A First-In-Human Study of the First-In-Class Fatty Acid Synthase (FASN) Inhibitor TVB-2640

Results of Dose Escalation in Mono and Combination and Evidence of Preliminary Activity

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Introduction

- FASN inhibition is a novel approach to cancer treatment.
- Selective disruption of palmitate biosynthesis leads to apoptosis in many tumor cells.
- TVB-2640 is the only selective FASN inhibitor in clinical trials.
- Broadly active, oral, once-daily treatment.
- Monotherapy activity in multiple solid tumors, including NSCLC.
- Well-tolerated with grade 1-2 adverse events at the MTD; even when combined with paclitaxel.
- Safety profile and schedule enable combination regimens.
- Synergistic activity in combination with paclitaxel preclinically.
- No discernible PK interference of either drug.

FASN-Integrated Target in Tumor Biology

Objectives

- Exposure by Dose and DLT’s
- Treatment Related Adverse Events
- SAE Update: Calculated
- Pharmacodynamics Changes in Sebum Lipids
- Preliminary Anti-Tumor Activity with TVB-2640
- Escalation and Expansions
- Monotherapy with TVB-2640
- Combination TVB-2640 and paclitaxel

Pharmacodynamics Changes in Sebum Lipids

- Significant reductions in sebum saturated triglycerides were observed after one week of treatment and generally remained low throughout subsequent cycles of treatment.

Conclusions

- An MTD of 100mg/m² TVB-2640 has been defined for both mono and paclitaxel combination therapy.
- TVB-2640 demonstrates a favorable tolerability profile with no significant GI, hematologic or serum chemistry adverse events; no evidence of QTc prolongation by Holter monitoring; no additive toxicity with paclitaxel.
- Biomarker analysis demonstrates target engagement (FASN pathway inhibition), and inhibition of lipogenesis in patients.
- Promising early signs of clinical activity have been seen in heavily pre-treated patients, in monotherapy and in combination with paclitaxel.
- Further exploration of biological activity is underway in expansion cohorts.

Thank You to the Patients and Their Families