NGM313, a Novel Activator of β-Klotho/FGFR1c: A Single Dose Significantly Reduces Steatosis (Liver Fat by MRI-PDFF), Inflammation (ALT, AST) and Fibrogenic Activity (Pro-C3) in NAFLD Subjects

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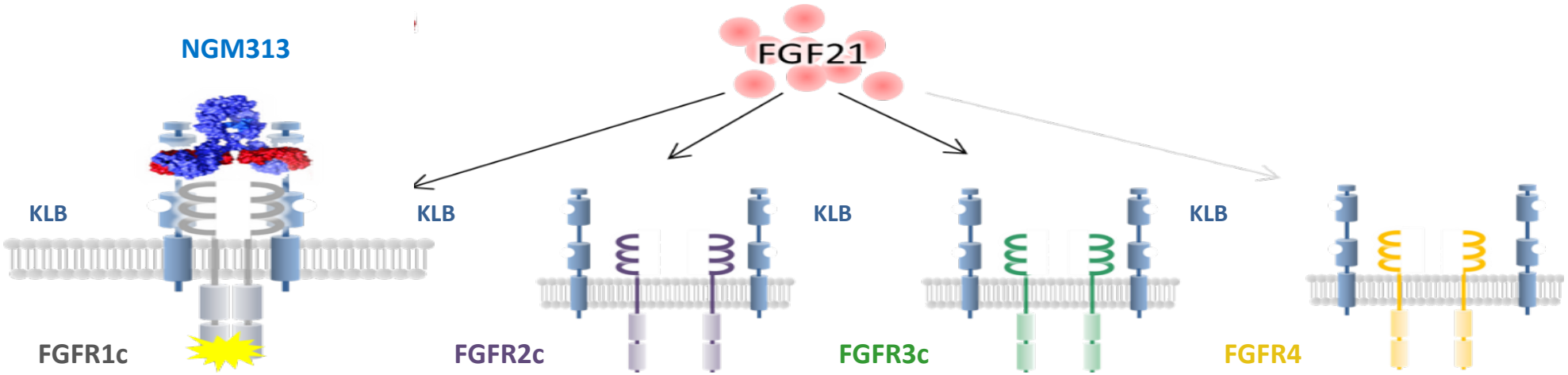
EASL The International Liver Congress 2019
Vienna, Austria
12 April 2019

NGM313 Selectively Targets β-Klotho/FGFR1c to Modulate the Insulin Sensitizing Effects of FGF21



β-Klotho (KLB)/FGFR1c: A Validated Pathway

- FGF21 Analogs: Demonstrated Clinical Efficacy in Metabolic Syndrome/NASH
- Important Regulator of Glucose and Lipid Homeostasis
- Pathway Complements Existing Therapeutic Classes (*e.g.*, GLP-1, DPP-IV)

NGM313

- Allosteric Agonistic Monoclonal Antibody with Long Half-life

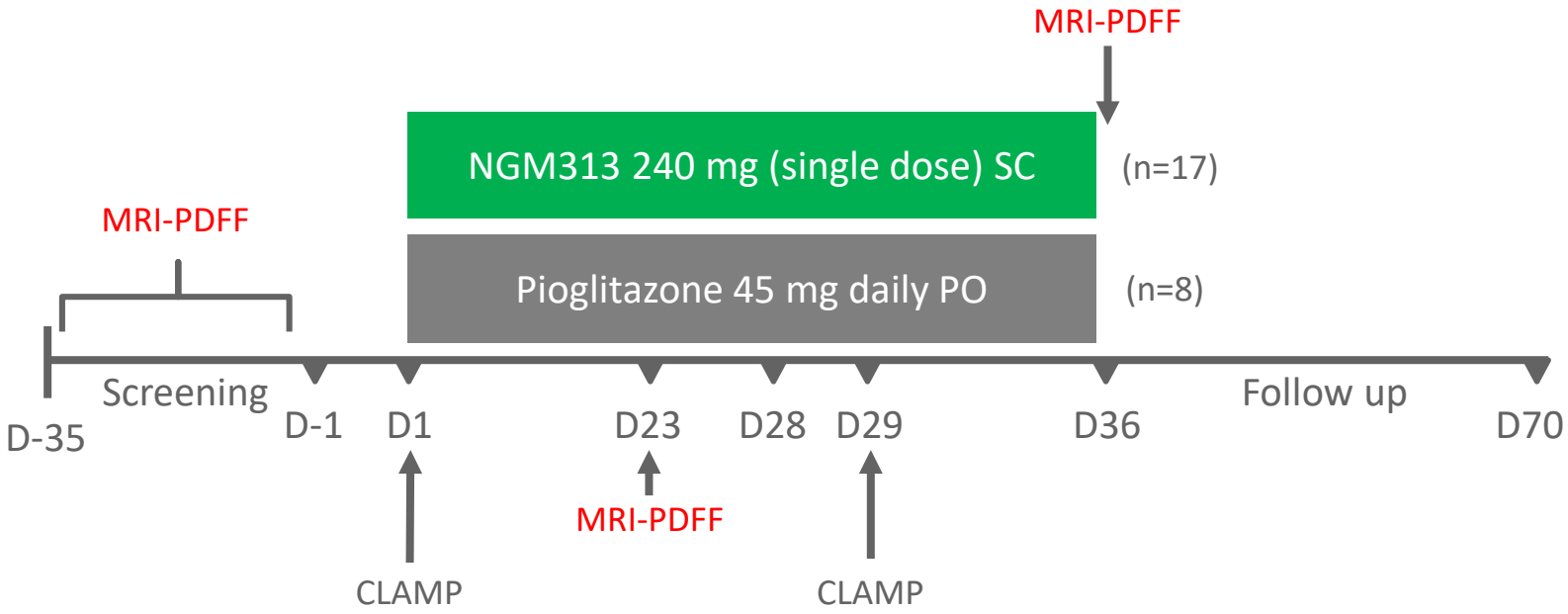
- Highly Specific, No Signaling Through Other Receptors
- Reduced Immunogenicity vs. Ligand Analogs
- Does Not Compete with Endogenous FGF21 / FGF19 Binding to FGFR1c

NGM313 is a Monoclonal Antibody Activator of β-Klotho/FGFR1c in Development for NASH

- NGM313 has completed Phase 1 studies in normal subjects [1-2]
  - Single ascending dose: 4-week treatment
  - Multiple ascending dose: 12-week treatment
- NGM313 has demonstrated favorable safety and tolerability profile in Phase 1 studies:[1-3]
  - No significant lab, vital sign or adverse event signals observed
  - No evidence for changes in blood pressure or gastrointestinal symptoms
- A single dose of NGM313 produced rapid, robust and significant decreases in TG and increases in plasma adiponectin, consistent with insulin-sensitizing action [1-3]
- Data support Phase 1b metabolic study in insulin-resistant NAFLD subjects

[1] *DePaoli et al. NASH-TAG Conference 2019*
[2] *NGM Data on File*
[3] *DePaoli et al. AASLD Conference 2018*

Ph1b Metabolic Study Design and Key Enrollment Criteria



- Twenty-five insulin-resistant patients with NAFLD were randomized 2:1 to either a single dose of NGM313 240 mg SC or pioglitazone 45 mg QD for 36 days
- Inclusion criteria included fasting glucose <125 mg/dL, fasting insulin >10 mIU/mL, BMI >30 kg/m^2 and NAFLD with ≥8% liver fat content by MRI-PDFF
- Primary objectives
  - Change in **insulin sensitivity** from baseline to Day 29
  - Change in **liver fat content (LFC)** from baseline to Day 36

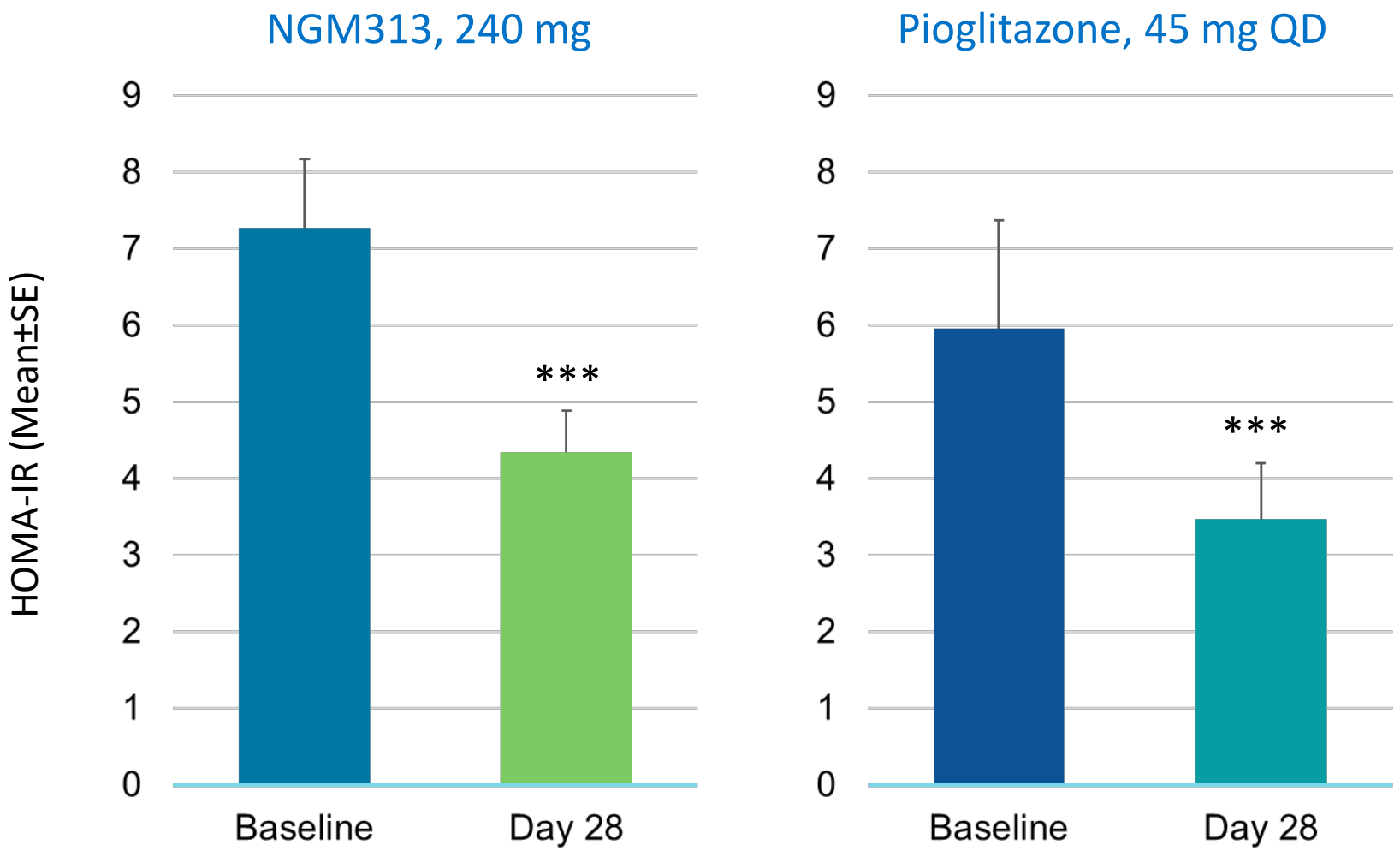
Baseline Demographics and Patient Characteristics

Parameter	NGM313 (n=17[#])	Pioglitazone (n=8)
Age (years)	41.9 ± 11.8	47.0 ± 10.2
Weight (kg)	106.0 ± 15.4	100.4 ± 18.7
BMI (kg/m^2)	36.8 ± 3.1	33.7 ± 3.2
Fasting Glucose (mg/dL)	101.7 ± 9.6	101.5 ± 10
Fasting Insulin (mU/mL)	27.0 ± 13.9	20.0 ± 5.9
HbA1c (%)	5.81 ± 0.37	5.70 ± 0.33
Hepatic Fat Fraction (%)	18.4 ± 6.4	17.3 ± 7.7
LDL-C (mg/dL)	105 ± 25	111 ± 41
HDL-C (mg/dL)	39 ± 8	42 ± 10
Triglyceride (mg/dL)	148 ± 91	136 ± 61
ALT (IU/L)	30.7 ± 14.0	43.0 ± 24.4
AST (IU/L)	20.7 ± 6.3	23.0 ± 10.9

Shown are mean ± SD

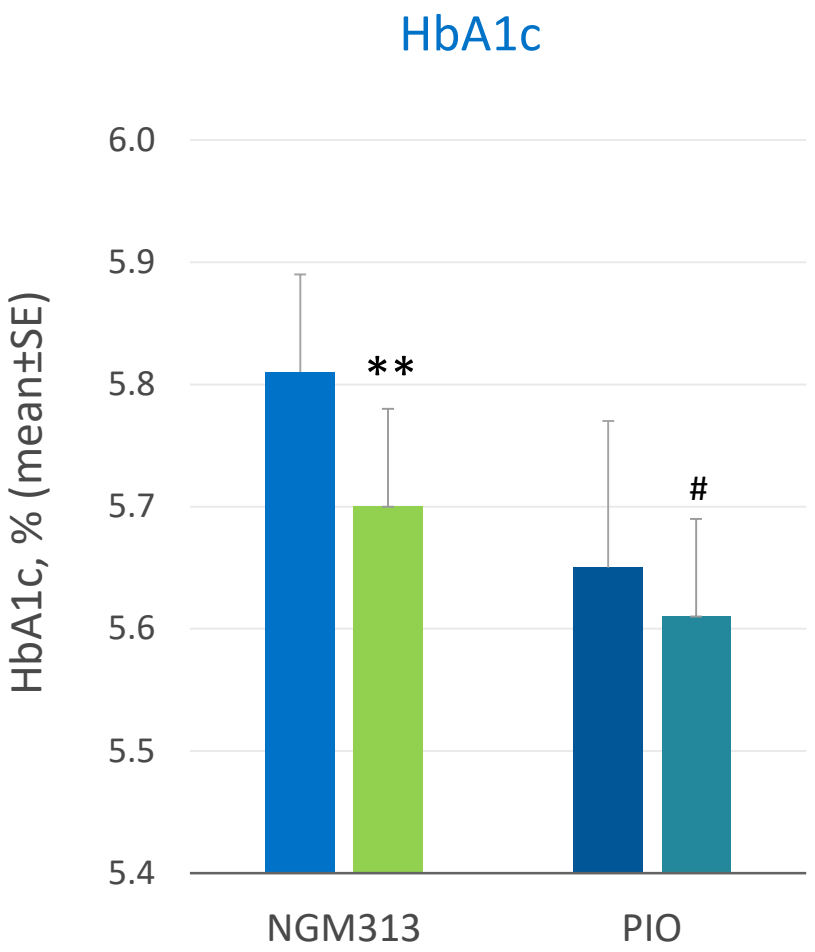
[#]One subject declined to complete the Day 28 and Day 29 procedures and was excluded from the pharmacodynamic analysis; all patients were included in the safety analysis

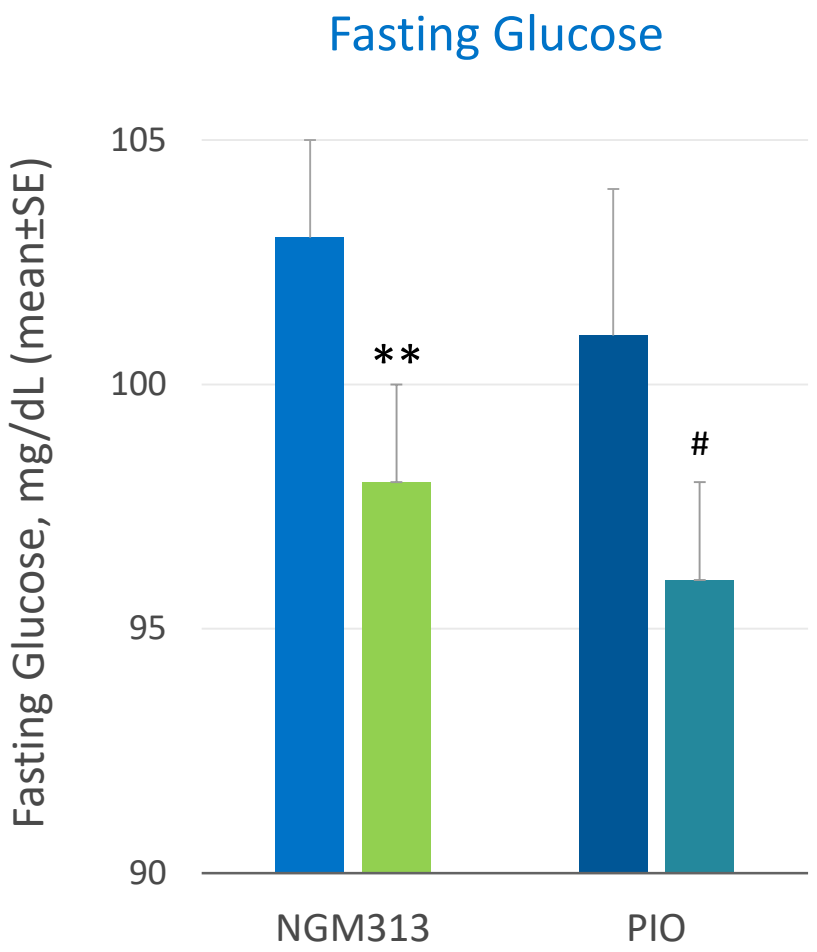
Robust Lowering of HOMA-IR is Consistent with the Insulin-Sensitizing Action of NGM313



****p<0.0001 vs baseline*

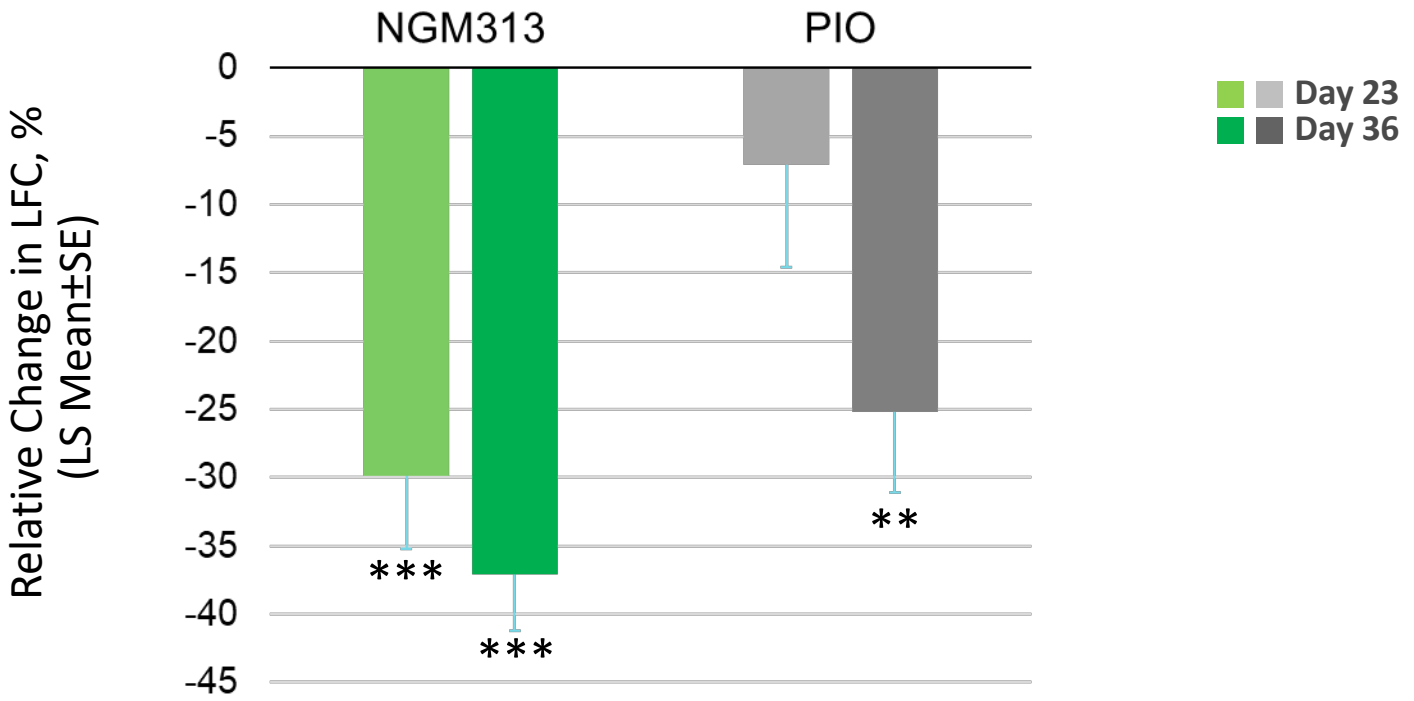
NGM313 Lowered HbA1c and Fasting Glucose Levels





***p<0.001*
**p<0.01*
#p<0.05 vs baseline

A Single Dose of NGM313 Resulted in Significant Reductions in Absolute and Relative Liver Fat Content



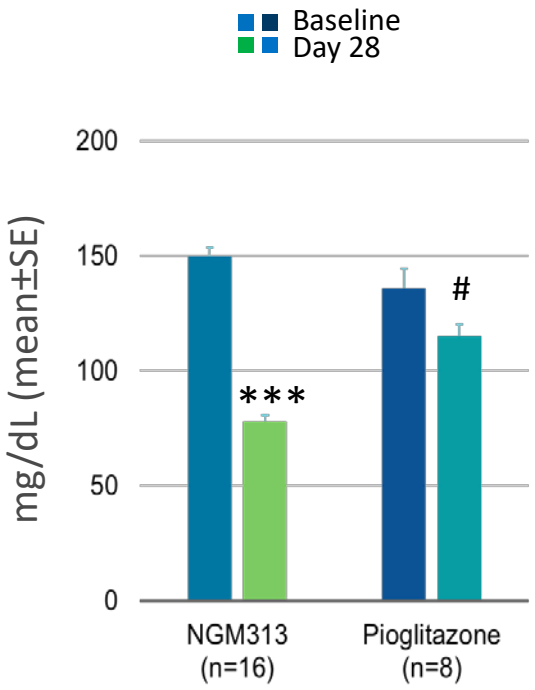
	NGM313		PIO	
# (%) of Subjects with Relative Reduction in LFC ≥ 30%	Day 23	Day 36	Day 23	Day 36
	8 / 16 (50%)	10 / 16 (63%)	1 / 8 (13%)	2 / 8 (25%)
# (%) of Subjects with Absolute Reduction ≥ 5% LFC	Day 23	Day 36	Day 23	Day 36
	6 / 16 (38%)	10 / 16 (63%)	1 / 8 (13%)	2 / 8 (25%)

****p<0.0001*
***p<0.001*
**p<0.01 vs baseline*

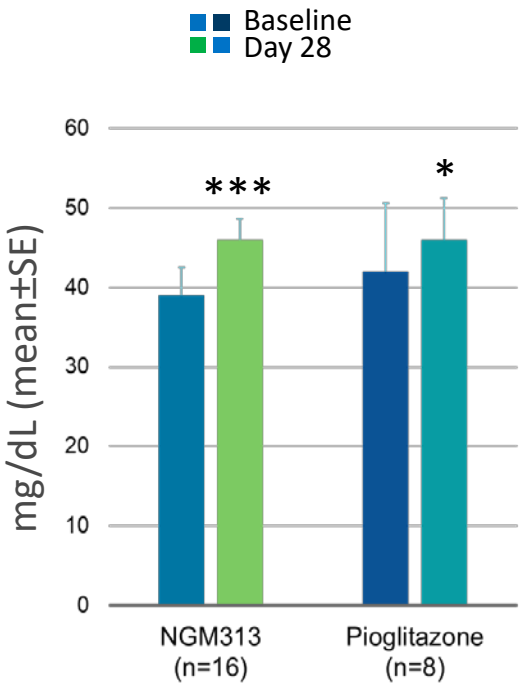
PIO, pioglitazone
LFC, liver fat content

NGM313 Produced a Favorable Lipid Profile

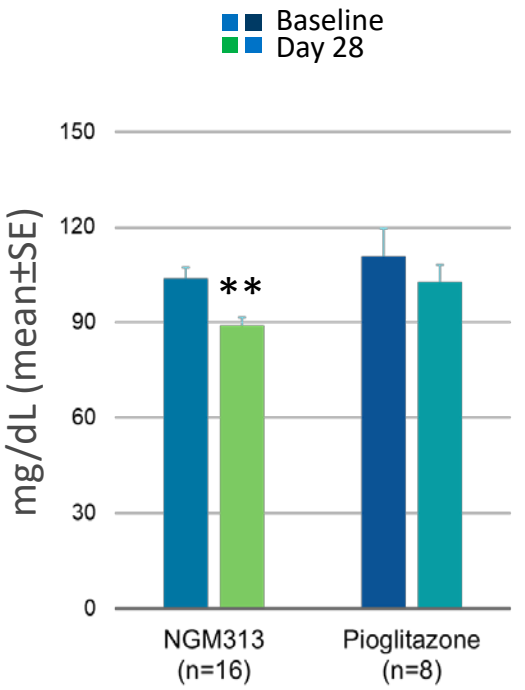
Triglycerides



HDL-C



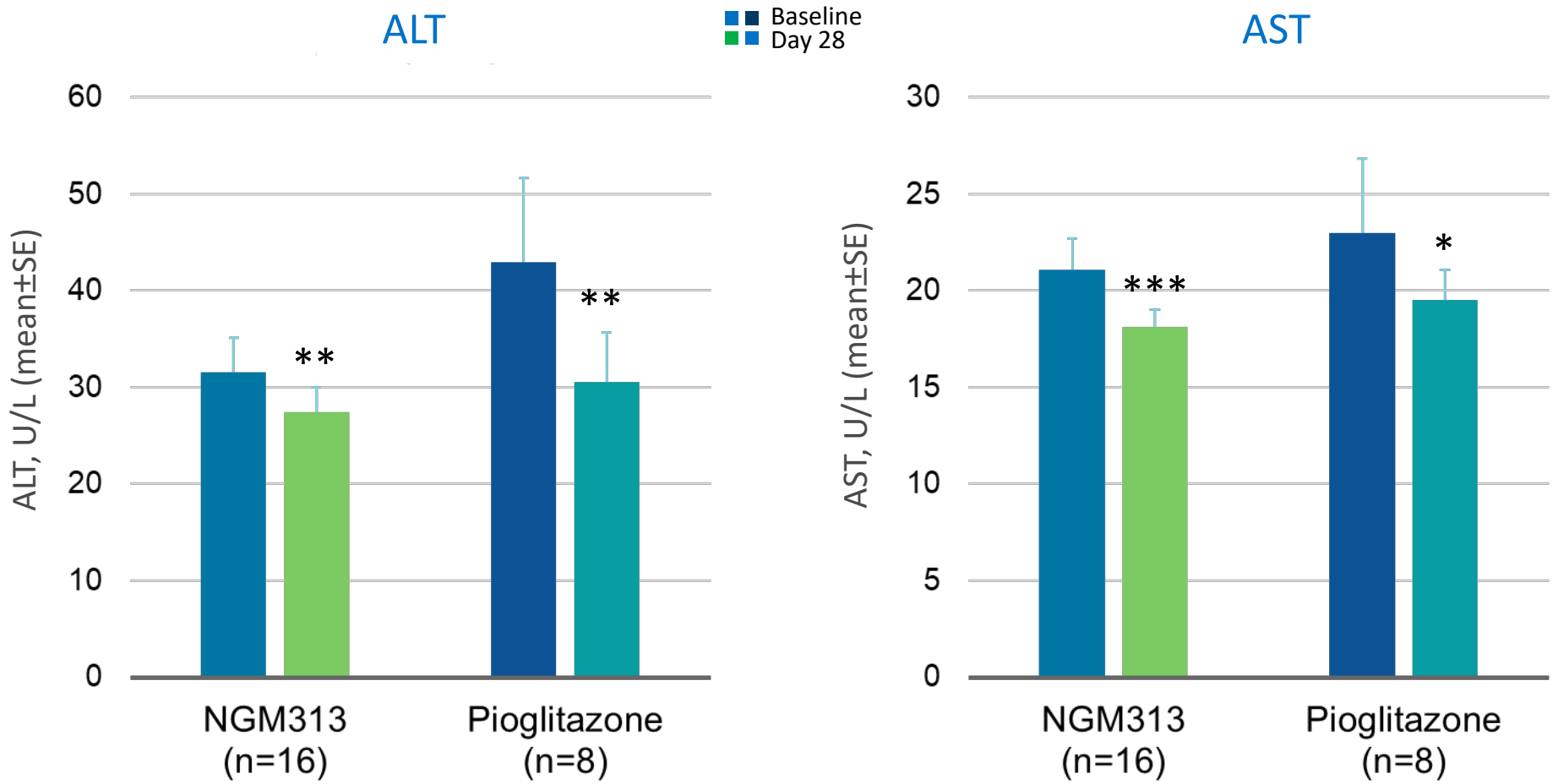
LDL-C



- Administration of a single dose of NGM313 resulted in a favorable lipid profile in patients with NAFLD
  - o ↓Triglycerides, ↑HDL-C, ↓LDL-C

****p<0.0001*
***p<0.001*
**p<0.01*
#p<0.05 vs baseline

Decreases in ALT and AST Suggest Potential for Improvement in Hepatic Injury and Inflammation by NGM313

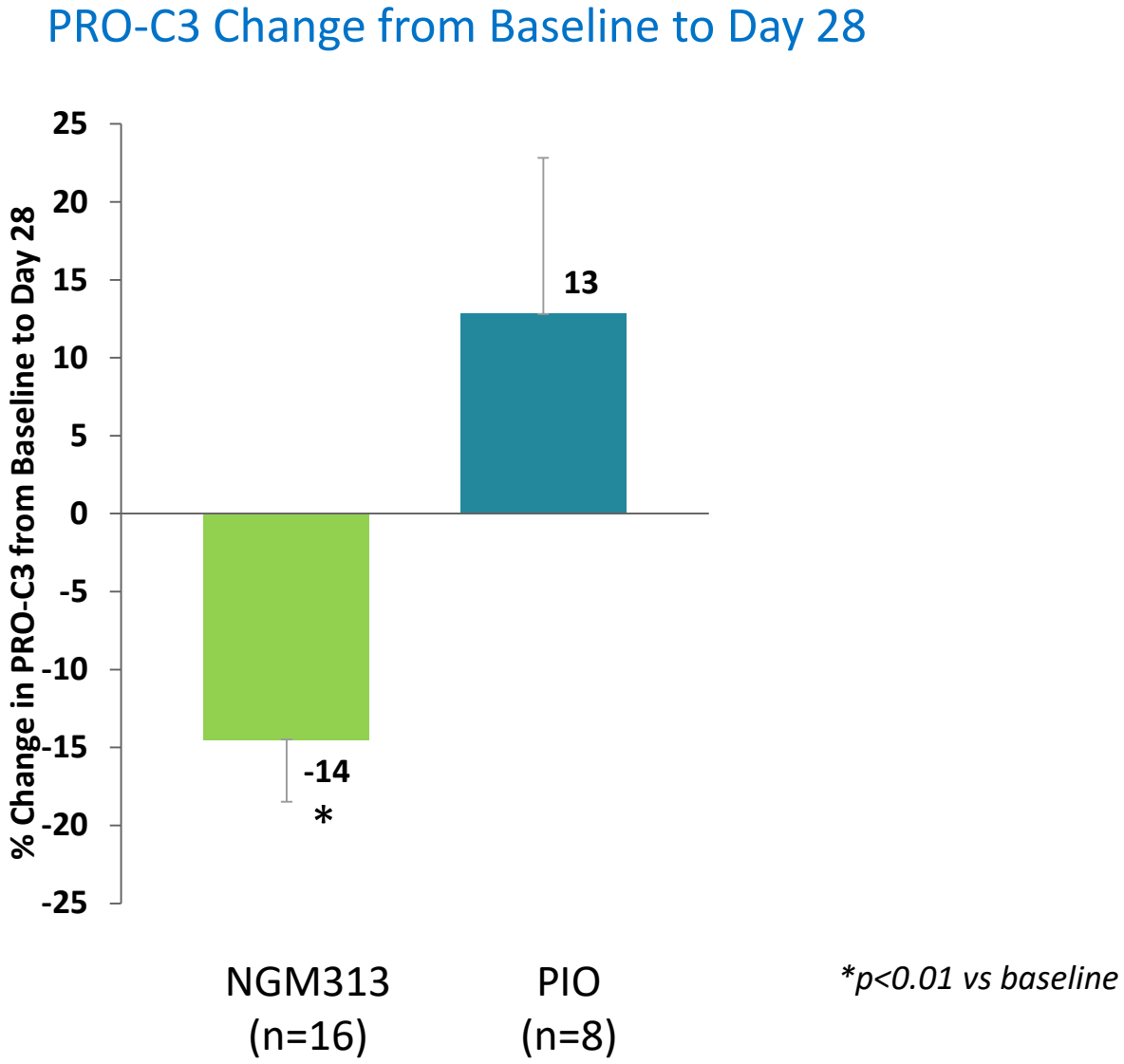


****p<0.0001,**p<0.001*
**p<0.01 vs baseline*

Fibrosis Marker Pro-C3 is Significantly Reduced by NGM313 But Not Pioglitazone

- Pro-C3 measures a neo-epitope of type III collagen during collagen formation and reflects fibrogenic activity [1]

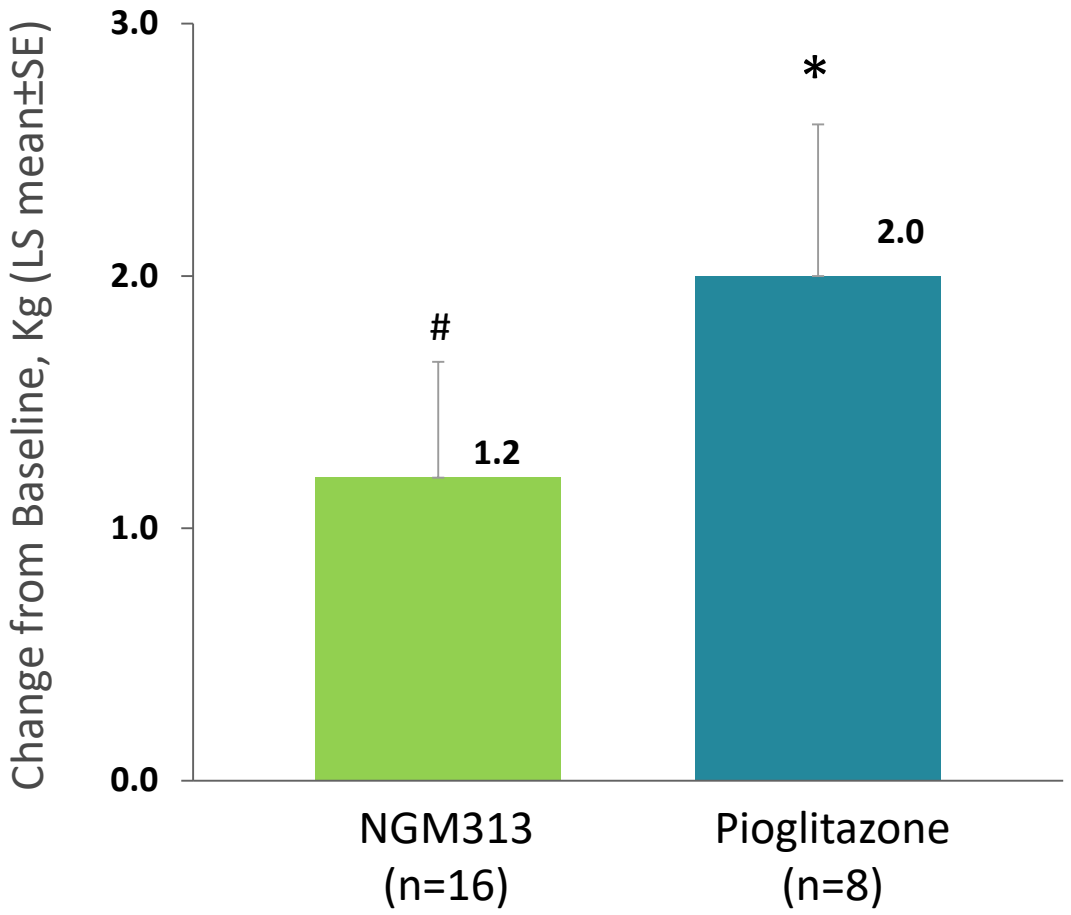
- PRO-C3 increases with fibrosis stage and is independently associated with advanced fibrosis in patients with NAFLD [2]



[1] *Nielsen et al., Am J Transl Res 2013;5:303-315*
[2] *Daniels et al., Hepatology 2018; doi: 10.1002*

Numerically Less Weight Gain in Subjects Treated with NGM313 than Pioglitazone

Body Weight Change from Baseline to Day 28



*p<0.01
#p<0.05 vs baseline

Summary of NGM313 Safety and Tolerability

- Favorable safety and tolerability profile consistent with other NGM313 studies
  - No new safety signals identified
- All AEs were mild in severity
- No SAEs or Grade 3/4 AEs
- No pattern or organ system AEs of note
- Most common AEs (>10%) were increased appetite (12%)
- No evidence of safety issues that were associated with FGF21 analogues in clinical development
  - No significant change in blood pressure
  - A previously conducted multiple-ascending dose study showed no significant change in bone mineral density or bone turnover markers [1]

[1] *NGM data on file*

NGM313 Demonstrates Significant Improvements in Multiple Non-Invasive Markers of NASH

- Administration of a single dose of NGM313 resulted in robust **reductions in liver fat content** in obese, insulin-resistant, non-diabetic subjects with NAFLD
  - 5.1% (Day 23) and 6.3% (Day 36) reduction in absolute liver fat content
  - 30% (Day 23) and 37% (Day 36) relative reduction in liver fat content
- NGM313 also demonstrated robust metabolic effects on insulin sensitivity and lipid homeostasis
  - Improved insulin sensitivity
  - Reduced HbA1c and fasting glucose levels
  - Lowered triglycerides and LDL-C
  - Raised levels of HDL-C
- Safe and well-tolerated
- These data support advancing NGM313 to Phase 2b studies in patients with biopsy-proven NASH with or without type 2 diabetes

Acknowledgments

Jin-Long Chen
David Shen
Jian Luo
Kalyani Mondal
Betty Li
Bernard Allan

Linda Morrow
Carine Beysen
Marcus Hompesch

We thank all of the patients who participated in this study, and the investigators, study coordinators, and staff for their support and assistance