Novel Gene Therapy Shows Three-Fold Improvement in Recurrence-Free Survival in High-Risk, Early-Stage Bladder Cancer Patients Where Current Gold-Standard Treatment Fails

Durable responses in 35 percent of patients reported in Phase II data published in the *Journal of Clinical Oncology*

Schaumburg, IL., [August 24, 2017] – The Society of Urologic Oncology and the Society of Urologic Oncology Clinical Trials Consortium (SUO-CTC) announced today that the *Journal of Clinical Oncology* (JCO) has published results from a Phase II clinical study led by the SUO-CTC demonstrating the potential effectiveness of Instiladrin® (rAD-IFN/Syn3) in patients with high grade, BCG refractory or relapsed Non-Muscle Invasive Bladder Cancer (NMIBC). The paper, titled, "A Phase II, Randomized, Open Label, Parallel Arm Study to Evaluate the Safety and Efficacy of rAD-IFN/Syn3 Following Intravesical Administration in Subjects with High Grade, BCG Refractory or Relapsed Non-Muscle Invasive Bladder Cancer (NMIBC)" can be found on the Journal of Clinical Oncology website at http://ascopubs.org/doi/full/10.1200/JCO.2017.72.3064.

The JCO paper reports durable responses in 35 percent of patients, which represents more than a three-fold improvement in recurrence-free survival compared to Valrubicin, the only agent currently approved for this indication. Instiladrin was well tolerated and no patient discontinued treatment due to a treatment-related adverse event. The data are consistent with a previous Phase I clinical trial. The study was organized and run by SUO-CTC and sponsored by FKD Therapies Oy, Finland (FKD).

"These data are encouraging and hold promise in improving the treatment outcomes for patients with high-risk non–muscle-invasive bladder cancer that persists or recurs despite standard treatment with Bacillus Calmette-Guérin (BCG)," said Colin Dinney, M.D., Professor and Chair of the Department of Urology at The University of Texas MD Anderson Cancer Center (MDACC), and the Principal Investigator of the Phase II study. "Today, such patients have very limited medical options."

Instiladrin is a gene therapy consisting of an adenovirus containing the gene interferon alfa-2b. Instiladrin is given by catheter into the bladder where the virus enters the cells of the bladder wall. Inside the cells, the virus breaks down leaving the active gene to do its work. The cell's internal gene/DNA machinery picks up the gene and translates its DNA sequence, resulting in the cells secreting high quantities of interferon alfa-2b protein, a naturally occurring protein the body uses to fight cancer. This novel gene therapy approach turns the patient's own bladder wall cells into multiple interferon microfactories, enhancing the body's natural defenses against the cancer.

SUO-CTC, has now launched a Phase III registration trial of Instiladrin, sponsored by FKD Therapies, in patients with BCG-unresponsive NMIBC. The trial which opened in 2016, is recruiting across the USA now and is expected to enroll approximately 135 patients at 35 centers.

"If similar efficacy and tolerability are demonstrated in the Phase III trial, Instiladrin, with FDA approval, may represent an effective alternative to radical cystectomy for patients with recurrent

NMIBC where BCG therapy has not been successful," commented Stephen Boorjian, MD, Professor of Urology and Vice Chair of Research for the Department of Urology at the Mayo Clinic in Rochester, Minnesota, and the SUO-CTC's Principal Investigator for the Phase III trial. "As with the Phase II trial, the SUO-CTC will ensure a high-quality study is undertaken in a timely manner for the pivotal evaluation of this promising new approach."

Because of the high risk of progression of BCG-unresponsive NMIBC, and lack of effective therapeutic options, the safest option is cystectomy; however, many patients are understandably reluctant to undergo this procedure. An alternative is second-line chemo therapy, but the only U.S. Food and Drug Administration (FDA)–approved drug for BCG-refractory disease, Valrubicin, provides a durable (12 month) complete response for only about 8-10 percent of patients.

Although IFNα protein is an established anticancer agent, instillation into the bladder has had only limited efficacy against bladder cancer because the drug is cleared from the bladder in a few hours. Interferon-α gene therapy causes the cells lining the bladder to produce high levels of their own IFNα for a protracted period of time, up to 3 weeks, resulting in more extended exposure and an enhanced anti-tumor activity.

About the SUO-CTC

The Society of Urologic Oncology (SUO) developed a clinical trials network in 2008. Created and operated by its members, the Society of Urological Oncology Clinical Trials Consortium (SUO-CTC) is a clinical research investigator network of over 340 members from more than 180 clinical sites in the U.S. and Canada. This national alliance of leading academic and community-based uro-oncologists is committed to furthering urology research. The SUO-CTC is a registered 501c3 not-for-profit corporation and maintains a cooperative relationship with the Society of Urologic Oncology. SUO-CTC pursues clinical trials, in concert with sponsors, to investigate therapeutic interventions which address urological cancers including, but not restricted to bladder cancer, prostate cancer and renal cancer. Together with industry, the SUO-CTC offers enhanced research options for ultimately delivering better quality of life to our patients.

Information for Patients

Details of the Phase III trial can be found on ClinicalTrials.gov and on the Bladder Cancer Advocacy Network website.

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