**KEY TAKEHOME MESSAGE**

In a Phase 2a study (DUET), TERN-501 significantly improved liver fat content, cT1 (a marker of fibroinflammation), and liver volume following 12 weeks of treatment in patients with presumed MASH including those with at-risk MASH, metabolic comorbid conditions, or risk factors associated with MASH.

1 **INTRODUCTION**

- THR-β, the major form of thyroid hormone receptor in the liver, regulates key aspects of energy and lipid metabolism including liver fat removal via fatty acid oxidation.1
- TERN-501 is a potent, highly selective THR-β agonist.2

- In a 12-week Phase 2a MASH study, (DUET, Figure 1), TERN-501 was evaluated as a pioneer in the development of MASH therapeutics.3
- The late Dr. Stephen Harrison, acknowledged for his significant contributions to the field of liver disease, passed away in 2023; 77(5):1797-1835

2 **METHODS**

- This study was a 12-week, randomized, double-blind, placebo-controlled study in patients with clinically diagnosed or previous biopsy confirmed MASH.4
- Changes in liver fat content measured by MRI-PDFF, fibroinflammation measured by cT1, and LV were evaluated at 12 weeks using MRI in the following patient subgroups:
  - cT1 >875 msec at baseline (at-risk MASH)
  - Obesity (BMI ≥30 kg/m²)
  - Hypertension
  - Dyslipidemia
  - Type 2 diabetes
  - Hispanic ethnicity

3 **RESULTS**

- Significant reductions in liver fat content at Week 12, as assessed by relative change in MRI-PDFF, were observed in the overall TERN-501 6 mg group vs. placebo, as previously reported.1,4
- TERN-501 6 mg vs. placebo (LS Mean change (%): TERN-501 6 mg: -17.5 (5.28)%; Placebo: -17.3 (5.75)%; p<0.001)
- As previously reported, significant reductions in MRI-cT1 at Week 12 were observed in the TERN-501 6 mg vs. placebo (72 mcsec vs. 4 mcsec, respectively, p<0.001),1 suggesting improvement in fibroinflammation.
- Significant reduction in cT1 (≥72 mcsec) was associated with 3-point reduction in NAS.3
- The cT1 improvement was statistically significant vs. placebo in all key patient subgroups except the type 2 diabetes subgroup.

4 **CONCLUSIONS**

- Overall, TERN-501 6 mg, given once daily for 12 weeks consistently demonstrated significant improvement in MRI-PDFF, cT1, and liver volume compared to placebo in key patient subgroups including those with at-risk MASH, metabolic comorbid conditions, or risk factors associated with MASH.
- These results demonstrate TERN-501, a highly selective THR-β agonist, has the potential to be an effective therapeutic agent across common liver subtypes associated with adverse outcomes in MASH including the presence of common metabolic comorbidities or a high degree of fibroinflammation.

**REFERENCES**

2. Dennis et al.
3. Stine et al.
5. Harrison et al.

**ABBREVIATIONS**

- ANCA: Antinuclear antigen; cT1, corrected T1; FDR, forward k- space; k-space; IQR, interquartile range; LAS, liver stiffness assessment; LVEF, left ventricular ejection fraction; LV, liver volume; MASH, metabolic dysfunction-associated steatohepatitis; NAS, NAFLD activity score; THR-β, thyroid hormone receptor β; QD, once-daily; T1rho, T1 relaxation time; T2, tissue relaxation time; TERN-501, Terns Pharmaceuticals' unique, first-in-class selective THR-β agonist that is designed to improve liver fat content and volume in patients with presumed MASH.

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