The University of Texas Health Science Center at San Antonio

TITLE:	Phase II Trial of Encapsulated Rapamycin (eRapa) for Bladder Cancer Prevention
PROTOCOL NO.:	ER-B01 UT IRB Protocol #STUDY00001422
SPONSOR:	NIH-NCI
INVESTIGATOR:	Robert S Svatek, MD, MSCI 7703 Floyd Curl Drive San Antonio, Texas 78229-3900 United States
STUDY-RELATED PHONE NUMBER(S):	210-567-3224 (24 hours)

Concise Summary

Important Information
This information gives you an overview of the research. More information about these topics may be found in the pages that follow. You may choose not to take part in the study, or you may choose to leave the study at any time. Deciding not to participate or deciding to leave the study later will not result in any penalty or loss of benefits which you are otherwise entitled to and will not affect your relationship with us.

1. What problem is this study trying to solve?
You are being asked to participate in a research study. Scientists do research to answer important questions which might help change or improve the way we do things in the future**.**

We are investigating if the oral medication called encapsulated rapamycin (eRapa) decreases the risk of cancer relapse for patients with non-muscle invasive bladder cancer. Additionally, we will also determine if eRapa can improve certain immune parameters and improve cognition and physical function without adversely affecting patient-reported outcomes and quality of life.

For more information, please see the "***Why is this Study Being Done****"* section below.

2. What will happen to me during the study and how is this different from continuing with usual care? What are all my options for treatment, including the pros and cons?
While you are taking part in this study, you will be asked to take an oral medication every weekday for one year. This oral medication will be eRapa or a placebo, depending on which group you are randomized to. We will measure immune response, rapamycin levels, and tests to monitor safety through blood draws at four different time points. We are also capturing information on quality of life, physical and cognitive function, and patient reported outcomes.

For more information, please see the "***What will be done if you decide to be in the research****"* section below.

3. How much time will I spend on the study?
You will be asked to attend approximately 15 visits with the research staff. The total number of visits will depend on your study entry time. Every effort will be made to schedule study visits in conjunction with your regular clinic visits. However, some of the research visit may need to be scheduled in addition to your

regular clinic visit. During the visit, you will be asked to spend approximately 30 minutes to 180 minutes completing study procedures. You may be in this study for up to 5 years.

4. **Could taking part in the study help me and are there risks?**
   Possible benefits of your participation in the study include decreasing the risk of cancer relapse and improvement in cognition and physical function. However, there is no guarantee or promise that you will receive any benefit from this study. We hope the information learned from this study will benefit other people with similar conditions in the future. Although previous studies have shown low doses of eRapa to be relatively well tolerated, the most common side effects reported were mild mouth sores.

For more information, please *see "**How could you or others benefit from your taking part in this study"*** section below. For details and a list of risks you should know about, please see the "***What are the risks of participation in the research**"* section below.

5. **What else should I consider before I make my decision?**
   There are other treatments available for bladder cancer. You do not have to participate in this study to get access to treatment.

6. **Will I be paid for my participation in this study?**
   There is no compensation for participation in this study.

   The results from this study may lead to new commercial products or tests. If this happens you will not receive any compensation.

Please review the rest of this document for additional details about these topics and other information you should know before making a decision about participating in this research.

Consent to Be Part of a Research Study
To be conducted at
University of Texas Health Science Center at San Antonio
University Health

Information about this form

You may be eligible to take part in a research study. This form gives you important information about the study.

Please take time to review this information carefully. You should talk to the research staff about the study and ask them any questions you have. You may also wish to talk to others (for example, your friends, family, or a doctor about your participation in this study.) If you decide to take part in the study, you will be asked to sign this form. Before you sign this form, be sure you understand what the study is about, including the risks and possible benefits to you.

Please tell the research staff if you are taking part in another research study.

Voluntary Participation - You do not have to participate if you do not want to. You may also leave the study at any time. If you leave the study before it is finished, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled.

General Information – "Who is conducting this research?"

Principal Investigator
The Principal Investigator (PI) is the researcher directing this study; the PI is responsible for protecting your rights, safety, and welfare as a participant in the research. The PI for this study is Robert Svatek, M.D., Department of Urology, The University of Texas Health Science Center at San Antonio (UTHSCSA).

Funding
The National Institutes of Health (NIH), a federal agency that promotes scientific research, is funding this study. This organization is providing money to University of Texas Health Science Center at San Antonio, (UTHSCSA) so that the research staff can conduct the study.

Purpose of this study – "Why is this study being done?"

You are asked to participate in this research study of bladder cancer. The purpose of this research study is to investigate a new experimental approach to the treatment of bladder cancer. In particular, this study addresses "superficial" bladder cancer. Superficial bladder cancer has not invaded or inserted into the muscle of the bladder. Currently, patients with superficial bladder cancers may be treated with Bacillus Calmette-Guérin (BCG) or chemotherapy. This medication is instilled directly into the bladder through a soft tube (catheter). This research is trying to look at the effects of encapsulated rapamycin (eRapa) on decreasing the risk of bladder cancer relapse on superficial bladder cancer.

The research staff hope to learn that if by adding oral eRapa, it will decrease the possibility of cancer returning in your bladder, while also improving cognition and physical function without adversely affecting patient-reported outcomes and quality of life.

Investigational Use of Drug
This study involves the use of an investigational drug called eRapa. "Investigational" means that the drug has not yet been approved by the U.S. Food & Drug Administration (FDA) for treating bladder cancer.

Phase 2 Clinical Trial

UT Health SA
Study: STUDY00001422
IRB Approved:
4/1/2025

This study will help find out what effects, good and/or bad, this drug has on people who take it and on its effect on the condition/disease. The safety of this drug in humans has been tested in prior research studies; however, some side effects may not yet be known.

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.

Information about Study Participants – "Who is participating in this research?"

You are being asked to be a participant in this study because you have been diagnosed with non-muscle invasive bladder cancer stage (Ta, Tis, T_1). This means your cancer is confined only to your bladder and has not spread to any other part of your body including the muscles that surround your bladder.

How many people are expected to take part in this study?
This study will enroll approximately 166 study participants across all sites.

Information about Study Procedures – "What will be done if you decide to be in the research?"

While you are taking part in this study, you will be asked to attend approximately 15 visits with the research staff. The majority of these study visits will be scheduled at the same time as your standard of care visits. Your total participation time for this study is up to 5 years. The total study duration is expected to last up to 10 years.

Screening – After you sign this consent to participate, exams, tests, and/or procedures may be done as described below to find out if you can continue in the study; this is called screening. We may be able to use the results of exams, tests, and/or procedures you completed before enrolling in this study. You will be told which results we will need to obtain after enrollment and which procedures will not have to be repeated. Many of the procedures are described below as "standard of care" and would be done even if you do not take part in this research study. You will be told which ones are for "research only".

Screening Procedures

- As part of the screening procedures, the research staff will review your medical records and ask you questions about your health and any immune compromising illnesses or drugs you may be taking. It is important to tell the research staff of any change in medications you take (even vitamins and over the counter supplements/medications) and in your health. You must also tell the research staff about any visits to your doctor that are not part of this study. It is also a good idea to tell your doctor that you are in this study. (**standard of care**)
- Physical examination – we will conduct a complete physical exam including for example, measuring your height and weight. (**standard of care**)

The screening procedures will add approximately 5 minutes of length of a routine care visit.

The results of the screening exams, tests, and/or procedures will be reviewed to determine whether you will be allowed to continue in the study. If you are not allowed to continue in the study, the research staff will discuss the reasons with you and will discuss other possible options.

Study Calendar

Visit #	1 (Baseline)	2	3	4	5	6	7	8	9	10	11	12	13	14	15	EOT[5]
Month	**0**	**1**	**3**	**6**	**9**	**12**	**15**	**18**	**21**	**24**	**30**	**36**	**42**	**48**	**60**	
Visit Windows[10]	-90 days	± 14 days	± 14 days	± 14 days	± 14 days	± 14 days	± 14 days	± 14 days	± 14 days	± 14 days	± 14 days	± 14 days	± 14 days	± 14 days	± 14 days	
Eligibility Assessment/ Informed Consent	R															
Patient Assessment Medical History Physical Exam Vital Signs ECOG Concomitant Meds	S		S	S	S	S										S
Cystoscopy[3]	S		S	S	S	S	S	S	S	S	S	S	S	S	S	S
Urine Cytology[3]	S		S	S	S	S	S	S	S	S	S	S	S	S	S	S
Randomization[9]	R															
Drug Compliance Assess. Drug Diary Pill Count			R	R	R	R										R
PPD placement & read[1]	S[4]		R													R[7]
Safety Labs (25 mL)	S/R[11]			S/R[11]		S/R[11]										S/R[11]
Blood – Rapa Level (4 mL)	R			R		R										R
Blood – Immune Cells (30-50 mL)	R 30 mL			R 30mL		R 30mL		R 50mL								R 30mL
Adverse Event Assessment [2]		R	R	R	R	R	R	R								R
PROs and other Assessments																
FOR	R			R												R[8]
HL	R			R												R[8]
QLQ-C30	R			R		R				R						R
AUASS	R		R	R		R				R						R
QLQ-BLS24	R		R	R		R				R						R

Visit #	**1 (Baseline)**	**2**	**3**	**4**	**5**	**6**	**7**	**8**	**9**	**10**	**11**	**12**	**13**	**14**	**15**	**EOT[5]**
Month	**0**	**1**	**3**	**6**	**9**	**12**	**15**	**18**	**21**	**24**	**30**	**36**	**42**	**48**	**60**	
Visit Windows[10]	-90 days	± 14 days	± 14 days	± 14 days	± 14 days	± 14 days	± 14 days	± 14 days	± 14 days	± 14 days	± 14 days	± 14 days	± 14 days	± 14 days	± 14 days	
EXIT	R					R				R						R
SLUMS	R					R				R						R
TAPS	R			R		R				R						R
Handgrip	R			R		R				R						R
SPPB	R			R		R				R						R
Tissue Collection for CGH array [6]	R															
Biopsy	S			S[3] CIS only												

*Patients may also receive BCG treatment as per standard of care
1 - Only for those concurrently receiving BCG; PPD read is required at 48-72 hours after placement
2 - May be done via telephone or during the standard of care cystoscopy visits
3 - At treating physician's discretion, per clinic standard of care
4 - PPD testing is optional at Baseline and is based on the site's procedures
5 - EOT visit will be conducted for any subject who has a high-grade recurrence after enrollment but prior to completing a full year of dosing at Month 12
6 - The tissue sample should be 1 block, if possible; if 1 block is not possible, then tissue sample should be 10 slices cut 10 microns thick.
7 - PPD testing should only be done at EOT if EOT is prior to Month 3
8 - Questionnaire should only be completed at EOT if EOT is prior to Month 6
9 - Once randomization occurs, first dose of eRapa or placebo must occur within 14 days.
10 - Visit Windows are calculated from Randomization date
11 - Complete Blood Count and Complete Metabolic Panel considered as standard of care procedures. Fasting blood sugar and hemoglobin A1c, and fasting lipids considered as research procedures; however, if these tests have been collected as standard of care within the visit window, they may be used for study purposes

AUASS – American Urological Association Symptom Score
BCG – Bacillus Calmette-Guérin
CGH – comparative genomic hybridization
CIS – Carcinoma in Situ
ECOG – Eastern Cooperative Oncology Group
EOT – End of Treatment
EXIT – Executive Interview
FOR – Fear of Recurrence
HL – Health Literacy
PPD – Purified Protein Derivative
PROs – Patient Reported Outcomes
QLQ – Quality of Life Questionnaire
R - Research Procedure
S - Standard of Care Procedure
SLUMS – St. Louis University Mental Status exam
SPPB – Short Physical Performance Battery
TAPS – Texas Assessment of Processing Speed

Study Procedures – as a participant, you will undergo the following procedures:

Visit 1 (Baseline) Study Procedures:

1. Your demographic data including race, ethnicity, and gender, the results of the physical examination and prior biopsy done as part of your standard of care will be used. As well as any medical history you have provided.
2. Physical examination **(standard of care)**
3. Vital signs – we will record your pulse, temperature, and blood pressure **(standard of care)**
4. Questionnaires about your health literacy, quality of life, and urinary symptoms. **(research only)**
5. Blood draw – 25mL may be drawn for safety labs **(standard of care and research)** and 34 mL may be drawn for laboratory analysis to identify specific markers found in patients with bladder cancer and to look for additional markers we believe to help the immune response of patients with bladder cancer. **(research only)**
6. Purified Protein Derivative (PPD Test) - If you are concurrently taking BCG during this study, your physician may have you take a PPD test. This test is done by injecting a small amount of solution into the surface skin of the forearm. On this day of the study, antigens will test your immune response towards tuberculosis (TB). **(standard of care)**
    a. You will be asked to return 48-72 hours after the skin tests have been placed. Results of the skin test will be determined by qualified clinic personnel. State law requires positive test results for certain communicable diseases, including HIV, hepatitis, sexually transmitted infections, and tuberculosis, to be reported to a local health agency. The study doctor can discuss this with you.
7. Tissue collection – tissue blocks/slides from your most recent TURBT (Transurethral Resection of Bladder Tumor) will be requested from the pathologist after consent is signed. **(research only)**
8. Cognitive and Physical Assessments – cognitive function will be measured using validated assessments that entail a brief interview with trained research staff and an exam to evaluate memory. Physical performance will be measured using Short Physical Performance Battery and handgrip strength. **(research only)**

Assignment to Study Groups –
When it is determined that you are eligible for the study, you will be assigned by chance (like flipping a coin) to one of two study groups.

- eRapa 0.5 mg/weekday (Monday – Friday) for 1 year or until high-grade disease recurrence
- Placebo 0.5 mg/weekday (Monday – Friday) for 1 year or until high-grade disease recurrence

You will have a one in two chance of being in the placebo group. A placebo is an inactive, harmless substance that looks like the other study drugs.

Neither you nor the research staff will know whether you are receiving the study drug or a placebo. In the event of an emergency, there is a way for the research staff to find out which you are receiving.

Once you are randomized, study staff will provide you with your prescription and you will start the medication. You will be given three bottles of either the study drug (eRapa) or the placebo, and it will be refilled every 3 months as long as you remain high-grade recurrence free at time of your next cystoscopy. You should take the medication once daily Monday – Friday at the same time every day for approximately 1 year. (**research only**)

Visit 2 (Month 1) Study Procedures:

A member of the research staff will contact you at Month 1 in order to review if any adverse events have occurred during the first month of treatment. **(research only)**

Visits 3-6 (Months 3-12) Study Procedures:

1. Every 3 months as part of normal standard of care, you will undergo an examination of your bladder (cystoscopy) to evaluate for any bladder cancer recurrence. The urologists will look into the bladder to see if any tumors have returned. In the event that a tumor(s) has developed, you will most likely undergo another surgery to remove this tumor as this is standard of care. (**standard of care**)
    a. You will be given instructions on how to discontinue eRapa prior to surgery.
    b. If the biopsy does show a high-grade tumor recurrence, you will be withdrawn from the study.
    c. If the biopsy does not show a high-grade tumor recurrence, you will restart the study drug
2. Drug compliance assessment – you will be asked to bring your study medication and patient dosing calendar to each cystoscopy visit so the research staff can assess your drug compliance. **(research only)**
    a. As long as there is no recurrence of high-grade bladder cancer, your study drug will be refilled.
3. If you are concurrently taking BCG during this study, you will have a Purified Protein Derivative (PPD test) at Visit 3 (Month 3). This test is done by injecting a small amount of solution into the surface skin of the forearm. On this day of the study, antigens will test your immune response towards tuberculosis. **(research only)**
    a. You will be asked to return 48-72 hours after the skin tests have been placed at Visit 3. Results of the skin test will be determined by qualified research staff.
4. At Visits 4 and 6 (Month 6 and 12) – you will complete questionnaires about your health, quality of life, and urinary symptoms. **(research only)** If your cancer comes back; you will be treated for that. That treatment will usually involve the surgical removal of the tumor using a cystoscope.
5. Blood draw – Approximately 50-60 mL may be drawn at each visit for laboratory analysis to assess any hematological, metabolic, lipid or diabetogenic effects, identify specific markers found in patients with bladder cancer and to look for additional markers we believe to help the immune response of patients with bladder cancer. **(standard of care and research)**
6. Cognitive and Physical Assessments – At Visits 4 and 6 (Months 6 and 12) cognitive function will be measured using validated assessments that entail a brief interview with trained research staff and an exam to evaluate memory. Physical performance will be measured using Short Physical Performance Battery and handgrip strength. **(research only)**

Remaining Visits

After you have completed 1 year of study drug, you will continue to have cystoscopies as part of your standard of care every 3 months for an additional year, then every 6 months for 2 years, and a final exam at year 5. We will continue to follow your results from the cystoscopies and meet with you to check for any adverse events. Additionally, we will have a final blood draw (50 mL) to look for additional markers we believe to help the immune response of patients with bladder cancer at Visit 8 (Month 18) and a final set of questionnaires about your health, quality of life, urinary symptoms, and assessment of physical and cognitive function at Visit 10 (Month 24). We will continue to collect information on disease progression for up to 5 years from enrollment.

Ending Participation Early

Could your participation end early? There are several reasons why the researchers may need to end your participation in the study (early withdrawal). Some reasons are:

1. The research staff believe that it is not in your best interest to stay in the study.
2. You become ineligible to participate.
3. Your condition changes and you need treatment that is not allowed while you are taking part in the study.
4. You do not follow instructions from the research staff.
5. The study has been stopped or terminated.
6. If you have a recurrence of high-grade bladder cancer you will stop the study drug and be withdrawn from the study.
7. You have adverse events that you have not completely recovered from and your study doctor believes that it is in your best interest not to continue in the study.

The research staff will discuss your options for medical care when your participation in this study ends. If you end study participation early, the researchers will ask that you come in for a final visit called an End of Treatment (EOT) visit.

Future Use of Your Information or Biospecimens Collected as Part of Your Participation

Information or biospecimens will not be used for future research, even if identifiers are removed.

Return of Research Test Results for Genetic Tests to Subjects

It is possible that this study will identify information about you that was previously unknown, such as disease status or risk. There are no plans to provide this information to you or your physician.

Risks – "What are the Risks of Participation in the Research?"

Risks from the Research

The investigators have designed this study to learn how well the new treatment(s) compares to commonly accepted treatment(s). There is a risk that the effectiveness and/or safety of the treatment for the eRapa group may not be as good as the most commonly accepted treatments. You may get a treatment or drug that does not help treat your disease or that makes your condition or disease worse.

Risks from the Specific Research Procedures (drug(s), interventions, or procedures)

There are risks to taking part in this research study. It is possible that you may have side effects while on the study. Side effects from this study will usually go away soon after you stop taking the drug.

Everyone taking part in the study will be watched carefully for any side effects. However, the study doctors don't know all the side effects that may happen. Be sure to tell your study doctor or research staff immediately, about any side effect that you have while taking part in the study.

The following section will describe the risks related to your participation in this research study. You should talk to your study doctor or research staff about any side effects or other problems that you have while taking part in the study.

Side effects can range from mild to serious. Serious side effects are those that may require hospitalization, are life threatening or fatal (could cause death). The frequency that people experience a certain side effect can range from many (likely), few (less likely) or only one or two (rarely).

Risks and side effects related to **eRapa** include those which are:

Likely (greater than 10%):

1. Stomatitis (sores in the mouth)
2. Diarrhea
3. Abdominal pain
4. Nausea
5. Nasopharyngitis (inflammation of your nasal passages and the back of your throat)
6. Acne
7. Chest pain
8. Peripheral edema (swelling of the hands and legs)
9. Upper respiratory tract infection
10. Headache
11. Dizziness
12. Myalgia (body aches)
13. Hypercholesterolemia (increased cholesterol levels) , Hypertriglyceridemia (increased triglyceride levels) , or Hyperlipidemia (increased lipid levels)

14. Impaired wound healing

Less Likely (1 - 10%):
1. Hypersensitivity (5.4%)
2. Indigestion (2.8%)
3. Fatigue (2.8%)
4. Blood cholesterol (high density lipoprotein – HDL) increased (2.8%)
5. Blood cholesterol (low-density lipoprotein – LDL) increased (2.3%)
6. Tongue sores (2.3%)
7. Sleeplessness (1.8%)
8. Dry mouth (1.4%)
9. Abnormally low level of white blood cells (Neutropenia) (1.4%)
10. Mouth, gum, or tooth (Oral) pain (1.4%)
11. Itching (1.4%)

Rare but Serious (less than 1%):
1. Rash
2. Laryngeal Inflammation (Sore Throat)

Risks and side effects related to the **blood collection** include those which are:

Likely, some may be serious
In 100 people, approximately 15-20 may have:
- Inflammation (redness and swelling of the vein)
- Pain
- Bleeding
- Bruising

Less Likely, some may be Serious
In 100 people, approximately 5-15 may have:
- Formation of blood clots
- Fainting
- Infection at puncture site

Risks and side effects related to **Purified Protein Derivative (PPD skin test)** include those which are:

Likely, some may be serious
In 100 people, approximately 15-20 may have:
- Inflammation (redness and swelling)
- Pain
- Bleeding
- Bruising

Less Likely, some may be serious
In 100 people, approximately 5-15 may have:
- Infection at test site

Rare and Serious
In 100 people, approximately 0-5 may have:
- An allergic reaction to the drug such as rash, hives, difficulty breathing, tightness in the chest, swelling of the mouth, face, lips, or tongue

- Blisters, open sores

For more information about risks and side effects, ask the research staff.

We will tell you about any significant new findings which develop during the course of this research study which may relate to your willingness to continue taking part of this study.

Are there Risks related to withdrawing from the study?
If you decide to withdraw from this study early, please discuss your decision with your study doctor or research staff. The research staff may ask you to complete study withdrawal procedures at a final study visit. There is no risk to you if you do not complete the final withdrawal procedures and you can choose not to participate in them.

Reproductive Risks -
Concerns for sexually active men and women: Women should not become pregnant and men should not father a baby while taking part in this study because we do not know how the study drugs/procedures could affect a man's sperm (for some drugs/procedures, the concern may be that the sperm might be affected and, in some cases drugs could be carried by the semen into the vagina and cause harm) or a fetus, if a woman becomes pregnant during the study.

In order to prevent pregnancy, if you are able to become pregnant or to father a child you must use effective pregnancy prevention from screening through to the end of your study participation or at minimum to 12 weeks after ending treatment. Effective pregnancy prevention will be a use of **one** of the following choices:

- Hormonal pregnancy prevention
- Double Barrier method (condom, or diaphragms, with spermicidal cream)
- Intrauterine device
- Male Partner vasectomy

It is important that you talk to your study doctor about avoiding pregnancy during this study. If you think you might have become pregnant or if you believe your female partner has become pregnant while you are in this study, you must tell one of the study doctors right away If you become pregnant, you will no longer be given the study drug and your pregnancy will be followed to outcome. If your female partner becomes pregnant, your partner will be asked to consent to the pregnancy being followed to its outcome.

If you are a woman who is pregnant or could be pregnant, you cannot take part in this study because we do not know how the study drug might affect a developing fetus. We will do a pregnancy test before you start treatment to make sure you are not pregnant.

Risks to babies who are being breastfed: Women who are breastfeeding cannot take part in this study because we do not know what effect the drugs/procedures might have on their breast milk.

Are there risks if you also participate in other research studies?
Being in more than one research study at the same time may increase the risk to you. It may also affect the results of the studies. You should not take part in more than one study without approval from the researchers.

What if a research-related injury occurs?
The researchers have taken steps to minimize the known or expected risks. However, you may still experience problems or side effects, even though the researchers are careful to avoid them. In the event of a research-related injury or if you experience an adverse reaction, please immediately contact your study doctor. See the section “Contact Information” for phone numbers and additional information. You may also need to tell your regular doctors.

If you are injured or made sick from taking part in this research study, medical care will be provided. This care may be billed to you or your insurance. Depending on the circumstances, this care may be provided at no cost to you. We have no plans to give you money if you are injured. The investigator can provide you with more information.

If you sign this form, you do not give up your right to seek additional compensation if you are harmed as a result of being in this study.

Benefits – "How could you or others benefit from your taking part in this study?"

The possible benefit of your participation in this study is that you may decrease the chances of having a bladder cancer recurrence. There is no guarantee or promise that you will receive any benefit from this study.

We hope the information learned from this study will benefit other people with similar conditions in the future.

Alternative procedures or course of treatment – "What other options are there to participation in this study?"

There are other options available to you. Your other choices may include:

- Getting treatment or care without being in a study
- Getting no treatment
- Taking part in another study

The research staff will discuss all of your options with you. You do not have to be part of this research to receive treatment for your condition.

Costs – Will taking part in this study cost anything?

You or your health insurance company will be responsible for the cost of treatments and procedures that would be done whether or not you took part in this study (standard of care), such as clinic visits, BCG treatments and cystoscopy. It is important to understand that some insurance companies do not cover some costs (for example, approved drugs used in a way different from the package instructions). If your insurance company does not cover these treatments or procedures, you will be required to pay for them. Ask the research staff if you have any questions about what it will cost you to take part in this study (for example bills, fees, or other costs related to the research).

The sponsor will provide the study drug free of charge during this study. At the end of your participation, you must return all unused study drug to the research staff.

Confidentiality – How will your records be kept confidential?

Information we learn about you in this study will be handled in a confidential manner, within the limits of the law. If we publish the results of the study in a scientific journal or book, we will not identify you. The Institutional Review Board and other groups that have the responsibility of monitoring research may want to see study records which identify you as a subject in this study.

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the Federal Government. With this certificate, the research staff cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The researchers will use the certificate to resist any demands for information that would identify you, except as explained below. The certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of federally funded projects or for information that must be disclosed in order to meet the requirements of the U.S. Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you or a member of your family

from voluntarily releasing information about yourself or your involvement in this research. If an insurer, employer, or other person obtains your written consent to receive research information, then the research staff may not use the certificate to withhold that information.

The Certificate of Confidentiality does not prevent the research staff from disclosing voluntarily, without your consent, information that would identify you as a participant in the research project under certain circumstances. Circumstances that warrant the release of your information without your permission include: abuse and/or neglect, intention to harm yourself or others, or certain communicable diseases.

Limits of Confidentiality
Even without your consent, suspected or known abuse or neglect of a child, disabled, or elder abuse, threatened violence to self or others or other local health reporting requirements will be reported to appropriate authorities.

Research policies require that private information about you be protected and this is especially true for your health information. However, the law sometimes allows or requires others to see your information. The information given below describes how your privacy and the confidentiality of your research records will be protected in this study.

What is Protected Health Information (PHI)?
Protected Health Information (PHI) is information about a person's health that includes information that would make it possible to figure out whose health information it is. According to the law, you have the right to decide who can see your protected health information (PHI). If you choose to take part in this study, you will be giving your permission to the investigators and the research staff (individuals carrying out the study) to see and use your health information for this research study. In carrying out this research, the health information we will see and use about you will include:

- Medical history and blood work,
- Pathology, imaging and radiology reports and results of medical tests,
- Information from interviews or from questionnaires,
- Demographic information like your age, marital status, the type of work you do and the years of education you have completed.

We will get this information by asking you, asking your doctor, and/or by looking at your chart at the Medical Arts and Research Center at University of Texas Health Science Center at San Antonio (UTHSCSA) and University Health.

How will your PHI be shared?
Because this is a research study, we will be unable to keep your PHI completely confidential. We may share your health information with people and groups involved in overseeing this research study including:

1. Emtora Biosciences, the company that makes the study drug and is providing the study drug.
2. The following collaborators at other institutions that are involved with the study: UT Southwestern Medical Center at Dallas;
3. The committee that checks the study data on an ongoing basis, to determine if the study should be stopped for any reason;
4. The members of the local research team;
5. UT Health San Antonio IRB, the group providing independent review of the clinical study, and oversees the protection of your rights as a research participant;
6. The Compliance Office of the University of Texas Health Science Center at San Antonio, and other groups that oversee how research studies are carried out;
7. The Research offices at the University of Texas Health Science Center at San Antonio, University Health; and/or,

8. The U.S. Food and Drug Administration (FDA) and other U.S. and international governmental regulatory agencies involved in overseeing drug or device research.

If you decide to participate in this study, you will be giving your permission for the groups named above, to collect, use and share your health information. If you choose not to let these groups collect, use and share your health information as explained above, you will not be able to participate in the research study.

Some of the health information collected during the research study may also be kept in your medical record. This is for purposes of treatment and billing. The information will be maintained, used, and disclosed in accordance with laws and regulations applicable to medical records. It will also be in compliance with the policies and procedures of UT Health San Antonio, which are outlined in the Notice of Privacy Practices. The Notice of Privacy Practices explains how UT Health San Antonio may use and disclose health information kept in your medical record. As a patient of UT Health San Antonio, you should have received a copy of the Notice of Privacy Practices which are located here: https://uthscsa.edu/university/notice-of-non-discrimination/notice-privacy-practices.

Parts of your PHI may be photocopied and sent to a central location or it may be transmitted electronically, such as by e-mail or fax. The groups receiving your health information may not be obligated to keep it private. They may pass information on to other groups or individuals not named here.

How will your PHI be protected?
In an effort to protect your privacy, the study staff will use code numbers instead of your name, to identify your health information. Initials and numbers will be used on any photocopies of your study records, and other study materials containing health information that are sent outside of the University of Texas Health Science Center at San Antonio, University Health or UT Southwestern Medical Center at Dallas for review or testing. If the results of this study are reported in medical journals or at meetings, you will not be identified.

Do you have to allow the use of your health information?
You do not have to allow (authorize) the research staff and other groups to see and share your health information. If you choose not to let the research staff and other groups use your health information, there will not be any penalties, but you will not be allowed to participate in the study.

After you enroll in this study you may ask the research staff to stop using your health information at any time. However, you need to say this in writing and send your letter to:

Robert Svatek, M.D.
UTHSCSA, Department of Urology,
7703 Floyd Curl Drive, Mail Code 7845,
San Antonio, Texas 78229-3900

If you tell the research staff to stop using your health information, your participation in the study will end and the research staff will stop collecting new health information from you and about you for this study. However, the study staff will continue to use the health information collected up to the time they receive your letter asking them to stop.

Can you ask to see the PHI that is collected about you for this study?
The federal rules say that you can see the health information that we collect about you and use in this study. Contact the research staff if you have a need to review your PHI collected for this study.

You will only have access to your PHI until the study is completed.

How long will your PHI be used?

By signing this form, you agree to let us use and disclose your health information for purposes of the study until the end of the study. This permission to use your personal health information expires when the research ends, and all required study monitoring is over.

Contact Information – Who can you contact if you have questions, concerns, comments, or complaints?

If you have questions now, feel free to ask us. If you have additional questions, concerns, comments, or complaints later or you wish to report a problem which may be related to this study please contact:

Primary contact:
Robert Svatek, MD at 210-567-3224 (24 hours).

If primary is not available, contact
Study Coordinator at 210-567-3224 (24 hours).

This research is being overseen by UT Health San Antonio ("IRB"). The IRB will not be able to answer some study-specific questions, such as questions about appointment times. However, you may contact the IRB if the research staff cannot be reached or if you wish to talk to someone other than the research staff. You may talk to them at (210) 567-8250 or email at IRB@uthscsa.edu:

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

Research Consent & Authorization Signature Section

If you agree to participate in this research and agree to the use of your protected health information (PHI) in this research sign this section. You will be given a signed copy of this form to keep. You do not waive any of your legal rights by signing this form.

SIGN THIS FORM ONLY IF THE STATEMENTS LISTED BELOW ARE TRUE

- You have read the above information.
- Your questions have been answered to your satisfaction about the research and about the collection, use and sharing of your protected health information.

PRIMARY CARE PHYSICIAN / SPECIALIST NOTIFICATION OPTION

Please initial below whether you want us to notify your primary care physician or your specialist of your participation in this study

- _____ Yes, I want my study doctor to inform my primary care physician/specialist of my participation in this study.
- _____ No, I do not want my study doctor to inform my primary care physician/specialist of my participation in this study.
- _____ I do not have a primary care physician/specialist.
- _____ My study doctor is my primary care physician/specialist

Adult Signature Section

- You have voluntarily decided to take part in this research study.

- You authorize the collection, use and sharing of your protected health information as described in this form.

Printed Name of Subject	Signature of Subject	Date	Time AM PM
Printed Name of Witness	Signature of Witness	Date	Time AM PM

☐ *Check if consent and authorization obtained from an individual who is unable to read and/or write but can otherwise communicate and/or comprehend English. Have witness initial below.*
Declaration of witness: I was present for the entire consent process. _____ ←(initials of witness)

Printed Name of Person Obtaining Consent and Authorization	Signature of Person Obtaining Consent and Authorization	Date	Time AM PM

☐Consent and authorization were obtained from this individual who is unable to read and/or write but can otherwise communicate and/or comprehend English. The method used for communication with the subject was:

_____.
The specific means by which the subject communicated agreement to participate was:

_____