTATIVE:

Main Research Study: *I hereby agree to participate in the research study described to me during the informed consent process and described in this informed consent form.* ***You will be given a signed copy of this form.***

Name of Participant (Print) Signature of Participant Date of Signature

If participant is unable to sign the form, please state the reason below:

Signature of Legal Representative Relationship to the Participant Date of Signature

Authorization for Use and Disclosure of Identifiable Health Information (Research): *I hereby agree that my identifiable health information may be used and/or disclosed in accordance with the "Authorization for Use and Disclosure of Identifiable Health Information (Research)" form attached as an Appendix to this form.*

Name of Participant (Print) Signature of Participant Date of Signature

If participant is unable to sign the form, please state the reason below:

Signature of Legal Representative Relationship to the Participant Date of Signature

SIGNATURE BY THE INVESTIGATOR: *I attest that all the elements of informed consent described in this form have been discussed fully in non-technical terms with the participant. I further attest that all questions asked by the participant were answered to the best of my knowledge.*

Name of Investigator (Print) Signature Date Signed

SIGNATURE BY THE INTERPRETER/WITNESS (if applicable)
(Signature of an interpreter is only required when a non-English speaking subject is consented with the assistance of an interpreter. The interpreter may be any person who is conversant in both English and the language of the Non-English speaking subject, such as the interpreter (the certified hospital interpreter), study staff, a family member, or other person. The interpreter signs the consent forms to confirm that the oral interpretation occurred.)

Signature of Interpreter/Witness Date of Signature

SIGNATURE BY THE IMPARTIAL WITNESS (if applicable)
Signature of an impartial witness is required when an English-speaking subjects who has been determined to have capacity to consent is unable to read or physically sign the consent form, but choses to indicate via a "mark" or verbally that he/she agrees to participate. The impartial witness signs the consent form to confirm that an oral consent process occurred and that the individual verbally consented to participate in the research.

Signature of Impartial Witness Date of Signature

TO BE MARKED AT TIME OF SIGNATURE:
Consent obtained:
☐ *From non-English speaking individual with assistance of interpreter*
☐ *From individual who is not physically able to sign the consent document*

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APPENDIX: EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

In accordance with California Health and Safety Code 24172, any person who is required to consent to participate as a subject in a research study involving a medical experiment or who is requested to consent on behalf of another has the right to:

1. Be informed of the nature and purpose of the experiment.

2. Be given an explanation of the procedures to be followed in the medical experiment, and any drug or device to be utilized.

3. Be given a description of any attendant discomforts and risks to the subject reasonably to be expected from the experiment.

4. Be given an explanation of any benefits to the subject reasonably to be expected from the experiment, if applicable.

5. Be given a disclosure of any appropriate alternative procedures, drugs or devices that might be advantageous to the subject, and their relative risks and benefits.

6. Be informed of the avenues of medical treatment, if any, available to the subject after the experiment if complications should arise.

7. Be given an opportunity to ask any questions concerning the experiment or the procedure involved.

8. Be instructed that consent to participate in the medical experiment may be withdrawn at any time and the subject may discontinue participation in the medical experiment without prejudice.

9. Be given a copy of any signed and dated written consent form used in relation to the experiment.

10. Be given the opportunity to decide to consent or not to consent to a medical experiment without the intervention of any element of force, fraud, deceit, duress, coercion, or undue influence on the subject's decision.

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AUTHORIZATION FOR USE AND DISCLOSURE OF IDENTIFIABLE HEALTH INFORMATION FOR RESEARCH

- **USE AND DISCLOSURE OF HEALTH INFORMATION**

If you agree to this Authorization, you give permission to the Sponsor, Principal Investigator, other investigators and their research team described in the Consent Form for Research ("Research Team") to use or disclose your identifiable health information ("private information") for the research study titled "**LOW-DOSE TENECTEPLASE IN COVID-19 PATIENTS WITH ACUTE PULMONARY EMBOLISM**" which is described in the Consent Form for Research ("Consent Form") to which this Authorization is attached. In particular, you authorize the research team acting under the direction of the Principal Investigator to review your medical records and collect your private information from the following sources:

- ☒ Laboratory tests
- ☐ Pathology reports
- ☒ Imaging reports (e.g., x-rays or scans)
- ☐ Photographs or videos of your image
- ☒ Doctor/clinic records
- ☒ Hospital/medical records
- ☐ Mental health records
- ☐ Billing records
- ☐ Other tests or other types of medical information:

- **WHO WILL HAVE ACCESS TO YOUR PRIVATE INFORMATION?**

Your private information will be used by and/or shared with the Research Team.

In addition to the research team, if applicable, the following parties may receive your private information and inspect your records:

- The reviewing Institutional Review Boards and Cedars-Sinai offices with authority to oversee research compliance.
- U.S. government agencies, such as the Food and Drug Administration and the Department of Health and Human Services.
- Researchers at other organizations who are participating in this research study.
- The Study Sponsor, its business partners, and Cedars-Sinai's business partners for matters related to research study oversight, data analysis and use of research results in product development, and payment or reimbursement.
- Representatives from regulatory agencies in other countries may join in the review of your research records, including research-related medical reports and information, with the Sponsor and/or the FDA.

Cedars-Sinai is required by law to protect your private information. However, the recipients described above may re-disclose (or share) your information with other parties unless such sharing is prohibited by law.

- **WHEN WILL MY AUTHORIZATION EXPIRE?**

By signing this document, you authorize the use and sharing of your private information until the end of the research study and any related optional sub-study you choose to participate in.

- **REVOKING AUTHORIZATION**

You may change your mind and revoke (take back) this Authorization at any time. Even if you revoke this Authorization, the research team may still use or disclose private information they already have obtained about you as necessary to maintain the integrity or reliability of the current research. To revoke this Authorization, you must write to the Principal Investigator of the research study by writing to the Office of Research Compliance and Quality Improvement, 6500 Wilshire Blvd, Suite 1800, Los Angeles, Calif. 90048 and/or emailing to ResearchConcerns@cshs.org.

- **NOTICE OF RIGHTS AND OTHER INFORMATION**

You do not have to agree to this Authorization, but if you do not agree, you may not participate in the research study. The Research Team may not condition (withhold or refuse) treating you on whether you agree to this Authorization.

If you agree to this Authorization, please sign on the appropriate signature line on the Signature Page. You will receive a copy of this Authorization.

APPENDIX: Detailed Description of Common Medical Procedures Performed for Research Purposes and Associated Risks

The procedures listed below are often performed as part of routine care for a person with your condition. They are being repeated, or performed more frequently as part of this research. However, the risks associated with each procedure should be comparable to what you would experience even if you were undergoing the procedure outside this research study.

Study Procedure	Related Risks
Blood draw: A needle is placed in the vein in your arm to draw blood.	Blood drawing may cause some pain and has a small risk of bleeding, bruising, or infection at the puncture site. There is also a small risk of fainting.
Bolus Procedure: A bolus is the very quick administration of drugs directly into your bloodstream using intravenous (IV) lines. For this study, the study drug will be administered as a 5 second bolus.	Occasionally, people have allergic reactions (including life-threatening reactions) when taking any medication. Symptoms of any allergic reaction can include a rash, hives, itching, and/or difficulty breathing, closing of the throat, swelling of the lips, tongue or face, and rarely death. If you experience any difficulty breathing, closing of the throat, swelling of the lips, tongue or face, or hives, you should stop taking your study drug and immediately seek emergency medical attention. In general, allergic reactions to medicines are more likely to occur in people who have allergies to other drugs, foods, or things in the environment, such as dust or grass. If you have allergies to other medicines, foods, or other things in the environment, or if you have asthma, you should let your researcher know.
Physical Exam: Includes height, weight, vital signs (heart rate and blood pressure).	There are no physical risks associated with these procedures.
Concomitant Medications: You will be asked about your previous and current medications that you take.	There are no physical risks associated with these procedures.
Medical History Review: You will be asked about your medical and surgical history with attention to smoking and alcohol habits, menopausal history (females only) and your physical activity.	There are no physical risks associated with this procedure.
Echocardiogram: a test that uses ultrasound waves to create a moving picture that shows how strong your heart muscle is pumping or if there are areas not pumping normally. The picture is much more detailed than an x-ray image and involves no radiation exposure.	You may feel some discomfort similar to pulling off an adhesive bandage when the technician removes the electrodes placed on your chest during the procedure.

Urine Sample: If you are a woman who is able to become pregnant, we will collect a urine sample in a collection cup to run a pregnancy test.	There are no physical risks associated with this procedure.
Pregnancy Test: If you are a woman who is able to become pregnant, urine samples will also be used to do a pregnancy test. If the urine pregnancy test is positive, a blood pregnancy test will be conducted.	If your test is positive, you will be told and at that point you should discuss options available with your primary physician.
Demographic Information: You will be asked about your age, gender, race, whether you are a fraternal or identical twin, and ethnicity.	There are no physical risks associated with these procedures.