



# LIFT Study Topline Results

A 12-Week Phase 2a Trial of TERN-101 in NASH Patients

June 14<sup>th</sup>, 2021

NASDAQ: TERN

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# Acknowledgements



Terns would like to acknowledge and thank the patients, investigators, and LIFT study team, especially during the COVID pandemic – thank you!

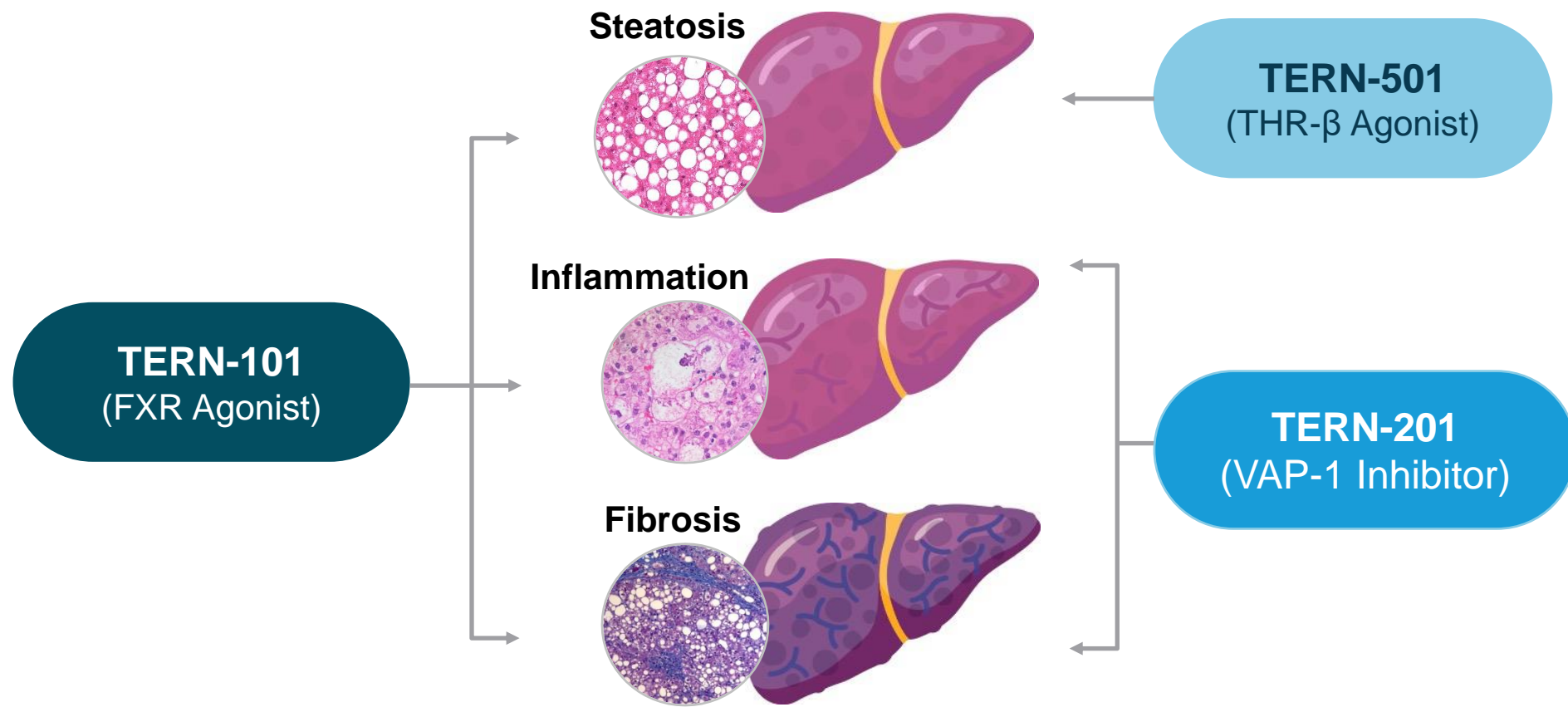
# 3 Important Firsts for NASH Treatment

1. First FXR agonist trial to demonstrate no discontinuations due to AEs, including pruritus
  - TERN-101 was generally well-tolerated with similar incidence of AEs across treatment groups
  - No treatment-related SAEs
2. First 12-week controlled trial in NASH to show significant improvements in cT1
  - cT1 is an imaging marker of liver inflammation and fibrosis linked to clinical outcomes<sup>1</sup>
  - Also observed improvements in PDFF and liver enzymes
3. First NASH trial of an FXR agonist (TERN-101) in combination with a THR- $\beta$  agonist (TERN-501) planned for 1H22 initiation
  - TERN-501 Phase 1 MAD portion started in June 2021 with data expected in 2H 2021

# Terns Pipeline:

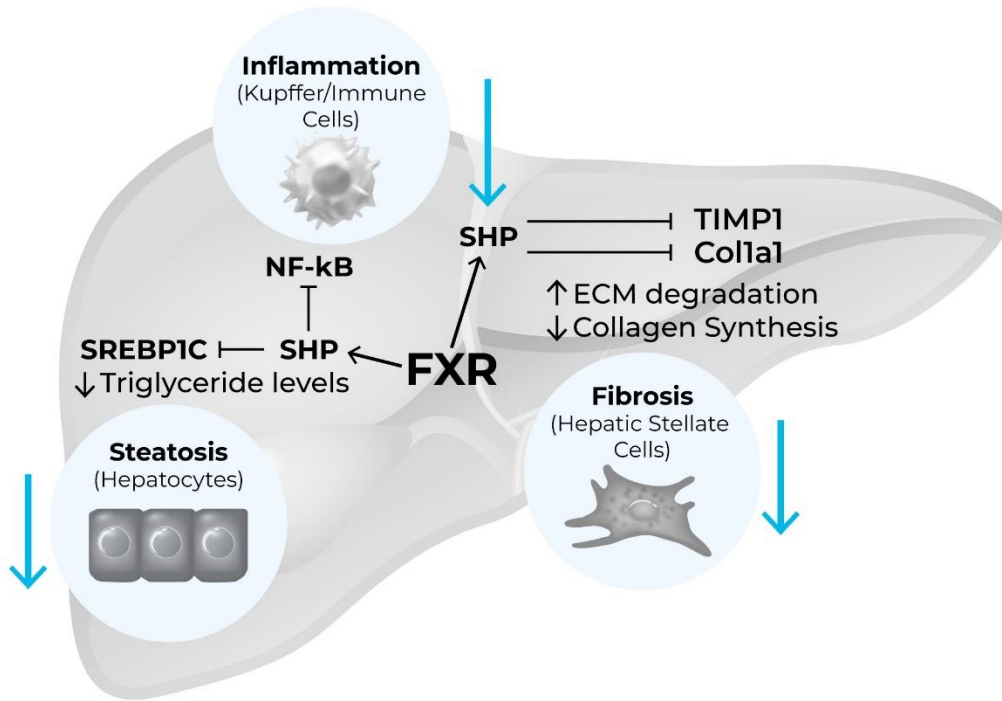
## Designed to Address Multifaceted Nature of NASH

*Combining candidates with complementary mechanisms to maximize NASH response rates*



# TERN-101: A Differentiated Liver-Distributed FXR Agonist

A liver-distributed FXR agonist has the potential to address NASH by acting on the three key disease processes and cell types

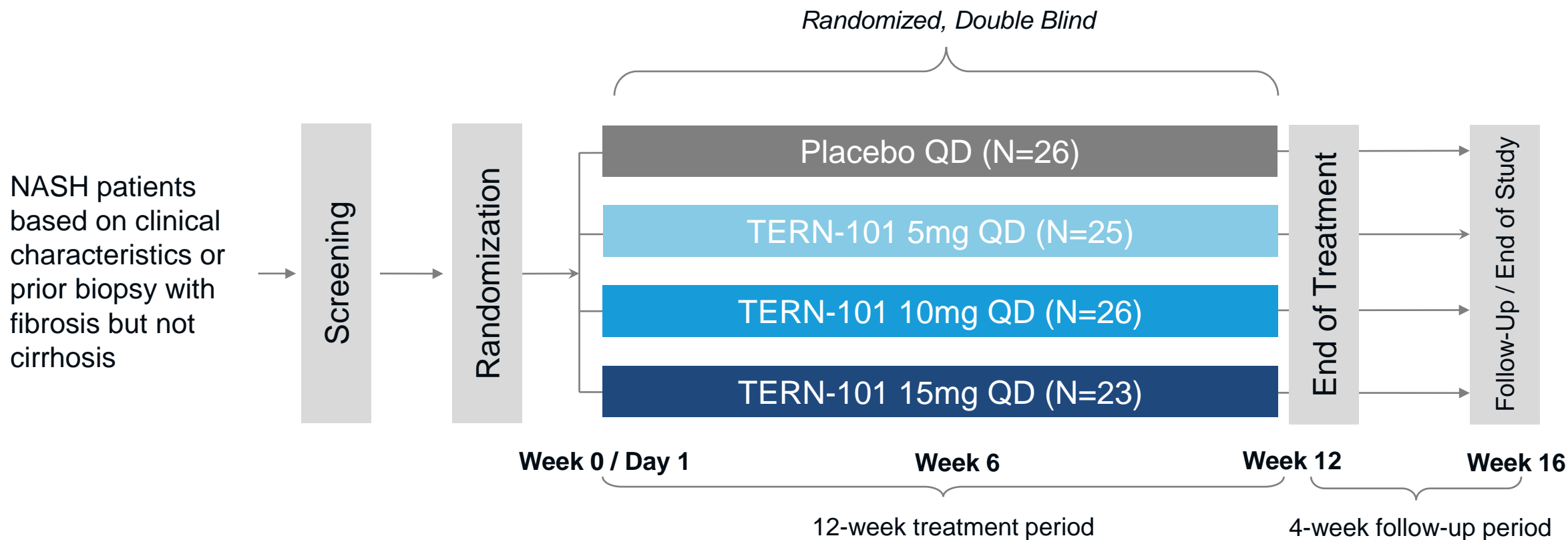


- Liver-distributed, non-bile acid FXR agonist with **differentiated tolerability profile & improved target engagement**
- Some FXR agonists have demonstrated **significant histological NASH improvements** in clinical trials
  - But also resulted in substantial pruritus, adverse lipid changes & discontinuations
- TERN-101 demonstrated **sustained liver FXR activation & favorable tolerability profile** in multiple Phase 1 trials (in addition to the LIFT Study)

# LIFT Phase 2a Trial in Patients with NASH

*Primary objective: Safety assessment*

*Secondary / exploratory objectives: ALT, PK, cT1, MRI-PDFF, and other biomarkers*

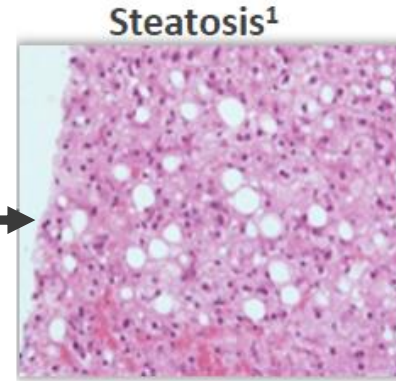
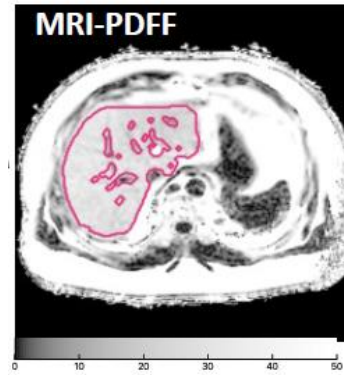


# Exploratory Endpoints Include Multi-parametric MR Imaging: MRI-PDFF & Corrected T1 (cT1)

**LiverMultiScan** 

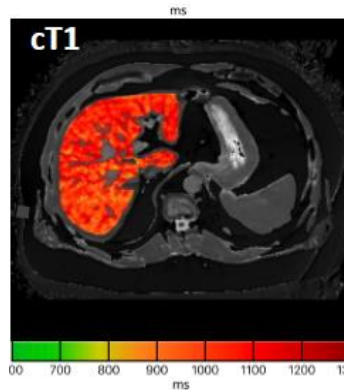


*Quantitative MRI metrics that correlated with histological markers of liver disease*

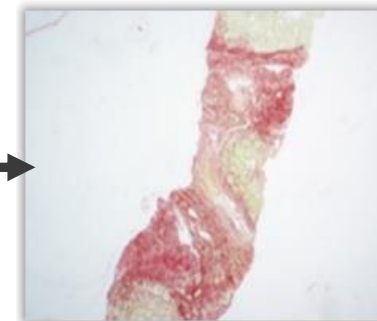


## MRI-PDFF

Shown to correspond to histological measures of **steatosis**



## Fibroinflammation³



## Corrected T1

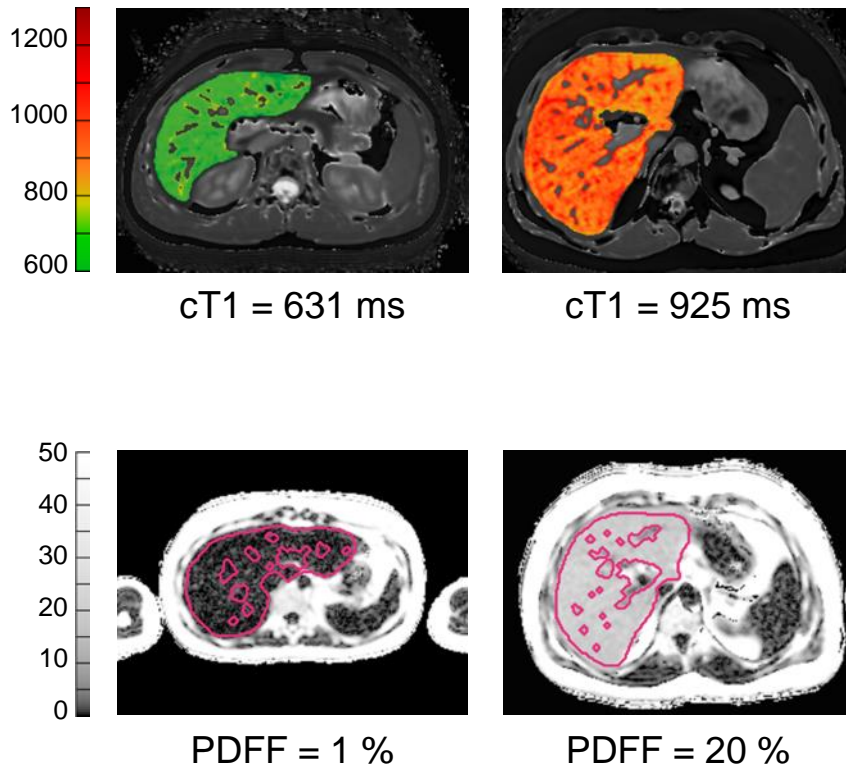
Free-water content in tissue shown to increase in **inflammation and fibrosis**

$$2 \text{ point } \Delta \text{NAS} \propto 88 \text{ ms } \Delta \text{cT1}^4$$

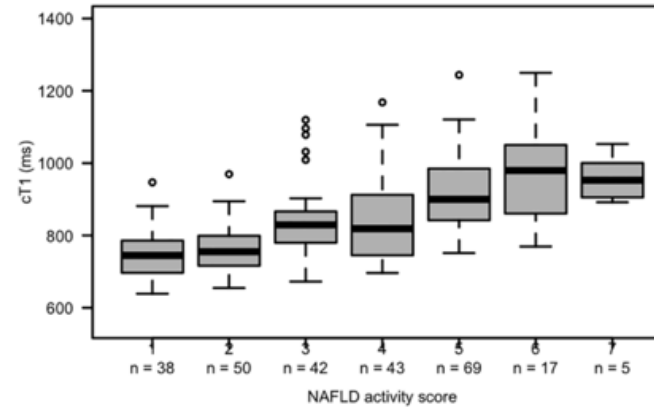
# cT1 is Correlated with Liver Histology

*Both PDFF and cT1 correlated with NAS, but only cT1 correlates with fibrosis*

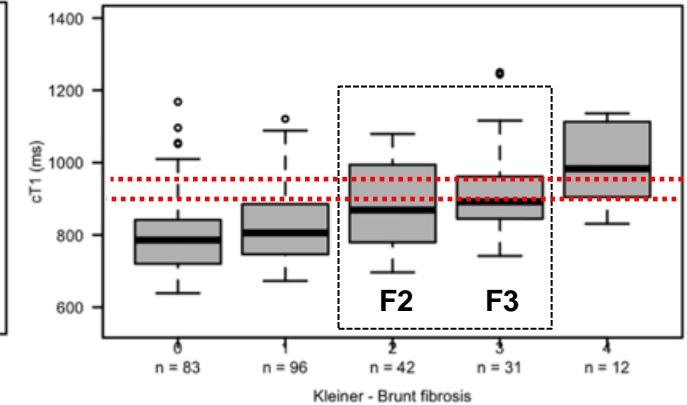
## Example cT1 and PDFF Maps for Range of Values



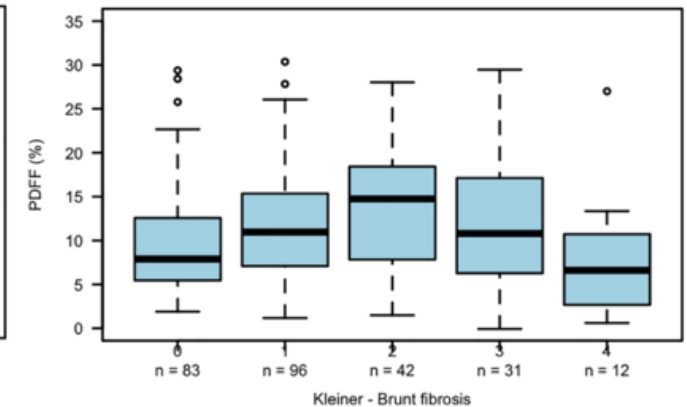
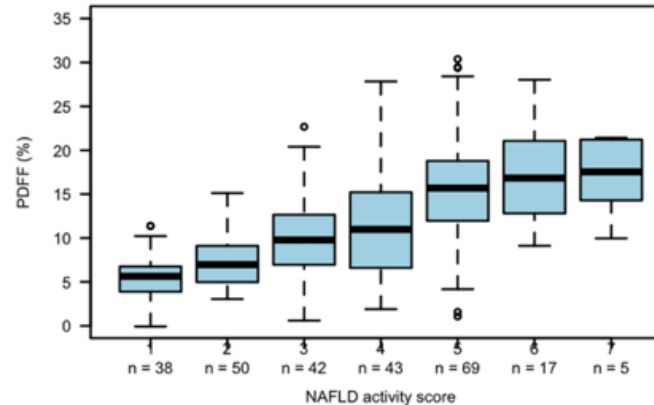
## NAFLD Activity Score



## Kleiner Brunt-Fibrosis Score



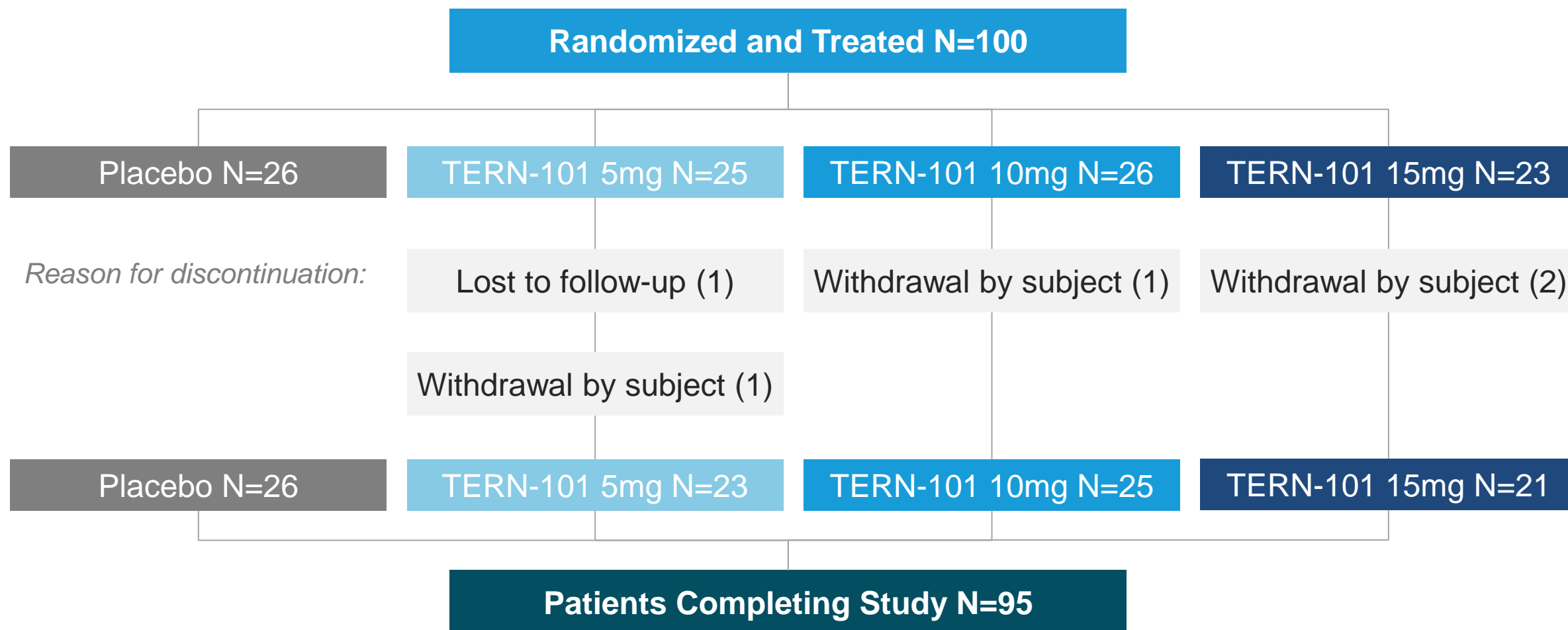
LIFT<sup>1</sup>



*cT1 was also correlated with fibrosis and was superior to PDFF for detection of fibrosis and inflammation*

# Patient Disposition: High Rate of Completion

*No patient discontinued TERN-101 or placebo due to adverse events including pruritus*



# Baseline Characteristics: Balanced Across Treatment Arms, Representative of High-risk F2/F3 NASH Population

	Placebo (N=26)	TERN-101 5mg (N=25)	TERN-101 10mg (N=26)	TERN-101 15mg (N=23)
Age, mean [years]	50	48	53	52
<b>Female, n (%)</b>	<b>16 (62%)</b>	<b>15 (60%)</b>	<b>17 (65%)</b>	<b>17 (74%)</b>
BMI, mean [kg/m <sup>2</sup> ]	36.5	37.2	36.3	36.2
<b>Patients with diabetes, n (%)</b>	<b>11 (42%)</b>	<b>11 (44%)</b>	<b>16 (62%)</b>	<b>8 (35%)</b>
A1c, mean	6.3	6.2	6.5	6.1
LDL cholesterol, mean [mg/dL]	103.4	105.4	99.2	105.8
ALT, mean [IU/L]	55.5	56.2	60.8	55.8
Stiffness by TE, mean [kPa]	10.4	12.0	9.6	9.8
<b>MRI-PDFF, mean [%]</b>	<b>21.4</b>	<b>21.1</b>	<b>20.1</b>	<b>22.8</b>
<b>cT1, mean [msec]</b>	<b>908.9</b>	<b>925.4</b>	<b>942.0</b>	<b>974.7</b>
<i>cT1 conducted at available sites:</i>	<i>n=22</i>	<i>n=24</i>	<i>n=20</i>	<i>n=18</i>

# Primary Objective Safety Summary:

## Well Tolerated with No Discontinuations Due to Any AE

*No treatment-related serious adverse events were observed*

Patient incidence TEAEs by category	Placebo (N=26)	TERN-101 5mg (N=25)	TERN-101 10mg (N=26)	TERN-101 15mg (N=23)
Any TEAE	10 (39%)	13 (52%)	14 (54%)	15 (65%)
Serious TEAE	1 (4%)	-	-	1 (4%)
TEAE leading to death	-	-	-	-
Treatment-related AEs	5 (19%)	6 (24%)	7 (27%)	7 (30%)
Treatment-related serious AE	-	-	-	-
<b>TEAE leading to discontinuation</b>	-	-	-	-

# Most Frequent Treatment-Emergent Adverse Events

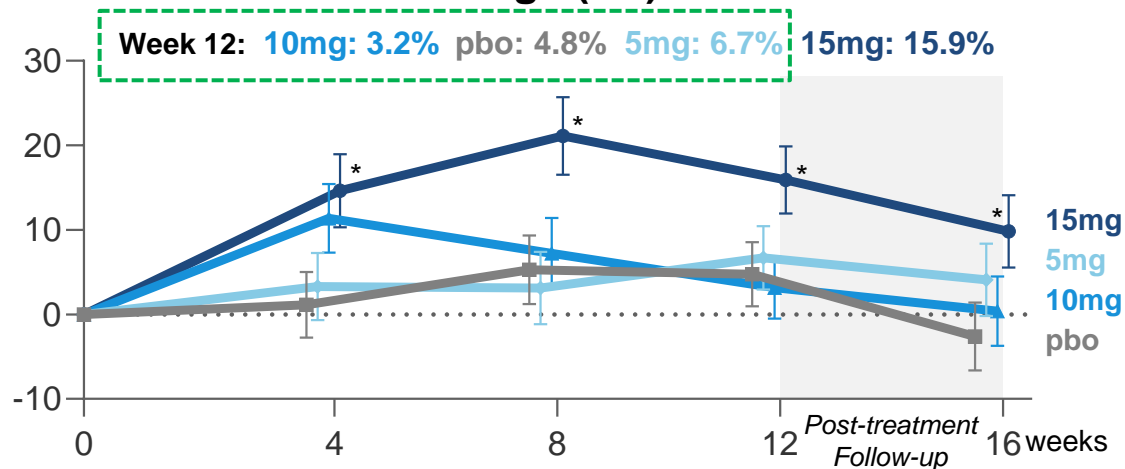
*All treatment-related AEs were mild/moderate with no apparent dose-relationship*

*Pruritus: no Grade 3; no discontinuations; most resolved with continued dosing*

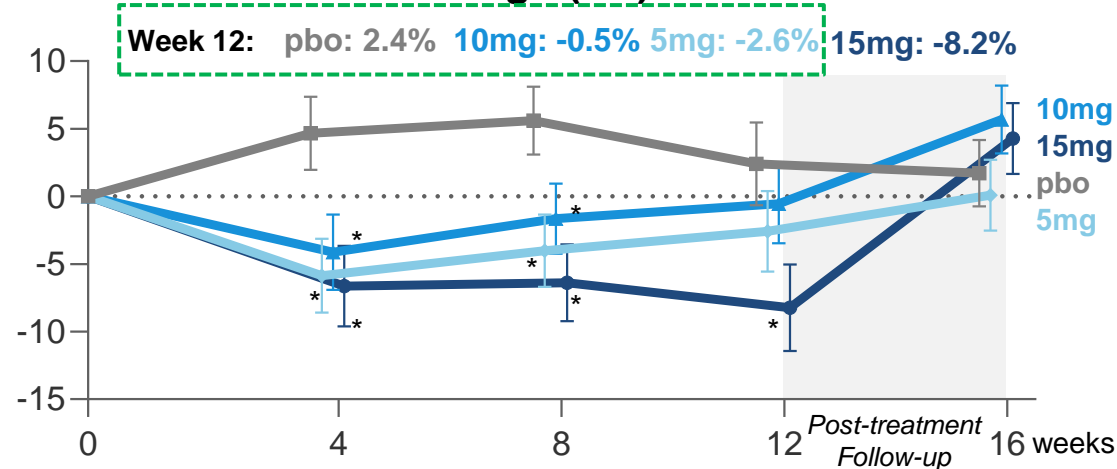
Treatment-Emergent AE ≥ 5% of patients in any arm	Placebo (N=26)	TERN-101 5mg (N=25)	TERN-101 10mg (N=26)	TERN-101 15mg (N=23)
Pruritus	-	4 (16%)	3 (12%)	4 (17%)
<i>Grade 1 (mild or localized)</i>	-	4 (16%)	1 (4%)	3 (13%)
<i>Grade 2 (widespread &amp; intermittent)</i>	-	-	2 (8%)	1 (4%)
<i>Grade 3 (widespread &amp; constant)</i>	-	-	-	-
Headache	2 (8%)	1 (4%)	3 (12%)	2 (9%)
Constipation	2 (8%)	1 (4%)	1 (4%)	1 (4%)
Diarrhea	2 (8%)	-	-	2 (9%)
Decreased appetite	1 (4%)	-	2 (8%)	1 (4%)
Dizziness	1 (4%)	1 (4%)	2 (8%)	-

# Minimal Lipid Changes in TERN-101 5mg and 10mg Cohorts

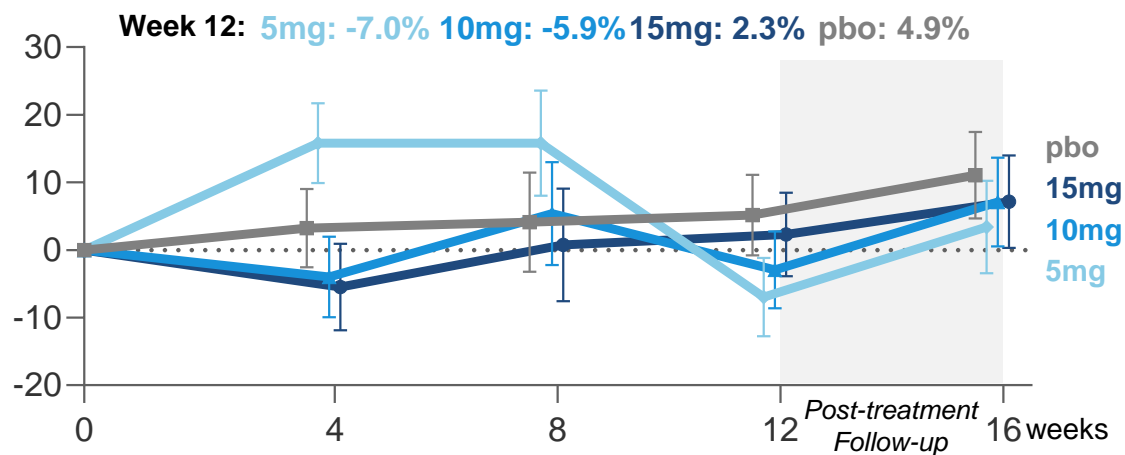
**LDL: Mean % Change (SE) from Baseline**



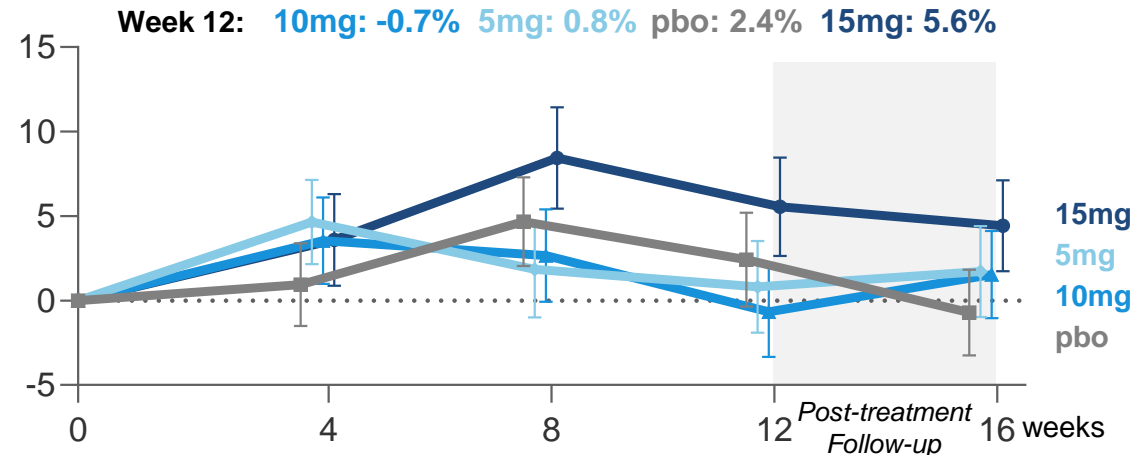
**HDL: Mean % Change (SE) from Baseline**



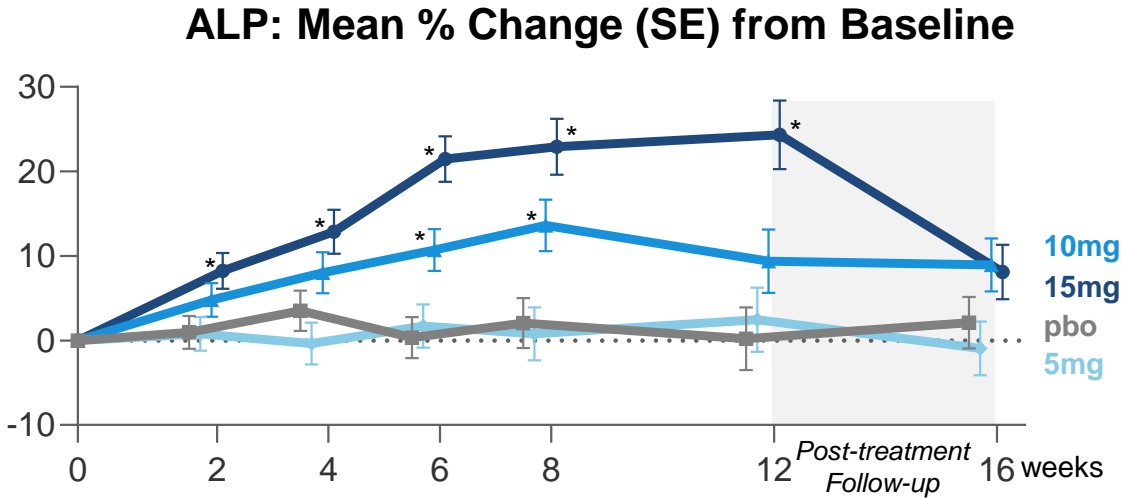
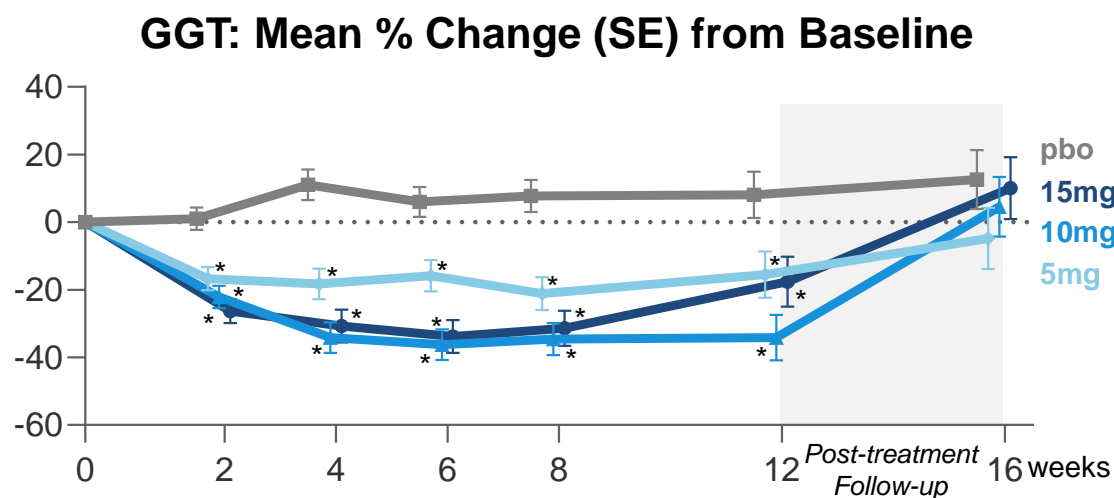
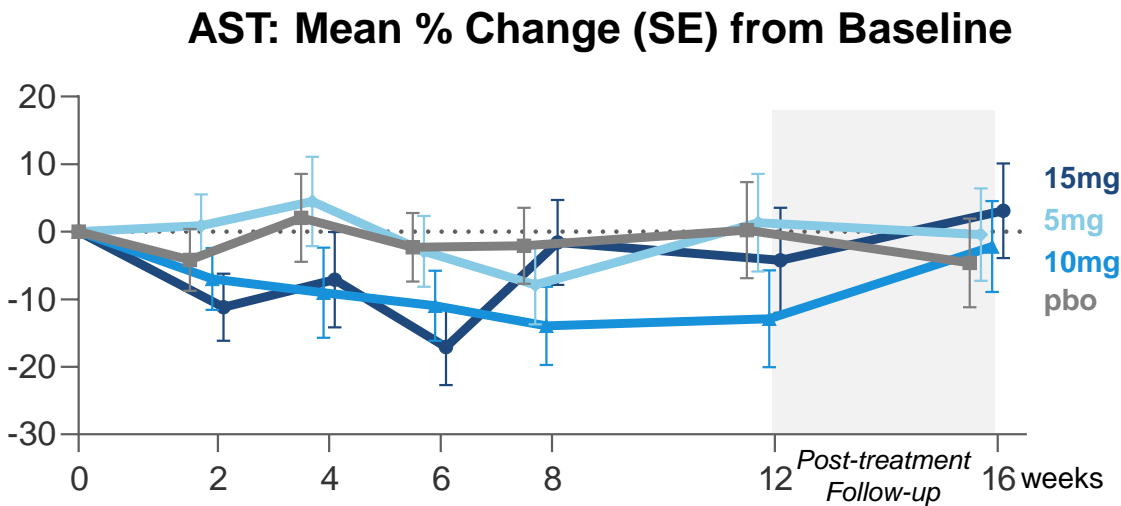
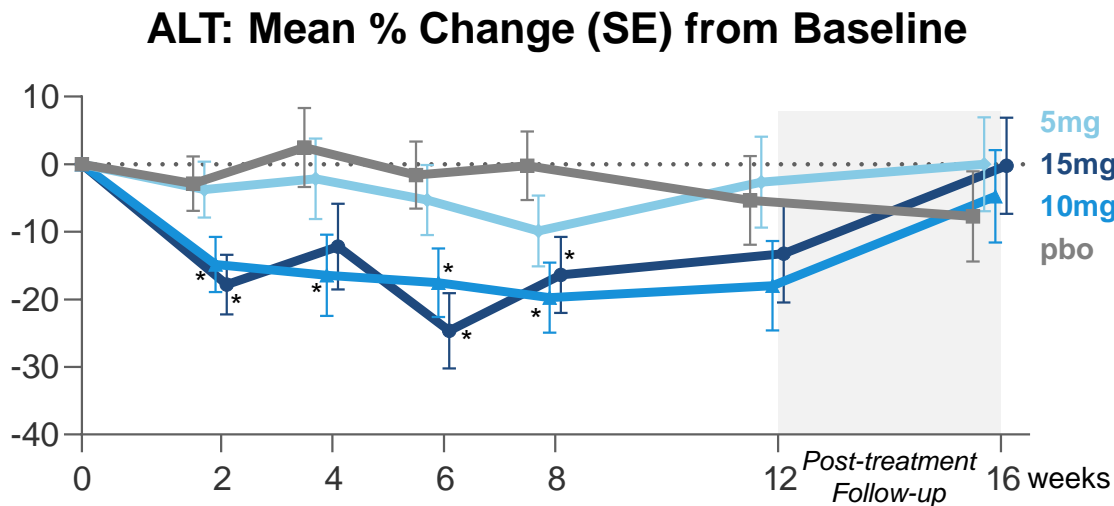
**Triglycerides: Mean % Change (SE) from Baseline**



**Total Cholesterol: Mean % Change (SE) from Baseline**

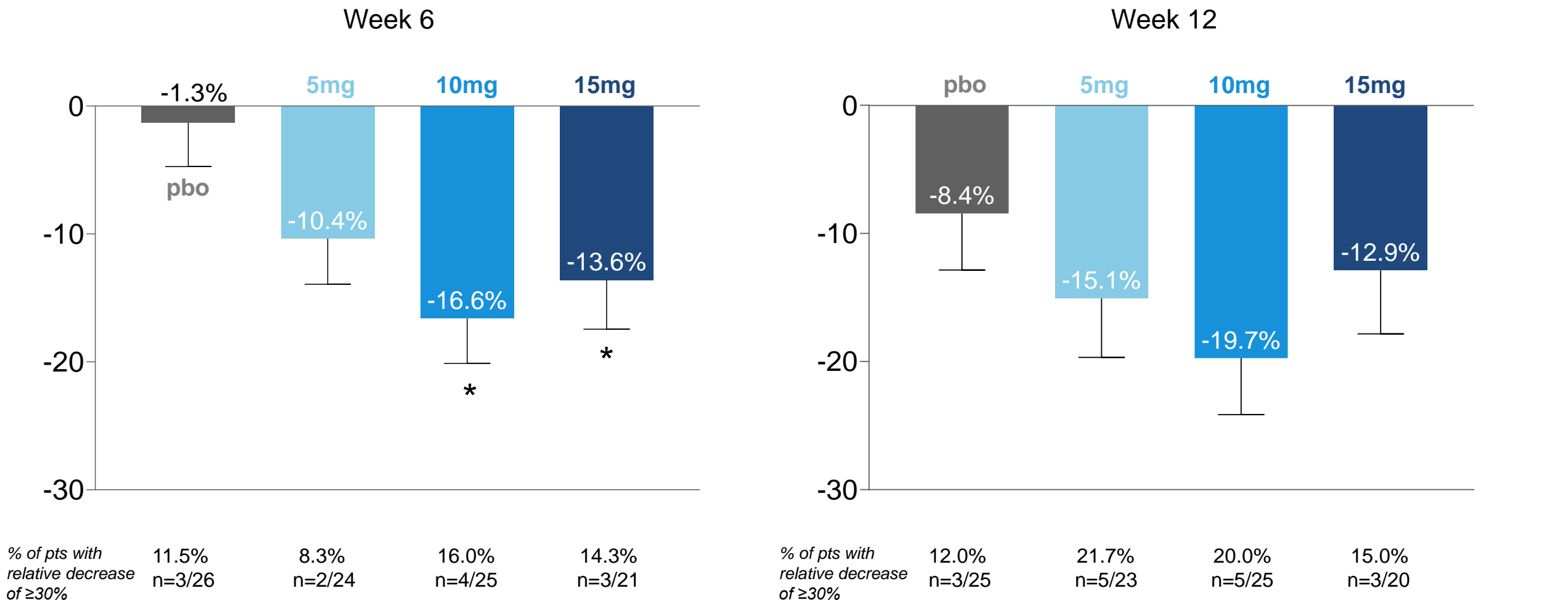


# Response in Markers of Liver Injury and Target Engagement



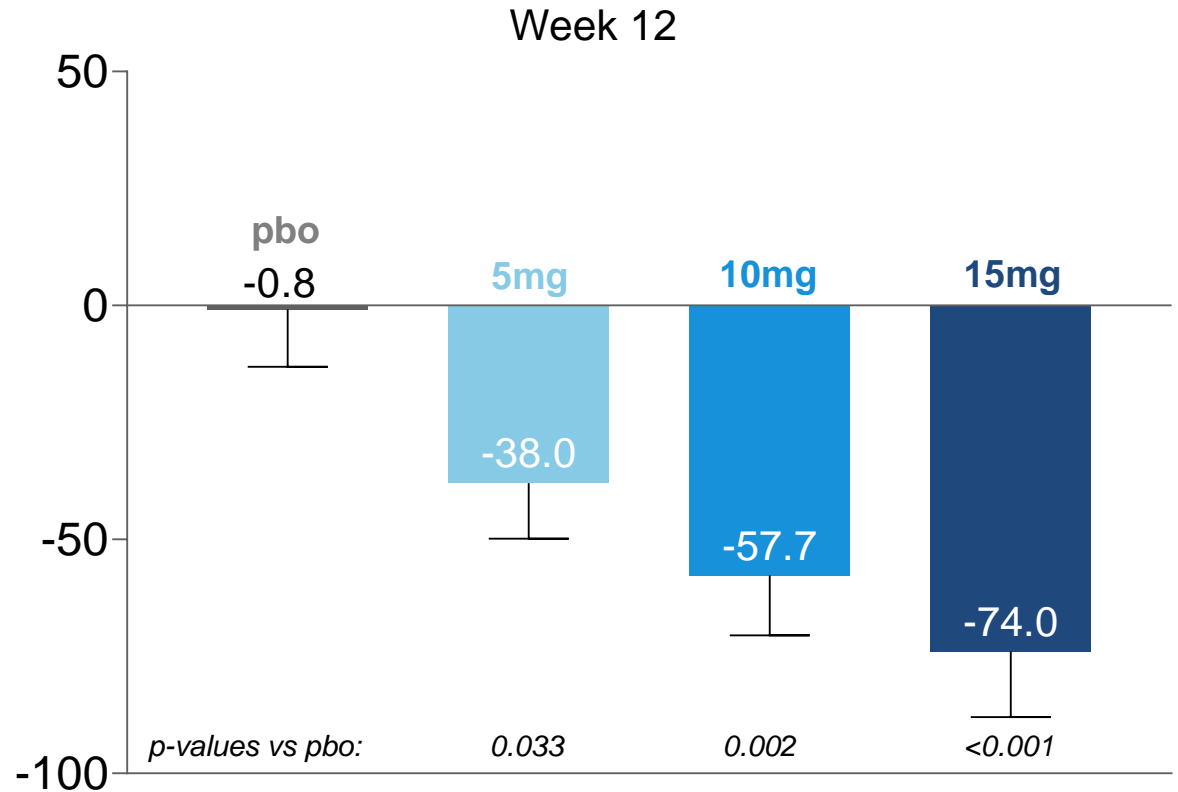
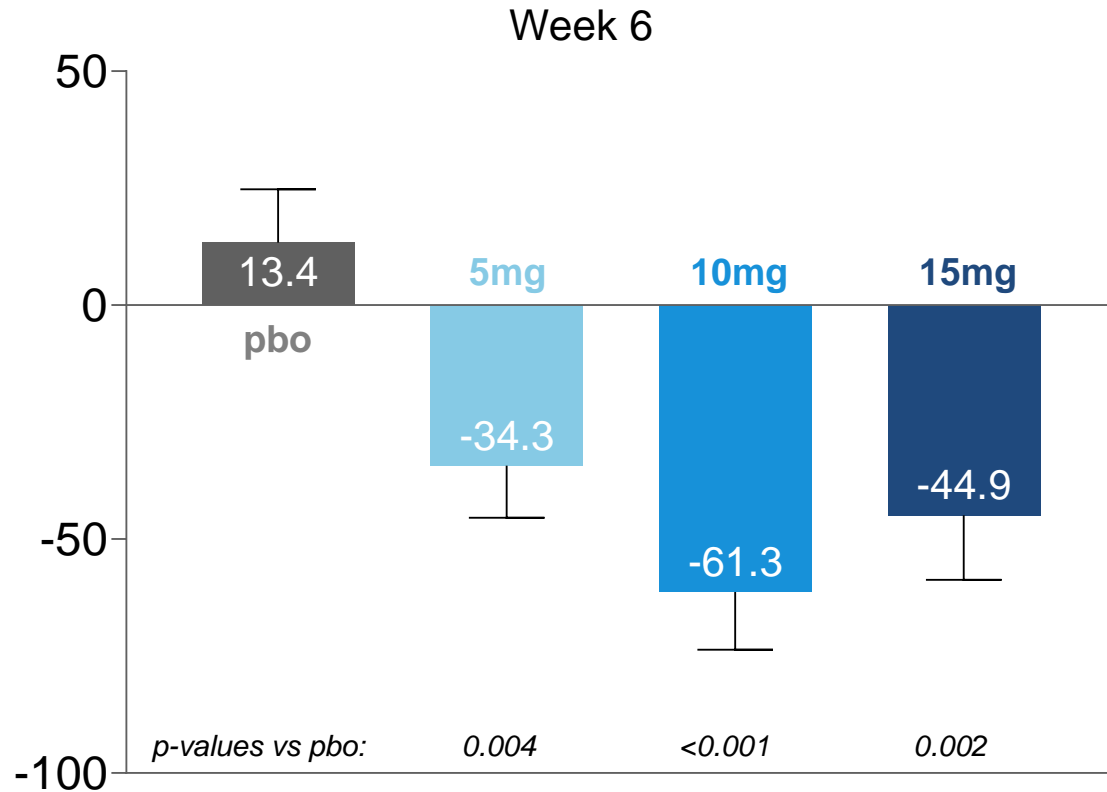
# Improvement in Liver Fat Content (MRI-PDFF)

MRI-PDFF Mean Relative Change (SE) from Baseline [%]

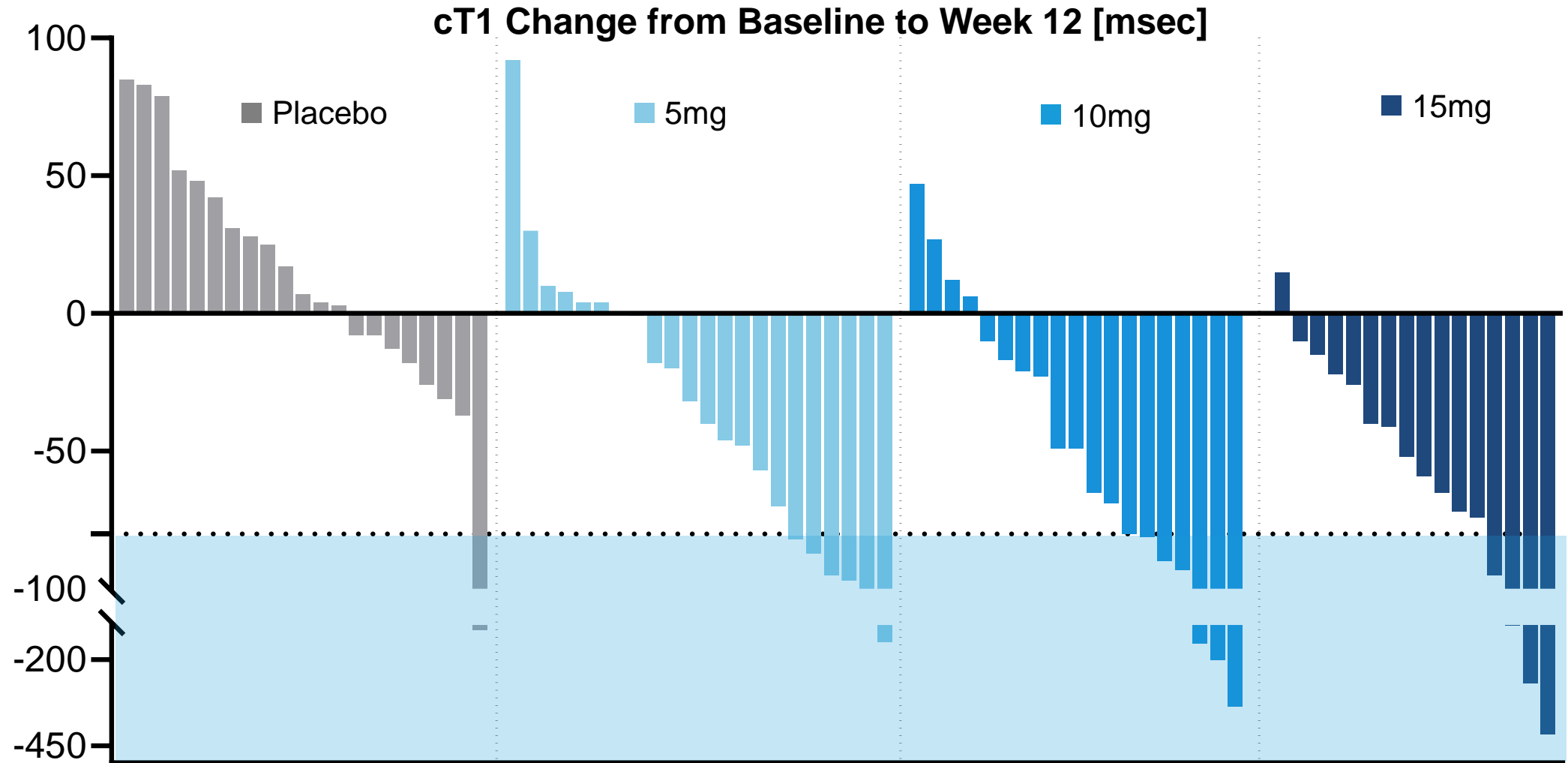


# LIFT is the First Trial in NASH Patients to Show Significant Improvements in cT1 Starting as Early as 6 Weeks

cT1 Mean Change (SE) from Baseline [msec]



# Substantially More Patients in Each TERN-101 Cohort Had Improvements in cT1



*% with  $\geq 80$  msec decline at Week 12*

**4.8%**

**27.3%\***

**36.8%\***

**25.0%**

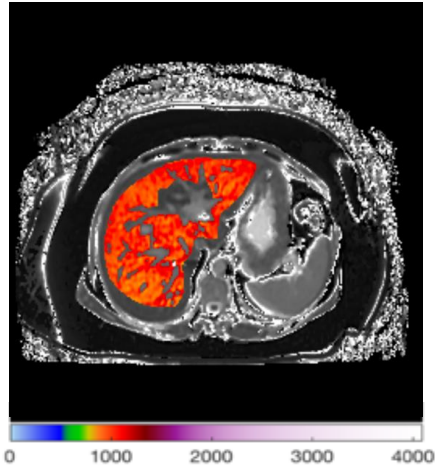
\* p-value < 0.05

# LIFT Patient Case Studies: Changes in cT1

**TERN-101  
10mg**

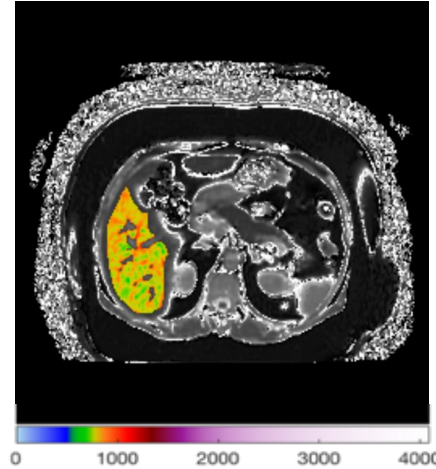
**Baseline**

cT1 – 1028ms



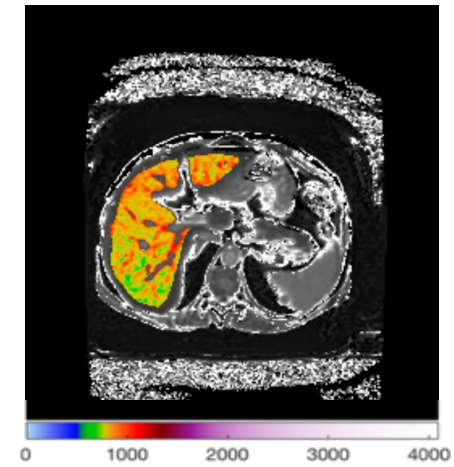
**Week 6**

cT1 – 808ms



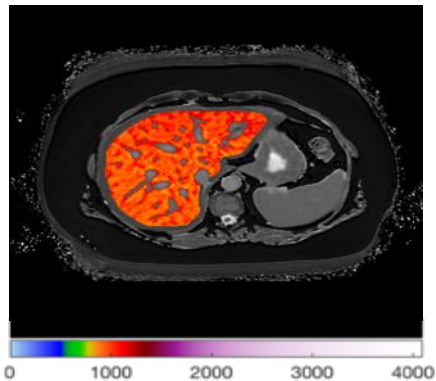
**Week 12**

cT1 – 826ms

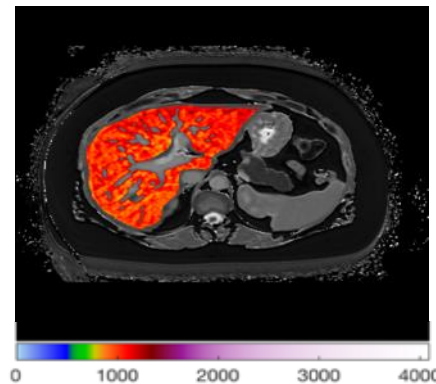


**Placebo**

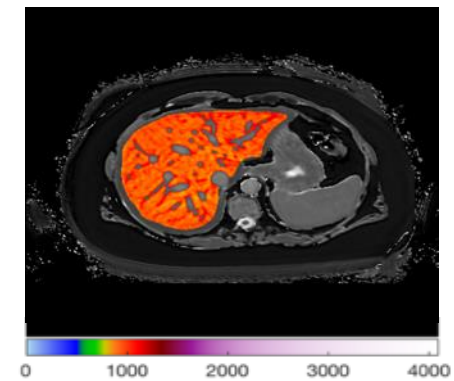
cT1 – 984 ms



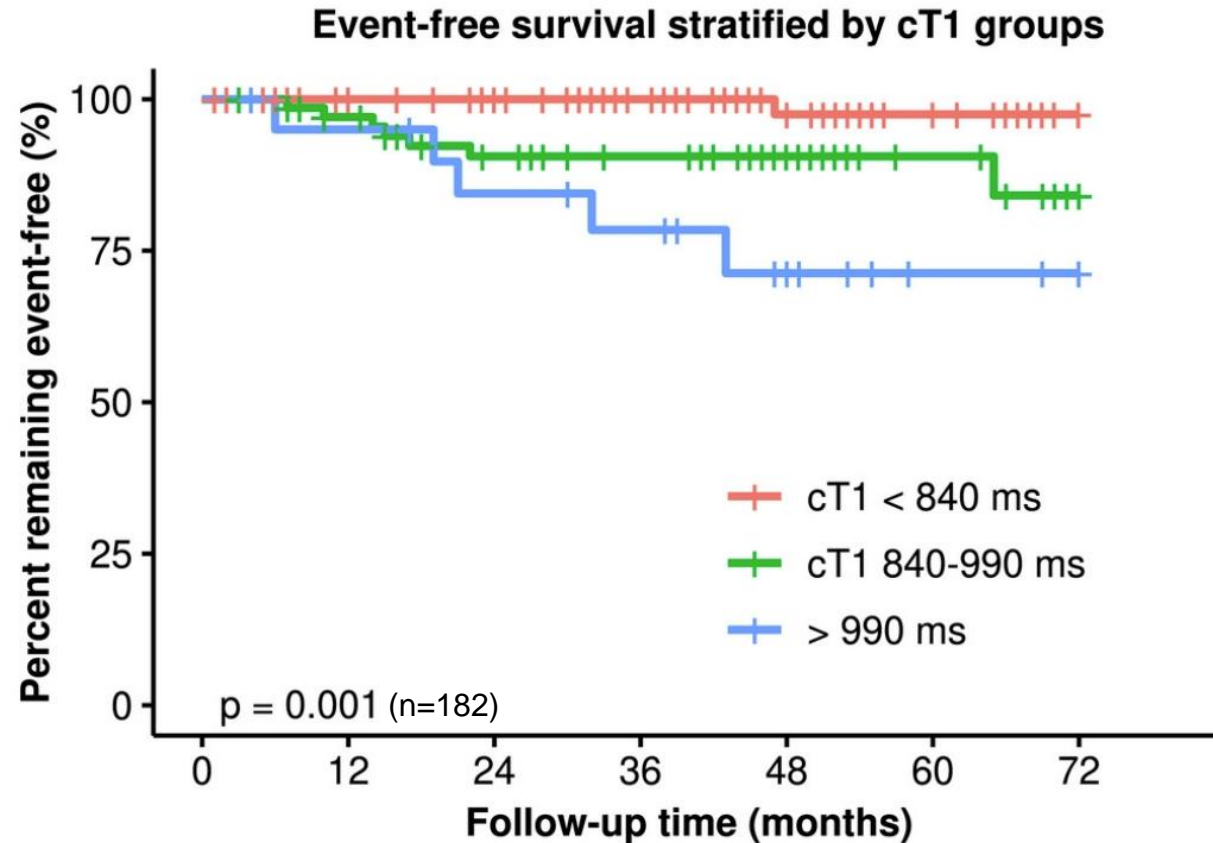
cT1 – 1015 ms



cT1 – 966 ms



# cT1 is Significantly Correlated with Clinical Outcomes

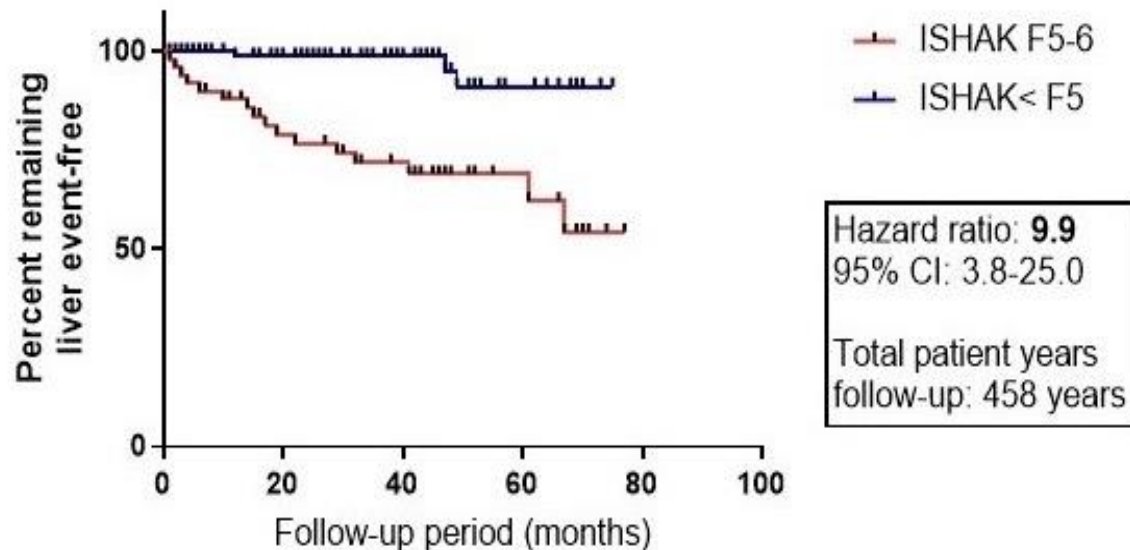


- Corrected T1 (cT1)
  - Magnetic resonance measurement that quantifies liver inflammation and fibrosis<sup>1</sup>
- Established correlation with clinical outcomes<sup>2</sup>
  - Liver cT1 (but not PDFF) is shown to strongly predict clinical outcomes in patients with chronic liver disease including NAFLD
  - Long-term outcomes being tracked in UK Biobank Imaging study of 100,000 individuals

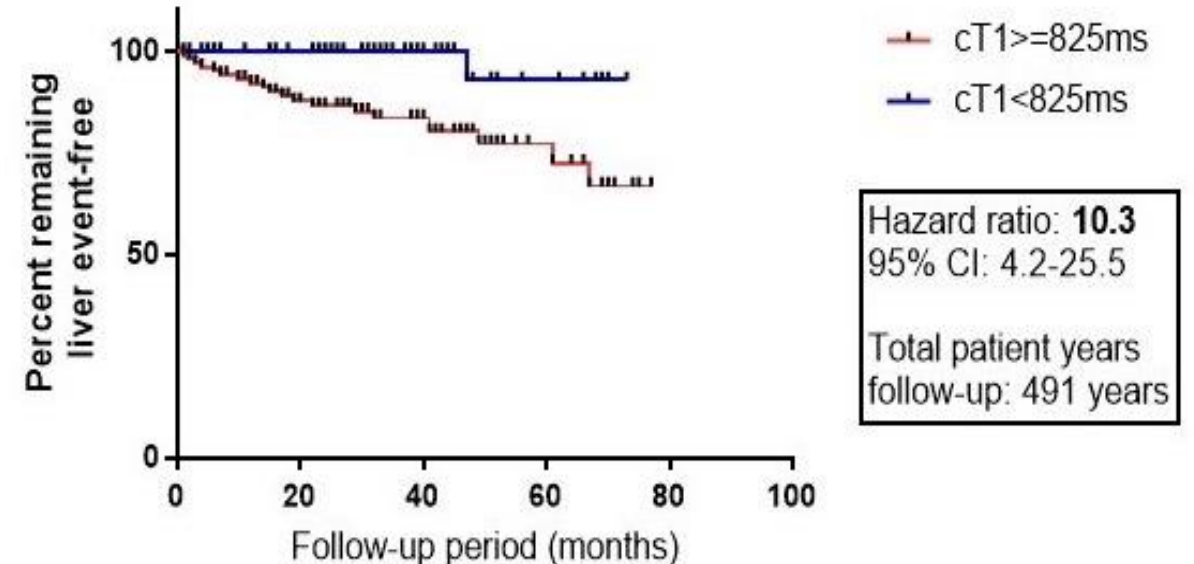
# cT1 and Histology Have Shown Equivalent Performance for Predicting Clinical Outcomes

*cT1, but not MRI-PDFF, correlated with clinical outcomes*

**Kaplan-Meier curve for liver-related event free survival with patients stratified according to ISHAK score**  
(n=150, median follow-up period: 35 months)



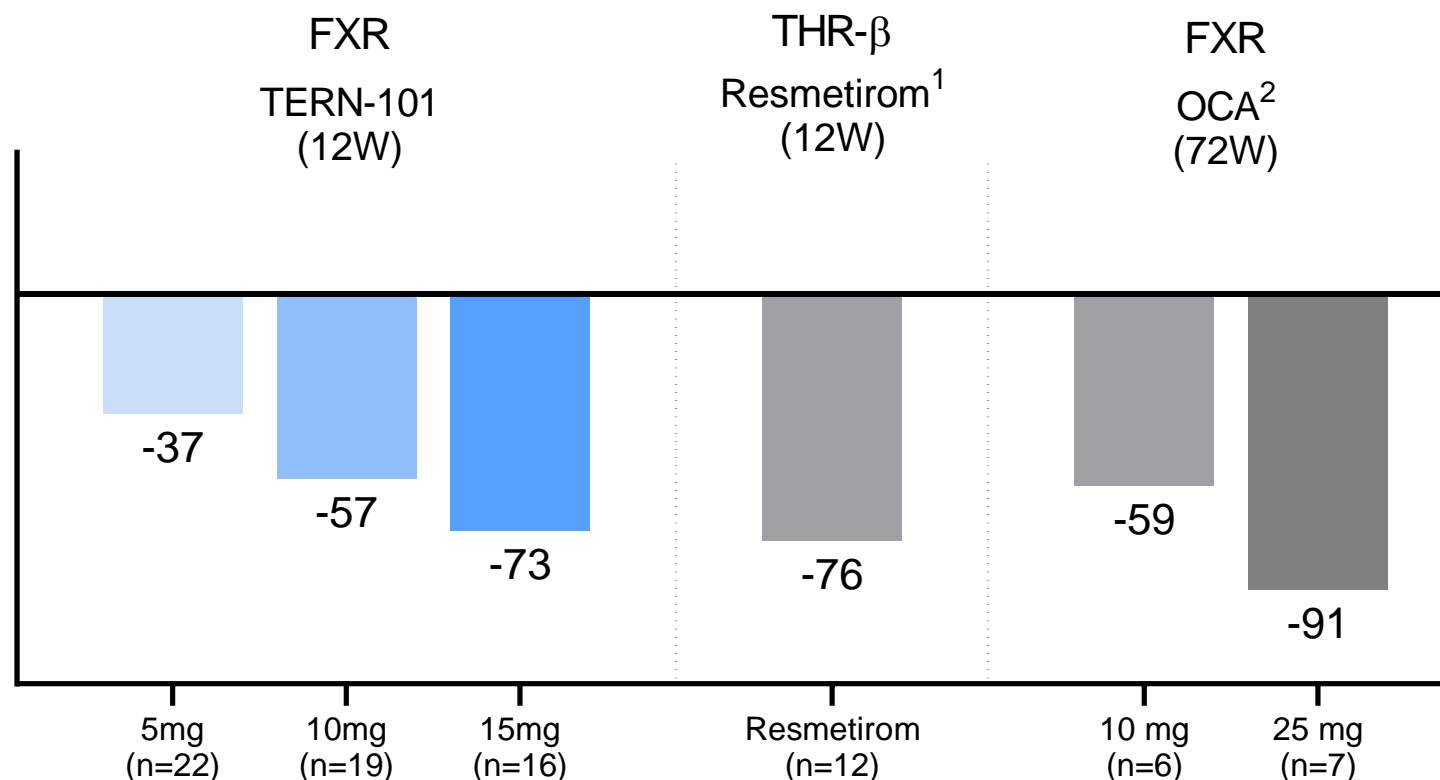
**Kaplan-Meier curve for liver-related event free survival with patients stratified according to cT1**  
(n=166, median follow-up period: 35 months)



# cT1 Results in Context of Late-Stage NASH Investigational Products

*TERN-101 cT1 changes comparable to late-stage development candidates*

## Placebo Adjusted Mean Change in cT1 (msec)



1. Data from resmetirom Phase 2 study extension [Madrigal 2018 corporate presentation](#); 2. Data from OCA Phase 3 REGENERATE study, [Loomba et al. Intercept poster at DDW 2020](#)

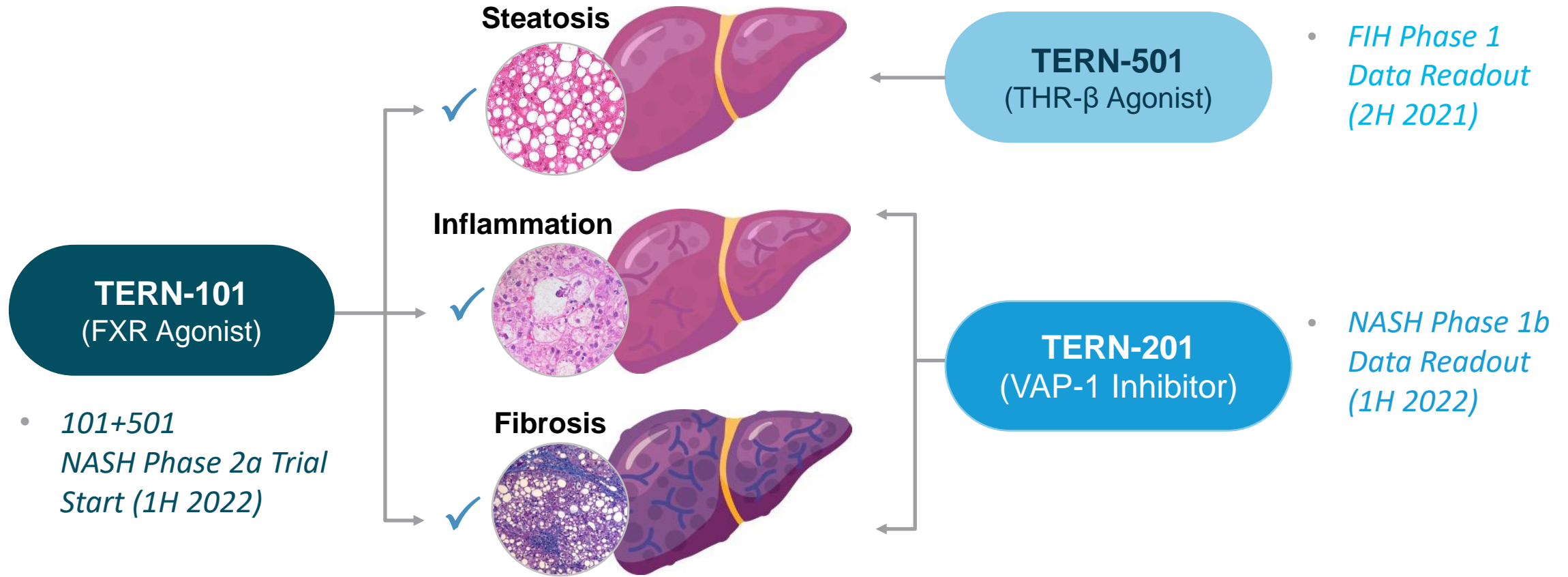
Note: Cross-trial comparisons involve the inherent bias of post-hoc manipulation of data and choice of analytical methods, as well as methodological issues surrounding heterogeneity among studies contributing to the analyses; therefore, it is important to view such results in light of the totality of all available information, such as individual study results on pre-specified analyses of endpoints

# 3 Important Firsts for NASH Treatment

1. First FXR agonist trial to demonstrate no discontinuations due to AEs, including pruritus
  - TERN-101 was generally well-tolerated with similar incidence of AEs across treatment groups
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  - cT1 is an imaging marker of liver inflammation and fibrosis linked to clinical outcomes<sup>1</sup>
  - Also observed improvements in PDFF and liver enzymes
3. First NASH trial of an FXR agonist (TERN-101) in combination with a THR- $\beta$  agonist (TERN-501) planned for 1H22 initiation
  - TERN-501 Phase 1 MAD portion started in June 2021 with data expected in 2H 2021

# Terns Pipeline: Multiple Catalysts Over the Next 12 Months

*Combining candidates with complementary mechanisms to maximize NASH patient benefit*





**TERNs**

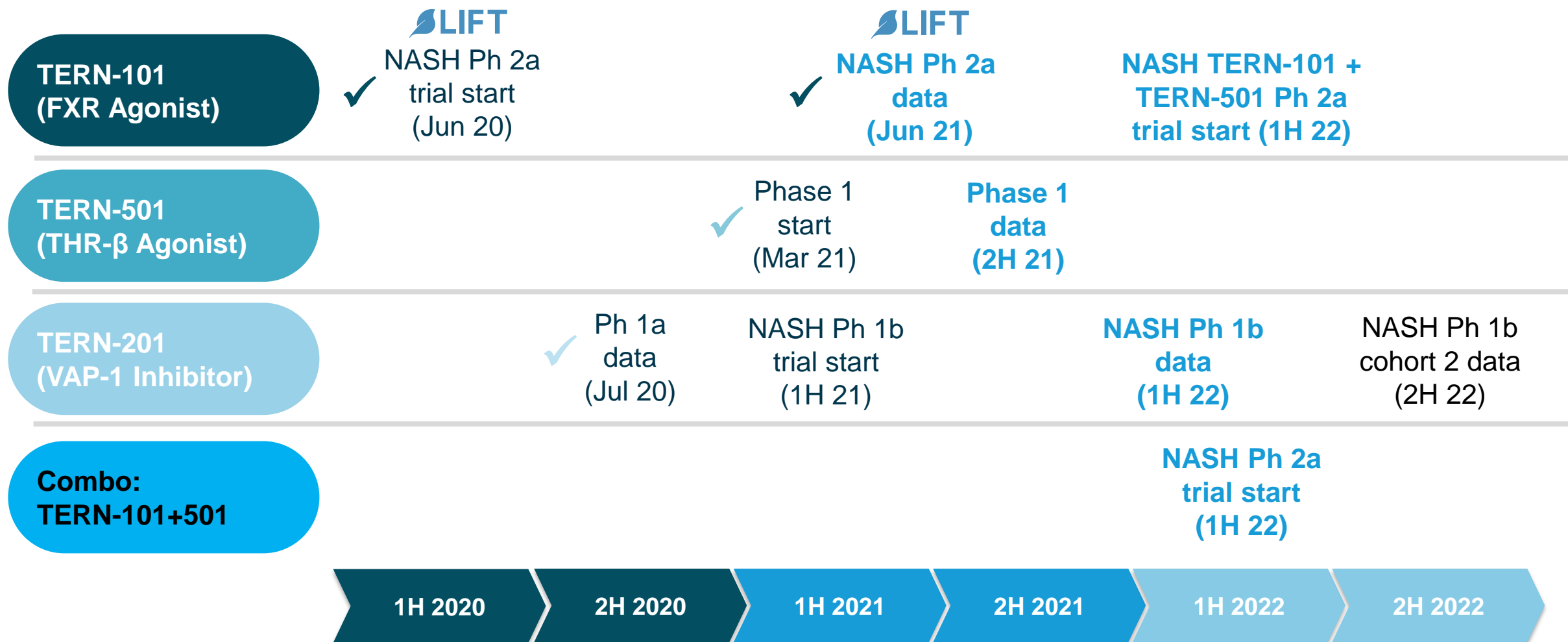
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# Appendix

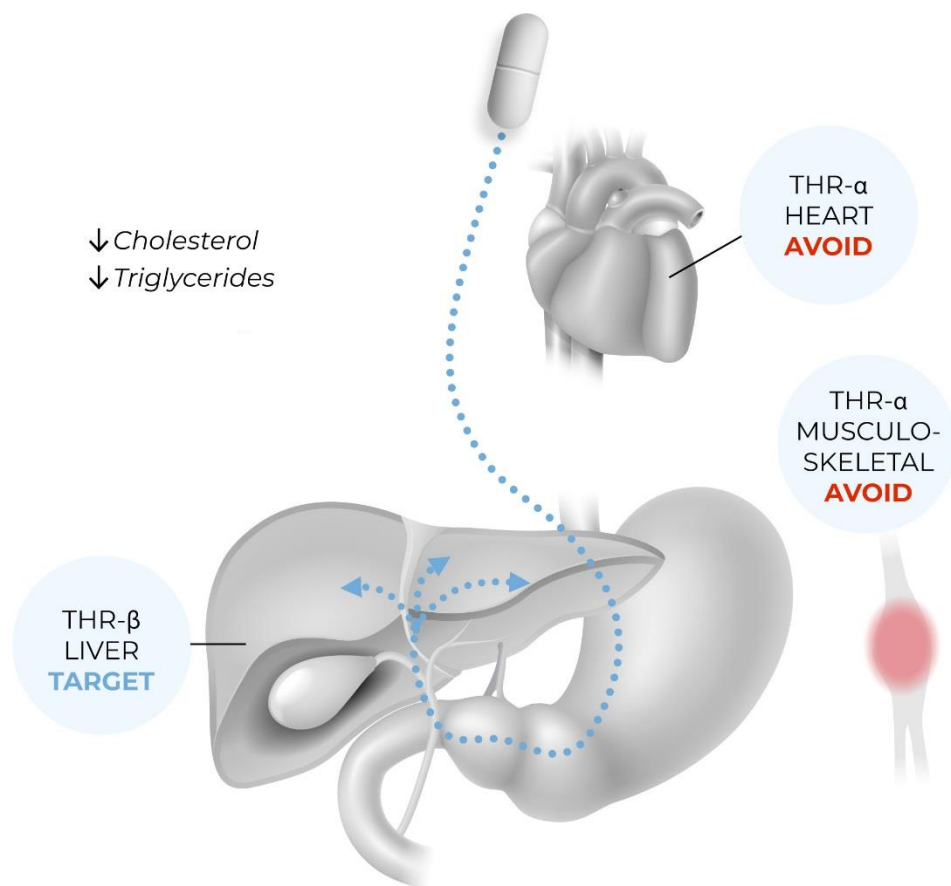
# Key Completed and Upcoming Milestones

*Multiple clinical milestones in 2021/2022 in preparation for combo trials*

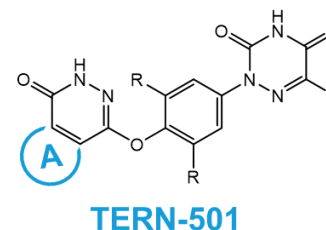


# TERN-501: Differentiated THR- $\beta$ Agonist

THR- $\beta$  regulates key aspects of energy metabolism (e.g., fatty acid & lipid synthesis, liver fat removal through fatty acid oxidation)



- TERN-501 is a selective Thyroid Hormone Receptor beta (THR- $\beta$ ) agonist with **enhanced metabolic stability and liver distribution**
- Other THR- $\beta$  agonists face limitations with off-target effects or unpredictable PK due to CYP metabolism

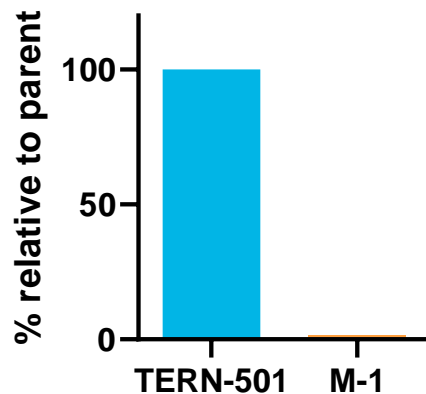
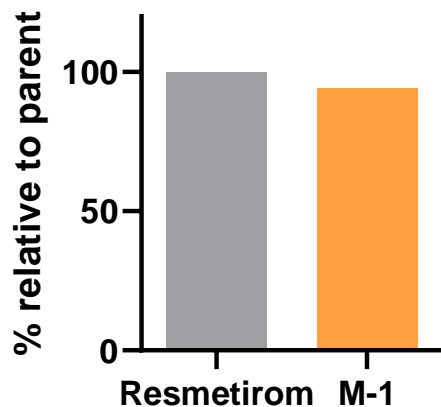
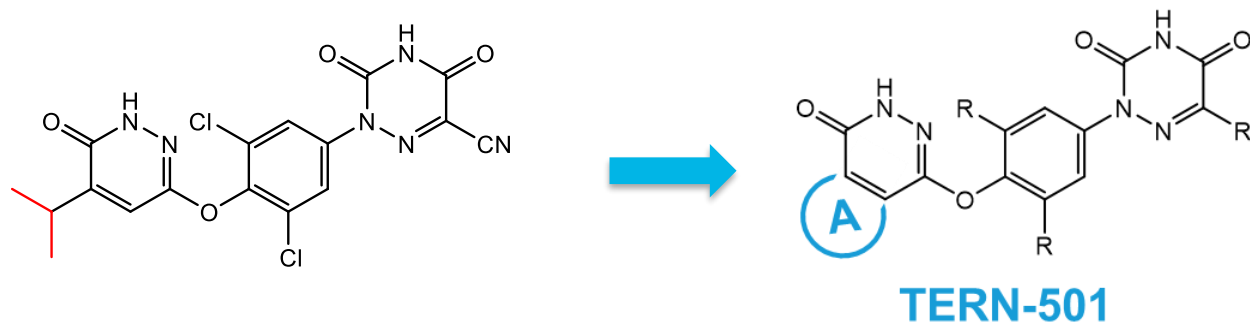


- TERN-501 was screened for **greater selectivity and enhanced metabolic and PK stability**
  - Expected low clinical dose
  - Attractive for monotherapy or combination therapy
- Phase 1 SAD/MAD clinical trial ongoing; top-line data expected **2H 2021**

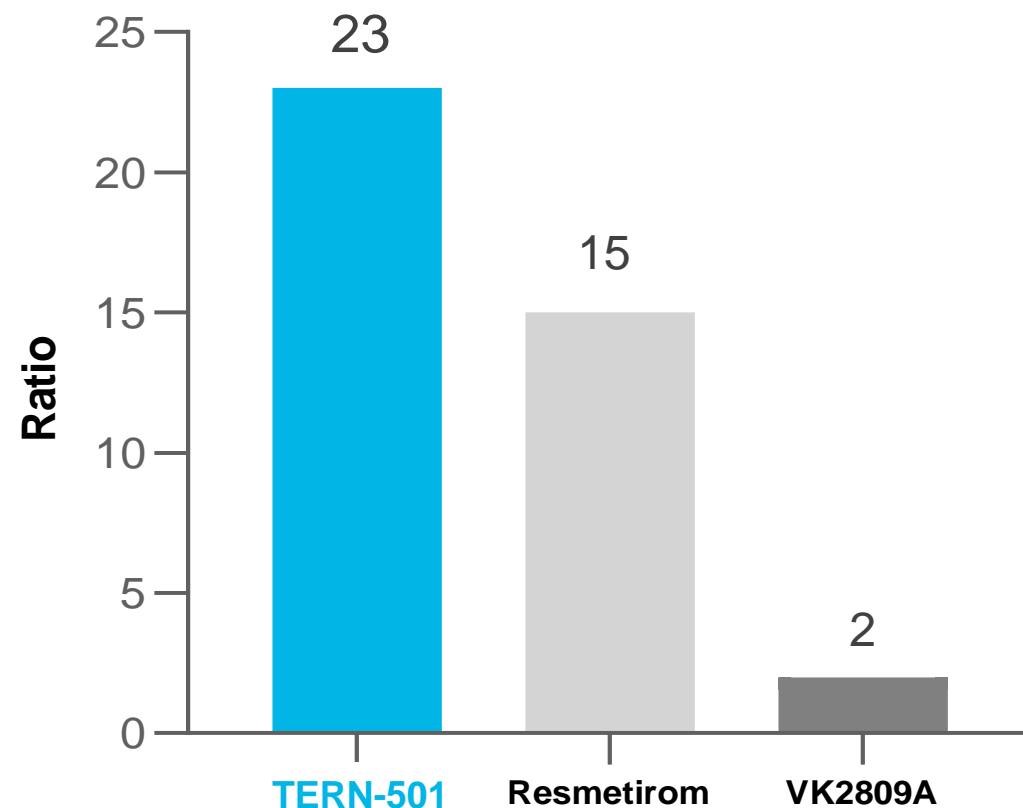
# TERN-501: Improved PK & THR- $\beta$ Selectivity

*Differentiated and excellent candidate for co-formulation*

## TERN-501: Improved Pharmacokinetics

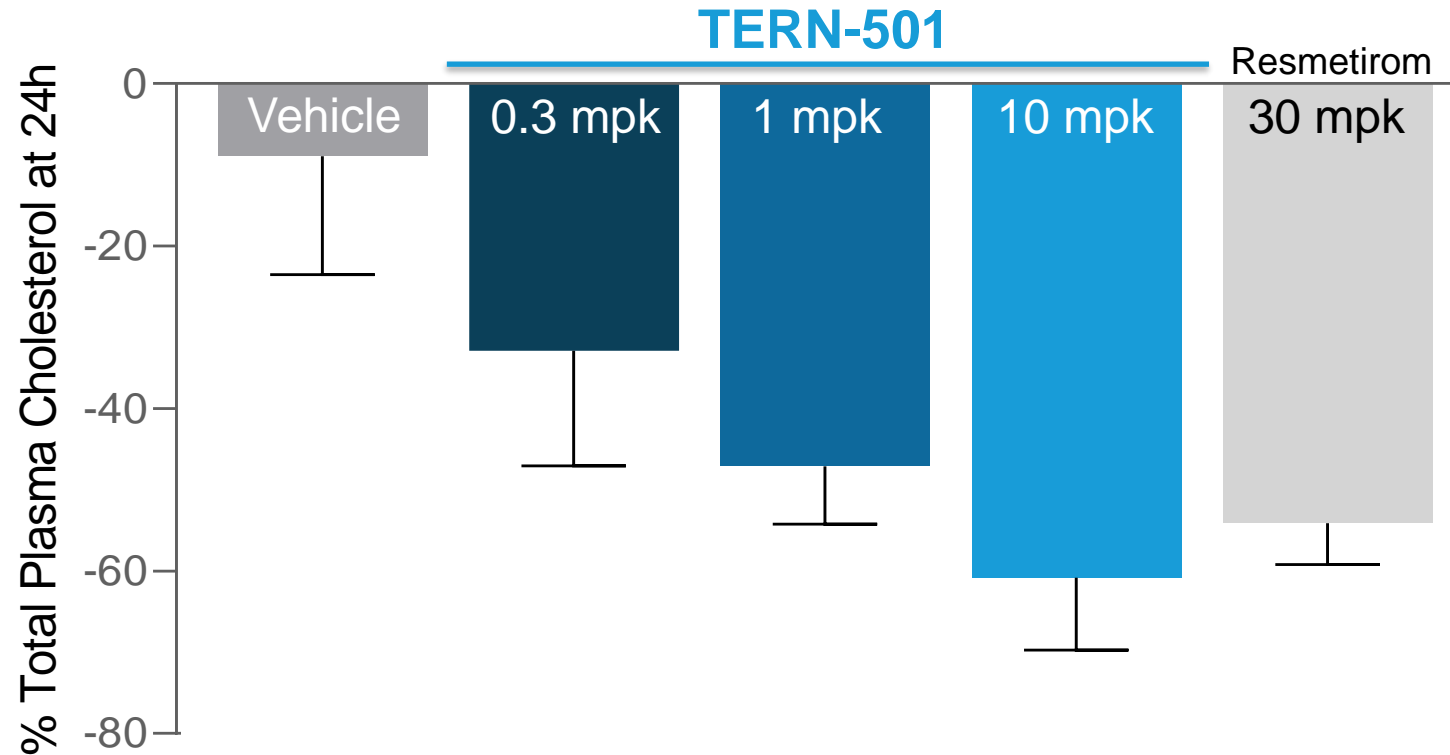


## TERN-501: Improved THR- $\beta$ ratio



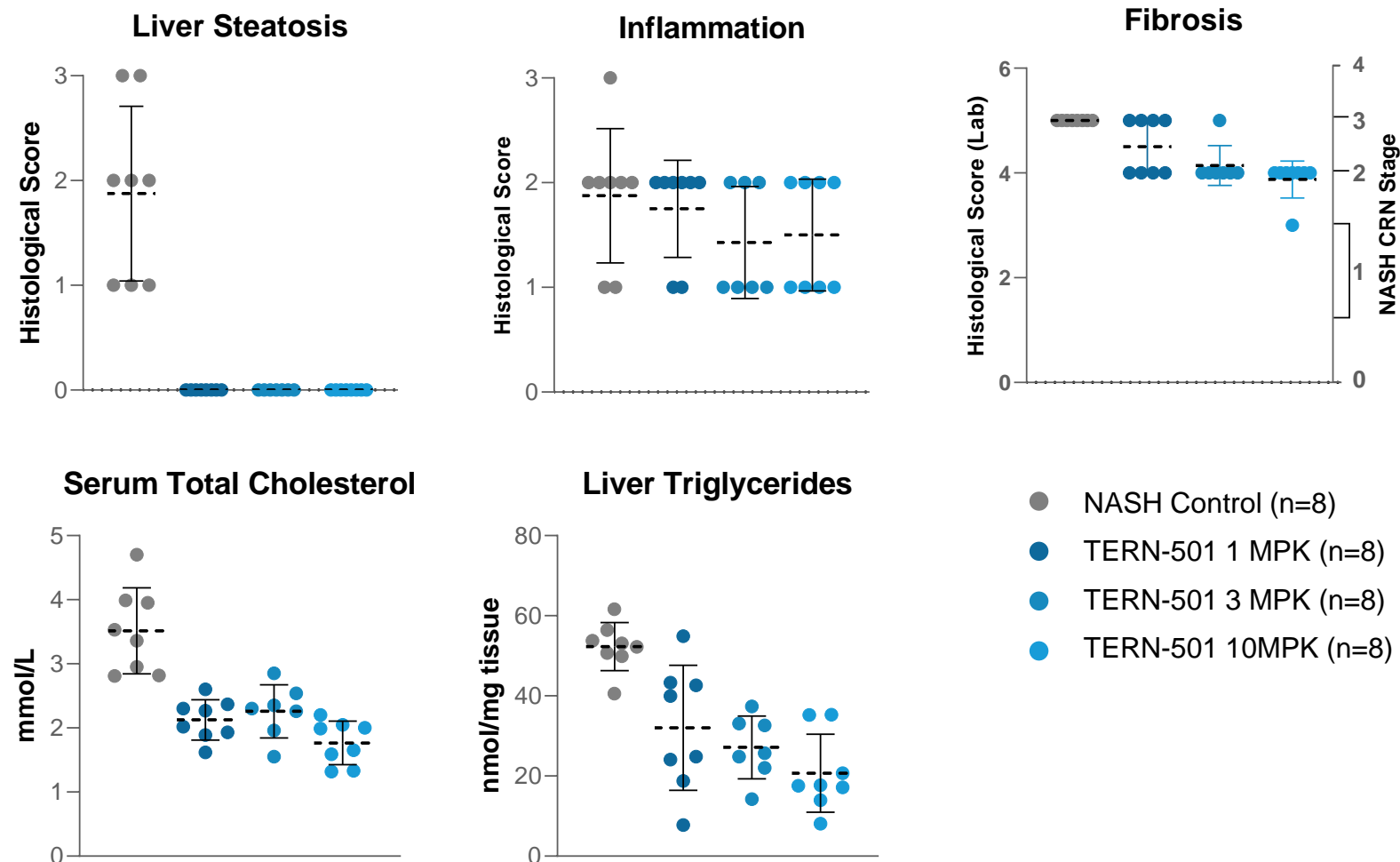
# TERN-501: Single Dose Suppresses Cholesterol

*Improved potency relative to resmetirom*



# TERN-501 Activity in DIO/CCl4 NASH Model

*Liver histology, liver function, lipid parameter improvements*



## Results

### Histology

- **Complete resolution of steatosis**
- Reductions in inflammation and fibrosis

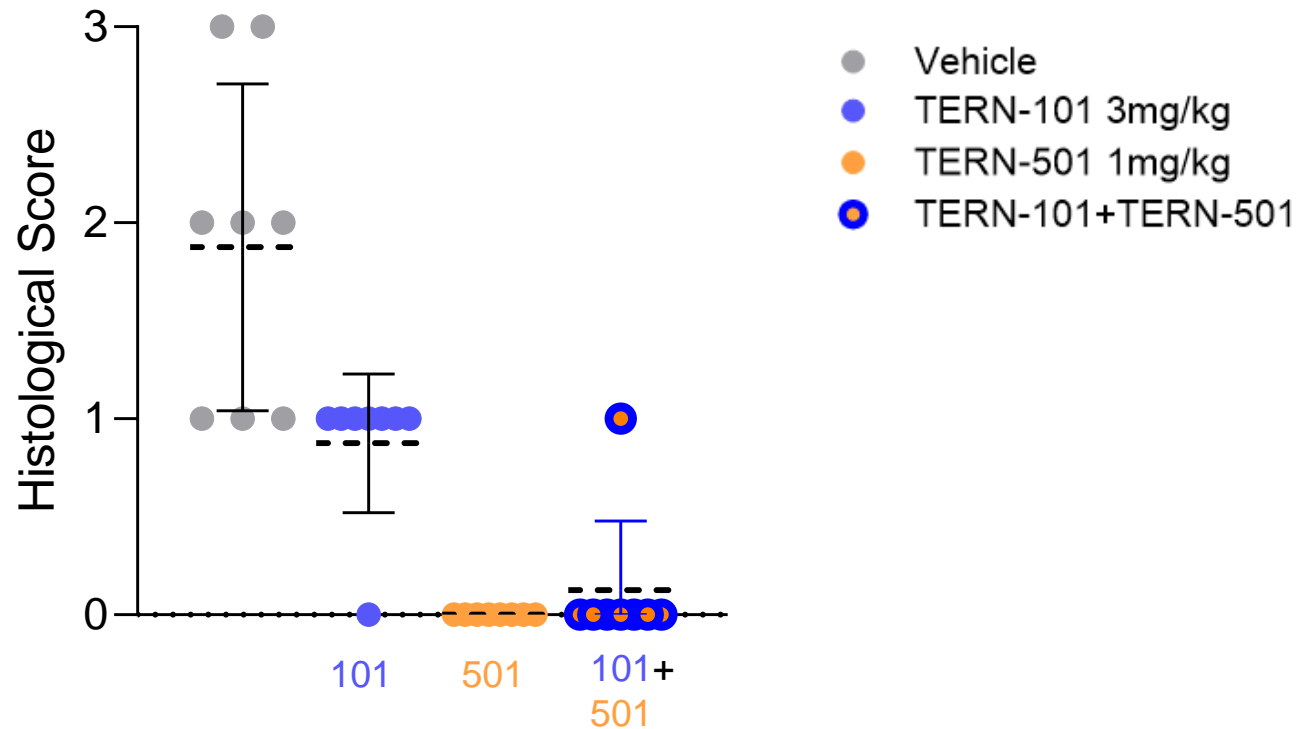
### Lipids

- Reduced serum cholesterol
- Dose-dependent reduction in liver triglycerides

# TERN-101+TERN-501 Combination NASH Model

*Combination shows additional effects on steatosis and fibrosis improvement*

## 101+501: Improvement in Steatosis



## 101+501: Improvement in Fibrosis

