Informed Consent Form
AND AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

Sponsor / Study Title:	**AzurRx BioPharma, Inc. / "OPTION2: A Phase 2, Open-Label, Multicenter, 2x2 Crossover Trial to Assess the Safety and Efficacy of MS1819 in Enteric Capsules in Patients with Exocrine Pancreatic Insufficiency due to Cystic Fibrosis"**
Protocol Number:	**AZ-CF2002**
Principal Investigator: (Study Doctor)	**«PiFullName»**
Telephone:	**«IcfPhoneNumber»**
Address:	**«PiLocations»**

Important

This informed consent ("permission") form may contain words that you do not understand. Please ask the study doctor or the study staff to explain any words or information that is not clear to you.

Joining a study is an important decision. You should ask the study team any questions you may have about the study and this informed consent form before making a decision to participate.

Also, you may have your primary doctor call the study doctor to ask any questions he/she feels are necessary to evaluate the study and your possible participation in it.

You may take home an unsigned copy of this informed consent form to think about it or discuss it with family or friends before making your decision to take part in the study.

Why is this study being done?

AzurRx BioPharma, Inc. (AzurRx) has begun a study of an investigational drug (also known as the "study drug") called MS1819 in enteric (extended-release) capsules as a possible treatment for exocrine pancreatic insufficiency (EPI) due to cystic fibrosis (CF). An investigational drug is one that has not been approved by the United States (US) Food and Drug Administration (FDA) or the European Union (EU). You are being asked to take part in this study because you have been diagnosed with EPI due to CF.

To control EPI, people with CF take pancreatic enzymes (your prescribed porcine pancreatic enzyme replacement therapy [PERT]) by mouth to help them digest foods better. Pancreatic enzymes help the body absorb nutrients from food, reduce the number and bulk of stools, and reduce the amount of gas and stomach pain. Enzymes that are currently available are made from pig pancreases. These enzymes contain many other things found in pig pancreases, not just the enzymes needed by CF patients. Also, as the enzymes pass through the harsh acidic conditions of the stomach, they may not work as well. The PERTs that are currently available have to be coated to prevent the enzymes from being broken down by the normal stomach acid resulting in "beads" that are then placed inside a capsule.

The biotechnology-derived study drug (MS1819 in enteric[extended-release] capsules) is similar to a naturally occurring enzyme (lipase) made in the pancreas that digests fat. In animal studies, the enzyme has demonstrated the potential to compensate the pancreatic lipase (enzyme) deficiency that is common with EPI due to CF patients. The main purpose of this study is to learn how well the study drug works and how safe the study drug is compared to your already prescribed PERT.

Your participation in this study is voluntary. If you decide not to take part in this study, you can continue with your current medical care. This study involves research.

Participation in one clinical research study may mean that you are not eligible to participate in other clinical research studies.

How many people will take part in this study?

Approximately 30 subjects with EPI due to CF, aged 18 years and older, are expected to take part in this study. This study will take place in approximately 15 centers in the US and Europe.

How long will my participation in this study last?

If you are eligible for this study and complete all visits, then your participation may last up to 11 weeks including the screening (approximately 3 weeks), study treatment (approximately 6 weeks), and end of study (approximately 2 weeks) periods. You will need to come to the study center at least 5 times and be available for a telephone call at least 5 times over this period. As described below (in the 'Study Procedures and Assessments' section) for Visit 6 and Visit 9, you will be required to stay overnight in a supervised confinement facility for a maximum of 7 days (typically 4 to 5 days).

What will happen during this study?

The study is divided into 4 time periods: a screening period (up to 3 weeks), a first study treatment period (approximately 3 weeks), a second study treatment period (approximately 3 weeks), and one End of Study/Early Termination visit (approximately 2 weeks after the second study treatment period). During each study period, you will have 1 or more visits with your study doctor at the study center.

Before any study-related tests and procedures can be done, you will be asked to read, sign, and date this informed consent form. After you sign and date this informed consent form, the study will begin with a screening visit. The purpose of the screening visit is to determine whether you meet the requirements to take part in this study. If you do not meet the requirements, the study doctor will explain why and you will continue on with your usual treatment.

You will receive study treatment for about 6 weeks in this study. You will be randomized (chosen to receive) to either take your prestudy porcine PERT for the first 3 weeks, then receive the study drug (MS1819 in enteric capsules) at a fixed dose of either 2240 mg/day or 4480 mg/day for the following 3 weeks, or you will receive MS1819 in enteric capsules at a fixed dose of either 2240 mg/day or 4480 mg/day for the first 3 weeks followed by your prestudy porcine PERT for the following 3 weeks. The first study treatment you are randomized to is determined by chance (50:50), like the flip of a coin. After the 6 weeks of study treatments are done, you will resume therapy with your prescribed prestudy porcine PERT and you will be asked to come back to the study center in 2 weeks for a final check-up.

Study Procedures and Assessments

A description of the procedures and assessments that will be performed during the study, including the screening visit, is provided below. In addition to the visits described below, the study doctor may ask you to come in for extra visits, if necessary for your safety.

Screening Period

Visit 1 (Day -21 to Day -1)

A member of the study staff will interview you to discuss your eligibility and to explain the study to you. After you understand the study and agree to participate in this study by signing and dating this consent form, you will be evaluated for overall eligibility for the study.

If you are eligible to participate, a member of the study team will review your medical history with you, record any medications being taken, and ask you how you are feeling. You will be asked demographic information (age/date of birth, sex, race, and ethnic origin). A complete physical exam in addition to vital signs (temperature, blood pressure, heart rate, and respiratory rate) will be performed. Your height and weight will also be measured.

You must not have anything to eat for at least 8 hours before you come to clinic so that blood can be drawn to check your blood cell count, general body functions, and blood clotting. The blood sample taken may also be used for additional testing if test results show that your liver is not working properly in order to see whether your liver is inflamed due to a virus. The blood samples will also check your levels of vitamins A, D, E, and K in addition to measuring any study drug (MS1819) and anti-lipase (antibodies against MS1819 enzyme lipase) concentrations. Females of childbearing potential (able to have a baby) will also have blood taken to test for pregnancy. You must have a negative pregnancy test (if applicable), and sexually active subjects must agree to use a reliable method of birth control for the duration of their participation in the study. The overall estimated blood that will be taken from you at Visit 1 is about 18 teaspoons (90 mL) at the most. For comparison, you have about 1000 teaspoons (5000 mL) of blood in your body. A standard blood donation is about 2 cups (480 mL).

A urine sample will be collected to assess the health of your kidneys and bladder. A stool sample will be collected to see whether you need to take enzymes to treat your CF. A breathing test called spirometry will also be performed to check lung function. It may additionally be necessary to collect samples of your sweat in order to measure how much of an element known as chloride there is in your sweat. People with CF have a higher level of chloride in their sweat.

At the end of the visit, the study staff will confirm that they will call you once all of the laboratory results are available to confirm your eligibility in the study.

Visit 2T

This will be the first study telephone call in the study. This visit will occur once your eligibility is determined. If your results from Visit 1 showed that you are eligible for the study, then the study doctor or study staff will call you to provide instructions for the randomization visit, which will occur at Visit 3. These instructions will include a reminder to bring in your current PERT medication as well as to refrain from alcohol for 24 hours prior to your visit. However, there may be reasons why you are not allowed to take part in this study. If you are not eligible to participate in the study, then the study doctor or study staff will discuss these reasons with you.

Initial (First) Study Treatment Period

Visit 3 (Day 1)

This visit will be conducted at the study center. This is the first visit where you will start to receive study treatment (either MS1819 in enteric capsules or continuation of your own prestudy porcine PERT). The following assessments will be conducted at this time:

- You will be asked about any medications that you are taking, any other products that you are currently using, or medications that have changed since your first visit.
- You will be asked how you are feeling. Please make sure you tell study staff as much information about this as possible.

- The study doctor or study staff will perform a focused physical exam, including evaluations of your gastrointestinal (GI) tract (stomach and intestines), heart, and lungs, as well as record your height, weight, and vital signs (including temperature, blood pressure, heart rate, and respiratory rate).
- The study doctor or study staff will ask questions about your GI tract (stomach and intestines) such as abdominal pain, bloating, and gas as well as the frequency and characteristics of your stools.
- Blood samples will be taken to check your levels of vitamins A, D, E, and K in addition to measuring any study drug (MS1819) and anti-lipase (antibodies against MS1819 enzyme lipase) concentrations. The overall estimated blood that will be taken from you at Visit 3 is about 10 teaspoons (50 mL) at the most.
- The study doctor or study staff will collect a urine sample to test for pregnancy (for females of childbearing potential).
- A urine sample will be collected to assess the health of your kidneys and bladder.
- After these procedures are complete, then the study staff will instruct you to either continue taking your prescribed porcine PERT or to take the study drug. If you are randomized to MS1819, instructions will vary depending on the dose to which you are randomized (either 2240 or 4480 mg/day).
- If the study doctor or study staff instructs you take the study drug, then you will be provided with the study drug to take home with you.
- If the study doctor or study staff instructs you to continue taking your prescribed porcine PERT, then you must make sure you have enough left for the duration of the study. The study staff can help you with this. You will be required to obtain your prescribed PERT through your normal doctor.

Visit 4T and Visit 5T (Day 8 plus or minus 2 and Day 15 plus or minus 2)

Visit 4T and Visit 5T will be conducted over the telephone. The study doctor or study staff will discuss the following assessments with you at this time:

- You will be asked about any medications that you are taking, any other products that you are currently using, or medications that have changed since your first visit.
- You will be asked how you are feeling. Please make sure you tell study staff as much information as possible.
- The study doctor or study team will assess and record whether there are any signs or gastrointestinal symptoms of malabsorption like abdominal pain, bloating, constipation, diarrhea=, nausea or steatorrhea (oily, fatty stools).
- The study doctor or study team will remind you that you will need to fast for at least 8 hours before your next visit at the study center.
- You will be asked to confirm the scheduled date for your next visit (Visit 6, the overnight visit at the supervised confinement facility).

Visit 6 (Day 17 +5)

At this visit, you will be required to stay in a supervised confinement facility for a maximum of 7 days (typically 4 to 5 days) to measure how your body is absorbing fat from the foods you eat. A laboratory test will be performed on stool samples collected during your stay. To accommodate your schedule for the supervised confinement, a +5 day visit window is permitted, meaning that Visit 6 can start between Day 17 and Day 22. You will need to have completed at least 16 days of dosing before starting Visit 6.

If you are currently taking your prescribed PERT, you will be required to obtain your prescribed PERT through your normal doctor prior to this visit. You will also need to bring your medication with you to this visit (either your prescribed porcine PERT or study drug). When you arrive at the research facility, the following assessments will be conducted at this time:

- You will be asked about any medications that you are taking, any other products that you are currently using, or medications that have changed since your first visit.
- You will be asked how you are feeling. Please make sure you tell study staff as much information as possible.
- The study doctor or study staff will perform a focused physical exam, including evaluations of your GI tract (stomach and intestines), heart, and lungs, as well as record your height, weight, and vital signs (including temperature, blood pressure, heart rate, and respiratory rate).
- The study doctor or study staff will ask questions about your GI tract such as abdominal pain, bloating, and gas as well as the frequency and characteristics of your stools.
- Blood samples will also be collected for a lipid test, a test that measures the amount of cholesterol and triglycerides (fats) in your body. You will be required to fast for at least 8 hours before this visit. Prealbumin levels will also be tested at this time to measure how much protein is in your liver. Low prealbumin levels could mean you are malnourished. The blood samples will also check your levels of vitamins A, D, E, and K in addition to measuring any study drug (MS1819) and anti-lipase (antibodies against MS1819 enzyme lipase) concentrations. The blood sample will also be used to check your blood cell count, general body functions, and blood clotting. The blood sample taken may be used for additional testing if test results show that your liver is not working properly to see whether your liver is inflamed due to a virus. The overall estimated blood that will be taken from you at Visit 6 is about 23 teaspoons (115 mL) at the most.
- A urine sample will be collected to assess the health of your kidneys and bladder.
- The study doctor or study staff will collect a urine sample to test for pregnancy (for females of childbearing potential).
- Fat and protein intake, in addition to study drug intake, will be recorded during the 72-hour controlled diet period and on the morning of Day 4 of the supervised visit by the study staff.

- You will begin a controlled diet (approximately 100 grams of fat per day) with 3 meals and 2 snacks per day for 72 hours. With breakfast on Day 1 of the supervised visit, 2 capsules containing a blue dye marker will be given to you to take with your meal to mark the start of the controlled diet. The blue dye marker is an FDA-approved food coloring used in foods, drugs, and cosmetics. Two more capsules containing the blue dye marker will be given at the beginning of breakfast on Day 4 of the supervised visit to mark the end of the controlled diet. Once you have passed the first blue dye marker in your stool (likely within 24 hours), all of your stool will be collected for 3 to 5 days to test how much fat and protein (or nitrogen) is being digested. You will be asked to tell the study staff each time you have a bowel movement. These stools will be collected for testing. If the first blue dye marker has not passed within 4 days, or the second dye marker has not passed within 2 days after ingesting the capsules, 5 to 10 mg of oral bisacodyl (a laxative) may be given. Once you have passed the second blue dye marker in your stool (likely within 24 hours), this sample will be collected and you will be allowed to go home.
- At the end of the supervised stay, the study doctor or study staff will instruct you to either take your prescribed porcine PERT or to take the study drug.
- If you were treated with study drug during this study treatment period, then you will return the study drug to the supervised facility.
- Before leaving, the study doctor or study staff will confirm the study treatment you will take in the next study period. If you are scheduled to take the study drug in the next study treatment period, then the study doctor or study staff will provide this to you. If you are scheduled to continue taking your prescribed porcine PERT, then you will be asked to switch back to your normal treatment.

Second Study Treatment Period

Visit 7T and Visit 8T (Day 29 and Day 36)

Visit 7T and Visit 8T will be conducted over the telephone. The study doctor or study staff will discuss the following assessments with you at this time:

- You will be asked about any medications that you are taking, any other products that you are currently using, or medications that have changed since your first visit.
- You will be asked how you are feeling. Please make sure you tell study staff as much information as possible.
- The study doctor or study team will remind you that you will need to fast for at least 8 hours before Visit 9.
- You will be asked to confirm the scheduled date for your next visit (Visit 9, the supervised confinement facility).

Visit 9 (Day 38 +5)

At this visit, you will be required to stay in a supervised confinement facility for a maximum of 7 days (typically 4 to 5 days) to measure how your body is absorbing fat from the foods you eat. This is a measurement that is commonly used to test whether the PERT is working. A laboratory test will be performed on stool samples collected during your stay. To accommodate your schedule for the supervised confinement, a +5 day visit window is permitted, meaning that Visit 9 can start between Day 38 and Day 42. You will need to have completed at least 16 days of dosing before starting Visit 9.

If you are currently taking your prescribed PERT, you will be required to obtain your prescribed PERT through your normal doctor prior to this visit. You will also need to bring your medication with you to this visit (either your prescribed porcine PERT or study drug). When you arrive at the research facility, the following assessments will be conducted at this time:

- You will be asked about any medications that you are taking, any other products that you are currently using, or medications that have changed since your first visit.
- You will be asked how you are feeling. Please make sure you tell study staff as much information as possible.
- The study doctor or study staff will perform a focused physical exam, including evaluations of your GI tract (stomach and intestines), heart, and lungs, as well as record your height, weight, and vital signs (including temperature, blood pressure, heart rate, and respiratory rate).
- The study doctor or study staff will ask questions about your GI tract such as abdominal pain, bloating, and gas as well as the frequency and characteristics of your stools.
- Blood samples will also be collected for a lipid test (fatty acid), a test that measures the amount of cholesterol and triglycerides (fats) in your body. You will be required to fast for at least 8 hours before this visit. Prealbumin levels will also be tested at this time to measure how much protein is in your liver. Low prealbumin levels could mean you are malnourished. The blood samples will also check your levels of vitamins A, D, E, and K in addition to measuring any study drug (MS1819) and anti-lipase (antibodies against MS1819 enzyme lipase) concentrations. The blood sample will also be used to check your blood cell count, general body functions, and blood clotting. The blood sample taken may be used for additional testing if test results show that your liver is not working properly to see if your liver is inflamed due to a virus. The overall estimated blood that will be taken from you at Visit 9 is about 23 teaspoons (115 mL) at the most.
- A urine sample will be collected to assess the health of your kidneys and bladder.
- The study doctor or study staff will collect a urine sample to test for pregnancy (for females of childbearing potential).
- Fat and protein intake, in addition to study drug intake, will be recorded during the 72-hour controlled diet period and on the morning of Day 4 of the supervised visit by the study staff.

- You will begin a controlled diet (approximately 100 grams of fat per day) with 3 meals and 2 snacks per day for 72 hours. With breakfast on Day 1 of the supervised visit, 2 capsules containing a blue dye marker will be given to you to take with your meal to mark the start of the controlled diet. The blue dye marker is an FDA-approved food coloring used in foods, drugs, and cosmetics. Two more capsules containing the blue dye marker will be given at the beginning of breakfast on Day 4 of the supervised visit to mark the end of the controlled diet. Once you have passed the first blue dye marker in your stool (likely within 24 hours), all of your stool will be collected for 3 to 5 days to test how much fat and protein (or nitrogen) is being digested. You will be asked to tell the study staff each time you have a bowel movement. These stools will be collected for testing. If the first blue dye marker has not passed within 4 days, or the second dye marker has not passed within 2 days after ingesting the capsules, 5 to 10 mg of oral bisacodyl (a laxative) may be given. Once you have passed the second blue dye marker in your stool (likely within 24 hours), this sample will be collected and you will be allowed to go home.
- At the end of the supervised stay, the study doctor or study staff will instruct you to take your prescribed porcine PERT.
- If you were treated with study drug during this study treatment period, then you will be asked to switch back to your prescribed PERT and to continue as you were before you started the study and to return any unused study drug.
- At the end of this visit, the study doctor or study staff will remind you of the End of Study/Early Termination Visit.

End of Study/Early Termination Visit

Visit 10 (Day 56 ±2)

The last study visit will be conducted at the study center approximately 2 weeks after your last dose of study drug (either MS1819 in enteric capsules or your prestudy porcine PERT). In the event that you do not complete Visit 9, an Early Withdrawal visit will be held approximately 2 weeks after the last dose of study drug. The procedures scheduled for the End-of-Study visit are the same as those that should be conducted for the Early Withdrawal visit. The following assessments will be conducted at this time:

- You will be asked about any medications that you are taking, any other products that you are currently using, or medications that have changed since your first visit.
- You will be asked how you are feeling. Please make sure you tell study staff as much information as possible.
- A focused physical exam will be performed, including evaluations of your GI tract (stomach and intestines), heart, and lungs.
- You will be asked questions about your GI symptoms such as abdominal pain, bloating, and gas as well as the frequency and characteristics of your stools.

- The blood samples will also check your levels of vitamins A, D, E, and K in addition to measuring any study drug (MS1819) and anti-lipase (antibodies against MS1819 enzyme lipase) concentrations. The overall estimated blood that will be taken from you at Visit 10 is about 10 teaspoons (50 mL) at the most.
- A urine sample will be collected to test for pregnancy (for females of childbearing potential).

What do I have to do?

During the study, you will have the following responsibilities:

- Follow directions from the study staff.
- Make and keep all study appointments.
- You will need to make sure you have enough of your prescribed porcine PERT for the duration of the study.
- Take your study drug or prescribed porcine PERT as instructed.
- Give blood, urine, and stool samples.
- Tell the study staff about all of the medicines you take during the study. You may call your study doctor at any time during the study if you are not feeling well or notice any changes in your overall health.
- Tell the study staff about any changes to your health, including changes to digestive symptoms related to pancreatic insufficiency, during the study.
- Not allow anyone else to use your study drug.
- Return all empty study drug bottles or packaging and all study drug that you do not use.
- You must also be willing to fast for at least 8 hours before attending Visit 1, Visit 6, and Visit 9.
- Tell the study doctor of any changes to your current medications, illnesses or injuries, unexpected or troublesome side effects, or problems that occur during the study.
- Tell the study doctor if you plan to have an elective surgery or any other medical treatment or procedure.
- Females who are able to get pregnant and all males must use a reliable form of contraception during the study. If you or your partner becomes pregnant while you are in the study, be sure to tell the study doctor as soon as possible.
- You will be encouraged to maintain your normal level of physical activity, diet, and lifestyle throughout the entire study (that is, you will not begin a new exercise program or participate in any unusually strenuous physical exertion).
- You will be advised that the consumption of alcohol is discouraged for the duration of the study. You will be specifically be advised to refrain from alcohol consumption for 24 hours before you attend clinic visits.

What are the benefits of being in this study?

You may benefit as a result of your participation in this study, but this is not guaranteed and there may be no clinical benefit from participating in this study. Additionally, if the results of the trial are favorable, you may be contributing to the future of your own healthcare or the healthcare of other patients with EPI.

What are the risks and possible discomforts?

Any study has risks, which may include things that could make you sick, make you feel uncomfortable, or harm you. You might experience side effects related to the study drug while participating in the study. All participants in the study will be watched carefully for any side effects; however, the study team does not know all the side effects that the study drug may have on you. These side effects may be mild or serious. In some cases, these side effects might be long lasting or permanent.

Taking part in this study involves some risks and possible discomfort to you as noted below:

- If MS1819 in enteric (extended-release) capsules does not work for you, you may see an increase in your EPI due to CF symptoms.
- The study drug may increase your chance of having a rare bowel disorder called fibrosing colonopathy, which can present with severe belly pain and swelling, vomiting and constipation.
- Because the study drug is investigational, there may be risks and side effects that are unknown. All drugs have a possible risk of an allergic reaction. A severe allergic reaction can cause itchy rash, facial swelling including swelling of the throat and tongue, breathing difficulties, a drop in blood pressure, and possibly death. If any of these symptoms occur, you should dial 911 immediately and, as soon as it is practical, contact the study doctor. Your treatment may include the administration of various drugs, which may include adrenaline, antihistamines, or hydrocortisone.

MS1819 in enteric capsules:

The study drug may cause unpleasant side effects or reactions. The most commonly reported side effects in other studies of MS1819 were:

- Abdominal pain
- Diarrhea
- Abdominal distension (swelling or bloating)
- Nausea
- Constipation
- Hypoglycemia (low blood sugar levels)
- Fatigue

Because the study drug is a modified form of a natural enzyme found in your body, it is not anticipated to cause an immune reaction, but any time a protein is administered, it is possible to form antibodies (immune reaction) to that protein. If this were to occur, it could cause itching and/or redness of the skin, hives, or swelling of the throat.

Bisacodyl:

Common side effects include; abdominal cramping, excessive diarrhea, nausea, vomiting, electrolyte imbalance, dizziness, and rectal burning.

Blood samples:

Taking blood from your arm may cause faintness and/or swelling, pain, redness, bruising, bleeding at the collection site, or infection (infection rarely happens) at the site where the needle is inserted.

Dye Marker:

The dye markers used in this study will result in colored stools, which are harmless.

Spirometry Test:

Risks and discomforts associated with spirometry measurement may include a sensation of shortness of breath while doing the breathing tests.

Fasting:

Fasting for 8 hours could cause dizziness, headache, stomach discomfort, or fainting.

Pregnancy/Birth Control

Women

Taking the study drug may involve unknown risks to a pregnant woman, an embryo, fetus (unborn baby), or nursing infant. Therefore, if you are pregnant, planning to become pregnant, or are breastfeeding a child, you cannot take part in this study.

Before entering the study, a pregnancy test will be done for all women who are able to become pregnant. This test might not detect an early pregnancy. Pregnancy tests will be repeated during the study.

If you are female and sexually active with a male partner, then you must be willing to use a reliable method of birth control during the study. A reliable method of birth control is defined as one of the following: oral or injectable contraceptives, intrauterine device, contraceptive implants, tubal ligation, hysterectomy, or a double-barrier method (diaphragm with spermicidal foam or jelly, or a condom), abstinence (avoiding sexual intercourse) or vasectomy in your partner. If you become or are found to be pregnant while in this study, you must let the study doctor know immediately so that management of the pregnancy can be discussed. You will be

asked to allow the following of your pregnancy and the outcome of the baby. The study drug will be stopped and your involvement in this study will end.

Men

If you are male and sexually active with a female partner, then you must be willing to use a reliable method of birth control (as defined above for women) during the study. If your sexual partner becomes pregnant while you are taking part in this study, you should also inform your study doctor or study staff. Because the risk to your partner and the baby are unknown, your partner will be asked to agree to medical follow-up during her pregnancy and for the outcome of the baby. Your partner will be asked to sign a separate consent form to allow the study staff to collect information about the pregnancy, its outcome, and the health of the child after birth.

What if there are new findings?

If new findings that would affect your safety and willingness to participate in the study are identified while you are in the study, you will be told as soon as possible so you can decide whether to leave the study or continue. If you continue, you will be required to sign and date a new informed consent form.

What other options are available if I do not take part in this study?

You do not have to take part in the study to treat your EPI due to CF. Pancreatic enzyme replacement therapy is the standard of care for EPI due to CF.

Your primary doctor or the study doctor can answer any questions that you have about other treatments.

You should also contact your primary doctor to ask about other research currently being done in the treatment of EPI due to CF.

Who is paying for this study?

This study is being funded by AzurRx. The study doctor will be paid for his/her work in this study.

What are the costs?

The study drug will be given at no cost to you, and you will not be charged for any study doctor visits, laboratory work, tests, or procedures that are needed for the study. You or your insurance company may be billed for any standard medical care given during this research study.

You may want to talk with your insurance company about its payment policy for standard medical care given during a research study. If your insurance company does not pay, you may be billed for those charges.

You might have unexpected expenses from being in this study. Ask your study doctor to discuss the costs that will or will not be covered by the sponsor. These expenses may include the cost of

your prestudy PERT while you are on study. This discussion should include who will pay the costs of treating possible side effects.

Will I be paid for being in the study?

«Compensation»

You will be reimbursed for any travel-related expenses such as transportation, parking payments, hotel stays, etc. related to visiting the study center. Acceptable reimbursements will be discussed with the study doctor and study staff. You will need to provide receipts to your study doctor or study staff.

All subjects will be paid **up to $4490** to cover the expenses and time for participating in the study. The following amounts will be paid for each completed:

Visit 1	$90	Visit 7 (Telephone)	$10
Visit 2 (Telephone)	$10	Visit 8 (Telephone)	$10
Visit 3	$60	Visit 9 $300 per day, up to 7 days maximum	$2100
Visit 4 (Telephone)	$10	Visit 10	$45
Visit 5 (Telephone)	$10	Unscheduled Visit	$45
Visit 6 $300 per day, up to 7 days maximum	$2100		

You will be paid after each visit.

You will be paid only for the portions of the study that you complete. Therefore, you will not be paid for any portions of the study you do not complete. Your payments will be provided via a contracted third-party vendor and will require you to provide personally identifiable information including your name, address, phone number, and date of birth upon registration.

Because payments made to you for participating in this study may be reported to the Internal Revenue Service (IRS) as income, you may be required to provide your Social Security number in the U.S.

Note: Because CF is a rare disease, if you are currently receiving Supplemental Security Income, Medicaid, or Medicare low-income subsidies, you may be able to receive up to $2,000 in a calendar year as payment for study participation without it affecting your continued eligibility for these benefits. Please ask your study coordinator for details.

What if I get sick or hurt?

If you become ill or are injured while you are in the study, get the medical care that you need right away. You should inform the healthcare professional treating you that you are participating in this study. If you tell the study staff that you think you have been injured, then they will help you get the care you need.

If you require medical treatment for an illness or injury that is a direct result of taking the study drug, then AzurRx will pay for reasonable and routine costs of such treatments if either of the following conditions are met:

- The illness or injury was a result of taking part in the study.
- The cost of treatment or any part of the costs is not covered by any other health insurance, government health program, or other institutions providing coverage for health care.

To pay medical expenses, the sponsor will need to know some information about you like your name, date of birth, and Medicare Beneficiary Identifier (MBI). This is because the sponsor has to check to see whether you receive Medicare and if you do, report the payment it makes to Medicare.

You will not lose any of your legal rights or release the sponsor, the Investigator, the study staff, or study site from liability for mistakes by signing and dating this consent document.

Can I leave the study after it has begun?

Yes. Taking part in this study is voluntary, and you can leave the study at any time for any reason. There will also not be any penalty or loss of benefits to which you are entitled at this site if you decide not to take part or if you decide to leave the study.

If you decide to leave the study, then you should contact the study doctor who will explain the safest way to end participation, which may involve completing some final tests and examinations. You should also contact your primary doctor so he or she can provide you with the best course of continuing care.

The study doctor or AzurRx can remove you from the study without your permission for any reason. Possible reasons for doing so include the following:

- Any change in your medical condition that might make continuation in the study harmful to you
- Your failure to follow the study doctor's instructions
- Discovery that you do not meet the study requirements
- Cancellation of the study
- Administrative purposes

What will happen to the samples that I provide?

Blood and stool samples collected throughout the study are a mandatory part of the study. The blood and stool samples that you give will be used only for specific tests that are needed for this study. They are for research purposes only and will be analyzed by a central laboratory. Only authorized study and laboratory staff will have access to your samples and results. The study doctor or study team will inform you if any of the samples reveal sensitive medical information. Your collected samples will be destroyed according to standard operating procedures as soon as possible after those specific tests are completed.

Your samples and information will be stored in a secure storage area. To protect your privacy, your samples and information will be identified only by a coded subject identification number.

Signing and dating this informed consent form means you agree to have this testing; it will not be done without your consent.

What happens when this study stops?

When the study stops, you will be under the care of your primary doctor who will decide the best way to treat your EPI due to CF. The study drug will no longer be available to you.

You have the right to be informed of the overall results of the study.

Will my records be kept private?

To participate in this study, you must read, sign, and date the Privacy Notice at the end of this form (see Appendix 1).

Whom to contact about this study

During the study, if you experience any medical problems, suffer a research-related injury, or have questions, concerns or complaints about the study, please contact the Investigator at the telephone number listed on the first page of this consent document. If you seek emergency care, or hospitalization is required, alert the treating physician that you are participating in this research study.

An institutional review board (IRB) is an independent committee established to help protect the rights of research subjects. If you have any questions about your rights as a research subject, and/or concerns or complaints regarding this research study, contact**:**

- By mail:
  Study Subject Adviser
  Advarra IRB
  6940 Columbia Gateway Drive, Suite 110
  Columbia, MD 21046
- or call **toll free**: 877-992-4724
- or by **email**: adviser@advarra.com

Please reference the following number when contacting the Study Subject Adviser:Pro00043375.

Consent to Participate

By signing and dating this informed consent form, I agree to the following:

- I have read and I understand this informed consent form.
- I have been given the chance to ask any questions that I had about the study, and all questions that I asked were answered to my satisfaction.
- I understand the risks of taking part in this study as described in this informed consent form.
- I understand that there is no guarantee that I will receive any benefits from taking part in this study.
- I freely consent to be treated with the study drug under the study doctor's care.
- I confirm that all information that I have given about my medical history is correct to the best of my knowledge.
- I understand that I am free to withdraw from the study at any time for any reason. I will tell the study doctor if I decide to withdraw so that my participation may end in an orderly manner, and my future care can be discussed.
- I understand that I will be told of any new information that might relate to my willingness to continue in the study.
- I will tell the study doctor if I have any physical or psychiatric ("mental health") symptoms or problems.
- I understand that I will receive a signed and dated copy of this informed consent form for my records.

My consent to participate in this study does not take away any legal rights in the case of negligence (carelessness) or other legal fault of anyone who is involved with this study.

_____

Name of participant (print)

_____ _____

Signature of participant Date (dd/Mmm/yyyy)

_____

Name of study doctor or person administering consent (print)

_____ _____

Signature of study doctor or person administering consent Date (dd/Mmm/yyyy)

Appendix 1: Privacy Notice

AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

Identification of Data Controller:

The study center may also be considered as a data controller of your personal data under applicable data protection laws. You may contact the study doctor using the contact information for the study doctor on the first page of this informed consent form.

If you have any questions or would like to see the data collected about you for this study, you should contact the study doctor.

Data to be Collected and Processed: The study staff will collect data about you for the study. This data may include your name or initials, date of birth, gender, contact details (email, telephone number, etc.), and information needed for payment processing. In addition, the following sensitive personal data about you will be collected: health, ethnicity, and race.

How Your Personal Data Will be Used: The personal data collected about you will be recorded in your study file by the study staff to run the study and to monitor your safety as a participant. Your personal data may be processed on a computer and/or on paper. The collection of this data is necessary to conduct the study and comply with applicable laws. You will not be able to participate in the study if you fail or refuse to provide your information.

There are laws about the recording, forwarding, storage, and analysis of your personal data, including sensitive personal data. These laws require your voluntary and explicit consent before you participate in the study. If you do not consent to the collection and use of your personal information, you will not be able to be in the study.

Results of this study may be presented at meetings or in publications; however, your identity will never be shared. Your personal data will not be used for any direct marketing purposes.

Storage of Your Personal Data: According to legal requirements, your personal data will be stored in the study databases and/or paper files for whichever time period is longer, as required by applicable laws:

- At least 15 years after the study ends, OR
- At least 2 years after the study drug being studied has received its last approval for sale, OR
- At least 2 years after the study drug's development has stopped.

Transferring the Personal Data to a Third Party: Records of your participation in this study will be held confidential except when sharing the information is required by law or as described in this informed consent. To keep your identity private, all data sent or provided outside of the study center will show only a coded identification number instead of your name. Only the study doctor and authorized personnel will be able to connect this code to your name. They will use a list that will be kept in a secure place to link this code to your name in case of an emergency. The coded data from the study showing your involvement (including uncoded personal information) will be provided to the Sponsor and other individuals and/or companies that act on the Sponsor's behalf. Also, your medical records (including uncoded personal data) may be reviewed by the Sponsor and other individuals and/or companies that act on the Sponsor's behalf; government agencies in countries where the study drug may be considered for approval (such as the US FDA); Advarra IRB, a group that reviews and approves studies; and independent auditors for the purposes of confirming your participation in the study, monitoring your safety during the study, and monitoring the conduct of the study. This means that absolute confidentiality cannot be guaranteed. Further, your personal information may be disclosed in response to lawful requests by public authorities, including those to meet national security or law enforcement requirements. Once your health data has been shared with authorized users, it may no longer be protected by federal privacy law and could possibly be used or disclosed in ways other than those listed here.

If your personal data are shared with other companies that are located outside of the country where you live, the Sponsor will make sure your data are protected as required by your country's data protection laws. Some of these other companies may be located in countries whose data protection and privacy laws may be less

strict than in your own country. You may contact the study doctor to get more information about the precautions used to protect your personal data outside of your country. You may also ask the study doctor for a copy of those precautions.

With your permission, the study doctor will tell your primary doctor about your role in this study.

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.

A description of this clinical study will be available on the European clinical trials database at https://www.clinicaltrialsregister.eu as required by European Law. This website will not include information that can identify you. At most, this website will include a summary of the results. You can search this website at any time. Information about what will happen to the results of the research and how the results will be made available to participants should be added.

Your Rights as a Data Subject: You have the right to access and correct the data collected about you during the study and submit any questions or concerns about the collection or processing of your personal data. If applicable, you may also have the right to request

- The deletion of your personal data,
- Restriction on or objection to the processing of your personal data, and
- The receipt of your personal data (data portability).

You may make these requests by contacting the study doctor. You may also have the right to file a complaint regarding the handling of your personal information with your local data protection authority.

Your permission to use and share health data about you will end in 50 years unless you revoke it (take it back) sooner. You have the right to withdraw your authorization for the processing of your personal data at any time by writing to the study doctor at the address listed on the first page of this form. However, data collected before you remove your consent are still legally allowed to be used. If

you withdraw your authorization, you will no longer be able to take part in the study.

Authorization to the Collection, Processing, and Use of Personal Data

By signing and dating below, I agree that:

(1) My personal data, including sensitive personal data, can be collected, used, and archived for purposes of carrying out the study as described in this Privacy Notice;

(2) My personal data, including sensitive personal data, can be transferred to and shared with other companies both within and outside of the European Economic Area (EEA), including to countries that may not have the same level of data protection as the EEA, as described in the Privacy Notice;

I understand that I will receive a signed and dated copy of this form for my records.

_____

Name of participant (print)

_____ _____

Signature of participant Date (dd/mm/yyyy)

_____

Name of study doctor or person obtaining authorization (print)

_____ _____

Signature of study doctor or person obtaining authorization Date (dd/Mmm/yyyy)