**Introduction**

- FASN inhibition is a novel approach to cancer treatment involving the selective disruption of palmitate biosynthesis that, in tumor cells, causes changes in cell signaling, induces apoptosis, and enhances sensitivity to other chemotherapeutic agents, in addition to other effects.
- TVB-2640 is an oral, first-in-class, small-molecule reversible inhibitor of FASN that demonstrates in vitro and in vivo anti-tumor effects with an acceptable non-clinical safety profile.
- This is a dose-escalation study in patients with metastatic or advanced-stage malignant disease refractory to standard therapy and for whom no therapy exists that would be curative or might provide significant benefit.

**FASN-Integrated Target in Tumor Biology**

*Oral, First-in-Class, Potent FASN Inhibitor TVB-2640*

**Objectives**

Primary: Safety, MTD, recommended phase 2 dose
Secondary: Pharmacokinetics, preliminary anti-tumor activity (monotherapy and in combination with Paclitaxel)
Exploratory: Biomarkers of response

**Study Design & Key Eligibility Criteria**

- **Multicenter, open label, phase 1 study**
- **Oral, once daily with 21 day monotherapy continuous cycles (or 28 days in combination with paclitaxel)**
- **Single patient, accelerated titration followed by “3+3” design after ≥ Grade 2 toxicity**

**Inclusion**

- Adult patients with adequate bone marrow, hepatic and renal function and metastatic or advanced-stage solid malignant tumor
- Up to 4 prior regimens
- ECOG 0-1

**Exclusion**

- History of clinically significant dry eye
- Clinically significant ophthalmologic findings
- History of risk factors for torsade de pointes (e.g., heart failure, hypokalemia)
- Conditions that might interfere with oral absorption

**Time on Study**

- **TVB-2640 Monotherapy Doses Explored**
- **TVB-2640 + 90mg/m² Weekly Paclitaxel Doses Explored**

**Grade 1 and 2 Related Adverse Events**

**Reversible Adverse Events**

**Demographics**

Note: All patients to date are enrolled in the United States

**Pharmacokinetic Plasma Levels**

**Pharmacodynamics**

**Evidence of FASN Inhibition in Patients**

**Conclusions**

- TVB-2640 is an oral, selective, potent, reversible FASN inhibitor and is the first FASN inhibitor in clinical trials
- TVB-2640 demonstrates a favorable tolerability profile with no significant GI, hematologic, serum chemistry adverse events or evidence of QTc prolongation by Holter monitoring
- Skin and ophthalmological toxicity are on-target and reversible
- Ophthalmological toxicity occurs at doses much higher than the projected MTD
- Exposures of 60 mg/m² and above demonstrate target modulation and are above those associated with efficacy in preclinical models
- Skin toxicity also occurs higher than but close to the MTD
- Biomarker profile demonstrates FASN inhibition in patients
- Early data in combination with weekly paclitaxel show expected PK results and no newly emergent toxicities. The combination has been well tolerated to date
- Two patients with NSCLC (one monotherapy and 1 in combination) have evidence of stable disease after >12 weeks of treatment

**Thank You to the Patients and Their Families**