Abstract 6039: Phase 1b/2, Open-Label Multicenter Study of Intratumoral SD-101 in Combination With Pembrolizumab in Anti-PD-1 Treatment-Naive Patients with Recurrent or Metastatic Head and Neck Squamous Cell carcinoma (SYNERGY-001/KEYNOTE-184, NCT0251870)

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Background: SD-101 (Lympholyzed™, Medcape Ltd) is a dermalized, well-characterized, recombiant lymphokine GM-CSF, IFNγ, IL6, IL8, IL10 and IL21; histocompatible with human tissue; and designed to prime and activate innate and adaptive immune responses. SD-101 was developed based on SD-101-1 RPA clinical trial providing an estimated overall response rate (ORR) of 27% in a Phase 2b clinical trial of head and neck cancer (SD-101-1, NCT01835469). Phase 2/3 clinical trials of SD-101-2 in Non-Small Cell Lung Cancer (NSCLC) (NCT02353396) and SD-101-3 in head and neck squamous cell carcinoma (HNSCC) (NCT0251870) in combination with Pembrolizumab (pembrolizumab) are currently ongoing. The current study was a Phase 1b/2 dose escalation study of SD-101 in combination with pembrolizumab in anti-PD-1 treatment-naive patients with recurrent or metastatic HNSCC. The primary endpoints included safety and best overall response (BOR).

Methods: The efficacy and safety of SD-101 in combination with pembrolizumab was assessed in a Phase 1b/2, open-label, multicenter study of anti-PD-1 treatment-naive patients with recurrent or metastatic HNSCC. Eligible patients received intratumoral SD-101 injection at one of six dose levels (20-600 mg) followed by pembrolizumab intravenous infusion (200 mg fixed dose) every 3 weeks. The primary objective was to evaluate the safety and BOR in this study. Other secondary objectives included: responses per treatment arm and BOR rates per tumor stage, subgroup, and immune-related biomarkers. Safety was assessed on a weekly basis for at least 4 weeks prior to SD-101 administration.

Results: The study enrolled 84 patients with advanced or recurrent HNSCC. The median age was 63 years (range: 28-81 years). The majority of patients had advanced or recurrent HNSCC. The most common tumor sites included oropharynx (45%), oral cavity (36%), and hypopharynx (18%). The most common primary histology was squamous cell carcinoma (92%). All patients were positive for PD-L1 expression by immunohistochemistry. Patients received pembrolizumab at a median of 10 cycles (range: 1-37 cycles). The median duration of follow-up was 9 months (range: 1-47 months). The most common adverse events (AEs) were injection site reactions (91%) and fatigue (65%). The overall response rate (ORR) was 11% (95% CI: 5-20%), with 1 (3.7%) partial response and 6 (21.7%) patients with stable disease. The most common adverse events were injection site reactions (91%), fatigue (65%), rash (51%), and pruritus (35%). The median time to response was 1.5 months (range: 0.6-2.4 months). The median duration of response was 17.5 months (range: 4.1-30.9 months). The median duration of overall survival was 8.4 months (range: 1.1-30.9 months).

Conclusion: Phase 1b/2 clinical trials of SD-101 in combination with pembrolizumab showed a clinically promising safety profile. The ORR was 11% with 1 (3.7%) partial response, 6 (21.7%) patients with stable disease, and 58 (69%) patients with disease progression. The most common AEs were injection site reactions (91%), fatigue (65%), rash (51%), and pruritus (35%). The median duration of response was 17.5 months. The median duration of Overall Survival was 8.4 months. The study provides important insights into the use of SD-101 in combination with pembrolizumab in anti-PD-1 treatment-naive patients with recurrent or metastatic HNSCC. Further studies are needed to evaluate the role of this combination therapy in the treatment of HNSCC.