SCLC is an aggressive disease with limited treatment options beyond first-line chemotherapy and no approved third-line therapy. 

Delta-like ligand 3 (DLL3) is a Notch ligand that is upregulated and aberrantly expressed on the cell surface in most SCLC, making it a compelling therapeutic target. TARLATAMAB, a HLE BiTE® designed to bind DLL3 on target cancer cells and CD2 on T cells, engages endogenous DLL3 on target cancer cells and CD3 on T cells, forming a cytolytic synapse and resulting in T cell activation & expansion and T cell-dependent killing of tumor cells (Figure 1).

Key Takeaways:

1. Phase 1 FIH (NCT03319940) data shows tarlatamab has an overall manageable and reversible AE profile and delivers promising and durable efficacy in relapsed/refractory SCLC.

2. Based on promising outcomes from the phase 1 study, a phase 2 study (NCT05060016) is being conducted to evaluate the efficacy, safety, tolerability, and PK of tarlatamab in third line and later SCLC patients.

- Two different doses of tarlatamab will be evaluated in Part 1 (Dose Characterization).

- In Part 2 (Dose Expansion) enrollment will continue at the selected target dose based on Part 1 results.

- Enrollment is ongoing.

Figure 1. Tarlatamab: A HLE BiTE® Therapy Targeting DLL3

**Background**

- SCLC is an aggressive disease with limited treatment options beyond first-line chemotherapy and no approved third-line therapy.

- Delta-like ligand 3 (DLL3) is a Notch ligand that is upregulated and aberrantly expressed on the cell surface in most SCLC, making it a compelling therapeutic target.

- TARLATAMAB, a HLE BiTE® designed to bind DLL3 on target cancer cells and CD2 on T cells, engages endogenous DLL3 on target cancer cells and CD3 on T cells, forming a cytolytic synapse and resulting in T cell activation & expansion and T cell-dependent killing of tumor cells (Figure 1).

- Interim results of an ongoing first-in-human study of tarlatamab in patients with relapsed/refractory SCLC (NCT03319940) show promising and durable efficacy with an acceptable safety profile.

- These findings support further study of tarlatamab in SCLC.

**Figure 2. Study Design - Phase 2 Study of Tarlatamab in 3L or Later SCLC (DeLLphi-301 Study)**

**Study Overview**

DeLLphi-301 (NCT05060016) is a phase 2, open-label, registration study in subjects with relapsed/refractory SCLC (Figure 2).

**Objectives and Endpoints**

**Part 1 Only**

- Primary Objective: To evaluate safety and efficacy (per RECIST 1.1 by investigator) of 2 dose levels of tarlatamab

**All Parts**

- Primary Objective: Evaluate anti-tumor activity of tarlatamab as determined by ORR per RECIST 1.1 by BICR

- Secondary Objectives: Evaluate anti-tumor activity of tarlatamab as determined by other measures per RECIST 1.1 (DOR, DCR, PFS, OS); safety and tolerability; pharmacokinetics; immunogenicity

**Key Eligibility Criteria**

- Adults with histologically or cytologically confirmed SCLC

- ECOG performance status ≤1

- Treated brain metastases permitted provided defined criteria are met

**References**

3. Leyland J, et al. Cell Oncol (S fundamental domain; PH-like in human; HLE BiTE; half-life extended bispecific T cell agonist; ORR, objective response rate; OS, overall survival; PK, pharmacokinetics; PFS, progression-free survival; RECIST 1.1, Response Evaluation Criteria in Solid Tumors version 1.1; SCLC, small cell lung cancer.

**DISCLOSURES**

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