

## INFORMED CONSENT TO PARTICIPATE IN A CLINICAL RESEARCH STUDY

**Study Title:** A Phase I Open Label Study To Evaluate The Safety, Tolerability, And Pharmacokinetics Of Intravenous Dalbavancin (VER001) in Subjects With Mild and Moderate Renal Impairment and Healthy Subjects with Normal Renal Function

**Sponsor:** Versicor, Inc.  
455 South Gulph Road  
King of Prussia, PA 19406

**Protocol No.:** VER001-13

**Principal Investigator:** Thomas C. Marbury, M.D.  
Orlando Clinical Research Center  
4401 South Orange Avenue, Suite 108  
Orlando, FL 32806  
24-Hour Telephone Number: [REDACTED]

### **INTRODUCTION**

The following information describes the study and your role as a participant. This document is intended to inform you about the nature and risks of the clinical study in which you have been asked to participate. The study doctor or his designee will answer any questions you may have about this consent form and about the study. Please read this consent form carefully and do not hesitate to ask any questions you may have about the information provided below or about any words that you may not understand.

### **DESCRIPTION AND PURPOSE OF THE STUDY**

You have been invited to participate in a clinical research study of dalbavancin, an investigational drug. "Investigational" means that the drug being tested has not been approved by the United States Food and Drug Administration (FDA) as a prescription or over-the-counter medicine, but may be tested in research studies such as this one. This study is sponsored by Versicor, Inc. This study is designed for research purposes only and is not designed to treat any medical condition.

Dalbavancin is an experimental antibiotic being developed to help treat infections.

The main purpose of this study is to determine if dalbavancin is safe and well tolerated. Also, the purpose of this study is to find out how much dalbavacin is passed into the urine of volunteers with decreased kidney function as well as healthy volunteers with normal kidney function.

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This study is being conducted at approximately 2 centers in the United States and will involve approximately 24 subjects. Approximately 12 subjects will participate at Orlando Clinical Research Center.

### **STUDY DURATION**

You will make one screening visit within 21 days of entering the study. If you qualify, you will take part in the study for approximately 60 days. The study procedures require that you complete one 4 day/4 night clinic confinement followed by 6 out patient visits. In addition, you will be required to have 2 Audiology (hearing) assessments one at the beginning of the study and one at the end.

### **STUDY PROCEDURES**

**If you agree to participate in this research study, you must sign this consent form before having any study-related tests or procedures performed.**

To be in this study, you must be at least 18 years of age. The study staff will ask you questions about your health and medical history, your medication history in the previous 6 months and if you are currently taking any medications, (over-the counter or prescription) or vitamins.

Volunteers for this study must meet certain requirements. Since this is a study of an investigational drug, it is important to answer all questions honestly and to tell the study staff your complete health history.

### **SCREENING VISIT**

Once you have consented to participate in this study you must undergo the following screening procedures

- General examination including vital signs (blood pressure, temperature and, pulse), and weight.
- Electrocardiogram (ECG - monitoring of the heart).
- Blood draw for laboratory testing.
- Collection of a urine sample for urinalysis, and a urine drug screen (for drugs and/or alcohol abuse).
- Female volunteers only will have a pregnancy test (must be negative in order to participate in the study).
- Audiologic assessment to evaluate hearing function (a non-invasive testing that evaluate your hearing)

The study doctor will review your screening tests and decide if you qualify to continue participating in the study. If you do, you will be scheduled to return to the study site for admission (Day -1) to the Orlando Clinical Research Center and will undergo additional assessments of any new medical history or medications since the initial evaluation. If you are a female of childbearing potential a repeat pregnancy test will be performed.

**Admittance to the study is not final until all laboratory tests that were performed at screening and/or check-in have been returned and judged to be satisfactory by the study doctor.**

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### **TREATMENT PERIOD**

If you are eligible to continue participating in this study based on the results of the screening tests and procedures you will come to the Clinical Research Center in the evening of Day -1 and begin the 4 night clinic confinement. Your medical and medication history will be updated, your vital signs will be measured and if you are a woman the pregnancy test will be repeated.

During the study, your vital signs will be measured periodically and you will be monitored closely for possible side effects. At each visit, you will be asked about any symptoms or illnesses that you may have experienced. In addition, you will be asked to inform the investigator and/or study staff of any medications or therapies you are taking while you are participating in this study.

If you develop symptoms you must inform the study doctor or study staff immediately.

On Day 1 two catheters (small plastic flexible tubes) will be inserted into your vein, one in each arm. The catheter will allow the study personnel to administer the study drug through one tube and obtain blood samples from the other. The catheter will be inspected, maintained and may be changed if necessary during the clinic confinement. Before study medication is given, you will be asked to empty your bladder, blood samples will be drawn and vital signs will be taken. You will receive a single dose of 1000mg of Dalbavancin (study drug) through one of the catheters in your arm over 30 minutes.

Blood samples will be taken to measure the levels of the study drug in your blood at the end of infusion (dose), and at 1, 4, 8 and 16 hours after the start of infusion. Additional blood samples will be taken to measure blood levels of the study drug on Days 2, 3, and 4 at approximately the same time that the study drug was started on Day 1. All of your urine will be collected from Day 1 through 3 (72-hours) beginning immediately after the start of the study drug infusion. The urine collected will be used to measure levels of the study drug over the course of the study. Your blood pressure, pulse, respiration, and temperature will be taken at the end of the infusion and 1, 2, 4, and 12 hours after the start of the infusion. A 12-lead ECG (test to evaluate your heart rhythm) will be taken shortly after the completion of the study drug infusion. Blood will be drawn on Days 2 and 4 for laboratory testing. You will also be given a physical examination including vital signs (heart rate, temperature, and blood pressure) on Day 4. You will go home on Day 4 following the final 24-hour urine collection and after all procedures have been completed. You will be given instruction when to return to the clinic for out patient visits.

### **Out Patient Visits**

You will return to the Clinical Research Center on days 7, 14, 21, 28 and 42 for outpatient visits. At each visit, blood samples will be taken at approximately the same time that the study drug was started on Day 1 and urine samples will be collected to measure levels of the study drug over the course of the study. You will also be given a physical examination including vital signs (heart rate, temperature, and blood pressure) on days 14 and 42. Blood will be drawn on day 14 for laboratory testing.

### Final Visit Day 60

On study day 60, you will return to the clinic for a final outpatient visit, you will have a complete physical exam performed including vital signs. Blood and urine samples will be taken. At this visit you will be scheduled for your final Audiology Assessment.

### **BLOOD SAMPLING**

Blood samples may be drawn by individual needle-sticks or from an indwelling catheter directly from a vein in your arm. An indwelling catheter is a special needle device designed to be placed in a vein and then remain in the vein over a period of time and is used to obtain multiple blood samples, thus lessening the number of needle punctures. If the use of the catheter is not possible, the location of the needle puncture will be varied to lessen discomfort.

There will be at least 16 blood draws during the course of this study. The total volume of blood drawn will be about 215 mL (less than ½ pint). Additional blood samples may be drawn during the study if the study doctor considers it necessary for monitoring your health.

### **RISKS AND DISCOMFORTS**

Dalbavancin has been well tolerated in healthy subjects administered up to 1120 mg dalbavancin as a single IV dose. Possible side effects are similar to those associated with taking currently available antibiotics that work in a similar manner as dalbavancin. Possible side effects may include diarrhea, abdominal pain, heartburn, liver damage, and kidney damage. Side effects associated with the administration of the drug include pain, redness or discomfort at the infusion site. In exceptional cases, hearing impairment was observed with other drugs in this class that work in a similar manner.

Thirty nine (39) healthy volunteers have received dalbavancin in a study conducted at the University of Medicine and Dentistry of New Jersey. There were no signs of any of the above-mentioned side effects. In several of the volunteers, a slight increase in body temperature of about 1-2 degrees Fahrenheit was observed.

The drug may stay in the blood stream longer in a person whose kidneys are not working normally. In addition, the drug may might act on the body longer, and it might also have more side effects.

If you have any injury, bad effect, or any other unusual health experience during this study, it is important that you tell the study doctor or the study staff immediately.

***Unforeseen Risks/New Risks:*** Since the study drug is experimental, there may be risks that are unknown when the study drug is taken alone or in combination with other drugs. Serious, and in rare instances fatal, allergic reactions can occur with any medication. To date, there have been no such serious allergic reactions in patients exposed to dalbavancin. **You should notify the study doctor immediately if you experience allergy symptoms such as rash, hives, or itching. Untreated allergic symptoms can lead to a medical emergency.**

You will be informed verbally and in writing of any new information, findings or changes to the way the research will be performed that might influence your willingness to continue your participation in this study.

**Blood drawing:** Local pain, bruising, swelling, bleeding, blood clot formation, and in rare instances an infection and nerve damage (some numbness and tingling) might occur at the site of the needle stick where blood is drawn and at the site where the catheter is placed.

There is also the possibility of dizziness or fainting while your blood is being drawn. The decision to use a catheter for blood collecting is made by the study staff or study protocol not by the individual volunteer.

**Additional risks:** The electrocardiogram (ECG) procedure may cause minimal discomforts during the attachment and removal of the ECG leads to and from the skin.

**Pregnancy/Fetal Risks:** The effects of the study medication to the pregnant women, the embryo, the human fetus and the nursing child are not known and may be harmful. Birth defects, including physical deformities, mental retardation, and other problems, as well as premature birth are known risks of some drugs. Women who are pregnant or nursing may not take part in this study. Dalbavancin has not been studied in pregnant women.

If you are a woman who is able to become pregnant, you must have a negative pregnancy test at the Screening Visit and check-in. Women will only be allowed to enter this study if they are using contraception for at least one month prior to the study and agree to continue using it for six weeks after the last dose of study medication. Acceptable forms of birth control include (either oral contraception, IUD, condoms with spermicide or diaphragm with spermicide), are surgically sterile (have undergone a bilateral tubal ligation, removal of both ovaries, or total hysterectomy), or are postmenopausal (at least 1 year without periods).

If you suspect you are pregnant at any time during the study, you must notify the study doctor immediately. If you do become pregnant during your participation in this study, you will be discontinued from the study and all costs for care related to your pregnancy, childbirth, and post-partum/newborn care will be your responsibility.

The effects of the study medication on sperm are not known and may be harmful. You should not father a child during your participation in this study.

### **BENEFITS OF THE STUDY**

This study is not designed to benefit you directly. Future patients may benefit from the overall conclusions drawn from the results of the study. Information obtained from this study may also benefit the sponsor of the study.

### **ALTERNATE TREATMENT**

This study is not designed to provide treatment. You have the alternative of not participating in this study.

### **COSTS AND REIMBURSEMENT**

Study drug will be supplied free of charge. You will not be responsible for any of the costs of the tests and evaluations required by this protocol that go beyond what you would normally receive as part of the routine treatment of your condition.

You will be paid for taking part in this study as outlined below. This is to compensate you for your time and travel. Each portion of the study has a monetary value assigned to it, which accumulates as you participate in the study. You will be paid within 7 days of the completion of your participation in this study. No additional financial compensation will be provided.

#### **Schedule of Payments**

<b>Visit</b>	<b>Amount</b>
Screening	No Compensation
Screening audiology test visit	\$ 50.00
Day -1 (check-in/admittance)	\$ 50.00
Days 1, 2, & 3	\$ 150.00 each day
Days 4, 7, 14, 21, 28, 42, 60	\$ 45.00 each visit
Day 60 audiology test visit	\$ 50.00

If, at the completion of the study, you have been on time and participated in all clinic visits, study unit confinements, and procedures, you will receive an additional \$85.00. Thus, the total compensation for complete participation in this study will be \$1,000.00. If your participation in this study is terminated by the study doctor in the interests of your safety, you will still receive the extra \$85.00 in addition to compensation for the visits that you have completed. If you choose to withdraw from the study, you will receive a prorated amount based on the procedures and visits that you have **completed** as outlined above.

In agreeing to participate in this study, you will be acting as an independent contractor, not as an employee of Orlando Clinical Research Center. Because payments made to you for participating in this study may be reported to the IRS as income, you are required to provide your social security number. No deductions for any state or federal withholding or any other similar taxes will be made. It is the responsibility of the participant to report this compensation on state and federal tax returns and for the payment of any taxes that are due on this compensation.

### **RESEARCH-RELATED INJURIES**

If you have any adverse reaction (side effect) to the study medicine during the course of the study, you should immediately contact Dr. Marbury or study personnel at (407) 240-7878, day or night.

If you become injured during this study and your injury is a direct result of the study drug or the administration of the study drug according to the study directions, medical treatment will be

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available to you. The costs of treatment will be paid by the Sponsor to the extent it is not covered by your health insurance. No further compensation for research related injury is available.

Further information regarding medical treatment for research-related injuries can be obtained from the study doctor or other authorized personnel. You must notify the study doctor immediately of any research-related injury.

**By signing this form you have not waived any of your legal rights.**

**PARTICIPATION INFORMATION**

I understand that I am free to withdraw from this study at any time, and I agree to inform the physician immediately if I intend to withdraw. It is understood that my decision to participate in this study or to withdraw from this study will not influence the availability of my future medical care and will involve no penalty or loss of benefits to which I am otherwise entitled. I may withdraw from this study at any time.

I agree that the physician in charge of the study can remove me from this study without my consent for any reason, including, but not limited to:

- a. His/her judgment that any condition or circumstance may jeopardize my welfare or the integrity of the study.
- b. My failure to follow the instructions of the investigator(s).
- c. If the study is stopped by the sponsor and/or doctors participating in the study prior to completion.

The sponsor, IRB or the FDA may stop the study at any time.

Any time your participation is terminated or if you withdraw voluntarily from the study, you will be asked questions about your participation in the study and to complete final laboratory tests and study procedures possibly including the audiology evaluation. It is important for your health and safety to have these final procedures completed.

**CONFIDENTIALITY**

Information from this study, medical records which identify you and the consent form signed by you, may be submitted to, inspected and or copied by; the study sponsor, the Sponsor's representatives (such as contract research organizations), Orlando Clinical Research Center, the FDA, governmental agencies in other countries where the study drug may be considered for approval, and the Independent Investigational Review Board, Inc. Because of the need to release information to these parties, absolute confidentiality can not be guaranteed. The results of this research study may be presented at meetings or in publications, however, your identity will not be disclosed in these presentations.

### **PERSONS TO CONTACT**

You have the right to ask any questions concerning the potential and/or unknown hazards of this study at any time. If you have any questions concerning your participation in this study, or if at any time you feel you have experienced a research-related injury or a reaction to the study medication, contact Dr. Marbury or his research staff at (407) 240-7878, 24-hours a day.

If you have any questions about your rights as a research subject, please contact Kim Lerner, Chairman of the Independent Investigational Review Board, Inc. toll free at (866) 475-8666 during regular working hours. The Independent Investigational Review Board is a committee established for the purpose of protecting the rights of volunteers in a research study.

Do not sign this form unless you have had a chance to ask questions and have received satisfactory answers to all of your questions.

### **CONSENT**

You have read and understood the information that has been stated above and have received satisfactory answers to all of the questions that you have asked and you willingly sign this consent form. You will receive a copy of the signed informed consent and you hereby consent to be a participant in this study.

### **SIGNATURES**

I have read in a language that I understand well, the above information. The content and meaning of this information has been explained to me. I hereby voluntarily consent and offer to take part in this study.

\_\_\_\_\_  
Print Subject Name

\_\_\_\_\_  
Subject Signature

\_\_\_\_\_  
Date/Time

The information contained in this document was fully and carefully explained to the study participant. Furthermore, the study participant has been given the opportunity to ask any questions regarding the nature, risks, and benefits of his/her participation in this research study.

\_\_\_\_\_  
Printed Name of Person  
conducting the Informed  
Consent discussion

\_\_\_\_\_  
Signature of Person conducting the  
Informed Consent discussion

\_\_\_\_\_  
Date/Time

Independent Investigational Review Board, Inc.  
Approved: 9/10/02

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