Pharmacological inhibition of FASN prevents high fat diet induced liver damage in mice and significantly reduces de novo lipogenesis in humans

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3-V’s FASN Inhibitors:
• Excellent PK – liver enhanced distribution
• Reduce high fat diet liver damage in mice
• Treat established disease with short therapy
• Evaluate low doses of TVB-2640 to inhibit hepatic lipogenesis

Next step: Phase 1b – Identify dose for hepatic DNL in metabolic syndrome

3-V FASN inhibitors – preclinical studies
Prevent diet induced steatosis & inflammation

TVB-2640 – serum metabolomics – inhibition of FASN in humans

TVB-2640 inhibits lipogenesis in human skin (sebum)

Sebutape: A non-invasive biopsy

FASN (fatty acid synthase)
Critical lipogenesis & inflammatory target in NASH

TVB-2640 – clinical experience
Oral, potent, FASN inhibitor

Excellent pharmacokinetics

Phase 1 – Cancer patients treated with TVB-2640 (n=62)
PK, PD and AE profiles point to promising opportunity for NASH

MALOY Reduces AEs at lower doses
Ph1b Study – DNL Metabolic syndrome

IL-1β response inhibited by 3-V FASN inhibitors

TVB-3664 and TVB-2640 direct human T-cell differentiation away from pro-inflammatory TH17 and toward anti-inflammatory Treg

TVB-3664* and TVB-2640 direct human T-cell differentiation away from pro-inflammatory TH17 and toward anti-inflammatory Treg

3-V FASN inhibitors:
• Reduce high fat diet liver damage in mice
• 38% reduction in liver steatosis
• Inhibited IL-1β production in serum
• Treated established disease with short therapy
• Ex vivo stimulated human PBMC
• Inhibited IL-1β production
• Inhibited differentiation to Th17 – replaced with Treg

TVB-2640: oral, potent, first-in-class FASN inhibitor
• Demonstrated inhibition of FASN & lipogenesis in humans
• Excellent PK – liver enhanced distribution
• Potential to significantly reduce dose for NAFLD/NASH

Next step: Phase 1b – Identify dose for hepatic DNL in metabolic syndrome
• Evaluate low doses of TVB-2640 to inhibit hepatic lipogenesis (collaboration with E. Parks at University of Missouri)