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ENHANCING HEALTH

LPCN 1144

Oral Testosterone (T)

Non Alcoholic Steatohepatitis (NASH) and NASH Cirrhosis

LPCN 1144: Well Positioned for Success

Differentiated Mechanism of Action and Well Tolerated Safety Profile

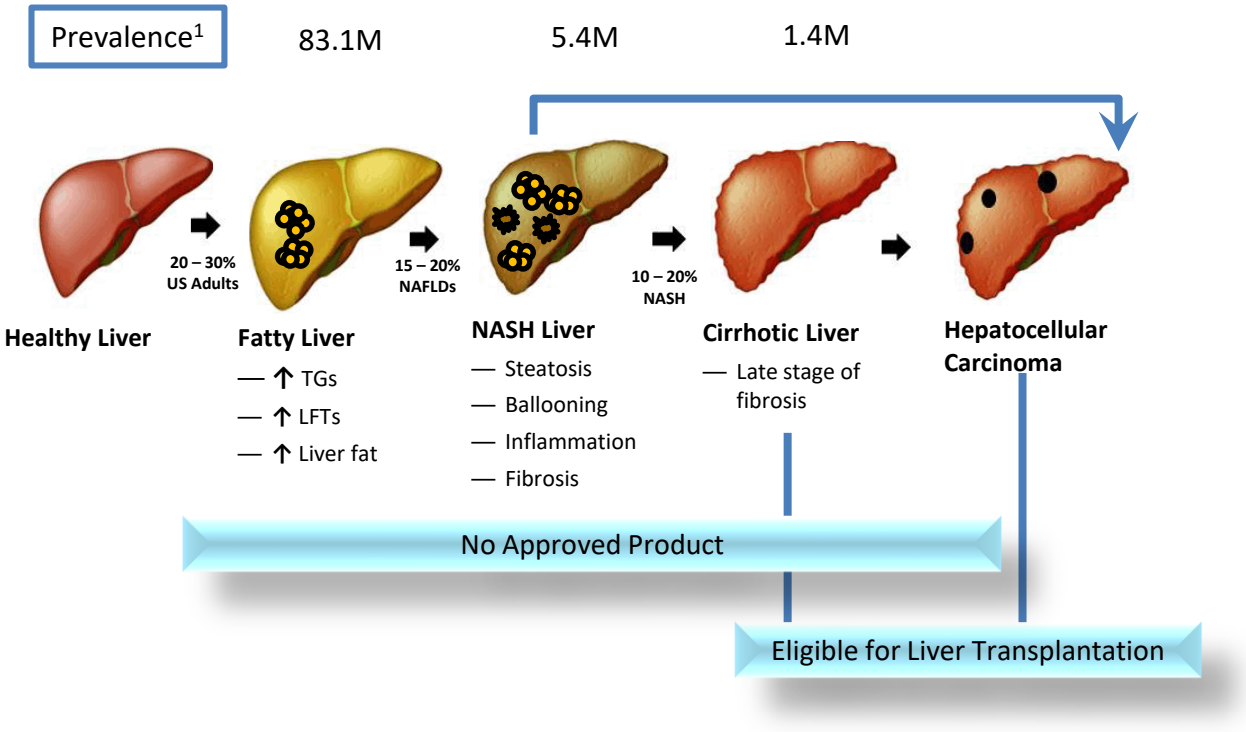
- Targeted for NASH Epidemic with No Approved Product
  - The NASH market could peak at $30-40 billion by 2025[1]
- Unique Mechanism Targeting Full Spectrum of NASH Pathogenesis + Collateral Health Benefits
  - Testosterone deficiency induces NAFLD/NASH
  - Testosterone treatment improves liver functions
- Well Tolerated Safety Profile
  - Prodrug of a bio-identical hormone
  - Demonstrated with 591 subjects in 12 studies with up to 52 week exposure
- Compelling Clinical Biomarker Data
  - Significant reductions in both the key ALT and TG serum NASH biomarkers
  - Good potential of histological improvement in NASH and Fibrosis

1. Deutsche Bank industry report, "NASH – the next big global epidemic in 10 years?", 2014

Non-Alcoholic Fatty Liver Disease (NAFLD)

Clinical Progression

Fatty liver is a reversible condition wherein large vacuoles of triglyceride fat accumulate in liver cells via the process of steatosis



1 . Estes et.al. Hepatology, 2018:

LFTs: Liver function test, especially Alaninine amino transferase (ALT) and Aspartame amino transferase (AST)
NASH: Non-alcoholic Steatohepatitis, TG: Triglyceride

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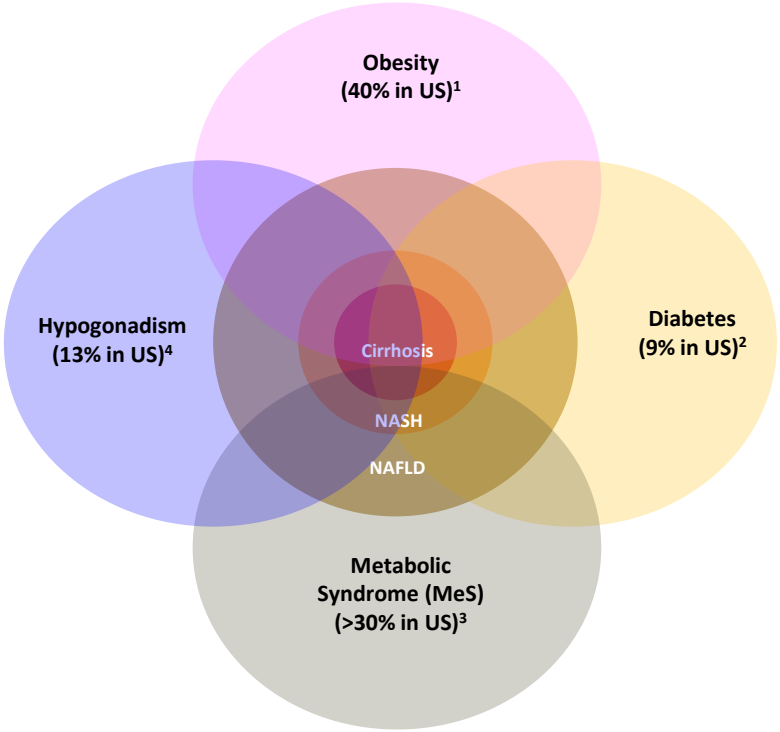
Co-Morbidities Associated with NASH

Fatty Liver Related Diseases



* Kim et al, Male hypogonadism and liver disease in Male hypogonadism and basic clinical and therapeutic, Contemp Endocrin (2017) p219-234

1. CDC, Jun 2018
2. CDC, Jul 2017
3. Moore et al, Prev Chronic Dis, 2017 (CDC)
4. Dandona and Rosenberg, Int J Clin Pract, 2010 (US Census Bureau, Aug 2008

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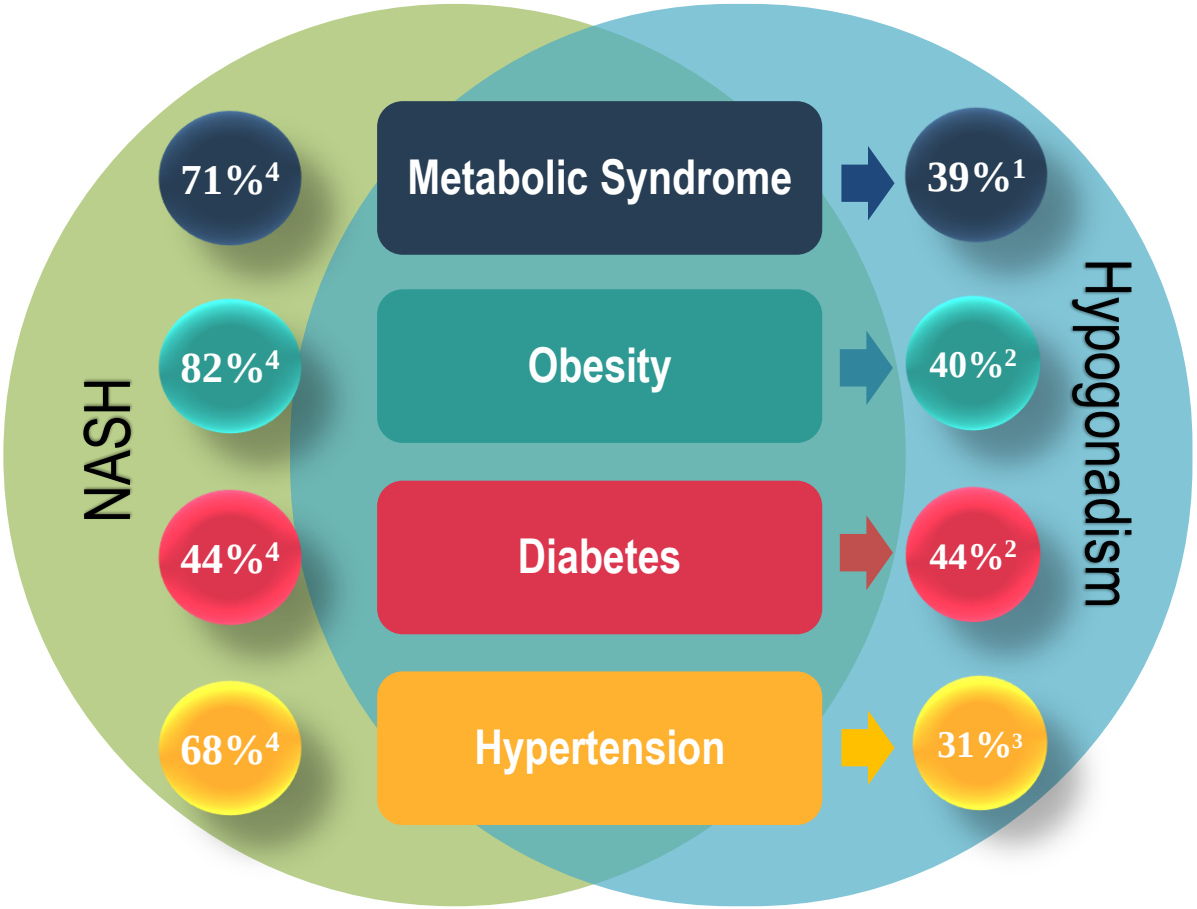
Testosterone Deficiency Relevant in Chronic Liver Diseases*

Significant Overlap of NASH with Hypogonadism



Liver fat is highly correlated with components of metabolic syndrome[5]

* Kim et al, Male hypogonadism and liver disease in Male hypogonadism and basic clinical and therapeutic, Contemp Endocrin (2017) p219-234

1. Guay A.T., J Androl 2009; 2. Dhindsa et al., Diabetes Care 2010; 3. Guay et al., Int J Impotent Res 2010; 4. Younossi et al., Hepatol 2016; 5. Rector et al., Gastroenterol 2008

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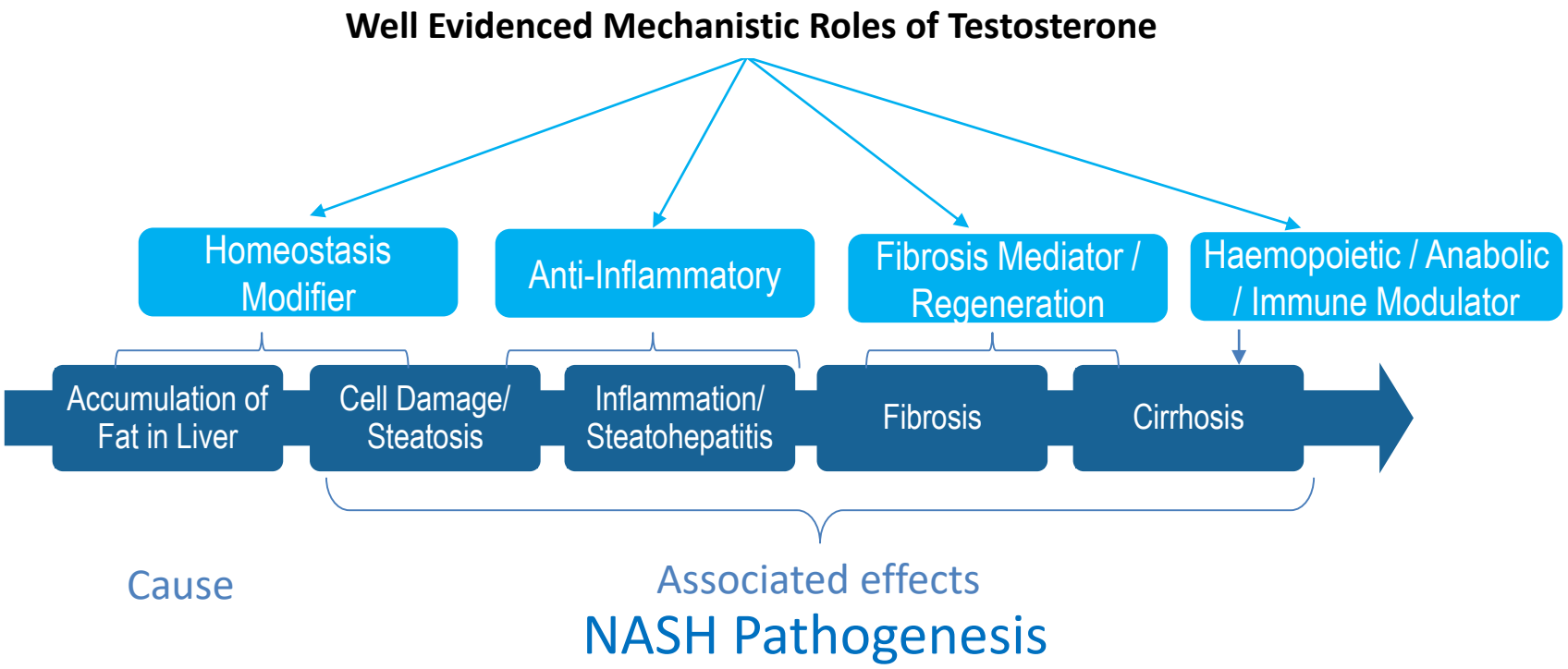
LPCN 1144: Targeting Full Spectrum Of NASH Pathogenesis

Plus Collateral Health Benefits



- Reduction of elevated ALT levels generally predicts histological improvement of NASH and fibrosis[1]
- Liver fat (TG) reduction typically associated with steatosis reduction

1 Hoffnagle et al. APT 2013

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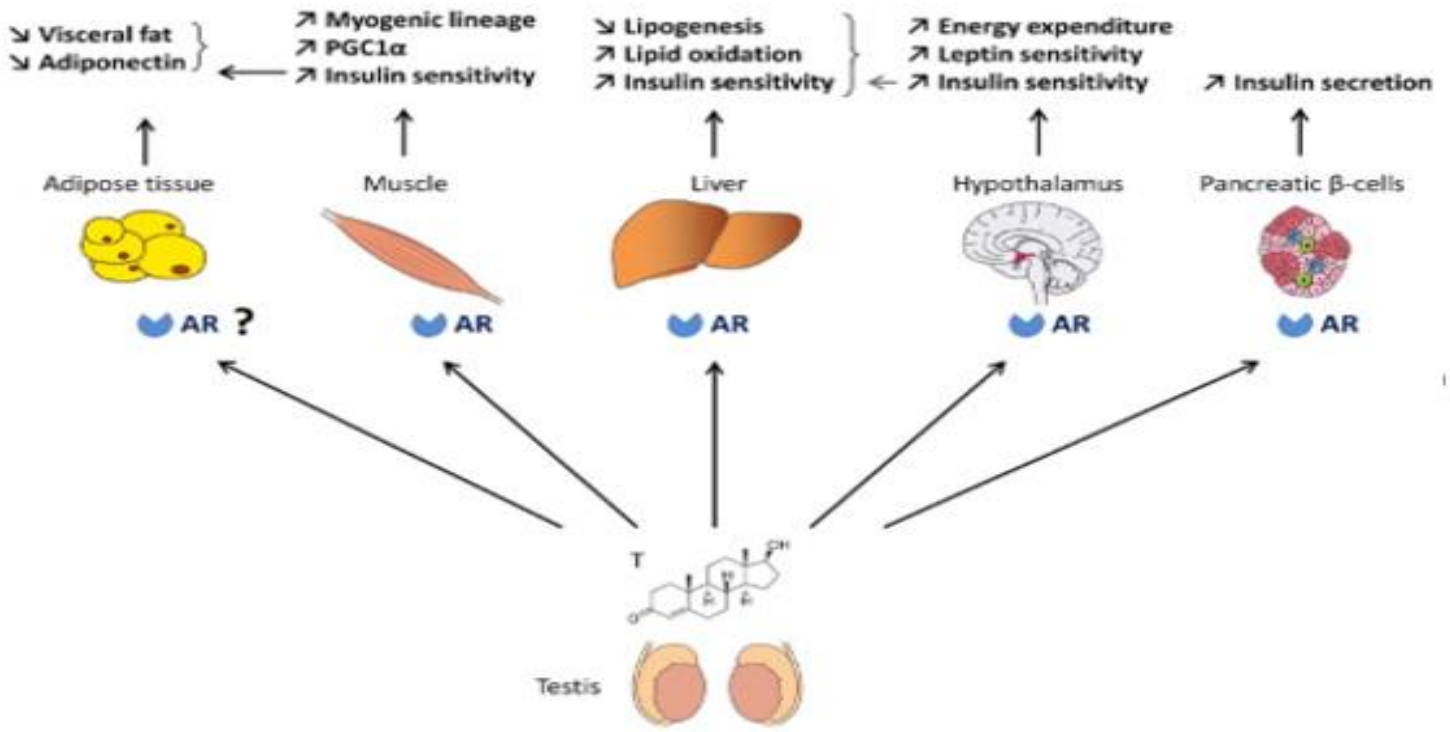
Proposed Mechanism of Androgen Action via Androgen Receptor (AR) in Males*



Normal level and signaling of androgens prevent hepatic fat accumulation in males**

* Navarro et al, Obesity 2015

** Shen and Shi, Int J Endocrinol 2015

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LPCN 1144: Oral T

Proposed Multidimensional Mechanism of Actions

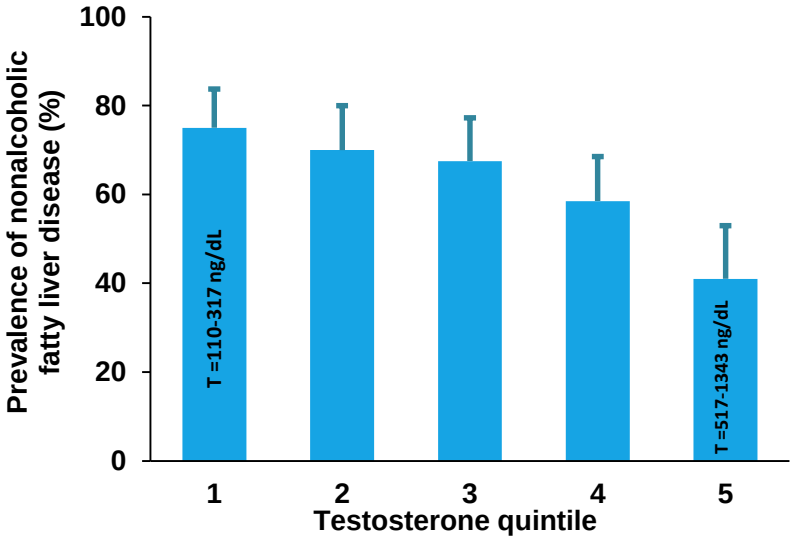
- **Homeostasis Modifier[1, 2]**
  - Alter lipid, cholesterol, and glucose metabolism
  - Reduce visceral abdominal fat
  - Modify activity of hepatic lipase, and skeletal muscle/ adipose lipoprotein lipase
- **Anti-inflammatory[2]/ Immuno-modulator[3]**
  - Low T results in compromised immune system
  - Inflammatory Cytokines, IL-6, TNF-α and IL-1β, inhibit testosterone secretion by their influence on the central (hypothalamic-pituitary) and peripheral (testicular) components of the gonadal axis.
- **Regenerative**
  - Stimulate satellite cells and myocyte precursor resulting in cell differentiation and myocyte proliferation
  - Clinical data demonstrate that adult males who undergo a 40–60% partial hepatectomy experience T levels decline similar to those observed in male rats following a 70% hepatectomy.[4,5]
- **Anabolic effects on muscle, bone and hematopoiesis**
  - Low T is a predictor of mortality in men with advanced liver disease.[6]

1. Shen and Shi, Int J Endocrinol 2015
2. Kelly and Jones, J Endocrinol 2013
3. Sinclair et al, J Gastroenterol
4. A. Francavilla et al., Digestive Disease ans Sciences, 1989
5. Vic et al, Hepatol 1982
6. Sinclair et al, J Gastroenterol Hepatol 2016 Hepatol 2015

Low T Association with NAFLD and Cirrhosis

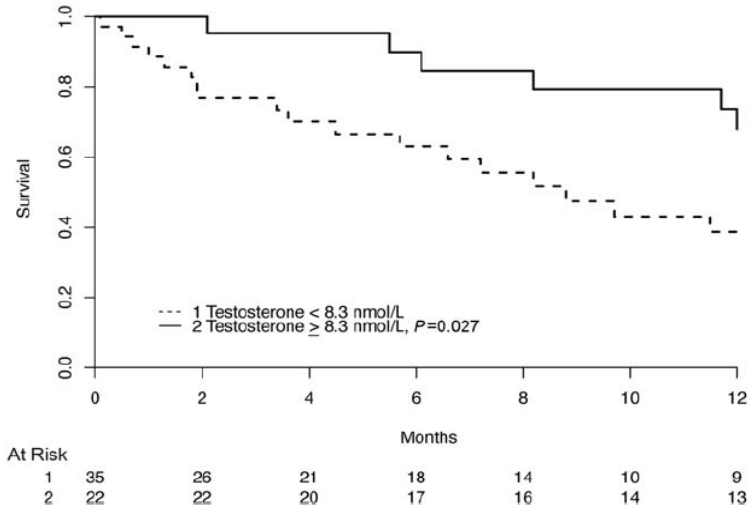
Hepatic steatosis is associated with low serum testosterone in men*

NAFLD and Low T[1]



✓ After adjusting for age, smoking, diabetes, exercise, BMI, TG and HDL, the lowest T quintile (110 – 317 ng/dL) have OR† of 5.12 (2.43 – 10.77) for NAFLD

Cirrhosis survival and Low T[2]



✓ Low T (<8.3 nmol/L; 239 ng/dL) remained a significant predictor of reduced survival in cirrhotic patients

1. Kim et al, Gastroenterol 2012
2. Sinclair et al, Liver Trans 2016

* Volzke et al, Int J Androl 2010

† OR: Odds Ratio

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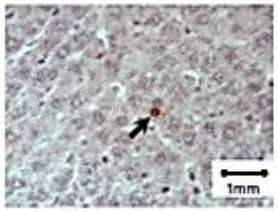
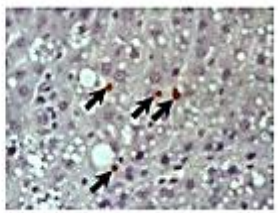
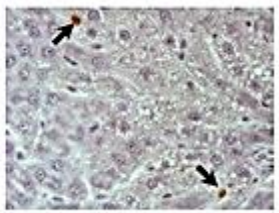
Testosterone Deficiency Induces NAFLD/NASH

Testosterone Treatment Improves Liver Functions[1]

Groups	Intact + Normal Diet *I + RCD (Control)*	Intact + High Fat Diet *I + HFD*	Castrated + High Fat Diet C + HFD	Castrated + High Fat Diet + Testosterone C + HFD + T
Histology				
Histopathology lipid deposits	*Normal*	Similar to control	Increase in score	Similar to control
Hepatocyte Apoptosis	Rare occurrence	Higher than control	Significantly higher than control	Similar to I + HFD
ALT	40.7 ± 4.4 IU/L	47.4 ± 3.8 IU/L	60.6 ± 6.4 IU/L	44.4 ± 4.5 IU/L
Macrovascular Inflammation	Normal	No	Yes	No

1 Rat Study (Nikolaenko et al, Endocrinol 2014)

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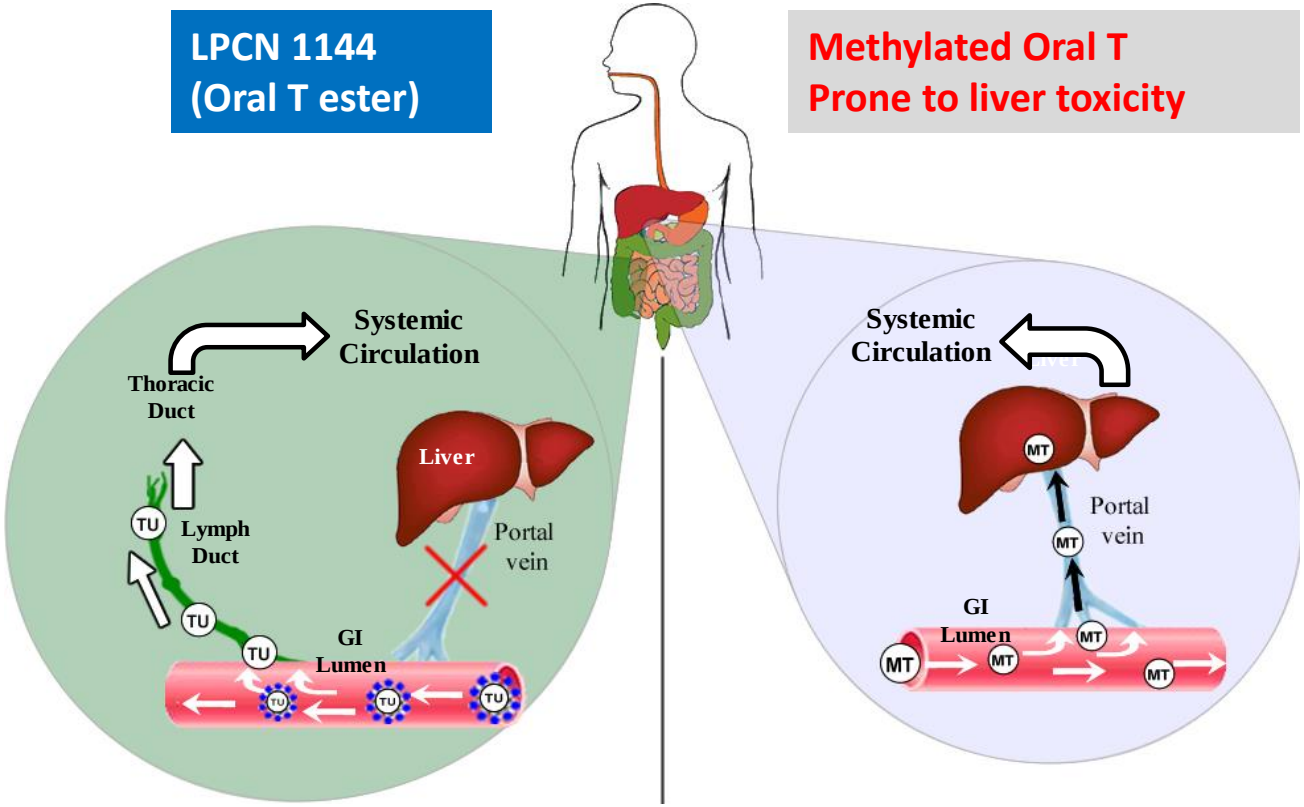
LPCN 1144: Lymphatic Delivery of Oral T Via Chylomicron



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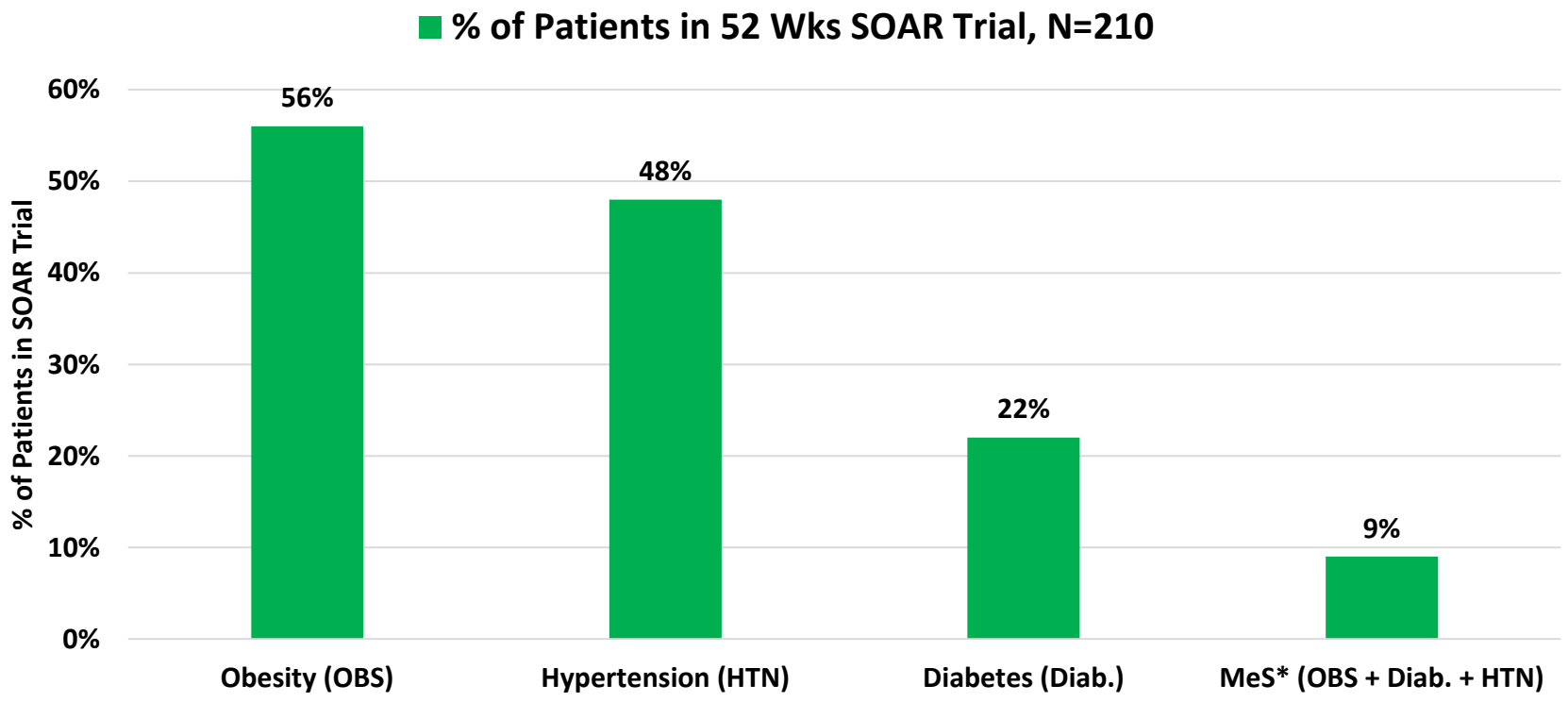
LPCN 1144: Study Details for Serum Biomarker Data Analyses

- Oral Testosterone, twice daily dosing regimen
  - Included subjects with typical comorbid conditions associated with NASH
  - Liver enzymes, lipids and cholesterol (NASH biomarkers) levels were monitored
  - Key serum NASH biomarkers were evaluated via mean change from baseline
  - Subjects were not confirmed with biopsy for NASH

- **M12-778 Study (Double Blind Placebo-controlled Study)**: 3 week therapy with oral T vs. placebo control in hypogonadal subjects
- **13-001 Study (Study of Oral Androgen Replacement [SOAR] Trial)**: 52 week therapy with oral T and topical T active control in 314 hypogonadal subjects
- **16-002 Study (Dosing Validation [DV] study)**: 3 week therapy with oral T in 94 hypogonadal subjects

- Subgroup of subjects are categorized as "potential NASH patients" based on elevation of key NASH biomarkers at baseline
  - Key NASH biomarkers: Alanine aminotransferase (ALT), Aspartate aminotransferase (AST), Alkaline phosphatase (ALP), Gamma-glutamyl transpeptidase (GGT), Triglyceride (TG)

LPCN 1144: SOAR Trial Comorbidity Distribution



* MeS: Metabolic Syndrome

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LPCN 1144: Liver Enzymes and TG Mean BL Levels in Patients with Comorbidities Typical of NASH

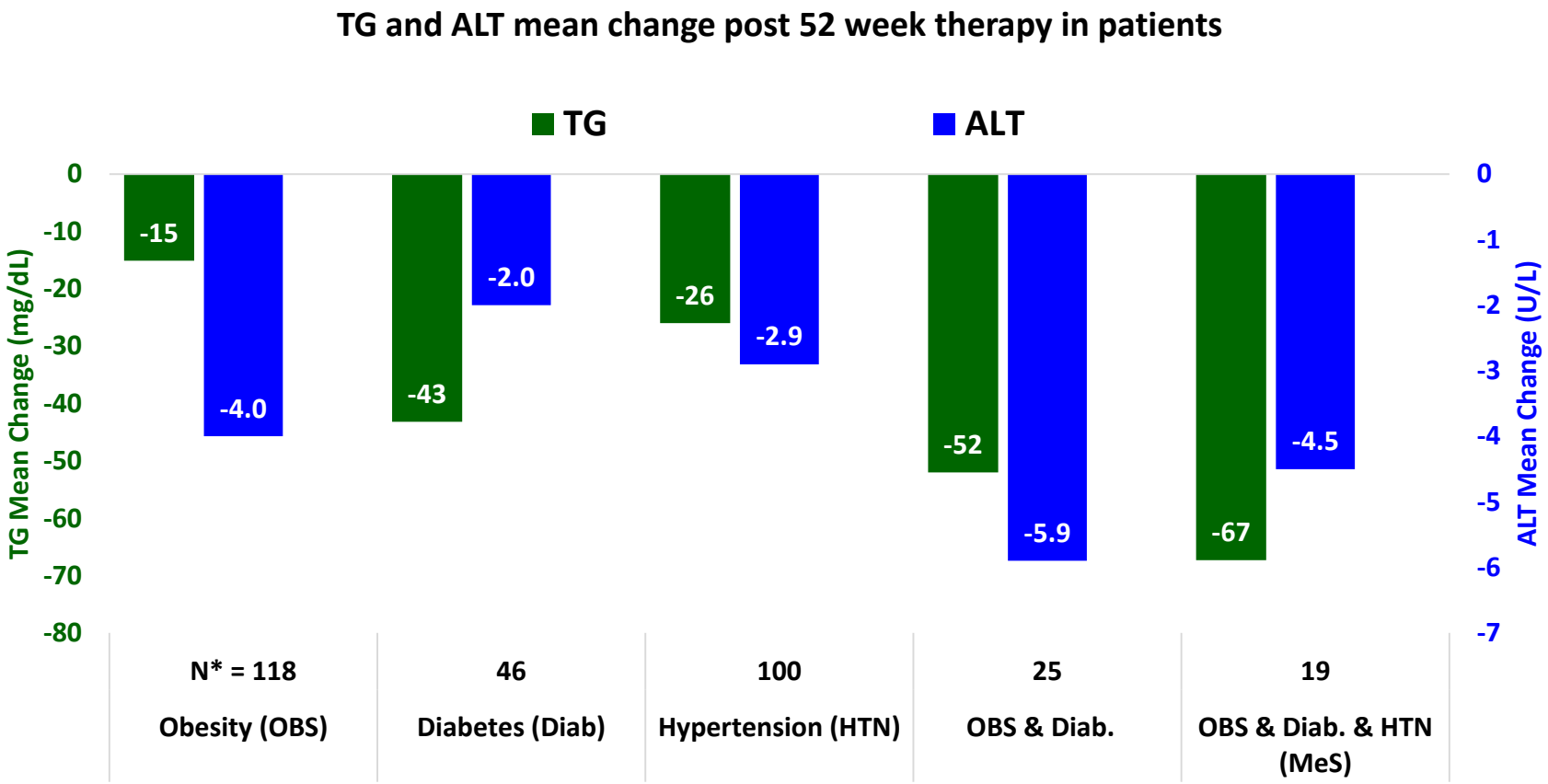
SOAR Trial (13-001)	Overall (N=210)	Obesity (N=118)	Diabetes (N=46)	Hypertension (N=100)	OBS + Diab. (N=25)	MeS (OBS + Diab + HTN) (N=19)
ALT (U/L)	30.5	33.3	29.4	29.0	33.4	30.2
AST (U/L)	24.2	24.7	21.1	23.5	22.3	22.4
ALP (U/L)	71.8	71.7	73.3	69.4	69.2	66.0
GGT (U/L)	36.0	36.8	41.7	34.0	35.2	29.4
TG (mg/dL)	192	205	209	187	237	253

LPCN 1144: General Safety

- **LPCN 1144 is a prodrug of bioidentical sex hormone**
  - History of safe Ex-US Oral TU use for decades
  - 8,400 patients / 15,600 patient years of use of over 19 years
    - Data assures well-characterized safety with respect to prostate, hypertension, polycythemia and liver disease

- **Extensive clinical safety database with LPCN 1144**
  - 591 subjects in 12 studies with up to 52 week exposure
  - Safety profile well-characterized and demonstrated no unexpected risks
  - Well tolerated with no adverse liver enzyme signals, no deaths or MACE events
  - No drug related SAEs

LPCN 1144: Substantial Reduction of Clinical Biomarker Levels in Cohorts with NASH Risk Factors



* N = Total N for subgroup

MeS: Metabolic Syndrome

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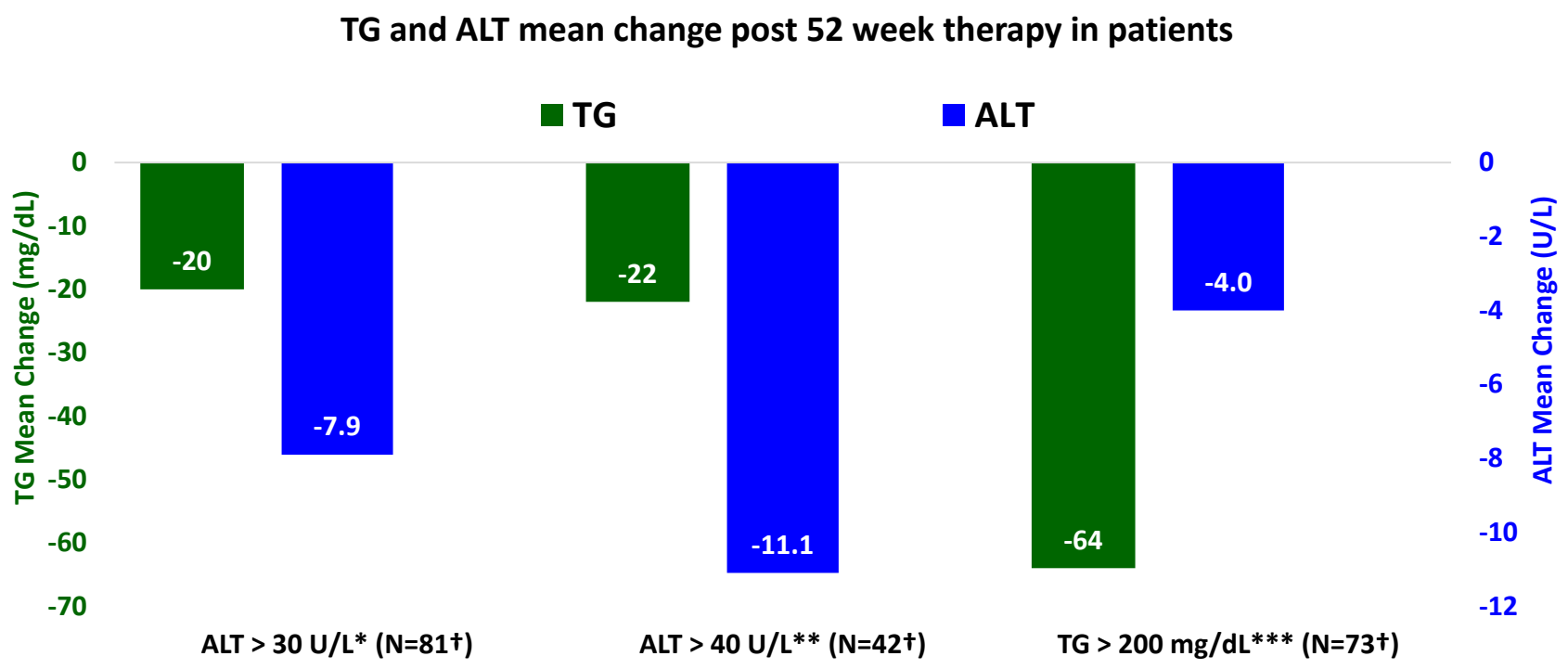
LPCN 1144: Significant Reduction of Clinical Biomarker Levels in Cohort with Elevated ALT and TG at BL



Mean BL:	TG	ALT	TG	ALT	TG	ALT
	214	44.5	227	53.6	320	34.4

† N = Total N for subgroup

* Barritt 4th et al, Contemp Clin Trials, 2017

** Sanyal et al, Hepatol, 2015

*** TG normal range 45 – 200 mg/dL

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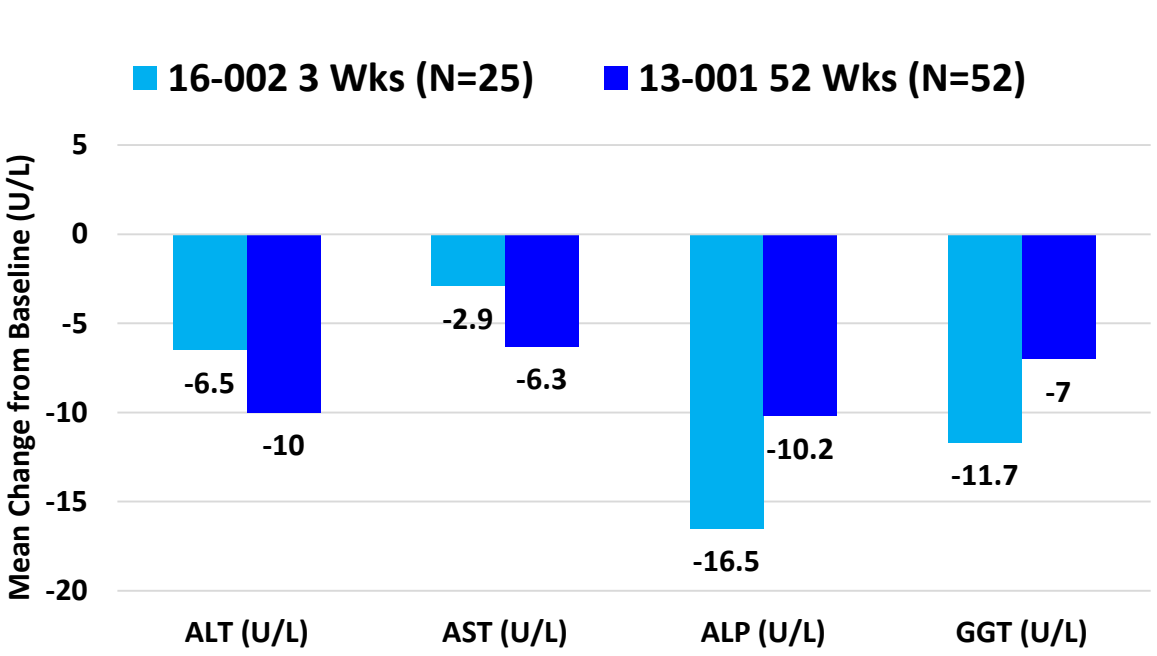
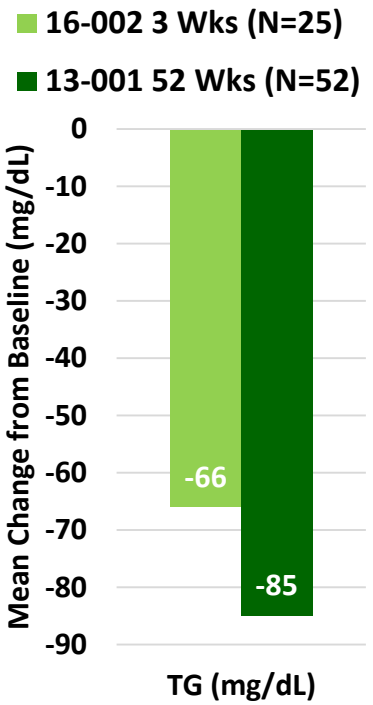
LPCN 1144: Consistent Effects on Key Clinical Biomarkers Across Studies

Liver enzymes and TG mean change post therapy in patients in two separate studies*





Mean BL	ALT (U/L)	AST (U/L)	ALP (U/L)	GGT (U/L)
16-002	46.5	29.5	92.8	61.9
13-001	51.1	35.1	97.6	70.7

TG (mg/dL)
346
360

* Patients are for 4th Quartile (above or upper normal level) of each lab at baseline

Alanine amino transferase (ALT), Aspartate amino transferase (AST), Alkaline phosphatase (ALP), Gamma-glutamyl transpeptidase (GGT), Triglyceride (TG)

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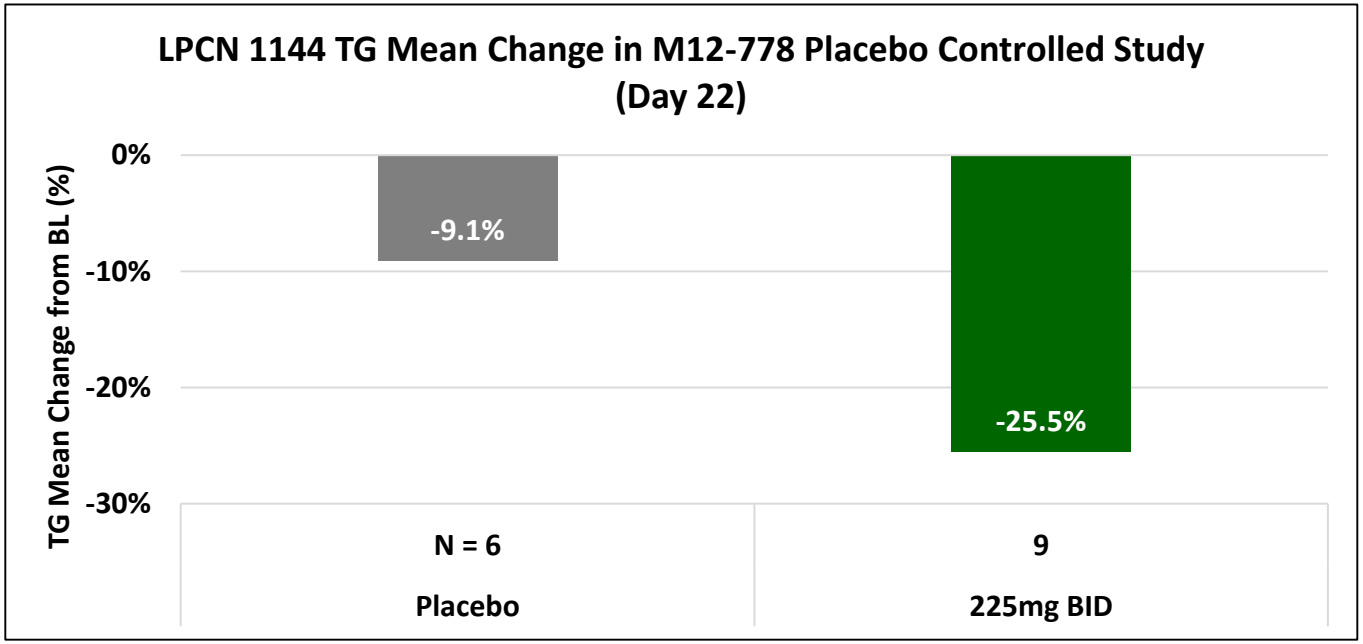
M12-778 Study: TG Mean Change from Baseline



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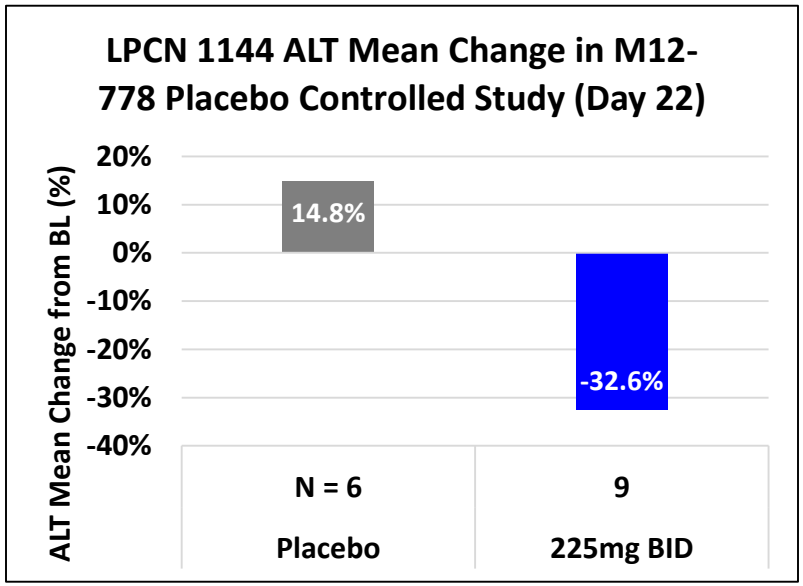
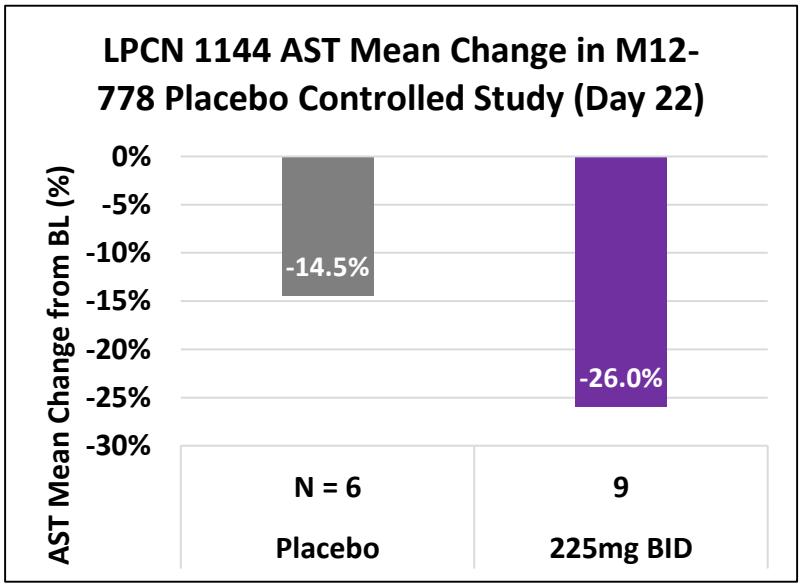
M12-778 Study: ALT and AST Mean Change from Baseline





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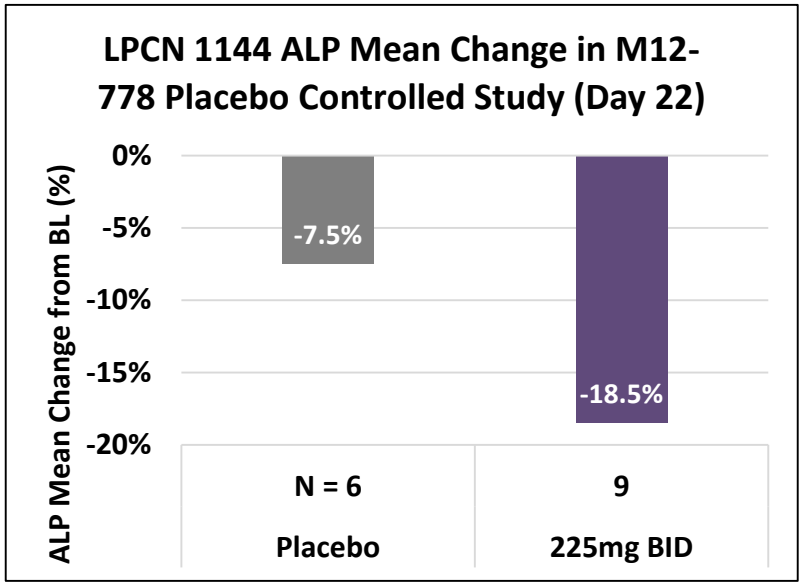
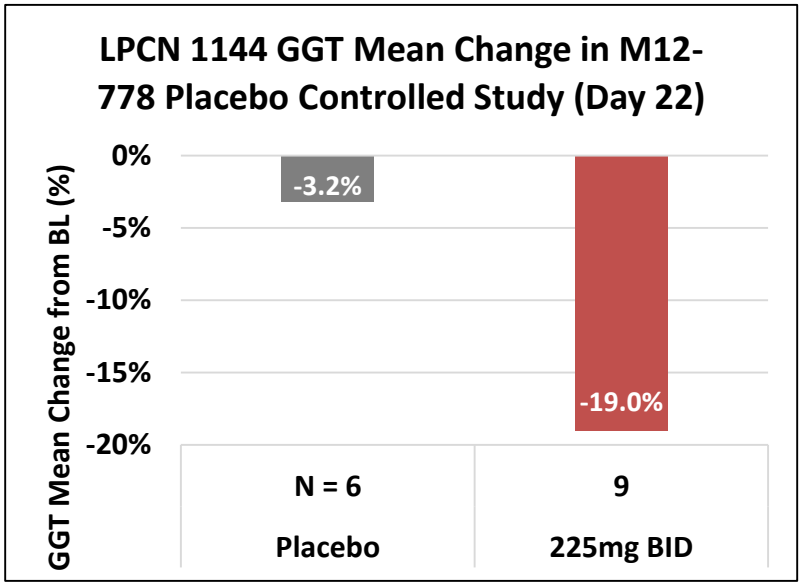
M12-778 Study: ALP and GGT Change from Baseline





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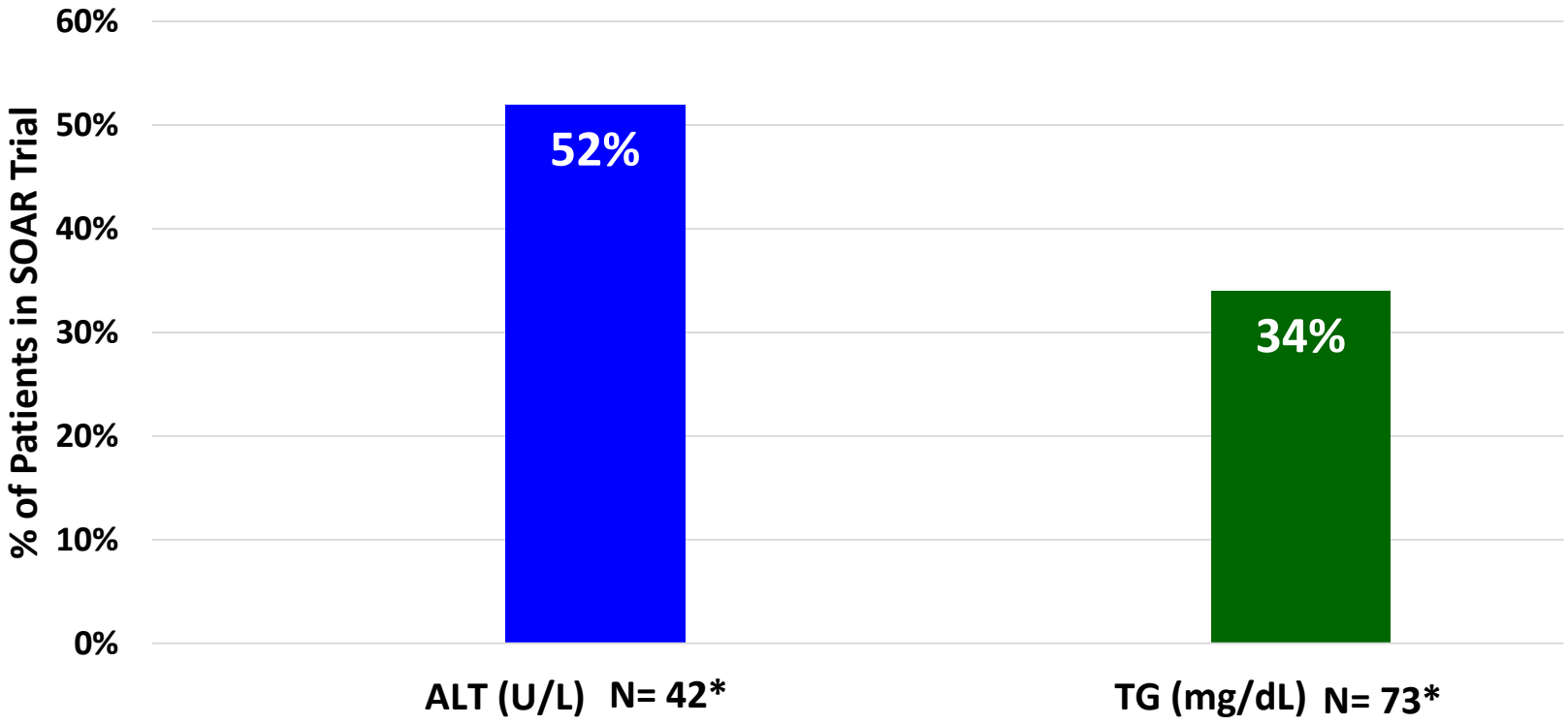
LPCN 1144: Significant Number of Patients for ALT and TG Shift from Above-Normal Levels at BL to Normal† Levels at EOS



* N = Total N for subgroup with above normal biomarker levels at baseline

† Normal range: ALT (10-40 U/L), TG (45-200 mg/dL)

BL: Baseline, EOS: End Of Study

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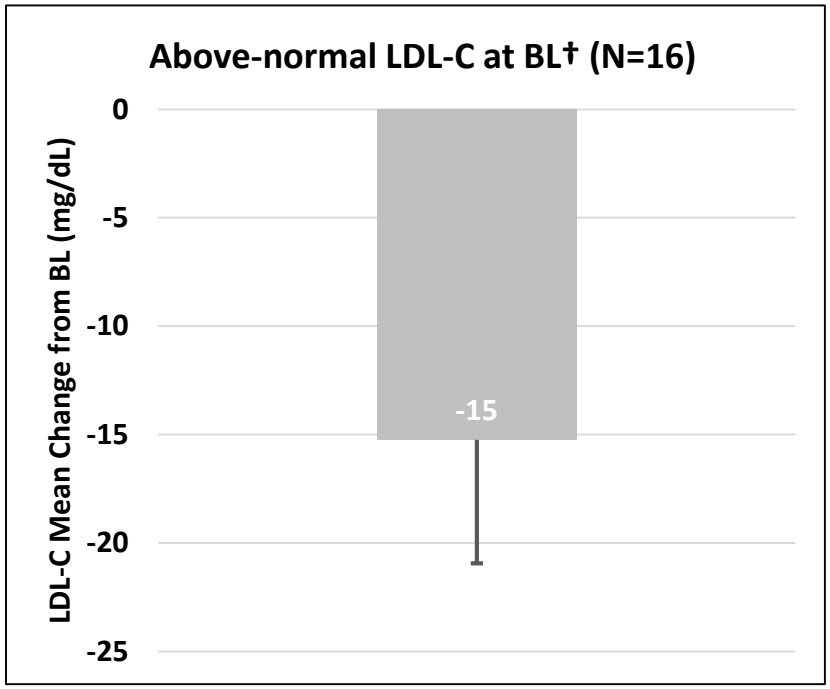
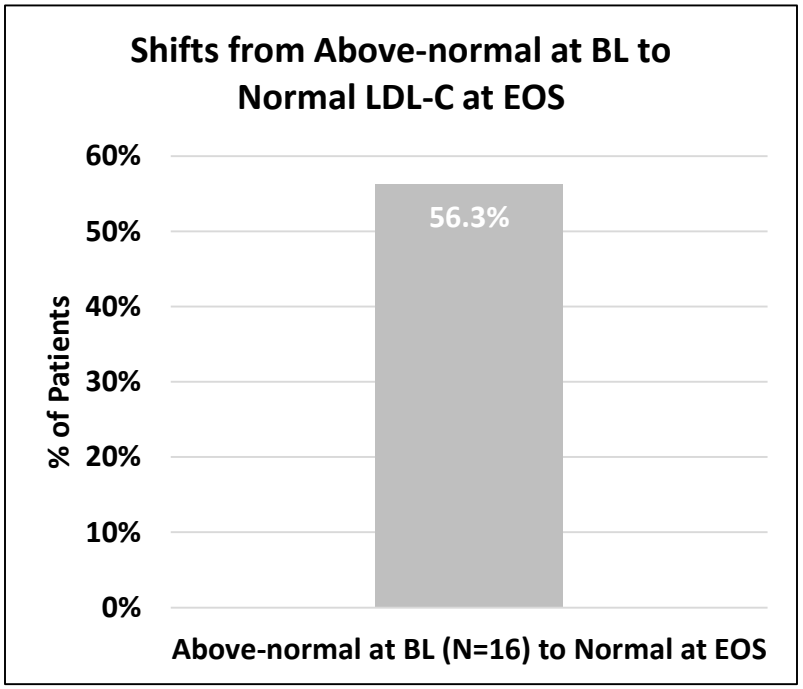
LPCN 1144: LDL Reduction and Significant Number of Patients for LDL-C Shift from Above-normal Levels at BL to Normal* Levels at EOS





*LDL-C normal range in SOAR trial is 50 – 160 mg/d.
†SOAR trial patients with mean BL LDL = 175 mg/dL

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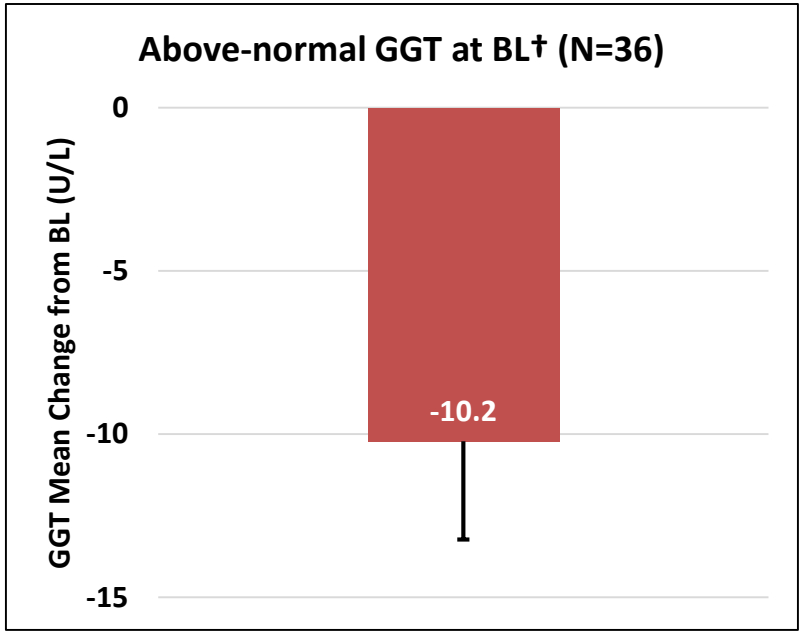
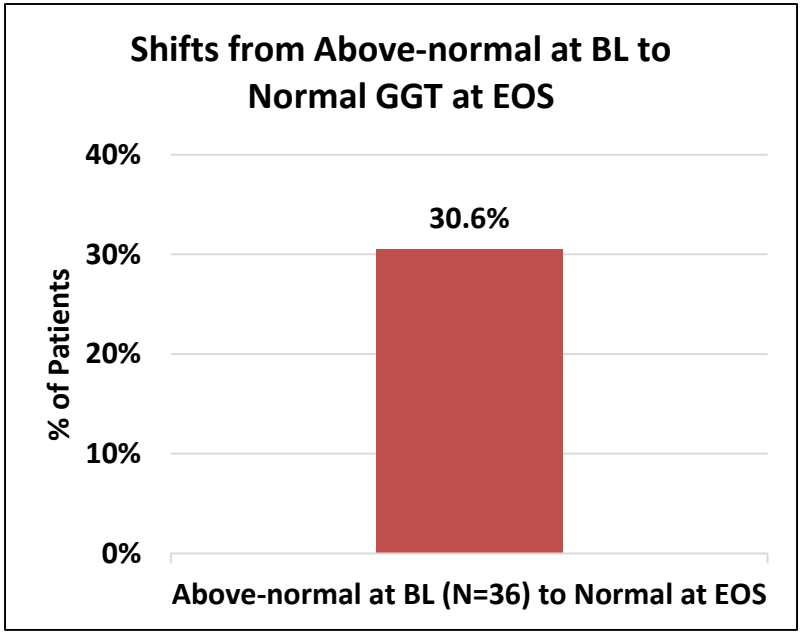
LPCN 1144: Significant Patient Number of Shifts from Above-normal GGT at BL to Normal* GGT at EOS

- GGT can also be an early marker of oxidative stress and indirect serum marker of fibrosis





* GGT normal range in SOAR trial is 10 – 49 U/L
† Mean BL = 82 U/L

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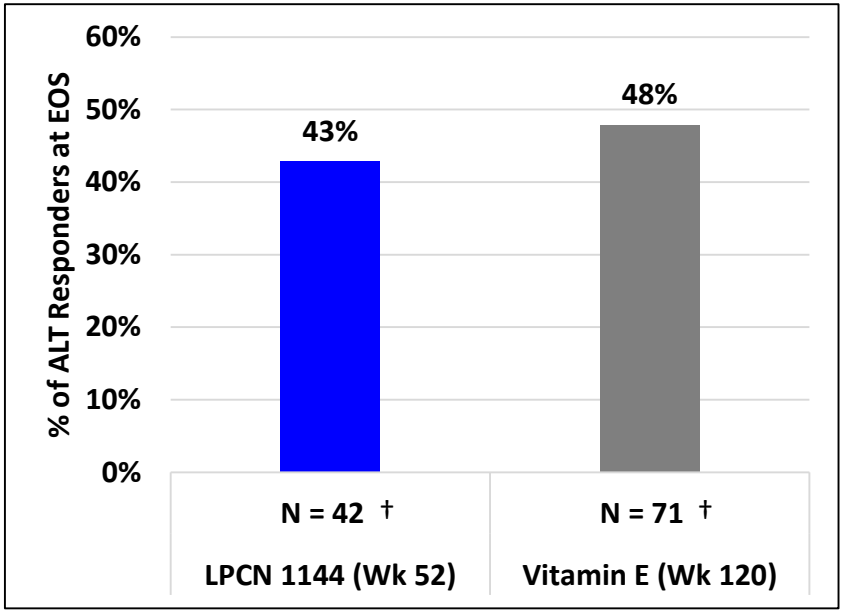
LPCN 1144: Robust ALT Response

Good Potential for Histological Improvement in NASH and Fibrosis[1]

Comparable LPCN1144 ALT response to Vitamin E in PIVENS Trial[2]

	Vitamin E		
Histological feature	**ALT R* (*n* = 34)**	**ALT NR* (*n* = 37)**	***P* value**
Mean change in steatosis score	−1.1	−0.4	<0.001
Mean change in inflammation score	−1.1	−0.3	<0.001
Mean change in Ballooning score	−0.8	−0.2	0.01
Mean change in NAS† score	−3.0	−0.8	<0.001
Mean change in Fibrosis score	−0.5	−0.2	0.34
Decrease in NAS by ≥2 points	82%	32%	<0.001
Resolution of NASH‡	44%	22%	0.07
Mean change in Weight (kg)	−0.9	1.8	0.03

* ALT Responders: Patients with ALT > 40 U/L at baseline, ending with ≤ 40 U/L and more than 30% reduction at end of study post therapy
† Total non-alcoholic fatty liver activity score (NAS), comprising the sum of scores for steatosis, inflammation, and ballooning cell injury
‡ Resolution of histological features that fulfil the criteria for diagnosis of NASH



† Total N is for patients with ALT > 40 U/L at baseline (ALT normal range is ≤ 40 U/L)

1 Hoffnagle et al. APT 2013

2 Sanyal et al, New Eng J Med, 2010

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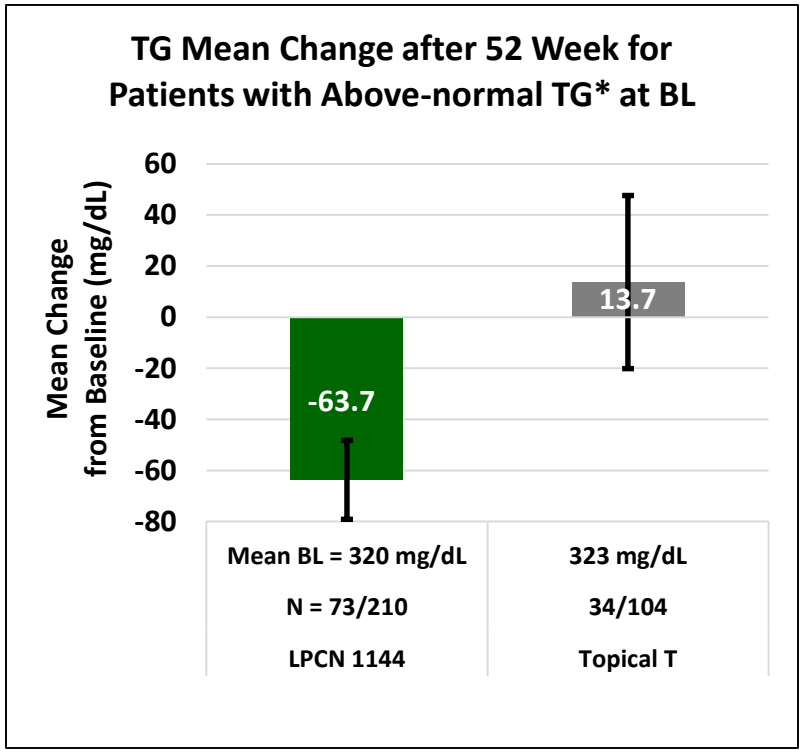
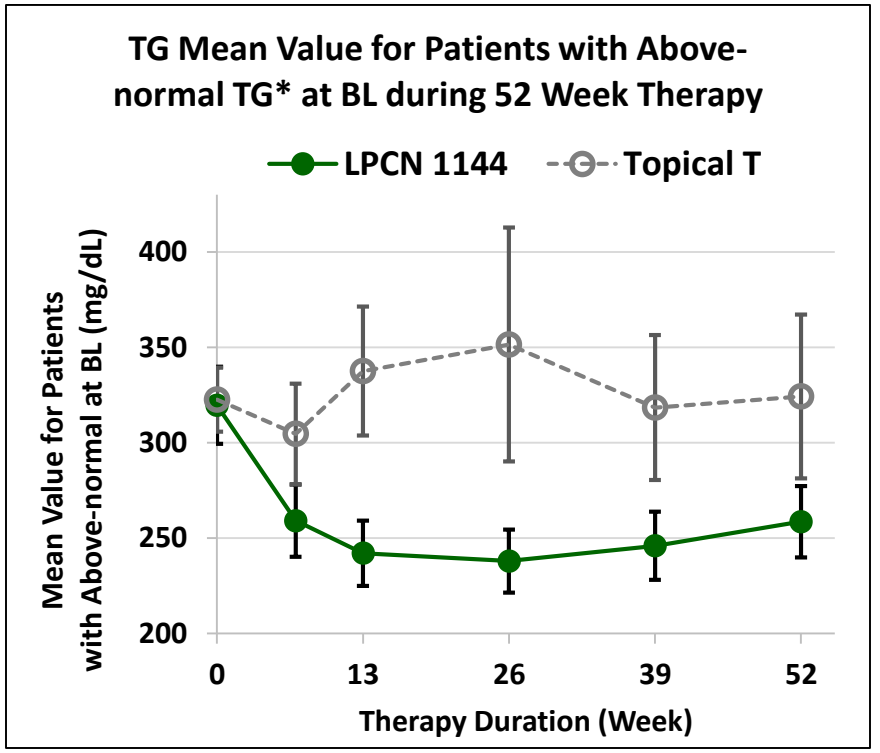
Comparison with Topical Testosterone

LPCN 1144: Unique TG Reduction

- TG mean change post therapy in patients on oral T vs non-oral T therapy





* TG normal range in SOAR Trial: 45 – 200 mg/dL

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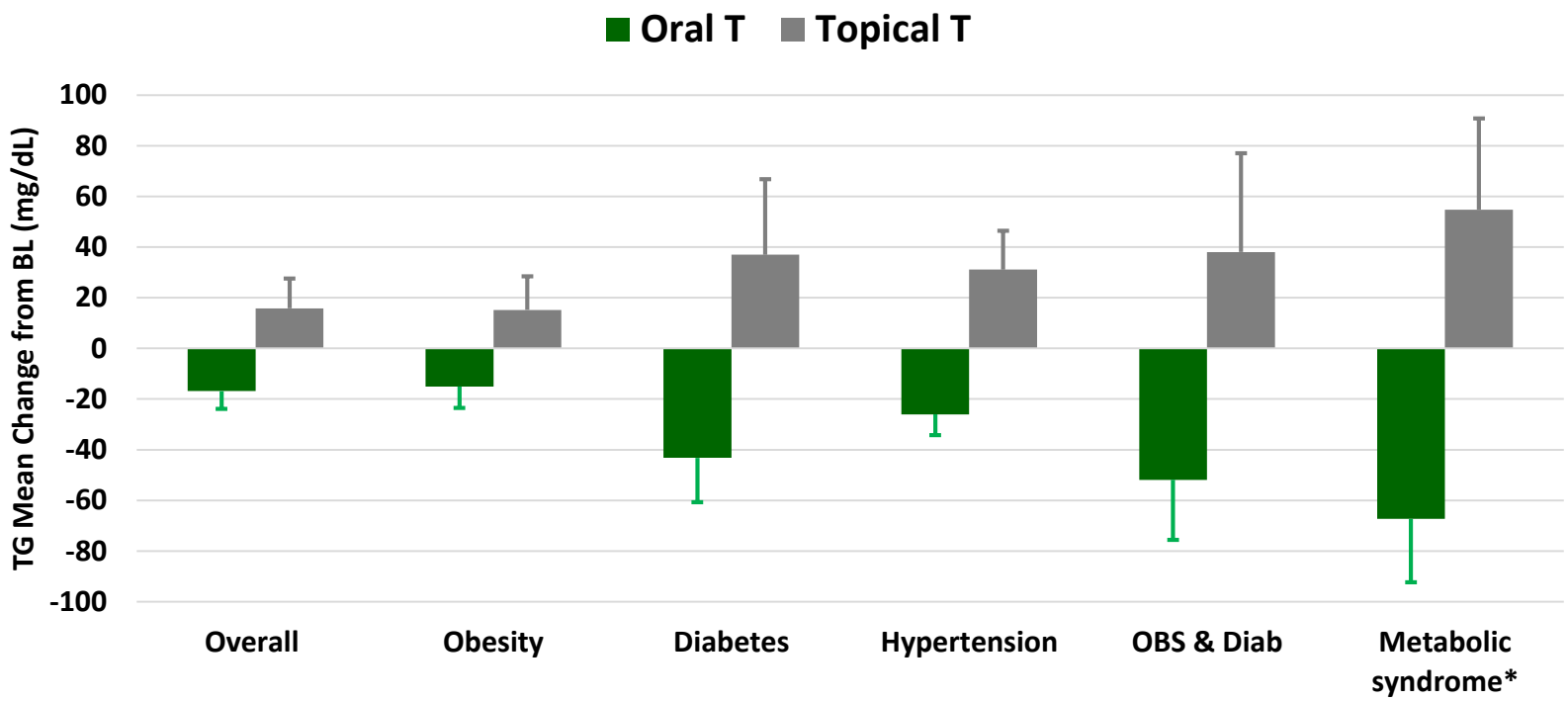
LPCN 1144: Oral T

TG Comparison with Topical T Across Various Co-Morbidities

Unique Oral T Therapy in TG Reduction Post 52 Week Therapy in Patients with Comorbidities



N	Overall	Obesity	Diabetes	Hypertension	OBS & Diab	MeS
Oral T	210	118	46	100	25	19
Topical T	104	65	36	49	21	15

* Metabolic syndrome: Obesity + Diabetes + Hypertension

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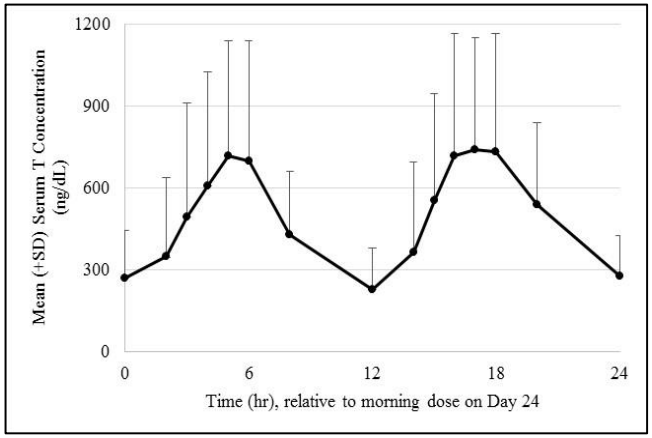
LPCN 1144: Comparison of PK Profile with Topical T and Injectable T

Fluctuating levels during the day

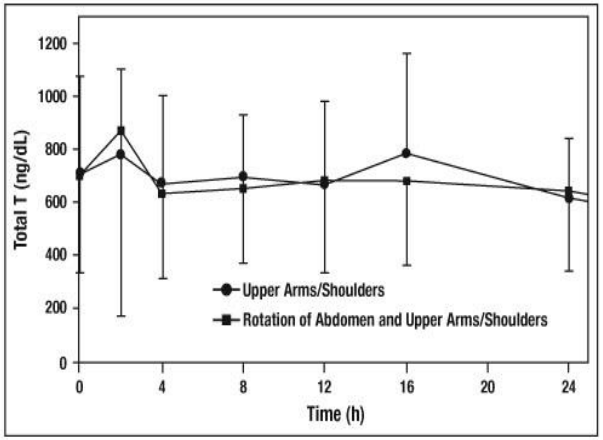
Oral (LPCN 1144)



Mean (+SD) Serum Total Testosterone Concentrations on Day 24, LPCN 1021-16-002 study results (PK Set, N=90)

Sustained high levels during the day

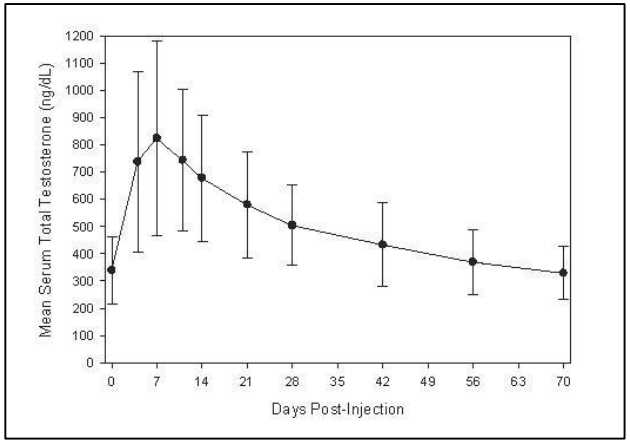
Topical (AndroGel*)



Mean (±SD) Serum Total Testosterone Concentrations on Day 7 in Patients Following AndroGel 1.62% Once-Daily Application of 81 mg of Testosterone (N=33) for 7 Days

Sustained high levels for weeks

Injectable (Aveed)**



Mean (SD) Serum Total Testosterone Concentrations (ng/dL) at 14-24 Weeks

* AndgroGel 1.62% label

** Aveed label

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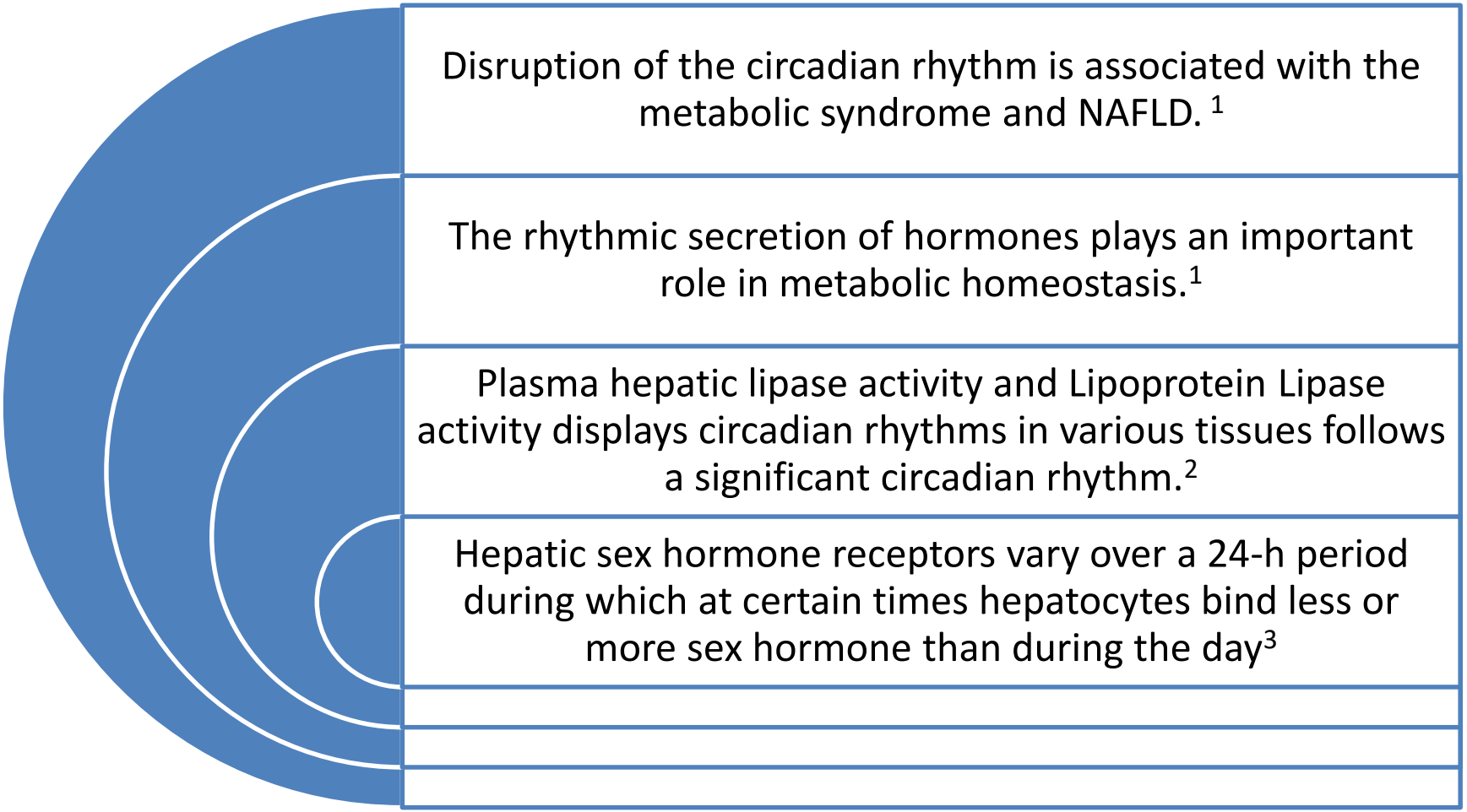
Oral T Delivery is More “In Tune” with Normal Circadian Variation of Plasma Sex Steroids



1. Shetty et al, Digest Dis Sci 2018 2. Benavides et al, Am J Physiol 1998 3. Antonio et al, Gastroenterol 1986

LIPOCINE® ENHANCING HEALTH

LPCN 1144: Oral Testosterone for the Treatment of NASH

Summary and Next Steps

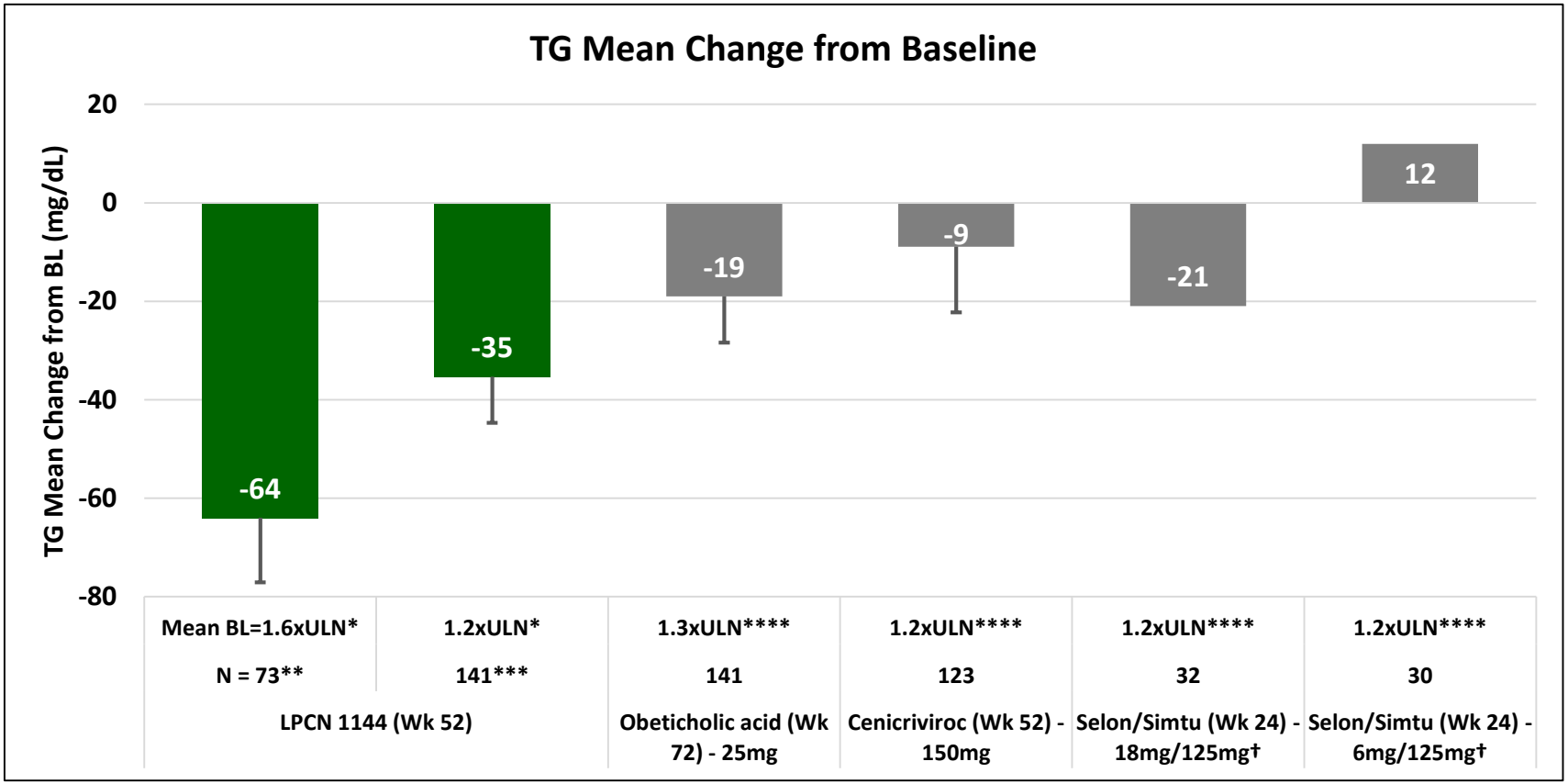
- Targeted for NASH epidemic with no currently approved product
- Unique mechanism targeting full spectrum of NASH pathogenesis + collateral health benefits
- Well tolerated safety profile
- Compelling clinical biomarker data
- Next Steps
  - In-vivo model Proof-Of-Concept (POC) study in biopsy-confirmed NASH
  - POC clinical study to assess liver fat changes via MRI-PDFF imaging in confirmed NAFLD/NASH patients

LPCN 1144

Competitive Biomarker Data Comparison

(Separate Studies/Not Head to Head)

LPCN 1144: Comparison of TG Mean Change from BL with Phase 3 Drug Candidates



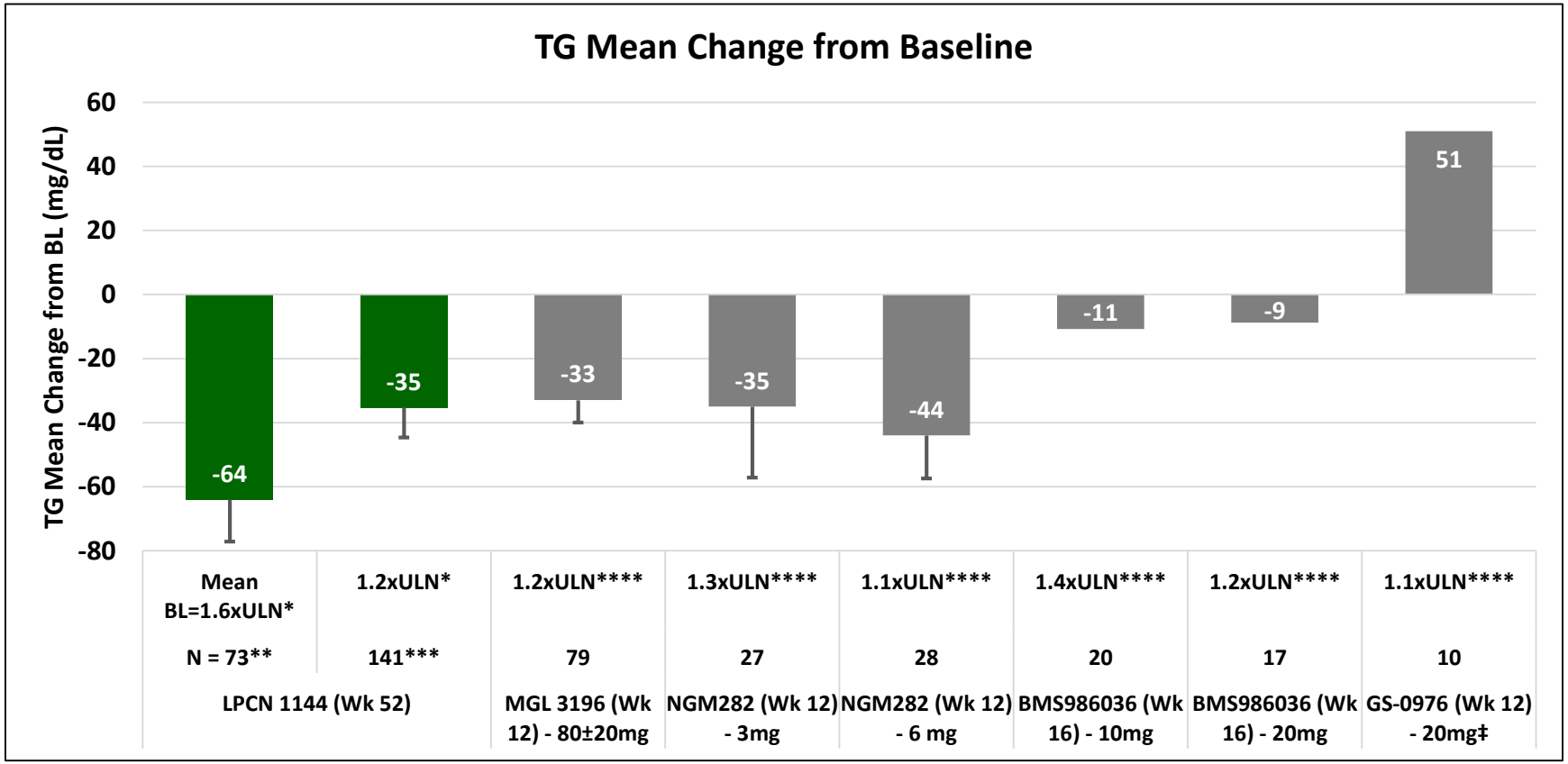
* Upper limit of normal range (ULN) is 200 mg/dL
, * SOAR Trial patients with TG > 200 mg/dL and >120 mg/dL at baseline, respectively
**** ULN is not reported; typical ULN is 150 mg/dL
† Mean change values for Selonsertib/Simtuzumab are median in interquartile range

Obeticholic acid: Neuschwander-Tetri et al, Lancet 2015
Selonsertib/Simtuzumab: Loomba et al, Hepatology 2018

Cenicriviroc: Friedman et al, Hepatology 2018, Suppl. Table 5

LIPOCINE® ENHANCING HEALTH

LPCN 1144: Comparison of TG Mean Change from BL with Phase 2 Drug Candidates

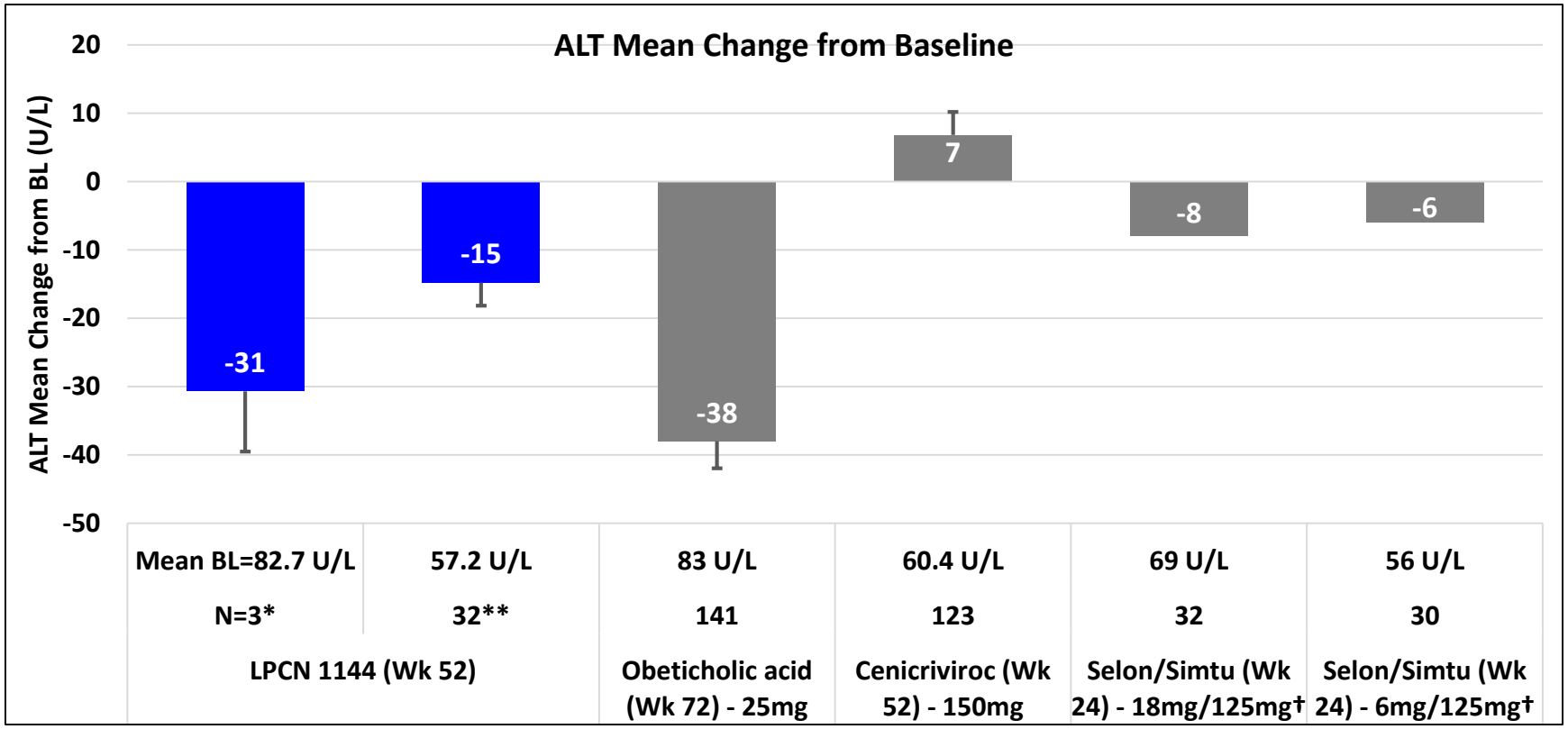


* Upper limit of normal range (ULN) is 200 mg/dL.
, * SOAR Trial patients with TG > 200 mg/dL and 120 mg/dL at baseline, respectively.
**** ULN is not reported; typical ULN is 150 mg/dL.
‡ Mean change for GS 0976 is recalculated from mean values at BL and EOS.

MGL 3196: EASL International Liver Congress 2018, April 2018
BMS986036: Sanyal et al, AASLD, Oct 2017
NGM282: Harrison et al, The Lancet 2018
GS0976: Lawitz et al, Clin Gasteroenterol Hepatol 2018

LIPOCINE® ENHANCING HEALTH

LPCN 1144: Comparison of ALT Mean Change from BL with Phase 3 Drug Candidates



* SOAR Trial Patients with ALT > 75 U/L at baseline
** SOAR Trial Patients with ALT ≥ 45 U/L at baseline
† Mean change values for Selonsertib/Simtuzumab are median in interquartile range

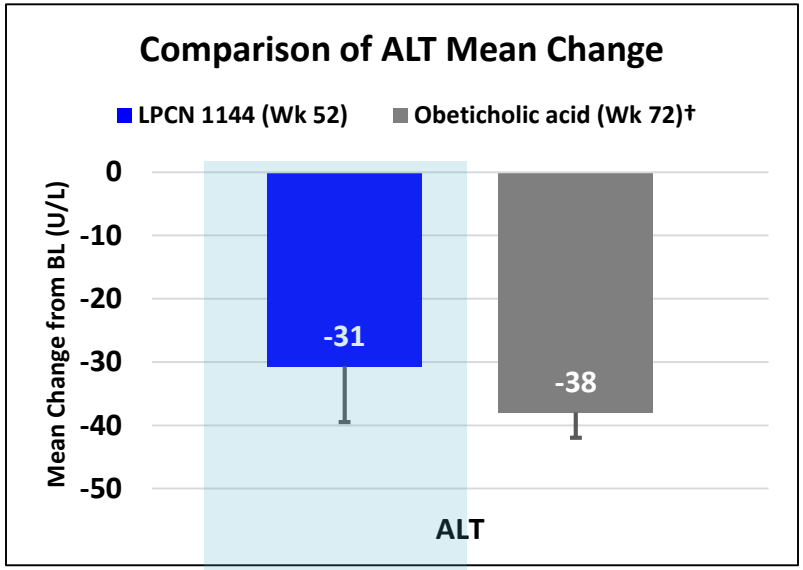
Obeticholic acid: Neuschwander-Tetri et al, Lancet 2015
Selonsertib/Simtuzumab: Loomba et al, Hepatology 2018

Cenicriviroc: Friedman et al, Hepatology 2018, Suppl. Table 5

LIPOCINE® ENHANCING HEALTH

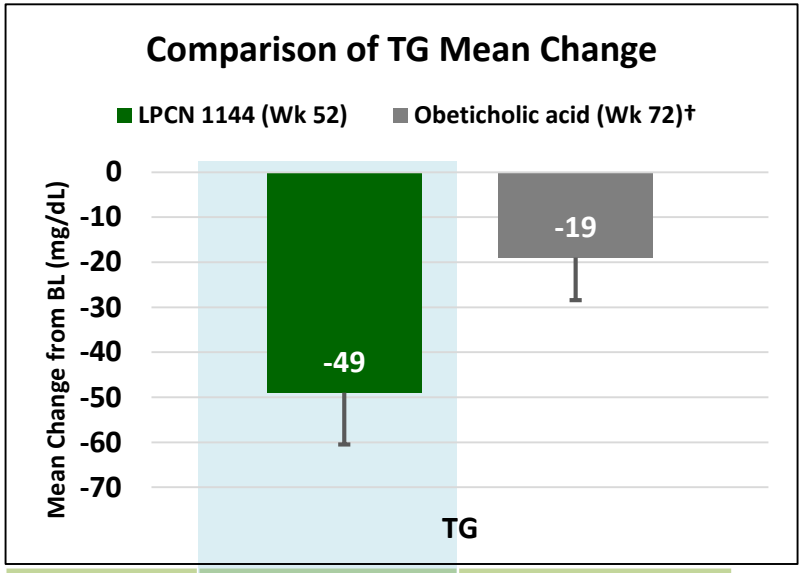
LPCN 1144: Comparison of Key NASH Biomarker Mean Change from BL with Obeticholic Acid

- Obeticholic Acid (FXR agonist) – FLINT Study, P2, 72 weeks, 25mg dose ‡



Mean BL	82.7 U/L	83 U/L**
N	3*	126

* SOAR Trial patients with ALT > 75 U/L at baseline
** Reported mean baseline level for Obeticholic Acid (N=141)
† Reported placebo mean change for Obeticholic Acid is -18 U/L



Mean BL	1.3xULN*	1.3xULN***
N	109**	126

* Upper limit of normal range (ULN) is 200 mg/dL
** SOAR Trial patients with TG > 150 mg/dL at baseline
*** ULN is not reported; typical ULN is 150 mg/dL
† Reported placebo mean change for Obeticholic Acid is -7 mg/dL

‡ Neuschwander-Tetri et al, Lancet 2015

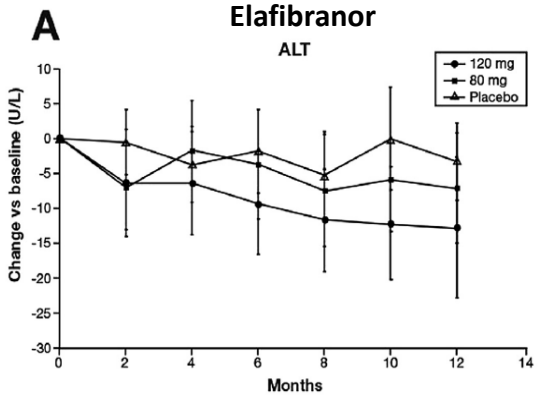
LIPOCINE® ENHANCING HEALTH

LPCN 1144: Comparison of Key NASH Biomarker Mean Change from BL with Elafibranor

- Elafibranor (PPAR-α, δ agonist) – P2, 52 weeks, 120mg dose ‡

LPCN 1144 ALT	
Mean BL	62.2 U/L
N	22*
Mean Change from BL, (SE)	-20 (±3.1) U/L

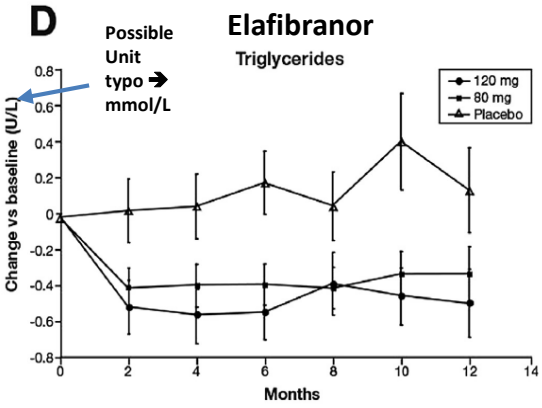
* SOAR Trial patients with ALT > 50 U/L



Elafibranor ALT	
Mean BL	63.8 U/L
N	78
Mean Change from BL, (SE)	-12 U/L

LPCN 1144 TG	
Mean BL	1.2xULN**
N	141***
Mean Change from BL, (SE)	-0.4 (±0.1) mmol/L

** Upper limit of normal range (ULN) is 200 mg/dL
*** SOAR Trial patients with TG > 120 mg/dL at baseline



Elafibranor TG	
Mean BL	1.2xULN†
N	78
Mean Change from BL, (SE)	-0.5 mmol/L

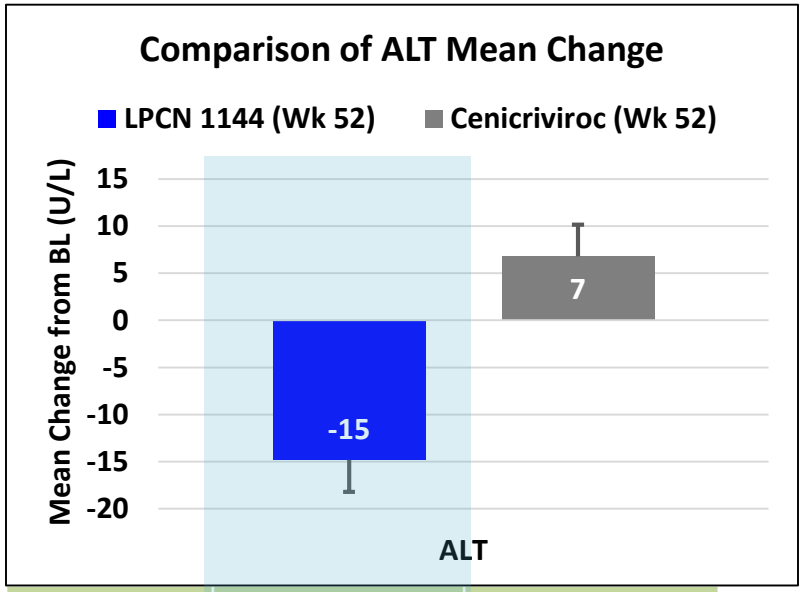
† ULN is not reported; typical ULN for TG is 150 mg/dL.

‡ Ratziu et al, Gastroenterol, 2016

LIPOCINE® ENHANCING HEALTH

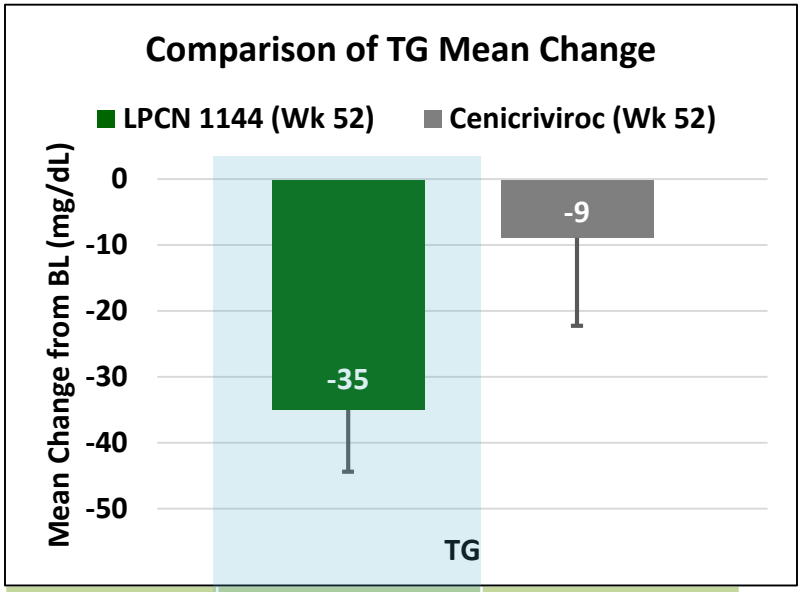
LPCN 1144: Comparison of Key NASH Biomarker Mean Change from BL with Cenicriviroc

- Cenicriviroc (CCR2/CCR5 inhibitor) – P2, 52 weeks, 150mg dose ‡



Mean BL	57.2 U/L	60.4 U/L
N	32*	123

* SOAR Trial patients with ALT ≥ 45 U/L.



Mean BL	1.2xULN*	1.2xULN***
N	141**	123

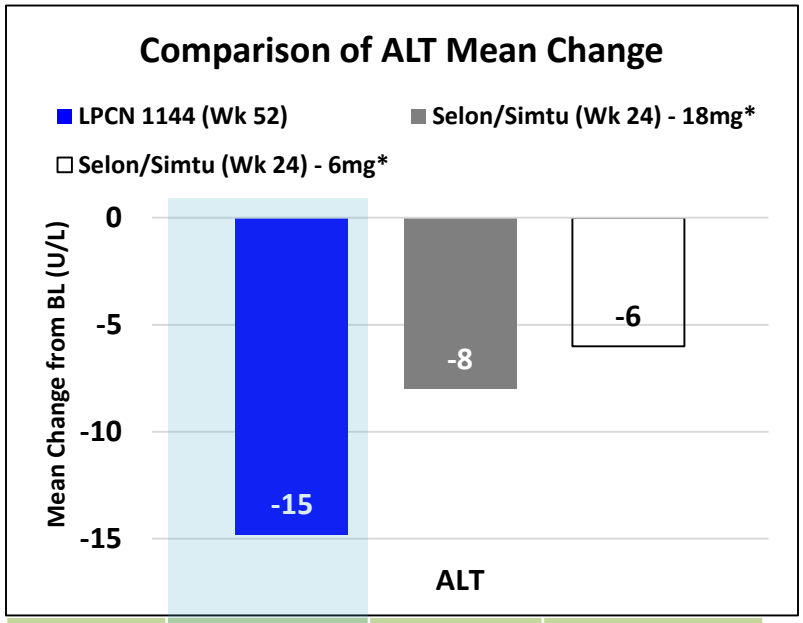
* Upper limit of normal range (ULN) is 200 mg/dL.
** SOAR Trial patients with TG > 120 mg/dL at baseline.
*** ULN is not reported; typical ULN is 150 mg/dL.

‡ Friedman et al, Hepatology 2018, Suppl. Table 5

LIPOCINE® ENHANCING HEALTH

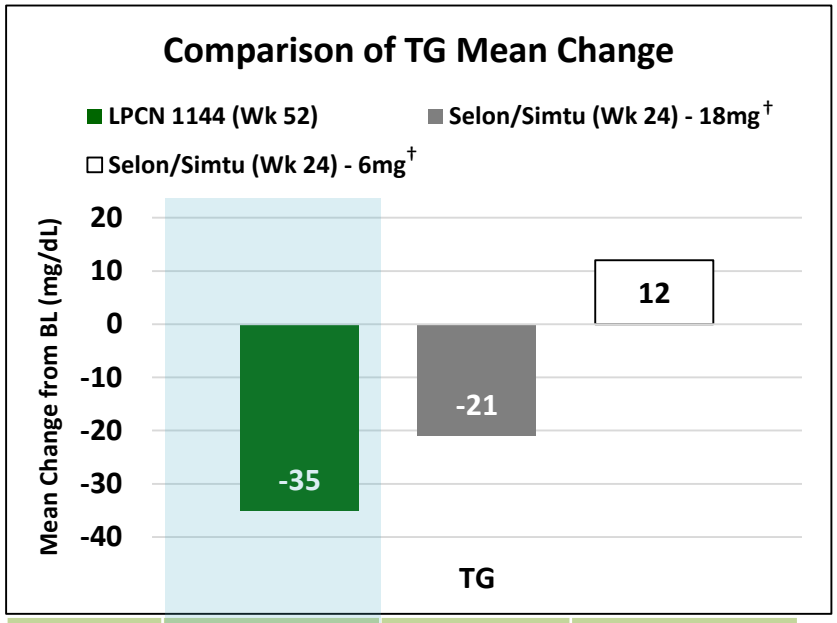
LPCN 1144: Comparison of Key NASH Biomarker Mean Change from BL with Selonsertib/Simtuzumab

- Selonsertib/Simtuzumab (ASK1 inhibitor) – P2, 24 weeks, 18mg or 6mg Selonsertib with fixed Simtuzumab dose ‡



Mean BL	57.2 U/L	69 U/L	56 U/L
N	32†	32	30

† SOAR Trial patients with ALT ≥ 45 U/L
* Mean change values for Selonsertib/Simtuzumab are median in interquartile range



Mean BL	1.2xULN*	1.2xULN***	1.2xULN***
N	141**	32	30

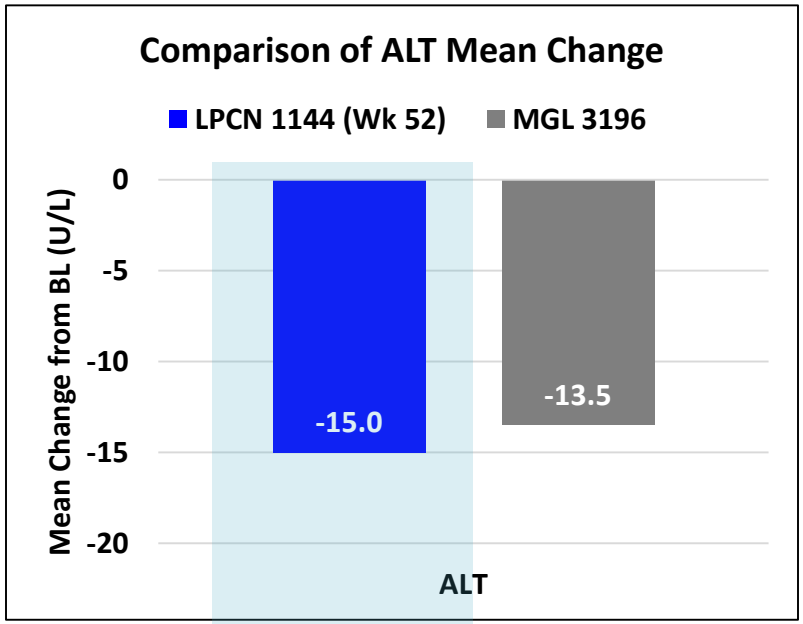
* Upper limit of normal range (ULN) is 200 mg/dL
** SOAR Trial patients with TG > 120 mg/dL at baseline
*** ULN is not reported; typical ULN is 150 mg/dL
† Mean change values for Selonsertib/Simtuzumab are median in interquartile range

‡ Loomba et al, Hepatology 2018

LIPOCINE® ENHANCING HEALTH

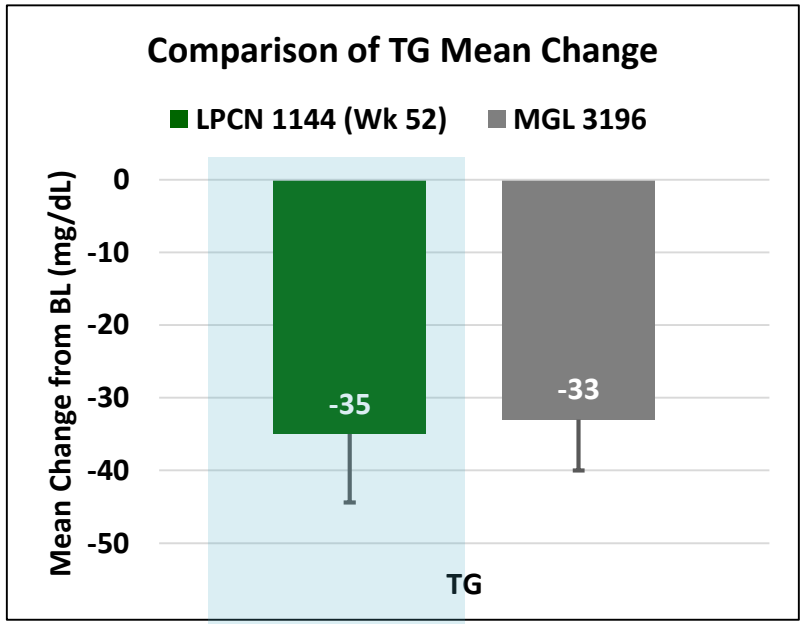
LPCN 1144: Comparison of Key NASH Biomarker Mean Change from BL with MGL 3196

- MGL 3196† (THR-β agonist) – P2, 12 weeks, 80mg ± 20mg dose ‡



N	32*	47**

* SOAR Trial Patients with ALT ≥ 45 U/L for males
** Patients of MGL 3196 are with ALT ≥ 45 U/L for males and > 30 for females; mean BL for these patients of MGL 3196 is not reported
† Reported placebo ALT mean change is -7.7 U/L.



Mean BL	1.2xULN*	1.2xULN***
N	141**	79

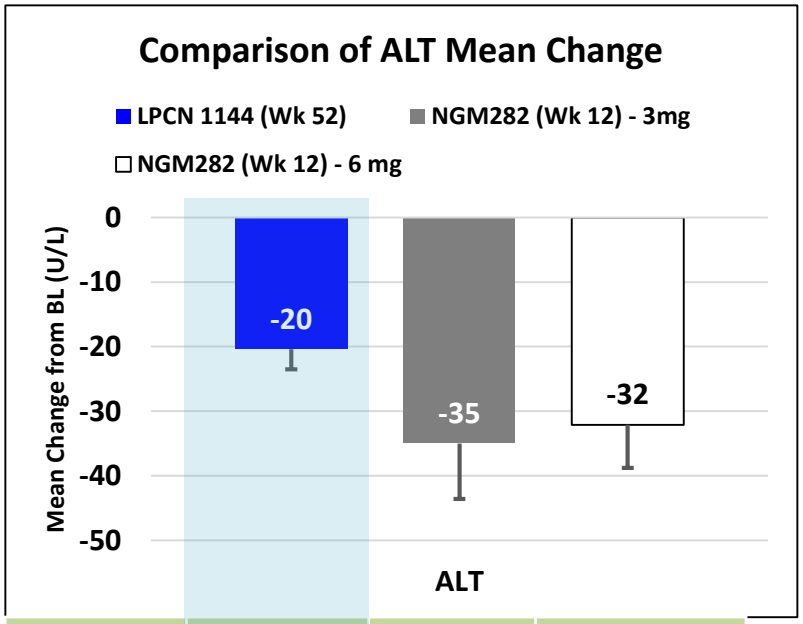
* Upper limit of normal range (ULN) is 200 mg/dL
** SOAR Trial patients with TG > 120 mg/dL at baseline
*** ULN is not reported; typical ULN is 150 mg/dL

‡ EASL International Liver Congress 2018. Paris, France – April 11-15, 2018

LIPOCINE® ENHANCING HEALTH

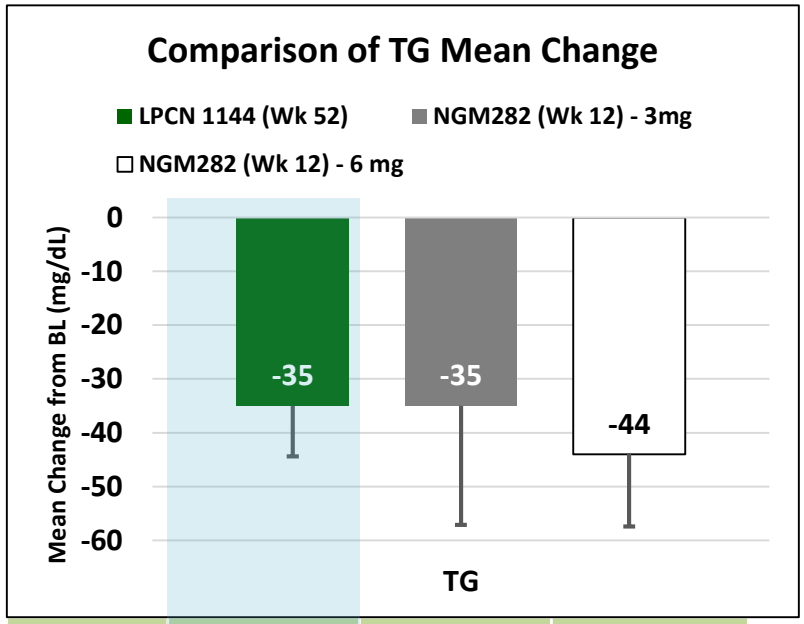
LPCN 1144: Comparison of Key NASH Biomarker Mean Change from BL with Injectable NGM282

- NGM282 (FGF19 analog) – P2, 12 weeks, 3mg and 6mg dose‡



Mean BL	62.2 U/L	67.4 U/L	61.8 U/L
N	22*	27	28

* SOAR Trial Patients with ALT > 50 U/L at baseline.



Mean BL	1.2xULN*	1.3xULN***	1.1xULN***
N	141**	27	28

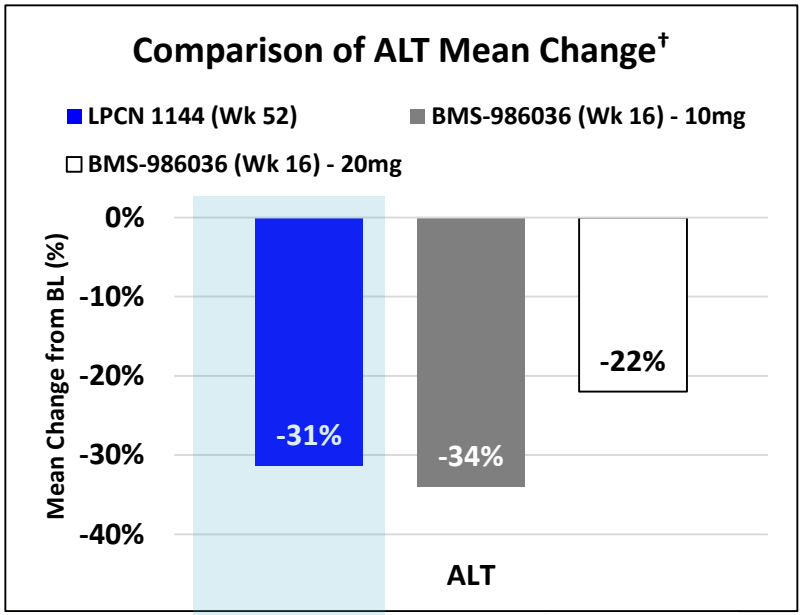
* Upper limit of normal range (ULN) is 200 mg/dL.
** Patients are with TG > 120 mg/dL at baseline.
*** ULN is not reported; typical ULN is 150 mg/dL.

‡ Harrison et al, The Lancet 2018

LIPOCINE® ENHANCING HEALTH

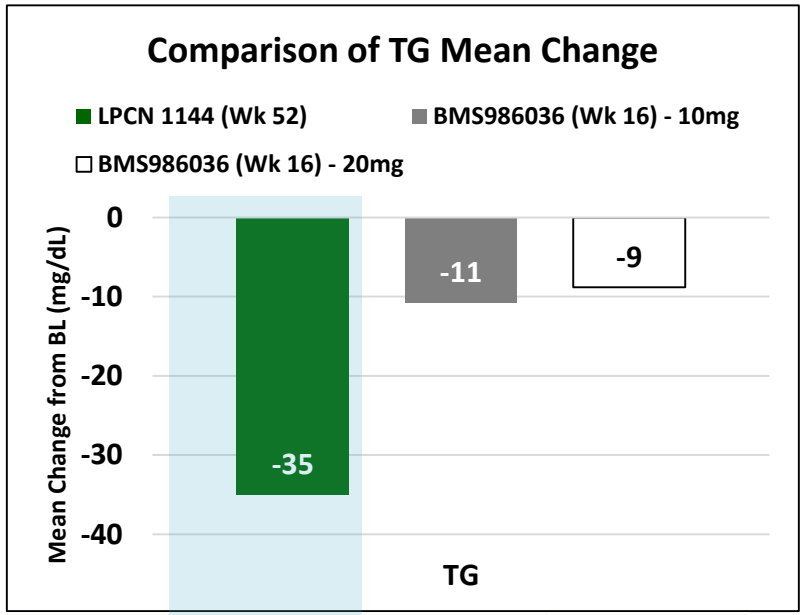
LPCN 1144: Comparison of Key NASH Biomarker Mean Change from BL with BMS-986036

- BMS 986036 (Peg-FGF21) – P2, 16 weeks, 10mg and 20mg dose‡



Mean BL	62.2 U/L	66 U/L	70 U/L
N	22*	24	22

* SOAR Trial Patients with ALT > 50 U/L at baseline.
† ALT mean change from baseline for BMS 986036 was obtained from graph image in reference.



Mean BL	1.2xULN*	1.4xULN***	1.2xULN***
N	141**	27	28

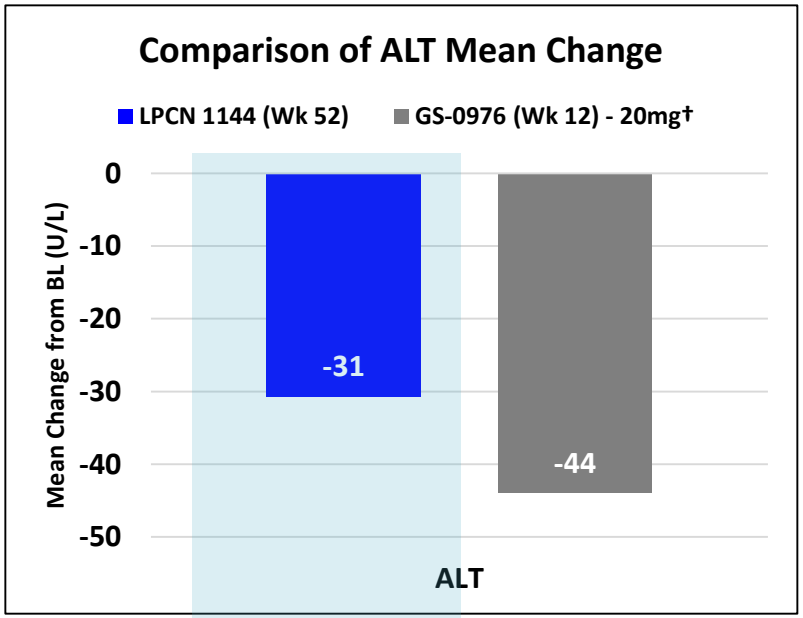
* Upper limit of normal range (ULN) is 200 mg/dL.
** Patients are with TG > 120 mg/dL at baseline.
*** ULN is not reported; typical ULN is 150 mg/dL.

‡ Sanyal et al, AASLD, Oct 2017

LIPOCINE® ENHANCING HEALTH

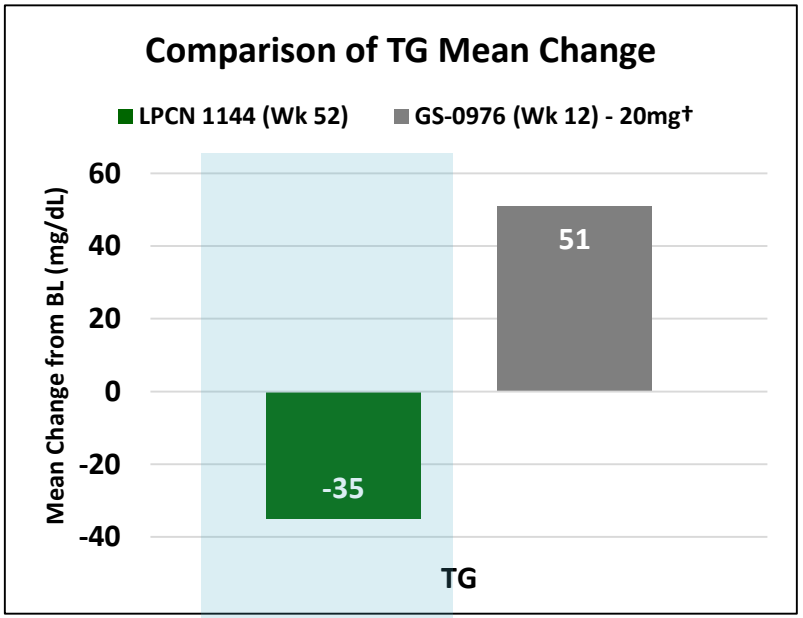
LPCN 1144: Comparison of Key NASH Biomarker Mean Change from BL with GS 0976

- GS 0976 (ACC inhibitor) – P2, 12 weeks, 20mg dose‡



Mean BL	82.7 U/L	101 U/L
N	3*	10

* SOAR Trial Patients with ALT > 75 U/L at baseline.
† Mean Change value is obtained from Mean values at BL and EOS.



Mean BL	1.2xULN*	1.1xULN***
N	141**	10

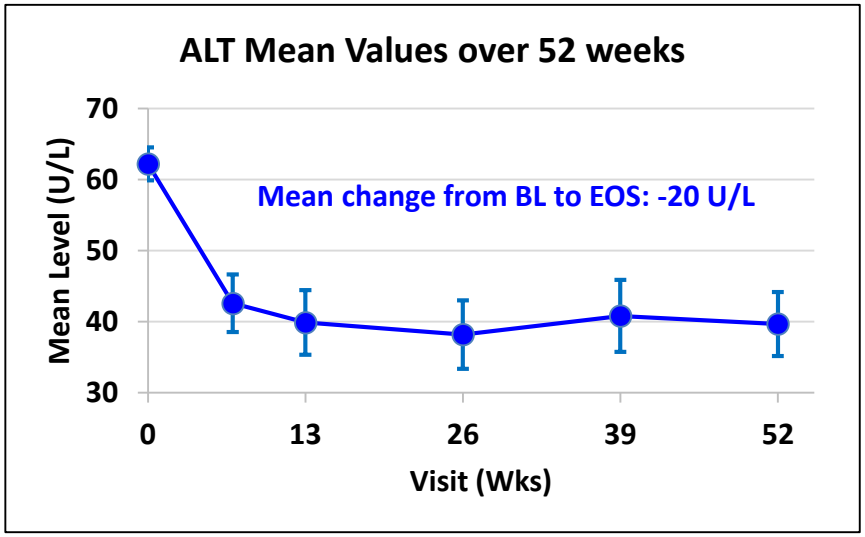
* Upper limit of normal range (ULN) is 200 mg/dL.
** Patients are with TG > 120 mg/dL at baseline.
*** ULN is not reported; typical ULN is 150 mg/dL.
† Mean Change value is obtained from Mean values at BL and EOS.

‡ Lawitz et al, Clin Gasteroenterol Hepatol 2018

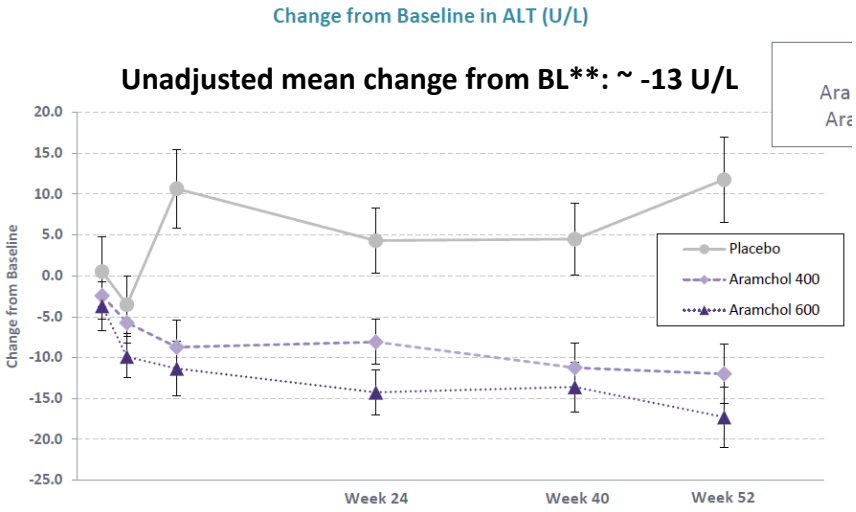
LIPOCINE® ENHANCING HEALTH

LPCN 1144: Comparison of Key NASH Biomarker Mean Change from BL with Aramchol

- LPCN 1144*
  - 52 weeks, randomized
- Aramchol‡
  - P2, 52 weeks, 600mg dose



* SOAR Trial patients with ALT > 50 U/L at baseline (Mean BL = 62.2 U/L), N=22



** Mean BL for 600mg dose: 62.8 U/L, N=98

‡ Galmed Corp PPT, Jun 2018

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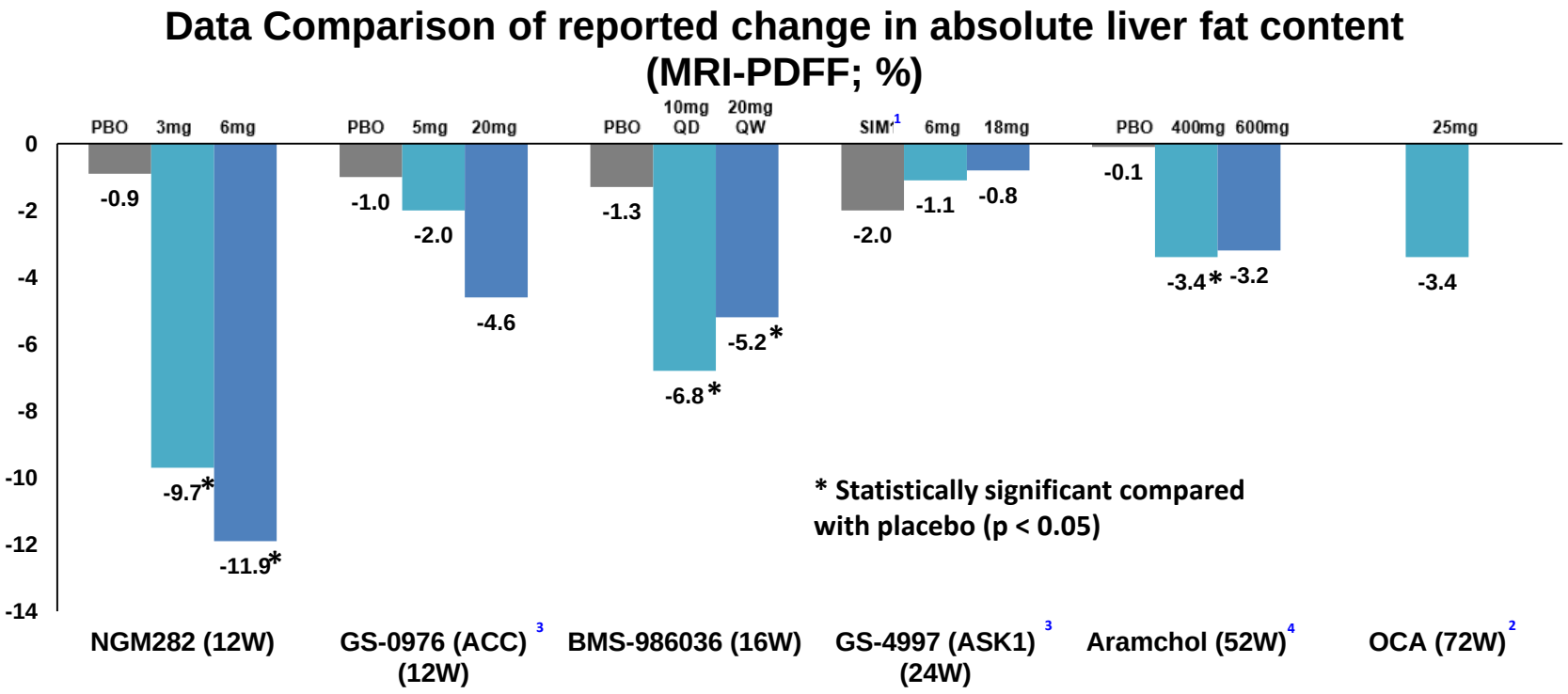
Absolute Liver Fat Change of Select NASH Drugs in Development



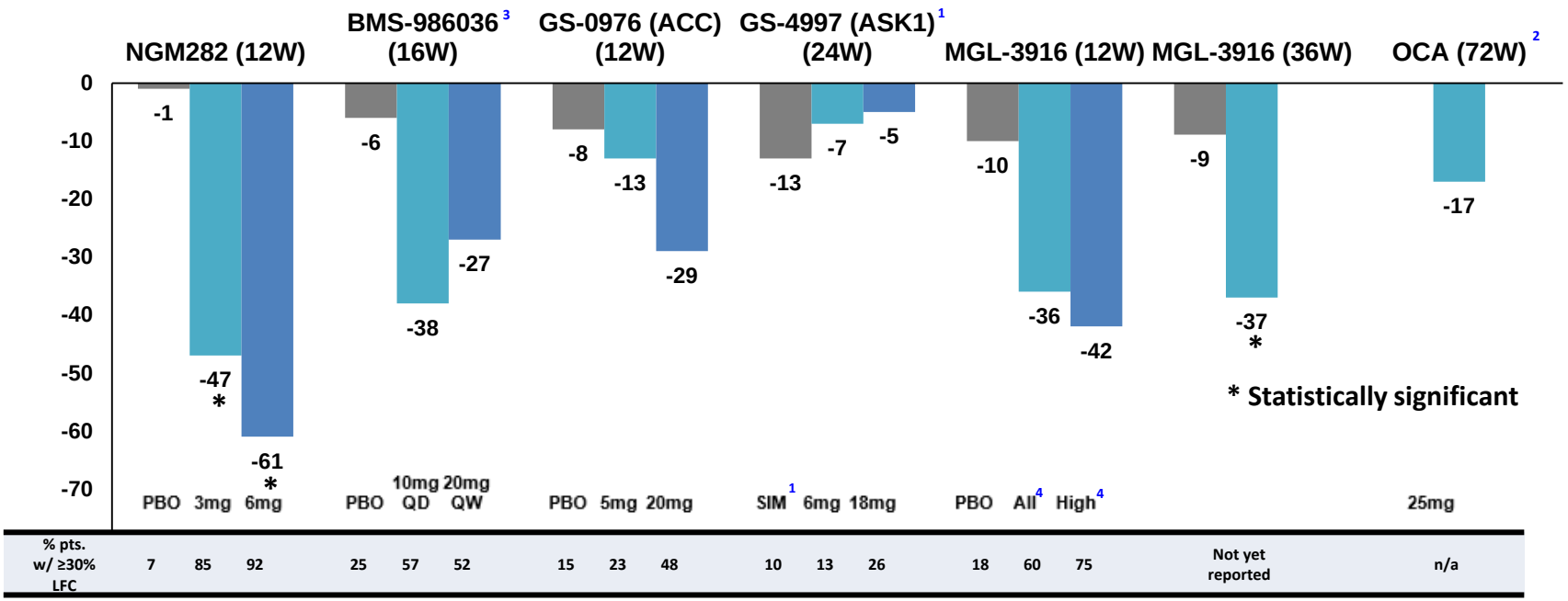
1 Selonsertib(SEL) +/-Simtuzumab (SIM) open label pooled study data; simtuzumab data used as proxy for placebo data
2 Placebo-subtracted data; secondary analysis of OCA FLINT trial
3 Absolute changes in LFC for GS-0976 and GS-4997 calculated from baseline values and relative median change values
4 LFC assessed by MRS

BMS-986036 (EASL 2017); Galmed (Press release June 12, 2018); GS-0976 (AASLD 2017); GS-4997 (Loomba et al, Hepatology 2017); OCA(AASLD 2017); NGM282 (Harrison et al. The Lancet 2018)

LIPOCINE® ENHANCING HEALTH

Relative Liver Fat Change of Select NASH Drugs in Development

Data Comparison of reported change in relative liver fat content (MRI-PDFF; %)

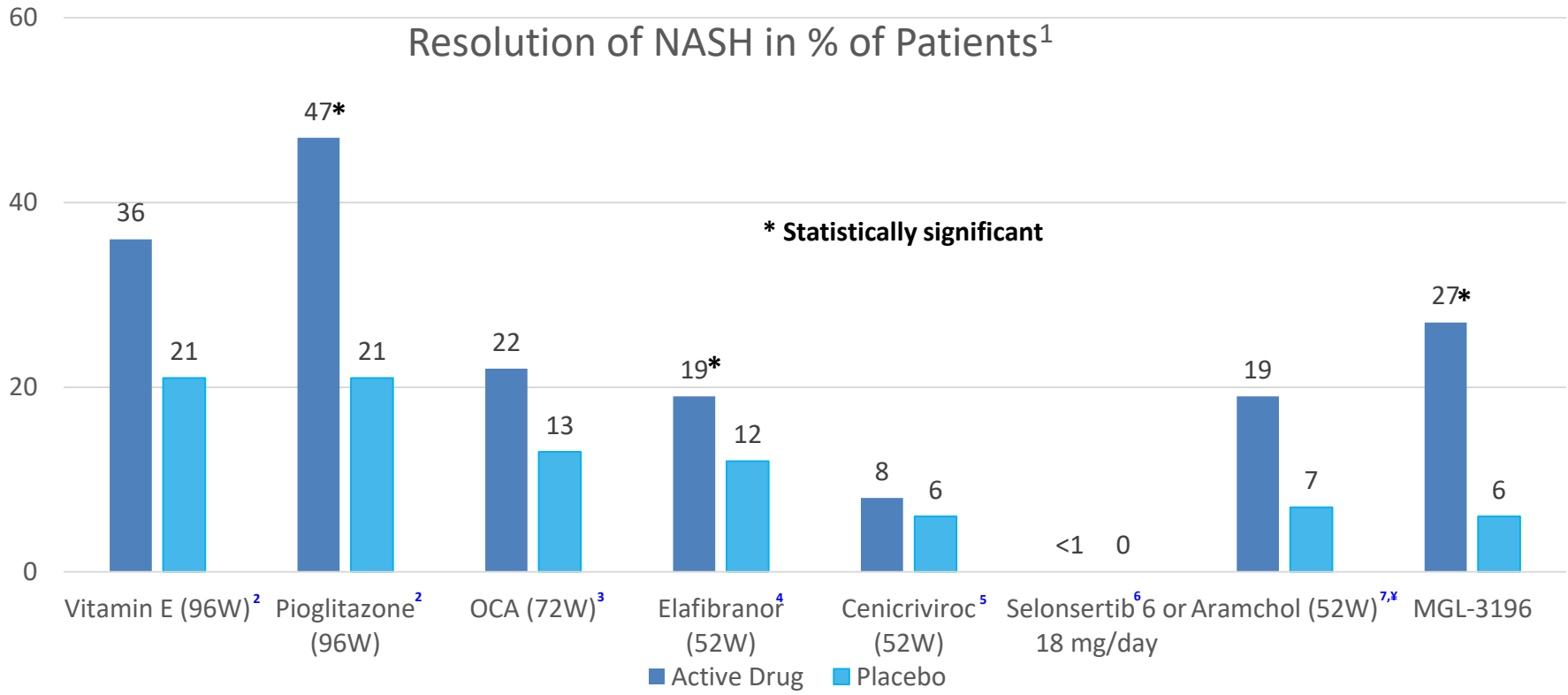


1 Selonsertib(SEL) +/-Simtuzumab(SIM) open label pooled study data; simtuzumabdata used as proxy for placebo data
2 Placebo-subtracted data; secondary analysis of OCA FLINT trial
3 Relative change in LFC for BMS-986036 calculated from reported baseline values and absolute changes
4 Absolute change in LFC for MGL-3196 calculated from baseline value (across entire study) and relative median change from baseline; data from ongoing blinded study where "High MGL-3196" was a pre-specified group of patients with relatively higher drug levels as measured by sex hormone binding globulin (marker of MGL-3196 hepatic level and activity) and "All MGL-3196" include low and high levels as measured by sex hormone binding globulin

BMS-986036 (EASL 2017); GS-0976 (AASLD 2017); GS-4997 (Loomba et al, Hepatology 2017); OCA (AASLD 2017); MGL-3196 (Press release Dec. 6, 2017 and transcript of webcast , and Press release June 12, 2018)

LIPOCINE ENHANCING HEALTH

Select NASH Biopsy Results – Reported Effect on Resolution of NASH



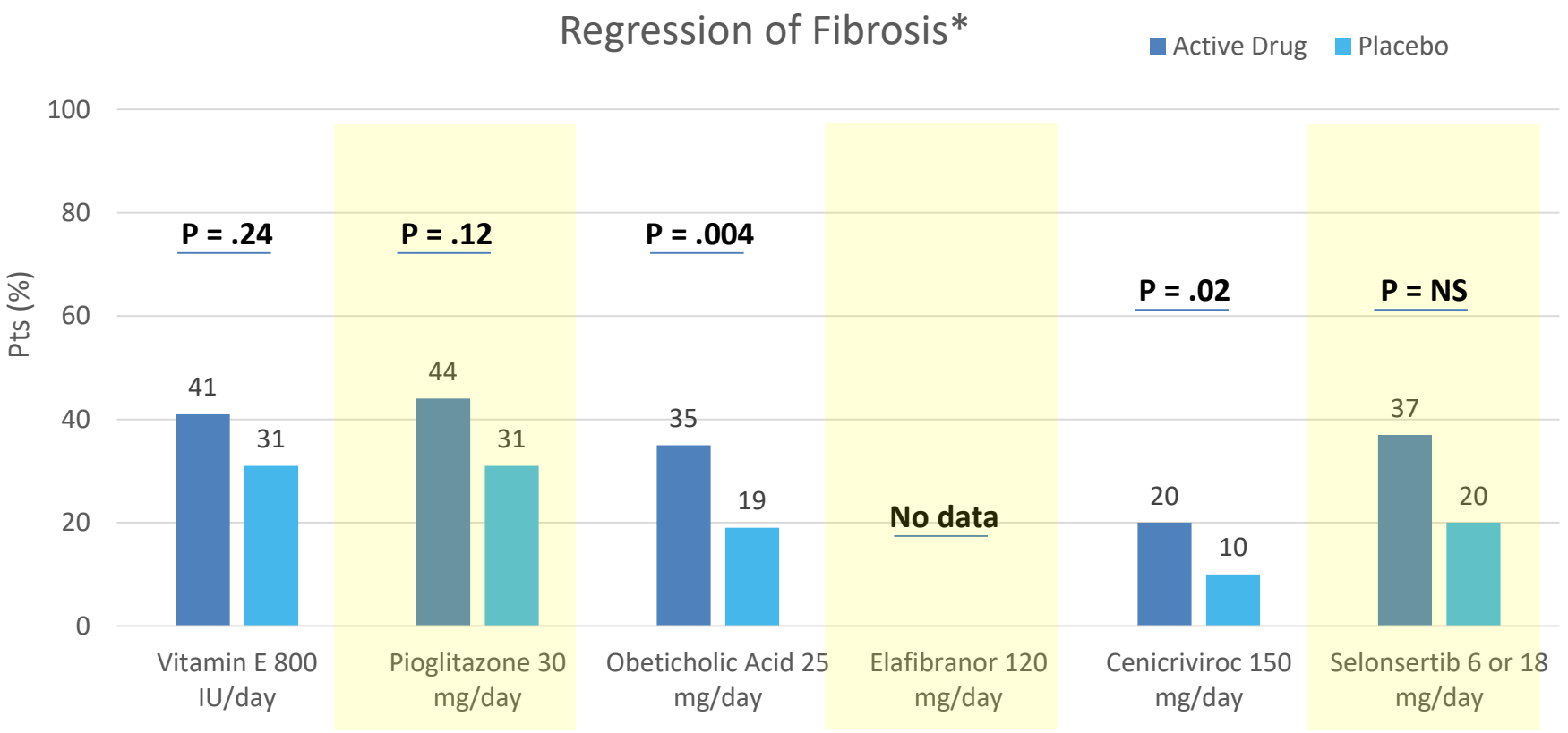
# pts	**80**	**72**		**70**	**72**		**102**	**98**		**78**	**77**		**126**	**126**		**23**	**22**		**Not Reported**		**73**	**34**

1 Resolution of NASH as defined by each study below; 2 PIVENS (Resolution of definite NASH); 3 FLINT (Not NAFLD, or NAFLD but not NASH at 72W biopsy; no requirement for absence of worsening of fibrosis);
4 GOLDEN-505 modified definition (Ballooning (score = 0) together with lobular inflammation (score = 0 or 1) and resulting in an overall pathologic diagnosis of steatosis alone or steatosis with mild inflammation, without worsening of fibrosis (any stage increase in fibrosis is considered fibrosis progression)); ITT population; 5 CENTAUR study 1Y data (Complete resolution of NASH and no worsening of fibrosis stage);
6 Loomba R, et al. AASLD 2016. Abstract LB3; 7 ARREST (Ballooning score = 0 and lobular inflammation score = 0 or 1); ¥ 600mg dose vs placebo

Sanyal et al, NEJM 2010 (PIVENS); Armstrong et al, Lancet 2016 (LEAN); Neuschwander-Tetri et al, Lancet 2014 (FLINT); Ratziu et al, Gastro 2016 (GOLDEN-505); Friedman et al, Hepatology 2017 (CENTAUR); MGL-3196 (Press release June 12, 2018); Galmed (Press release June 12, 2018)

LIPOCINE® ENHANCING HEALTH

Select NASH Biopsy Results† – Reported Effect on Fibrosis



n/N	33 /80	22 /72	31 /70	22 /72	36 /102	19 /98	29 /145	15 /144	21 /57	2 /10

*Calculated from publication, which reported separate results for each dose.
† Results from separate studies, not head to head, with different endpoint definitions; Time points and populations may differ among studies.

LIPOCINE® ENHANCING HEALTH

Comparison* of Advanced Candidates with Biopsy Results

Phase 2 end points:

- At least 2 point reduction in NAFLD NAS: at least one point reduction either in lobular inflammation or hepatocellular ballooning with no worsening of fibrosis stage

Phase 3 approvable regulatory end points:

- Complete resolution of NASH with no worsening of fibrosis and/or
- At least one point improvement in Fibrosis with no worsening of NASH

Agent	Primary target mechanism	Reported Trial Results	Patient Characteristics	Serum TG reduction	ALT Reduction	Improvement in NASH	Improvement in Fibrosis
Elafibranor PPAR α δ agonist	Homeostasis modifier Anti-inflammatory Fibrosis mediation	GOLDEN	NAS Score ~4.9 Fib score ~1.7	Robust	mild	Met NASH resolution	Failed to achieve 1 point improvement
AramChol SCD1 modulator	Anti-steatogenic Anti-oxidant	ARREST	NAS Score ~5.3 Fib score 2.1 Only diabetics	Not reported	modest	Met NASH resolution	Failed to achieve 1 point improvement
MGL-3196 THR-β agonist	Homeostasis modifier	P2	NAS Score ~4.9 F0-F1: 57% F2-F3: 43%	Robust	modest	Met NASH resolution	Maybe Positive trend
Obeticholic acid FXR agonist	Anti-inflammatory antifibrotic Control Bile acid synthesis	FLINT	NAS Score ~5.3 Fib score ~1.9	mild	Robust	Improved NAS score >2	1 point improvement
Selonsertib ASK1 inhibitor	Anti-inflammatory antifibrotic	Open label, No placebo	NAS Score ~6 71% more than NAS>6 60-66% F3	negligible	marginal	Failed NASH resolution	1 point improvement
Cenicriviroc CCR2/5 antagonist	Anti-inflammatory antifibrotic	CENTAUR	NAS Score ~5.3 Fib score ~2.06	negligible	negligible	Failed NASH resolution	Maybe Mixed results

* From separate studies not “head to head”

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