

## Sample Informed Consent

### **Study OCSI-004: An Open Label, Phase 1 Trial Comparing the Safety and Pharmacokinetics of a Single Infusion of Oritavancin in Subjects with Moderate Liver Insufficiency and in Healthy Controls**

#### **Introduction and Purpose of the Study**

You are invited to take part in a research study for an experimental antibiotic known as oritavancin. Antibiotics are used to treat infections caused by bacteria. Oritavancin is an antibiotic that interferes with the way bacteria build and maintain the cell membranes that surround and protect them. If the bacteria cannot maintain these membranes, they usually die and the infection goes away. Some bacteria are no longer affected by the antibiotics currently available, so new antibiotics are needed to treat these bacteria.

Oritavancin is a new, investigational antibiotic that has not yet received approval by the U.S. Food and Drug Administration (FDA). The Sponsor of the study, InterMune, is doing studies on oritavancin to get information that the FDA requires for drug approval. Studies previously conducted in humans have shown that oritavancin can treat infections caused by bacteria that are resistant to some of the antibiotics that are approved by the FDA and that are now being used to treat those infections.

The purpose of this study is to make sure that this dose of oritavancin is safe in people with liver disease in comparison to normal healthy people treated with the same dose of oritavancin. This particular study is being conducted at a dose of oritavancin that may make it more powerful for treatment of bacteria. Patients in another study (H4Q-MC-ARRM) have been treated for 10-14 days with doses similar to the dose proposed for this study.

#### **Study Overview**

A total of up to 40 volunteers will be enrolled in this study, with up to 20 people who have moderate liver disease and up to 20 normal healthy people. Your participation in the study may last up to 45 days. The first 2 days of the study will be spent in a research unit during which time you will receive a single dose of oritavancin. You will then be discharged from the research unit and asked to return at regular times for check-ups and tests.

## Study Procedures

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If you are interested in participating in this study, you will have screening procedures to determine if you qualify for entry into the study.

The following tests will be performed during the Screening Visit to determine if you are eligible to participate in the study:

1. A complete medical history will be obtained, including a description of any medications you are taking (including vitamins, herbals and medications available over the counter) and any medication allergies that you are aware of.
2. A complete physical examination, including your height, weight, frame size determination and vital signs (pulse, heart rate, blood pressure, breathing rate and temperature). Females will not receive a breast or pelvic exam. Neither males nor females will receive a rectal exam.
3. Approximately 30 mL of blood (about 2 tablespoons) will be taken from a vein in your arm to assess your complete blood count, the function of your kidneys and liver, your electrolytes (such as sodium and potassium), and total cholesterol. The tests will also determine if you have any evidence of Hepatitis B or C or HIV infection and will include a screen for alcohol. You will be asked to provide a urine sample for routine testing and drug screening. Females of child-bearing potential will have an additional blood test, approximately 7mL of blood (about 1 heaping teaspoon) to determine if they are pregnant.
4. You will also have a chest x-ray and an electrocardiogram (ECG). During the ECG 10 adhesive electrode pads will be placed on your chest, arms, and legs. These connect to the ECG machine. In order to get a good picture of your heart's electrical activity small areas of hair may have to be shaved from the chest, arms and legs.
5. If you are one of the subjects with moderate liver disease, you will be asked to take a test that will provide information about your mental status.

The doctor will then review the results of the examination and the tests to determine if you are eligible for the study. If you qualify for the study, the doctor or nurse will arrange the time for you to be admitted to the research unit.

**Day Before the Dosing**—You will be admitted to the research unit the evening before the dosing. You will have about 2 tablespoons of blood drawn for laboratory tests. You will be asked to provide a urine sample for routine testing and for females of child-bearing potential, a pregnancy test will be performed on the urine sample. Alcohol and/or drug screening may be repeated at this time. If you are one of the subjects with moderate liver disease, you will be asked to take the mental status test again. You will be allowed only liquids beginning at midnight on the day of admission, until after administration of the drug. You may

walk freely about the research area except during the period when the drug is being administered.

**Study Day 1**—On the morning of Study Day 1, your weight, blood pressure and pulse will be measured. You will have 6 ECGs prior to receiving study drug. Each ECG will be separated by a 15-20 minute interval and all 6 ECGs will be completed within a two-hour period. This ECG regimen will be repeated several times after you receive the study drug.

A trained member of the study staff will place an intravenous (IV) line in your arm that will be used to administer the oritavancin. You will receive a single 800 mg dose of oritavancin over a ninety minute time period. You must lie down in bed about 30 minutes before the start of the infusion and remain in bed during the infusion and for at least 30 minutes after the end of the infusion, except to go to the bathroom.

Blood will be collected by either venipuncture (a needle stick) or by catheter (a small tube placed in your arm to keep the vein open for collecting blood) up to 10 times from just prior to the start of the study drug until 24 hours after the study drug has been given to measure the amount of oritavancin in your blood. Each of these blood draws will remove about 1 teaspoon of blood.

You will be allowed to eat breakfast 1 hour after the study drug infusion is complete, but after breakfast, you should not eat anything else until lunch is served. Between breakfast and lunch you may have liquids, but caffeine-containing food and beverages should be consumed only at meal times. After lunch you can return to your regular diet.

**Study Day 2**—The morning after the study drug infusion, you will have another physical examination, your blood pressure and pulse will be measured, and another blood sample will be taken. Six ECGs will be performed according to the same schedule used previously. You will be sent home from the research unit on Study Day 2 if there are no significant findings in the results of the laboratory tests or physical examination.

**Other Study Days**—You will be required to return to the study doctor 8 more times. On Days 3, 4, 5, 8, 15, 21, 28, and 45, you will have repeat blood tests. These tests will be performed to check your blood counts and chemistry, to determine the level of study drug in your blood, and to determine how your liver is functioning.

**Last Study Day**—On Day 45 you will also have another ECG, physical examination and will have repeat blood tests.

The visits from Day 1 through Day 45 will take place over a 6- to 7-week period. The expected number of blood samples over the study period that may be drawn from you is approximately 20 (about 1 1/2 cups). A standard blood donation is about 1 pint (about 2 cups) of blood.

Your blood and/or urine sample may be randomly selected to be tested for alcohol or certain types of drugs (known as controlled substances in the United States) that may affect behavior and that may be regulated by law. If your test results show that you have taken these types of drugs, you will be notified of the test results and may be discontinued from the study based on the investigator's decision. The results of this test will be kept confidential and disclosed only as required by law.

## **Risks of Taking Part in This Study**

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### ***Risks from Oritavancin***

All drugs have side effects and there may be risks associated with participation in this study. There may also be risks involved, which are currently not known. You will be told of any important new information developed during the course of the study that may affect your decision to participate or continue your participation in the study.

As of May 1, 2002 approximately 1150 subjects have taken oritavancin. Adverse events from completed and ongoing studies for which information is available are included in the discussion below.

The most common side effects possibly related to oritavancin include rash, pain, diarrhea and reactions at the site of the study drug infusion. Allergic reactions, such as rash/redness, flushing, nausea, vomiting, diarrhea, shortness of breath and low blood pressure have been reported in some studies with oritavancin. To reduce the chance of these side effects, oritavancin will be given over a period of 90 minutes.

Other side effects associated with oritavancin include a decrease in the number of red blood cells (anemia), fast breathing rate, reversible changes in liver enzyme tests that are not accompanied by symptoms, abnormal kidney function, abnormal pain, water retention (edema), shaking chills (rigors), chest tightness, fever, itching, difficulty sleeping and thrush.

Oritavancin may interfere with some blood clotting tests, but no bleeding problems have been noted. Based on in vitro data (data obtained from studies done in a test tube), oritavancin could cause changes in the heart rhythm (arrhythmia). Electrocardiograms (which measure the electrical activity of the heart) have been done on subjects and animals that have been exposed to oritavancin. At this time, there is no evidence that oritavancin causes abnormalities of the heart rhythm and no evidence that it causes any changes in the electrocardiogram over and above those of a similar antibiotic that has been on the market for many years—vancomycin.

Because oritavancin is similar to the antibiotics vancomycin (Vancocin<sup>®</sup>) or teicoplanin (Targocid<sup>®</sup>), people who are known to be allergic to either of these

two antibiotics should not receive oritavancin. Antibiotics can cause diarrhea with or without blood in some people, so this could also occur with oritavancin. Oritavancin may stay in the body for a longer period of time than most drugs. Therefore, side effects may take longer to go away.

### ***Women of Childbearing Potential/Pregnancy Information***

Females of childbearing potential have additional risks to consider. Use of oritavancin may involve risks to the embryo or fetus, which are unforeseeable, if you become pregnant.

Animal studies that might indicate whether oritavancin has potential risks for your embryo, fetus, or unborn child have not been done. If you are a female of childbearing potential, you will be admitted to the study only if you are not pregnant as determined by a pregnancy test and you agree to use at least a barrier method of contraception while you are taking the study medication. If you are pregnant, there may be unknown risks to your embryo, fetus or unborn child as a result of participating in this study.

If you are pregnant, become pregnant or are currently breast-feeding, you may not participate in this study. If you are pregnant or currently breast feeding, you understand that the embryo, fetus, or child may be exposed to unknown risks. If you do become pregnant while on this study, you must inform your doctor immediately, so that you can be counseled, withdrawn from the study, and referred for appropriate care. The study sponsor, InterMune, Inc., and the study doctor will follow the progress of your pregnancy until the termination of the pregnancy or a minimum of 6 months following the birth of your child.

### ***Other Possible Risks***

You will be undergoing tests and procedures as part of this study, some of which may be associated with potential side effects or risks. For example, blood being taken from a vein for tests may cause some discomfort and may occasionally cause some bleeding or bruising, infection, fainting, pain at the needle site, dizziness or the development of a collection of blood under the skin (hematoma).

If you have an injury, bad effect or any other unusual health experience during this study, make sure that you tell the nurses, study coordinator, or the physician immediately.

There may be unknown risks of possible harmful interaction with other medication you take. Therefore, it is very important that you tell the study staff if you take any medications (including over-the-counter medications and vitamins) other than the study drug during course of the study.

### **Possible Benefits of Taking Part in the Study**

Study drug and study procedures will be provided at no cost to you. You may receive information about your health from any physical examinations and laboratory tests to be done in this study.

Since you do not have any of the conditions for which oritavancin is being developed, you will not medically benefit from being a part of this study.

Information obtained from this study may benefit the sponsor of the study, InterMune, and may benefit people in the future.

### **Alternative Treatments**

You do not have the illness for which oritavancin is being developed. Because you do not have this illness, no alternative treatments are applicable for this study.

### **Reporting Health Experiences**

If you have any injury, bad effect, or any other unusual health experience during this study, make sure that you immediately tell the nurses or Dr. \_\_\_\_\_ at [phone #]. You may call at any time, day or night, to tell us about your health experiences.

### **Patient's Rights**

Your participation in this study is entirely voluntary, and you may elect to withdraw from this study at any time. You may withdraw from the study at any time without jeopardizing your future medical care or possible involvement in subsequent clinical studies. If you do not want to participate in this experimental study, you can still have your medical questions answered to the best of your physician's ability. Refusal to participate will not involve any penalty or loss of benefits to which you are otherwise entitled.

You may also be withdrawn from the study, and the study medication may be stopped without your consent, for some of the following reasons: 1) changes in your health that might make continued participation harmful to you, 2) your failure to keep appointments, 3) if you decide that you do not want to take the study drug, 4) if the investigator considers that it would not be in your best interest to continue, 5) if the investigator or the sponsor decide to suspend or stop the study. If the study medication is stopped or you withdraw from the study and you have taken any dose of study medication, the procedures outlined in the End of Study Visit will be completed.

You will also be informed of any new findings that may affect your willingness to continue participating in the study.

If you have any questions about this research, you may contact:

Dr. \_\_\_\_\_  
Telephone: \_\_\_\_\_ Fax: \_\_\_\_\_

## Compensation \_\_\_\_\_

You will not be charged for your participation in this study, for the study medication or for any study related procedures or tests. All costs for routine treatment of any pre-existing medical condition that you may have, including Emergency Room visits, hospitalizations, and tests that are not outlined in the study protocol, will be borne by you or your health insurer.

In the event that you are physically injured as a direct result of the study drug, the Institution, in this case \_\_\_\_\_ will provide medical treatment to you. InterMune will pay such medical treatments that are not covered by your medical insurance. No other compensation of any type shall be provided by InterMune. InterMune will not pay for the treatment of medical complications that are part of the natural course of your illness. If you have questions about compensation if you have a research-related injury or about the medical treatments that are available to you in the event of a research-related injury, you may contact Dr. \_\_\_\_\_ at [phone number].

You will receive up to \$ \_\_\_\_\_ as reimbursement of expenses for participation in this study if you complete all parts of this study, including the scheduled visits before drug infusion and the visits scheduled after drug infusion. If you do not complete this study for any reason, the amount you will receive will be prorated. In that case, you will receive \$ \_\_\_\_\_ for the completion of the screening visit and \$ \_\_\_\_\_ for each scheduled visit.

## Confidentiality \_\_\_\_\_

All information will be held confidential and will not be released without your written permission to the extent permitted by law.

You will be issued a code number, known only to you and the study personnel. All information about you will be identified only by this code number, and not by your name. Information about the code will be kept in a locked, secure location and access limited only to study personnel, the sponsor InterMune and/or its designee(s), the FDA or the Institutional Review Board. Any information about you, including your test status, will not be shared with anyone else (including your spouse or family or health providers), without your written permission.

In certain circumstances, the Sponsor, InterMune, Inc., and/or its designee(s), the FDA or Institutional Review Board may request to review your records. If this happens, their request will be honored.

If you decide to participate in the study, it is important that you understand that you will also be giving consent for the medical investigators and their study staff to review your medical records for the purpose of this study.

Your records and results will not be identified in any publication resulting from these studies as pertaining to you specifically. Information obtained from this study that does not identify you individually will be given to InterMune, Inc., and/or its representatives and may be published or given to regulatory authorities in the United States or other countries in which regulatory approval of oritavancin may be sought.

Your original medical records may be reviewed by the sponsor and/or its representatives, the Ethical Review Board for this study, and regulatory authorities (FDA) for the purpose of verifying clinical trial procedures and/or data. Your medical information may be held and processed on a computer.

By signing this consent form, you authorize the record review, information storage, and data transfer described above.

Finally, it is possible that collected information relating to the study will be analyzed by the InterMune in the future to evaluate oritavancin for other possible uses or for other medical or scientific purposes other than those currently proposed.

### **Contacts for Questions**

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If you have any questions about this study please contact Dr. \_\_\_\_\_ at [address and phone #]

If you have any questions about your rights as a participant in a research study, please feel free to contact the [ERB contact] at [address and phone #]

### **Volunteer's Statement**\_\_\_\_\_

You, the undersigned, hereby voluntarily consent to participate in the research study OCSI-004 entitled "An Open Label, Phase 1 Trial Comparing the Safety and Pharmacokinetics of a Single Infusion of Oritavancin in Subjects with Moderate Liver Insufficiency and in Healthy Controls".

You understand that Dr. \_\_\_\_\_ is the Principal Investigator of this study. You further understand that this Investigator is in charge of the study and will be responsible for safeguarding your welfare while you participate in the study. You understand that the Institutional Review Board has approved this study. If you believe that there is any infringement on your rights or if you have questions about your rights as a research subject, you may contact \_\_\_\_\_ at \_\_\_\_\_.

You are satisfied that study personnel have explained the nature of the study, the procedures, the benefits and the risks adequately to you. You understand that you may contact them if you have further questions. You understand the statements in all of the preceding sections of this Informed Consent document.

This version of the Informed Consent replaces all versions previously signed.

You will receive a copy of this consent statement for your own information.

\_\_\_\_\_  
**Printed Name of Study Participant**

\_\_\_\_\_  
**Signature of Study Participant**

\_\_\_\_\_  
**Date**

\_\_\_\_\_  
**Printed Name of Witness**

\_\_\_\_\_  
**Signature of Witness**

\_\_\_\_\_  
**Date**

\_\_\_\_\_  
**Printed Name of Investigator**

\_\_\_\_\_  
**Signature of Investigator**

\_\_\_\_\_  
**Date**