Fatty Acid Synthase (FASN)

- Central mediator of neoplastic lipogenesis
- Generates palmitate, the building block of long chain fatty acids, providing a mechanism to convert glucose and other carbon sources into lipids to support cancer cell signaling
- Upregulated in tumor vs normal tissue, and correlates with poor prognosis in certain tumor types

TVB-2640, FASN inhibitor

- Oral, first-in-class, small-molecule reversible inhibitor of FASN.
- IC<sub>50</sub> < 0.05 μM.
- In vitro and in vivo anti-tumor effects previously shown.

MALONYL CARNITINE (MAL) response to TVB-2640

- Multi-center, open label, ongoing phase 1 study
- Oral, once daily with 21/28 day continuous cycles
- Multicenter, ongoing phase 1 study
- Oral, once daily with 21/28 day continuous cycles
- To date, 23 patients enrolled in monotherapy dose escalation at dose levels of 60, 80, 120, 240 mg/m² or 250 mg flat dose. 7 patients enrolled in combination with paclitaxel.

Analysis of biomarkers in TVB-2640 monotherapy

- TVB-2640 at 60 mg/m² on day 1 and day 8, trough blood samples twice on day 1 and day 8, trough blood samples twice on day 1 and day 8.
- TVB-2640 QD, starting on day 13.
- Pre-dose on day 1 and day 8, trough blood samples twice on day 1 and day 8.
- Tumor Size (mm<sup>3</sup>)

Biomarker and PK/PD analyses of first-in-class FASN inhibitor TVB-2640 in a first-in-human phase 1 study in solid tumor patients

- TVB-2640 is a first-in-class FASN inhibitor currently in a Phase 1 oncology clinical study (TVB-2640-CLIN-002).
- Excellent QD oral PK profile.
- Pharmacodynamic biomarkers identified in patient sera and target engagement observed in ongoing Phase 1 study.
- Increased malonyl carnitine.
- Decreased TG 16:0 palmitate.
- Good correlation with TVB-2640 plasma exposure.
- Similar pharmacodynamic activity in rat model.
- Pharmacodynamic activity observed in patient tumors.
- Decreased pAKT S473 in 2/2 patients, also in xenografts.
- Comprehensive biomarker analysis is underway with analysis in additional patients in ongoing 3V2640-CLIN-002 Phase 1 study.
- Poised to understand the clinical impact of FASN inhibition.