NGM282 (Engineered FGF-19 Variant)

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Disclosure Information:

Dr. Stephen Harrison discloses the following relevant financial relationships with commercial interests within the past twelve months:

- Speakers' Bureau: Alexion, Abbvie
- Consultant, Advisory Board: Allergan, Chronic Liver Disease Foundation, Cirius, Second Genome, CiVi Biopharma, CanFite Biopharma, Echosens, Fibrogen, Galmed, Genfit, Gilead, Intercept, Madrigal, NGM Bio, Novartis, Perspectum, Pfizer, BMS, Prometheus, Cymabay
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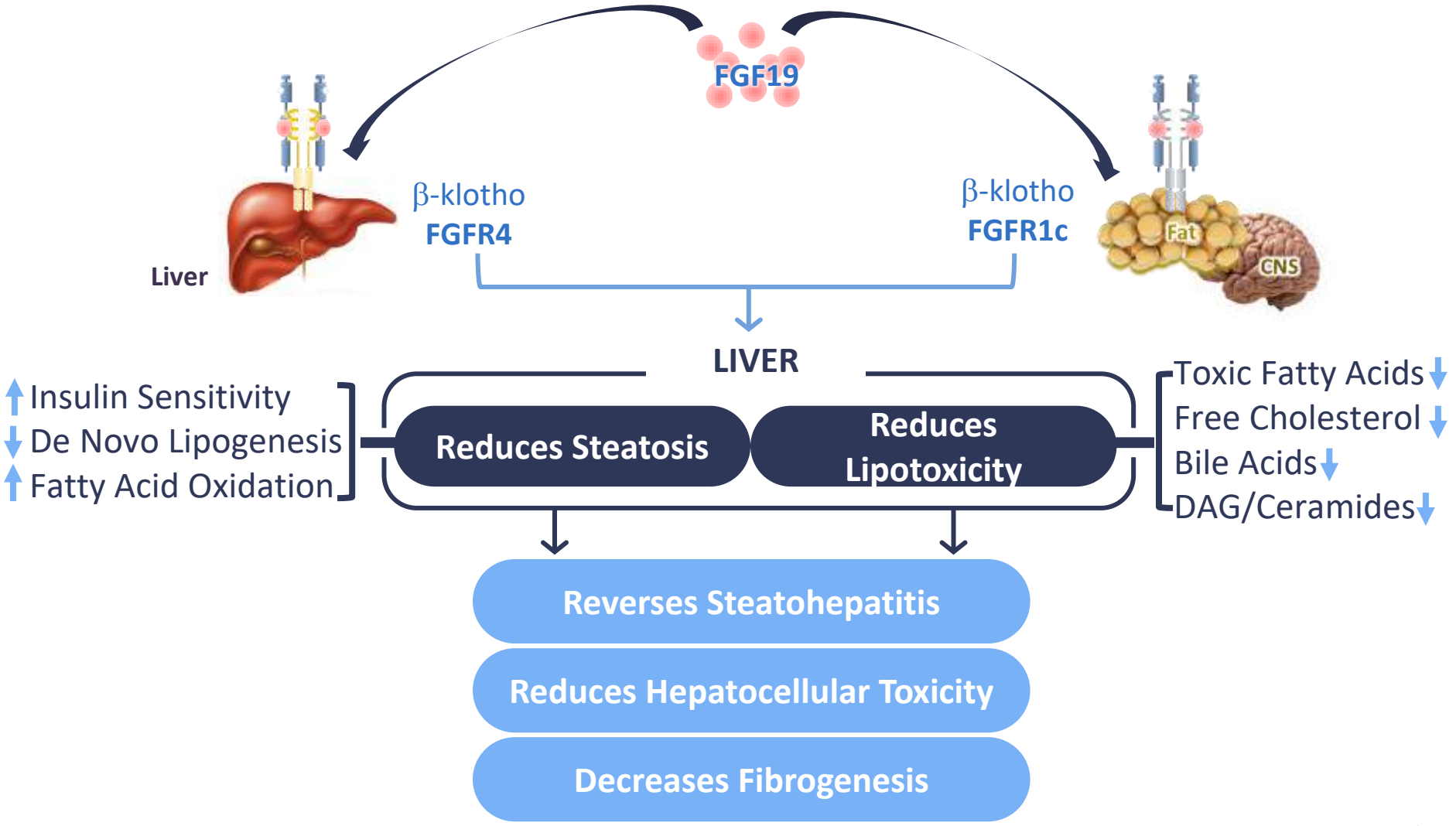
FGF19 Has Multiple Biological Activities Relevant to the Pathogenesis of NASH



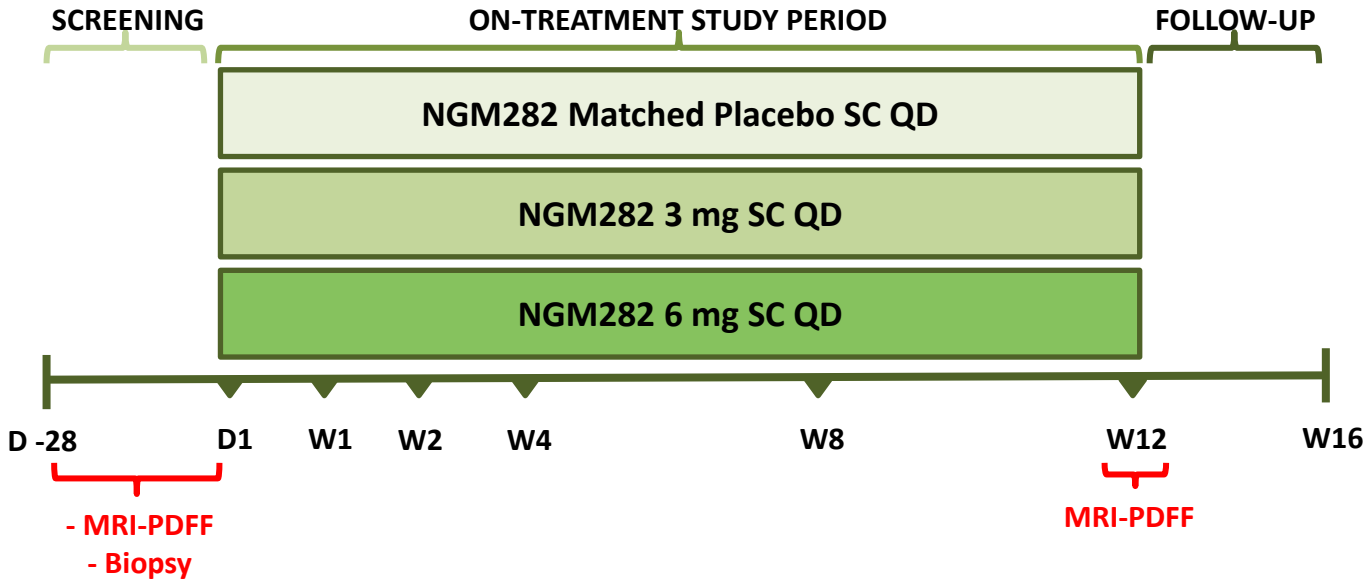
NGM282: A Novel Non-tumorigenic, Engineered Variant of Human FGF19

- Over 150 variants screened to identify molecules retaining the metabolic activity of FGF19 while eliminating the tumorigenic effects
- Engineered variant devoid of IL6/STAT3 activation associated with the tumorigenic effects of FGF19
- Studied in multiple animal models of NASH with consistent activity:
  - Normalization of liver enzymes
  - Improvements in all components of NAS
  - Anti-fibrotic activity
  - No tumorigenicity
- Studied in over 400 subjects, including patients with type 2 diabetes, PBC, PSC and NASH

NGM282 Demonstrates Robust Activity in Animal Models of NASH and Fibrosis

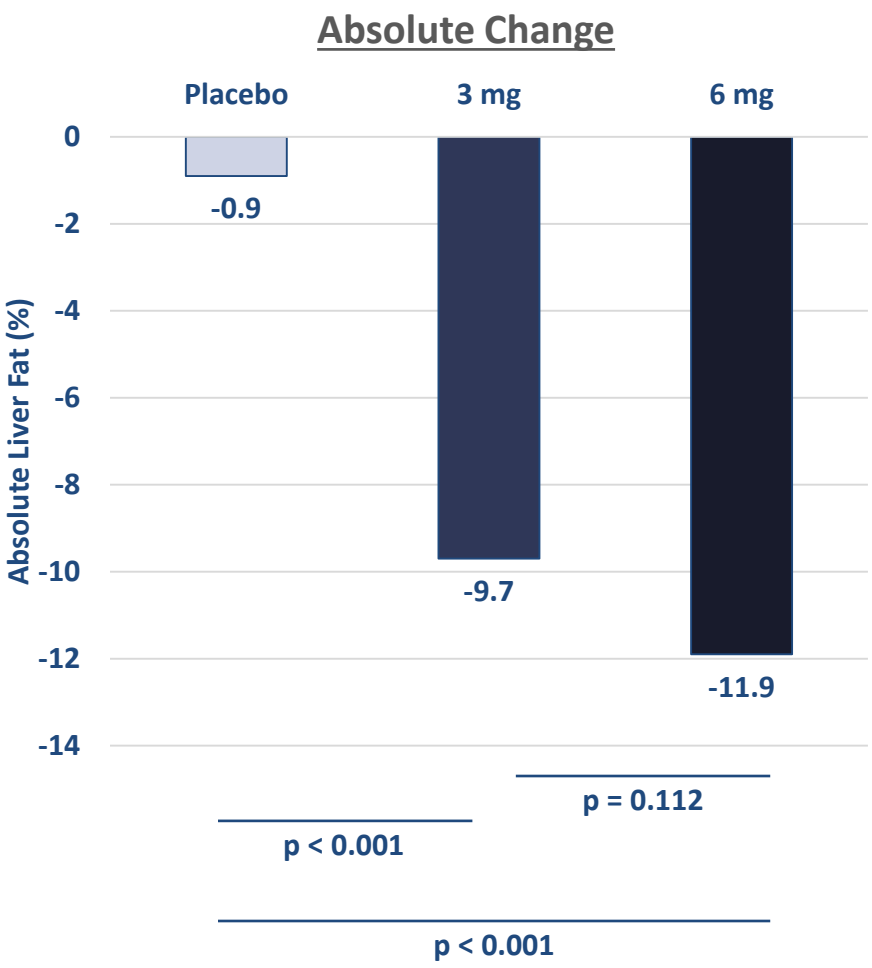
	MODEL	NGM282 ACTIVITY
STAM	• STAM™ model of NASH (STZ and high-fat diet-induced)	• Significantly improves steatosis, lobular inflammation and hepatocyte ballooning • Decreases liver enzymes and triglycerides
High Fat, High Carbohydrate	• Diet-induced model of NASH	• Reduces hepatic steatosis • Prevents liver fibrosis and inflammation
High Fat, Fructose & Cholesterol	• Diet-induced model of NASH	• Reduces hepatic steatosis • Prevents liver fibrosis and inflammation
Aged FXR KO	• Aged FXR-deficient mice display findings resembling NASH histopathology	• Normalizes liver enzymes • Improves NAFLD activity score (NAS) • Reduces hepatocellular fibrosis
BDL	• Bile duct ligation (BDL) model of severe cholestatic fibrosis	• Significantly reduces fibrosis and suppresses fibrotic gene expression • Reduces bile duct proliferation and inflammation
MDR2 KO	• MDR2-deficient mice develop bile duct injury and fibrosis	• Reverses liver injury and decreases hepatic inflammation • Improves liver fibrosis

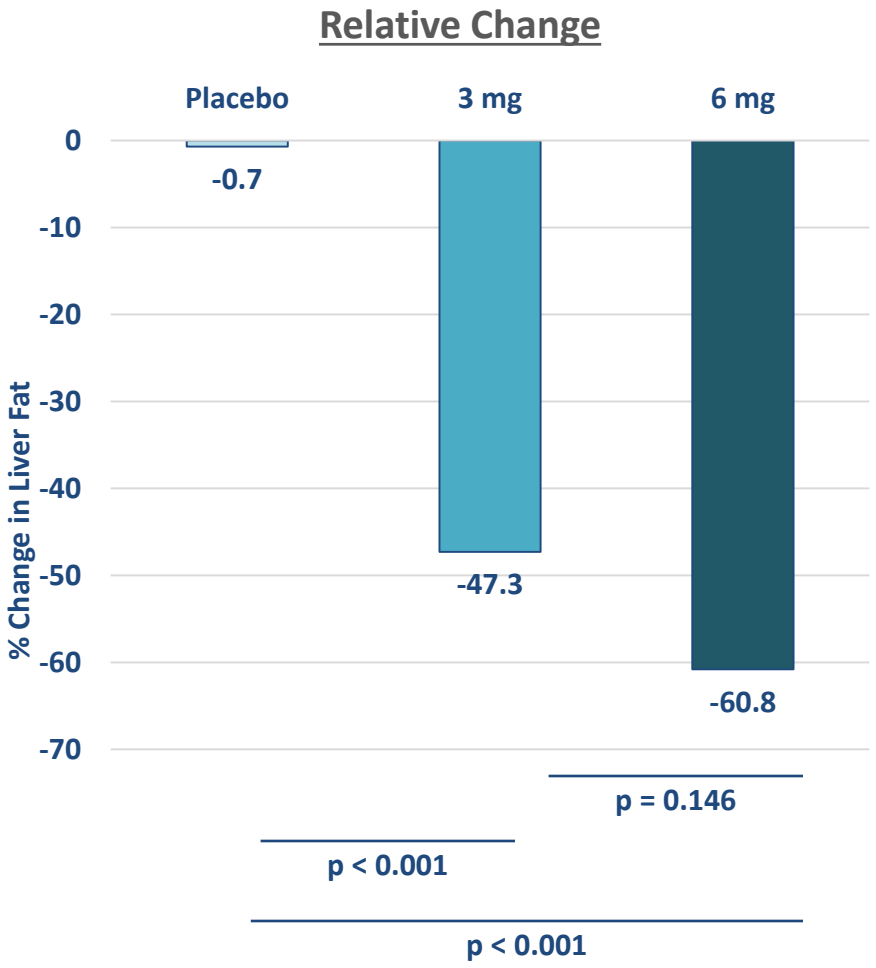
Phase 2 Study of NGM282 in NASH: Overview of Study Design



- Randomized, double-blinded, placebo controlled
- Eighty-two subjects enrolled at 18 sites in Australia and the United States
- Biopsy confirmed NASH with a minimum NAS $\geq$ 4 (1 point in each component)
- Stage 1, 2 or 3 fibrosis
- Minimum 8% absolute liver fat content by MRI-PDFF
- ALT $\geq$ 19 IU/L in females; $\geq$ 30 IU/L in males
- ***Primary endpoint is a decrease in absolute liver fat content $\geq$ 5%***

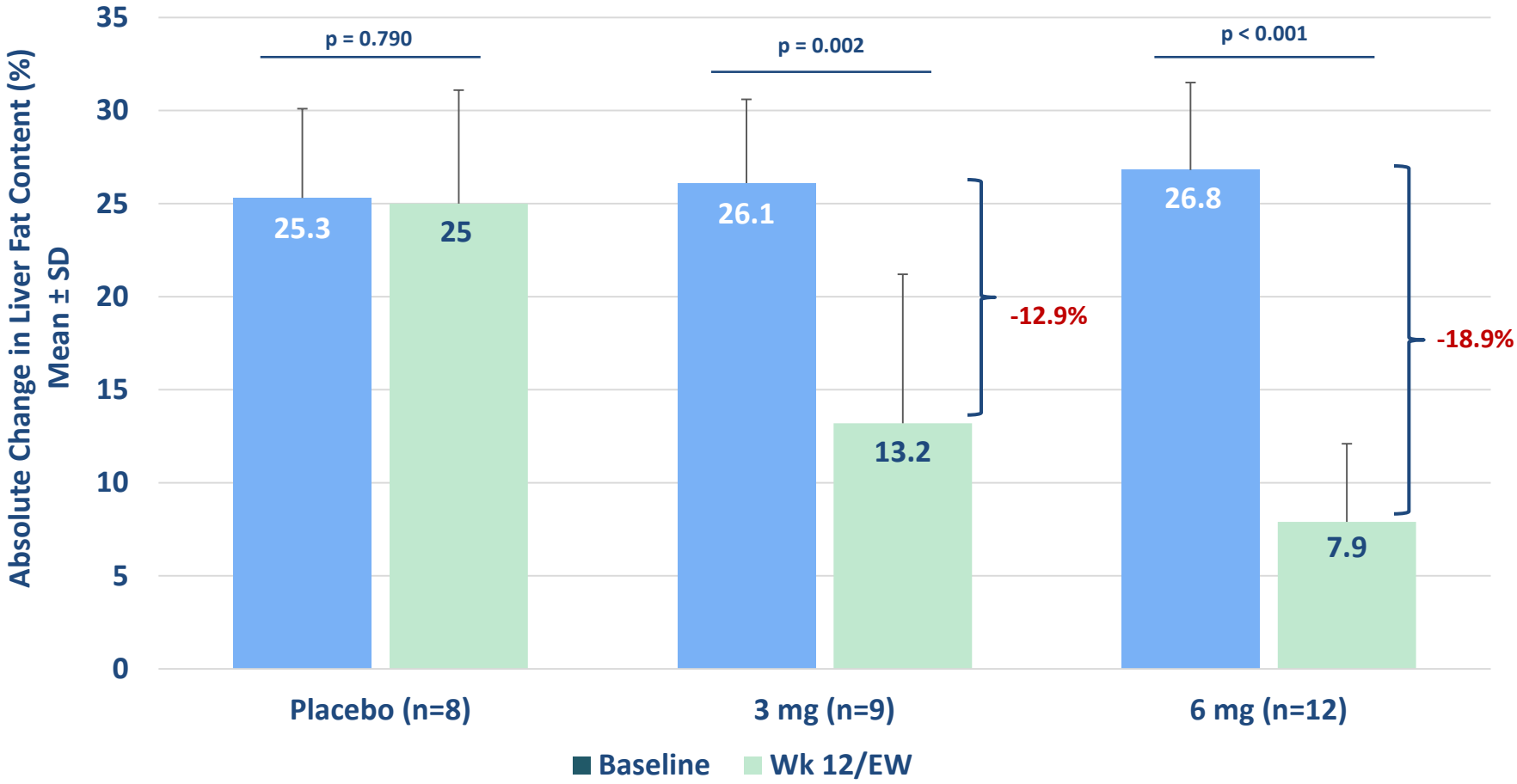
Primary Endpoint Met with Clinically Meaningful Changes in Liver Fat Content



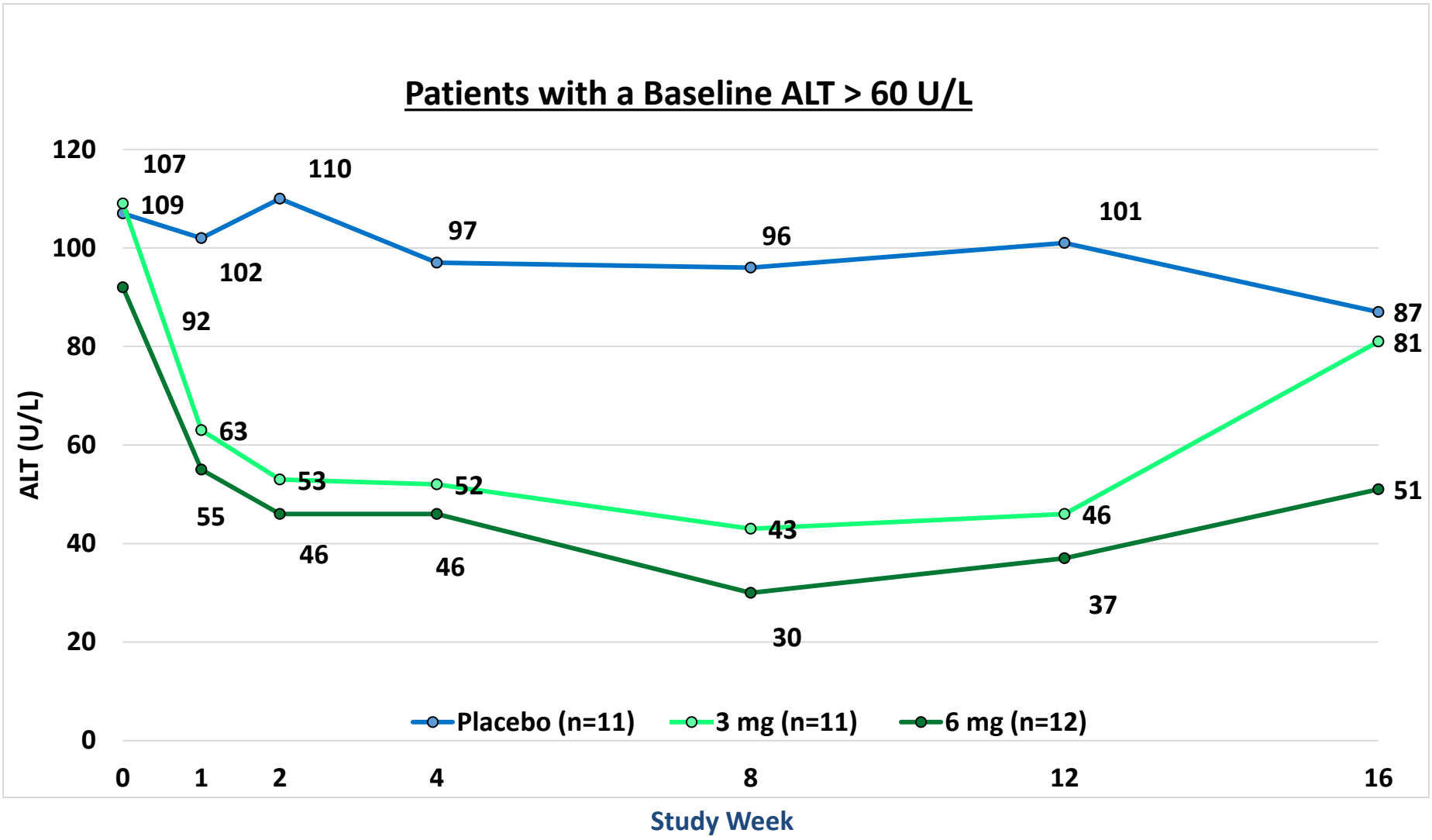


Decreases in liver fat strongly correlate with a reduction in ALT, AST and C4

Greatest Magnitude of Effect in Subjects with Most Active Disease: Baseline MRI-PDFF >20%



Rapid and Sustained Reductions in ALT in Patients with High Baseline Levels



Significant Correlations Between Decreases in LFC and NASH or Target Engagement Biomarkers

Correlation Between Absolute LFC and Key Biomarkers

PARAMETER	r-value	p-value
C4 (ng/ml)	0.53	< 0.0001
LDL Cholesterol (mg/dL)	-0.54	< 0.001
ALT (U/L)	0.46	< 0.001
Total Cholesterol (mg/dL)	-0.43	< 0.001
AST (U/L)	0.37	< 0.001
HbA1c (%)	0.32	0.004
Triglycerides (mg/dL)	0.31	0.006

Noninvasive Parameters in Open-Label Dose Finding Study for 12 weeks

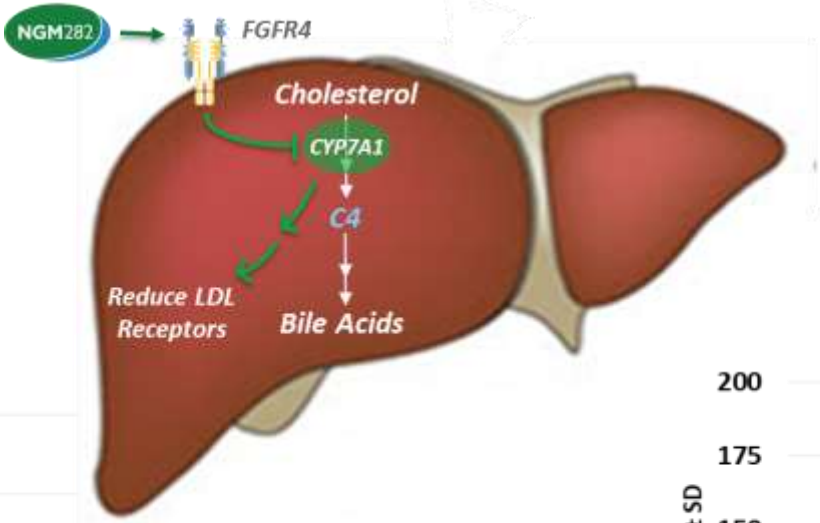
OPEN LABEL

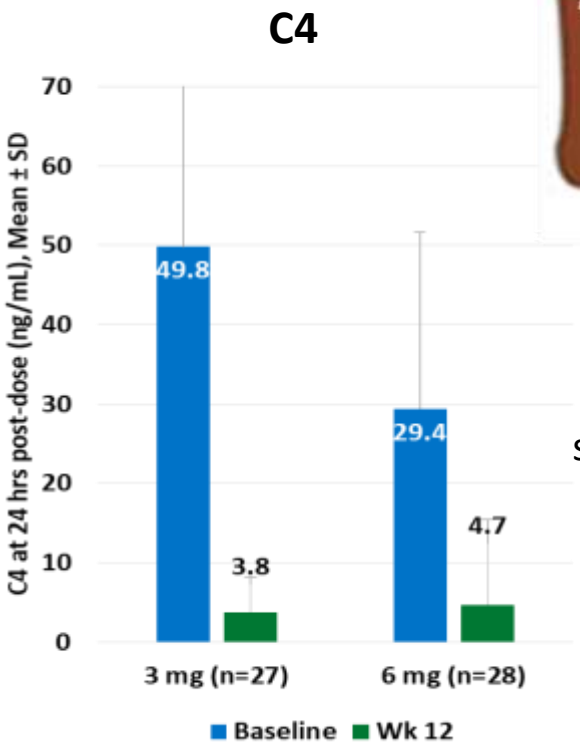
Parameter	0.3 mg (n=23)	1 mg (n=21)	3 mg (n=16)
MRI-PDFF, Absolute %	-5.3%	-11.0%	-10.9%
Absolute ≥5% (% of pts.)	57%	90%	100%
MRI-PDFF, Relative %	-29%	-57%	-66%
Relative ≥30% (% of pts.)	48%	85%	100%
ALT, Absolute (IU)	-21	-44	-54
ALT, Relative %	-30%	-59%	-59%

1 mg NGM282 dose has comparable efficacy *vs*. 3 mg (MRI, ALT)

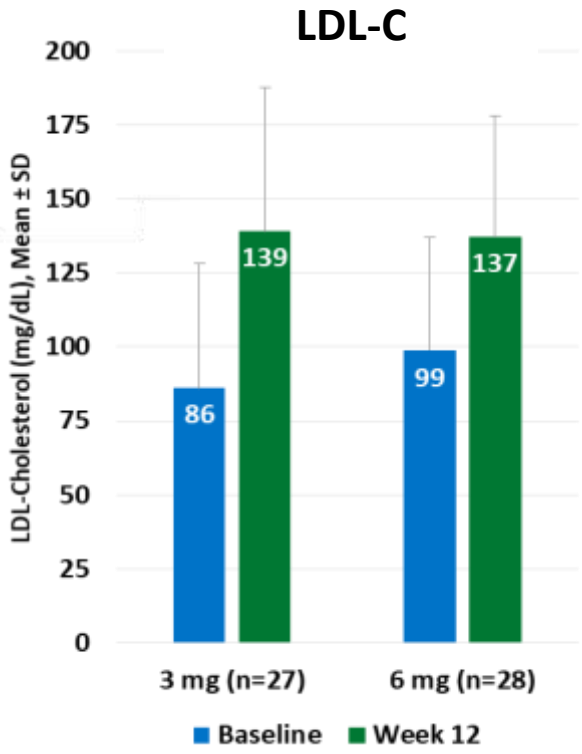
Abdelmalek et al, NASH-TAG 2018

Decreased C4 and Increased LDL-C Levels Reflect Potent FGFR4-Mediated CYP7A1 Inhibition



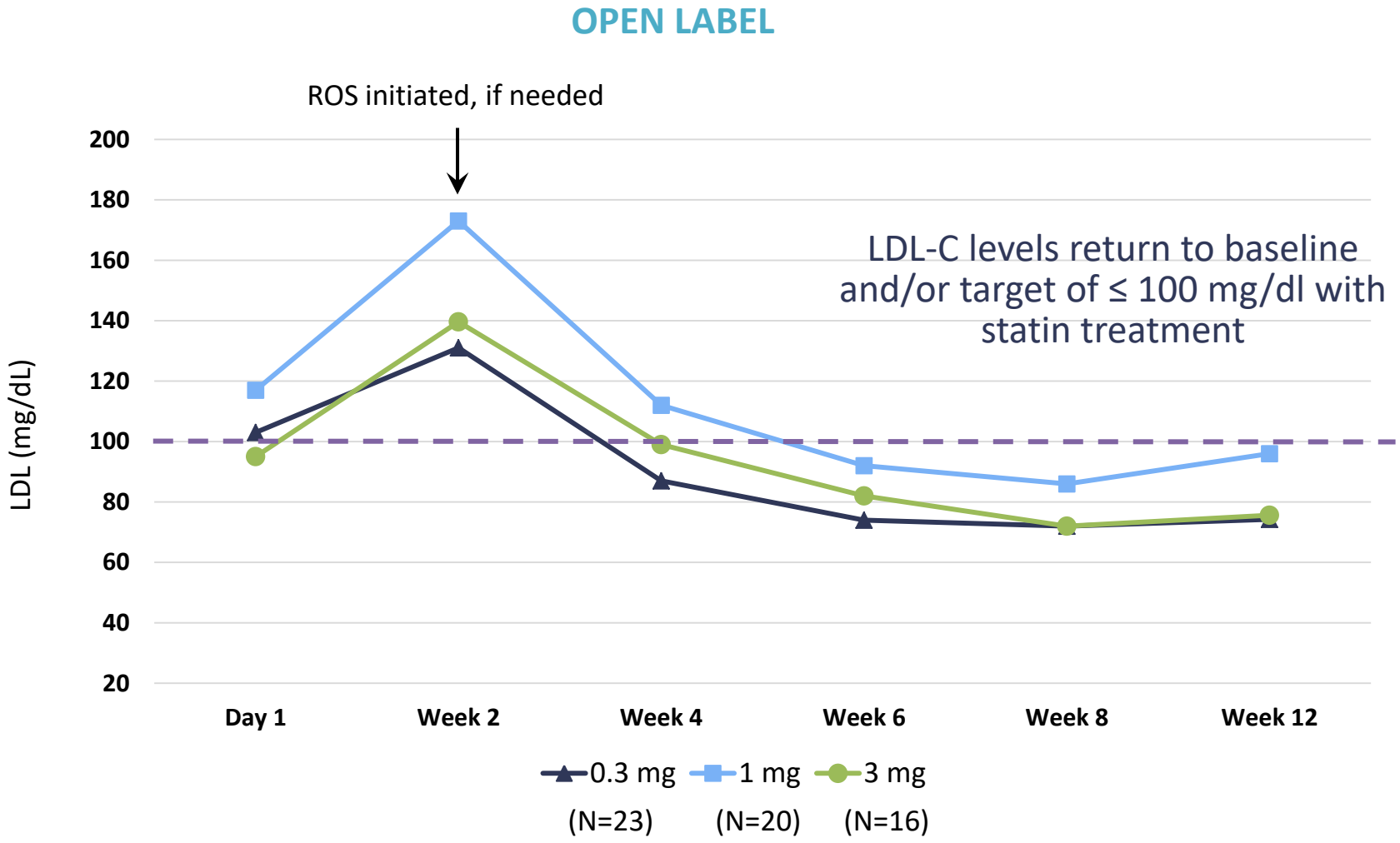


C4 (intermediate in bile acid synthetic pathway) and LDL-C are negatively correlated



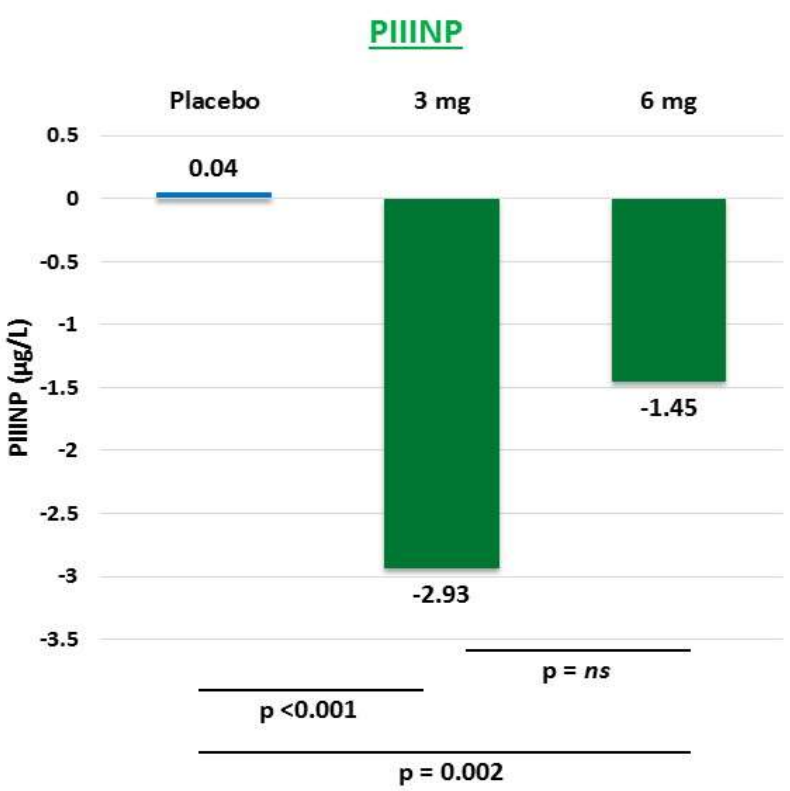
Loomba et. al, AASLD 2017 Abstract 2178

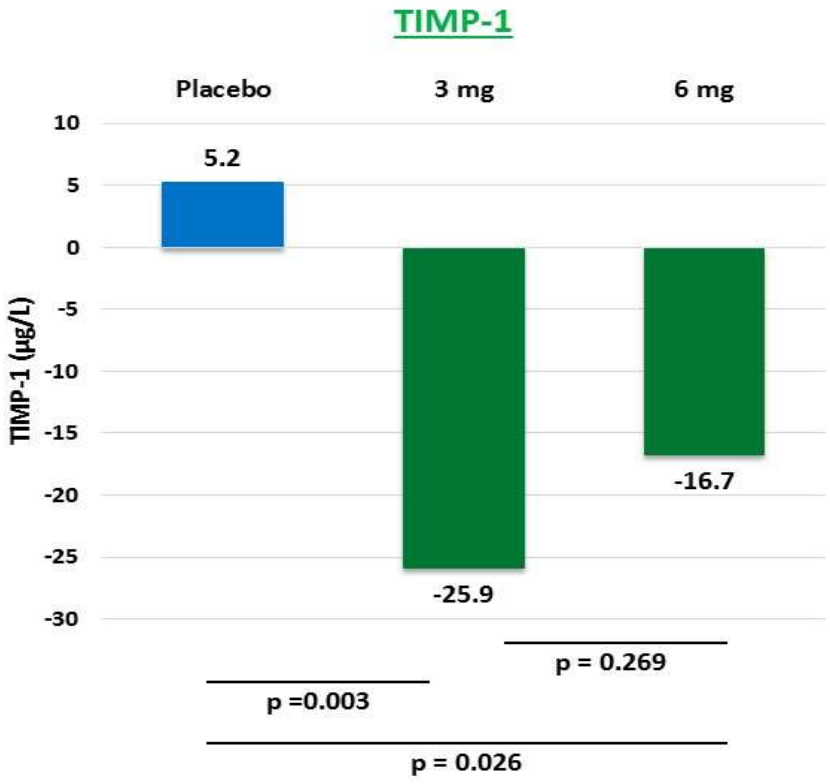
Rapid and Complete Reversal of LDL-C Elevations Achieved with Statin Co-administration



Rinella et. al, AASLD 2017 Abstract 2143

Significant Decreases in PIIINP and TIMP-1 Supportive of Potential Anti-fibrotic Activity





- Significant absolute and percentage change in total ELF score for 3 mg NGM282 cohort with numeric decreases observed with 6 mg cohort
- No significant changes observed in hyaluronic acid

Summary of Safety/Tolerability and Other Lab Parameters

- Injection site reactions and lower GI symptoms (increased stool frequency/diarrhea, loose stools, cramping) remain the most common AEs
  - Dose dependent in frequency, severity and persistence on treatment
  - < 10% of GI symptoms were continuing at end of treatment
- No significant impact on peripheral glucose and insulin sensitization parameters
  - Some evidence of lipid mediated and hepatic insulin sensitization
- Significant decreases in triglycerides and stable HDL
- No significant changes observed in vital signs or ECG
- No evidence of nephrotoxicity or hepatotoxicity
- No significant changes in hematologic parameters
- Measures of bile acid-mediated absorption (Vitamin D, INR) were stable

Summary and Conclusions

- Rapid and profound reduction of multiple parameters relevant to the pathogenesis of NASH
- Favorable and consistent safety and tolerability profile
  - GI symptoms are generally mild at relevant doses and mitigated with timing of injection and decreased meal size
  - Mitigation of LDL increases rapidly managed with a statin
- Translation of noninvasive measures to 12 week histology are currently being generated