**1 INTRODUCTION**

- FXR is a nuclear receptor hormone that is highly expressed in the liver and small intestine. FXR agonists have demonstrated a histological liver fibrosis without progression of NASH in a late-stage study, demonstrating the potential for FXR agonists for use in the treatment of nonalcoholic steatohepatitis (NASH).

- TERN-101 is a potent, non-steroidal FXR agonist with enhanced liver distribution, being developed for the treatment of NASH. TERN-101 induced robust FXR agonism in rodent liver and significantly reduced steatosis, inflammation, and fibrosis in NASH rodent models.

- The Phase 2a LIFT Study (TERN101-2001) assessed 5, 10, or 15 mg TERN-101 vs placebo for 12 weeks in non-cirrhotic patients with presumed NASH and histology was graded according to the NASH clinical characteristics or prior biopsy.

**2 OBJECTIVES/METHODS**

**LIFT Study overall:**
- The primary objective of the LIFT Study was to assess the safety and tolerability of dose levels of orally administered TERN-101 versus placebo for 12 weeks in non-cirrhotic presumed NASH patients, based on clinical characteristics or prior biopsy.
- The secondary endpoint was ALT percent change from baseline to Week 12, and exploratory endpoints included change from baseline in other liver enzymes, MRI-PDFF, and cT1.

**Current analysis:**
- cT1 was collected at baseline, Week 6, and Week 12, at sites with cT1 MRI scannability.
- The following cT1 exploratory endpoints were presented:
  - cT1 change from baseline to Week 6 and to Week 12 by treatment group.
  - Placebo-level resistant patient with cT1 response defined as a ≥80 msec decrease from baseline to Week 6 or Week 12.
  - A ≥80 msec increase in cT1 at Week 12 with low (≤400) or high (≥475) cT1 values, reflecting increasing risk of liver fibrosis/ inflammation and disease progression.

**3 RESULTS**

**Disposition, Safety, Demographics and Baseline Characteristics**
- 100 patients were randomized and received at least one dose-level of study drug. The numbers per treatment group were as follows:
  - Placebo, n = 22
  - 5 mg, n = 18
  - 10 mg, n = 25
  - 15 mg, n = 21

- All dose levels of TERN-101 were overall safe and well-tolerated, with no discontinuations due to adverse events.
- Mean cT1 at baseline was >500 msec in all treatment groups, indicating a patient population with advanced NASH and high levels of fibroinflammation at baseline.
- TERN-101 treatment resulted in significant decreases in ALT, cT1, and MRI-PDFF (oral presentation #1435).

**Fig. 2 cT1 is Correlated with NAFLD Activity Score and Fibrosis on Liver Histology**

- cT1 is a stronger predictor of clinical outcomes in patients with chronic liver disease including NAFLD.
- Low (<400 msec), elevated (400-875 msec), or high (>875 msec) cT1 values reflect increasing liver fibroinflammation and increased risk of NASH disease progression.

**4 CONCLUSIONS**

- TERN-101 was overall safe and well-tolerated in the LIFT Study, and resulted in significant dose-dependent decreases in cT1 at Weeks 6 and 12.
- Mean cT1 values significantly decreased from baseline for all TERN-101 dose groups, and cT1 may serve as a biomarker of TERN-101 treatment response as early as Week 6.
- A higher proportion of patients treated with TERN-101 had a cT1 response (decrease ≥80 msec from baseline) at Week 12 compared to placebo.
- TERN-101 treatment led to study population shifts to cT1 categories associated with lower risk of clinical events in chronic liver disease patients, particularly in the TERN-101 10 and 15 mg dose groups.
- Overall, TERN-101 treatment in the LIFT Study indicates improvements in fibroinflammation between baseline and Week 12.
- Further clinical studies of TERN-101 for the treatment of NASH, either alone or in combination with other agents, are warranted.
- A clinical trial of TERN-101 co-administered with the thyroid hormone receptor beta agonist TERN-101 is planned to initiate in the fall of 2022.

**5 REFERENCES**

- Terns Pharmaceuticals, Inc., Foster City, California.

**6 ACKNOWLEDGEMENTS**

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**7 CONTACT**

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