UNIVERSITY OF CALIFORNIA, SAN FRANCISCO CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Study Title: *Developing a Heart Failure Polypill to Reduce Total Pill Burden: A Pilot Crossover Randomized Controlled Trial*

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This project is being conducted by researchers from University of California, San Francisco. The objective of this research study is to test whether a combination pill, or "polypill," for congestive heart failure (CHF) makes it easier for patients with CHF to take their heart failure medications. Some participants also have HIV, which increases total daily pill burden. The Principal Investigator, who is the person in charge of the study, or another member of the study team from the UCSF Division of Cardiology at Zuckerberg San Francisco General will explain this study to you.

STUDY SUMMARY

Introduction: We are asking you to consider taking part in a research study being done at UCSF.

The first part of this consent form gives you a summary of this study. We will give you more details about the study later in this form. The study team will also explain the study to you and answer any questions you have.

Research studies include only people who choose to take part. It is your choice whether or not you want to take part in this study. Please take your time to make a decision about participating. You can discuss your decision with your family, friends and health care team.

Purpose of the study: The purpose of this study is to find out the effects, good and/or bad, of a combination pill for congestive heart failure (CHF) among patients with CHF. Instead of taking several CHF medications as individual pills, study participants' CHF medications will be over-encapsulated into a single combination pill ("polypill").

Study Procedures: If you choose to be in this study, you will first meet with a cardiology doctor, who will evaluate your CHF medication regimen and may prescribe additional medications for your heart failure. You will then be assigned at random to study group A or B. Group A will receive the medications as a combination pill ("polypill") for one month, and then as individual tablets for one month. Group B will receive the medications as individual tablets for one month, and then as a polypill for one month. Your medication doses may be adjusted at

study follow-up visits. You will attend monthly study visits and undergo blood draws at least every month during the study, with additional blood draws if needed, for example, if your medications are adjusted. The study team will also call you for a telephone visit at the halfway point between in-person visits, or more frequently if needed. After the study, you will complete a 30-60 minute exit interview to discuss your experience with the CHF polypill.

Any medications that are started during this study will be continued after you complete the study, and you will be referred to cardiology clinic if you do not already have a cardiologist. You will be in this study for 2-3 months and visit the research site approximately 4-6 times. If you consent to be in the study, the research team will also review your medical record at regular intervals to gather additional information about your health and your medical care.

Possible Risks: There are risks to taking part in a research study. Some of the most likely risks of participation in this study include:

- **Known side effects of your CHF medications**: Through participation in this research study, you may continue taking some of the same medications for CHF, or may be started on new medications that are effective in treating CHF. If you are started on new CHF medications, or if the CHF polypill makes it easier to take your CHF medications, you may experience more side effects. The side effects of these medications could include low blood pressure, low heart rate, high potassium, engorgement of breast tissue (gynecomastia), or acute kidney injury.
- **Drawing blood (venipuncture) risks:** Drawing blood may cause temporary discomfort from the needle stick, bruising, infection, and fainting.

There are also rare but serious risks of participation, like:

- **Increased side effects due to dose adjustments:** In order to allow your CHF medications to fit into a single capsule, the study clinician may need to switch you to another medication in the same drug class, or make a small adjustment to your medication dose. These dose adjustments would be disclosed to you in advance, and your primary cardiologist or primary care provider would be notified of any changes.
- **Medication error:** As with a Bubble Pack or Medi-Set, the CHF polypill will involve having a pharmacist co-package several of your medications into a single capsule. Any medication repackaging entails some risk of medication error, for example, having too much of one medicine or none of another medicine included in the CHF polypill.

We'll tell you about the other risks later in this consent form.

Possible Benefits: You may or may not benefit from participating in the study.

Your Other Options: You do not have to participate in this study. Your other choices may include:

- Getting treatment or care for your condition without being in a study.
- Taking part in another study.

Please talk to your doctor about your choices before agreeing to participate in this study.

Following is a more complete description of this study. Please read this description carefully. You can ask any questions you want to help you decide whether to join the study. If you join this study, we will give you a signed copy of this form to keep for future reference.

DETAILED STUDY INFORMATION

Research studies include only people who choose to take part. Please take your time to make your decision about participating, and discuss your decision with your family or friends if you wish. If you have any questions, you may ask the researchers. You are being asked to take part in this study because you have been diagnosed with CHF.

Why is this study being done?

The purpose of this study is to find out the effects, good and/or bad, of a combination pill for congestive heart failure (CHF) among patients with CHF. Some participants also have HIV, which further increases their daily pill burden. Instead of taking several CHF medications as individual pills, study participants' CHF medications will be over-encapsulated into a single combination pill ("polypill"). The administration of these CHF medications via polypill is investigational, which means it is being tested and the polypill is not approved for marketing by the FDA.

The investigators do not have any relevant conflicts of interest for this study. This study received funding from the ACC/ABC Merck Research Fellowship Award, the CAPS-HIV Innovative Grant, and the CFAR-ARI HIV Research Boost Award.

What is the usual care for my condition?

Usual care for patients with CHF is to take several medications that act together to strengthen the function of the heart. These medications are prescribed by your cardiologist, and are each taken as individual pills. There is no combination pill currently available for CHF.

How many people will take part in this study?

Up to 40 people will take part in this study at the University of California, San Francisco.

What will happen if I take part in this research study?

Before you begin the main part of the study...

You will need to have an intake visit and blood test to find out if you can be in the main part of the study. These blood tests are part of regular CHF care and may be done even if you do not join the study. If you have had some of them recently, they may not need to be repeated. This will be up to your study clinician. The research team will also review your chart in the electronic medical record.

- Intake visit with a study clinician
- Review of your current medication regimen
- Blood tests
- Questionnaires about how you currently take your medications

- If you are not currently prescribed all recommended medications for CHF, the study clinician may start you on additional medications for CHF

During the main part of the study...

If the intake visit and blood tests show that you can be in the main part of the study, and you choose to take part, then you will need the following tests and procedures. They are part of regular CHF care, but they will be done more often because you are in this study.

- Monthly visit with a member of the research team. At these visits, we will measure the following:
    - Vital signs (blood pressure, heart rate, and oxygen saturation)
    - Weight
    - Pill counts. You will be asked to bring in your medications to each visit, and we will keep track of the number of pills in each pill bottle
    - Questionnaires about your CHF symptoms and your medication-taking practices
- Regular blood tests (every month, or as needed according to the study clinician)
- You may be started on additional medications for CHF, or your doses may be adjusted if recommended by the study clinician
- The study research team will review your chart in the medical record at regular intervals, in order to gather information about your health and the medical care you receive

At the first visit, a study clinician will review your CHF medications with you. The study clinician may adjust your medication doses or prescribe additional CHF medications if clinically indicated. The study physician will notify your primary care doctor and your main cardiologist of any medication changes that are made. During the study, you will be able to contact the study team with any issues with your CHF medications. You will still be under the care of your regular doctors, and should contact your regular doctors for any symptoms or health concerns.

At the end of the first study visit, you will be "randomized" into one of the study groups described below. Randomization means that you are put into a group by chance. A computer program will place you in one of the groups. Neither you nor your doctor can choose the group you will be in. You will have an equal chance of being placed in either group.

- **If you are in group 1**, you will receive a CHF polypill for one month, followed by usual care for one month. You can choose to receive the polypill by mail, or pick it up at Daniel's Pharmacy or the ZSFG cardiology clinic.
    - The "polypill" is a strategy for reducing the number of CHF pills that you need to take every day. While you are in the polypill group, the pharmacist will package some of your CHF medications into a single, larger plastic capsule. If any of the medications are twice a day, you will continue taking a second dose of the medication separately, outside of the polypill. Your doctor will still be able to prescribe new medications or adjust the doses of these medications. The goal of the polypill is to reduce your pill burden and make it easier to take your CHF medications each day. We

may need to modify some of your CHF medications so that they fit into the polypill. This could involve cutting the tablets in half, switching to another medication in the same drug class, or making minor dose adjustments if considered safe by the study clinician. You and your primary care provider or primary cardiologist would be notified of any changes. Many of your medications will not be included in the polypill, and will still be taken as individual tablets.

- After one month, you will stop taking the CHF polypill and will resume taking your CHF medications as individual tablets, as you do now. Any new medications that were started as part of the polypill will be continued as individual tablets.

- **If you are in group 2,** you will receive usual care for 1 month, followed by the polypill intervention for 1 month.
- After completing the trial, any CHF medications that were started or increased during the study will be continued as individual tablets. If you do not already have a cardiologist, you will be referred to cardiology clinic for ongoing care of your heart failure.

While you are receiving the treatment, you will continue to complete regular study visits and blood tests:

- Monthly in-person visit with a member of the research team. At these visits, we will measure the following:
  - Vital signs (blood pressure, heart rate, and oxygen saturation)
  - Weight
  - Pill counts. You will be asked to bring in your medications to each visit, and we will keep track of the number of pills in each pill bottle
  - Questionnaires about your CHF symptoms and your medication-taking practices
- Telephone visit with the member of the research team, at the halfway point between monthly visits or more frequently if needed
- Blood tests, at least every month or as medically necessary
- Regular review of your medical record by the study team

These are part of the usual care for CHF, but they are more frequent because you are participating in the study. Standard care for CHF usually involves follow-up visits and blood tests every 1-6 months. While in the study, you will have follow-up visits every month, as well as blood tests at least every month.

After the treatment is complete, you will be asked to participate in a 30-60 minute exit interview to learn more about your experience with the CHF polypill.

- A study researcher will interview you for about 30-60 minutes in a private office or by phone. The researcher will ask you to describe your experiences with the CHF polypill compared to usual care.
- The researcher will make a sound recording of your conversation. After the interview, someone will write down a transcription of what's on the tape and will remove any

mention of names. The sound recording will then be destroyed.

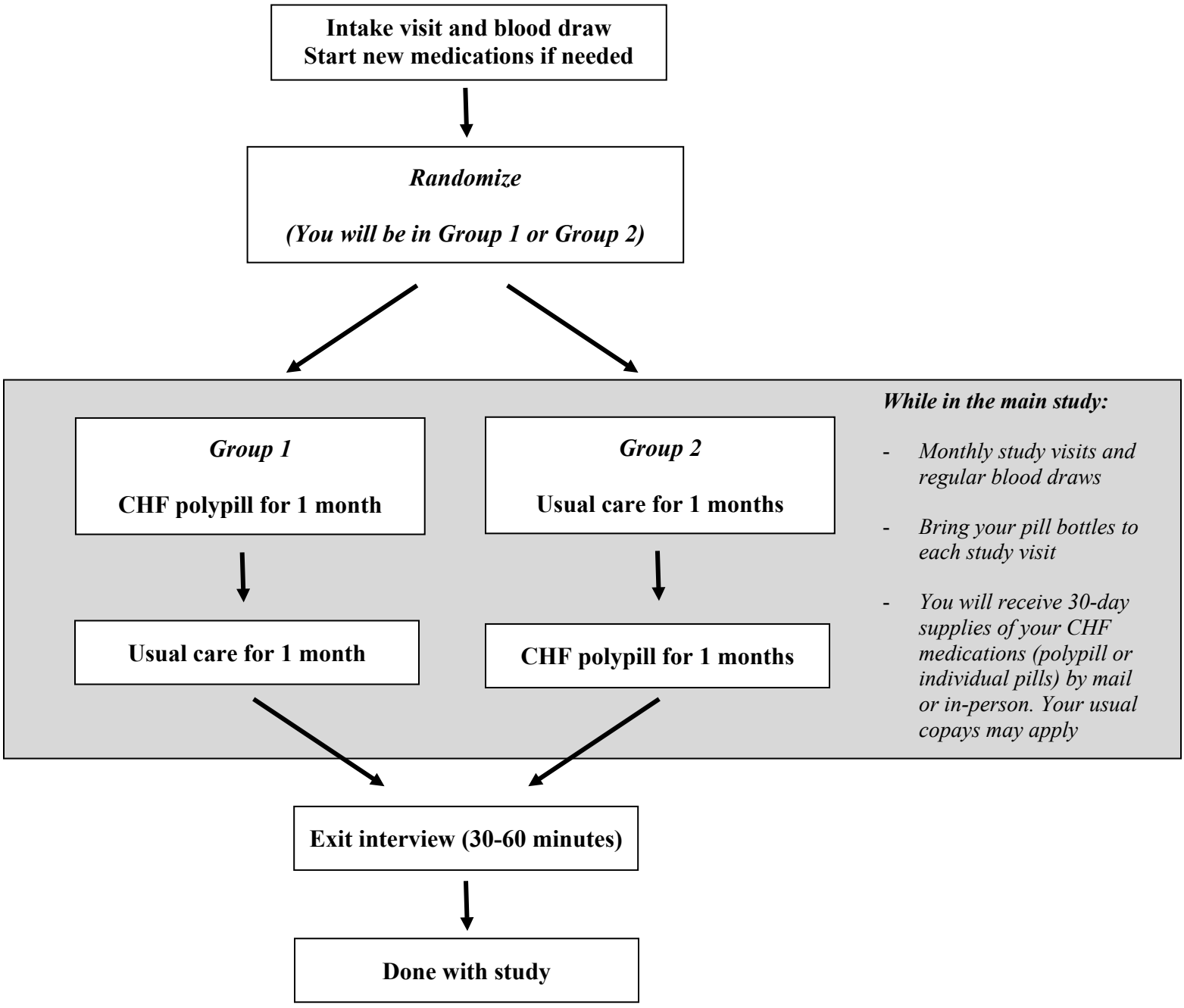
Study location: All study procedures will be done at Zuckerberg San Francisco General Hospital or by telephone.

Blood drawing (venipuncture): When recommended by the study physician, a blood sample will be drawn by inserting a needle into a vein in your arm. Each sample will be less than 2 teaspoons. For most participants, no more than 10 teaspoons will be drawn for the whole study.

Study team will contact your primary doctors: If you consent to participate in this study, the study team will contact your primary care provider and primary cardiologist (if applicable) and will update them about any medication changes.

STUDY PLAN

Another way to find out what will happen to you during the study is to read the chart below. Start reading at the top and read down the list, following the lines and arrows.



How long will I be in the study?

After the intake visit, you will be asked to take the CHF polypill for 1 month and your individual CHF pills for 1 month. After you have completed the study, you will be contacted for a 30-60

minute exit interview. In total, the study will take 2-3 months to complete from the time of the first study visit.

Will I be contacted after the conclusion of the study?
The study team will only reach out to participants who are willing to be contacted again in the future. Contact will be by email or by telephone. Please share whether your preferences on future contact from the study team at the end of this form.

Can I stop being in the study?

Yes. You can decide to stop at any time. Tell the study doctor if you are thinking about stopping or decide to stop. They will tell you how to stop your participation safely.

It is important to tell the study doctor if you are thinking about stopping so any risks from the CHF polypill can be evaluated by your doctor. Another reason to tell your doctor that you are thinking about stopping is to discuss what follow-up care and testing could be most helpful for you.

If you withdraw from the study, any data or specimens we have already collected from you will remain part of the study records. After you withdraw, the researchers may still get information from your medical records if it is relevant to the study (e.g., laboratory results, treatment courses, health outcomes). You must tell the study team you do not want this information to be collected when you withdraw, otherwise it will be collected.

The study doctor may stop you from taking part in this study at any time if they believe it is in your best interest, if you do not follow the study rules, or if the study is stopped.

What side effects or risks can I expect from being in the study?

You may have side effects while participating in the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen. Side effects may be mild or very serious. Your health care team may give you medicines to help lessen side effects. Many side effects go away soon after you stop taking the medications. In some cases, side effects can be serious, long lasting, or may never go away.

While you are in the study, you will still be under the care of your regular doctors (i.e., your primary care doctor and/or cardiologist). You should call your regular doctors about any new symptoms or health problems.

You will also have a contact number to reach the study team. You should contact the study team about any problems specifically related to the study medications (for example, difficulty taking the study medications, or questions about side effects from the study medications). Your study team will communicate with your regular doctors about any medication changes that are made as part of the study.

Risks and side effects related to the CHF polypill study include those which are:

Likely

- **Known side effects of CHF medications:** Through participation in this research study, you will continue taking your CHF medications, and you may be started on additional CHF medications or undergo adjustments in the medication type or dose. You may be started on new CHF medications more quickly than you would have if you were not in the study. If you start new CHF medications, if the doses are increased, or if the CHF polypill makes it easier to take your CHF medications, then you may experience more side effects. Side effects from common CHF medications could include low blood pressure, slow heart rate, high potassium ("hyperkalemia") leading to potentially life-threatening cardiac arrhythmias, enlargement of breast tissue ("gynecomastia"), or acute kidney injury.
- **Drawing blood (venipuncture) risks:** Drawing blood may cause temporary discomfort from the needle stick, bruising, infection, and fainting.

Less Likely

- **Increased side effects due to dose adjustments:** In order to allow your CHF medications to fit into a single capsule, the study clinician may need to switch you to another medication in the same drug class, or make a small adjustment to your medication dose. These dose adjustments would be disclosed to you in advance, and your primary cardiologist or primary care provider would be notified of any changes. In addition, we may need to split some of your usual CHF medications in half in order to fit them comfortably into the CHF polypill capsule. These adjustments could carry risk of exacerbating the side effects of CHF medications, which are described above. We will monitor you closely throughout the study period for any signs of adverse effects. You may stop the study any time and return to usual care, i.e., receiving each CHF pill individually from the pharmacy.
- **Alterations to medication efficacy:** It is possible that splitting tablets or co-packaging medications into a single capsule could lead to changes in the effectiveness of the medications, or could lead to small variations in the dose that you take each day. To minimize this risk, we will follow the regulations of the California State Board of Pharmacy. The CHF polypill will need to be taken within 6 months of production in accordance with regulations.
- **Discomfort related to pill size:** the polypill will be larger than the individual tablets, which could cause discomfort for some participants.
- **Missed doses:** If you miss a dose of the polypill, it will mean missing several medications at once, which could lead to adverse health effects.
- **Breach of confidentiality:** Any participation in a research study entails risk of breach of confidentiality if identifying data becomes available to someone outside of the study team. To minimize this risk, we will store data on secure servers and ensure that all study personnel are appropriately trained.
- **Impact on adherence to medications:** The CHF polypill may make it easier or harder to take some of your medications. As a result of participating in the study, you may be less likely to take some of your medications.
- **Exit interviews:** Some questions at the end of the study could cause discomfort, for example, as they pertain to medication-taking adherence or personal health practices. You may skip or decline to answer any questions. There can also be a risk of breach of

confidentiality if the exit interviews are overheard. We will mitigate this risk by conducting the interviews in private rooms, or via telephone or secure video conferencing.

Rare but serious

- **Medication error:** As with a Bubble Pack or Medi-Set, the CHF polypill will involve having a pharmacist co-package several of your medications into a single capsule to see if this makes it easier to take your medications. Any repackaging of medications entails some risk of medication error, for example, having too much of one medicine or none of another medicine included in the CHF polypill. To minimize this risk, we will partner with a board-certified pharmacy with experience with medication repackaging, including experience with medication over-encapsulation. In addition, when you are switched from the polypill to individual tablets (or vice versa), there could be a risk of taking a double dose of the same medication. To minimize this risk, we will ask you to bring in your pill bottles at each study visit, and we will collect duplicate pill bottles to avoid medication errors. However, medication error could have serious consequences, for example, depriving you of the benefits of your CHF medications or causing severe adverse effects.

Unknown Risks: The experimental treatments may have side effects that no one knows about yet. The researchers will let you know if they learn anything that might make you change your mind about participating in the study.

For more information about risks and side effects, ask your study doctor.

Are there benefits to taking part in the study?
You may or may not benefit from participating in this study.

What other choices do I have if I do not take part in this study?
You are free to choose not to participate in the study. If you decide not to take part in this study, there will be no penalty to you. You can continue getting care for your CHF without being in a study. You will not lose any of your regular benefits, and you can still get your care from our institution the way you usually do.

How will my specimens and information be used?
Researchers will use your specimens and information to conduct this study. Blood samples may be analyzed at the ZSFG laboratory or sent to an outside laboratory, and the specimens may be tied to your personal information, such as your name, date of birth or medical record number. Your specimens will only be used for the purposes of this study and then will be discarded. After the study is completed, we may use deidentified information for future research studies or share it with other researchers so they can use it for other studies in the future. We will not share your name or any other personal information with other researchers outside of this study. We cannot guarantee that this will prevent future researchers from determining who you are. We will not ask you for additional permission to share this de-identified information.

How will information about me be kept confidential?

Participation in research involves some loss of privacy. We will do our best to make sure that information about you is kept confidential, but we cannot guarantee total privacy. Some information from your medical records will be collected and used for this study. Your signed consent form and some of your research tests will be added to your ZSFG medical record. Therefore, people involved with your future care and insurance may become aware of your participation and of any information added to your medical record as a result of your participation. Study tests that are performed by research labs, and information gathered directly from you by the researchers will be part of your research records and may be added to your medical record. 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 personal information will not be used.

Authorized representatives from the following organizations may review your research data for the purpose of monitoring or managing the conduct of this study:

- Representatives of the University of California
- Representatives of the Sponsor, the UCSF-CAPS HIV Innovative Grant
- Representatives of the Food and Drug Administration (FDA)
- Representatives from Washington University in St. Louis may review deidentified data

Are there any costs to me for taking part in this study?
Two types of procedures will be done during this study. Some are part of your standard medical care and others are only for research. You or your insurer will be billed for standard medical care. You will be responsible for your co-pays, deductibles, and any other charges that your insurer will not pay. There is a possibility that your insurer may not cover all standard medical care costs if you are receiving medical services out of network. Any procedures done only for research will not be charged to you or your insurer.

If you have questions about what costs you will be responsible for, please talk with the study investigator before deciding to enroll in the study. Depending on the type of study, some of your costs could be substantial.

Will I be paid for taking part in this study?

In return for your time and effort, you will be paid $10 for each on-site visit in the form of a gift card, with an additional $30 gift card for bringing in your medication bottles to your visit. You will also receive an additional $10 gift card any time a blood draw is required, and will receive a $20 gift card for participating in an exit interview. You will receive a gift card at the conclusion of each completed visit or blood draw. You will not be paid for telephone visits. There will be up to 6 on-site visits and up to 6 blood draws over the course of 2-3 months, as well as an exit interview, for a maximum payment of approximately $260.

Will I be reimbursed if I pay expenses related to my participation in this study?
You may be eligible for reimbursement of travel expenses if you take part in this study.

What happens if I am injured because I took part in this study?

It is important that you tell your study doctor, Dr. Colette DeJong, if you feel that you have been injured because of taking part in this study. You can tell the doctor in person or call the study coordinator at 628-206-5801. For urgent issues, you can contact Dr. DeJong directly at 217-649-1482.

Treatment and Compensation for Injury: If you are injured as a result of being in this study, the University of California will provide necessary medical treatment. The costs of the treatment may be billed to you or your insurer just like any other medical costs, or covered by the University of California, depending on a number of factors. The University and the study sponsor do not normally provide any other form of compensation for injury. For further information about this, you may call the office of the Institutional Review Board at 415- 476-1814.

What are my rights if I take part in this study?

Taking part in this study is your choice. You may choose either to take part or not to take part in the study. If you decide to take part in this study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your regular benefits. Leaving the study will not affect your medical care. You can still get your medical care from our institution.

We will tell you about new information or changes in the study that may affect your health or your willingness to continue in the study.

In the case of injury resulting from this study, you do not lose any of your legal rights to seek payment by signing this form.

You may request a copy of the health information collected from you as part of this research after the study is completed. You may not have access to this information while the study is still being conducted.

Who can answer my questions about the study?

For questions about the study medications, can contact the research team at 628-206-5801. You can also contact the research team with any questions, concerns, or complaints you have about this study. For any new symptoms or health concerns, please contact your regular doctors (your primary care doctor or regular cardiologist), or call 911. If you wish to ask questions about the study or your rights as a research participant to someone other than the researchers or if you wish to voice any problems or concerns you may have about the study, please call the office of the Institutional Review Board at 415-476-1814.

A description of this clinical trial will be available on http://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. The National Clinical Trial (NCT) number for this study is NCT06029712.

Permission for study team to contact someone who helps with your medications: If there is someone that helps you with your medications (such as an IHSS worker, nurse, or adult family member), do you consent for the study team to contact that person to assist with safe medication changes?

□ YES □ NO

Permission to be contacted after the study:
Please indicate whether you would be willing to be contacted by the study team to answer additional questions or discuss the study's results:

□ YES □ NO

Please indicate whether you would be willing to be contacted about opportunities to participate in similar research in the future:

□ YES □ NO

CONSENT

You have been given a copy of this consent form and the Experimental Subject's Bill of Rights to keep.

You will be asked to sign a separate form authorizing access, use, creation, or disclosure of health information about you.

PARTICIPATION IN RESEARCH IS VOLUNTARY. You have the right to decline to be in this study, or to withdraw from it at any point without penalty or loss of benefits to which you are otherwise entitled.

If you wish to participate in this study, you should sign below.

_____ _____
Date Participant's Signature for Consent

_____ _____
Date Person Obtaining Consent