Poster No. SAT-142

FAVORABLE SAFETY PROFILE OF TERN-201, A HIGHLY SELECTIVE INHIBITOR OF VASCULAR ADHESION PROTEIN-1, IN THE NONALCOHOLIC STEATOHEPATITIS PHASE 1B AVIATION STUDY

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SCAN ME!

KEY TAKEHOME MESSAGE

TERN-201 was well-tolerated with a safety profile similar to placebo in patients with baseline multiparametric magnetic resonance imaging and liver stiffness (LS) values indicative of nonalcoholic steatohepatitis with at least stage 2 fibrosis and showed near complete suppression of plasma VAP-1 activity.

1 • INTRODUCTION •

- Vascular adhesion protein-1 (VAP-1) levels are elevated in nonalcoholic steatohepatitis (NASH) patients, where it contributes to liver injury (Figure 1)[1,2]
- TERN-201 is a highly specific irreversible inhibitor of VAP-1 and has demonstrated sustained target engagement in healthy human volunteers without off-target effects[3]
- Here we report results from Part 1 of the TERN-201, Phase 1b AVIATION trial in patients with NASH

Figure 1: VAP-1 Recruits White Blood Cells To The Liver And Increases Inflammation And Fibrosis

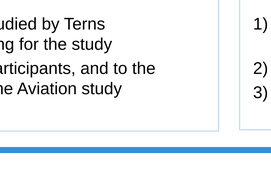


Figure 2: Study Design

Key inclusion criteria:
- Adults 18-75 years
- BMI ≥ 25 kg/m^2
- ALT ≥ 28 IU/L (women) or ≥ 43 IU/L (men)

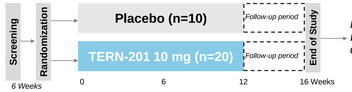
Key exclusion criteria:
- ALT > 5x ULN

NASH based on clinical characteristics:
- TE 6.5-21 kPa
- CAP > 280 dB/m; cT1> 800 msec

Or prior biopsy:
- F1-3 in last 2 years and stable weight; cT1> 800 msec

Part 1

Initiated June 2021



Pre-specified Part 1 Interim analysis completed

Part 2: TERN-201 20 mg vs. placebo initiated 1Q 2022 and is ongoing

Magnetic resonance imaging-proton density fat fraction (MRI-PDFF) and corrected T1 (cT1) at Baseline, Week 6, and Week 12

2 • METHODS •

- Part 1 of the two-part AVIATION trial was a double-blind, placebo-controlled study (NCT04897594) in 30 adults with non-cirrhotic NASH phenotype evaluating 10 mg TERN-201 once daily (QD) for 12 weeks followed by off-treatment evaluation at Week 16 (Figure 2)
- The prespecified Part 1 interim analysis primary endpoint was safety assessed by adverse events (AEs) and laboratory tests; percent change from baseline (BL) in plasma VAP-1 activity was a secondary endpoint
- Exploratory imaging and blood-based biomarkers of liver inflammation and fibrosis were also assessed
- Least square means (LSM) and standard errors (SE) for change and percent change from BL are estimated using an ANCOVA model with change (or percent change) from BL as the dependent variable including treatment group and randomization strata as fixed effects and BL as a covariate.

3 • RESULTS •

- Demographics and baseline characteristics were overall similar (Table 1)
- Nearly all patients (28/30, 95% of TERN-201 and 90% of placebo) completed Part 1. No patient discontinued due to any AE (Figure 3). 10 mg TERN-201 was well-tolerated with a similar incidence of AEs as placebo (Table 2). All AEs were mild or moderate with no serious AEs or trends in AEs or laboratory abnormalities reported
- There were no significant changes in body weight from baseline to end of treatment
- 10 mg TERN-201 resulted in >98% inhibition of plasma VAP-1 activity in most patients by Week 2 and sustained inhibition through Week 12 (Figure 4)
- There were no statistically significant differences between placebo and 10 mg TERN-201 in change from BL cT1, liver enzymes, cytokeratin-18, or relative change from BL MRI-PDFF
- Significant differences in tissue inhibitor of metalloproteinase-1 (TIMP-1), a component of the ELF score and a marker of hepatic fibrogenesis, were observed at Week 12 (Figure 6)
- Significant differences from placebo in a markers of cell adhesion, ICAM-1 (at Week 8) and VCAM-1 (at Week 12) were observed (Figure 7)

Table 1: Patient Demographics and Baseline Characteristics

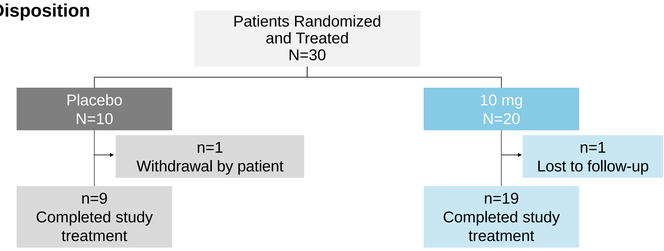
	Placebo (N=10)	10 mg (N=20)
Age, years, mean (SD)	54.9 (13.48)	47.1 (11.85)
Sex, n (%), Female	9 (90%)	13 (65%)
Race, n (%), White	8 (80%)	18 (90%)
Ethnicity, n (%), Hispanic or Latino	5 (50%)	14 (70%)
ALT, mean (SD) [IU/L]	62.1 (29.00)	69.8 (32.72)
AST, mean (SD) [IU/L]	44.7 (15.60)	46.1 (17.45)
GGT, mean (SD) [IU/L]	63.2 (45.72)	39.9 (33.19)
BMI, mean (SD) [kg/m^2]	38.8 (5.54)	36.6 (6.59)
Baseline statin use, n (%)	3 (30%)	5 (25%)
Patients with diabetes, n (%)	4 (40%)	6 (30%)
LS by TE, mean (SD) [kPa]	9.9 (2.55)	8.1 (1.42)
CAP, mean (SD) [dB/m]	340.7 (46.07)	327.4 (35.92)
cT1, mean (SD) [msec]	933.4 (175.54)	883.2 (55.32)
MRI-PDFF, mean (SD) [%]	18.0 (9.03)	17.4 (6.83)

Table 2: Overall Summary of Adverse Events

Patient incidence AEs by category	Placebo (N=10) n (%)	10 mg (N=20) n (%)
Any AE, all CTCAE grades	6 (60%)	11 (55%)
CTCAE Grade 3 or higher AEs	0	0
Serious AE	0	0
AE leading to death	0	0
Treatment-related AEs, all CTCAE grades	3 (30%)	1 (5%)
Treatment-related CTCAE Grade 3 or higher AE	0	0
AE(s) in >1 TERN-201 patient:		
Nausea	2 (20%)	2 (10%)

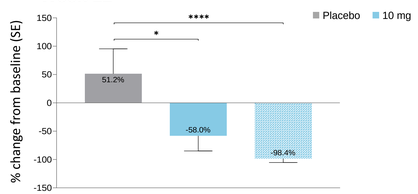
- The only AE in > 1 TERN-201 patient was nausea, occurring in a higher % of placebo patients
- Only TERN-201 AE reported as related per investigator was Grade 1 frequent bowel movements
- No trends in laboratory or ECG abnormalities

Figure 3: Patient Disposition



No patient discontinued TERN-201 or placebo due to an adverse event

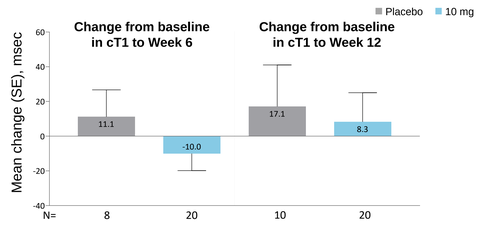
Figure 4: VAP-1/SSAO Activity % Change from Baseline at Week 12



Excludes patients (n=4) with low VAP-1/SSAO activity at baseline (<10% of total assay signal).
*p-value <0.05; ****p-value <0.0001 vs. placebo

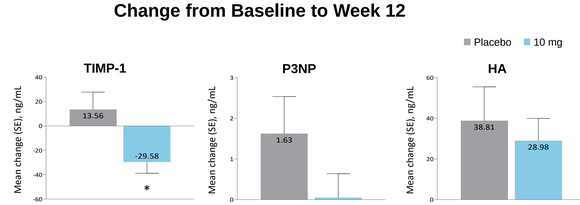
10 mg TERN-201 dose achieved significant suppression of plasma VAP-1/SSAO activity.

Figure 5: cT1 Changes in Week 12



cT1 change from BL was not statistically significant compared to placebo. No patients had a cT1 decline ≥ 80 msec at Week 12.

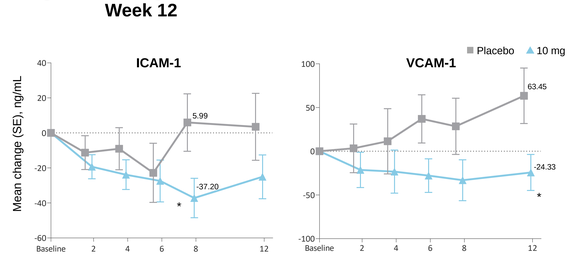
Figure 6: ELF Components (TIMP-1, P3NP, HA) Change from Baseline to Week 12



*p-value <0.05 vs. placebo. One 10 mg patient with high baseline TIMP-1 had large decrease of 51% at Week 12.

ELF change from baseline at Week 6 and 12 was not statistically significant compared to placebo. TIMP-1 change from baseline at Week 12 was statistically significant compared to placebo (p< 0.05).

Figure 7: Change in ICAM-1 and VCAM-1 from baseline to Week 12



*p-value <0.05 vs. placebo

Significant decreases from baseline in cell adhesion proteins, ICAM-1 at Week 8 and VCAM-1 at Week 12 (p<0.05 vs. placebo).

4 • CONCLUSIONS •

- TERN-201 was well-tolerated with a safety profile similar to placebo in patients with baseline multiparametric MRI and LS values indicative of NASH with at least stage 2 fibrosis
- There were no statistically significant differences between 10 mg TERN-201 and placebo on imaging biomarkers (cT1 and MRI-PDFF)
- 10 mg TERN-201 led to near complete inhibition of plasma VAP-1 activity, decreased levels of the hepatic fibrogenesis marker TIMP-1, and statistically significant decreases in the cell adhesion biomarkers, ICAM-1 (at Week 8) and VCAM-1 (at Week 12), compared to placebo
- Overall, these data support further assessment of safety and activity of 20 mg TERN-201 in the ongoing Part 2 of the AVIATION Trial in phenotypic NASH

5 • ACKNOWLEDGEMENTS •

- TERN-201 is an investigational drug studied by Terns Pharmaceuticals, which provided funding for the study
- The authors are grateful to the study participants, and to the research staff for their participation in the Aviation study

6 • REFERENCES •

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2) Weston et al (2015) *J Clin Invest* 125(2): 501-520
3) Fenaux et al (2020) *Hepatology* 72(1 Suppl): 1025A-1026A

7 • CONTACTS •

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