Subject Informed Consent Form

Protocol Title:	A Phase 1 Dose Escalation Study to Evaluate Safety, Tolerability, and Pharmacokinetics/Pharmacodynamics of APR003 in patients with Advanced Colorectal Cancer (CRC) with Malignant Liver Lesions
Sponsor:	Apros Therapeutics, Inc.
Protocol Number:	*APR003-001*
Investigator:	<*Insert Principal Investigator name*>
Investigator Telephone:	<*Insert Principal Investigator telephone number*>
Subject Identification:	_____

INTRODUCTION

You are being invited to take part in a clinical research study because you have been treated for advanced, unresectable colorectal cancer and have not responded to conventional therapy or the cancer has come back. This study involves research and is being conducted to determine the safety, efficacy of the study drug, how your body process the study drug, APR003.

Taking part in this clinical research study is strictly voluntary meaning that you may or may not choose to take part. Before you give your consent to be in this study, we ask you to read the following information. It is also important that you ask as many questions as you need to understand what is involved in this study. You will be given as much time as needed to decide whether you want to take part in this study.

This document is called an informed consent form. This form explains the purpose of the study and describes what is expected of you during the study. It also explains the possible risks and discomforts of taking part in this study and how being in the study may help you or others. Medical information will be collected about each person who participates in this study. This form will explain how your medical information will be used and provides information about your rights while you are taking part in this study. If you do not sign the consent form, you will be unable to take part in this study.

The study drug, APR003, is made by the pharmaceutical company, Apros Therapeutics, Incorporated (Inc.). As the sponsor of the study, Apros Therapeutics is supporting the research study and providing money for some of the costs of performing the study. Your study doctor's institution is being paid by the study sponsor to perform this research study.

PURPOSE OF THE STUDY

The study drug, APR003, used in this study is experimental. That means the United States Food and Drug Administration (FDA) has not approved it for the treatment of cancer.

APR003 might stop tumor cells (cancers) from growing and living and is being studied as a possible treatment for cancer. This is the first study in which APR003 will be given to humans. APR003 is a drug that changes the immune system within the liver. The hope is that by changing the immune system in the liver, the immune system will be better able to find and kill the cancer, both in the liver and in other places of the body.

The people who take part in research studies are called "subjects".

The purpose of this study is to:

- Determine the highest dose that can safely be given without unacceptable (intolerable) side effects to subjects who have cancer.
- Determine the amount of APR003 in the blood of subjects who have cancer and have been given APR003.
- Determine if APR003 might work to kill cancer or stop cancer from growing and, thus be used in the treatment of cancer.

NUMBER OF STUDY SUBJECTS

Approximately 36 subjects from about (4) study centers (US) will participate in the study to find the highest dose of study drug that can safely be given to advanced colorectal cancer patients with metastases to the liver without unacceptable side effects. This is called the dose escalation phase. <Approximately <XX> Subjects will be enrolled at <Insert Institution Name>.

STUDY OVERVIEW

This study will evaluate the safety, levels of drug in the blood and antitumor activity of APR003. Laboratory, imaging and safety assessments will be performed throughout the study to understand how APR003 moves through your body and how your body and your cancer respond to APR003.

On the study, you will receive APR003 in 3-week (21 days) treatment cycles. Your study doctor will inform you of which dose group you are assigned to. APR003 is a capsule that is taken by mouth once a week in the morning, at approximately the same time of day, and with an empty stomach (2 hours before or 1 hour after breakfast).

How long you stay on the study drug depends on how well you tolerate the study drug and how your cancer responds. You can continue on the study drug as long as your study doctor feels that you are benefitting. If your cancer progresses (gets worse), you may not be able to continue to receive the study drug, but you will take part in the follow-up period of the study.

The study is divided into the following periods:

- A 28-day screening period
- A study treatment period, which may last up to 1 year
- A follow-up period, during which you will be contacted by telephone or e-mail every 3 months, which may last up to 2 years

SUBJECT RESPONSIBILITIES

If you are enrolled in this study, you will have the following responsibilities:

- Go to all scheduled clinic visits
- Take the study drug as directed
- Record the date and time of when you take the study drug into a dosing diary
- Bring your dosing diary to all of your clinic visits
- Tell your study doctor of all medications that you are currently taking, and before taking any new medications
- Follow the study staff's directions about the study
- Tell the study doctor about any illnesses or injuries
- Tell the study doctor about any side effects or problems that occur during the study
- Tell the study doctor if you plan to have any surgery or any other medical treatment or procedure

It is important for your safety that you are completely honest with your study doctor throughout the duration of the study.

Diet: You will be asked to follow instructions to fast (with the exception of clear liquids) for 2 hours before and at least 1 hour after each APR003 dose. No other specific dietary restrictions are required.

Medications: During the study, you will not be allowed to take certain medications. You need to tell your study doctor what drugs you are taking and let your doctor know you are participating in this study. You may need to adjust the dose of some prescription medications or use an alternative medication while participating in this study. Medications such as antacids may decrease the drug's absorption into your body. For this reason, you should not take antacids within 7 days of your first dose of study drug. If antacids medication is necessary, some examples of preferred antacids include Pepto Bismol®, Milk of Magnesia, or Tums ® but these must not be used within 24 hours of taking the study drug. The study staff will let you know which medications you cannot take during the study. If a doctor other than your study doctor prescribes a drug for you to take during the course of the study, please inform the study doctor so that we may determine if it can be taken with the study drug.

Therapies: While you are participating in the study, you will not be allowed to receive certain therapies. This includes chemotherapy, surgery tumor control, radiation therapy for tumor control, investigational products other than APR003 or other prescribed drug that is part of this protocol therapy. The study staff will let you know which therapies you cannot receive during the study.

If, for any reason, the study drug is stopped before your last treatment visit, you will be asked to come into the clinic. You will be asked to have all end-of-treatment testing done for your safety.

STUDY PROCEDURES

Before any study-related tests and procedures are performed, you will be asked to read, sign and date this consent form. If you decide you want to participate in the study, the study staff will need to perform screening tests and procedures to find out if you qualify for the study and to determine the current status of your cancer.

These tests and procedures are often used as regular care for colon cancer patients and might be done even if you do not take part in the research study. If you have had some of these tests done within the last few weeks, they might or might not need to be repeated. Screening tests and procedures may be done over a period of approximately 28 days (4 weeks) and include the following:

Screening within 28 days before Day 1 (first Day of study medication)

- **Health and Medical Questions:** You will be asked about your overall health, medical history, previous medical procedures and treatments. You will also be asked about your current health and how well you are able to perform your daily activities.
- **Medication History:** You will be asked to list all the medication you have taken and are currently taking.
- **Demographic questions:** You will be asked to give personal information about yourself, such as your date of birth, sex and race.
- **Physical Examination:** You will have a physical exam and your height and weight will be recorded.
- **Vital signs:** Your vital signs will be measured, including blood pressure, heart rate body temperature, oxygen saturation and respiration rate.
- **Electrocardiogram (ECG):** An ECG will be performed to measure the electrical activity of your heart.

- **Blood Tests:** A small needle will be placed into a vein in your arm to draw blood for testing, unless you have a central venous catheter where blood will be drawn. The blood samples will be used for the following tests:
    - **Clinical chemistry:** To evaluate your general health, liver and kidney function
    - **Complete blood count (CBC) with platelets and differential:** To evaluate white blood cells, red blood cells and other blood components that give an indication of your general health and safety
    - **Coagulation function:** To measure your body's blood clotting function.
    - **Virology:** To test for the presence of hepatitis B (HBV), hepatitis C (HCV), or human immunodeficiency virus (HIV).
    - **Thyroid function:** To measure how much of this hormone is in your blood.
    - **Pregnancy test:** Blood or urine will be collected from women of children bearing potential.
- **Urinalysis:** A urine sample will be collected to test for problems with your kidneys or urinary tract.
- **Radiography Examination:** You will be asked to have a radiology examination using computed tomography (CT), positron emission tomography (PET) /CT or magnetic resonance imaging (MRI) scans. The scans take pictures of the inside of your body and provide important information about the status of the cancer. Your study doctor will explain which type of scan will be best for you.

Study Procedures during Treatment Period (3-week Cycles)

The following tests and procedures will be performed at every visit or as indicated:

Cycle 1 Day 1:

- **Physical Examination:** You will have a physical exam and your weight will be recorded.
- **Health and Medical Questions:** You will be asked about your current health and how well you are able to perform your daily activities.
- **Vital signs:** Your vital signs will be measured, including blood pressure, heart rate, body temperature, oxygen saturation and respiration rate.
- **Medication History:** You will be asked to list all the medication you have taken and are currently taking.
- **Electrocardiogram (ECG):** An ECG will be performed to measure the electrical activity of your heart.
- **Blood Tests:** Blood samples will be collected before your morning dose (pre-dose) of APR003. Samples collected after your morning dose (post-dose) are indicated as follows.
    - **Clinical chemistry and hematology**
    - **Coagulation function:** as deemed necessary by your investigator
    - **Pregnancy test:** A blood or urine sample will be collected pre-dose.
    - **PK testing for APR003**: *Pharmacokinetic (PK) test:* PK measures the amount of study drug in your blood to understand how the drug is absorbed and removed from your body. Blood samples will be collected pre-dose and 30 mins, 1 hour, 2 hours, 4 hours, 6 hours, and 8 hours post-dose.
    - **PD/biomarkers for APR003:** *Pharmacodynamic (PD) test*: Blood samples will be taken to measure the effect of study drug on tumor materials that may be in your blood. These samples will be collected pre-dose, 1 hour, 2 hours, 4 hours, 6 hours, and 8 hours post dose.
- **Urinalysis:** A urine sample will be collected to detect problems with your kidneys or urinary tract.
- **Study Medication:**
    - You will take your first dose of APR003 in the clinic.

- After receiving the study drug, you will need to remain in the clinic for a minimum of 6 hours post-dose for observation or you may be admitted to a hospital for overnight observation. During this time, the study team will take your vital signs every 2 hours and perform other health checks to ensure your safety.

Cycle 1 Day 2:

- **Physical Examination:** To be performed as deemed necessary by your investigator; your weight will be recorded.
- **Health and Medical Questions:** You will be asked about your current health and how well you are able to perform your daily activities.
- **Vital signs:** Your vital signs will be measured, including blood pressure, heart rate and respiration rate.
- **Medication History:** You will be asked to list all the medication you have taken and are currently taking.
- **Electrocardiogram (ECG):** An ECG will be performed to measure the electrical activity of your heart as deemed necessary by your investigator.
- **Blood Tests:** Blood samples will be collected before your morning dose (pre-dose) of APR003. Samples collected after your morning dose (post-dose) are indicated as follows.
  - **Clinical chemistry and hematology**
  - **Coagulation function:** as deemed necessary by your investigator
  - **PK testing for APR003**: Blood sample to be collected at 24 hours post-dose.
  - **PD/biomarkers for APR003:** *Pharmacodynamic (PD) test*: Blood sample will be taken at 24 hours post dose
  - **Other specialty tests:** as deemed necessary by your investigator
- **Urinalysis:** A urine sample will be collected to detect problems with your kidneys or urinary tract

Cycle 1 Day 8:

- **Physical Examination:** To be performed as deemed necessary by your investigator; your weight will be recorded
- **Health and Medical Questions:** You will be asked about your current health and how well you are able to perform your daily activities.
- **Vital signs:** Your vital signs will be measured, including blood pressure, heart rate, body temperature, oxygen saturation and respiration rate.
- **Medication History:** You will be asked to list all the medication you have taken and are currently taking.
- **Electrocardiogram (ECG):** An ECG will be performed to measure the electrical activity of your heart as deemed necessary by your investigator.
- **Blood Tests:** Blood samples will be collected before your morning dose.
  - **Clinical chemistry and hematology**
  - **Other specialty tests:** as deemed necessary by your investigator
- **Urinalysis:** A urine sample will be collected to detect problems with your kidneys or urinary tract
- **Study Medication:**
  - You will take your dose of APR003 in the clinic.

- After receiving the study drug, you will need to remain in the clinic for a minimum of 6 hours post-dose for observation or you may be admitted to a hospital for overnight observation. During this time, the study team will take your vital signs every 2 hours and perform other health checks to ensure your safety.

Cycle 1 Day 15:

- **Physical Examination:** To be performed as deemed necessary by your investigator, your weight will be recorded.
- **Health and Medical Questions:** You will be asked about your current health and how well you are able to perform your daily activities.
- **Vital signs:** Your vital signs will be measured, including blood pressure, heart rate, body temperature, oxygen saturation and respiration rate.
- **Medication History:** You will be asked to list all the medication you have taken and are currently taking.
- **Electrocardiogram (ECG):** An ECG will be performed to measure the electrical activity of your heart as deemed necessary by your investigator.
- **Blood Tests:** Blood samples will be collected before your morning dose.
  - **Clinical chemistry and hematology**
  - **PK testing for APR003:** Blood samples will be collected pre-dose, 30 min, 1 hour, 2 hours, 4 hours, 6 hours, and 8 hours post dose.
  - **PD/biomarkers for APR003:** *Pharmacodynamic (PD) test*: Blood sample will be taken at collected pre-dose, 1 hour, 2 hours, 4 hours, 6 hours, and 8 hours post-dose.
  - Other specialty tests: as deemed necessary by your investigator
- **Study Medication**: You will take your dose of APR003 in the clinic.
  - After receiving the study drug, you will need to remain in the clinic for a minimum of 6 hours post-dose for observation or you may be admitted to a hospital for overnight observation. During this time, the study team will take your vital signs every 2 hours and perform other health checks to ensure your safety.
- **Urinalysis:** A urine sample will be collected to detect problems with your kidneys or urinary tract

Cycle 2 and Cycle 3 Day 1:

- **Physical Examination:** To be performed as deemed necessary by your investigator, your weight will be recorded
- **Health and Medical Questions:** You will be asked about your current health and how well you are able to perform your daily activities.
- **Vital signs:** Your vital signs will be measured, including blood pressure, heart rate, body temperature, oxygen saturation and respiration rate.
- **Medication History:** You will be asked to list all the medication you have taken and are currently taking.
- **Electrocardiogram (ECG):** An ECG will be performed to measure the electrical activity of your heart.
- **Blood Tests:** Blood samples will be collected before your morning dose (pre-dose) of APR003. Samples collected after your morning dose (post-dose) are indicated as follows.
  - **Clinical chemistry and hematology**

- **Coagulation:** To measure your body's blood clotting function
- **Cycle 2 only: PD/biomarkers for APR003:** Blood samples will be collected pre-dose and 30 mins, 1 hour, 2 hours, 4 hours, and 6 hours post-dose
- **Cycle 2 only: PK testing for APR003**: Blood samples will be collected pre-dose and 30 mins, 1 hour, 2 hours, 4 hours, and 6 hours post-dose
- **Other specialty tests**: as deemed necessary by your investigator

- **Urinalysis:** A urine sample will be collected to detect problems with your kidneys or urinary tract
- **Study Medication:** You will take your dose of APR003 in the clinic. At every visit, you will be asked to return the empty, partially used or full drug bottles of APR003 and bring your dosing diary at each of your clinic visits
    - After review how you tolerated APR003 during the first 3 doses and if deemed necessary by your investigator you may need to continue taking APR003 in clinic and after receiving the study drug, you will need to remain in the clinic for a minimum of 6 hours post-dose for observation or you may be admitted to a hospital for overnight observation. During this time, the study team will take your vital signs every 2 hours and perform other health checks to ensure your safety or:
    - When taking APR003 at home, it is important you immediately report any side effects, such as fever, weakness, dizziness, chills, headache, rash, difficulty breathing and/or wheezing, or seizure to your study team. If you experience side effects, the study team may request you return to the clinic for further observation and testing.
    - NOTE: If there is a dose interruption of greater than or equal to 21 consecutive days, the monitoring as described above will be restarted as if it was your first day of dosing.

Cycle 2 and Cycle 3 Day 11:

- **Health and Medical Questions:** You will be asked about your current health and how well you are able to perform your daily activities.
- **Vital signs:** Your vital signs will be measured, including blood pressure, heart rate, body temperature, oxygen saturation and respiration rate.
- **Electrocardiogram (ECG):** An ECG will be performed to measure the electrical activity of your heart as deemed necessary by your investigator.
- **Medication History:** You will be asked to list all the medication you have taken and are currently taking.
- **Blood Tests:** Blood sample will be collected pre-dose.
    - **Clinical chemistry**
    - **Other specialty tests**: as deemed necessary by your investigator
- **Study Medication:** At every visit, you will be asked to return the empty, partially used or full bottles of APR003 and bring your Dosing Diary at each of your clinic visits.
    - After review how you tolerated APR003 during the first 3 doses and If deemed necessary by your investigator you may need to continue taking APR003 in clinic and after receiving the study drug, you will need to remain in the clinic for a minimum of 6 hours post-dose for observation or you may be admitted to a hospital for overnight observation. During this time, the study team will take your vital signs every 2 hours and perform other health checks to ensure your safety or:
    - When taking APR003 at home, it is important you immediately report any side effects, such as fever, weakness, dizziness, chills, headache, rash, difficulty breathing and/or wheezing, or seizure to your study team. If you experience side effects, the study team may request you return to the clinic for further observation and testing.

- NOTE: If there is a dose interruption of greater than or equal to 21 consecutive days, the monitoring as described above will be restarted as if it was your first day of dosing. .

Cycle 4 Day 1 (and all remaining cycles): Study procedures and assessment to be performed on Day 1 of Cycle 4 and for the remainder of time you stay on the study.

- **Physical Examination:** To be performed as deemed necessary by your investigator.
- **Health and Medical Questions:** You will be asked about your current health and how well you are able to perform your daily activities.
- **Vital signs:** Your vital signs will be measured, including blood pressure, heart rate, body temperature, oxygen saturation and respiration rate.
- **Urinalysis:** A urine sample will be collected to detect problems with your kidneys or urinary tract.
- **Electrocardiogram (ECG):** An ECG will be performed to measure the electrical activity of your heart as deemed necessary by your investigator.
- **Medication History:** You will be asked to list all the medication you have taken and are currently taking.

- **Blood Tests:** The blood samples will be used for the following tests:
  - **Clinical chemistry:** To evaluate your general health, liver and kidney function
  - **Complete blood count (CBC) with platelets and differential:** To evaluate white blood cells, red blood cells and other blood components that give an indication of your general health and safety
  - **Coagulation function:** To measure your body's blood clotting function as deemed necessary by your investigator.
  - **Thyroid function:** To measure how much of this hormone is in your blood.
  - **Cycle 4 (every 3 cycles thereafter) PD biomarkers for APR003:** Blood samples will be collected pre-dose.
  - **Other specialty tests:** as deemed necessary by your investigator
- **Radiography Examinations/Tumor Measurement:** Imaging studies, such as a CT, CT/PET or MRI scan will be performed at Cycle 4 and then every 3 cycles thereafter.
- **Study Medication:** You will take your dose of APR003 in the clinic. At every visit, you will be asked to return the empty, partially used or full bottles of APR003 and bring your Dosing Diary at each of your clinic visits
  - After review how you tolerated APR003 during the first 3 doses and If deemed necessary by your investigator you may need to continue taking APR003 in clinic and after receiving the study drug, you will need to remain in the clinic for a minimum of 6 hours post-dose for observation or you may be admitted to a hospital for overnight observation. During this time, the study team will take your vital signs every 2 hours and perform other health checks to ensure your safety or:
  - When taking APR003 at home, it is important you immediately report any side effects, such as fever, weakness, dizziness, chills, headache, rash, difficulty breathing and/or wheezing, or seizure to your study team. If you experience side effects, the study team may request you return to the clinic for further observation and testing.

NOTE: If there is a dose interruption of greater than or equal to 21 consecutive days, the monitoring as described above will be restarted as if it was your first day of dosing.

Study Procedures at the End of Treatment visit

- **Health and Medical Questions:** You will be asked about your current health and how well you are able to perform your daily activities.

- **Medication History:** You will be asked to list all the medication you have taken and are currently taking.
- **Physical Examination.**
- **Vital signs:** Your vital signs will be measured, including blood pressure, heart rate, body temperature, oxygen saturation and respiration rate.
- **Urinalysis:** A urine sample will be collected to detect problems with your kidneys or urinary tract
- **Electrocardiogram (ECG):** An ECG will be performed to measure the electrical activity of your heart.
- **Blood Tests**
    - Clinical chemistry and hematology
    - Coagulation
    - Thyroid
    - Pregnancy test
    - PD/Biomarkers for APR003
    - Other specialty tests
- **Radiography Examination**: A CT, CT/PET or MRI scan may be performed.
- **Study Medication** will be collected. The study staff will ask you to return all bottles of used, partially used, or unused APR003 to the clinic and bring your Dosing Diary.

Study Procedures during the Follow-Up Period

Long-Term Safety Follow-Up

You will continue to be followed after you have taken the last dose of study drug on this study. Follow-up will occur approximately every 3 months for 2 years. Information on treatments you receive after being on the study and on your general well-being will be collected via telephone or email with your caregiver or your referring doctor.

BLOOD DRAWS

The total amount of blood taken during the study will depend on how long you remain on the study. For the initial 3 cycles including Screening, a total of approximately 140 mL or 28 teaspoons will be drawn. If you stay on the study for 6 months, the approximate total amount of blood drawn will be 221.5 mL or 45 teaspoons. For comparison, the standard blood donation is about 480 mL (two cups).

KNOWN SIDE EFFECTS

Related adverse events include:

- Shivering and chills
- Feeling sick to the stomach
- Feeling tired, tiredness, weakness.
- Decreased number of a type of white blood cells. This is associated with an increased risk of infection.
- Fever
- Pain at the tumor site
- Vomiting

- Cytokine release syndrome: A group of symptoms caused by release of chemicals from cells during the infusion. This can include nausea, headache, rapid heartbeat, shortness of breath, kidney damage, and rash. It can be-life threatening and may be reversible.
- Sudden reddening of the face and/or neck
- Pain in the head
- Abdominal pain
- Dizziness
- Sweating
- abnormal digestive blood test
- Muscle spasms, body aches
- Condition in which the number of white bloods cells called neutrophils is abnormally low. This increases the risk of infection, which may be serious or life-threatening. Symptoms of infection may include fever, pain, redness, and/or difficulty breathing.
- Inflammation of the pancreas causing pain in the upper abdomen. This could become severe and cause nausea and vomiting, fever and rapid heart rate. This could require hospitalization and may be life threatening.
- Sudden growth in tumor or worsening of tumor related problems.
- Weight decrease

After you receive your dose of APR003, you'll be watched closely for side effects. Cytokine release syndrome (CRS) has occurred and neurological changes are possible side effects of APR003 administration. CRS is a group of symptoms that happen when T cells attack cancer cells. T cells help your immune system tell which antigens don't belong in your body. T cells are a type of white blood cell (lymphocyte). T cells have receptors that attach to certain antigens. Antigens are substances that activate (turn on) your immune system. Antigens are found on the surface of some things made inside your body, such as cells. They're also found on the surface of some things from outside your body, such as bacteria and viruses. Once a T cell attaches to an antigen, it sends messages to other cells in your immune system. These cells help kill the thing with the antigen and get it out of your body.

Common symptoms of CRS include:

- A fever of 100.4 °F (38 °C) or higher
- Flu-like symptoms, such as:
- Muscle aches
- Headaches
- Chills
- Feeling unusually tired
- Nausea or vomiting
- A faster heart rate than usual
- Feeling dizzy or lightheaded

Common neurologic changes include:

- Confusion
- Trouble finding words
- Tremors
- Seizures
- Sleeping more than usual
- Feeling very drowsy and responding more slowly than usual

Not everyone gets the same symptoms, and everyone responds differently to each dose of APR003.

These side effects aren't permanent. Your care team will watch you carefully for side effects. They'll manage any side effects you have. It's very important for you or your caregiver to tell a member of your healthcare team if you think you're having any of these side effects.

If the symptoms become serious, your doctors will use medications (such as tocilizumab, prednisone, Benadryl, Tylenol, and NSAIDS) to try to reverse the immune reaction. There is a small possibility that CRS can be so severe that it leads to death.

POSSIBLE SIDE EFFECTS AND RISKS/DISCOMFORT OF THE STUDY DRUG

Participating in a research study can be an inconvenience to your daily life. Please consider the study time commitments and responsibilities as a research subject when you are deciding if you will participate. It is important that you disclose all relevant medical history and medications to the study staff. You must carefully follow any instructions given to you concerning the study.

All drugs can cause side effects in some people. Since the study drug is experimental there may be other risks that are unknown. All patients in the study will be monitored for side effects. The study staff may give you medications to help lessen some of the side effects.

There may be rare and unknown side effects, some of which may be irreversible and/or life-threatening.

You must tell the study doctor or study staff about all side effects that you have. If you are not honest about your side effects, it may not be safe for you to stay in the study.

Potential Risk Related to APR003

- Gastritis (inflammation of the stomach), that may lead to nausea, upset stomach, abdominal bloating, vomiting, indigestion or hiccups
- Hepatitis (liver inflammation) and/or liver failure that may lead to fatigue, flu-like symptoms dark urine, abdominal pain, loss of appetite/weight loss, or jaundice (yellowing of the eyes and skin)
- Enteritis (inflammation of the small intestine) that may lead to abdominal pain/cramps, diarrhea, nausea, vomiting, loss of appetite, bleeding or mucus in the stool
- Colitis (inflammation of the colon) that may lead to diarrhea, abdominal pain/cramps, pain in the rectum, blood in the stool, weight loss, fatigue
- Diabetes that may lead to increased thirst, frequent urination, unexplained weight loss, fatigue, blurry vision
- Nephritis (inflammation of the kidneys) that may lead to pain in the pelvis, burning sensation while urinating, increased need to urinate or frequency or urination, pain in the kidney area or abdomen, vomiting, blood in the urine, swelling of the face, hands, legs and/or feet, or increase blood pressure
- Increased risk of bleeding
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These are not all the possible side effects of APR003. Your study doctor can provide you with more information about APR003.

Unforeseen Risks

Sometimes people have allergic reactions to drugs. A serious allergic reaction can be life threatening. Some signs that you may be having an allergic reaction are:

- Rash or hives
- Having a hard time breathing
- Wheezing when you breathe
- Sudden change in blood pressure (making you feel dizzy or lightheaded)
- Swelling around the mouth, throat or eyes
- Fast pulse
- Sweating

You should get medical help and contact the study doctor or staff if you have any of these or any other side effects during the study.

Potential Risks of Additional Study Procedures

Blood Draw Risks

Blood samples will be taken during the study. Using a needle to remove blood from a vein is called “a blood draw”. Side effects associated with routine blood draws can include pain, bruising, bleeding, swelling, or scarring of the skin where the blood is drawn. You may also feel light-headed, faint, or dizzy when the blood is taken.

Electrocardiogram Risks

During an ECG, electrode patches/sensors are applied to the chest area, as well as your arms and legs. You may experience temporary discomfort (pulling on the skin/skin hair) during removal of the sensors. You may also develop some minor skin irritation from the ECG patch adhesive.

CT, PET/CT or MRI Scan Risks

Computed tomography (CT), positron emission tomography (PET) /CT or magnetic resonance imaging (MRI) MRI scanners use special equipment to take pictures of the inside of your body. The scanner is usually a large machine shaped like a doughnut and has a bed in the middle of the circle that you lie on. The bed can slide backwards and forwards through the hole of the doughnut. Pictures of your internal organs are taken as you move through the machine.

The most accurate method for following your cancer and how you respond to the study drug, is CT scanning. If the study doctor uses these scans, you will have some radiation exposure. Generally, the amount of radiation received during this procedure is the same as a normal person gets from exposure to natural sources of radiation in the environment in a 2- to 3-year period. The potential long-term risks from this radiation are uncertain, but have not been associated with any definite change in overall medical condition.

A contrast drug or radioactive tracer is commonly injected in a vein before a CT scan to make the organs, tumors and the inside of your bones easier to see. One form of contrast dye contains iodine and if you are allergic to iodine or shellfish you should notify your study doctor and radiology lab prior to having the CT scan. Rarely, some people have allergic reactions (such as hives or itching) due to the contrast agent. Severe reactions (for example, drop in blood pressure, difficulty in breathing, or kidney problems) are rare. You should inform your study doctor if you have had an allergic reaction in the past. Your doctor will then be able to make sure that you are protected during the scan.

Some doctors may use MRI scans, rather than CT scans, to measure your cancer and your response to the study drug. If the study doctor uses MRI scans, you will be exposed to powerful magnetic fields. There are no known risks resulting directly from exposure to these magnetic fields. However, it possible to feel muscle twitches and tingling sensations or a slight increase in body temperature during the test.

The MRI scanner produces tapping sounds that can reach very loud levels. To avoid any discomfort from this noise, you can wear earplugs or headphones that are available in the MRI scanning room.

A contrast agent is commonly injected in a vein before the MRI scan. The contrast agent usually used in MRI is associated with a low risk of mild problems like headache, nausea, or a tingling sensation around the mouth. Allergic reactions are possible but very rare. Subjects who have reduced kidney function may have severe scarring reactions that can cause permanent disability or death. The contrast agent should not be given to pregnant subjects, so if there is a possibility that you could be pregnant, you should ask to undergo a pregnancy test before having the MRI.

Some people have reported feeling anxious or claustrophobic (like being trapped) during the CT or MRI scans because they are performed in a narrow, enclosed space. You can ask for the scan to be stopped at any time if you cannot stand being in the scanner. Medicine can also be provided to relieve anxiety during these scans.

Incidental Findings

It is possible that the study procedures could detect a medical problem that was previously unknown to you and that is unrelated to the purpose of this study. If the research procedures uncover findings that may be important for you to know about, such as the possibility of a previously unknown medical condition, you will be informed by a member of the study staff. Or, you may authorize the release and communication of the findings to your primary physician. These findings may require additional testing or treatment. The cost of any additional tests or related treatment will be your responsibility.

Pregnancy Risks

The effects of APR003 on pregnancy, an unborn baby, or a nursing child is not known at this time. Therefore, if you are pregnant, planning to become pregnant or are breastfeeding a child, you cannot participate in this study. You must confirm that, to the best of your knowledge, you are not pregnant, and that you do not intend to become pregnant during the study.

If you are a woman of childbearing potential you must agree to use a recommended method of contraception during heterosexual intercourse throughout the study dosing period and for up to 6 months after stopping the study drug.

Female subjects are considered to be of childbearing potential in this study unless you meet the following criteria:

- Surgical hysterectomy
- Bilateral tubular ligation
- Bilateral oophorectomy
- Menopause > 55 years of age with last menses > 6 months ago

Males who can father a child must use one, or a combination, of the approved forms of birth control, for up to 6 months following stopping the study dosing. Females of childbearing potential must use of combination of two of the following methods.

- Individual methods:
  - IUD (Intrauterine device)
  - Tubal sterilization
  - Vasectomy
  - Hysterectomy
- Combined with barrier methods (diaphragm with spermicide and/or male condom with spermicide)

Your study doctor or other personal health care provider can discuss birth control options with you.

Males must also refrain from sperm donation from the start of the study therapy until at least 90 days after the last dose of the study drug.

Females who become pregnant or think they may be pregnant while taking study drug or within 30 days after the last dose of the study drug, you must stop taking the study drug and notify your study doctor immediately. The study doctor will request to track your pregnancy and will report the outcome of the pregnancy to the study sponsor.

Males with female partners who become pregnant or suspects that she has become pregnant while you are taking study drug or within 30 days after the last dose of study drug, you must notify your study doctor immediately. Because the risk to your partner and baby is unknown, it is recommended for your partner to agree to medical supervision during her pregnancy and for the baby after it is born. If you agree, your partner will be invited to sign a consent document to allow medical supervision. Your study doctor may need to disclose to your partner details of this study and your participation in it. The study sponsor, through the study doctor, will request your consent and your partner's consent to collect confidential information about her health and that of the baby. Neither the study sponsor nor the study doctor will be responsible for providing routine medical care relating to the pregnancy.

Because the effects of the study drug on a nursing child are not known, you may not enroll in this study if you are a woman who is breastfeeding a child. You should not nurse a baby while taking study drug because of the risk that the baby might be exposed to the study drug that comes out of your body into the breast milk.

POTENTIAL BENEFITS

The study therapy may reduce the amount of cancer in your body or slow the growth of your cancer. Your participation in the study may lead to possible improvements in the symptoms of your cancer, but, there is no guarantee that this study will help you. Your disease may improve, stay the same, or get worse due to your participation in this study.

Your participation in this study may benefit subjects, scientists, and doctors by providing increased knowledge and information about the treatment of cancer. The study sponsor may benefit if it is found that the study drug is effective in treating cancer**.**

TREATMENT ALTERNATIVES

You should discuss participation in this protocol and other potential treatment options with your doctor. Other treatment options that have been shown to prolong life expectancy in some patients include different chemotherapy regimens that include drugs like 5-Flourouracil, Oxaliplatin and Irinotecan or treatments directed against new blood vessel formation in the tumor (VEGF). You do not have to be in the study to get treatment for your cancer. You can choose to get treatment from your regular doctor that may include supportive care, drugs, or combinations of drugs that are currently approved or are being tested in other clinical studies investigating the treatment of advanced colorectal cancer. However, by participating in this study, you will not be able to receive those treatment option(s) while on study. Your Study Doctor will discuss with you the risks and benefits of other treatments.

NEW FINDINGS

If Apros Therapeutics, Inc obtains any new information about the study medication that might change your decision to be in the study, you or your legally authorized representative will immediately be made aware of this information.

If additional procedures or tests are required for this study, you will be notified of these requirements. Before any new procedures or tests are performed, you will be asked to sign a new consent form which details the potential additional risks, discomforts and benefits.

CONFIDENTIALITY AND DATA PROTECTION

During this study, the study doctor and the study staff will record information about you, your health and your participation in the study on forms provided by the sponsor. These forms are known as case report forms. You will not be able to participate in this study if you do not consent to the collection of this information about you.

Your name and any other information that allows you to be identified directly will not be entered on the case report forms or included in any records or samples the study doctor provides to the sponsor or the sponsor's representatives. Instead, you will only be identified by a code. The code is used so that the study doctor can identify you if necessary. The study doctor will keep the list connecting that code to your name, but the study doctor will not send that list to the sponsor or its representatives. However, the study forms will contain other information about you that could be used to identify you even though your name does not appear. Although efforts will be made to protect your privacy, absolute confidentiality of your records cannot be guaranteed.

Your coded study information will be entered into and kept in a database by the sponsor. This coded information will be used by the sponsor, its affiliates and collaborators to analyse the study results and may be used for additional unanticipated medical and/or scientific research projects in the future relating to the development of the study drug (but at all times in compliance with applicable law and regulation).

The results of this study may be published and presented to the public, and used for educational purposes. Information that could identify you will not be used in any publication or presentation.

Other groups may also need to look at your medical records and study records to make sure that the information is correct and to evaluate the conduct of this study. These include the following:

- The sponsor, its affiliates and its representatives, including any contract research organization helping the Sponsor with the study, and any collaborators of the sponsor working with the sponsor to develop the study drug.
- The Institutional Review Board (IRB) responsible for overseeing the study. An IRB is a group of qualified people that evaluates the ethical merits of a study and looks out for the rights and welfare of research subjects.
- The United States Food and Drug Administration and regulatory agencies in other countries where the study is taking place.

Storage of blood and biological samples

During this study, you will be asked to provide blood, urine and tissue samples. These samples will be used for checking the safety of the study drug, the amounts of study drug in the blood, the effects of the drug on blood cells, and the effects of the drug on proteins that are produced by certain cells of the body. Some of these samples will be stored in case the sponsor wishes to examine additional drug breakdown products or effects of the drug on cellular function at a later time. In signing this consent form, you voluntarily donate all collected and stored blood samples to the study sponsor to perform these types of foreseen or unforeseen tests as part of the evaluation of the study drug.

You may change your mind and take back your consent at any time. If you take back this consent, no further information will be collected about you. If you withdraw from the study, any sample collected prior to your withdrawal may still be analyzed as described in the Informed Consent Form, unless you specifically ask for your samples to be destroyed or local laws require destruction of the samples. However, if samples have been tested prior to withdrawal, results from those tests will remain as part of the overall research data. However, the sponsor and those identified above will still be able to use and disclose coded information about you from this study that has already been collected.

A description of this clinical trial will be available on 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.

COSTS OF PARTICIPATION

You (and/or your insurance company) will not be expected to pay for any of the procedures that are obtained solely for the purposes of this study. Also, you (and/or your insurance company) will not be expected to pay for the study medication or tests that are part of this research study.

You will still need to pay for your usual medical care. You (and/or your insurance company) will be responsible for costs of care that are associated with usual cancer care. This could include any non-study procedures and/or non-study medication that are needed while you are in the study. You should contact your medical insurance company to find out if they will pay for routine medical care while you are in this study. If you have any questions, please ask the study doctor or a member of the study staff.

For more information on insurance coverage for clinical trials, you can visit the National Cancer Institute's Web site at http://www.cancer.gov. You can print a copy of the "Clinical Trials and Insurance Coverage" information from this Web site.

Another way to get the information is to call 1-800-4-CANCER (1-800-422-6237) and ask them to send you a free copy.

COMPENSATION

You will not be paid for participating in this study. You will not be paid for expenses like lost wages, disability, discomfort due to injury, or meals obtained while waiting at the study clinic.

You may ask to be reimbursed for the reasonable cost of travel required to participate in this study. Discuss this with the study clinic staff. To receive payment for travel, you will need to submit the original travel receipts to the research study clinic staff at the clinic.

COMPENSATION FOR INJURY

If you become sick or injured as a direct result of taking the study drug and/or following the study procedures, the study doctor will provide you with medical treatment. The study sponsor will reimburse you or your study doctor for the reasonable and necessary costs of such medical treatment, provided that you have followed the instructions of the study doctor and that these expenses are not paid by medical insurance. No other form of reimbursement for study-related injury or illness is offered by the study sponsor. You should immediately contact your study doctor if you believe you have experienced any study-related illness or injury.

If you receive Medicare benefits in the United States, the study sponsor is required by law to report payments made to you for treatment, complications, and injuries that arise from this study. Information that you are taking part in the study, medical treatments received, Medicare claims, and other personal information about you such as your name, social security number, and date of birth, will be provided to the Centers of Medicare and Medicaid Services and its agents and/or contractors for this purpose.

By signing and dating this form, you have not waived any of the legal rights, which you would have otherwise, if you were not a participant in a medication research study.

EMERGENCYAND IRB CONTACT

You have the right to ask questions about the known and unknown risks of this study at any time.

The study doctor will be available and on call during the whole study. Please call the study doctor at the phone number listed on page 1 if:

- You have any questions about this study
- You experience a study-related injury
- You have a medical emergency

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

This study has been reviewed by an IRB and has received a positive opinion, meaning that the study was deemed ethically sound to conduct.

If you have any questions about your rights as a research subject, or complaints about this study, you should call <INSERT IRB NAME, ADDRESS, and PHONE NUMBER>.

VOLUNTARY PARTICIPATION/ WITHDRAWAL FROM THE STUDY

You do not have to be in this study. Your participation is voluntary. Refusal to participate will involve no penalty or loss of benefits. If you decide that you do not want to be in the study anymore, you should tell the study staff before you stop taking the study drug. This is called withdrawal. Withdrawal will not affect your future medical care at this clinic nor your ability to participate in future studies. You can withdraw at any time without having to give a reason. But, if you withdraw because of side effects, it is important that you tell this to the study doctor.

You may be asked to stop being in this study at any time by the study doctor, Apros Therapeutics, Inc or the Food and Drug Administration (FDA), without your consent and for any reason. Some of these reasons are:

- You do not follow the study instructions.
- You no longer fulfill the criteria for the remainder of the study.
- You need medicine that is not allowed during the study.
- You develop a medical condition that makes you unqualified for the study.
- The study doctor thinks it is best for you to discontinue your participation in the study.
- You have an injury or side effect that is “serious or severe”.
- The study is cancelled or stopped.
- If you are female and become pregnant
- If the study is stopped by Apros Therapeutics, Inc., you will be given the reason for this decision.

You may also be asked to stop being in the study for other reasons including not taking the study medication as directed and not coming to the clinic for your scheduled visits.

If you do not finish the study for any reason, you will be asked to come to the clinic to have all end-of-study tests and procedures done. You will be required to return all unused, partially used, and/or used containers of study drug.

FINANCIAL DISCLOSURE

If a commercial product is developed from the research performed in the Study, Apros Therapeutics, Inc., will own all rights to the product. By participating in the Study, you do not acquire any rights to the commercial product.

CONSENT

I have read and understand the information in this informed consent document. I have had an opportunity to ask questions and all of my questions have been answered to my satisfaction. I voluntarily agree to participate in this study until I decide otherwise. I do not waive any of my legal rights by signing this consent document. I will receive a copy of this signed consent document.

_____
Subject's Printed Name

_____ _____
Subject's Signature Date

I certify that under law I am the legally authorized representative of the participant named above and that I am authorized by law to sign this consent to his/her participation in the research study described above.

_____
Printed Name of Legal Representative

_____ _____
Signature of Legal Representative Date

Person Conducting the Consent Discussion:

_____
Printed Name of the Person Conducting the Consent Discussion

_____ _____
Signature of the Person Conducting the Consent Discussion Date

The study subject has indicated that he/she is unable to read. The consent document has been read to the subject by a member of the study staff, discussed with the subject by a member of the study staff, and the subject has been given an opportunity to ask questions of the study staff.

_____
Printed Name of Impartial Witness

_____ _____
Signature of Impartial Witness* Date

*Impartial Witness: A person, who is independent of the study, who cannot be unfairly influenced by people involved with the study, who attends the informed consent process if the subject or the subject's legally acceptable representative cannot read, and who reads the informed consent and any other written information supplied to the subject. Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance

AUTHORIZATION TO USE AND DISCLOSE PROTECTED HEALTH INFORMATION

During your participation in this research study, the study doctor and study staff will collect or create personal health information about you (for example, medical histories and results of any tests, examinations or procedures you undergo while in the study) and record it on study documents. The study doctor will keep this personal health information in your study-related records (that we will refer to as "your study records"). In addition, the study doctor may obtain, and include in your records, information regarding your past, present and/or future physical or mental health and/or condition. Your study doctor may ask you to sign a separate authorization to obtain some or all of your medical records from your doctor. Your study records may include other personal information (such as social security number, medical record numbers, date of birth, etc.), which could be used to identify you. Health information that could identify you is called "Protected Health Information" (or "PHI").

Under federal law (the "Privacy Rule"), your PHI that is created or obtained during this research study cannot be "used" to conduct the research or "disclosed" (given to anyone) for research purposes without your permission. This permission is called an "Authorization." Therefore, you may not participate in this study unless you give your permission to use and disclose your PHI by signing this Authorization. By signing, you are agreeing to allow the study doctor and staff to use your PHI to conduct this study.

By signing this Authorization, you also are agreeing to allow the study doctor to disclose PHI as described below:

- The sponsor of this study and anyone working on behalf of the sponsor to conduct this study (referred to as "the sponsor"). The sponsor will analyze and evaluate the PHI and may use it to develop new tests, procedures and commercial products. The study staff will assign a code number and/or letters to your records, which means that you will not ordinarily be identified in the records sent to the sponsor. The sponsor may, however, look at your complete study records that identify you. In addition, the sponsor may visit the study site to oversee the way the study is being conducted and may review your PHI during these visits to make sure the information is correct.
- The Institutional Review Board ("IRB") may have access to your PHI in relation to its responsibilities as an Institutional Review Board.

The study doctor or sponsor may disclose your PHI to the United States Food and Drug Administration (“FDA”) or similar regulatory agencies in the United States and/or foreign countries.

These disclosures also help ensure that the information related to the research is available to all parties who may need it for research purposes.

Except for the disclosures described above, your PHI will not be shared with others unless required by law. If your PHI is given to the parties listed above and/or to others who are not required to comply with the federal law, your PHI will no longer be protected by this law and could possibly be used or disclosed in ways other than those listed here.

You have a right to see, request corrections to errors, and make copies of your PHI. You are agreeing, however, by signing this document, not to see or copy some or all of your PHI until the sponsor has completed all work related to this study. At that time, you may ask to see your records**.**

This Authorization will expire 50 years from the date you sign it unless you revoke (cancel or withdraw) it sooner.

You have a right to revoke your Authorization at any time. If you revoke it, your PHI will no longer be used for this study, except to the extent the parties to the research have already taken action based upon your Authorization or need the information to complete analysis and reports for this research. To revoke your Authorization, you must write to the study doctor, stating that you are revoking your Authorization to Use and

Disclose Protected Health Information. If you revoke this Authorization, you will not be allowed to continue to be in this study.

You will receive a copy of this Authorization after you have signed it.

_____ _____

Signature of Subject Date

_____

Printed Name of Subject

I certify that under law I am the legally authorized representative of the participant named above and that I am authorized by law to sign this consent to his/her participation in the research study described above.

_____

Printed Name of Legal Representative

_____ _____

Signature of Legal Representative Date

Person Obtaining the Authorization.

_____ _____

Signature of the Person Obtaining the Authorization Date

_____

Printed Name of the Person Obtaining the Authorization

The study subject has indicated that he/she is unable to read. The consent document has been read to the subject by a member of the study staff, discussed with the subject by a member of the study staff, and the subject has been given an opportunity to ask questions of the study staff.

_____

Printed Name of Impartial Witness

_____ _____

Signature of Impartial Witness* Date

*Impartial Witness: A person, who is independent of the study, who cannot be unfairly influenced by people involved with the study, who attends the informed consent process if the subject or the subject's legally acceptable representative cannot read, and who reads the informed consent and any other written information supplied to the subject. Guidance for Industry E6 Good Clinical Practice: Consolidated Guidance