Biomarker Analyses from Dose Escalation and Expansion Phases of FASN Inhibitor TVB-2640 Phase 1 Study Shows Target Engagement in Solid Tumor Patients

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Comprehensive Biomarker Sampling in CLIN-002 for First-In-Class FASN Inhibitors

**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 tumors vs normal tissue, and correlates with poor prognosis in certain tumor types

**Malonyl Carnitine and Tripalmitin Show Inhibition of FASN in Patients**
- TVB-2640: FASN Inhibitor in Phase 1 in Solid Tumors (Study 3V6240-CLIN-002)
- Oral, first-in-class, small-molecule reversible inhibitor of FASN
- IC50 < 0.05 μM
- Multicenter, open label, ongoing phase 1 study (1)
- Oral, once daily with 21/28 day continuous cycles
- Currently in expansion phase at RPDG of 100 mg/m2
- TVB-2640 as monotherapy or in combination with paclitaxel
- Approximately 90 patients enrolled to date

**Decreases in Sebum Composition Show Inhibition of Lipogenesis in Patients**
- Novel Non-Invasive Collection
- TVB-2640 Once daily
- Lipidomic profiling of sebum from Sepatuban® >30 readouts

**Exploratory Assessment of Tumor Biopsies from CLIN-002 Patients**
- Matched pre and post dose tumor IHC for 9 patients to date
- pAKT S4737 detected after 1 cycle in 5/9 patients, including 2/2 breast cancer patients. No change in total AKT.
- FASN expressed at moderate to high levels (H score >100) in most biopsies to date
- RNA-Seq showed significant gene expression changes compared to adjacent normal tissue in 2 breast cancer patients (3): Additional testing ongoing with emphasis on gene expression signatures and genotype analyses

**Summary**
- TVB-2640 is a first-in-class FASN inhibitor
- Excellent GD oral PK profile, previously published
- FASN inhibition consistently shown across patients using novel biomarker approaches in two surrogate tissues, serum and sebum, including dose level used in expansion cohorts
- Exploratory tumor analysis shows inhibition of pAKTS473 and gene expression changes after TVB-2640 treatment consistent with decreased de novo lipogenesis
- Poised to understand the clinical impact of FASN inhibition

Thanks to the patients and their families. Also to Mechanistic, Personal, and Stockists for sample analysis in this study.Poster available at www.3vbio.com

**Comprehensive Biomarker Sampling in CLIN-002 for First-In-Class FASN Inhibitors**

- Serum
- Metabolomics
- Global metabolite profiling, mechanism studies, PD (pharmacodynamic) biomarkers including altered secreted FASN, cytokines, disease markers
- Lipids
- PD lipid biomarkers in surrogates tissue
- Tumor
- Genotype
- Characterize population, direct PD biomarkers, potential patient enrichment biomarkers.
- Gene expression
- Real-time PCR
- Characterize population, direct PD biomarkers, potential patient enrichment biomarkers.
- Blood
- Gene expression
- Assess blood cells as a surrogate tissue.

**Decreases in Sebum Composition Show Inhibition of Lipogenesis in Patients**
- TVB-2640 Once daily
- Lipidomic profiling of sebum from Sepatuban®, >30 readouts

**Exploratory Assessment of Tumor Biopsies from CLIN-002 Patients**
- TVB-2640 Once daily
- Immunohistochemistry
- Gene expression
- Genotyping (baseline)