Background CG0070, is an Ad5-based oncolytic vaccine engineered to express GM-CSF and replicate selectively in tumor cells with mutated or deficient RB. The CG0070 mechanism of action includes cell lysis and immunogenic cell death which is enhanced in the presence of GM-CSF. In an open label ph. 2 study, an overall CR rate of 62% and a CR at 12 months (m) of 29% have been observed in patients with high risk NMIBC previously treated with BCG.

IV pembrolizumab, was recently approved by the FDA for patients with BCG-unresponsive CIS (with or without papillary tumors) with an overall complete RR of 41% and a 12 m CR rate of ~20%.

This ph. 2 study will assess the potential synergy of the two agents in the treatment of BCG-unresponsive NMIBC.

Methods 35 pts with BCG-unresponsive CIS with or without concurrent Ta or T1 disease will be treated with intravesical CG0070 (1x10^12 vp) in combination with pembrolizumab at a dose of 400 mg IV q6 weeks. CG0070 will be administered weekly x 6 as induction followed by weekly x 3 maintenance instillations at months 3, 6, 9, 12, and 18. Patients with persistent CIS or HG Ta at 3 m may receive re-induction with weekly x 6 of CG0070. Pembrolizumab will be administered up to 24 m. Assessment of response will include q 3 m cystoscopy with biopsy of areas suspicious for disease, urine cytology, CTU/MRU, and mandatory bladder mapping biopsies at 12 m. Recurrence of HG disease will be enumerated as disease recurrence.

The primary endpoint of the study is CR at 12 m. Secondary endpoints will include CR at any time, progression free survival, duration of response, cystectomy free survival and the safety.

Results Enrollment has been completed. Based on follow up thus far, CR rate of 92% (22/24) at 3 m has been observed. All patients in CR at 3 m remain in CR at downstream time-points including: 14/16 at 6 m, 9/11 at 9 m, and 6/8 at 12 m. Treatment related AE are consistent with those observed in studies of each agent alone.

Conclusions This initial data on the efficacy and safety of CG0070 plus pembrolizumab for the treatment of BCG unresponsive NMIBC is encouraging. Data on efficacy and safety for all enrolled patients, N=35, as well as biomarker (CAR, E2F, and PDL1) assessment will be presented at the time of the conference.

Trial Registration NCT04387461
Ethics Approval CENTRAL IRB Castle: Protocol Number: CORE-001 (CG2003C)
Sponsor CG Oncology, Inc
Study Title A Phase 2, Single Arm Study of CG0070 Combined with Pembrolizumab in Patients with Non- Muscle Invasive Bladder Cancer (NMIBC) Unresponsive to Bacillus Calmette-Guerin (BCG)