A 12-WEEK, RANDOMIZED, DOUBLE-BLIND, PLACOBO-CONTROLLED PHASE 2A STUDY WITH FACTORIAL DESIGN TO EVALUATE SAFETY, EFFICACY, PHARMACOKINETICS, AND PHARMACODYNAMICS OF TERN-501 ALONE AND IN COMBINATION WITH TERN-101 IN PATIENTS WITH NASH

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1· BACKGROUND

TERN-501
- TERN-501 is a potent, highly selective THR-β agonist
- In a first-in-human (FIH) study1, once daily dosing of TERN-501 at 1, 3, 6, and 10 mg for 14 days was overall safe and well-tolerated. No clinical signs or symptoms consistent with hypothyroidism or THR-α agonism and no dose limiting stopping criteria met. Nonvariate, dose proportional TERN-501 PK was observed from 1 mg to 6 mg with overlapping PK at 6 mg and 10 mg. Significant increases in sex hormone binding globulin (SHBG) were dose proportional between 1 and 6 mg with less than dose proportional SHBG increases between 6 and 10 mg (Figure 1)1,2. TERN-501 resulted in atherogenic lipid decreases (Figure 1)1,2
Figure 1: 14-day Once Daily Administration of TERN-501 Led to Significant Increases in SHBG and Decreases in LDL-c

2· DUET – STUDY DESIGN

Figure 3: DUET Study Schema - First NASH trial Evaluating a THR-β agonist and an FXR agonist Combination

Randomized, Double-Blind, Placebo-Controlled, Factorial Design, Phase 2a Study (N=140)

- Placebo QD (n=20)
- 5 mg QD + Placebo (n=20)
- 6 mg QD + Placebo (n=20)
- 10 mg QD + Placebo (n=20)
- 10 mg QD + 5 mg QD (n=20)
- 10 mg QD + 6 mg QD (n=20)
- 10 mg QD + 10 mg QD (n=20)

Enrollment is underway with data expected in the 2nd half of 2023

3· DUET – STUDY OBJECTIVES

Primary objective
- To evaluate the effect of TERN-501 monotherapy on liver fat content as assessed by MRI-PDFF compared to placebo

Secondary objectives
- To evaluate the effect of TERN-501 on cT1 relaxation time compared to placebo
- To evaluate the effect of TERN-501+TERN-101 on liver fat content as assessed by MRI-PDFF and on cT1 relaxation time compared to placebo

4· ELIGIBILITY CRITERIA

Key Inclusion Criteria
- Male or female, 18 to 75 years of age on the day of consent
- Overweight or obese with a body mass index (BMI) ≥ 25 kg/m²
- Presumed NASH diagnosed by prior biopsy and/or imaging criteria

Key Exclusion Criteria
- History or clinical evidence of chronic liver diseases other than NASH
- History or known clinical evidence of cirrhosis, esophageal varices, hepatic decompensation or other severe liver impairment
- History of liver transplant, or current placement on a liver transplant list
- Current diagnosis or history of pituitary or thyroid disorders - except for patients with primary hypothyroidism on a stable dose of thyroid hormone replacement therapy
- Abnormal TSH or free T4 levels
- Weight loss of > 5% total body weight within 3 months prior to Screening
- Uncontrolled diabetes or hyperlipidemia; unstable cardiovascular disease
- Excessive alcohol consumption

Key Exclusions
- Unstable cardiovascular disease
- Excessive alcohol consumption

6· ACKNOWLEDGEMENTS

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REFERENCES

3) Loomba R, et al. AASLD 2021 Oral Presentation

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