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NOVEMBER 12, 2019**

**INFORMED CONSENT DOCUMENT  
AGREEMENT TO BE IN A RESEARCH STUDY**

**NAME OF SPONSOR COMPANY:** Division of Microbiology and Infectious Disease (DMID)

**PROTOCOL NUMBER AND TITLE OF STUDY:** 17-0088 “A Phase 1, Three-Part, Randomized, Double-Blind, Single and Multiple Subcutaneous Dose Escalation Study to Determine the Safety, Tolerability, and Pharmacokinetics of Rezafungin in Healthy Adult Subjects”

**NAME OF PERSON IN CHARGE OF THE RESEARCH  
STUDY (STUDY DOCTOR/INVESTIGATOR):** Dennis Ruff, MD

**TELEPHONE NUMBER(S), DAYTIME:** (210) 283-4500  
**AFTER HOURS:** (210) 283-4510

**INTRODUCTION**

You are deciding if you would like to volunteer for a medical research study. You must read and sign this form before you agree to take part in this study. This form will give you more information about this study. Please ask as many questions as you need to before you decide if you want to be in the study. Do not sign this form if you have any questions that have not been answered.

The Study Doctor (investigator) is being paid by the sponsor, the National Institute of Health’s Division of Microbiology and Infectious Disease (DMID), to conduct this research study.

You must be honest with the Study Doctor about your health history or you may harm yourself by participating in this study.

**PURPOSE OF THE STUDY**

The drug being tested in this study, rezafungin, is being developed by a drug company (Cidara Therapeutics) to treat or prevent fungal infections. This study drug (rezafungin) has not been approved for use by the FDA and has been given to patients by intravenous (IV) infusion (put directly into the vein by way of a tube) in clinical trials. For the study you will participate in, the study drug would be given to you by injecting it under the skin, which is called subcutaneous (SC) dosing, or by injecting it into a vein in your arm, which is called intravenous (IV) dosing. When rezafungin is given by SC dosing, it is called an “investigational route of dosing”. “Investigational” means the FDA has not yet approved giving rezafungin to patients, either by IV dosing or SC dosing.

The purpose of this study is:

- to see how safe the study drug is and how the body tolerates the study drug when given under the skin (SC) one time (single dose) as well as several times (multiple dose);
- to see how the body absorbs and breaks down the study drug when given SC one time (single dose) as well as several times (multiple dose);

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- to see how the body acts and how much of the drug circulates in the body when given by SC compared to when given IV.

In this document, you may see the terms “medication”, “treatment”, and “treatment period”; these are terms used in research studies as mentioned above. This does not mean that you will be receiving medical treatment for any condition that you may have. These terms apply to the investigational drug and parts of the study where you will be receiving this drug.

Once enrolled in the study, each participant, including yourself, will be called a “subject” while being part of the study. For Parts 1 and 2, there will be 8 subjects in each group, called a “cohort”. However, the first cohort will only have 4 subjects. For Part 3, there will be 5 subjects in each group. In Parts 1 and 2 of the study, two subjects in each cohort will be called “sentinels”. However, there will be no sentinel subjects in the first cohort. The 2 sentinel subjects will receive the study drug or placebo first, before the other 6 subjects. After the Study Doctor reviews the information collected on the 2 sentinel subjects through Day 30 for Parts 1 and 2, and there are no safety concerns, the other 6 subjects in the cohort will be admitted to the study unit and receive study drug.

This study is divided into three parts, Part 1, Part 2, and Part 3. If you agree to be in the study (enrolled), you will be assigned to either Part 1, Part 2, or Part 3. All three parts of the study are designed to evaluate how safe the study drug is when given SC, how the body tolerates the study drug when given SC, and how it is broken down and absorbed by the body when given SC. Part 3 also compares any differences between giving the study drug by SC vs. IV. Part 1 subjects receive one dose of study drug; Part 2 subjects receive three (3) doses of study drug (one dose per week for 3 weeks), and Part 3 subjects receive one dose of study drug by SC and one dose of study drug by IV. These parts will be described in more detail below.

If you qualify for the study, you will receive either the investigational study drug (rezafungin) or what is called a placebo. Placebo looks like the study drug but does not contain any active ingredient. The first cohort will have 4 subjects, 3 will receive rezafungin and 1 will receive placebo. In cohorts 2-6 of Part 1 and all cohorts of Part 2, 6 subjects receive rezafungin, and 2 subjects receive placebo. However, there is no placebo in Part 3. The drug you receive will be assigned by chance, like a lottery.

The amount of drug you are given at one time is called a dose. The doses are measured in weight (milligrams, or mg) and volume (in milliliters, or mL). For comparison, 1/8 teaspoon of sugar weighs about 500 mg and 1/8 teaspoon of liquid is a little over 1/2 mL (0.60).

**If you are assigned to Part 1, Cohorts 1, 2, 3, 4, 5, or 6, you will receive one the following doses given subcutaneous (SC, under the skin) injections in the abdomen (stomach area) once (on Day 1):**

- Cohort 1: 1 mg rezafungin subcutaneous or placebo given in **one** 0.10 mL injection
- Cohort 2: 10 mg rezafungin subcutaneous or placebo given in **one** 0.10 mL injection
- Cohort 3: 30 mg rezafungin subcutaneous or placebo given in **one** 0.30 mL injection
- Cohort 4: 60 mg rezafungin subcutaneous or placebo given in **one** 0.60 mL injection
- Cohort 5: 100 mg rezafungin subcutaneous or placebo given in **one** 1.00 mL injection
- Cohort 6: 200 mg rezafungin subcutaneous or placebo given in **two** 1.00 mL injections (given in different areas of your abdomen)

**The first cohort of 4 subjects will be dosed together. At each dosing level for cohorts 2-6, 2 subjects will be dosed and observed for at least 4 weeks after dosing for safety before the other 6 subjects in**

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NOVEMBER 12, 2019**

**the group are dosed. Of those 2 subjects, 1 subject will receive placebo and 1 will receive active study drug.**

**If you are assigned to Part 2**, Cohorts 7, 8, 9, or 10, you will receive one of the following doses given as subcutaneous injections in the stomach area on **three** separate days (Day 1, Day 8 and Day 15):

- Cohort 7: 30 mg rezafungin subcutaneous or placebo given in **one** 0.30 mL injection every 8 days (total 3 injections)
- Cohort 8: 60 mg rezafungin subcutaneous or placebo given in **one** 0.60 mL injection every 8 days (total 3 injections)
- Cohort 9: 100 mg rezafungin subcutaneous or placebo given in **one** 1.0 mL injection every 8 days (total 3 injections)
- Cohort 10: 200 mg rezafungin subcutaneous or placebo given in **two** 1.0 mL injections every 8 days (total 6 injections)

**At each dosing level, 2 subjects will be dosed and observed for at least 4 weeks after the final dose for safety before the other 6 subjects in the group are dosed. Of the first 2 subjects, one (1) subject will receive placebo and 1 will receive active study drug.**

Parts 1 and 2 of this study are called “double-blind”, which means that neither you nor the investigators or study team you work with will know which drug (rezafungin or placebo) you are given. However, in case of emergency, the study staff can get this information.

**If you are assigned to Part 3**, Cohort 11, you will receive one dose given either as a subcutaneous (SC) injection on Day 1, or you will receive the following dose level study drug into the vein (intravenous -IV) on Day 1. Then on Day 22 you will receive the study drug in the route you did not receive study drug (i.e. Day 1 (SC) and Day 22 (IV) OR Day 1 (IV) and Day 22(SC)).

- 100 mg rezafungin SC or placebo given in two 1.0 mL injections once AND; 100 mg rezafungin IV infusion in 250 mL of normal saline over 60 minutes once.

The dose amount you end up receiving may be adjusted to something different than what is shown above but it will not be more than 100 mg of rezafungin. The dose will be by the highest level of rezafungin in the blood that was proven to be safe and well tolerated, as determined by evaluating the information gathered from Cohorts 1-6 in Part 1 of this study. Part 3 is unblinded with no placebo. This means you will receive study drug and that you and the study team will know what you are receiving.

A Safety Monitoring Committee (SMC), made up of at least 3 independent experts, will monitor subject safety. The SMC, along with the sponsor (DMID), will review all information and any specific safety issues during the study. They will meet at the end of Part 1 before deciding that the study is safe to continue to Parts 2 and 3. The Food and Drug Administration (FDA) will be reviewing this same information, and will only give permission to continue to Parts 2 and 3 if the study is safe. In addition to these reviews, there is an Independent Safety Monitor (ISM) assigned to this study. An ISM is a doctor that is not part of the study who can provide quick safety assessments, because they are located close to the study site. The ISM participates voluntarily and is not paid for providing this service.

If changes are made to any of the above cohorts or cohort(s) are added once you are enrolled, you would be informed of these changes and asked to review and sign a new consent form.

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**HOW LONG THE STUDY WILL LAST AND HOW MANY PEOPLE WILL BE IN THE STUDY**

Approximately 86 healthy male and female participants aged 18 through 45 will be included in this study. The study will last approximately 58 to 80 days including an up to 28-day screening period between screening and dosing (timing depends on the Part and Cohort you will participate in). Refer to the chart below for timing of visits. You will be informed of which part and Cohort you will be participating in.

**Part 1 (Cohort 1, 2, 3, 4, 5, and 6):**

Visit	Study day	Type	Description
Visit 1	Within 28 days of Visit 2	Screening	Outpatient visit; must fast (no food or drink other than water) for at least 8 hours before visit
Visit 2	Check in Day -1; Check out Day 7	Dosing on Day 1	In house stay (7 days); must fast (no food or drink other than water) for at least 8 hours before check-in
Visit 3	Day 14	Follow-up	Outpatient visit
Visit 4	Day 21	Follow-up	Telephone follow-up to discuss any changes to the injection site(s) since Visit 3 (Day 14).
Visit 5	Day 30	Follow-up (End of Study)	Outpatient visit; must fast (no food or drink other than water) for at least 8 hours before visit

A full safety review is performed before proceeding with Part 2.

**Part 2 (Cohorts 7, 8, 9, and 10):**

Visit	Study day	Type	Description
Visit 1	Within 28 days of Visit 2	Screening	Outpatient visit; must fast (no food or drink other than water) for at least 8 hours before visit
Visit 2	Check in Day -1; Check out Day 21	Dosing on Day 1 Dosing on Day 8 Dosing on Day 15	In house stay (21 days); must fast (no food or drink other than water) for at least 8 hours before check-in
Visit 3	Day 30	Follow-up	Outpatient visit
Visit 4	Day 45	Follow-up (End of Study)	Outpatient visit; must fast (no food or drink other than water) for at least 8 hours before visit

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NOVEMBER 12, 2019**

**Part 3 (Cohort 11):**

Visit	Study day	Type	Description
Visit 1	Within 28 days of Visit 2	Screening	Outpatient visit; must fast (no food or drink other than water) for at least 8 hours before visit
Visit 2	Check in Day -1; Check out Day 7	Dosing on Day 1	In house stay (7 days); must fast (no food or drink other than water) for at least 8 hours before check-in
Visit 4	Day 14	Follow-up	Outpatient visit
Visit 5	Check in Day 21; Check out Day 28	Dosing on Day 22	In house stay (7 days); must fast (no food or drink other than water) for at least 8 hours before check-in
Visit 6	Day 35	Follow-up	Outpatient visit
Visit 7	Day 52	Follow-up (End of Study)	Outpatient visit; must fast (no food or drink other than water) for at least 8 hours before visit

**WHEN ARE YOU ELIGIBLE TO PARTICIPATE IN ANOTHER DRUG STUDY?**

The decision for when you can participate in another study is determined by the drug safety information gathered from the previous study. Usually, you can participate in another study as soon as 30 days after you received the last dose of drug in the study you were in. This information is true for most drugs. Some drugs may stay in your body longer and that may mean you may have to wait longer before starting another study. These results are usually only known after the last blood sample taken from you is tested to look for left-over drug. We will always make this information available to you as soon as we know. Our goal is to keep you from doing anything that may be potentially harmful to you. Your safety while participating in these studies is our primary concern.

**TO BE ENROLLED IN THIS STUDY**

You cannot be enrolled in the study if, at screening you:

- Report a history of allergic reactions or oversensitivity to drugs like rezafungin or the inactive ingredients (mannitol, polysorbate 80, histidine) of the injectable form of rezafungin (Rezafungin for Injection);
- experience symptoms of an illness within 14 days before the first dose of study drug, or if the Study Doctor feels you are not in good health;
- if you weigh less than 50 kg (110 lbs.) and/or have a body mass index (BMI) calculated from your height and weight that is less than 18.5 kg/m<sup>2</sup> or more than 35.0;
- have a positive HIV or hepatitis test result, abnormal laboratory test results that are not due to a transient (passing) condition, or an abnormal electrocardiogram (ECG);

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NOVEMBER 12, 2019**

- Are pregnant or planning to become pregnant during the study or a minimum of 30 days after the study, or if you are breastfeeding, or if you have any medical conditions that could make it potentially unsafe for you to participate in the study (for females);
- are planning to have unprotected intercourse or donate sperm for at least 18 weeks (126 days) after receiving the study drug (for males);
- have taken prescription drugs within 14 days of first receiving the study drug and throughout the study, except for birth control pills (hormonal contraceptives only);
- had a vaccination with a live or killed vaccine or immunoglobulin within 14 days receiving the study drug;
- if you have taken or if you take any non-prescription medications, vitamins or dietary supplements (including herbal supplements) within 14 days of getting the first dose of study drug, except for intermittent (not every day) normal doses of acetaminophen (i.e., Tylenol®) and ibuprofen (i.e. Advil®).
- if you have used illicit (illegal) drugs, smoked or used nicotine products (smoking or smokeless tobacco, vaping, nicotine patches or gum) within 90 days before the Screening visit or during the study\*;
- if you have consumed alcohol or alcohol-containing food or beverages within 48 hours of the Screening visit\*;
- consumed foods or beverages containing caffeine or xanthines (coffee, tea, chocolate, energy drinks and colas) for 24 hours before dosing day(s) and until discharge;
- if you have (or had within 6 months of screening and throughout the study) an alcohol or substance (illegal or prescription drugs) abuse problem\*;
- donated blood or blood products (such as plasma) or experienced significant blood loss within 60 days of screening, and throughout the study;
- had a blood transfusion within 14 days of screening;
- if you previously participated in this trial, any other rezafungin trial, or had a treatment with any investigational products or treatments within 28 days before the dosing visit and during the study;
- if it would be difficult or unsafe to draw blood samples from you or place a catheter in your arm;
- if the results of your clinical evaluations or lab tests are abnormal, even after repeating (tests may be repeated one time to double-check);
- if the Study Doctor feels you have a condition that would impact how the drug acts in your body or feels you should not participate for any reason not related to the above.

\*A urine test will be performed at Screening to check for the use of these drugs: amphetamines, barbiturates, cocaine, opiates, cannabinoids (marijuana), benzodiazepines, phencyclidine (PCP), and also for alcohol and cotinine (a chemical that indicates tobacco use).

**Subject Responsibilities:**

While participating in this research study, you will need to:

- men must be vasectomized or agree to use barrier contraception (condom with spermicide) from first dose of study drug until 18 weeks (126 days) following the last dose of study drug, and refrain from sperm donation from first dose of study drug through 18 weeks (126 days) after last dose of study drug;

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NOVEMBER 12, 2019**

- women who are able to become pregnant must agree to use allowable methods from 30 days before the first dose of study drug until 30 days after the last dose of study drug:
  - under the skin hormone (progestin) implants (for example, Nexplanon and Implanon);
  - copper IUD (intrauterine devices; for example, ParaGard);
  - hormone (levonorgestrel) releasing IUDs (for example, Mirena, Skyla, and Liletta)
- be willing and able to follow the study directions and procedures;
- tell the study staff about any side effects or problems;
- ask questions as you think of them;
- tell the Study Doctor or the study staff if you change your mind about staying in the study;
- you must not use drugs of abuse throughout this study;
- refrain from taking any over-the-counter medications (except for acetaminophen or ibuprofen), prescription medications (except for hormonal birth control), vitamins, or dietary supplements (including herbal supplements) within 14 days of dosing;
- refrain from consuming caffeine or xanthine containing food or beverages (coffee, tea, chocolate, energy drinks and colas) 24 hours before dosing day and until discharge;
- alcohol is not allowed for the duration of this study and you must refrain from use for at least 48 hours before dosing day and until discharge; refrain from eating or drinking anything at least 8 hours before safety lab blood collection. (may have water only);
- you must not smoke or use any tobacco products while enrolled in this study (tobacco use includes vaping, smoke tobacco, the use of snuff and chewing tobacco, and other nicotine or nicotine-containing products);
- you must refrain from strenuous physical activity that could cause muscle aches or injury, including contact sports, at any time from screening until completion of the trial;
- you must not donate any blood or blood products (like plasma) while participating in this study and for at least 8 weeks after receiving the study drug;
- be willing to avoid sun and ultraviolet (tanning bed) exposure during this study (using i.e. wide brim hat, sunscreen, etc.);
- you will be given a “Memory Aid”. This is a diary to help you track any reactions you may be having to the study drug;
- be willing to have a photograph taken of the skin in the area of your body where the drug is injected (abdomen) if you have a reaction to the drug.

You cannot participate in any other clinical study during your participation in this study. This is a precaution to protect your safety and the conclusions of this study.

**WHAT WILL HAPPEN DURING THE STUDY**

**Screening (all Parts and all Cohorts):**

Before the study starts, you will be asked to sign this consent form, give your health history, and tell study staff if you take any over-the-counter or prescription medicines, vitamins or herbs.

The Study Doctor will do some tests to find out if you can be in the study. These tests include:

- We will ask you how you are feeling and about any medications you may have taken;
- the study doctor will review the study requirements to determine your eligibility to participate in this study;

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NOVEMBER 12, 2019**

- we will ask you some personal information such as your race, date of birth, etc.;
- we will ask you about your medical history, including any psychiatric, surgical, smoking, alcohol and/or drug history;
- your vital signs (Blood Pressure, Heart Rate, Oral Temperature, and Respiratory Rate) will be measured;
- you will have an electrocardiogram (ECG – a recording of the heart’s electrical activity);
- you will have a physical examination;
- if female, we will ask about your menstrual cycle;
- we will ask about current use of contraceptives (male and female);
- your weight will be measured and your body mass index (BMI- a way of relating your weight to your height) will be calculated;
- you will have blood drawn for lab tests: Must not eat or drink anything for at least 8 hours, water only. These tests will be on the blood and urine, and include Chemistry tests (such as blood sugar, potassium, etc.), Hematology (such as red/white blood cell counts), Coagulation (how quickly your blood clots) and Urinalysis (testing your urine for protein, bacteria, etc.);
- if a female of post-menopausal status, a blood test will be drawn to confirm;
- if you are a female who is able to get pregnant, a blood pregnancy test will be performed;
- you will be tested for hepatitis (A, B, and C) and human immunodeficiency virus (HIV). If the Screening HIV test is positive you will be referred to your personal physician or Medical Clinic of your choice for follow-up evaluation. You will be told your results in private.;
- you will give urine to be tested for drugs of abuse, cotinine (to test for tobacco use), and alcohol;
- you be informed of which group you will be assigned to, either Part 1, Part 2, or Part 3;
- you will be counseled on the avoidance of pregnancy for women able to get pregnant, and use of barrier contraception for men, and on the avoidance of vaccines, drugs, dietary supplements and dietary restrictions before admission.

**Day -1: Admission to the Clinical Research Unit (CRU) Study Procedures Parts 1-3 (All Cohorts):**

You will be admitted to the study site 1 day before you receive the study drug (Day -1). You must be fasting for at least 8 hours before your visit. The following procedures may be done on this study day:

- Review the study requirements to determine that you are still able to participate in this study;
- review any changes to your health and/or medications you have taken since screening visit;
- measure weight;
- vital signs after resting for at least 5 minutes;
- lab tests: Must not eat or drink anything for at least 8 hours, water only. These tests will be on the blood and urine, and include Chemistry tests (Coagulation) and Urinalysis ;
- blood pregnancy test for female subjects who have the potential to become pregnant;
- urine test for drugs of abuse (illegal and/or prescription), alcohol, and for tobacco use
- physical exam;
- standard meals (Lunch, Dinner, Snack).

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NOVEMBER 12, 2019**

**Part 1 (Cohorts 1-6):**

**Day 1 – Inpatient CRU**

- On the morning of Day 1, you will be assigned (randomized) to a cohort;
- review any changes to your health and/or medications you have taken since being admitted;
- vital signs after resting for at least 5 minutes; this is done again at multiple timepoints following study drug dosing;
- physical exam;
- electrocardiogram (ECG) after lying down for at least 5 minutes (to measure the electrical function of your heart) before study drug dosing and again at around 4 hours after dosing (and after lying down for at least 5 minutes);
- on the morning of Day 1, study drug or placebo will be given by SC injection (using a syringe with needle) in the abdomen at a slow steady pace;
- you will be given a “Memory Aid”. This is a diary to help you track any reactions you may be having to the study drug;
- collect blood samples at multiple time points to measure the amount of study drug in the body; blood samples on this day will go into the night and possibly disturb your sleep; (we will not collect these samples from you if you are assigned to Cohort 1);
- inspection of the injection site before and after injection, at multiple timepoints.

**Day 2 – Inpatient CRU**

- Review any changes to your health and/or medications;
- vital signs after resting for at least 5 minutes;
- physical exam;
- collect fasting (must not eat or drink anything for at least 8 hours, water only) blood and urine for lab tests;
- collect blood sample to measure the amount of study drug in the body; (we will not collect these samples from you if you are assigned to Cohort 1);
- inspection of the injection site.

**Day 3 – Inpatient CRU**

- Review any changes to your health and/or medications you have taken since Day 1;
- collect blood sample to measure the amount of study drug in the body; (we will not collect these samples from you if you are assigned to Cohort 1);
- inspection of the injection site.

**Day 4 – Inpatient CRU**

- Review any changes to your health and/or medications you have taken;
- vital signs after resting for at least 5 minutes;
- physical exam;
- inspection of the injection site.

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NOVEMBER 12, 2019**

**Day 5 – Inpatient CRU**

- Review any changes to your health and/or medications you have taken since Day 4;
- collect blood sample to measure the amount of study drug in the body; (we will not collect these samples from you if you are assigned to Cohort 1);
- inspection of the injection site.

**Day 6 – Inpatient CRU**

- Review any changes to your health and/or medications you have taken;
- inspection of the injection site.

**Day 7 – Inpatient CRU**

- Review any changes to your health and/or medications you have taken since Day 6;
- vital signs after resting for at least 5 minutes;
- electrocardiogram (ECG) after lying down for at least 5 minutes (to measure the electrical function of your heart)
- physical exam;
- collect fasting (must not eat or drink anything for at least 8 hours, water only) blood and urine for lab tests;
- collect blood sample to measure the amount of study drug in the body; (we will not collect these samples from you if you are assigned to Cohort 1);
- inspection of injection site;
- counselling on birth control and post-discharge instructions (dietary and medication/nonmedication restrictions);
- instructions on how to properly complete the Memory Aid;
- discharge from clinical research unit.

**Day 14 (±1 Day) – Follow-Up – Outpatient**

- Review any changes to your health and/or medications you have taken since Day 7;
- review Memory Aid;
- vital signs after resting for at least 5 minutes;
- collect blood sample to measure the amount of study drug in the body; (we will not collect these samples from you if you are assigned to Cohort 1);
- inspection of injection site;
- reminder of birth control and post-discharge instructions (dietary and medication/nonmedication restrictions).

**Day 21 (±1 Day) –Telephone Follow-Up**

- Study Doctor or study staff will call you to review any changes to your injection site (s) since the Day 14 visit.
- Review Memory Aid

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**VERSION CONTROL**

tr/9-3-19 jbm/ 11-12-19

**APPROVED BY  
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NOVEMBER 12, 2019**

**Day 30 (±1 Day) – Follow-Up – Final Study Visit**

- Review any changes to your health and/or medications you have taken since Day 14;
- review Memory Aid;
- vital signs after resting for at least 5 minutes;
- electrocardiogram (ECG) after lying down for at least 5 minutes (to measure the electrical function of your heart)
- physical exam;
- weight;
- collect fasting (must not eat or drink anything for at least 8 hours, water only) blood and urine for lab tests;
- collect blood sample to measure the amount of study drug in the body; (we will not collect these samples from you if you are assigned to Cohort 1);
- inspection of injection site;
- perform blood (serum) pregnancy test (females only),
- review post-study instructions (birth control, pregnancy reporting).

**Part 1 Blood Samples:**

Blood samples will be taken by single needle-sticks or by a tube that is left in your arm. You cannot choose how the blood is taken.

There will be 6 blood draws for participants in Cohort 1; there will be about 30 blood draws for participants in Cohorts 2-6. The total amount of blood drawn will be about 90 ml (about 50 ml for first cohort) or a little over 1/3 cup. For comparison, the standard blood donation is about 480 mL (two cups).

**Part 2 (Cohorts 7, 8, 9, and 10):**

**Days 1, 8, and 15 – Inpatient CRU**

- On the morning of Day 1, you will be assigned (randomized) to a cohort. On Days 1, 8 and 15, the following procedures will be performed;
- review any changes to your health and/or medications you have taken since being admitted;
- review the study requirements to determine that you are still able to receive study drug;
- vital signs (Blood Pressure, Heart Rate, Oral Temperature, and Respiratory Rate) after resting for at least 5 minutes; this is done at multiple timepoints;
- physical exam;
- electrocardiogram (ECG) after lying down for at least 5 minutes (to measure the electrical function of your heart) before dosing and again at around 4 hours after dosing (and after lying down for at least 5 minutes);
- collect blood samples at multiple time points to measure the amount of study drug in the body; blood samples on this day will go into the night and possibly disturb your sleep;
- inspection of the injection site before and after injection, at multiple timepoints;
- give the study drug by SC injection (using a syringe with needle) in the abdomen at a slow steady pace;
- you will be given a “Memory Aid”. This is a diary to help you track any reactions you may be having to the study drug.

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tr/9-3-19 jbm/ 11-12-19

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**Days 2, 9, and 16 – Inpatient CRU**

- Review any changes to your health and/or medications you have taken;
- vital signs after resting for at least 5 minutes;
- physical exam;
- collect fasting (must not eat or drink anything for at least 8 hours, water only) blood and urine for lab tests;
- collect blood sample to measure the amount of study drug in the body;
- inspection of the injection site.

**Days 3, 10, and 17 – Inpatient CRU**

- Review any changes to your health and/or medications you have taken since Day 1, 9 or 15;
- inspection of the injection site;
- collect blood sample to measure the amount of study drug in the body.

**Days 4, 11, and 18 – Inpatient CRU**

- Review any changes to your health and/or medications you have taken;
- vital signs after resting for at least 5 minutes;
- physical exam;
- inspection of the injection site.

**Days 5, 12, and 19 – Inpatient CRU**

- Review any changes to your health and/or medications you have taken since Day 4, 11 or 18;
- collect fasting blood (must not eat or drink anything for at least 8 hours, water only) for lab tests;
- collect blood sample to measure the amount of study drug in the body;
- inspection of the injection site.

**Days 6, 13, and 20 – Inpatient CRU**

- Review any changes to your health and/or medications you have taken since Day 5, 12 or 19;
- inspection of the injection site.

**Days 7, 14, and 21 – Inpatient CRU**

- Review any changes to your health and/or medications you have taken since Day 6, 13 or 20;
- vital signs after resting for at least 5 minutes;
- electrocardiogram (ECG) after lying down for at least 5 minutes (to measure the electrical function of your heart) (Day 21 only)
- physical exam;
- collect fasting blood (must not eat or drink anything for at least 8 hours, water only) and urine for lab tests;
- collect blood sample to measure the amount of study drug in the body;
- inspection of the injection site;

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**VERSION CONTROL**

tr/9-3-19 jbm/ 11-12-19

**APPROVED BY  
INTEGREVIEW IRB  
NOVEMBER 12, 2019**

- counselling on birth control and post-discharge instructions (dietary and medication/nonmedication restrictions);
- instructions on how to properly complete the Memory Aid;
- DAY 21 ONLY: discharge from clinical research unit.

**Day 30 (±1 Day) – Follow-Up – Outpatient**

- Review any changes to your health and/or medications you have taken since the last study visit
- review Memory Aid;
- vital signs after resting for at least 5 minutes;
- electrocardiogram (ECG) after lying down for at least 5 minutes (to measure the electrical function of your heart)
- physical exam;
- collect blood sample to measure the amount of study drug in the body;
- inspection of injection site;
- review post-discharge instructions (birth control, pregnancy reporting).

**Day 45 (±1 Day) – Follow-Up – Final Study Visit**

- Review any changes to your health and/or medications you have taken since Day 30;
- review Memory Aid;
- vital signs after resting for at least 5 minutes;
- electrocardiogram (ECG) after lying down for at least 5 minutes (to measure the electrical function of your heart)
- physical exam;
- weight;
- collect fasting blood (must not eat or drink anything for at least 8 hours, water only) and urine for lab tests;
- collect blood sample to measure the amount of study drug in the body;
- inspection of injection site;
- perform blood (serum) pregnancy test (females only);
- review post-study instructions (birth control, pregnancy reporting).

**Part 2 Blood Samples:**

Blood samples will be taken by single needle-sticks or by a tube that is left in your arm. You cannot choose how the blood is taken.

There will be about 55 blood draws. The total amount of blood drawn will be about 163 ml or slightly over 2/3 cup. For comparison, the standard blood donation is about 480 mL (two cups).

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**VERSION CONTROL**

tr/9-3-19 jbm/ 11-12-19

**APPROVED BY  
INTEGREVIEW IRB  
NOVEMBER 12, 2019**

**Part 3 (Cohort 11):**

**Days 1 and 22 – Inpatient CRU**

- On the morning of Day 1, you will be assigned (randomized) to a cohort;
- review any changes to your health and/or medications you have taken since being admitted;
- vital signs (Blood Pressure, Heart Rate, Oral Temperature, and Respiratory Rate) after resting for at least 5 minutes; this is done at multiple timepoints;
- physical exam;
- you will receive the study drug by two SC injections into the abdomen (100 mg each, using a syringe and needle) in the morning on Day 1 and as an IV infusion (into a catheter placed in the vein of one arm) over 60 minutes in the morning on Day 22; or the study drug will be given via IV infusion over 60 minutes in the morning on Day 1 and by SC injection in the morning on Day 22;
- you will be given a “Memory Aid”. This is a diary to help you track any reactions you may be having to the study drug;
- electrocardiogram (ECG) after lying down for at least 5 minutes (to measure the electrical function of your heart) before dosing
- electrocardiogram (ECG) after lying down for at least 5 minutes (to measure the electrical function of your heart) at around 4 hours after dosing if you had the SC injection
- electrocardiogram (ECG) after lying down for at least 5 minutes (to measure the electrical function of your heart) at around 1 hour from the start of your infusion; if you had the IV
- collect blood samples at multiple time points to measure the amount of study drug in the body; blood samples on this day will go into the night and possibly disturb your sleep;
- inspection of the injection site/IV site before and after injection, at multiple timepoints.

**Days 2 and 23 – Inpatient CRU**

- Review any changes to your health and/or medications you have taken;
- vital signs (Blood Pressure, Heart Rate, Oral Temperature, and Respiratory Rate) after resting for at least 5 minutes;
- physical exam;
- collect fasting blood (must not eat or drink anything for at least 8 hours, water only) and urine for lab tests (hematology/chemistry and urine for urinalysis);
- collect blood sample to measure the amount of study drug in the body;
- inspection of the injection site/IV site.

**Days 3 and 24 – Inpatient CRU**

- Review any changes to your health and/or medications you have taken since Day 1 or Day 22;
- collect blood sample to measure the amount of study drug in the body;
- inspection of the injection site/IV site.

**Days 4 and 25 – Inpatient CRU**

- Review any changes to your health and/or medications you have taken;
- vital signs (Blood Pressure, Heart Rate, Oral Temperature, and Respiratory Rate) after resting for at least 5 minutes;

**THIS IS AN IMPORTANT DOCUMENT - KEEP FOR FUTURE REFERENCE**

**VERSION CONTROL**

tr/9-3-19 jbm/ 11-12-19

**APPROVED BY  
INTEGREVIEW IRB  
NOVEMBER 12, 2019**

- physical exam;
- inspection of the injection site/IV site.

**Days 5 and 26 – Inpatient CRU**

- Review any changes to your health and/or medications you have taken since Day 4 or 25;
- collect blood sample to measure the amount of study drug in the body;
- inspection of the injection site/IV site.

**Days 6 and 27 – Inpatient CRU**

- Review any changes to your health and/or medications you have taken;
- inspection of the injection site/IV site.

**Days 7 and 28 – Inpatient CRU**

- Review any changes to your health and/or medications you have taken since Day 5 or 26;
- vital signs after resting for at least 5 minutes;
- physical exam;
- collect fasting blood (must not eat or drink anything for at least 8 hours, water only) and urine for lab tests;
- collect blood sample to measure the amount of study drug in the body;
- inspection of the injection site/IV site;
- counselling on birth control and post-discharge instructions (dietary and medication/nonmedication restrictions);
- instructions on how to properly complete the Memory Aid;
- discharge from clinical research unit.

**Days 14 and 35 (±1 Day) – Follow-Up – Outpatient**

- Review any changes to your health and/or medications you have taken since Day 7 or 28;
- review Memory Aid;
- vital signs after resting for at least 5 minutes;
- physical exam;
- inspection of injection site;
- collect blood sample to measure the amount of study drug in the body;
- review post-discharge instructions (birth control, pregnancy reporting).

**Day 52 (±1 Day) – Follow-Up – Final Study Visit**

- Review any changes to your health and/or medications you have taken since Day 35;
- review Memory Aid;
- vital signs after resting for at least 5 minutes;
- electrocardiogram (ECG) after lying down for at least 5 minutes (to measure the electrical function of your heart)
- physical exam;

**THIS IS AN IMPORTANT DOCUMENT - KEEP FOR FUTURE REFERENCE**

**VERSION CONTROL**

tr/9-3-19 jbm/ 11-12-19

**APPROVED BY  
INTEGREVIEW IRB  
NOVEMBER 12, 2019**

- weight;
- collect fasting blood (must not eat or drink anything for at least 8 hours, water only) and urine for lab tests;
- collect blood sample to measure the amount of study drug in the body;
- perform blood (serum) pregnancy test (females only),
- review post-study instructions (birth control, pregnancy reporting).

**Part 3 Blood Samples:**

Blood samples will be taken by single needle-sticks or by a tube that is left in your arm. You cannot choose how the blood is taken.

There will be about 49 blood draws. The total amount of blood drawn will be about 146 mL or just over 1/2 cup. For comparison, the standard blood donation is about 480 mL (two cups).

**HIV AND HEPATITIS TESTING**

As required by the study, and in the event anyone is exposed to your blood, you must have your blood tested for the hepatitis viruses and for HIV. HIV is the virus that causes AIDS. If you have a positive HIV or hepatitis test, you cannot be in the study. If the HIV test is positive, a follow-up confirmatory test will be done. If the follow-up test is also positive, you will be told in private and you will also be told about counseling.

It may take weeks or months after being infected with HIV for the test to be positive. The HIV test is not always right.

According to Texas State Laws, cases of positive HIV, hepatitis B antigen, and hepatitis C antibody are all reportable to the Department of Health. In the event that your results are positive for any of these lab tests, the following personal information will be reported to the Department of Health via a “Notifiable Disease Report” form supplied by the local Health Department:

- Your Name
- Date of Birth
- Sex
- Race
- Ethnicity
- Address
- Telephone Number

If you have any questions, please ask the study doctor or staff. Although this testing is supposed to be private, this cannot be guaranteed. For example, it is possible for a court of law to get health or study records without your permission.

**POSSIBLE SIDE EFFECTS AND RISKS**

**If you do not understand what any of these side effects mean, please ask the Study Doctor or study staff to explain these terms to you.**

**THIS IS AN IMPORTANT DOCUMENT - KEEP FOR FUTURE REFERENCE**

**VERSION CONTROL**

tr/9-3-19 jbm/ 11-12-19



**APPROVED BY  
INTEGREVIEW IRB  
NOVEMBER 12, 2019**

Because this route of dosing of the study drug is investigational, all the side effects for this way of giving it may not be known. There may be rare and unknown side effects. Some of these may be life threatening.

You must tell the Study Doctor or study staff about all side effects that you have. If you are not honest about your side effects, you may harm yourself by staying in this study.

You may be asked to return to the clinical unscheduled safety follow-up visits if deemed necessary by the study investigators.

**What are the possible side effects or harms of taking part?**

The study drug (rezafungin) is a new drug from the antifungal drug family called “echinocandins”. The study drug is not yet approved for use by the FDA and is currently being studied by giving it to patients by intravenous (IV) infusion (put directly into the vein by way of a tube). The study drug has not been given to patients in the same way it will be given to you, should you choose to participate in the study (by injecting it under the skin). **The following information describes the side effects observed when giving the study drug to patients by IV infusion and to animals.** We do not know whether these side effects are also possible when giving the study drug by injection under the skin or by IV injection, as it will be given in this study. It is also unknown whether side effects observed in animal studies will also be observed in human study participants.

**Risks to Healthy Human Participants**

So far, 42 healthy participants have received rezafungin in two studies in doses up to 400 mg (twice as much as the highest dose being given in this study) once weekly given for three weeks. All side effects were mild (easy to tolerate and did not affect daily living) or moderate (caused some discomfort and changed normal routine to a limited amount). There were no serious side effects observed. There were no abnormal results from routine laboratory tests for participants taking rezafungin at any dose. All side effects occurred in less than 10% of participants taking rezafungin. The most commonly reported side effects in these two studies were:

- Constipation
- Flushing (redness of the skin, typically over the cheeks or neck, which is usually temporary)
- Nausea

**Risks to Participants with Candidemia or Invasive Candidiasis (yeast infections)**

Additionally, 71 participants with candidemia or invasive candidiasis were treated with rezafungin. The most commonly reported side effects for rezafungin were:

- Decreases in potassium in the blood, which may cause muscle cramps, constipation, weakness, and abnormal heart rhythms, especially in people with heart disease. This can cause you to feel lightheaded or faint. A very low potassium level can even cause your heart to stop.
- Diarrhea
- Nausea
- Anemia

**THIS IS AN IMPORTANT DOCUMENT - KEEP FOR FUTURE REFERENCE**

**VERSION CONTROL**

tr/9-3-19 jbm/ 11-12-19

**APPROVED BY  
INTEGREVIEW IRB  
NOVEMBER 12, 2019**

**Heart Beat Risks**

One serious side effect that was possibly related to the study drug was reported in this study, the side effect was a delay in the timing of the way the heart normally beats and resolved without treatment.

**Other Possible Risks**

In the group of participants with candidemia or invasive candidiasis, one participant in the rezafungin group had a side effect of sunburn (dosing group 400 mg on Day 1 and Day 8, with optional dosing on Days 15 and 21) following substantial sun exposure (photosensitivity). There were two side effects (reported in 2.8% of participants) that may represent tremor or nerve injury causing numbness or weakness: intensive care unit acquired weakness (reported as moderate intensity), and tremor (reported as mild intensity). These events of tremor/neuropathy that were potentially related to rezafungin were followed until resolution and both resolved.

**Risks seen in animal studies**

Based on a fertility study in male rats, there is a potential risk for decreased sperm motility (sperm may not swim properly), abnormal sperm morphology (change in size and shape of the sperm), and testicular seminiferous tubular epithelial degeneration (Seminiferous tubules are tubes located within the testicles, they are the specific location that produces sperm cells.) Damage to these specific cells was observed in mice at doses of rezafungin 2.5 times greater than the amounts used in this study. However, the risk in participants taking rezafungin is currently unknown. If you are a male and agree to participate on this study, you will be asked to avoid fathering a child or donating sperm until at least 18 weeks (126) days after your last dose of study drug. If you are a female and agree to participate in this study, you will be asked to avoid becoming pregnant until at least 30 days after your last dose of study drug.

Results from a 3-month animal study suggest a potential risk of unexpected tremors (shaking or movements of one or more body parts). There were observations of tremors and intention tremors (increased tremors when attempting to make a movement) in animals after 6 weeks of dosing with rezafungin at amounts 11 times greater than the amounts of rezafungin used in this study. These effects disappeared after rezafungin was stopped. These effects were not observed in animals after 13 weeks of dosing with rezafungin at 4 times greater than the amounts of rezafungin used in this study. These effects have also not been observed in clinical trials in patients taking IV rezafungin at similar doses to the highest dose to be given in this study. Given the late timing, absence of these effects in IV rezafungin trials, and high amounts of drug necessary to cause this effect relative to this rezafungin dosing group regimen, the risk to study participants is believed to be low but cannot be sure. At the highest dose (about 20 times greater than the proposed human dose), severe neurobehavioral effects were observed. These effects were not seen in the levels at 11.4 times the maximum exposure proposed for humans.

Results from an animal study suggest a potential risk of skin sores at the site of subcutaneous injection. In animals, there was inflammation and, in the most severe cases, open sores at the injection sites after 4 or more injections of a total volume and dose equal to the top dose per injection planned in this study. There was partial recovery of the sores after 4 weeks. If you agree to participate in this study, you may develop sores on your abdomen (stomach) area where the drug is given. If you do develop sores on your abdomen, you are to contact the study doctor immediately once you first notice the sores.

**THIS IS AN IMPORTANT DOCUMENT - KEEP FOR FUTURE REFERENCE**

**VERSION CONTROL**

tr/9-3-19 jbm/ 11-12-19

**APPROVED BY  
INTEGREVIEW IRB  
NOVEMBER 12, 2019**

**Risks of other drugs like rezafungin**

Side effects for other drugs like rezafungin include:

- Abnormal liver tests
- Hepatitis (inflammation of the liver)
- Liver failure
- Tremors (shaking)
- Ataxia (loss of control of body movements, stumbling, slurred speech)
- Hypoesthesia (loss of sensitivity to touch)
- Paraesthesia (tingling, “pins and needles” sensations)
- Chest discomfort
- Flushing
- Nausea
- Myalgia (muscle pain)
- Rash
- Dyspnea (shortness of breath)
- Pruritus (itching)
- Urticaria (Hives)
- Hypotension (Low blood pressure)
- Facial Swelling
- Nodules, thickening of the skin
- Open sores at the injection site(s)
- Phototoxicity (reaction to the sun that may cause damage to the skin)
  - It is recommended that you try to reduce direct sun exposure during this study

**ADDITIONAL RISKS OR DISCOMFORTS**

**Blood Samples (taken by single needle-sticks or by a tube that is left in your arm):**

There may be side effects of having blood drawn such as:

- Fainting
- Redness
- Pain
- Bruising
- Bleeding
- Infection
- Nerve damage
- Blood clots, which may cause inflammation, swelling and pain

If you feel faint tell the study staff right away.

**Risks of Subcutaneous (SC) Injections:**

- Infection
- Pain

**THIS IS AN IMPORTANT DOCUMENT - KEEP FOR FUTURE REFERENCE**

**VERSION CONTROL**

tr/9-3-19 jbm/ 11-12-19

**APPROVED BY  
INTEGREVIEW IRB  
NOVEMBER 12, 2019**

- Redness
- Bruising
- Local Swelling

**Risks of Using an Intravenous (IV) Catheter:**

- Infection
- Pain
- Redness
- Bruising
- Vein irritation from the fluids or medication being given
- Local swelling due to IV fluid accidentally entering the tissue rather than the vein
- Blood clots, which may cause inflammation, swelling and pain
- Nerve Damage

If you feel faint tell the study staff right away.

**Electrocardiogram (ECG):**

The ECG test is a recording of the electrical activity of your heart. The sticky pads used may be cold when applied and sometimes cause some discomfort such as redness or itching. If the hair under the patches needs to be shaved, irritation from shaving also could occur.

**What if new information becomes available?**

If any new information about the study product, study procedures or risks becomes available which could affect your willingness to participate or which have an impact on your follow-up, the study doctor will discuss what this will mean for you. If you choose to continue, you may have to sign a new subject informed consent. If you choose to discontinue, the study doctor will decide for your future care and treatment.

**BIRTH CONTROL, DANGERS OF PREGNANCY AND BREASTFEEDING**

**Females who are able to get pregnant and who cannot get pregnant**

Females who are pregnant or breastfeeding must not participate in this study.

Even if you use birth control during the study, there is a chance you could become pregnant. If you are pregnant or become pregnant during the study, the study drug may involve unforeseeable risks to the unborn baby. A pregnancy test is not always right, especially in the early stages of pregnancy.

**If you are a female, you must not get pregnant while in this study.** The only certain way to not get pregnant is to not have sex. If you are a female and choose to have sex, you must use a type of birth control listed below. Females must meet one of the following criteria to participate in the study.

**THIS IS AN IMPORTANT DOCUMENT - KEEP FOR FUTURE REFERENCE**

**VERSION CONTROL**

tr/9-3-19 jbm/ 11-12-19

**APPROVED BY  
INTEGREVIEW IRB  
NOVEMBER 12, 2019**

- Post-menopausal defined as no menses for at least 12 months after stopping all hormone treatments and with follicle stimulating hormone (FSH) level in the post-menopausal range (confirmed by lab test);
- documentation of irreversible surgical sterilization (but not tubal ligation only);
- if of child bearing potential, you must agree to one of the acceptable methods of birth control listed below, starting at least 30 days before receiving the first dose of rezafungin and continue to use for at least 30 days after the last dose of rezafungin:
  - progestin-releasing subdermal implants (for example, Nexplanon and Implanon);
  - copper intrauterine devices (IUD) (for example, ParaGard);
  - levonorgestrel-releasing IUDs (for example, Mirena, Skyla, and Liletta).

If at any time during the study, you think you may be pregnant, you must immediately contact the study doctor. You cannot be in the study if you are breastfeeding.

**Males**

The effects of rezafungin on reproduction (i.e. abnormalities in offspring or a decrease in the ability to get a partner pregnant) have shown potential risks in men (sperm abnormalities).

Even if you use birth control during the study, there is a chance your partner could become pregnant. If your partner becomes pregnant during the study, the study drug may involve unforeseeable risks to the unborn baby.

Therefore, if you have not had a vasectomy, you must agree to use condoms with spermicide for birth control from the first day of the study until at least 18 weeks (126 days) after your last dose of rezafungin.

You must also not donate sperm from the first day of the study until at least 18 weeks (126 days) after the last dose of rezafungin.

If at any time during the study, your female partner becomes pregnant, you must immediately contact the study doctor.

**Questions/Questionnaires**

You may get tired or bored when we are asking you questions. You do not have to answer any question you do not want to answer.

**Confidentiality**

There is the risk that information about you may become known to people outside this study.

**POSSIBLE BENEFITS OF THE STUDY**

You will get no medical benefit from this study. However, the knowledge gained in this study may help those requiring treatment for fungal infections in the future.

**THIS IS AN IMPORTANT DOCUMENT - KEEP FOR FUTURE REFERENCE**

**VERSION CONTROL**

tr/9-3-19 jbm/ 11-12-19

**APPROVED BY  
INTEGREVIEW IRB  
NOVEMBER 12, 2019**

**ALTERNATIVES TO PARTICIPATING IN THE STUDY**

Since this study is for research only, the only other choice would be not to be in the study.

**AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR RESEARCH PURPOSES**

Federal regulations give you certain rights related to your health information. These include the right to know who will be able to get the information and why they may be able to get it. The research center (including the study doctor and study staff) must get your authorization (permission) to use or give out any health information that might identify you (protected health information). By signing this form, you allow the research center to use your information to carry out the study and to share your information for the study, as described in this form.

**PROTECTING THE PRIVACY OF YOUR HEALTH DATA**

The medical information obtained in this study that identifies you will be handled with the strictest confidence. It will be protected as required by laws and/or regulations. It will not be made publicly available. If the results of this study are published, you will not be identified by name. Certain people and organizations will need to see, copy, and use your health data so that they can do their part in the study, and some of these people and organizations will see your health data together with information that identifies you. This is necessary to ensure the trial is conducted properly, to verify the accuracy of data collected about you and for regulatory purposes. They are called “authorized users.” Authorized users will be given access to and may make copies of your health data. In general, before the information about your health leaves the research clinic facility, it will be labeled with a code identifying you only by study subject number, and will not contain name, initials, or other items that could identify you personally; however there may be circumstances that require your health information along with information that identifies you be disclosed to authorized users outside of the study location. Specimens of your blood, urine or other samples will also be labeled with your study subject number and will not be labeled with your name or initials. The following people will have access to your study records and will use the information for purposes of conducting the study, for regulatory purposes or as described below.

The following people will have access to your study records:

- The study doctor and the study staff including other ICON Early Phase Services staff;
- sponsor company, the sponsor’s associated companies, and representatives [including monitor(s) and auditor(s)];
- Cidara Therapeutics, the manufacturer of the study drug, and its collaborators will use the study data in furtherance of its research and development of the study drug;
- The United States Food and Drug Administration (FDA);
- other country, state or federal regulatory agencies;
- IntegReview IRB.

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.

**THIS IS AN IMPORTANT DOCUMENT - KEEP FOR FUTURE REFERENCE**

**VERSION CONTROL**

tr/9-3-19 jbm/ 11-12-19

**APPROVED BY  
INTEGREVIEW IRB  
NOVEMBER 12, 2019**

The Institutional Review Board (IRB), IntegReview, and accrediting agencies may inspect and copy your records, which may have your name on them. Therefore, total confidentiality cannot be guaranteed. If the study results are presented at meetings or printed in publications, your name will not be used.

**CERTIFICATE OF CONFIDENTIALITY**

To help us protect your privacy, we have a Certificate of Confidentiality from the National Institutes of Health (NIH). The researchers can use this Certificate to legally refuse to give information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other Proceedings, for example, if there is a court subpoena. The researchers will use the Certificate to resist any demands for information that would identify you, (except for reporting of communicable diseases to State and local health departments, or as explained below, see “Disclosure is permitted only when”).

The Certificate of Confidentiality cannot be used for information in your medical records.

Disclosure is permitted only when:

- Required by Federal, State, or local laws (e.g., as required by the Federal Food, Drug, and Cosmetic Act, or state laws requiring the reporting of communicable diseases to State and local health departments), excluding instances of disclosure in any Federal, State, or local civil, criminal, administrative, legislative, or other proceeding;
- necessary for the medical treatment of the individual to whom the information, document, or biospecimen pertains and made with the consent of such individual;
- made with the consent of the individual to whom the information, document, or biospecimen pertains; or
- made for the purposes of other scientific research that follows Federal regulations governing the protection of human subjects in research.

Certificate of Confidentiality does not prevent release of your information to the NIH, Food and Drug Administration (FDA), or federal funding agency.

A Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If you give your consent to release information to a medical care provider, an insurer, or other person to receive research information, then the researchers will not withhold that information.

**IN CASE OF STUDY RELATED INJURY**

If you are injured during your participation in this study, you should contact the study doctor as soon as possible. Contact the study doctor in person or at the telephone number listed on page one of this consent form. If you need immediate medical care, you should seek it in the same way you would ordinarily get emergency medical treatment.

If you suffer a study-related injury, the reasonable costs of necessary medical treatment of the injury may be reimbursed to the extent these costs are covered by your private insurance or other third party coverage. A clinical trial insurance has been established to cover such reasonable and foreseeable costs. A study-related injury is a physical injury that is directly caused by the study drug that has been given as described in the study protocol or by medical procedures that are required by the study. The NIH and/or

**THIS IS AN IMPORTANT DOCUMENT - KEEP FOR FUTURE REFERENCE**

**VERSION CONTROL**

tr/9-3-19 jbm/ 11-12-19

**APPROVED BY  
INTEGREVIEW IRB  
NOVEMBER 12, 2019**

Government and/or ICON do not provide long-term medical care or financial compensation for study-related injuries.

Injuries directly caused by any of the following are not considered study-related injuries:

- The natural course of a disease or medical condition that you already had or have;
- not following the instructions provided in this consent form or by study staff.

No other forms of payment or compensation are offered for study-related injuries (for example, for lost wages or discomfort).

Please be aware that some insurance plans may not pay for research-related injuries. You should contact your insurance company for more information.

No other form of compensation is offered for non-study related injuries.

**LEGAL RIGHTS**

You will not lose any of your legal rights by signing this consent form.

**CONTACT INFORMATION**

If you have questions, concerns, or complaints about this study or to report a study related injury, contact:

Dennis Ruff, M.D.  
Daytime: 210-283-4500  
After hours: 210-283-4510

**If you are unable to reach anyone at the number(s) listed above and you require immediate (life threatening) medical attention, please go to the nearest emergency room.**

If you do not want to talk to the Study Doctor or study staff, if you have concerns or complaints about the research, or to ask questions about your rights as a study subject you may contact IntegReview. IntegReview is a group of people that has reviewed this research study. The main goal of this review is to protect the rights and well-being of the human subjects participating in research studies. IntegReview's policy indicates that all concerns/complaints are to be submitted in writing for review at a convened IRB meeting to:

<b>Mailing Address:</b>	<b>OR</b>	<b>Email Address:</b>
Chairperson IntegReview IRB 3815 S. Capital of Texas Highway Suite 320 Austin, Texas 78704		integreview@integreview.com

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tr/9-3-19 jbm/ 11-12-19



**APPROVED BY  
INTEGREVIEW IRB  
NOVEMBER 12, 2019**

If you are unable to provide your concerns/complaints in writing or if this is an emergency regarding subject safety, contact our office at:

512-326-3001 or  
toll free at 1-877-562-1589  
between 8 a.m. and 5 p.m. Central Time

IntegReview has approved the information in this consent form and has given approval for the Study Doctor to do the study. This does not mean IntegReview has approved your being in the study. You must consider the information in this consent form for yourself and decide if you want to be in this study.

**COSTS AND PAYMENT FOR BEING IN THE STUDY**

There is no cost to you for participating in the study.

**PAYMENT FOR BEING IN THE STUDY**

**Part 1 (Cohorts 1-6) Payment**

If in Part 1, you may receive up to \$3300.00 for being in the study. You will be paid per completed visit as follows: You will receive two separate payments within 10 business days from Day 14 and Day 30.

<b>Visit</b>	<b>Payment (amount)</b>
Screening	\$0.00
Day -1	\$200.00
Day 1	\$250.00
Day 2	\$250.00
Day 3	\$250.00
Day 4	\$250.00
Day 5	\$250.00
Day 6	\$250.00
Day 7	\$250.00
Day 14	\$150.00
Day 21	\$25.00
Day 30	\$200.00
Bonus	\$975.00
*Total Payment*	\$3,300.00

To ensure that each dosing group reaches the maximum number of subjects, extra subjects will be recruited. All participants will be asked to complete research study procedures up to the time of dosing. In the event that a study subject is unable to dose, another qualified subject will take that subject's place on the study. If you complete all the requirements, but are not dosed, you will receive a pro-rated stipend check based on information below.

If you not selected to be in the study, you will be paid \$200.00 if you are released on day -1 and \$400.00 if released on day 1. As an alternate, you may be asked to participate in the next dosing group, which may require you to repeat Day -1 and Day 1 procedures.

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**Part 2 (Cohorts 7, 8, 9, and 10) Payment**

If in Part 2, you may receive up to \$6,400.00 for being in the study. You will be paid per completed visit as follows: You will receive two separate payments within 10 business days from Day 21 and Day 45.

<b>Visit</b>	<b>Payment (amount)</b>
Screening	\$0.00
Day -1	\$200.00
Day 1	\$250.00
Day 2	\$250.00
Day 3	\$250.00
Day 4	\$250.00
Day 5	\$250.00
Day 6	\$250.00
Day 7	\$250.00
Day 8	\$250.00
Day 9	\$250.00
Day 10	\$250.00
Day 11	\$250.00
Day 12	\$250.00
Day 13	\$250.00
Day 14	\$250.00
Day 15	\$250.00
Day 16	\$250.00
Day 17	\$250.00
Day 18	\$250.00
Day 19	\$250.00
Day 20	\$250.00
Day 21	\$250.00
Day 30	\$175.00
Day 45	\$175.00
Bonus	\$600.00
*Total Payment*	\$6,400.00

To ensure that each dosing group reaches the maximum number of subjects, extra subjects will be recruited. All participants will be asked to complete research study procedures up to the time of dosing. In the event that a study subject is unable to dose, another qualified subject will take that subject's place on the study. If you complete all the requirements, but are not dosed, you will receive a pro-rated stipend check based on information below.

If you are not selected to be in the study, you will be paid \$200.00 if you are released on day -1 and \$400.00 if released on day 1. As an alternate, you may be asked to participate in the next dosing group, which may require you to repeat Day -1 and Day 1 procedures.

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**Part 3 Payment (Cohort 11)**

If in Part 3, you may receive up to \$6000.00 for being in the study. You will be paid per completed visit as follows: You will receive two separate payments within 10 business days from Day 21 and Day 44.

<b>Visit</b>	<b>Payment (amount)</b>
Screening	\$0.00
Day -1	\$200.00
Day 1	\$250.00
Day 2	\$250.00
Day 3	\$250.00
Day 4	\$250.00
Day 5	\$250.00
Day 6	\$250.00
Day 7	\$250.00
Day 14	\$250.00
Day 21	\$250.00
Day 22	\$250.00
Day 23	\$250.00
Day 24	\$250.00
Day 25	\$250.00
Day 26	\$250.00
Day 27	\$250.00
Day 28	\$250.00
Day 35	\$250.00
Day 44	\$250.00
Bonus	\$1,300.00
*Total Payment*	\$6,000.00

To ensure that each dosing group reaches the maximum number of subjects, extra subjects will be recruited. All participants will be asked to complete research study procedures up to the time of dosing. If a study subject is unable to dose, another qualified subject will take that subject's place on the study. If you complete all the requirements, but are not dosed, you will receive a pro-rated stipend check based on information below.

If you not selected to be in the study, you will be paid \$200.00 if you are released on day -1 and \$400.00 if released on day 1. As an alternate, you may be asked to participate in the next dosing group, which may require you to repeat Day -1 and Day 1 procedures.

You must follow the study and site unit rules, which will be explained and given to you. Failure to follow the rules may result in a \$50.00 deduction for each offense. You may be dropped from the study without your consent for any reason. If you are dropped from the study, you will be paid for the study visits that you completed before being dropped from the study.

The research facility reserves the right to conduct an unscheduled drug, alcohol, and cotinine screen. Should you test positive for drugs, alcohol, or cotinine during the study you may be removed from participation and forfeit study payment.

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No subject is officially enrolled into a study until the Study Doctor makes a final decision, usually upon review of all screening and admission procedures. All subjects are in an alternate status and may be dismissed from the unit at any time before dosing. Enrollment is generally based on timing of consent, prompt arrival, and acceptable screening results. No guarantee of enrollment is offered.

You must give your social security number to receive payment. No deductions for state or federal withholdings (or other taxes) will be made on your behalf. You are responsible for reporting study payments on your federal and state tax returns for the payment of taxes. Taking part in this study does not make you an employee of the Sponsor, study site, or the US Food and Drug Administration.

**VOLUNTEERING TO BE IN THE STUDY**

It is your choice if you want to be in the study. No one can force you to be in the study. You may not want to be in this study or you may leave the study at any time without penalty or loss of benefits to which you are otherwise entitled. You can still get healthcare in the future. You may want to inform your personal doctor of your choice to participate in this study.

The Study Doctor, the sponsor company, IntegReview, or the FDA may take you out of the study without your permission, at any time, for the following reasons:

- If you do not follow the Study Doctor's instructions
- If we find out you should not be in the study
- If the study is stopped
- If it becomes harmful to your health

If you leave the study or if you are taken out of the study, you may be asked to return for a final visit to have some end of study evaluations or tests. If information generated from this study is published or presented, your identity will not be revealed. If you leave the study, no more information about you will be collected for this study. However, all the information you gave us before you left the study will still be used.

**NEW FINDINGS**

If there is new information or any significant new findings that could relate to your willingness to continue participation we will tell you. You can then decide if you still want to be in the study.

**Consent for Future Use of Stored Specimens and Data**

This consent form contains important information to help you decide if you want the residual (remaining/ left over) clinical samples collected during this study to be available for future research use by the sponsor company. These clinical samples will be shipped to and stored for up to 2 years at the Fisher Biorepository (DMID CMS) and may be shared with investigators at the participating site and with other investigators at other institutions. The samples will not be sold or used directly for production of any commercial product. No human genetic tests will be performed on the samples. Each sample will be encoded (labeled) only with a barcode and a unique tracking number to protect subject confidentiality. The recipients of specimens will be informed that these specimens have a NIH certificate of confidentiality. There will be no benefit to you in the collection, storage, and use of these specimens for

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future research. Reports that may occur in the future will NOT be kept in your health records. If you have any questions that are not answered in this consent form, ask one of the study staff.

**CONSENT**

- ☐ I **AGREE** to let my samples be used for future research and I also understand that I have the right to change my decision at any time by notifying the study doctors or study management team in writing.  
*(Any data from previously collected samples may still be used for future research)*  
*OR*  
☐ I **DO NOT AGREE** and wish my samples to be destroyed at the end of the trial

\_\_\_\_\_  
Printed Name of Adult Study Subject

\_\_\_\_\_  
Signature of Adult Study Subject

\_\_\_\_\_  
Date

\_\_\_\_\_  
Printed Name of Person Explaining Consent Form

\_\_\_\_\_  
Signature of Person Explaining Consent Form

\_\_\_\_\_  
Date

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**PHOTO RELEASE FORM**

Photographs may be taken to document side effects, such as a rash, for this study. You give the company paying for this research study the right to use, copy, and give out any pictures taken of you.

Your pictures may be used in scientific journals or magazines.

Your pictures may be used as part of a larger presentation, along with other pictures, videotapes or things like that. Your pictures may also be edited.

The company paying for this research study may give other people or companies permission to use your pictures.

We will try to hide your identity. Your name will not be on the pictures. You have the right to review your pictures and cancel this Photo Release Form.

**Statement of Consent:**

I have read this release and understand its meaning. I understand I do need to sign this Photo Release Form in order to be in the study.

\_\_\_\_\_  
Printed Name of Adult Study Subject

\_\_\_\_\_  
Signature of Adult Study Subject Date

\_\_\_\_\_  
Printed Name of Person Explaining Release Form

\_\_\_\_\_  
Signature of Person Explaining Release Form Date

You will be given a signed and dated copy of this release consent form to keep.

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**AGREEMENT TO BE IN THE STUDY**

This consent form contains important information to help you decide if you want to be in the study. If you have any questions that are not answered in this consent form, ask one of the study staff.

Please answer **YES** or **NO** to the following questions:

- A. Is this document in a language you understand? \_\_\_\_\_
- B. Do you understand the information in this consent form? \_\_\_\_\_
- C. Have you been given enough time to ask questions and talk about the study? \_\_\_\_\_
- D. Have all your questions been answered to your satisfaction? \_\_\_\_\_
- E. Do you think you received enough information about the study? \_\_\_\_\_
- F. Do you volunteer to be in this study of your own free will and without being pressured by the Study Doctor or study staff? \_\_\_\_\_
- G. Do you know that you can leave the study at any time without giving a reason and without affecting your health care? \_\_\_\_\_
- H. Do you know that your health records from this study may be reviewed by the sponsor company and by government authorities? \_\_\_\_\_
- I. Do you know that you cannot be in another study while you are in this study? \_\_\_\_\_

**IF YOU ANSWERED “NO” TO ANY OF THE ABOVE QUESTIONS,  
OR YOU ARE UNABLE TO ANSWER ANY OF THE ABOVE QUESTIONS,  
YOU SHOULD NOT SIGN THIS CONSENT FORM.**

\_\_\_\_\_  
Printed Name of Adult Study Subject

\_\_\_\_\_  
Signature of Adult Study Subject

\_\_\_\_\_  
Date

\_\_\_\_\_  
Printed Name of Person Explaining Consent Form

\_\_\_\_\_  
Signature of Person Explaining Consent Form

\_\_\_\_\_  
Date

You will be given a signed and dated copy of this consent form to keep.

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