RX-3117, An Oral Hypermethylating Agent to Treat Advanced Solid Tumors (ST): Interim results from an Ongoing Phase 2a Study in Advanced Urothelial Cancer (aUC)

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Background: RX-3117 is an oral small molecule hypermethylating agent, cyclopentyl pyrimidyl/nucleoside that is activated by uridine cytidine kinase 2. RX-3117 shows efficacy in various xenograft models, including those of gemcitabine resistant bladder cancer. Preliminary data from Stage 2 of a Phase 2a clinical study of RX-3117 as a single agent in subjects with aUC is described below.

Methods: This Phase 2a study (2-stage design, NCT0030067) evaluates the efficacy of RX-3117 in eligible patients (aged ≥ 18 years) with refractory aUC. Primary objectives include safety and efficacy of the recommended Phase 2 dose and schedule identified in the Phase 1 portion of the study. Patients received 700 mg of oral RX-3117 daily for 4 weeks, followed by 1 week off in each 4-week cycle or 4 continuous weeks. The primary endpoint is a ≥20% rate of progression free survival benefit (i.e., proportion of patients with disease for at least 4 months) and/or a 10% of evaluable patients with a partial response or better.

Results: As of October 2017, 17 patients (12 males, 5 females) with aUC were treated with RX-3117. The median age was 66 years, ECOG performance status was 0 to 1 and 53% received ≥ 3 prior therapies. Metastatic disease sites included lung, liver, lymph nodes, and peritoneum. Four patients achieved stable disease for 4 cycles of RX-3117 treatment; one patient received treatment for 168 days and another patient for 301 days. One patient showed tumor shrinkage as measured by RECIST (15.5%) after 4 cycles of RX-3117; another patient showed a 19% tumor reduction after 1 cycle. The most frequent related adverse events were G1 diarrhea (13%), fatigue (13%), nausea (10%), G1/G2 anemia (10%), vomiting (10%) and G3 thrombocytopenia (10%).

Conclusions: RX-3117 is safe and well tolerable and shows preliminary evidence of anti-tumor activity. The study continues to enroll patients with aUC in Stage 2.