Trial In Progress: Phase 1b Study of AMG 757, a Half-Life Extended Bispecific T Cell Engager (HLE BiTE®) Immuno-Oncology Therapy, Combined With AMG 404, an Anti-PD-1 Antibody, in Patients With Small Cell Lung Cancer (SCLC)

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Background

- Delta-3 cytokine-3 (D3L3) is a promising therapeutic target because it is highly expressed in small cell lung cancer (SCLC) and internally expressed in normal tissues.
- AMG 757, a bispecific T cell engager (HLE BiTE®) therapy that binds D3L3 on cancer cells and CCT 3 on T cells to redirect T cell dependent killing of tumor cells.
- In a phase 1 study in SCLC, talirentuzumab gave every 2 weeks was safe, with encouraging efficacy up to 100 mg in early trials.
- In a multiple, cohort expanded dose (PDI) or (BDI) 1 antitumor efficacy and provided also efficacy in relapsed/refractory (RR) SCLC.

Rationale for Tarlatamab and AMG 404 (Zeluvalimab) Combination

- Upregulation of PD1 in the tumor microenvironment has been shown to blunt effectiveness of BITE molecule.
- Combining anti-PD1 antibody with a BITE molecule could increase T cell activity and antitumor response.

Tarlatamab + Zeluvalimab

- Dose levels evaluated to date, talirentuzumab was well tolerated with no dose limiting toxicities reported.
- Preclinical data showed that talirentuzumab treatment upregulates PD1- TPD1 and the combination with talirentuzumab increased T cell mediated types of tumor cells compared with talirentuzumab alone (Figure 1).*1
- Based on these preclinical findings, the purpose of this study is to evaluate the safety and efficacy of talirentuzumab in combination with zeluvalimab in patients with SCLC.

Figure 1. Tarlatamab With Zeluvalimab Increases Cytotoxicity in Vitro

Key Messages

- The combination of talirentuzumab, an HLE BiTE therapy, and zeluvalimab, an anti-PD-1 antibody, may be well tolerated and have the potential to further increase antitumor activity compared with talirentuzumab alone.
- We are conducting a phase 1b study to evaluate talirentuzumab in combination with zeluvalimab in patients with SCLC.
  - ClinicalTrials.gov identifier: NCT04885998
  - The study is currently open and recruiting patients.

For more information, please contact Amgen Medical Information: medinfo@amgen.com

[ENDPOINTS]

- Primary Endpoints:
  - Dose-limiting toxicities (DLTs)
  - Treatment-emergent and related adverse events (AEs)
  - Clinically significant changes in vital signs
  - Clinical laboratory tests
  - PD2D of the talirentuzumab and zeluvalimab combination

- Secondary Endpoints:
  - Antitumor activity
  - Pharmacokinetics of talirentuzumab in combination with zeluvalimab

[REFERENCES]


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