UroGen Highlights New Real-World Safety Data Published in The British Journal of Urology International That Showed a Low Rate of Ureteral Stenosis When Antegrade Administration of JELMYTO® was Used in Patients with Upper Tract Urothelial Carcinoma

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-- 32-patient, multi-center study showed 9% occurrence of ureteral stenosis and 10% discontinuation rate
-- All three stenosis patients were treated without later recurrence or chronic stenosis

PRINCETON, N.J.--(BUSINESS WIRE)--Nov. 14, 2022-- UroGen Pharma Ltd. (Nasdaq: URGN), a biotech company dedicated to developing and commercializing innovative solutions that treat urothelial and specialty cancers, today highlights results from a retrospective multi-center study of 32 patients evaluating the safety of antegrade administration of *JELMYTO* (mitomycin) for pyelocalyceal solution via percutaneous nephrostomy tube for the treatment of patients with upper tract urothelial carcinoma (UTUC). The study titled, *"Antegrade Administration of Mitomycin Gel for UTUC via Percutaneous Nephrostomy Tube: A Multi-Institutional Retrospective Cohort Study,"* provides additional real-world evidence of a favorable safety and tolerability profile for JELMYTO when administered via percutaneous nephrostomy tube and is published in *The British Journal of Urology International,* November Issue.

This retrospective study assessed the safety and feasibility of antegrade administration of JELMYTO via a percutaneous nephrostomy tube (PCNT) in 32 patients from four institutions. Each patient received at least one dose of JELMYTO via PCNT for UTUC, 29 of whom completed induction (at least 5 of 6 doses) and underwent primary disease evaluation (PDE) at a median 17 weeks after the last dose of therapy. At a median follow-up of 15 months following initiation of induction therapy, ureteral stenosis (defined as a discrete narrowing of the ureter on direct visual ureteroscopy, or a constriction identified on retrograde pyelogram at the time of ureteroscopy that required dilation or stenting to pass a ureteroscope for upstream visualization) occurred in three (9%) of patients. None of these patients had recurrent stenosis at a median 16 months follow- up. Other adverse events included fatigue (27%), flank pain (19%), urinary tract infection (12%), sepsis (8%), and hematuria (8%). No patient had impaired renal function during follow-up and there were no treatment-related deaths. Seventeen patients (59%) had no evidence of disease at PDE and had not recurred at a median follow-up of 13 months post induction.

"We found that antegrade administration of JELMYTO via a nephrostomy tube offered a low rate of ureteral stenosis and a favorable safety and tolerability profile overall," said Kyle Rose, M.D., Urologic Oncology Fellow at Moffitt Cancer Center in Tampa, Fla., and study investigator. "This study adds to the evidence that this form of administration is beneficial in many ways, including the ability to treat the elderly without the use of anesthesia, which can have negative cumulative effects when used repetitively."

In both retrograde and antegrade approaches, JELMYTO can be administered as an outpatient procedure in the clinic. Retrograde administration requires administration by a physician via a ureteral catheter which requires fluoroscopic guidance. Antegrade administration may be performed by trained nursing professionals under clean rather than sterile conditions and does not require fluoroscopy once tube placement is confirmed via nephrostogram at the first instillation.

"JELMYTO is approved for antegrade and retrograde administration in patients with LG-UTUC, which gives physicians the added convenience of choosing a method that works best for them and their patients," said Mark Schoenberg, Chief Medical Officer, UroGen. "Retrograde administration was the only method used in the pivotal OLYMPUS trial. Therefore, UroGen is pleased that this study adds to the growing body of real-world evidence demonstrating that antegrade administration of JELMYTO is a feasible alternative for patients with LG-UTUC."

About the Retrospective Study

In this multi-center study, patients undergoing antegrade administration of JELMYTO via PCNT were retrospectively included for analysis from four tertiary referral centers between 2020 and 2022. The primary outcome was safety profile graded by Common Terminology Criteria for Adverse Events (v5.0). Post-therapy disease burden was assessed by primary disease evaluation (PDE) via ureteroscopy. Thirty-two patients received at least one dose of JELMYTO via PCNT for UTUC, 29 of whom completed induction and underwent PDE. Thirteen (41%) patients had residual tumor present prior to induction therapy. At a median follow up of 15 months following first dose of induction therapy, ureteral stenosis occurred in 3 (9%) patients, all of which were treated without later recurrence or chronic stenosis. Other adverse events included fatigue (27%), flank pain (19%), UTI (12%), sepsis (8%), and hematuria (8%). No patients had impaired renal function during follow up and there were no treatment related deaths. Seventeen patients (59%) had no evidence of disease at PDE and had not recurred at a median follow up of 13 months post induction.

Limitations of this study include the retrospective nature and sample size. Some complications and side effects of the antegrade approach were contingent on patient reporting, and thus may be under-reported. Ureteral stenoses were noted incidentally at the time of PDE, and no patients presented with obstructive symptoms. There is a need for larger studies with longer follow-up to study more conclusively any potential advantages of antegrade JELMYTO administration when compared to retrograde instillation.

About the Pivotal OLYMPUS Study

OLYMPUS (Optimized DeLiverY of Mitomycin for Primary UTUC Study) was an open-label, single-arm Phase 3 clinical study of UGN-101 JELMYTO (mitomycin) for pyelocalyceal solution, to evaluate the safety, tolerability and tumor ablative effect of JELMYTO in patients with low-grade Upper Tract Urothelial Cancer UTUC (LG UTUC). Seventy-one patients were treated at clinical sites across the United States and Israel. Study participants were treated with six weekly instillations of JELMYTO administered via a standard catheter. Four to six weeks following the last instillation, patients underwent a Primary Disease Evaluation (PDE) to determine Complete Response (CR), the primary endpoint of the study. PDE involved a ureteroscopy and wash cytology, a standard microscopic test of cells obtained from the urine to detect cancer and for cause biopsy. Patients who achieved a CR at the PDE timepoint were eligible for the maintenance phase of the trial, during which they could receive monthly maintenance instillations for up to 12 months and were assessed to determine the durability of response with JELMYTO.

In the OLYMPUS study, data was generated for the retrograde administration of JELMYTO. In that study, population ureteric obstruction was reported in 58% (n=41) of patients receiving JELMYTO, including 17% (n=12) of patients who experienced Grade 3 obstruction.

About LG UTUC

LG UTUC is a rare disease managed by endoscopic methods and radical nephroureterectomy. Endoscopic resection and laser ablation attempt to preserve the kidney, though there is a high risk of recurrence that may eventually necessitate removal of the kidney. Although kidney removal is the gold standard for treatment of high-grade UTUC, it may be over-treatment in LG UTUC, as kidney removal offers similar five-year survival as kidney-sparing procedures but is associated with significant morbidity. JELMYTO is efficacious as a primary chemoablative therapy in patients with LG UTUC.

About JELMYTO®

JELMYTO® (mitomycin) for pyelocalyceal solution is a mitomycin-containing reverse thermal gel containing 4 mg mitomycin per mL gel indicated for primary chemoablative treatment of LG UTUC in adults. It is recommended for primary treatment of biopsy-proven LG UTUC in patients deemed appropriate candidates for renal-sparing therapy. JELMYTO is a viscous liquid when cooled and becomes a semi-solid gel at body temperature. The drug slowly dissolves over four to six hours after instillation and is removed from the urinary tract by normal urine flow and voiding. It is approved for administration in a retrograde manner via ureteral catheter or antegrade through nephrostomy tube. The delivery system allows the initial liquid to coat and conform to the upper urinary tract anatomy. The eventual semisolid gel allows for chemoablative therapy to remain in the collecting system for four to six hours without immediately being diluted or washed away by urine flow.

APPROVED USE FOR JELMYTO

JELMYTO® is a prescription medicine used to treat adults with a type of cancer of the lining of the upper urinary tract including the kidney called low-grade Upper Tract Urothelial Cancer (LG-UTUC).

IMPORTANT SAFETY INFORMATION

You should not receive JELMYTO if you have a hole or tear (perforation) of your bladder or upper urinary tract.

Before receiving JELMYTO, tell your healthcare provider about all your medical conditions, including if you:

- are pregnant or plan to become pregnant. JELMYTO can harm your unborn baby. You should not become pregnant during treatment with JELMYTO. Tell your healthcare provider right away if you become pregnant or think you may be pregnant during treatment with JELMYTO.

Females who are able to become pregnant: You should use effective birth control (contraception) during treatment with JELMYTO and for 6 months after the last dose.

Males being treated with JELMYTO: If you have a female partner who is able to become pregnant, you should use effective birth control (contraception) during treatment with JELMYTO and for 3 months after the last dose.

- are breastfeeding or plan to breastfeed. It is not known if JELMYTO passes into your breast milk. Do not breastfeed during treatment with JELMYTO and for 1 week after the last dose.
- **Tell your healthcare provider if you take water pills (diuretic).**

How will I receive JELMYTO?

- Your healthcare provider will tell you to take a medicine called sodium bicarbonate before each JELMYTO treatment.
- You will receive your JELMYTO dose from your healthcare provider 1 time a week for 6 weeks. It is important that you receive all 6 doses of JELMYTO according to your healthcare provider's instructions. If you miss any appointments, call your healthcare provider as soon as possible to reschedule your appointment. Your healthcare provider may recommend up to an additional 11 monthly doses.
- JELMYTO is given to your kidney through a tube called a catheter.
- During treatment with JELMYTO, your healthcare provider may tell you to take additional medicines or change how you take your current medicines.

After receiving JELMYTO:

- JELMYTO may cause your urine color to change to a violet to blue color. Avoid contact between your skin and urine for at least 6 hours.
- To urinate, **males and females should sit** on a toilet and flush the toilet several times after you use it. After going to the bathroom, wash your hands, your inner thighs, and genital area well with soap and water.
- Clothing that comes in contact with urine should be washed right away and washed separately from other clothing.

JELMYTO may cause serious side effects, including:

- **Swelling and narrowing of the tube that carries urine from the kidney to the bladder (ureteric obstruction).** If you develop swelling and narrowing, and to protect your kidney from damage, your healthcare provider may recommend the placement of a small plastic tube (stent) in the ureter to help the kidney drain. Tell your healthcare provider right away if you develop side pain or fever during treatment with JELMYTO.
- **Bone marrow problems.** JELMYTO can affect your bone marrow and can cause a decrease in your white blood cell, red blood cell, and platelet counts. Your healthcare provider will do blood tests prior to each treatment to check your blood cell counts during treatment with JELMYTO. Your healthcare provider may need to temporarily or permanently stop JELMYTO if you develop bone marrow problems during treatment with JELMYTO.

The most common side effects of JELMYTO include: urinary tract infection, blood in your urine, side pain, nausea, trouble with urination, kidney problems, vomiting, tiredness, stomach (abdomen) pain.

You are encouraged to report negative side effects of prescription drugs to the U.S. Food and Drug Administration. Visit www.fda.gov/medwatch or call 1-800-FDA-1088. You may also report side effects to UroGen Pharma at 1-855-987-6436.

Please see JELMYTO Full Prescribing Information, including the Patient Information, for additional information.

About UroGen Pharma Ltd.

UroGen is biotech company dedicated to developing and commercializing innovative solutions that treat urothelial and specialty cancers because patients deserve better options. UroGen has developed RTGel™ reverse-thermal hydrogel, a proprietary sustained release, hydrogel-based platform technology that has the potential to improve therapeutic profiles of existing drugs. UroGen's sustained release technology is designed to enable longer exposure of the urinary tract tissue to medications, making local therapy a potentially more effective treatment option. UroGen's first commercial product JELMYTO (mitomycin) for pyelocalyceal solution, and investigational treatment UGN-102 (mitomycin) for intravesical solution for patients with low-grade non-muscle invasive bladder cancer, are designed to ablate tumors by non-surgical means. UroGen is headquartered in Princeton, NJ with operations in Israel. Visit www.urogen.com to learn more or follow us on Twitter, @UroGenPharma.

Forward-Looking Statements

This press release contains forward-looking statements as that term is defined in the Private Securities Litigation Reform Act of 1995, including, without limitation, statements regarding the potential benefits of antegrade administration as compared to retrograde instillation, including the ability to treat without the use of anesthesia. These statements are subject to a number of risks, uncertainties and assumptions, including, but not limited to: results from initial reports of the antegrade administration of JELMYTO in the publication may not be indicative of results that may be observed in future clinical practice; and potential safety and other complications from the antegrade administration of JELMYTO. In light of these risks and uncertainties, and other risks and uncertainties that are described in the Risk Factors section of UroGen's Form 10-Q filed with the SEC on November 10, 2022 and other filings that UroGen makes with the SEC from time to time (which are available at http://www.sec.gov), the events and circumstances discussed in such forward-looking statements may not occur, and UroGen's actual results could differ materially and adversely from those anticipated or implied thereby. Any forward-looking statements speak only as of the date of this press release and are based on information available to UroGen as of the date of this release.

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