Aim: This ongoing Phase I, multicenter, open-label study (NCT01693562) evaluates the safety and efficacy of MEDI4736 in patients (pts) with multiple solid tumor types including non-small cell lung cancer (NSCLC). MEDI4736 is a human IgG1 mAb, engineered to prevent ADCC activity, that blocks PD-L1 binding to PD-1 and CD-80. PD-L1 is expressed in many NSCLC tumors and may be associated with poor prognosis.

Methods: MEDI4736 was administered IV every 2 weeks (q2w) or every 3 weeks (q3w) using a standard 3 + 3 dose escalation (6 dose levels: 0.1–10 mg/kg q2w; 15 mg/kg q3w). In dose expansion, NSCLC pts were assigned to cohorts by histology and line of therapy and administered MEDI4736 10 mg/kg q2w. Retreatment was permitted for progression after 12 months of therapy. Response is assessed by immune-related response criteria in escalation and RECIST v1.1 in expansion.

Results: As of 14 April 2014, 114 NSCLC pts have been treated with MEDI4736 in dose escalation and expansion cohorts. Of the 101 pts treated at the 10 mg/kg q2w dose (median 3 doses received; range 1–14), mean age 63 y (37–83), all were PS 0–1, with a median of 2.5 prior treatments (range 1–8). In this group, treatment-related adverse events (AEs) were reported in 20% of pts; most frequently dyspnea (16%), fatigue (15%) and nausea (15%). Grade ≥3 treatment-related AEs were reported in 4 pts. AEs led to study discontinuation in 6 pts, none of which were treatment-related. Pneumonitis (grade 2) occurred in 1 pt. With a median follow up of 10 wks, 46 pts were followed ≥12 wks. Objective response + stable disease was observed in 18 pts to date. While some responses or stabilization were reported at first assessment (6 wks), others appeared following initial progression. Benefit was durable; 72/114 pts remain on study (including 4 pts >52 wks) at data cutoff. Assessment of clinical activity by PD-L1 expression, underlying mutation, smoking history, and line of therapy continues.

Conclusions: Durable clinical activity has been observed with manageable AEs, no grade ≥3 pneumonitis, and no colitis of any grade. Further development of MEDI4736 alone and in combination is ongoing in NSCLC.