Inovio Commences Phase 1b/2 bladder cancer trial

PLYMOUTH MEETING, Pa., Oct. 16, 2017 – **Inovio Pharmaceuticals {NASDAQ: INO}** announced initiation of a phase 1b/2 immuno-oncology trial to evaluate Genentech/Roche's atezolizumab (TECENTRIQ®) in combination with Inovio's INO-5401, a T cell activating immunotherapy encoding multiple antigens, and INO-9012, an immune activator encoding IL-12.

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Inovio Pharmaceuticals Begins Phase 1b/2 Cancer Efficacy Trial Combining Its T-cell Immunotherapy with a PD-L1 Checkpoint Inhibitor in Advanced Bladder Cancer

Trial to evaluate Inovio's INO-5401 and Genentech's TECENTRIQ® in patients with metastatic bladder cancer

PLYMOUTH MEETING, Pa., Oct. 16, 2017– Inovio Pharmaceuticals, Inc. **(NASDAQ:INO)** today announced initiation of a phase 1b/2 immuno-oncology trial to evaluate Genentech/Roche's atezolizumab (TECENTRIQ®) in combination with Inovio's INO-5401, a T cell activating immunotherapy encoding multiple antigens, and INO-9012, an immune activator encoding IL-12.

The multi-center, open-label efficacy trial will be managed by Inovio, and Genentech will supply atezolizumab. The trial will evaluate the safety, immune response and clinical efficacy of the combination therapy in approximately 80 patients with advanced bladder cancer, specifically advanced unresectable or metastatic urothelial carcinoma (UC), the most common type of bladder cancer. The majority of the patients to be enrolled in the trial will have previously received and failed to demonstrate meaningful response to an anti-PD-1 or PD-L1 checkpoint inhibitor alone. Thus the study will evaluate potential benefit of a checkpoint inhibitor combined with a DNA-based immunotherapeutic and T cell activator within a bladder cancer patient population with very limited treatment options and poor outcomes. The immunologic analyses accompanying the study will provide further insight into mechanisms of checkpoint inhibition and T cell activation in bladder cancer.

Dr. Joaquim Bellmunt, MD, PhD, Director of Bladder Cancer Center, Dana-Farber Cancer Institute and Associate

Professor, Harvard Medical School, said, “The unmet need for effective treatments for advanced UC patients remains very high even in the midst of approvals of multiple checkpoint inhibitors in this space – as only a small subset of patients respond to these therapies alone. Increasing evidence suggests that combinatorial approaches are needed to improve upon the initial success of checkpoint inhibitors; the benefit to this patient population may be significantly improved when combination therapies that also generate activated T cells are utilized. Furthermore, there is a very high need for effective treatment approaches in checkpoint-refractory patients.”

Dr. J. Joseph Kim**, Inovio’s President and CEO, said,** *“Combining INO-5401 with TECENTRIQ may provide a synergistic therapeutic effect as a result of generating high levels of activated T cells and simultaneously inhibiting PD-L1. Bladder cancer has often been described as an immunogenic tumor, and here our approach is to augment the anti-PD-1/PD-L1 driven efficacy by further enhancing the T cells against the tumor in a cancer antigen-specific manner. We believe we can demonstrate the immense potential of INO-5401 as a universal cancer immunotherapy to treat patients with multiple cancers.”*

Nearly 430,000 new cases of urinary bladder cancer are diagnosed each year worldwide; it accounts for about 165,000 deaths worldwide annually. Advanced unresectable or metastatic UC remains a high unmet medical need as survival remains poor for most patients who experience disease progression or intolerance to treatment during or after platinum-containing chemotherapy. The approval of several checkpoint inhibitors for advanced unresectable or metastatic UC has improved response and survival rates for some patients, however, the majority of patients do not experience meaningful clinical

responses to checkpoint inhibitor monotherapy.

Inovio’s INO-5401, an immunotherapy encoding multiple cancer antigens (HTERT, PSMA, and WT1), is designed to generate and activate T cells to many cancer types including bladder cancer. INO-9012, a DNA-based immune activator encoding IL-12, is designed to amplify and accelerate T cell immune responses to INO-5401. Combining INO-5401/INO-9012 with atezolizumab may provide a synergistic therapeutic effect as a result of generating higher levels of activated T cells and simultaneously inhibiting PD-L1. Atezolizumab is a monoclonal antibody designed to bind with a protein called PD-L1 expressed on tumor cells and tumor-infiltrating immune cells, blocking its interactions with both PD-1 and B7.1 receptors. By inhibiting PD-L1, atezolizumab may enable the activation of T cells.