UroGen Pharma Announces Encouraging Results from a Phase 1 Dose-Escalation Study Evaluating UGN-301 in Non-Muscle Invasive Bladder Cancer

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- UGN-301 was tolerated across all dose levels, with no dose-limiting toxicities or adverse events leading to treatment discontinuation
- UGN-301 formulated in a reverse thermal gel allowed sustained exposure in the bladder
- Some patients receiving UGN-301 (zalifrelimab) intravesical solution showed clinical activity at the week 12 disease assessment
- Data presented at the 2025 American Urological Association Annual Meeting in Las Vegas, Nevada

PRINCETON, N.J.--(BUSINESS WIRE)--Apr. 26, 2025-- UroGen Pharma Ltd. (Nasdaq: URGN), a biotech company dedicated to developing and commercializing innovative solutions that treat urothelial and specialty cancers, today announced encouraging safety data from the Phase 1 dose-escalation study for UGN-301 (zalifrelimab) intravesical solution, an investigational drug in development for the treatment of recurrent non-muscle invasive bladder cancer (NMIBC).

"The early safety profile and clinical activity results from this study are encouraging," said Jay Raman, M.D., Professor and Chair of Urology, and Professor of Surgery, Penn State Cancer Institute, PA. "This innovative approach of localized drug delivery combined with immune modulation merits additional investigation in the treatment of non-muscle invasive bladder cancer."

The multi-part clinical study included up to 30 patients per arm, aimed to assess safety and determine the recommended Phase 2 dose of UGN-301 as monotherapy and in combination with other agents. In the monotherapy arm, dose escalation continued to the maximum feasible dose. No dose-limiting toxicities and no treatment-emergent adverse events leading to treatment discontinuation were observed. This study also demonstrated that local delivery of UGN-301 formulated in our proprietary reverse thermal gel (*RTGel*®) allowed sustained exposure of zalifrelimab in the bladder with limited systemic exposure, which mitigated the risk of systemic immune-related toxicities associated with CTLA-4 inhibition.

With respect to clinical activity observed in the trial, among evaluable patients who received UGN-301, 46% (6 of 13) of those with Ta/T1 disease and 33% (2 of 6) of those with carcinoma in situ (CIS) ± Ta/T1 disease were recurrence-free or had achieved a complete response at week 12. Notably, 60% (3 of 5) of patients with Ta/T1 disease treated with 300 mg continued to remain recurrence-free at the 15-month disease assessment, including one patient with high-grade T1 disease. In the 500 mg cohort, 25% (1 of 4) of patients with CIS disease and 33% (1 of 3) of patients with Ta/T1 disease remained disease-free at six months, both of whom are still active participants in the study.

These findings highlight the potential of UGN-301 as a targeted treatment for NMIBC with an acceptable safety profile. Presentation of data from the combination arms is planned for later this year.

"Our hypothesis is that UGN-301's unique formulation could potentially offer the dual benefits of maximizing therapeutic activity while minimizing systemic side effects, a key challenge in cancer immunotherapy," said Mark Schoenberg, Chief Medical Officer, UroGen. "Although this requires additional clinical investigation, we are encouraged by the potential of UGN-301 as an investigational treatment for patients with recurrent NMIBC."

About Non-Muscle Invasive Bladder Cancer and High-Grade Disease

In the U.S., bladder cancer is the second most common urologic cancer in men. Bladder cancer primarily affects older populations with increased risk of comorbidities, with the median age of diagnosis being 73 years. High-grade non-muscle invasive bladder cancer (HG-NMIBC) is a serious and potentially life-threatening form of bladder cancer that remains confined to the inner layers of the bladder wall but exhibits aggressive behavior and a higher risk of progression. In the U.S., HG-NMIBC accounts for approximately 30–40% of all newly diagnosed NMIBC cases. Patients with HG-NMIBC face a significantly elevated risk of recurrence and progression to muscle-invasive disease, necessitating close surveillance and aggressive treatment. The standard of care includes complete transurethral resection of bladder tumor, often followed by intravesical therapy such as Bacillus Calmette-Guérin (BCG). However, BCG has a treatment failure rate of approximately 40-50%, leaving patients with limited treatment options short of radical cystectomy. Given the high recurrence and progression rates, HG-NMIBC presents a substantial clinical and quality-of-life burden. Upon recurrence, which occurs in approximately 70% of patients, the patients undergo another round of BCG therapy with a response rate of approximately 30%.

About UGN-301

UGN-301 is an anti-CTLA-4 monoclonal antibody (zalifrelimab), originally licensed from Agenus Inc. in 2019. It is formulated with *RTGel*, our proprietary reverse-thermal hydrogel, for intravesical administration into the bladder. Intravesical administration of UGN-301 is designed to increase drug concentrations in the bladder without significant systemic exposure, potentially diminishing the systemic toxicity associated with CTLA-4 blockade. UroGen is evaluating UGN-301 in a multi-arm Phase 1 study of UGN-301 as monotherapy and in combination with other agents. The safety of UGN-301 is being evaluated in the monotherapy arm of the study as combination therapy for HG-NMIBC.

About UroGen Pharma Ltd.

UroGen is a 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 the 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. Our first product to treat low-grade upper tract urothelial cancer and investigational treatment UGN-102 (mitomycin) for intravesical solution for patients with low-grade intermediate risk NMIBC 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 X (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 UGN-301, including as a targeted treatment for NMIBC; implications that may follow from the early clinical activity and safety profile observations; UGN-301's innovative approach of localized drug delivery combined with immune modulation meriting additional investigation in the treatment of NMIBC; the potential for UGN-301 to maximize therapeutic activity and minimize systemic side effects for patients with recurrent NMIBC; the potential benefits of the intravesical delivery of UGN-301 using UroGen's *RTGel* proprietary technology; statements regarding our ongoing clinical studies of UGN-301; the estimated patient population and demographics for bladder cancer and HG-NMIBC; the potential of UroGen's proprietary *RTGel* technology to improve therapeutic profiles of existing drugs; and UroGen's sustained release technology making local delivery potentially more effective as compared to other treatment options. Words such as "could," "potential" or other words that convey uncertainty of future events or outcomes to identify these forward-looking statements. These statements are subject to a number of risks, uncertainties and assumptions, including, but not limited to: UroGen's development plans for UGN-301, including in combination with other investigational agents; preliminary results may not be indicative of results that may be observed in the future; the timing and success of clinical trials and potential safety and other complications thereof; unforeseen delays that may impact the timing of progressing clinical trials and reporting data; the ability to obtain regulatory approval within the timeframe expected, or at all; the ability to obtain and maintain adequate intellectual property rights and adequately protect and enforce such rights; complications associated with commercialization activities; the labeling for any approved product; competition in UroGen's industry; the scope, progress and expansion of developing and commercializing UroGen's product candidates; the size and growth of the market(s) therefor and the rate and degree of market acceptance thereof vis-à-vis alternative therapies; UroGen's ability to attract or retain key management, members of the board of directors and other personnel; UroGen's *RTGel* technology may not perform as expected; and UroGen may not successfully develop and receive regulatory approval of any other product that incorporates *RTGel* technology. In light of these risks and uncertainties, and other risks and uncertainties that are described in the Risk Factors section of UroGen's Annual Report on Form 10-K for the year ended December 31, 2024, filed with the SEC on March 10, 2025. 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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