Single doses of TERN-201, a novel selective semicarbazide-sensitive amine oxidase (SSAO) inhibitor, are safe, well-tolerated, and result in sustained reduction of SSAO activity in healthy participants

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INTRODUCTION

Semicarbazide-sensitive amine oxidase (SSAO, also known as vascular adhesion protein-1 (VAP-1)) is expressed in vascular endothelium and functions as both a leukocyte adhesion molecule and a primary amine oxidase. SSAO contributes to hepatic inflammation and injury in non-alcoholic steatohepatitis (NASH) through recruitment of inflammatory cells to the liver and increasing oxidative stress via breakdown of primary amines (e.g., methylamine) to aldehyde, ammonium, and hydrogen peroxide (H₂O₂). Pharmacological inhibition of SSAO is anticipated to have therapeutic benefit in the treatment of NASH by reducing oxidative stress and recruitment of inflammatory cells to the liver.

TERN-201 is a novel, potent, and irreversible covalent inhibitor of SSAO-inhibition is selective for SSAO over other monoamine oxidases (e.g., MAO-A/B), reducing potential off-target safety concerns. Here we present interim, single-ascending dose results from TERN201-US-A101, a Phase 1 first-in-human study in healthy subjects receiving a single oral dose of TERN-201. The study remains ongoing and blinded.

METHODS

Single-ascending dose study of TERN-201 in healthy volunteers

- **Assay Workflows**
  - **Total amine oxidase activity**
    - Plasma
    - Hepatocytes
  - **SSAO-specific amine oxidase activity**
    - Plasma
    - Hepatocytes
  - **Plasma H₂O₂ levels**
    - Total amine oxidase activity
    - SSAO-specific amine oxidase activity
  - **Plasma SSAO activity**
    - Activity (IC₅₀, µM)

- **Results**
  - **Inhibition of plasma total amine oxidase activity**
    - Placebo: 1 mg, 3 mg, 6 mg, and 10 mg
  - **Plasma methyamine accumulation**
    - Placebo: 1 mg, 3 mg, 6 mg, and 10 mg

- **CONCLUSIONS**
  - **Safety and Tolerability**
    - TERN-201 was safe and well tolerated in healthy subjects administered a single oral dose ranging from 1 mg to 10 mg and exhibited greater than dose proportional plasma PK between 3 and 10 mg
  - **Pharmacodynamics**
    - Near complete inhibition of SSAO-specific activity was achieved for up to 7 days following a single dose of TERN-201
    - Dose-dependent increases in plasma methyamine levels were observed, indicative of SSAO target engagement

REFERENCES


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