Clinical Science Research & Development (CSR&D) Study Document Cover Sheet

Study Title: Re-purposing Probenecid for the Treatment of Heart Failure with Reduced Ejection Fraction: The Re-Prosper HF Study

NCT Number: NCT04551222

Initial cIRB Approval Date: 1/17/2023

Participant Name: _____ Date:_____

Title of Study: Re-purposing Probenecid for the Treatment of Heart Failure with Reduced Ejection Fraction: The Re-Prosper HF Study

Principal Investigator: Jack Rubinstein, MD and Joe Calkins, MD VA Facility: Cincinnati VAMC

Principal Investigators for Multisite Study: Jack Rubinstein, MD, Jacob Joseph, MD, Wen-Chih Wu, MD

KEY SUMMARY INFORMATION ABOUT THIS STUDY

You are being invited to take part in a research study that is being funded by VA CSR&D. Before you decide to take part, it is important for you to know why the research is being done and what it will involve. This includes any potential risks to you, as well as any potential benefits you might receive.

Read the information below closely and discuss it with family and friends if you wish. Ask one of the study staff if there is anything that is not clear or if you would like more details. Take your time to decide. If you do decide to take part in this study, your signature on this consent form will show that you received all of the information below, and that you were able to discuss any questions and concerns you had with a member of the study team.

WHAT IS THE STUDY ABOUT AND HOW LONG WILL IT LAST?

The purpose of this research is to gather information on the safety and effectiveness of probenecid for treatment of your heart failure. This medication is FDA approved for gout and has been proven a safe medication for the treatment of gout. Although you might not have gout, the study team is performing this research to determine if probenecid could also be a safe and effective treatment for heart failure. If an approved medication will be used for a different medical reason than for which it is currently approved by the FDA, a research study such as this must be conducted.

Your participation in this study will last approximately seven months.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE TO VOLUNTEER FOR THIS STUDY?

As a patient with heart failure, you may want to participate in this study to help discover if probenecid can be re-purposed safely and effectively to treat heart failure. You may also want to participate to help others or to possibly receive the newest treatment and to have the additional care and attention that will take place during this study**.**

WHAT ARE KEY REASONS YOU MIGHT CHOOSE NOT TO VOLUNTEER FOR THIS STUDY?

You may be anxious about whether you will receive the study drug or the placebo.

There is 50/50 chance of this occurring. However, you will continue to take your currently prescribed heart failure medications. You may be concerned about the results or the effects of the study medication. The results related to heart failure are unknown at this time. The

medication used in this study is an FDA approved medication for gout, which has been proven to have few side effects.

You may feel that you don't have time to join the study. Every effort will be made to coincide your regular clinic visits with the study visits. The study staff will do their best to work with your schedule.

For a complete description of alternate treatment/procedures, refer to the Detailed Information section of this consent.

DO YOU HAVE TO TAKE PART IN THE STUDY?

If you decide to take part in the study, it should be because you really want to volunteer. You will not lose any services, benefits, or rights you would normally have if you chose not to volunteer.

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS OR CONCERNS?

The person in charge of the study is Jack Rubinstein, MD and Joe Calkins, MD at the Cincinnati VAMC. If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study his/her contact information is: Jack Rubinstein @ 517-388-6217 or Joe Calkins, 513-475-6383.

DETAILED INFORMATION ABOUT THE STUDY

WHAT IS THE PURPOSE OF THIS STUDY?

By conducting this research study, we hope to learn if adding a drug called probenecid to the usual care in people with heart failure is better than usual care alone in preventing new or worsening symptoms. Probenecid is an investigational medicine for the treatment of heart failure. There is some information from other studies that this drug may be helpful in patients with heart failure, but it has not been adequately tested. Investigational means that this drug has not been approved for use for heart failure by the Food and Drug Administration (FDA).

HOW LONG WILL I BE IN THE STUDY?

You can expect to be in this study for approximately 7 months. Enrollment of people into the study will take up to 3.5 years. The study will end approximately 6 months after the last participant starts the study. Approximately 40 to 50 participants will likely take part in this study at your local facility.

WHAT WILL HAPPEN IF I TAKE PART IN THE STUDY?

There will be a total of 9 study visits, this will include 4 regular visits and 5 phone visits. You will be asked to come to the clinic for visits 1, 2, 5 and 8 at which you will meet with the study personnel which will be either one of the study physicians or the Study Nurse or Study Coordinator. Local COVID 19 protocols will be followed throughout the study.

Study Entry Visit (Visit 1)

This visit will involve several tests to confirm that you are eligible to participate in the study. This visit will take about 2 hours to complete. During this visit, the study team will:

- Go over this document with you and answer any questions. If you decide to participate in the study, you will need to sign the document before further study procedures can take place.
- Take your vital signs: This will include checks of your heart rate and blood pressure.
- Obtain your height and weight.
- Blood Draw and Testing: At this visit, 0.75 tablespoons (11.2mL) of blood will be drawn. A maximum of about 31 mL (2.1 tablespoons) will be drawn during the entire study (approximatively 7 months). Sometimes a blood test may need to be repeated. If this happens the total amount of blood drawn will be more than this. Your blood will be tested to check your kidneys.
- Blood will also be collected for Biomarker Discovery/ Future Research related to this trial only. A biomarker is something in your blood that can be used to measure the status of disease and/or the effects of probenecid on your body. These samples can be used to learn more about heart failure, how probenecid works, and/or the target of probenecid. At this visit we are collecting the biomarkers to observe results before you are given the study medication.
- Perform an electrocardiogram (ECG). Your doctor may use an ECG to determine or detect: a healthy heart, abnormal heart rhythm, if blocked or narrowed arteries in your heart are causing chest pain or a heart attack. You may have had this test before, but if not, an ECG is a recording of the electrical activity of your heart and is taken by placing adhesive tabs attached to wires on the skin of your chest, arms and legs.
- Perform an Echocardiogram: An echocardiogram helps your doctor determine whether all of the parts of your heart wall are contributing normally to your heart's pumping

activity. An echocardiogram (echo) is a test that uses high frequency sound waves (ultrasound) to make pictures of your heart. The test is also called echocardiography or diagnostic cardiac ultrasound.

- Ask about the other medications you are taking.
- Check the status of your heart failure and any signs or symptoms associated with heart problems.

Baseline/Randomization Visit (Visit 2)

During this visit, you will be randomly assigned by a computer (as if by the toss of a coin) to get either probenecid or placebo. Half the participants in this study will receive the probenecid and half will receive placebo. A placebo is an inactive medication, sometimes referred to as a sugar pill. We use placebos in clinical studies to learn if the effects seen in the trial are truly from the study medicine or from other reasons. Neither you nor the study staff can choose or will know your study drug assignment. You will not find out your assignment. This visit will take about 2-2.5 hours to complete. In addition to being randomized, the study team will do the following:

- Take your vital signs: This will include checks of your heart rate and blood pressure.
- Obtain your height and weight.
- Ask about the other medications you are taking.
- Check the status of your heart failure and any signs or symptoms associated with heart problems.
- You will complete 2 questionnaires (KCCQ and EQ5D) to assess your quality of life. Your answers will help the study doctor determine if the study drug treatment is helping you. If you feel the questionnaires make you uncomfortable you will not have to answer them
- Review your medical history and collect demographics.
- Perform an ECG.
- Pregnancy testing for pre-menopausal women
- Blood Draw and Testing: repeat standard overall health blood if > 30 days from Screening/V1.
- Answer any questions that you might have.

- Bike Exercise Stress Test (BEST): This test involves increasing the intensity level of exercise until you can no longer keep up, either because you are winded, or the ECG indicated there is a cardiac problem. By riding a stationary bike, we will see how your heart works during physical activity. Because exercise makes your heart pump harder and faster, an exercise stress test can reveal problems with blood flow within your heart.
- You will receive enough medication for 3 months. You will be asked to take the study drug twice a day every day, throughout the study. The study drug should be swallowed whole, not chewed, or split, and should be taken with water. It can be taken with or without food. We recommend that you take the study drug at the same time each day, preferably between 6-8am and 6-8pm. If you cannot take each dose at least 9 to 15 hours after the most recent dose, then the dose should not be taken, the next dose should be taken at the regular time. At every visit, we will ask you to bring in your unused study drug or empty bottle.

Study Visits 3, 4, 6 and 7 (Phone Calls)

After the Study Entry and Baseline/Randomization visits we will ask you to complete monthly phone visits. We will ask you the following:

- Ask about any changes in your health since the last contact and if you have any upcoming procedures.
- Ask about the other medications you are taking.
- Ask if there has been worsening in your overall health, specifically shortness of breath.
- Ask about any side affects you may have. Side effects are any unexpected, unwanted or sometimes unpleasant reactions that may result from your participation in this study, regardless of whether it is related to the study drug or not.

Study Visit 5

This visit will take about 1 hour to complete. During this visit, the study team will:

- Take your vital signs: This will include checks of your heart rate and blood pressure.
- Your weight will be checked.
- Ask about any changes in your health since the last contact and ask if you have any upcoming procedures.
- Ask about the other medications you are taking.

- Check the status of your heart failure and any signs or symptoms associated with your heart.
- The study doctor or staff will review your study drug and ask about any side affects you may have. Side effects are any unexpected, unwanted or sometimes unpleasant reactions that may result from your participation in this study, regardless of whether it is related to the study drug or not.
- Perform an ECG
- Blood Draw and Testing: 0.6 tablespoons (8.5ml) of blood will be collected. Sometimes a blood test may need to be repeated. If this happens the total amount of blood drawn will be more than this. Your blood will be tested to check your kidneys.
- Pregnancy testing for pre-menopausal women
- You will receive 3-month study drug supply. We will
-
- ask you to bring in your unused study drug or empty bottle.

Study Visit 8 (Final Visit or Early Termination)

This visit will take about 2-3 hours to complete. At this visit we will do the following:

- Vital signs: This will include checks of your heart rate and blood pressure.
- Your weight will be checked.
- Ask about any changes in your health since the last contact and if you have any upcoming procedures.
- Ask about the other medications you are taking.
- Check the status of your heart failure and any signs or symptoms associated with your heart.
- Perform an ECG.
- Perform an echocardiogram.
- You will complete 2 questionnaires (KCCQ and EQ5D) to assess your quality of life. Your answers will help the study doctor determine if the study drug treatment is helping you. If you feel the questionnaires make you uncomfortable you will not have to answer them.

- The study doctor or staff will review your study drug and ask about any side effects you may have. Side effects are any unexpected, unwanted or sometimes unpleasant reactions that may result from your participation in this study, regardless of whether it is related to the study drug or not.
- Blood Draw and Testing: At this visit we will collect 1.6 tablespoons (25mL) of blood for your overall health. Blood samples will be used to monitor your health and safety. Blood will also be collected for Biomarker Discovery/ Future Research related to this trial only. A biomarker is something in your blood that can be used to measure the status of disease and/or the effects of probenecid on your body. These samples can be used to learn more about heart failure, how probenecid works, and/or the target of probenecid. At this visit we are collecting the biomarkers to observe results before you are given the study medication.
- Pregnancy testing for pre-menopausal women
- Bike Exercise Stress Test (BEST): This test involves increasing the intensity level of exercise until you can no longer keep up, either because you are winded, or the ECG indicated there is a cardiac problem. By riding a stationary bike, we will see how your heart works during physical activity. Because exercise makes your heart pump harder and faster, an exercise stress test can reveal problems with blood flow within your heart.

Study Visit 8 (Early Termination Phone Call)

- Ask about any changes in your health since the last contact and if you have any upcoming procedures.
- Ask about the other medications you are taking.
- Ask about the status of your heart failure and any signs or symptoms associated with your heart.
- Complete 2 questionnaires (KCCQ and EQ5D) to assess your quality of life.
- Ask about any side effects or adverse events.

Study Visit 9 (Phone Call)

Study staff will call you 30 days after your last in person visit. This is to inquire how you have been feeling since your last dose of study drug and f you have any questions or concerns regarding the study.

Participant Name: _____ Date:_____

Title of Study: Re-purposing Probenecid for the Treatment of Heart Failure with Reduced Ejection Fraction: The Re-Prosper HF Study

Principal Investigator: Jack Rubinstein, MD and Joe Calkins, MD VA Facility: Cincinnati VAMC

Principal Investigators for Multisite Study: Jack Rubinstein, MD, Jacob Joseph, MD, Wen-Chih Wu, MD

Schedule of Assessments

Data Collection	Screening visit V1	*Baseline visit V2*	Monthly phone visits (28 days +/- 3 days) V3, V4, V5, V6, V7	In person - Visit 5 (28 days +/- 3 days)	Final Study V8 or ET (28 days +/-3 days)	30-day safety call V9 (+/- 3 days)
Complete screening Form/consent	X					
Echocardiogram	X	X (Repeat if > 3 months from V1)			X	
ECG	X	X		X	X	
Blood Draw and Testing; Renal function, CBC, Troponin (non-fasting)	X	X (repeat if > 30 days from V1)		X	X	
Blood Draw and Testing: Uric Acid	X	X (repeat if > 30 days from V1)			X	
Biomarker/Future Research Blood Collection	X				X	
Pregnancy testing for Pre-menopausal women		X		X	X	

FOR VA CENTRAL IRB USE ONLY

PI/SC Approval Date: 11/4/2022

LSI Approval Date: 1/17/2023

LSI Verification Date: N/A

Questionnaires		x			x	
Bike Exercise Stress Test		x			x	
Demographics & Medical history,		X				
Complete concomitant medication list	X	x	x	X	X	
Assessment of vital signs and/or weight	x	X		X	X	
Check status of heart failure	X	X	X	X	X	
Assess health status: Adverse Events/Serious Adverse Events	x	X	X	X	X	X

WHAT IS EXPECTED OF ME IF I TAKE PART IN THIS STUDY?

While you are part of this study, the study staff will follow you closely to determine whether there are problems that need medical care. It is your responsibility to do the following:

- Ask questions about anything you do not understand.
- Keep your appointments.
- Follow the study team's instructions.
- Report to the study team any injury or illnesses while you are on study, even if you do not think it is related. Do not take medications that are not allowed during your participation in this study or while taking the study drug. These include the following classes and/or specific medications; cephalosporins (a large group of antibiotics). If you have an infection and a Physician prescribes an antibiotic, please call the study staff so they can review the antibiotic to see if it safe to use with the study drug, quinolones, penicillin's, methotrexate, zidovudine, ganciclovir, and acyclovir. Your medication list will

be reviewed by the study staff. The study staff will tell you more about which medicines you can take during your participation in the study. Probenecid may reduce the excretion rate of certain pain medications, there is a possibility of increasing the effects of non-steroidal anti-inflammatory medications known as NSAIDS and including high dose aspirin (dose over 1600 mg daily). Please inform your doctor if they are starting or changing the dose of your NSAID. A list of medications will be given to you.

- Tell the study doctor about all drugs you are taking or are prescribed while you are participating in the study so that you can receive advice about its safety during the study.
- Consult with the study doctor before taking any new medications, supplements or herbal medications or changing the dose of any of your existing medications or taking any new medication. Always follow the study doctor's instructions during the study.
- Store all drugs at 20-25°C (68-77°F) and keep study drug out of reach of children.
- Take the study drugs twice a day as instructed.
- Return study drug that you have not taken and all empty bottles to study personnel at visit 5 and 8.
- It is important that you keep in touch with your study doctor until the end of the study for any required follow-up, even if you decide to stop the study drug earlier. You will also be asked to provide your contact details or a family member's contact information to allow the study doctor to contact you. Let the study team know if your telephone number or address changes.
- In case you need to contact your study doctor in an emergency, you will be given a contact card with all the relevant information about this study. This card must be kept with you always during your participation in the study because it gives details on the experimental study drug you are receiving.
- Inform your general practitioner or any other doctor who takes care of you of your participation in this study to avoid your being prescribed drugs not allowed during the study. Always consult with the study doctor before you take any new medicine.
- Tell the study doctor if you no longer want to take part in the study.

During the study, you will receive the study drug free of charge. The study drug will not be available as a prescription paid for by the health care system immediately after the end of the study. You will not continue to receive this drug when you have finished taking part in the study. The care you receive after the study has ended may involve a different drug or treatment that your study doctor considers to be the most suitable alternative.

WHAT POSSIBLE RISKS OR DISCOMFORTS MIGHT I HAVE IF I TAKE PART IN THIS STUDY?

The possible discomforts, side effects, and risks related to study drug are not all completely known. All drug may have side effects. Most side effects are mild to moderate, but some may be serious and/or require treatment or additional testing. Each person's reaction to a study drug may be different. You may have a side effect or be at risk for symptoms, illnesses and/or complications that could not be predicted by your study doctor or the Sponsor of this study.

For your safety, you must inform your study doctor about all medicines you are taking. In addition, you must inform your study doctor about any side effects.

The following side effects have been seen in patients treated with the study drug during clinical studies but none of the side effects were confirmed to have been caused by the study drug:

Most common possible side effects (2 out of 100 patients)

- Nausea, vomiting and loss of appetite. These can be reduced if you eat only a little at a time but eat often. Stick to simple foods such as dry toast. If you are sick drink plenty of liquid.
- It has been observed that sperm has an increased ability to travel (motility) in men who take probenecid.

Less common or rare possible side effects (less than 1 out of 100 patients.)

- Headache
- Flushed skin (skin redness typically over the cheeks or neck)
- Sore gums
- Difficulty sleeping and dizziness.
- Skin problems: Probenecid may cause a rash or flaking skin as well as boils, sore lips or mouth ulcers. If any of these occur, contact your doctor straight away.
- Kidney problems: Probenecid may cause kidney stones. If you get blood in the urine or severe back pain, see your doctor. Infrequently, probenecid may cause leakage of protein into the urine. Traces of protein in the urine are often not a problem; larger amounts usually mean that probenecid will be stopped. If protein leakage does occur, provided the probenecid is stopped, there is little chance of serious kidney damage developing.

If you receive placebo, there may be no additional effects on your current medications or treatments, so your condition may stay the same or become worse. It is possible that the symptoms of your condition will not improve during the study or may even worsen. Taking this study drug may also involve risks to your future health that we currently don't know about. Any side effects or other health issues occurring during the study will be followed up by the study doctor.

Blood Samples: You will need to have samples of blood taken during the trial for laboratory testing. You may experience temporary discomfort from this. The blood sampling may cause local pain, bruising, swelling, lightheadedness, dizziness and rarely, fainting and/or a possible infection at the blood sampling site.

Electrocardiogram (ECG): The study also includes ECGs at different times. Occasionally there may be some minor skin irritation from the adhesive tabs of the wire electrodes.

Echocardiogram: A transthoracic echocardiogram carries no risk. There is a chance for possible skin irritation. This may feel similar to pulling off a Band-Aid.

Bike Exercise Stress Test (BEST): Is generally safe, and complications are rare. But, as with any medical procedure, there is a risk of complications, including:

- Low blood pressure. Blood pressure may drop during or immediately after exercise, possibly causing you to feel dizzy or faint. The problem should go away after you stop exercising.
- Abnormal heart rhythms (arrhythmias). Arrhythmias brought on by an exercise stress test usually go away soon after you stop exercising.
- Heart attack (myocardial infarction). Although exceedingly rare, it's possible that an exercise stress test could cause a heart attack.
- You will be told about the other risks of BEST which may include the development of any of the following: (1) chest pain, (2) intolerable labored breathing, (3) leg and back, (4) staggering and dizziness, (5) sweating, (6) pale or ashen appearance, (7) falls and, (8) low blood sugar.
- If you are a diabetic patient, you will be asked to bring your glucometer to the BEST, as well as test your blood sugars prior to starting the test and at the end of the test. Glucose tablets or a sugared beverage will be available if your blood sugar drops below 70 mg/dL or if you are symptomatic at any point.

Pregnancy: The safe use of probenecid is the medication of choice during pregnancy for uric acid elimination. However, this trial is not for the elimination of uric acid. Therefore, women of childbearing potential enrolling in this study must (i) have been using a birth control measure (an intrauterine device (IUD), birth control pills, a condom, diaphragm, or abstinence) for the previous three months, (ii) must have a negative pregnancy test, and (iii) must agree to continue to use a birth control measure for the duration of the study. If, while participating in the study, you suspect you have become pregnant, please contact the study physician immediately. Women are considered to be of childbearing potential unless they have been surgically sterilized (for example tubal ligation or hysterectomy) or are post-menopausal, that is, no menstrual period for more than 6 months. Nursing mothers may not participate in this study.

There is always a chance that any procedure can harm you. The procedures in this study are no different. In addition to the risks described above, you may experience a previously unknown risk or side effect.

Risks of the usual care you receive are not risks of this study. Those risks are not included in this consent form. You should talk with your health care providers if you have any questions about the risks of usual care.

WHAT ARE THE POSSIBLE BENEFITS OF THIS STUDY?

We can't promise that you will receive any benefits from taking part in this research study. However, possible benefits might include: the contacts and tests occurring during study visits might help to detect a medical problem before it would otherwise be noticed. This might allow you to seek and receive earlier treatment. Also, what is learned from this study might help doctors treat other patients who have health problems, similar to yours in the future.

WHAT OTHER CHOICES DO I HAVE IF I DO NOT WANT TO JOIN THIS STUDY?

You can choose not to participate in this study. If you choose not to participate, the study doctor can discuss other healthcare choices for you.

Other healthcare choices may include but are not limited to; increasing the dose of medications you are already receiving to treat your heart failure or adding new treatments to your existing treatment.

HOW WILL MY PRIVATE INFORMATION BE PROTECTED?

Taking part in this study will involve collecting private information about you. Confidentiality cannot be guaranteed, but your private information will be protected in a number of ways. The study team will keep all research records that contain your identifiable health information confidential to the extent allowed by law. All hard-copy study forms with the information we collect from you as part of this study will be stored in locked cabinets to which only approved study staff will have access. Data will be entered on computers that are protected with passwords to which only approved study personnel will have access. Only approved study staff will have access to participant identifying information. This study is being conducted in multiple VA Medical Centers nationwide. Information shared among researchers will not be able to identify you individually.

We will include information about your study participation in your medical record. Your medical records and information will be kept confidential as described in this form and as allowed by the applicable laws. If you are currently receiving care through the VA, you already have a VA medical record. If you have not received care through the VA recently, we will create a VA medical record for you. A VA Medical Record includes your Social Security number.
We will put the following information into your electronic VA medical record from this study:

- A note that says you are participating in a research study. The note will contain the name of the study.
- A note for each of your study visits/contacts, including any changes in the dose of study drug.

The study team will collect your Social Security number for this research study. The study team will use your Social Security number only as necessary within the VA to search your medical records or when there is a need to check your non-VA hospitalizations during the study or to check your status with other healthcare and vital status databases. We use a unique code instead of your name or Social Security number to identify you in our study database. If you choose to withhold your Social Security number, you will not be able to participate in the study.

Information about you will be combined with information from other people taking part in the study. We will write about the combined data we have gathered. Any talks or papers about this study will not identify you individually. Research records, just like hospital medical records, may be released or disclosed according to applicable federal and state law as well as to federal and state agencies that are responsible for oversight of medical research. We will not share your

records or identify you unless we have to by law. Approved study personnel from another study site may review your data for quality assurance purposes.
There are times when we may have to show your records to other people including:

1. Representatives of the study sponsor: VA Clinical Science Research and Development (CSR&D)
2. VA Data Monitoring Committee
3. Food and Drug Administration (FDA)
4. Department of Health and Human Services, Office of Human Research Protections (OHRP)
5. Government Accountability Office (GAO)
6. Office of the Inspector General (OIG)
7. VA Office of Research Oversight (ORO)
8. VA Central Institutional Review Board (IRB)
9. Local VA Research and Development Committee
10. VA or VA-contracted personnel who may review study records for quality assurance purposes
11. Your study data will be sent to the University of Texas for analyses

All samples will be marked only with a unique study ID but will not include any Protected Health Information. These samples, however, can be linked with data collected as part of this research study. Your information or biospecimens collected as part of the research, even if identifiers are removed, will not be used or distributed for future research studies. The information or biospecimens will not be used for future research studies.

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.

Health Information Portability and Accountability Act (HIPAA)

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

The research team working on the study will collect information about you. This includes things learned from the procedures described in this consent form. The study team may also collect

other information including your name, address, date of birth, and information from your medical records.

The research team may also need to disclose the information to others as part of the study progress including:

1. Representatives of the study sponsor: VA Clinical Science Research and Development (CSR&D)
2. VA Data Monitoring Committee
3. Food and Drug Administration (FDA)
4. Department of Health and Human Services, Office of Human Research Protections (OHRP)
5. Government Accountability Office (GAO)
6. Office of the Inspector General (OIG)
7. VA Office of Research Oversight (ORO)
8. VA Central Institutional Review Board (IRB)
9. Local VA Research and Development Committee
10. VA or VA-contracted personnel who may review study records for quality assurance purposes
11. Your study data will be sent to the University of Texas for analyses

Your health information disclosed pursuant to this authorization may no longer be protected by Federal laws or regulations and may be subject to re-disclosure by the recipient.

While this study is being conducted you will not have access to your research related health records.

This will not affect your VA healthcare, including your doctor's ability to see your records as part of your normal care and will not affect your right to have access to the research records after the study is completed.

You can revoke this authorization, in writing, at any time. To revoke your authorization, you must write to the Release of Information Office at this facility or you can ask a member of the research team to give you a form to revoke the authorization. Your request will be valid when the Release of Information Office receives it. If you revoke this authorization, you will not be able to continue to participate in the study. This will not affect your rights as a VHA patient to treatment or benefit outside of the study.

If you revoke this authorization**,** Jack Rubinstein and his research team can continue to use information about you that was collected before receipt of the revocation. The research team will not collect information about you after you revoke the authorization.

Treatment, payment or enrollment/eligibility for benefits cannot be conditioned on you signing this authorization. This authorization will expire at the end of the research study unless revoked prior to that time.

WHAT ARE THE COSTS TO ME IF I TAKE PART IN THIS STUDY?

It is not expected that you will have any additional costs if you participate in this study. You will receive the study drug at no charge. There are no charges or co-pays for additional visits, tests or procedures that are required for this study. Some of the medical care you will receive while you are participating in this study is considered usual care for heart failure and would be recommended whether you are in the study or not. If you usually pay co-payments for VA care and medications, you will still pay these co-payments for the usual care and medications that are not part of this study.

Will you be paid for participating in this study?
You may receive up to $599.00 for your time and expenses. The payments are as follows:

- Visit 1/Screening - $50.00
- Visit 2/Baseline - $175.00
- Visit 3/Phone - $20.00
- Visit 4/Phone - $20.00
- Visit 5/In-person - $99.00
- Visit 6/Phone - $20.00
- Visit 7/Phone - $20.00
- Visit 8/In-person - $175.00 - if completed by phone - $35
- Visit 9/Phone - $20.00

You will be paid $50.00 if you fail the screening process. You will receive information on payment options available through your local VA facility. If you receive a debit card you will keep this debit card though out your participation in the study. Your Social Security number will be required for Internal Revenue Service reporting of income and payment processing.

Travel may be reimbursed if you require commercial transportation, please discuss with study staff.

You will not be paid for the use of your samples, or any information obtained from your samples or medical information. You do not have any rights to future inventions.

WHAT WILL HAPPEN IF I AM INJURED BECAUSE OF MY BEING IN THE STUDY?

If you are injured as a result of taking part in this study, the VA will provide necessary medical treatment at no cost to you unless the injury is due to non-compliance by a study participant with study procedures or if the research is conducted for VA under contract with an individual or non-VA institution.

If you should have a medical concern or get hurt or sick as a result of taking part in this study, call:
DURING THE DAY:

Ms. Julie Bunke at 513-861-3100 ext. 204339 and

AFTER HOURS:

Dr. Jack Rubinstein at 517-388-6217 or Joe Calkins at 513-475-6383.

DO I HAVE TO TAKE PART IN THE STUDY?

It is up to you to decide whether you want to take part in this study or not. By signing this consent, you are agreeing to participate in full. This means staying in contact with the research team, taking the study drug, and completing the required tests.

If you change your mind about taking part in any aspect of this study, please contact the research team. Leaving the study will not affect your heart disease. This study medication is added to your prescribe medication already taken for your heart disease. Study staff will call you 30 days after you withdraw to see how you are doing and to follow up on any issues or questions you may have.

If you have not informed your study doctor about your intent to completely leave the study and have had no form of contact with the study staff, and your study doctor is unable to contact you, the study staff may attempt to find you through contacting your emergency and alternate contacts or contacting your personal doctor.

Even if you decide to completely leave the study, public records and/or public sources of information may still be used to collect updates on your status, until the study ends, to the extent permitted by law.

If you do not wish to be in this study or leave the study early, you will not lose any benefits to which you are entitled. Your decision will not affect the relationship you have with your doctor or other staff. Your decision will not affect any of the usual care that you receive.

If you decide to leave the study early, please notify your Study Doctor Jack Rubinstein or Joe Calkins, or another member of the research team at 513-861-3100 ext. 204339. If you completely withdraw from the study, we will still use the information we have collected about you up to that time point.

RIGHT OF INVESTIGATOR TO TERMINATE MY PARTICIPATION

The study doctor may take you off the study for any of the following reasons:

- If your health changes and the study is no longer in your best interest.
- If new information becomes available.
- If you do not show up for study visits or follow the study procedures.
- If the study is stopped by the sponsor, local oversight committees, or the FDA.

Termination from the study will not affect your heart disease. This study medication is added to your prescribed medication already taken for your heart disease. We will inform your Primary Care Physician and/or your Cardiologist regarding our decision to terminate you from the study. Study staff will call you 30 days after your termination to see how you are doing and to follow up on any issues or questions you may have.

WHO DO I CONTACT ABOUT THIS STUDY IF I HAVE QUESTIONS?

If you have any questions, complaints, or concerns about this study, you may contact the study investigator at your VA Medical Center or the Study Coordinator during regular business hours.

The investigator is: Jack Rubinstein and Joe Calkins.

The study coordinator is: Julie Bunke.

VA patient Advocate is: 513-475-6492.

Participant Name: _____ Date:_____

Title of Study: Re-purposing Probenecid for the Treatment of Heart Failure with Reduced Ejection Fraction: The Re-Prosper HF Study

Principal Investigator: Jack Rubinstein, MD and Joe Calkins, MD VA Facility: Cincinnati VAMC

Principal Investigators for Multisite Study: Jack Rubinstein, MD, Jacob Joseph, MD, Wen-Chih Wu, MD

If you have questions about your rights as a study participant, or you want to make sure this is a valid VA study, you may contact the VA Central Institutional Review Board (IRB). This is the Board that is responsible for overseeing the safety of human participants in this study. You may call the VA Central IRB toll free at 1-877-254-3130 if you have questions, complaints or concerns about the study or if you would like to obtain information or offer input.

WILL I BE TOLD NEW INFORMATION ABOUT THIS STUDY?

If sometime during the course of this research study, new information becomes available about probenecid that might change your decision to stay in the study the study doctor will tell you about it and discuss with you whether you want to continue in the study. If you decide to withdraw from the study, your study doctor will arrange for your medical care to continue.

If you decide to continue in the study, you might be asked to sign an updated informed consent form. Your study doctor could also decide if it is in your best interest to withdraw you from the study. If so, he or she will explain the reasons and arrange for your usual medical care to continue.

AGREEMENT TO PARTICIPATE IN THE RESEARCH STUDY

Dr./Mr./Ms._____ _____ has explained the research study to you. You have been told of the risks or discomforts and possible benefits of the study. You have been told of other choices of treatment available to you. You have been given the chance to ask questions and obtain answers.

By signing this document below, you voluntarily consent to participate in this study and authorize the use and disclosure of your health information in this study. You also confirm that you have read this consent, or it has been read to you. You will receive a copy of this consent after you sign it. A copy of this signed consent will also be put in your medical record.

I agree to participate in this research study as has been explained in this document.		
_____ Participant's Name	_____ Participant's Signature	_____ Date

FOR VA CENTRAL IRB USE ONLY

PI/SC Approval Date: 11/4/2022

LSI Approval Date: 1/17/2023

LSI Verification Date: N/A