Title of research study: A Phase 3, Multicenter Trial Evaluating the Efficacy and Safety of MitoGel™ on Ablation of Upper Urinary Tract Urothelial Carcinoma

Investigator: Marc Dall'Era, M.D.

Why am I being invited to take part in a research study?

We invite you to take part in a research study because you have non-invasive, low grade upper urinary tract urothelial cancer and are seeking treatment.

This form may contain words that you do not understand. Please ask the study doctor or the study staff to explain any words or procedures that you do not clearly understand.

The purpose of this form is to give you information about the research study. This form describes the purpose, procedures, benefits, risks, discomforts and precautions of the research study and what will be expected of you.

You should only take part in the study if you want to do so. You can agree to be in the study now and change your mind later. Your decision will not affect your regular medical care. Please read this form and ask as many questions as needed. You should not sign this form if you have any questions that have not been answered to your satisfaction. By signing this form, you will be giving your consent to take part in this study.

What should I know about a research study?

(Experimental Subject's Bill of Rights)

- Someone will explain this research study to you, including:
  - The nature and purpose of the research study.
  - The procedures to be followed.
  - Any drug or device to be used.
  - Any common or important discomforts and risks.
  - Any benefits you might expect.
  - Other procedures, drugs, or devices that might be helpful, and their risks and benefits compared to this study.
  - Medical treatment, if any, that is available for complications.
- Whether or not you take part is up to you.
- You can choose without force, fraud, deceit, duress, coercion, or undue influence.
- You can choose not to take part.
- You can agree to take part now and later change your mind.
- Whatever you decide it will not be held against you.
- You can ask all the questions you want before you decide.
- If you agree to take part, you will be given a signed and dated copy of this document**.**

Who can I talk to?

For the duration of the study, you will be under the care of the study doctor. If at any time between your

visits you feel that any of your symptoms are causing you problems, or you have experienced a study related injury, please contact your study doctor.

If you have questions, concerns, or complaints, during regular business hours or think the research has hurt you, talk to the research team at 4860 Y St. #3500 Sacramento, CA 95817, or (916) 734-5173. The Clinical Research Coordinator will assist you in contacting the Investigator for this study.

For non-emergency issues you can call the UCDMC Hospital Operator (916-734-2011), tell the Operator you are participating in a research study and you wish to talk to the Urology Resident on call. In the case of an emergency, dial 911 from any phone.

This research has been reviewed and approved by an Institutional Review Board ("IRB"). Information to help you understand research is on-line at http://www.research.ucdavis.edu/policiescompliance/irb-admin/.You may talk to a IRB staff member at (916) 703-9151, IRBAdmin@ucdmc.ucdavis.edu, or 2921 Stockton Blvd, Suite 1400, Room 1429, Sacramento, CA 95817 for any of the following:

- Your questions, concerns, or complaints are not being answered by the research team.
- You cannot reach the research team.
- You want to talk to someone besides the research team.
- You have questions about your rights as a research subject.
- You want to get information or provide input about this research.

Why is this research being done?

To be in this Study, you must be at least 18 years of age and have been diagnosed with a low grade, non-invasive upper urinary tract urothelial cancer (UTUC).

UTUCs are cancerous changes of the cells lining the upper urinary tract, the kidneys and ureters.

You are being asked to take part in this research study which uses MitoGel™ (Mitomycin C). Mitomycin C (MMC) is FDA approved for other clinical indications and is commercially available for the treatment of bladder cancer. UroGen's MitoGel™ (a combination of MMC and TC-3 gel) has *not* been approved by the FDA and is *not* commercially available. The gel is designed to safely maintain the MMC within the body to treat the urinary tract urothelial carcinoma. The MitoGel™ treatment is delivered directly to the tumor area through a catheter in its liquid form, then turns to gel in the upper urinary tract. This slows down the loss of the drug, which would normally occur during regular urination. The gel helps keep the chemotherapy in direct contact with the tumor for serval hours, which increases its efficacy and is an improvement from current chemotherapy treatments.

This is an "open label" study, which means both you and your study doctor will know what study drugs you are taking. If you agree to take part in this study and meet all of the requirements, you will be given the following treatment:

MitoGel™ (Mytomycin C and TC-3 HydroGel) 60mg instilled into the kidney once a week for 6 weeks, with possible further maintenance instillations

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While you are receiving the study drug, you will be experiencing ongoing Urology related exams and bloodwork, have periodic cytologies (slides) and scopings done of your upper urinary tract, and receive x-rays, to gauge your progress.

It is possible for you to continue receiving maintenance treatment(s) after your 6 weeks of study treatment. If you have experienced a complete response, meaning your cancer completely disappears for a time, and after your Week11 visit (also known as: Primary Disease Evaluation visit), your study doctor may continue monthly maintenance instillation treatments until one month before the study ends (12 months after your Week11 visit).

The purpose of this study is to evaluate the possible benefits, risks and tolerability of MitoGel™ in UTUC patients. Information about any side affects you experience will also be collected.

How long will the research last?

We expect that you will be in this research study for approximately 16 months (a little over one year).

How many people will be studied?

We expect about 5 people at UC Davis will be in this research study out of 74 people in the entire study at approximately 45 study Sites in the United States, Canada, Europe and Israel.

What happens if I say yes, I want to be in this research?

You should know that typical standard of care received in Clinic depends on the patient, but can range from immunotherapy treatments, chemotherapy, radiation and/or removing the kidney, ureter and part of the bladder. Entering this study will delay any other method of care for your situation by at least 3 months. Such delay is considered low risk in patient with low grade upper tract urothelial carcinoma. If the study treatment succeeds, meaning, the tumor(s) disappeared after 6 instillations (Complete Response=CR), you will receive up to an additional 11 (eleven) maintenance instillations.

STUDY PROCEDURES

If you agree to take part in the study, no study-related procedures can start until this form is signed and dated. A description of all procedures performed at each visit appears below.

Screening

At this visit, you will discuss and have time to review this consent form in detail and you will have time to have all of your questions answered. You will be asked to give informed consent by signing and dating this form. In addition, you will be asked questions about your current and past health and any medications you are taking.

The following procedures will be done at the screening visit:

- You will be asked about your medical history information.
- You will have a full physical exam, including measurement of your weight, and vital signs (temperature, blood pressure, heart rate, and breathing rate), as well as a Urology oriented

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physical exam.

- You will be asked about what other medications you are taking or have taken and if you have experienced any side effects.
- Blood samples will be collected for safety tests (to check how your liver, muscles, kidney, blood cells, and other body systems are working). We will collect about four teaspoons of blood for laboratory testing.

  In addition, your blood will be tested for:

  - Coagulation tests to measures the time your blood takes to clot.
  - A serum pregnancy test, if you are a woman who could become pregnant (an additional teaspoon of blood). The study doctor or Study staff will tell you if the pregnancy test results are positive. The results of the pregnancy test must be negative in order for you to be in the Study.
- Urinalysis/urine culture: completed to determine if you have a current bladder infection.
- CTU Scan: a small amount of x-rays is used to visualize the overall health of the kidneys, ureters, and bladder. This would be required if there is no documented CTU Scan within three (3) months prior to screening or if your doctor believe it is necessary to a better evaluation of your current disease. Testing will take approximately 30 minutes. In the event that CTU cannot be performed due to any reason, an MRI should be performed instead.
- Ureteroscopy (under anesthesia): an examination (with a small scope) of the upper urinary tract that is passed through the urethra and the bladder, and then directly into the ureter. The upper urinary tract will be examined to record number, size, appearance and location of tumors, if any are present. This would be required if there is no documented Ureteroscopy within 8 weeks prior to screening, or if a current scoping is not informative enough for the trial. Testing will take approximately 30 minutes.

  A video recording or photography of the scoping and lesion assessment will occur as well.
- Cytology (wash-cytology): of the Upper Urinary Tract involves obtaining cells from the lesion(s) and viewing them on a slide. This would be required if there is no documented Cytology within 8 weeks prior to screening or if it is not informative enough for the study requirement.
- Biopsy: of lesions within the upper urinary tract. This would be required if there is no documented biopsy within 8 weeks prior to screening or if it is not informative enough for the study requirement. The biopsy will take approximately 30 minutes.
- We will also conduct the mentioned procedures (Ureteroscopy, Cytology, Biopsy) if they are not Recorded and slides are not available for the study sponsor for review.
- The volume of your kidney will be measured with a contrast agent during the Ureteroscopy or during the first treatment through the ureter catheter. This measured volume will be the volume of the MitoGel you will receive each treatment.

Part of the Screening process requires that we request, from the Pathology Department, any cytology or biopsy slides collected within 8 weeks prior to the Screening visit. If you have had a biopsy or cytology completed for your urothelial cancer, these slides will be sent to the Sponsor, UroGen, for review and will be returned to the Site after reading. By signing this Consent form, you agree to allow us to send these slides to UroGen's Central Laboratory for a second reading.

Your medical records and cytology/biopsy slides provided to UroGen and central lab, respectively will not contain your personal identification information (de-identified).

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Medications:
In order to facilitate the instillations, you will be given a prescription, during the Screening window, for Sodium bicarbonate, antibiotics, an anti-histamine (anti-allergy) and diazepam (for anxiety). Directions for these will be discussed below under Study Treatment.

If you cannot perform or do not want to do any of these procedures, you should not agree to be in this study.

Note: By signing this informed consent, you allow your Urologist to provide your relevant medical records to the Sponsor, UroGen, and to the coordinating investigator of this trial (whom is not your doctor) for review of Trail eligibility at screening. Your treatment records will be available to the Sponsor during the trial and for an additional two (2) years after this trial is over. . If you qualify and would like to take part, you will be asked to return to begin the study treatment phase within 21 days of your Screening visit.

If the screening tests show that you are not eligible to continue in the research Study, then you may not take part.

Study Treatment Phase
Study treatments will start on your Day 1 visit and will continue weekly for 6 weeks and the Study doctor will instill a volume of Study drug into the kidney during each treatment.

Directly prior to treatment:
Medications:
Prior to treatment, you will be prescribed 1.3 g Sodium bicarbonate tablets (a type of salt), to help lower the acid levels in your urine, as acidic urine can cause the fast breakdown of the Mitomycin C. *These tablets are to be taken the night before each instillation, the morning of instillation, and again 30 minutes prior to each instillation procedure*

In order to avoid allergic symptoms you will also be prescribed an anti-allergic treatment. *These tablets are to be taken the day before instillation, on the day of instillation and the day after the instillation.*

It is preferred that diuretics not be taken the night before and prior to the instillation. If you are on diuretic medications, your doctor will determine whether the medication can be skipped prior to the instillations.

Directions regarding drinking liquids:
To the extent that it is possible, drinking should be avoided in the 4-6 hours prior to the instillation.

- Post instillation drinking should be limited. A recommended drinking schedule follows:
- 0-2 hours post instillation: refrain from drinking any liquid
- 2-4 hours post instillation: 1 cup of water every 2 hours;
- 4 hours post instillation: resume normal liquids consumption

First, the urethra will be numbed with an anesthetic lubricating gel. The treatment then involves inserting a

small flexible tube (cystoscope) into your urethra, into the bladder and then into the ureter that provides the doctor a view of the lesions. This allows the doctor to visualize the instillation of the medication. Then the MitoGel™ will be instilled through the catheter into the necessary area of the kidney. The gel will thicken and dissolve over several hours, delivering the drug to cover the surface during that time. Each procedure will take approximately 30 minutes.

Instillation through a thin plastic tube inserted through the skin and into the kidney (AKA: nephrostomy tube) *may* also be an option, if necessary.

Upon consultation with your Urologist, in a very rare cases, the catheter *may* be kept in place for the 6 weeks duration, instead of having new ones put in every week (and removed). Your care team will provide home care instructions.

It may be required that an educational trainer from the Sponsor will be present during some of the treatments to support the clinical team with the proper instructions of use.

Following instillation, you will be carefully monitored for urine output and clinical symptoms, which might indicate urinary obstruction.

Aiming to minimize the risk for Urinary Tract Infections (UTI), an antibiotic will be prescribed, as is normal for a ureteroscopy.

Your doctor might prescribe you with Diazepam, an anti-anxiety medication to be taken 1 hour prior to each instillation.

You will be given separate written instructions for each of these steps, and will also receive a phone call from a member of the study team to remind you.

First instillation visit (Day of study treatment, Day 1)
If you meet all the requirements during your Day 1 visit, you will begin treatment. The following Day 1 procedures will include:

- Your study doctor will review the study entrance criteria to see if you are still able to participate
- Urology oriented physical exam
- Weight, and vital signs (temperature, blood pressure, heart rate, and breathing rate)
- You will be asked about how you are feeling and asked if you have taken any medicine including any over-the-counter medications.
- Blood samples will be collected.
- Urinalysis/urine culture.
- If you are a female able to become pregnant, a urine pregnancy test will be performed. The results of the pregnancy test must be negative in order for you to be in the Study.
- You will be counselled on pregnancy prevention.
- The Study Team will verify that you have taken the prescribed sodium bicarbonate the night before the treatment and 30min, prior to the treatment.
- If not done during screening, the volume of your kidney will be measured with a contrast agent during

the Ureteroscopy or during the first treatment through the ureter catheter. This measured volume will be the volume of the MitoGel you will receive each treatment

- Fluoroscopy: Administration of the gel will be performed under fluoroscopy, which is like an xray "movie." An x-ray beam is passed through the body part and its motion can be seen in detail, to allow the doctor to visualize the placement of the gel.
- Cystoscopy for catheterization: A thin tube with a camera is inserted through your urethra and into your bladder. This allows the doctor to see inside your bladder in order to place the catheter into the ureter.
- The treatment instillation procedure will take place.

After treatment, you will be requested to mark the degree of pain during the instillation procedure on a scale of 0-10. You will also be given a questionnaire to evaluate your post-treatment experience regarding urination.
Please keep the completed questionnaire as it will be collected at the next visit.

Following this first visit, we will monitor you for 6-32 hours after the instillation for observation, at the investigator's discretion, to monitor for side effects. This will include *staying on-Site (in the clinic/office or in the operating room with anesthesia), for periodic monitoring for 6 hours post-treatment*, as well as phone call(s) from Study staff until 32 hours post-treatment. Staying on-Site for 6 hours post treatment will *only* occur during your first treatment (on Day1) just to monitor if/how you might react to the new medications.

Instillation visits 2-6 (Wk1, Wk2, Wk3, Wk4, Wk5)
Your subsequent treatment visits will involve all of the above procedures done during your Day 1 visit, as well as the following procedures:

- You will be asked about any side effects you might have experienced since the last treatment.

After each treatment, you will be requested to mark the degree of pain during the instillation procedure on a scale of 0-10. You will also be given a questionnaire to evaluate your post-treatment experience regarding urination, as well as 24-32 hours post treatment, you will be contacted via telephone to review the completed questionnaire. Please keep the completed questionnaire as it will be collected at the next visit.

If necessary, you may be called for an unscheduled visit to follow up on any post-treatment issues or problems that require clinical evaluation or follow-up.

You will undergo safety evaluation after each instillation including adverse event rate and laboratory evaluation.

Five (5) weeks after the last treatment the anti-tumor effect of MitoGel will be evaluated in the PDE visit, (see below). Response will be determined based on visualization, biopsy, urine cytology, tumor size and location. The response to treatment will be determined by comparing the results of post-treatment tests to those obtained at the initiation of the treatment.

In the event of a UTI or another safety reason, the MitoGel treatment will be postponed until the event is resolved and not over 4 weeks. In case treatment has been delayed beyond 4 weeks due to a side effect to study

treatment, treatment will be discontinued, permanently however study follow-up will be continued.

Post-treatment labs (Wk 6 & Wk 8)
At the conclusion of your 6 week treatment, but before the evaluation of your response to treatment, the following labs will be collected:

- CBC (Complete Blood Count: evaluation of white/red blood cells, etc.) If necessary, this can be done at your local clinic or doctor's office.

Primary Disease Evaluation (PDE)
About five weeks following the completion of the instillation visits, you will be scheduled for an evaluation visit, which will include the following

- You will have a full physical exam, including measurement of your weight, and vital signs (temperature, blood pressure, heart rate, and breathing rate), as well as a Urology oriented Physical exam.
- You will be asked about what other medications you are taking or have taken within the last 30 days and if you have experienced any side effects.
- Blood samples will be collected.
- Urinalysis/urine culture
- If you are a female able to become pregnant, a urine pregnancy test will be performed. The results of the pregnancy test must be negative in order for you to be in the Study.
- Ureteroscopy
- Cytology (wash-cytology)
- Biopsy: if any remaining lesions, or a recurrence are suspected.
- You will be asked about any side effects you might have experienced since the last treatment.

At the evaluation, if no detectable disease is found, you will be considered a Complete Response patient, and continue with the study as below.

If you responded partially or did not respond to the treatment, you will be considered as a Non-Complete Response and your participation in the study will be terminated.

Note: The slides obtained from the biopsy/cytology completed during the PDE visit will also be sent to the Sponsor for review and will be returned to the Site after reading. By signing this Consent form, you agree to allow us to send these slides to UroGen's Central Laboratory for a second reading.

Your Urologist will discuss the results with you and will determine which standard of care treatment is best, and information about the disease will be collected.

Study continuation for Complete Response patients only:

Maintenance Instillation Visits (Months 1-11)
In the case that you are a Complete Response patient, you will be scheduled for monthly visits, during which MitoGel will be instilled in the same procedure as described in the visits above. This will occur approximately once per month for eleven months, or until tumor first recurrence. Expect the following procedures to occur

during this visit:

- You will have a Urology oriented physical exam, including measurement of your weight, and vital signs (temperature, blood pressure, heart rate, and breathing rate).
- You will be asked about what other medications you are taking or have taken and if you have experienced any side effects.
- Blood samples will be collected.
- Urinalysis/urine culture.
- If you are a female able to become pregnant, a urine pregnancy test will be performed. The results of the pregnancy test must be negative in order for you to be in the Study.
- You will be counselled on pregnancy prevention.
- The Study Team will verify that you have taken the prescribed sodium bicarbonate the night before the treatment and 30min, prior to the treatment.
- Fluoroscopy
- The treatment instillation procedure will take place.
- You will be asked about any side effects you might have experienced since the last treatment.

If you are a female able to become pregnant, a urine pregnancy test will be performed. The results of the pregnancy test must be negative in order for you to be in the Study.

If the disease reoccurs, you will stop the treatment in the study and your Urologist will assign you to the standard of care treatment according to the medical considerations. In any case of terminating your participation in the study, you will be asked to perform a safety visit to better control your health.

Follow-Up Phase

If you showed Complete Response and during the same window of your maintenance instillation visits, you will also have up to four (4) standard-of-care follow-up visits done every 3 months.

Follow Up visits (FU Month 3, FU Month 6, FU Month 9 & FU Month 12):

Three months after your Primary Disease Evaluation visit, the first follow-up (FU) visit will be conducted and the FU visits will continue every 3 months for approximately one (1) year. During these visits, follow-up data on your disease outcome will be collected. These visits may include:

- You will have a Urology oriented physical exam, including measurement of your weight, and vital signs (temperature, blood pressure, heart rate, and breathing rate).
- You will be asked about what other medications you are taking or have taken within the last 30 days and if you have experienced any side effects.
- Blood samples will be collected.
- Urinalysis/urine culture.
- If you are a female able to become pregnant, a urine pregnancy test will be performed. The results of the pregnancy test must be negative in order for you to be in the Study.
- You will be counselled on pregnancy prevention.
- The Study Team will verify that you have taken the prescribed sodium bicarbonate the night before the treatment and 30min, prior to the treatment.
- Biopsy (these slides will also be sent to the Sponsor, for review and will be returned to the Site

after reading).
- Cytology (wash-cytology)
- Ureteroscopy
- Fluoroscopy
- The treatment instillation procedure will take place.
- You will be asked about any side effects you might have experienced since the last treatment.

The final follow up visit will occur 12 months after the post-instillation evaluation visit, or until tumor first recurrence, at which time, additional follow-up data on disease outcome will be collected. During this last visit you will expect the above procedures, but you will not receive treatment instillation and all that relates to treatment (Fluoroscopy, Cystoscopy, etc.). However the last CTU Scan will be performed during this visit.

Note: In case of recurrence or progression at the original treated area found during the follow-up period, you will be considered as having completed the trial and will not be summoned for further follow-up visits, but for a single termination visit for safety evaluation.

Unscheduled Visit

An unscheduled visit may be performed at any time during the trial if the Investigator decides that your clinical state does not permit instillation of the study drug, for assessment of safety, at the Patient's request, or as deemed necessary by the Investigator.

Please provide the trial Urologist information about any medications you are taking. In addition, if you are taking any over-the-counter drugs or herbal supplements which you have obtained from the drug store, grocery store, etc., this information should also be provided to the Urologist, as well.

End of Study or Withdrawal Visit

At any time throughout the study, you may decide that you no longer want to participate in the study, new lesions have been found, or if it is determined by the Study doctor that your safety is at risk. The investigators may end your participation in this study for a number of reasons, such as if you do not follow instructions or if you miss scheduled visits. The investigators or the study sponsor might also decide to stop the study at any time. In this event, you *must* attend one final Clinic visit to terminate your involvement.

The data collected about you up to the point of withdrawal will remain a part of the study and may not be removed from the study database.

See below for an overview of the Study Calendar

All Patients - Up to Primary Disease Evaluation (PDE) Visit

Study Week	Wk (-)3-(-)1	Treatment period								Primary Disease Evaluation Wk 10 (±1 w)
		Wk 0 Day 1	Wk 1 (±3 d)	Wk 2 (±3 d)	Wk 3 (±3 d)	Wk 4 (±3 d)	Wk 5 (±3 d)	Wk 6 (±3 d)	Wk 8 (±3 d)	
Visit Number	**V0**	**V1**	**V2**	**V3**	**V4**	**V5**	**V6**	**V7**	**V8**	**V9**
Visit Name	**Screening**	**Rx #1**	**Rx #2**	**Rx #3**	**Rx #4**	**Rx #5**	**Rx #6**	**Lab 1**	**Lab 2**	**PDE**
Informed consent	X									
Demographics	X									
General and Urothelial Carcinoma Medical History, Smoking	X									
Concomitant Medicatio Review	X	X	X	X	X	X	X			X
Eligibility criteria	X	X								
Full Physical Examinatic	X									X
Urology oriented Physic Examination	X	X	X	X	X	X	X			X
Vital signs	X	X	X	X	X	X	X			X
CBC, liver and renal function, coagulation	X	X	X	X	X	X	X	X	X	X
Urinalysis/dipstick	X	X	X	X	X	X	X			X
Urine culture	X	X	X	X	X	X	X			X
CTU	X#									

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Study Week	Wk (-)3-(-)1	Treatment period								Primary Disease Evaluation Wk 10 (±1 w)
		Wk 0 Day 1	Wk 1 (±3 d)	Wk 2 (±3 d)	Wk 3 (±3 d)	Wk 4 (±3 d)	Wk 5 (±3 d)	Wk 6 (±3 d)	Wk 8 (±3 d)	
Visit Number	**V0**	**V1**	**V2**	**V3**	**V4**	**V5**	**V6**	**V7**	**V8**	**V9**
Visit Name	**Screening**	**Rx #1**	**Rx #2**	**Rx #3**	**Rx #4**	**Rx #5**	**Rx #6**	**Lab 1**	**Lab 2**	**PDE**
Biopsy for histopathology	X									X
Upper Urinary Tract Urine cytology-washing	X									X
Pregnancy blood test (only if urine is positive)	X	X	X	X	X	X	X			X
Pregnancy urine test		X	X	X	X	X	X			X
Ureteroscopy (URS)+C	X									X
Recording/ Photograph UUT lesions number, si appearance and location	X									X
Volumetric estimation o treatment area	X									
Provide prescription for sodium carbonate, Prophylaxis antibiotic, anti- histaminic and diazepam (optional) and written instructions	X									
Patient card, letter to GP, Guidance letter to patient	X									
Fluoroscopy		X	X	X	X	X	X			
Cystoscopy for catheterization		X	X	X	X	X	X			

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Study Week	**Wk (-)3-(-)1**	**Treatment period**								**Primary Disease Evaluation**
		Wk 0 Day 1	**Wk 1 (±3 d)**	**Wk 2 (±3 d)**	**Wk 3 (±3 d)**	**Wk 4 (±3 d)**	**Wk 5 (±3 d)**	**Wk 6 (±3 d)**	**Wk 8 (±3 d)**	**Wk 10 (±1 w)**
Visit Number	**V0**	**V1**	**V2**	**V3**	**V4**	**V5**	**V6**	**V7**	**V8**	**V9**
Visit Name	**Screening**	**Rx #1**	**Rx #2**	**Rx #3**	**Rx #4**	**Rx #5**	**Rx #6**	**Lab 1**	**Lab 2**	**PDE**
MitoGel™ Admixture administration		X	X	X	X	X	X			
VAS questionnaire for p evaluation		X	X	X	X	X	X			
6 hours observation pos treatment		X								
1.3 gr × 3 of sodium bicarbonate (|The night before, morning of and 30 min. prior to treatment)		X	X	X	X	X	X			
Phone reminder day prior to instillation:		X	X	X	X	X	X			
Supply questionnaire for 24-32 h Post treatment telephone contact		X	X	X	X	X	X			
24-32 h Post Treatment telephone contact		X	X	X	X	X	X			
Adverse Events	X	X	X	X	X	X	X			X

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Maintenance & Follow Up (FU) - Complete Response Patients

Study Week/Month	Maintenance Treatment											
	2-3 Weeks post PDE		FU1 +3mo Post PDE (±2 w)			FU2 +6mo Post PDE (±2 w)			FU 3 +9mo Post PDE (±2 w)			FU 4 +12mo Post PDE (±2 w)
Visit Number	**V10**	**V11**	**V12**	**V13**	**V14**	**V15**	**V16**	**V17**	**V18**	**V19**	**V20**	**V21**
Visit Name	**Maint. #1**	**Maint. #2**	**Maint. #3**	**Maint. #4**	**Maint. #5**	**Maint. #6**	**Maint. #7**	**Maint. #8**	**Maint. #9**	**Maint. #10**	**Maint. #11**	**FU4 Trial Completion**
Urology oriented Physical Examination	X	X	X	X	X	X	X	X	X	X	X	X
Vital signs	X	X	X	X	X	X	X	X	X	X	X	X
Lab work (CBC, liver and renal function, coagulation)	X	X	X	X	X	X	X	X	X	X	X	X
Urinalysis/dipstick	X	X	X	X	X	X	X	X	X	X	X	X
Urine culture	X	X	X	X	X	X	X	X	X	X	X	X
CT Scan												X
Biopsy			X			X			X			X
Upper Urinary Tract Urine cytology-washing			X			X			X			X
Pregnancy urine test	X	X	X	X	X	X	X	X	X	X	X	X

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Study Week/Month	Maintenance Treatment											
	2-3 Weeks post PDE		FU1 +3mo Post PDE (±2 w)			FU2 +6mo Post PDE (±2 w)			FU 3 +9mo Post PDE (±2 w)			FU 4 +12mo Post PDE (±2 w)
Visit Number	**V10**	**V11**	**V12**	**V13**	**V14**	**V15**	**V16**	**V17**	**V18**	**V19**	**V20**	**V21**
Visit Name	**Maint. #1**	**Maint. #2**	**Maint. #3**	**Maint. #4**	**Maint. #5**	**Maint. #6**	**Maint. #7**	**Maint. #8**	**Maint. #9**	**Maint. #10**	**Maint. #11**	**FU4 Trial Completion**
Pregnancy blood test (only if urine is positive)	X	X	X	X	X	X	X	X	X	X	X	X
Ureteroscopy (URS)			X			X			X			X
Recording/Photographing of UUT lesion appearance and location			X			X			X			X
Fluoroscopy	X	X	X	X	X	X	X	X	X	X	X	
Cystoscopy for catheterization	X	X	X	X	X	X	X	X	X	X	X	
MitoGel™ instillation	X	X	X	X	X	X	X	X	X	X	X	
1.3 g × 3 of sodium	X	X	X	X	X	X	X	X	X	X	X	
Phone reminder day prior to instillation: Bicarbonate, liquid limitation, diuretics	X	X	X	X	X	X	X	X	X	X	X	
Review of Disease Outcome and Complete Response Durability			X			X			X			X
Adverse Events /Concomitant	X	X	X	X	X	X	X	X	X	X	X	X

For IRB Use

Blood Sampling

Blood samples will be taken for the purpose of looking at how your liver, muscle, kidney, blood cells, and other body systems are functioning.

Based on the assumption that you show a Complete Response and complete the entire length of the Study, the total amount of blood taken per subject is anticipated to be approximately 440 mLs of blood, which is about 29 tablespoons. This amount will be taken throughout the course of the treatment and up to the Follow Up Month 12 visit.

This total does not include any unscheduled visit labs that are completed.

For comparison, a standard blood donation at a blood collection center, once in any 56 day period, is about 475 mLs of blood (32 tablespoons). This total volume does not include discarded blood from pre-draws used to remove fluid from flushed catheters. Additional blood samples may be drawn during the study if the study doctor considers it necessary for monitoring your health. It is possible that more than one attempt to obtain a blood sample may be necessary.

What are my responsibilities if I take part in this research?

If you take part in this research, there are certain rules you must follow before, during, and after the study period. Some are listed below, but there could be others that the study doctor will discuss with you as they arise:

• You must be able to provide written consent to be in this study.
• You must tell your study doctor all of the medications that you have been taking for at least 30 days before you take part in the study. This includes vitamins, minerals, and medications that do not require a doctor's prescription. Some medications are not allowed. Your study doctor will discuss these with you in detail.
• You must ask your study doctor before you take any new medications, even over the counter medications like vitamins and herbal treatments, during the study. You may not be allowed to participate in the study if you use certain medications.
• If you decide to take part in this study, it is very important that you attend all visits as scheduled, including all of the follow-up visits.
• For male subjects, you must not get a female partner pregnant during this study, and for a minimum of three months after your last does of Study drug. If your partner is able to get pregnant, you will need to use two acceptable forms of birth control: a condom AND at least one other form of birth control as described by your doctor.
• For female subjects, you must not get pregnant during this study, and for a minimum of six (6) months after your last does of Study drug.

Reliable or acceptable birth control methods (in addition to a male partner who correctly uses a condom) include:

- an intrauterine device (IUD) with a failure rate of <1% per year
- female barrier method: cervical cap or diaphragm with spermicidal agent
- tubal sterilization (having your tubes tied)
- vasectomy in male partner
- implants of levonorgestrel (AKA: Mirena, or Liletta)

For IRB Use

- injectable progesterone
- oral contraceptives (either combined or progesterone only)
- contraceptive vaginal ring
- transdermal contraceptive patch

• For male subjects, do not donate any sperm from Screening to six (6) months after your last dose of Study drug.
• Throughout the study, you are expected to notify your study doctor of any illnesses, ill effects or abnormalities you may suffer, whether or not you think they are related to the study.
• You must follow all instructions given to you while you are participating in this study. If you do not, you may be removed from the study. If you are unsure about what you are supposed to do, ask the study doctor.
• Some insurance companies require people who are renewing a policy or getting a new policy to tell them about participating in a clinical study. You should check with your insurer to determine if taking part in this study will affect your existing insurance policy.
• Tell the Study staff if you wish to stop being in the Study.

If you are allowed to participate, you will be informed by the study doctor as to which of your regular medications you are permitted to continue to take.

Your primary doctor will be notified that you are participating in this study and provided with the study doctor's contact information should they have any questions about your participation.

What happens if I do not want to be in this research?

You may decide not to take part in the research and it will not be held against you.

You should ask your study doctor about all the treatment options that are available for treatment of Urothelial carcinoma and experimental medicines. You should discuss with your study doctor whether you should receive treatment now or wait longer to begin treatment. It is possible that other therapies for Urothelial carcinoma may become available during your involvement in the study, so it may be in your best interest to wait. Your study doctor will discuss all of your treatment options with you. You do not have to take part in this study to get treatment for your Urothelial carcinoma.

If you decide not to take part in this study or decide to withdraw from the study, then your study doctor can talk with you about other treatment options and their risks and benefits. Other treatments might include:

- treatment with standard drugs and procedures (such as oral medications or injections)
- other experimental treatments that may be available (if they are available)
- other clinical research studies that may be available (if they are available)

You should discuss with your doctor whether this Study might be good treatment option for you. You will be made aware of any new findings during the course of the study that may affect your willingness to participate.

You may or may not receive any direct medical benefit from being in this study. Your condition may get

better, it may get worse, or it may stay the same.

If you withdraw from the study or decide not to participate, you will receive the standard of care treatment as determined by your doctor.

What happens if I say yes, but I change my mind later?

You can leave the research at any time and it will not be held against you.

If you decide to leave the research, you can refuse to take part or stop at any time without stating a reason. Your withdrawal will not affect your access to other medical care to which you would otherwise be entitled. If you decide to leave the research study, you are strongly urged to:

- Tell your study doctor.
- Return to the study doctor for one more visit. You will have an exam and plan for your upper tract urothelial carcinoma.
- Return any unused study supplies (as applicable) to the study doctor, if you have not already done so.

Special care will need to be taken when determining if you need to stop study drug. Your study doctor will supervise any discontinuation of the study drug with your health as the first priority. Your taking part in this study may be terminated at any time by a) your study doctor, b) the Sponsor UroGen, c) FDA, or d) the Institutional Review Board (IRB) which is a review group that gives approval to your study doctor to conduct this study, and other appropriate regulatory agencies. You may be removed from the study for various other administrative and/or medical reasons and this can be done without your consent.

Your study doctor may withdraw you from the study if it is considered important for your medical safety. If it is discovered that you did not give an accurate medical history or did not follow the instructions for the study given by your study doctor, you may be taken off the study at any time. Other reasons your study doctor may withdraw you from the study include: you need additional medication, you or your partner becomes pregnant, you do not consent to continue in the study after being told of changes in the research that may affect you, or for any other reason. If you are taken off the study, you will no longer receive the study drug.

If you decide to stop receiving the study treatment prior the 6th instillation, the investigator will ask you to continue being in the study up to the PDE visit. In the event that you didn't complete the study treatment, but have a Complete Response to the treatment, you will be advised to continue with the follow-up visits as long as possible, even without having the study treatment. But in consultation with your study doctor, it is possible that you may be re-considered for continuing monthly instillations until 1 year follow-up or disease recurrence. The data collected about you up to the point of withdrawal will remain a part of the study and may not be removed from the study database.

If you stop being in the research, already collected data may not be removed from the study database.

For IRB Use

You will be asked whether the investigator can collect data from your routine medical care. If you agree,

this data will be handled the same as research data.

Is there any way being in this study could be bad for me?

RISKS

Your condition may or may not improve and could even get worse if you take part in this study. The Study Doctor and study staff will monitor you for any signs of new or unexpected side effects. Please tell your Study Doctor if you have a side effect or feel unwell while in this study. Contact your Study Doctor immediately if you experience a side effect that concerns you or are unable to perform your daily functions.

Each treatment may have possible side effects. For example, there might be gel-related effects, Mitomycin C-related effects and catheter insertion related effects. Many side effects go away shortly after treatment is stopped, but in some cases, side effects may be serious, long-lasting or permanent, and may even result in hospitalization.

COMMON SIDE EFFECTS FOR MITOMYCIN C AND HYDROGEL COMBINED
Based upon limited information regarding upper urinary tract irrigation with Mitomycin C and gel (based on data from 18 compassionate treatments of upper tract urothelial carcinoma):

The following were reported more than once as probably or possibly related to study drug:

- Allergic Reaction (rash on the palms, or itching of the skin)
- Painful or difficult urination
- Urinary retention
- Urinary incontinence
- Weakness/ Fatigue
- Fever/chills
- Aggravation of kidney failure (if you have a history of kidney failure)
- Lower white blood cell count
- Nausea

Apart from the above, any side effect mentioned in the information leaflet of Mitomycin C may appear during the study.

Regarding Mitomycin C-related side effects, please note:

- Mytomycin C may cause burning sensation in the ureter, hand skin exfoliation (removal of dead skin cells), blood count changes, inflammation of the organ, soreness/pain in the area, soreness of the skin in the area around the openings of the urethra.
- Mitomycin C can have also some side effects, including cystitis (bladder infection), frequent and / or painful urination, night-time urination or blood in the urine, allergic reactions in form of rashes or erythema (redness of the skin or painful itching) of a portion of the skin (i.e. palms and feet) or of the entire skin surface, contact dermatitis, generalized exanthemas (skin breakouts), skin peeling on the palms with/without generalized rash.

For IRB Use

ANTICIPATED GEL (BY ITSELF) RELATED SIDE
EFFECTS Common:
When the when the Study drug is cold it is in a liquid state, but it will solidify once warmed to body temperature following instillations into the target organ. When the hydrogel arrives to the target organ

(kidney, ureter), contact with the cold hydrogel can cause muscle contractions in the following locations:

- Bladder
- Upper urinary tract (kidney, ureters)

If experienced, these contractions are not dangerous

Rare:

- Lower urinary tract obstruction- A blockage of the urinary tract might occur that impairs urine flow. If the liquid gel happens to slip further down in to the urinary tract (urethra) before solidifying, this could block the passage of urine. However this can be easily fixed by removing the gel. It is noted that this side effect has never occurred.
- Upper urinary tract obstruction which occurred once due to violation of treatment instructions.

Following are some side effects that were noticed and are mentioned despite of their rarity:

- "Cool" flank sensation due to low temperature of instilled drug
- Narrowing of previous tumor implantation site (resulting from either drug effect on the tissue or mechanical injury of tumor location)
- Bladder inflammation
- Upper tract inflammation (due to treatment drug)
- Frequency of urination and the swelling of the kidney due to a build-up of urine

****ANTICIAPTED MITOGEL RELATED PHENOMENA (NOT A SIDE EFFECT)****

- Purple colored urine
- Urination of gel particles

OTHER COMMON ADVERSE EVENTS

ALLERGIC REACTIONS
Occasionally, people have allergic reactions (including life-threatening reactions) when taking any medication. Symptoms of any allergic reaction can include: rash, hives, itching and/or trouble breathing, closing of the throat, swelling of the lips, tongue or face, and rarely death.
Immediately get emergency medical care if you have any of these symptoms. Stop taking your study drugs and let your study doctor know.

In general, allergic reactions to medicines are more likely to occur in people who already have allergies. If you are allergic to other drugs, foods or things in the environment, such as dust or grass, you should let your study doctor know. Also, if you have asthma, let your study doctor know.

SODIUM BICARBONATE (BAKING SODA)
Sodium bicarbonate (baking soda) is generally well tolerated. However, high doses may cause headache, nausea or irritability. If any of these effects continue or become bothersome, inform your study doctor.

BLOOD DRAWS
Drawing blood from a vein may cause local pain, bruising, occasional lightheadedness, fainting, and very rarely, infection at the site of the blood draw. Frequent blood collection may cause anemia (low red blood cell count), which may create a need for blood transfusions, but in this study the amount of blood drawn is limited and the risk for blood transfusion is extremely rare.

CATHETER INSERTION/NEPHROSTOMY TUBE PLACEMENT

Catheter insertion to the upper tract is well-practiced worldwide and widely used for many procedures, like during kidney stone removal. The following are the known side effects of this procedure, including those evident in the upper urinary tract instillations:

- Pain along the side(s)
- Mild pressure/fullness at medication instillation site
- Acute infection of the kidney
- Germs in urine without clinical signs
- Visible blood in urine
- Friction trauma to the urethra, ureter or kidney due to the presence of the scope, or catheter
- A tear or hole made in the urethra or bladder due to placement of the catheter
- Lower urinary tract symptoms, consisting of increased frequency and urgency of urination, painful urination, and/or excessive urination at night.
- A urinary tract infection due to the presence of the catheter

RADIOLOGICAL RISKS

This study involves a radiation exposure that is higher than other diagnostic tests using ionizing radiation. The exposure to radiation from this study might result in a slight increase in cancer risk in normal healthy individuals. However, since you already have cancer, a risk estimate cannot be accurately determined.

CT (Computed tomography) Scan
Risks and complications of a CT scan are very low but may include:

• An allergic reaction to the dye (contrast material).
• If you have diabetes or take metformin (Glucophage), the dye may cause problems. Your doctor will tell you when to stop taking metformin and when to start taking it again after the test so you will not have problems.

For IRB Use

Fluoroscopy
The probability that a person will experience these effects from a fluoroscopic procedure is statistically very small.

MRI Risks
An MRI scan is a painless radiology technique that has the advantage of avoiding x-ray radiation exposure. There are no known side effects of an MRI scan. During the MRI scan, patient lies in a closed area inside the magnetic tube. Some patients can experience a claustrophobic sensation during the procedure. If have history of claustrophobia please relate this to the treating urologist, as well as the radiology staff.

If you have any metallic materials within the body please notify your treating urologist prior to the examination or inform the MRI staff. Metallic chips, materials, surgical clips, or foreign material (artificial joints, metallic bone plates, or prosthetic devices, etc.) can significantly distort the images obtained by the MRI scanner. If you have a heart pacemakers, metal implants, or metal chips or clips in or around the eyeballs you should not be scanned with an MRI because of the risk that the magnet may move the metal in these areas. If you have artificial heart valves, metallic ear implants, bullet fragments, and chemotherapy or insulin pumps you should not have MRI scanning.

CYSTOSCOPY/URETEROSCOPY
Cystoscopy is generally a safe procedure. Serious complications are rare. As with any surgery, there is the risk of infection, bleeding, and complications from the anesthesia. In all but the simplest procedures, antibiotics are used before the surgery to reduce the incidence of urinary tract infection.

BIOPSY RISKS
Possible side effects from a biopsy include pain, stinging, bruising and/or swelling at the site of biopsy. It is common to have some soreness around the site and some mild pain in or around your kidney/side (flank). Less common side effects include bleeding from the area, infection and moderate or severe pain.
Having biopsies performed in the upper urinary tract may cause pain, local bruising, bleeding, redness, swelling, and/or infection at the site of the biopsies. An allergic reaction to the anesthetic may occur. A scar may form at the biopsy site.

PRIVACY RISKS
There may also be risks to your privacy. The Researchers will store study records and other information about you in a secure location and will grant access only to those with a need to know. However, just like with other personal information kept by your health care providers, your banks, and others, even these safeguards cannot guarantee absolute protection of the data. If private information gets into the wrong hands, it can cause harm. Although rare, there are reported cases of breaches that have resulted in discrimination in insurance or employment.

UNKNOWN/UNEXPECTED RISKS AND DISCOMFORTS
In addition to the risks listed above, there are risks that are not known or do not happen often when subjects take these study drugs, including severe or life-threatening allergic reactions, interactions

between study drugs, or interactions with another medication. You will be informed in a timely manner, both verbally and in writing of any new information, findings or changes to the way the research will be done that might influence your willingness to continue to take part in this study.

PREGNANCY AND BREAST-FEEDING

The effects of MitoGel™ on an unborn baby or a nursing infant are not known, so **extreme care must be taken to avoid pregnancy in female subjects during this study and for up to six (6) months following completion of study treatment and/or in female partners of male subjects during this study and for up to six (6) months following completion of study treatment.**

The use of Mitomycin during pregnancy is known to increase the risk of birth defects and miscarriage. Extreme care must be taken to avoid pregnancy in female patients during this study.

If you are a woman who is pregnant or a female with the intent of becoming pregnant or a female who is currently nursing (breastfeeding) a child, you cannot be in this study. If you are a man whose partner is currently pregnant, you cannot be in this study.

You must protect yourself or your partner from becoming pregnant before, during, and after the study. Women, and men with female partners capable of becoming pregnant, must use effective methods of birth control. Your study doctor will need to document what type(s) of birth control you are using.

Other unknown side events could occur to you or your baby (embryo, fetus) should you become pregnant during the time you participate in the study or after you have completed the study.

Women only:
If you are sexually active and able to become pregnant, you must agree to complete abstinence or use one of the birth control methods listed below, **in addition to a male partner who correctly uses a condom**, starting from 3 weeks prior to the Day 1 visit and for a minimum of six (6) months after last dose of study drug or longer as directed by your study doctor.

Acceptable birth control methods (in addition to a male partner who correctly uses a condom) include:

- an intrauterine device (IUD) with a failure rate of <1% per year
- female barrier method: cervical cap or diaphragm with spermicidal agent
- tubal sterilization (having your tubes tied)
- vasectomy in male partner
- implants of levonorgestrel
- injectable progesterone
- oral contraceptives (either combined or progesterone only)
- contraceptive vaginal ring
- transdermal contraceptive patch

You must tell your study doctor immediately if you become pregnant or think you have become pregnant while in this study and for a minimum 30 days after stopping study drug or for as long as you have been

directed by your study doctor to use contraception. The study doctor will tell you about the possible risks to your unborn child and options available to you. In the event of a positive urine pregnancy result, you will be instructed to stop study drugs immediately (if applicable) and return to the clinic as soon as possible for a serum (blood) pregnancy test. The pregnancy will be followed to its outcome. The outcome, including any premature termination, must be reported to the Sponsor.

You should be counseled and followed by your own doctor. As the risk to the unborn baby is unknown, it is recommended you seek medical supervision from your own doctor during the pregnancy and for the baby after it is born. Neither the study Sponsor nor the study doctor will be responsible for providing routine medical care relating to the pregnancy.

Men only:
If you have a female partner who can become pregnant, you must use a condom from baseline and your female partner must agree to use 1 of the methods of birth control listed above from screening until a minimum of six (6) months after your last dose of study drug or longer if directed by your study doctor.

If you cause your female sex partner to become pregnant while you are in the study and within six (6) months after your last dose of study drug, the study drug may harm an unborn baby. If you have a female partner who becomes pregnant or suspects that she has become pregnant while you are in the study and within six (6) months after your last dose of study drug, you will be required to notify your study doctor immediately. As the risk to your partner and unborn baby are not known, it is recommended for your partner to receive appropriate prenatal care. If you agree, your partner will be asked to sign a consent form to allow disclosure of medical information about the pregnancy.

Your study doctor may need to disclose to your partner details of this study and your taking part in it. The Study Sponsor and the study doctor will not be responsible for the costs related to the pregnancy, delivery, or care of your child.

Male subjects must also agree not to donate sperm to a sperm bank for the purposes of conception from screening until six (6) months after the last dose of study drug.

Please note: Hormonal birth control may be more effective when taken for at least 3 months. Even if you and your female partner use a medically proven birth control method, you could still cause your partner to become pregnant.

Please share this information with your partner.

Will being in this study help me in any way?

We cannot promise any benefits to you or others from your taking part in this research. However, possible benefits include:

- The tumors might disappear and subsequently no need for surgical removal would exist.
- Additionally, in case of reduction of the number or size of the lesion(s) in comparison with baseline, the following surgical removal would be more limited;

For IRB Use

- A more efficient preventive effect of tumor recurrence might be proven.

From what has been shown so far in the Sponsor trials for urothelial carcinoma in the bladder, Mitomycin C appears to have a high potential for tumor removal, with more than 70% of the patients showing complete response to the treatment, and more than 80% of the patients showing either complete response or partial response. The results suggest that the treatment appears to be generally safe and there has been no indication of a significant rise in risk related to the Mitomycin C dose used.

The information generated by your participation may help future patients with Low Grade Upper Urinary Urothelial Carcinoma (UTUC).

However, there is no guarantee that you will receive personal benefit from taking part in this study. The study drugs are not expected to cure you of urothelial cancer. However, clinical research studies such as this are a way for doctors to determine if a drug is useful in fighting a disease. By taking part in this study, you and the Sponsor, UroGen Pharma Ltd. , may benefit if the study drugs are effective in treating urothelial cancer**.** Your taking part in this study may benefit the community, scientists and doctors who work with urothelial cancer by providing increased knowledge and information about the treatment of your disease. By taking part in this study, you will have close medical monitoring of your health condition by blood tests and other evaluations during clinic visits.

What happens to the information collected for the research?

Efforts will be made to limit use or disclosure of your personal information, including research study and medical records, to people who have a need to review this information. We cannot promise complete confidentiality. Organizations that may inspect and copy your information include the IRB the Food and Drug Administration (FDA), the Sponsor (UroGen Pharma, Ltd.), or people who work for or with the Sponsor, the University of California representatives responsible for the management or oversight of this study and to regulatory authorities in other countries.

During your participation in this research, data will be collected about you. Your full identity will not be on any of the study documents or samples taken and kept by the sponsor for the study. Full date of birth will only be collected if medically relevant to this study, unless the use of full date of birth is legally restricted in the country. Only a unique patient number for the study will link the data or samples to you. These data may contain your gender and race, as well as any medical and scientific data required by the study. The de-identified data and any specimens, such as blood or tissue that are taken from you for this study, they will become the property of the University of California. The specimens may be used in this research, may be used in other research, and may be shared with other organizations. The specimens could lead to discoveries or inventions that may be of value to the University of California or to other organizations. Under state law you do not have any right to money or other compensation stemming from products that may be developed from the specimens.

Records identifying you will be kept confidential and, to the extent permitted by applicable laws and/or regulations, will not be made publicly available. In the event of any publication regarding this study, your identity will remain confidential. The sponsor and those who work for or with the sponsor, the IRB and national and international Regulatory Authorities will be able to see your personal medical files atthe study site, which contain your full name. All people involved in the study have the duty of confidentiality.

For IRB Use

The data or samples taken for this study may be sent to other countries in the world to be studied, for submission to their Regulatory Authorities and/or for publication. The data protection laws in these countries can be different, but all the parties involved in this process have a duty to protect your identity and use the data or samples for legitimate healthcare purposes only. If your data or samples are sent to third parties, all appropriate measures will be taken to protect your data or samples. If the data is published, it will be presented in a way so that it will not allow for you to be personally identified.

Representatives from government agencies, including the U.S. Food and Drug Administration

("FDA"), institutional review boards, the Sponsor and/or the Sponsor's authorized representatives may need access to your original medical records and study records for the purpose of checking data collected for the study. By signing this consent form, you authorize this access. Additional studies may be done by bringing together anonymous information from this study with information from other studies. By signing this form, you give consent for this activity.

By signing this consent form you agree that you will not be able to have access to your personal health information related to this study until the study is over. This is done to maintain the scientific integrity of the study. Your information will be available should an emergency arise that would require the treating physician to know this information in order to best treat you. After the study is complete, you can obtain access to your information through your Study Doctor.

The Sponsor, monitors, auditors, the IRB, the Food and Drug Administration will be granted direct access to your research records to conduct and oversee the study. We may publish the results of this research. However, we will keep your name and other identifying information confidential.

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.

If we access protected health information (e.g., your medical record), you will be asked to sign a separate form to give your permission. Your medical records may become part of the research record. If that happens, your research records may be looked at by the sponsor of this study and government agencies or other groups associated with the study. They may not copy or take your personal health information from your medical records unless permitted or required by law.

Federal law provides additional protections of your medical records and related health information. These are described in the UC Davis Health System Notice of Privacy Practices (http://www.ucdmc.ucdavis.edu/compliance/pdf/notice.pdf) and in an attached document.

Can I be removed from the research without my OK?

The person in charge of the research study or the sponsor can remove you from the research study without your approval. Possible reasons for removal include but are not limited to, not attending study visits, and not following patient responsibilities listed on page 16 of this document.

We will tell you about any new information that may affect your health, welfare, or choice to stay in the research.

For IRB Use

What else do I need to know?

This research is being funded by UroGen Pharam, Ltd., also called the sponsor. Sponsors may change or be added.
UC Davis is being paid to conduct this study, but the study doctor and research staff have not received any direct income from the sponsor.

You or your health plan will be billed for the costs of routine medical care you receive during the study. These costs may include operating room fees, pharmacy charges, treatments, hospitalization, scans, etc. You will be expected to pay for the usual deductibles and co-payments, and for any routine care that is not covered.

For more information about possible costs, please contact the research team. The research team can follow UC Davis Uninsured Non-Emergency Estimate Policy (Policy ID 1883) to work with their department and Decision Support Services to get you a cost estimate.

It is important that you promptly tell the person in charge of the research if you believe that you have been injured because of taking part in this study. If you are injured as a result of being in this study, the University of California, Davis will provide necessary medical treatment. Depending on the circumstances, the costs of the treatment may be covered by University or the study sponsor or may be billed to your insurance company just like other medical costs. The University and the study sponsor do not normally provide any other form of compensation for injury. For more information about compensation, you may call the IRB Administration at (916) 703-9151 or email at IRBAdmin@ucdmc.ucdavis.edu.

You will not be compensated for taking part in this study.

The results of this study, including specimens collected, may have commercial value to the sponsors, UC Davis, and/or the researchers. You will have no legal or financial interest in any commercial development resulting from the research or from the information or materials collected.

Note: By signing this informed consent, you will allow your Urologist to provide your safety data to UroGen for an additional 2 (two) years after this trial is over.

For IRB Use

Signature Block for Capable Adult

Your signature documents your permission to take part in this research.

Signature of subject	Date
Printed name of subject	
Signature of person obtaining consent	Date
Printed name of person obtaining consent	

For IRB Use