Updated Results of Phase 1b of Tarextumab (TRXT, OMP-59R5, anti-Notch 2/3) in Combination with Etoposide and Platinum Therapy (EP) in Patients (pts) with Untreated Extensive-Stage Small Cell Lung Cancer (ED-SCLC)


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Background
- The Notch pathway plays a central role in embryonic development and the regulation of progenitor cells, and is implicated centrally in many human cancers, including small cell lung cancer (SCLC).
- Aberrant Notch signaling is associated with poor survival and chemotherapy resistance in a number of solid tumors.
- Tarextumab (TRXT, OMP-59R5, anti-Notch2/3) is a fully human IgG2 that was originally identified by binding to Notch2. It inhibits the signaling of both Notch2 and Notch3.

Treatment Exposure (n=27)
- 7.5 mg/kg (n=3)
- 10 mg/kg (n=6)
- 12.5 mg/kg (n=3)
- 15 mg/kg (n=6)
- PD biomarkers, including Notch pathway related genes and proteins and tumor and surrogate tissue samples
- Exploratory: immunogenicity
- Secondary: PK of TRXT

Subject Time on Study (n=27)
- AE: activity was less than expected (based on single agent data). Co-administration of chemotherapy with TRXT may lessen GI tract toxicity.
- Incidence of diarrhea was higher at TRXT 15 mg/kg. However, Grade 3 diarrhea occurred only in three pts: 10 mg/kg (n=2, both unrelated); 12.5 mg/kg (n=1, unrelated).

TRXRT Pharmacodynamic Biomarkers: Whole Blood
- Greater tumor reductions noted in pts in 15 mg/kg dose cohorts (8/11 pts who had >60% SLD reduction were from 15 mg/kg dose).
- TRXRT 15mg/kg Q3W established as Ph2 dose with EP chemotherapy.
- No DLT was reported at TRXT 15 mg/kg.
- The incidence of diarrhea was less than expected (based on single agent data).
- Diarrhea, fatigue, nausea, decreased appetite and vomiting were the most common TRXT associated AEs (mostly Grade 1 or 2 events, and manageable with supportive care).

Progression Free Survival and Overall Survival Analysis By Dose Level
- Kaplan-Meier analysis was performed for PFS and OS separated by high and low dose.
- Potentially longer median OS (16.1 vs 8.7 months) seen in high dose group.

Phase 1b Study Schema and Objectives
- The randomized, double blinded Ph2 portion of the study is a Phase 1b/2 trial of TRXT in combination with etoposide and platinum therapy (EP) in pts with untreated extensive-stage small cell lung cancer (ED-SCLC).
- Phase 1b portion of the Pinnacle study aims to determine if the MTD of TRXT in combination with EP. Here we report the updated results of Phase 1b portion of the study based on the data cut as of April 21, 2016.

PIFOS and OS By Dose Level and Notch Gene Expression
- Due to small numbers, potential imbalances of baseline characteristics need to be explored in the Ph2, placebo-controlled portion of the study.

Summary
- The randomized, double blinded portion of the Pinnacle study is currently enrolling at 42 clinical sites in the United States (NCT01865471) and the efficacy endpoints of PFS, OS and OSR will be evaluated; results are expected in 2016/17.