the extracellular domain of TGF-βRII (a TGF-β "trap"). We report results in pts with Stage III/IV ≥2L SCCHN not amenable to local therapy with curative intent that progressed/recurred <6 months since last platinum dose.

Methods: In the phase 1 trial NCT02517398, pts with SCCHN received M7824 1200 mg q2w until confirmed PD, unacceptable toxicity, or trial withdrawal; continuation of M7824 beyond PD was permitted if AEs were manageable, PS maintained and no new treatment indicated. Biomarkers include tumor cell PD-L1 level (antibody clone 73-10) and HPV status (by RNAseq). The primary endpoint is BOR per RECIST; secondary endpoints include safety/tolerability.

Results: As of 12 March 2018, 32 pts (75% had ≥2 prior lines of therapy) received M7824 for a median duration of 12.1 (range, 2–74) weeks. 5 pts had a confirmed PR by investigator read (RECIST v1.1 ORR 15.6%). 2 additional pts developed delayed PRs after initial increase in index lesions per RECIST (total ORR 21.9%). 6 pts had SD (total DCR 40.6%). 4/5 pts with PR (DOR 4.1–12.5+ months) and both pts with PD→PR remain on treatment. The ORR (including pts with PD→PR) in HPV+ was 50% (4/8; HPV- ORR 13.6% [3/22]). PD-L1 expression was not predictive for ORR (20% [5/25 pts)] in PD-L1≥1%; 33% [2/6] in PD-L1<1%). 12-month OS rate was 51.2%. 10 pts (31.3%) had grade 3 TRAEs (increased liver enzymes [3 pts], hyperglycemia, maculopapular rash [2 pts each], anemia, hyperthyroidism, diabetic ketoacidosis + hypothyroidism, keratoacanthoma + folliculitis, skin SCC [1 pt each]); there were no grade 4 TRAEs and no treatment-related discontinuations or deaths.

Conclusions: M7824 showed promising early clinical activity and a manageable safety profile in pts with refractory/metastatic ≥ 2L SCCHN. A total ORR of 21.9% was observed (including 2 pts with initial tumor growth), with a possible trend toward higher activity in HPV + (ORR 50%) and evidence of clinical activity irrespective of PD-L1 status.

Clinical trial identification: NCT02517398.

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1048O M7824 (MSB0011359C), a bifunctional fusion protein targeting PD-L1 and TGF-β, in patients (pts) with advanced SCCHN: Results from a phase I cohort

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Background: The TGF-β pathway promotes tumor immunosuppression, and its inhibition may enhance the antitumor activity of PD-(L)1 mAbs. M7824 is an innovative first-in-class bifunctional fusion protein composed of an anti–PD-L1 mAb fused with