A Parallel Arm Phase 1b/2a Study of DKN-01 as Monotherapy or in Combination with Docetaxel for the Treatment of Advanced Prostate Cancer with Elevated DKK1

David R. Wise[1], Srinivasan Yegnasubramanian[2, 3], Jonathan Melamed[2], Fang-Ming Deng[2], Qinghu Ren[2], Luis Chiriboga[3], Michael Haas[3] Heidi Heath[3] Michael Kagey[4], Walter Newman[4], Cynthia A. Sirard[4]

1 Department of Medicine, Laura & Isaac Perlmutter Cancer Center, NYU Langone Medical Center, New York, New York.

2 Department of Pathology, New York University School of Medicine, New York, New York

3 Department of Pathology and DART Experimental Pathology Research Laboratory, NYU Langone Health, 160 East 34th Street, NY, NY 10016

4 Leap Therapeutics, Inc., Cambridge, MA

Background: Dickkopf-1 (DKK1) is a secreted Wnt target gene that contributes to tumor growth and immune evasion. DKK1 is activated by Wnt signaling and is upregulated in non-neuroendocrine AR-negative metastatic CRPC. Targeted inhibition of DKK1 delays prostate cancer growth in pre-clinical models through an NK-cell dependent anti-tumor immune response. DKN-01 is a potent humanized monoclonal antibody (IgG4) with neutralizing activity against DKK1. DKN-01 has been demonstrated to be safe as both a monotherapy and in combination with chemotherapy in other cancer types. This is the first clinical trial testing DKK1 depletion as a treatment for prostate cancer.

Methods: This is an investigator-initiated multicenter, parallel-arm, phase 1b/2a, study of DKN-01 as monotherapy or in combination with docetaxel in patients with advanced mCRPC with elevated DKK1 or pathogenic alteration in a Wnt pathway gene (APC, CTNNB1, RSPO2, RSPO3, AXIN2, AXIN3, RNF43, ZNRF3). All patients must have progressed on prior enzalutamide or abiraterone. Docetaxel naïve patients are eligible for the combination cohort whereas patients who have progressed on or intolerant of docetaxel are eligible for the monotherapy cohorts. Dose escalation and expansion parts will each consist of cohorts in which DKN-01 is combined with docetaxel or in which DKN-01 is administered as monotherapy. The primary endpoint of the phase 1b cohorts is the determination of DLTs. The primary endpoint of the phase 2 cohort is the determination of ORR (H_0 = 20%, H_A = 40%) to the combination of docetaxel with DKN-01. Exploratory endpoints, funded by PCF, include determination of the peripheral and intratumoral immunoprofile using high-dimensional flow cytometry in pre-treatment and on-treatment samples.

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