SUBJECT INFORMATION AND CONSENT FORM AND HIPAA AUTHORIZATION

Study Title: A 26-Week, Phase 3, Open Label Study with a 12-Week, Placebo-Controlled, Randomized Withdrawal Period Followed by an Open Label Long Term Safety Extension to Evaluate the Safety and Efficacy of Tenapanor to Treat Hyperphosphatemia in End-Stage Renal Disease Patients on Hemodialysis and Peritoneal Dialysis

Protocol #: TEN-02-301

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PURPOSE OF THE SUBJECT INFORMATION AND CONSENT FORM

Please note: This Subject Information and Consent Form may contain words you do not understand. Please ask the study doctor or the study staff to explain any words or procedures that you do not clearly understand.

The purpose of this form is to give you information about the research study and, if signed, will give your permission to take part in the study. The form describes the purpose, procedures, benefits, risks, discomforts and precautions of the research study. You should take part in the study only if you want to do so. You may refuse to take part or withdraw from this study at any time without penalty or loss of benefits to which you are otherwise entitled. Please read, or have read to you, this Subject Information and Consent Form and ask as many questions as needed.

You should not sign this form if you have any questions that have not been answered to your satisfaction.

Your study doctor and dialysis center will be paid by the sponsor to conduct this research study. If you agree to participate in this research study, your primary care doctor may be notified.

PURPOSE AND DESCRIPTION OF THE RESEARCH STUDY

You are being asked to take part in a research study of an experimental drug, tenapanor, because you are taking a phosphate binder medication for your hyperphosphatemia, you have end-stage renal disease (ESRD), and you have been on hemodialysis 3 times per week for at least the past 3 months or on peritoneal dialysis for a minimum of 6 months. Tenapanor is an experimental drug being developed to reduce the amount of phosphate that enters the blood from the food you eat. “Experimental” means that tenapanor is currently being tested and has not been approved for sale in the United States by the U.S. Food and Drug Administration (FDA).

The primary purpose of this research study is to compare the phosphate lowering effect of tenapanor with placebo (a tablet that looks like the study drug but does not contain any active ingredient). The term “study drug” refers to both tenapanor and placebo in this form. The change in serum phosphorus levels will be compared from the end of the 26-week treatment period to the end of the 12-week randomized withdrawal period. During the double-blinded 12-week randomized withdrawal period, half of the subjects who are taking tenapanor will stay on their current treatment and the other half will receive placebo. A secondary goal is to show the change in serum phosphorus levels from baseline (beginning of treatment) to the end of 26 weeks of treatment period. Another secondary goal is to assess the long-term safety of tenapanor. To achieve this, there will be an active control group that will receive, an approved phosphate binder, sevelamer carbonate based on standard of care according to the instructions in its package insert. The active control group is being used to compare to tenapanor for safety purposes only.

Tenapanor is minimally absorbed, which means that very little or no study drug should be found in your blood.

Earlier studies in healthy volunteers and ESRD patients given tenapanor, showed that there was an increase in the amount of sodium and phosphorus excreted in the stool (in their bowel movements) and a decrease in both sodium and phosphorus excreted in the urine due to a decrease in the absorption of both sodium and phosphorus. There were also changes in the stool form (how hard or soft your bowel movements are) and/ or frequency of stools (number of stools per day). Subjects had looser, softer, or watery stools which, in some cases, may be explained by the fact that water is attracted to sodium and the increased sodium in the stools was accompanied by an increase in water. You may also experience an increase in stool frequency.

If you qualify for this study, you will go through a washout period when you will stop taking your current phosphate lowering medication. The washout period can range from 1 to 4 weeks depending upon the rate your phosphorus levels rise. When your serum phosphorus level reaches (but does not exceed) the required level you will be randomly assigned (like drawing straws) to one of two study groups. You will either be assigned to take 30 mg of tenapanor bid (twice daily) or the active control, sevelamer carbonate for up to 52 weeks. If you are assigned to the tenapanor group, you will take 3 small tablets of tenapanor (orally) twice each day just before meals (breakfast and dinner; 6 total tablets). You should not take the study drug prior to the meal right before your dialysis session. You should still take 2 doses each day so your first or second dose may be taken just before lunch. If you are assigned to the active control group, sevelamer carbonate will be taken as instructed by the study doctor. There is a 3 out of 4 (75%) chance of being in the tenapanor group and a 1 in 4 (25%) chance of being in the active control group.

If you are assigned to the tenapanor group, you will be given 30 mg tenapanor bid (twice daily). The study doctor may reduce the dose depending on serum phosphorus and/or gastrointestinal (GI) tolerability to 20 mg bid, and 10 mg bid in a sequential manner. In other words, your dose will not be reduced directly from 30mg twice a day to 10mg twice a day without first being reduced to 20mg twice a day. After any decrease in dose, the dose may be sequentially increased back up to 30mg bid based on serum phosphorus levels and/or GI tolerability. Therefore, your dose could be 1-3 tablets (orally) twice each day just before meals (breakfast and dinner) for a total of 2-6 tablets.

If you are assigned to the tenapanor group, after the 26-week treatment period there is a 12-week randomized withdrawal period. For those 12 weeks, you will be randomized to either stay on your current dose of tenapanor or receive a placebo. There is a 1 in 2 (50%) chance of being in either group (like a coin toss).

Neither you nor your study doctor will know whether you receive tenapanor or placebo during this 12-week period, although this information can be made available to your study doctor in the event of an emergency.

After completing the randomized withdrawal period, you will continue into the safety extension period for an additional 14 weeks at the dose of tenapanor you were receiving at the end of the 26-week treatment period. The study doctor may reduce or increase the dose in the same way as the 26-week treatment period.

If your serum phosphorus level is greater-than or equal to 10.0 mg/dL or greater-than or equal to 9 mg/dL for two consecutive visits during the 26-week treatment period or safety extension period, your participation in the study will be discontinued and you will be put back on your pre-study phosphate binder medication.

If your serum phosphorus is greater than or equal to 9 mg/dL during the randomized withdrawal period, you will be discontinued from the study or you will have the opportunity to enter the 14-week safety extension period where you will receive the dose of tenapanor you were receiving at the end of the 26-week treatment period.

You will be discontinued if your serum phosphorus reaches less than or equal to 2.5 mg/dL at any time during the study.

The effectiveness of tenapanor in treating hyperphosphatemia has been previously studied in two double-blind, placebo-controlled clinical trials at twice a day doses between 1 and 30 mg for up to 12 weeks. Tenapanor produced a statistically significant decrease in serum phosphorus in both clinical trials; however, the phosphate lowering effect over a twenty-six (26) week period has not been determined and about half of the subjects will be receiving no active drug (placebo) during the 12 week randomized withdrawal period. Therefore, you should not expect this study to provide treatment for any medical condition.

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

This study will involve about 560 subjects at about 70-95 different study centers in the United States. Your participation in this study will last about 56 weeks. The screening period is up to 4 weeks; treatment period is 26 weeks; the randomized withdrawal period is 12 weeks; and the safety extension period is 14 weeks. If you are assigned to the tenapanor group at the end of the wash-out period, there are up to 23 visits to the study center (some of these visits will occur at the dialysis center if you are on hemodialysis). If you are assigned to the active control group at the end of the wash-out period, you will remain on the active control for the entire 52 weeks with up to 20 total visits. This study will use competitive enrollment. This means that when the targeted number of subjects have entered the study phase, all further enrollment will be closed. Therefore, it is possible that you could be in the screening phase, ready to enter the treatment phase, and be discontinued without your consent if the targeted number of subjects has already entered the study phase.

STUDY PROCEDURES (WHAT WILL HAPPEN DURING THE STUDY)

The following describes what will happen at each visit during the study:

Screening Visit (Visit 1; Study Day -21)
Before any study-related tests and procedures are performed, you will be asked to read and sign this consent document.

The following tests and procedures will be performed to determine if you qualify to take part in the study:

- You, the study staff, and the study doctor will review the requirements for being in the study.
- You will be asked about your medical and surgical history, including chronic kidney disease (CKD) history.
- You will be asked about the medications you are currently taking and have taken in the last 30 days.
- Your date of birth, sex, and ethnic origin will be collected.
- You will have a physical examination.
- Your height, pre-dialysis body weight (hemodialysis patients only) and vital signs (blood pressure and heart rate) will be measured.
- You will have an electrocardiogram (ECG). The ECG is an electrical tracing of your heart beat and heart rhythm.
- A pre-dialysis blood sample will be collected for:

    - Routine laboratory testing.
    - Measurement of Ca x P and FGF-23 (regulators of calcium and phosphorus concentration in the body).
    - Biomarker testing to see how indicators in your blood change in response to the study drug. These samples will be stored for future analysis.
    - Pregnancy will be tested on all females
    - Follicle-stimulating hormone (FSH) will be tested on all females.
    - Hepatitis B and C, and HIV testing. If you test positive for hepatitis B, C or HIV, we will notify you. We are required to notify state health authorities of positive results, as required by state law. If you do not want to be tested you should not take part in this study.

- You will complete the Kidney Disease Quality of Life Survey (KDQOLTM-36) and the Dialysis Symptom Index Survey (DSI). Please note: DSI survey is for English speakers only as it is only validated in English.
- After this visit you will stop taking your phosphate binders.

Wash Out Visits (Visit 2, Visit 3 and Visit 4; Study Days -14, -7, and -1)
During wash-out period, you will be off the phosphate binders and it can last up to 4 weeks. At one week intervals after Visit 1 you will have the following tests and procedures performed to determine if you continue to qualify to take part in the study:

- You and the study doctor will review the requirements for being in the study.
- You will be asked how you are feeling.

- You will be asked if there have been any changes to your medical or surgical history.
- You will be asked if there are any changes to the medication you are currently taking since your last visit.
- Your vital signs will be measured.
- A blood sample will be collected to measure serum phosphorus.
- If the phosphate level in your blood has reached and not exceeded the required level at visits 2, 3 or 4, you may be eligible to start the treatment phase of the study.
- If the phosphate level in your blood has not reached the required level, you will be scheduled for the next visit in one week.

If after Visit 4 the phosphate level in your blood has not reached the required level, you will be discontinued from the study.

Randomization Visit (Visit 5; Study Day 1)

When the phosphate level in your blood has reached the required level, you will have your randomization visit and start treatment with tenapanor or sevelamer carbonate.

The following tests and procedures will be performed to determine if you continue qualify to take part in the study:

- You and your doctor will review the requirements for being in the study.
- You will be asked how you are feeling.
- You will be asked if there have been any changes to your medical and surgical history.
- You will be asked if there are any changes to the medication you are currently taking since your last visit.
- You will have a physical examination.
- Your pre-dialysis weight (hemodialysis patients only) and vital signs will be measured.
- You will have an ECG.
- Blood samples will be collected pre-dialysis for:
    - Routine laboratory testing
    - Measurement of Ca x P and FGF-23
    - Biomarker testing to see how indicators in your blood change in response to the study drug. These samples will be stored for future analysis.
    - Pregnancy test, if necessary. The result of the pregnancy test must be negative for you to participate in the study.
- If, based on the results of these tests and procedures you qualify to take part in the study, you will be randomly assigned by chance (like drawing straws) to one of two treatment groups:

- Tenapanor 30 mg twice each day with possible reductions in the dose to 20 mg, and 10 mg depending on serum phosphorus and/or GI tolerability. Please note that all doses are taken twice each day prior to breakfast and dinner (unless dialysis will take place right after one of these meals, in which case, that dose should be taken prior to lunch).
- Active Control: Sevelamer carbonate will be prescribed for 52 weeks based on standard of care using package insert for guidance.

Visits 6, 7, 8, 9, 11 and 12 (Study Days 8 ± 5, 15 ± 5, 29 ± 5, 57 ± 7, 120 ± 7, 155 ± 7)
The following tests and procedures will be performed at study visits 6, 7, 8, 9, 11, and 12 unless otherwise noted:

- You will be asked about how you have been feeling.
- Your will be asked if there have been any changes to the medications you are currently taking since your last visit.
- Your pre-dialysis vital signs will be measured. Blood will be collected for pre-dialysis serum phosphorus testing.
- You will return any unused study drug or active control to the study center (except at Visit 7).
- You will receive your study drug or active control, if applicable (except at Visit 7).

Visit 10 (Study Day 85 ± 7)
The following tests and procedures will be performed at this visit:

- You will be asked about how you have been feeling.
- You will be asked if there have been any changes to the medications you are currently taking since your last visit.
- Your pre-dialysis body weight (hemodialysis patients only) and vital signs will be measured.
- You will have an ECG.
- Pre-dialysis blood samples will be collected for:
  - Routine laboratory testing
  - Serum pregnancy test, if necessary
  - Measurement of Ca x P and FGF-23
  - Biomarker testing to see how indicators in your blood change in response to the study drug. These samples will be stored for future analysis.
- You will return any unused study drug or active control to the study center. You will receive your study drug or active control, if applicable.
- You will complete the Kidney Disease Quality of Life Survey (KDQOLTM-36 survey) and the Dialysis Symptom Index Survey (DSI).

Randomized Withdrawal Visit or End of Treatment Visit (Visit 13, Study Day 183 ± 7)
The following tests and procedures will be performed at this visit:

- You will be asked about how you have been feeling.
- You will be asked if there have been any changes to the medications you are currently taking since your last visit.
- Your pre-dialysis body weight (hemodialysis patients only) and vital signs will be measured.
- You will have a physical examination.
- You will have an ECG.
- Pre-dialysis blood samples will be collected for:

    - Routine laboratory testing
    - Serum pregnancy test, if necessary
    - Measurement of Ca x P and FGF-23
    - Biomarker testing to see how indicators in your blood change in response to the study drug. These samples will be stored for future analysis.

- If you were assigned to the tenapanor group, you will be re-randomized for the withdrawal period of the study. During the 12-week period, you will either remain on the same dose of tenapanor you were on or you will be randomized to placebo.
- You will return any unused study drug or active control to the study center.
- You will receive a new supply of study drug or active control.
- You will complete the Kidney Disease Quality of Life Survey (KDQOLTM-36) and the Dialysis Symptom Index Survey (DSI).

Visits 14, 15, 16, 17, 18 (Study Days 197 ± 7, 211 ± 7, 225 ± 7 239 ± 7, 253 ± 7)

Visits 14, 16, and 18 will not be done if you are in the Active Control Group.
The following tests and procedures will be performed at these visits unless otherwise noted:

- You will be asked about how you have been feeling.
- You will be asked if there have been any changes to the medications you are currently taking since your last visit.
- Your pre-dialysis vital signs will be measured.
- Blood samples will be collected pre-dialysis for the following:

    - Serum phosphorus
    - Measurement of Ca x P and FGF-23(only at Visits 15 and 17)
    - Biomarker testing to see how indicators in your blood change in response to the study drug. These samples will be stored for future analysis(only at Visits 15 and 17).

- You will return any unused study drug or active control to the study center.
- You will receive your study drug or active control, if applicable.

Visit 19 (Study Day 267 ± 7)
The following tests and procedures will be performed at this visit:

- You will be asked about how you have been feeling.
- You will be asked if there have been any changes to the medications you are currently taking since your last visit.
- Your pre-dialysis body weight (hemodialysis patients only) and pre-dialysis vital signs will be measured.
- You will have a physical examination.
- You will have an ECG.
- Pre-dialysis blood samples will be collected for:
    - Routine laboratory testing
    - Serum pregnancy test, if necessary
    - Measurement of Ca x P and FGF-23
    - Biomarker testing to see how indicators in your blood change in response to the study drug. These samples will be stored for future analysis.
- You will return any unused study drug or active control to the study center.
- You will receive your study drug or active control, if applicable.
- You will complete the Kidney Disease Quality of Life Survey (KDQOLTM-36) and the Dialysis Symptom Index Survey (DSI).

When you complete the randomized withdrawal period, you will continue to the open label safety extension period for another 14 weeks. You will automatically be put on the dose of tenapanor you were on at the end of the 26-week treatment period. During the safety extension period, your doctor may increase or decrease your dose of tenapanor, similarly to the 26-week treatment period.

If you have a serum phosphorus level of greater-than or equal to 9 mg/dL during the randomized withdrawal period your participation in the study will be discontinued and you will be put back on your pre-study phosphate binder medication or you will have the opportunity to enter the 14-week safety extension period where you will receive the dose of tenapanor you were receiving at the end of the 26-week treatment period.

Safety Extension Period (Visits 20, 21, 22; Study Days 281 ± 7, 309 ± 7, 337 ± 7)
The following tests and procedures will be performed at these visits unless otherwise noted:

- You will be asked about how you have been feeling.
- You will be asked if there have been any changes to the medications you are currently taking since your last visit.
- Your pre-dialysis vital signs will be measured.
- A pre-dialysis blood sample will be collected to measure serum phosphorus.
- You will return any unused study drug or active control to the study center.
- You will receive your study drug or active control, if applicable.
- Your pre-dialysis weight will be measured (hemodialysis patients only at Visit 22).

End of Treatment (Visit 23, Study Day 365 ± 7)
The following tests and procedures will be performed at this visit:

- You will be asked about how you have been feeling.
- You will be asked if there have been any changes to the medications you are currently taking since your last visit.
- Your pre-dialysis body weight (hemodialysis patients only) and pre-dialysis vital signs will be measured.
- You will have a physical examination.
- You will have an ECG.
- Pre-dialysis blood samples will be collected for:
    - Routine laboratory testing
    - Serum pregnancy test, if necessary
    - Measurement of Ca x P and FGF-23
    - Biomarker testing to see how indicators in your blood change in response to the study drug. These samples will be stored for future analysis.
- You will return any unused study drug or active control to the study center.
- You will complete the Kidney Disease Quality of Life Survey (KDQOLTM-36) and the Dialysis Symptom Index Survey (DSI).

Upon study completion or early withdrawal, it is important for you to speak with your study doctor to arrange follow-up care and resume taking your phosphate binders as your doctor deems appropriate.

SUBJECT'S RESPONSIBILITIES
While participating in this research study, you will need to:

- Attend all study visits
- Follow all the instructions given to you by the study doctor and study staff
- Use the study drug or active control as instructed by the study doctor
- Keep the study drug or active control stored at room temperature.
- Return the study drug or active control bottles as instructed by your study doctor and study staff.
- Not participate in another research study
- Follow the study doctor's instructions regarding use of other medications
- Notify your study doctor or study staff before you take any new medications, as some are prohibited during the study.
- Notify your study doctor or study staff immediately if your health gets worse.
- Agree to use an effective method of birth control during your participation in the study and for 45 days after your last dose of study drug

RISKS AND DISCOMFORTS
There are risks, discomforts, and inconveniences associated with participation in any research study. You should talk with the study doctor if you have any questions.

Over 1800 subjects have been exposed to tenapanor in research studies; approximately 375 healthy subjects (people without any acute or chronic diseases), 1020 people with Irritable Bowel Syndrome with Constipation (IBS-C) and approximately 477 people with Chronic Kidney Disease (CKD).

The most common adverse events reported for the healthy subjects were gastrointestinal (GI) disorders (effecting the stomach and intestines) and included abdominal pain, abnormal GI sounds, abdominal discomfort (not necessarily pain), and diarrhea. No differences were seen in laboratory test results (measurements of chemicals and cells in the blood), vital signs (such as heart rate and number of breaths every minute) and Electrocardiogram (ECG).

In the most recent Phase 3 study in approximately 600 people with IBS-C, adverse events reported in more than 2% of people and greater than placebo include:

- Diarrhea (14.6%),
- Nausea (2.6%),

No serious adverse events associated with administration of tenapanor (for example, something life threatening, causing hospitalization) were reported. No differences were seen in laboratory test results (measurements of chemicals and cells in the blood), vital signs (such as heart rate and number of breaths every minute) compared to the people who received placebo.

In the most recent Phase 3 study in approximately 219 people on dialysis with hyperphosphatemia, adverse events reported in more than 2% of people include:

- Diarrhea (39%),
- Abdominal discomfort (2.8%),
- Flatulence (3.2%),
- Vomiting (3.7%),
- Hyperphosphatemia (5.5%),
- Cellulitis (2.8%),

It is expected that tenapanor will cause loose stools or diarrhea. People sensitive to loss of fluid volume should be monitored for dehydration (low body fluids) when they have diarrhea.

It is possible that taking tenapanor may change how your regular medications, vaccines, or supplements work. It is very important that you tell the study doctor about any medications, supplements, or vaccines before you take them during the study.

Some people in the study will get the active control, sevelamer carbonate, during the entire study. Sevelamer carbonate is a commercially available phosphate binder. Study doctor will determine the dose of sevelamer carbonate based on the standard of care using the package insert as guidance.

We will only be using sevelamer tablets in this study as the carbonate salt. As reported in the sevelamer package insert, most of the safety experience is with sevelamer tablets and sevelamer hydrochloride. In long-term studies with sevelamer hydrochloride, which contains the same active moiety as sevelamer carbonate, the most common adverse events reported in >5% of patients included:

- vomiting (22%)
- nausea (20%)
- diarrhea (19%)
- dyspepsia (16%)
- abdominal pain (9%)
- flatulence (8%)
- constipation (8%).

Serious cases of dysphagia, bowel obstruction, and perforation have been associated with sevelamer use, some requiring hospitalization and surgery.

Some people in the study will get placebo instead of tenapanor during the 12-week randomized withdrawal period (after the 26-week treatment period). Placebo is a tablet that looks like tenapanor but has no drug in it. Please ask the study doctor or study staff if you have any questions about placebo.

There may be side effects of the study drug that are not known at this time. A potential risk is allergic reaction.

Allergic Reaction Risks

Sometimes people have allergic reactions to drugs. If you have a very bad allergic reaction, you could die. Some things that may happen during an allergic reaction are:

- Rash or hives
- Having a hard time breathing
- Wheezing when you breathe
- Inability to breathe without assistance
- Sudden change in blood pressure, which may make you feel dizzy or lightheaded
- Swelling around the mouth, throat or eyes
- Fast pulse
- Sweating
- A feeling of dread

Seek medical help right away if you experience any of these symptoms.

Blood Draw Risks
Risks which may be associated with drawing blood from your arm include pain, swelling, bruising, lightheadedness, and, on rare occasions, infection. The maximum amount of blood drawn from you during this study is about 384 mL (about 25 tablespoons or 3/4th of a pint).

ECG Risks
As a result of the ECG you may have mild irritation, slight redness, and itching at the sites on the skin where the sticky tabs are placed.

You might have side effects or discomforts that are not listed in this form. Some side effects may not be known yet. The risks or discomforts described may occur more often or be more severe than has been seen before. Tell the study doctor or study staff right away if you have any problems.

REPRODUCTIVE RISKS
Since the effect of tenapanor in pregnant women has not been studied, the effects of tenapanor on a fetus or nursing infant are unknown.

To participate in this study, women must not be pregnant or planning on becoming pregnant during the study or for 45 days after the last dose of study drug, cannot be nursing a child and must fulfill one of the following:

1. Use of acceptable contraceptive method includes: IUD with spermicide, a female condom with spermicide, contraceptive sponge with spermicide, an intravaginal system (for example, NuvaRing®), a diaphragm with spermicide, a cervical cap with spermicide, or oral, implantable, transdermal, or injectable contraceptives; sexual abstinence, or a sterile sexual partner.
2. Post-menopausal, defined as amenorrhoea (absence of your menstrual period) for at least 12 months following discontinuation of all hormonal treatments or supplements, and with follicle stimulating hormone (FSH) levels in the laboratory defined post-menopausal range.
3. Documentation of irreversible surgical sterilization by hysterectomy, bilateral oophorectomy or bilateral salpingectomy but not tubal ligation.

Males must also agree to use appropriate birth control as it is not known if tenapanor has an effect on sperm.

Males must agree to avoid fathering a child (or donating sperm), and therefore be either sterile, have a sterile sexual partner, or agree to use, from the time of randomization until 45 days after end of study, one of the following approved methods of contraception: a male condom with spermicide, a sterile sexual partner, use by female sexual partner of an IUD with spermicide, a female condom with spermicide, contraceptive sponge with spermicide, an intravaginal system (such as, NuvaRing®), a diaphragm with spermicide, a cervical cap with spermicide, or oral, implantable, transdermal, or injectable contraceptives.

If you or your partner becomes pregnant during the study you should notify the study doctor right away. The study doctor will ask to follow your pregnancy to its outcome. If your partner becomes pregnant, she will be asked for permission to follow the pregnancy until its outcome.

Only you should take the study drug. It must be kept out of the reach of children or anyone else who may not be able to read or understand the label.

NEW INFORMATION
Your study doctor will tell you of any information learned during the course of the study that might cause you to change your mind about taking part in the study. You may be asked to sign a new consent form if this occurs. You may contact the study doctor at any time after your participation ends to find out if any new information about this study has become available.

POSSIBLE BENEFITS
There are no direct benefits of taking part in this study. Your symptoms of hyperphosphatemia may improve while participating in this study. Patients receiving placebo during the withdrawal period are not likely to receive the same benefit as those who continue to receive tenapanor. Your participation in the study will contribute to information about the study drug and may benefit other patients in the future.

PAYMENT TO SUBJECT FOR PARTICIPATION
For your time and inconvenience related to your participation in this study, you will be paid for the study visits you complete. If you do not complete the study, for any reason, you will be paid for each study visit you do complete. You will be paid $65.00 for each completed study visit. The IRS requires subjects that receive cumulative payments of $600 or more in a calendar year to report this income on their tax returns. Our site will request that every participant complete a W-9 tax form at the same time as signing the informed consent. If your study stipends are $600 or more for the calendar year, you will receive a 1099-MISC to report on your tax return. If your stipends are less than $600 per calendar year, you will not receive a 1099-MISC.

COSTS
You or your insurance company will not be charged for items or services that are provided solely for the purpose of the study, including the study drug and active control. You or your insurance company may still be charged for all routine costs including costs that are part of your usual medical care that you could have incurred regardless of your enrollment in this study.

ALTERNATIVE TREATMENTS
You do not have to take part in this study to receive treatment for your condition. If you decide not to take part in this study, there are other treatments for hyperphosphatemia, including continuing your current medications. Your study doctor will discuss alternative treatments with you.

CONFIDENTIALITY AND RELEASE OF MEDICAL RECORDS

All information that you give will be kept confidential. The information collected about you usually will not directly identify you (for example, by name, address, or social security number). Instead, your initials and a code number will be used for your information.

We will protect information about you and your taking part in this research study to the best of our ability. If information about this study is published, your identity will remain confidential. However, the U.S. Food and Drug Administration (FDA), Copernicus Group Independent Review Board (CGIRB), the sponsor of this research study, Ardelyx, Inc. and their respective business partners and agents and any other persons or entities working for the sponsor in connection with this research study may be granted direct access to your original medical records for verification of clinical trial procedures or data, without violating your confidentiality, to the extent permitted by the applicable laws and regulations. By signing this consent form, you are authorizing such access. A court of law could order medical records shown to other people, but that is unlikely. Therefore, absolute confidentiality cannot be guaranteed.

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.

COMPENSATION FOR RESEARCH-RELATED INJURY

If you have side effects during or after taking the study drug or are injured during your participation in this research study you should seek medical attention at the medical provider of your choice and notify your study doctor right away. If your injury or sickness is caused by the study drug or a required study-related procedure performed in accordance with the study protocol that would not have been performed if you were not participating in the study, the sponsor will cover the reasonable and necessary costs of diagnosis and medical expenses to treat the injury if:

- You followed the directions of the study doctor; and,
- You did not cause your own injury.

LEGAL RIGHTS

The above section does not restrict your right to seek legal assistance. You do not waive any legal rights by signing this Subject Information and Consent Form.

VOLUNTARY PARTICIPATION

Your decision to take part in this research study is completely voluntary. There will not be any penalty or loss of benefits to which you are otherwise entitled if you decide not to take part.

In addition, you may withdraw from the study at any time. There will be no penalty or loss of benefits to which you are otherwise entitled if you decide to withdraw from the

research study. Before withdrawing from this study, notify your study doctor that you wish to withdraw. This notice will allow your study doctor to inform you if there are any potential medical risks of withdrawal. You may be asked to return to the clinic for tests.

WITHDRAWAL
Your study doctor, the sponsor, or the FDA has the right to stop your participation in the study at any time, with or without your consent, for any of the following reasons:

- if you have an adverse effect from the study drug
- if you need a treatment not allowed in this study
- if you do not keep appointments
- if you do not take the study drug as instructed
- if you become pregnant
- if the study is canceled by the FDA or the sponsor.

The sponsor may decide to stop the study and your access to tenapanor under certain circumstances even if tenapanor appears to be safe and effective.

You may withdraw from the research study at any time. Your decision will not affect any benefits to which you are entitled.

If you decide to withdraw before the end of the study, you should notify your study doctor or study staff. If you leave the study for any reason, the study doctor may ask you to complete the Visit 23 tests and procedures for your safety.

CONTACT FOR QUESTIONS
If you have questions, concerns, or complaints, or think this research has hurt you or made you sick, talk to the study doctor / research team at the phone number(s) listed above on the first page.

This research is being overseen by an Institutional Review Board (IRB). You may talk to them at (888)-303-2224, irb@cgirb.com if:

- You have questions, concerns, or complaints that are not being answered by the research team.
- You are not getting answers from the research team.
- You cannot reach the research team.
- You want to talk to someone else about the research.
- You have questions about your rights as a research subject.

The IRB is a group of scientists and non-scientists who review the ethics of research. The goal of the IRB is to protect the rights and welfare of study subjects.

SUBJECT'S STATEMENT OF CONSENT

A 26-Week, Phase 3, Open Label Study with a 12-Week, Placebo-Controlled, Randomized Withdrawal Period Followed by an Open Label Long Term Safety Extension to Evaluate the Safety and Efficacy of Tenapanor to Treat Hyperphosphatemia in End-Stage Renal Disease Patients on Hemodialysis and Peritoneal Dialysis

- I have been told that this is a research study of an experimental drug, tenapanor.
- I have been given the chance to discuss this research and ask questions.
- I have been given sufficient opportunity to consider whether to participate in this study.
- My taking part in this research study is voluntary. I may decide not to take part or to withdraw from the research study at any time without penalty or loss of benefits or treatment to which I am entitled.
- If I meet the criteria and would like to take part in this research study, my doctor may enroll me in the research study.
- The research study may be stopped at any time without my consent either by the study doctor or by the company sponsoring the research.
- I have been told that my study doctor will be receiving payment from the sponsor to conduct the research.
- I have had an opportunity to ask my study doctor questions about this research study. My questions so far have been answered to my satisfaction.
- I have been told how long I may be in the research study.
- I have been told of the procedures and tests that may be performed during the research study.
- I have been told what the possible risks and benefits are from taking part in this research study. I may not benefit or my condition may worsen if I take part in this research study.
- I do not give up my legal rights by signing this form.
- I have been told that prior to any study-related procedures being performed, I will be asked to voluntarily sign this Subject Information and Consent Form.
- I will receive a copy of this signed and dated consent form.

I authorize access to my medical records by the sponsor, agent, and their business partners and agents, CRO, Copernicus Group IRB, the FDA or applicable regulatory agency.

I voluntarily agree to take part in this research study.

Signature of Subject **Date**

Printed Name of Subject

The information about the study was described to the subject in language he/she understood.

Signature of Person Obtaining Consent **Date**

Printed Name of Person Obtaining Consent

Statement of the Witness (when applicable*)
The information in the consent form was accurately explained to, and appeared to be understood by the subject. Informed consent was freely given.

Signature of Impartial Witness **Date**

Printed Name of Impartial Witness

*Impartial Witness: If the subject cannot read, the signature of an Impartial Witness is needed.

An impartial witness is:

- a person who is independent of the trial,
- who cannot be unfairly influenced by people involved with the trial,
- who attends the informed consent process, and
- who reads the informed consent form and any other written information supplied to the subject.

HIPAA AUTHORIZATION

The United States government has issued a privacy rule to protect the privacy rights of patients. This rule was issued under a law called the Health Insurance Portability and Accountability Act of 1996 (HIPAA). The Privacy Rule is designed to protect the confidentiality of your personal health information. The document you are reading, called an "Authorization," describes your rights and explains how your health information will be used and disclosed (shared).

In working with the sponsor, the study doctor will use and share personal health information about you. Except when required by law, you will not be identified by name, address, telephone number or other facts that could identify the health information as yours. This includes information in your medical record (from any doctor, hospital or other healthcare provider) and information created or collected during the study. This information may include your medical history, physical exam and laboratory test results. Some of these tests may have been done as part of your regular care. The study doctor will use this information about you to complete this research.

In most cases, the study doctor will use your initials and assign a code number to your information that is shared with the sponsor. The sponsor and their respective business partners and representatives may review or copy your personal health information at the study site. Regulatory authorities, such as the FDA and the Copernicus Group Independent Review Board (CGIRB) may also review or copy your information to make sure that the study is done properly or for other purposes required by law.

By signing this Authorization, you allow the study doctor to use your personal health information to carry out and evaluate this study. You also allow the study doctor to share your personal health information with:

- the sponsor and their respective business partners and agents
- the Copernicus Group Independent Review Board
- the U.S. Food and Drug Administration (FDA)
- Department of Health and Human Services (DHHS) agencies
- other regulatory agencies

Your personal health information may be further shared by the groups above. If shared by them, the information will no longer be covered by the Privacy Rule. However, these groups are committed to keeping your personal health information confidential.

You have the right to see and get a copy of your records related to the study for as long as the study doctor has this information. However, by signing this Authorization you agree that you might not be able to review or receive some of your records related to the study until after the study has been completed.

You may choose to withdraw this Authorization at any time, but you must notify the study doctor in writing.

Information that has already been gathered may still be used and given to others. If you withdraw from the study and withdraw your Authorization, no new information will be collected for study purposes unless the information concerns an adverse event (a bad effect) related to the study. If an adverse event occurs, your entire medical record may be reviewed. All information that has already been collected for study purposes, and any new information about an adverse event related to the study, will be sent to the study sponsor.

If you withdraw from the study but do not withdraw your Authorization, new personal health information may be collected until this study ends.

If you do not withdraw this Authorization, it will remain in effect.

If the research site is located in California, Delaware, Indiana, Washington, or Wisconsin, this authorization will expire on 31Dec2060.

There is no expiration of this authorization except for research conducted in the states listed above.

If you do not sign this Authorization, you cannot participate in this research study or receive study-related treatment. If you withdraw this Authorization in the future, you will no longer be able to participate in this study. Your decision to withdraw your Authorization or not to participate will not involve any penalty or loss of access to treatment or other benefits to which you are entitled.

AUTHORIZATION

I authorize the release of my medical records and personal health information related to this study to the sponsor and their respective business partners and representatives, Copernicus Group Independent Review Board, the FDA, and other regulatory agencies as described above. I have been told that I will receive a signed and dated copy of this Authorization for my records.

_____

Printed Name of Subject

_____

Signature of Subject Date

_____

Printed Name of Person Obtaining Authorization

_____

Signature of Person Obtaining Authorization Date

Statement of the Witness (when applicable*)
The information in the authorization was accurately explained to, and appeared to be understood by the subject. Authorization was freely given.

Printed Name of Impartial Witness

Signature of Impartial Witness Date

*Impartial Witness: If the subject cannot read, the signature of an Impartial Witness is needed.

An impartial witness is:

- a person who is independent of the trial,
- who cannot be unfairly influenced by people involved with the trial,
- who attends the Authorization process, and
- who reads the Authorization and any other written information supplied to the subject.