Company Overview

November 2018

NASDAQ: MDGL

Forward Looking Statements

Any statements, other than statements of historical facts, made in this presentation regarding our future financial or business performance, conditions, plans, prospects, trends, or strategies and other financial and business matters; our ability to obtain additional financing; the estimated size of the market for our product candidates, the timing and success of our development and commercialization of our anticipated product candidates; and the availability of alternative therapies for our target market, are, or may be deemed, forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995. In some cases, you can identify forward-looking statements by terms such as "may," "will," "could," "should," "would," "anticipate," "believe," "estimate," "continue," "design," "expect," "intend," "plan," "potential," "predict," "seek" or the negative of these words and similar expressions and their variants may identify forward-looking statements.

These forward-looking statements reflect management's current expectations, are based on certain assumptions and involve certain risks and uncertainties, which change over time. Our actual results may differ materially from the results discussed in these forward-looking statements due to various factors. Important factors that may cause actual results to differ materially from the results discussed in these forward-looking statements include, but are not limited to, risks related to securing and maintaining relationships with collaborators; risks relating to our clinical trials; risks relating to the commercialization, if any, of our proposed product candidates (such as marketing, regulatory, product liability, supply, competition, and other risks); dependence on the efforts of third parties; dependence on intellectual property; and risks related to our cash resources and ability to obtain working capital to fund our proposed operations. Further information regarding on the factors that could affect our business, financial conditions and results of operations are contained our filings with the U.S. Securities and Exchange Commission, which are available at www.sec.gov. These forward-looking statements represent management's expectations as of the date hereof only, and we specifically disclaim any duty or obligation to update forward-looking statements as a result of subsequent events or developments, except as required by law.

Madrigal Investment Highlights

1. MGL-3196: First-in-Class Thyroid Hormone Receptor (THR)-β Agonist
2. Large & Underserved Markets in NASH & Dyslipidemia
3. Multiple Possible Value-Creating Catalysts over Next 18 Months
4. Seasoned Management Team
5. Well-Financed with $490M of Cash & Securities at June 30, 2018

Pipeline: Madrigal has Two Phase 2 Programs and Is Nearing Potential Phase 3 Initiation

Madrigal is focused on the development of its pipeline of THR-β agonists for the treatment of NASH and Familial Hypercholesterolemia (FH) / Dyslipidemia

Compound	Indication	Pre-Clinical	Phase 1	Phase 2	Phase 3	Upcoming Catalysts
MGL-3196 Thyroid Hormone Receptor-β (THR-β) Agonist	Nonalcoholic Steatohepatitis (NASH)			→		■ Phase 3 initiation
	Dyslipidemia / FH			→		■ Dyslipidemia Phase 3 study in planning stage; additional potential Phase 3 study in FH
MGL-3745 THR-β Agonist	NASH and Dyslipidemia / FH	→				

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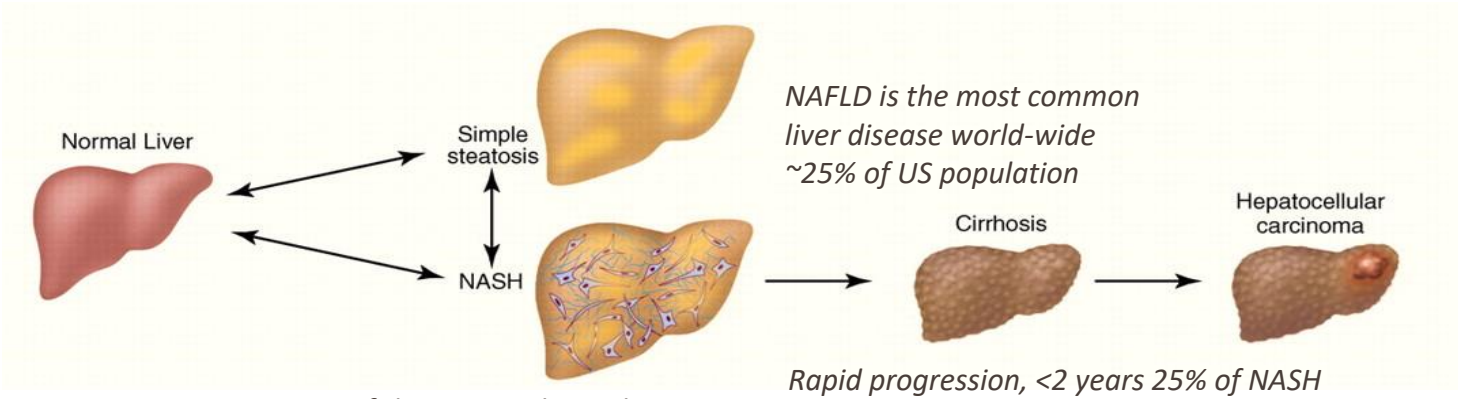
Unmet Need: Madrigal Aims to Treat Patients with NASH, a Large and Underserved Population

NASH is the most severe form of nonalcoholic fatty liver disease (NAFLD)

- Characterized by inflammation and damage caused by a buildup of fat in the liver that leads to cell death, fibrosis, and cirrhosis
- Develops most often in patients with obesity/metabolic syndrome, diabetes and dyslipidemia

NASH represents an indication with significant unmet need

- Estimated to affect 3-5% of the US adult population
- Expected to be the leading cause of liver transplant
- There are currently no approved therapies for the treatment of NASH



NAFLD is the most common liver disease world-wide
~25% of US population

~3-5% of the US population has NASH

Rapid progression, <2 years 25% of NASH
Stage 3 fibrosis progress to cirrhosis

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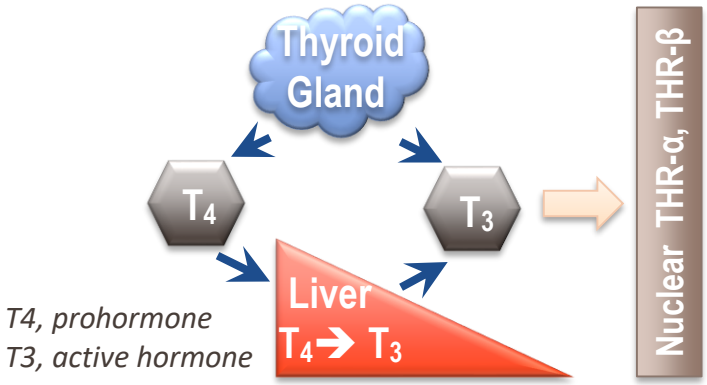
Mechanism of Action: The Importance of Liver THR-β in NASH



Thyroid Hormone Pathway

In humans, thyroid hormone receptor-β (THR-β) agonism:

- Lowers LDL-cholesterol
- Lowers triglycerides
- Lowers liver fat, potentially reducing lipotoxicity, NASH

No thyrotoxicosis (THR-α effect)

MGL-3196

- THR-β selective molecule with proven safety and efficacy in more than 300 subjects and patients treated
  - No exposure outside the liver or activity at the systemic THR-α receptor
- Pleiotropic effects with potential for addressing the underlying metabolic syndrome and hallmark features of NASH: steatosis/lipotoxicity, inflammation, ballooning, fibrosis (both directly and indirectly)
  - Reduction of liver fat through breakdown of fatty acids, normalization of liver function

Sinha and Yen Cell Biosci (2016) 6:46
DOI 10.1186/s13578-016-0113-7; Autophagy, 11:8, 1341-1357, DOI: 10.1080/15548627.2015.1061849

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Phase 2: MGL-3196 36 Week NASH Trial Read Out in 2018

Study Overview	
Drug	MGL-3196
Design	Blinded 2:1
Stage	Phase 2
Number of Patients	125
Centers	~30, USA
Treatment Duration	36 Weeks

Study Details

Inclusion/Exclusion

- NASH on liver biopsy: NAS≥4 with fibrosis
- ≥10% liver fat on MRI-PDFF
- Include diabetics, statin therapy

Comparator/Arms

- MGL-3196 or Placebo, once daily

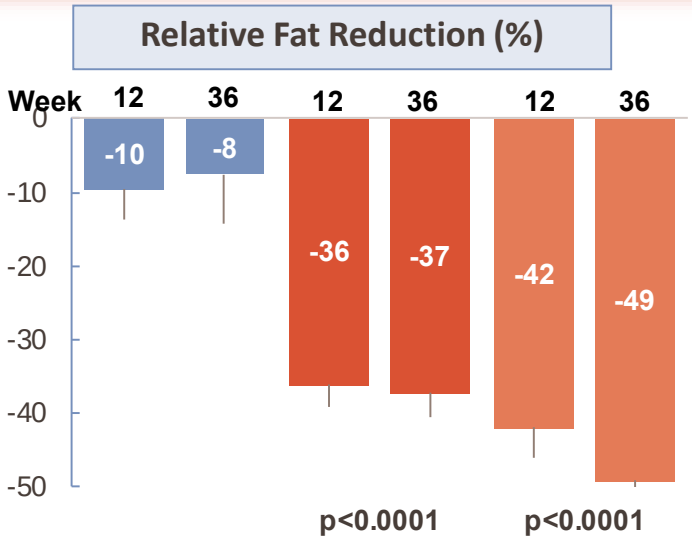
Primary Endpoint

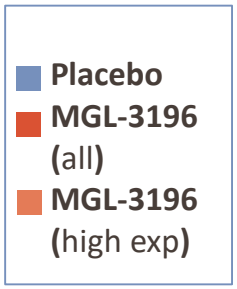
- Reduction of liver fat (MRI-PDFF) at 12 weeks

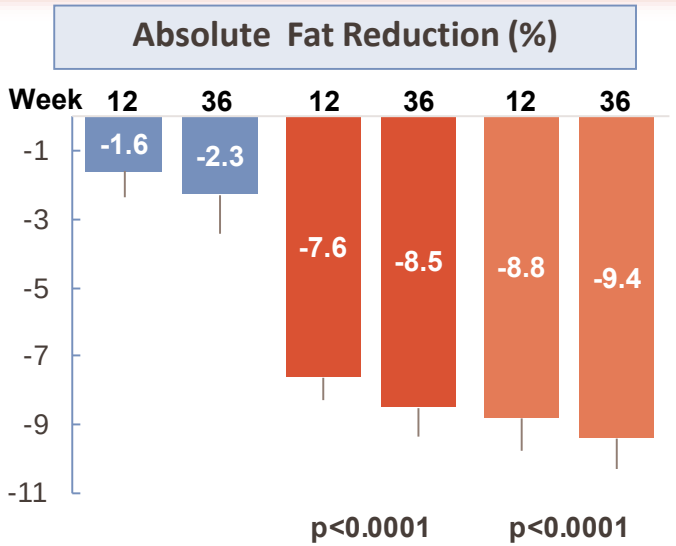
Secondary Endpoints

- NASH biomarkers and lipids at 12, 36 weeks
- Repeat MRI-PDFF at 36 weeks
- Liver biopsy at 36 weeks - reduction/resolution of NASH in patients on drug; reduction of fibrosis
- Ongoing extension study in a subset of patients who completed the Main 36 week study

Week 36: Sustained Reduction in Liver Fat on MRI-PDFF

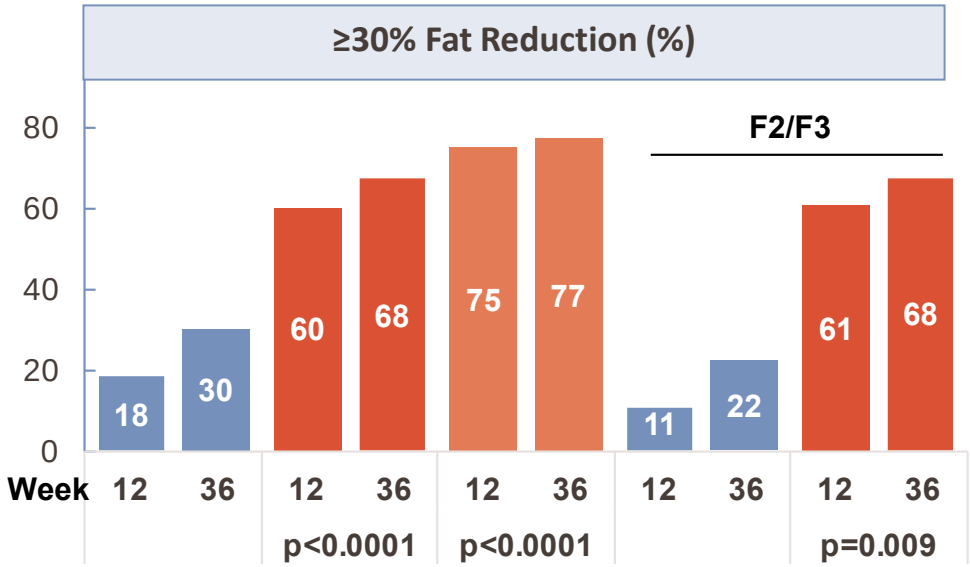






Main, 36 Week Study

- Sustained statistically significant reduction in hepatic fat Week 12 to Week 36
- Placebo response generally related to weight loss ≥5%



P value, placebo compared to MGL-3196; MGL-3196, n=78; placebo, n=38; prespecified high exposure (High Exp) n=44; F2/F3, placebo, n=19; MGL-3196, n=33

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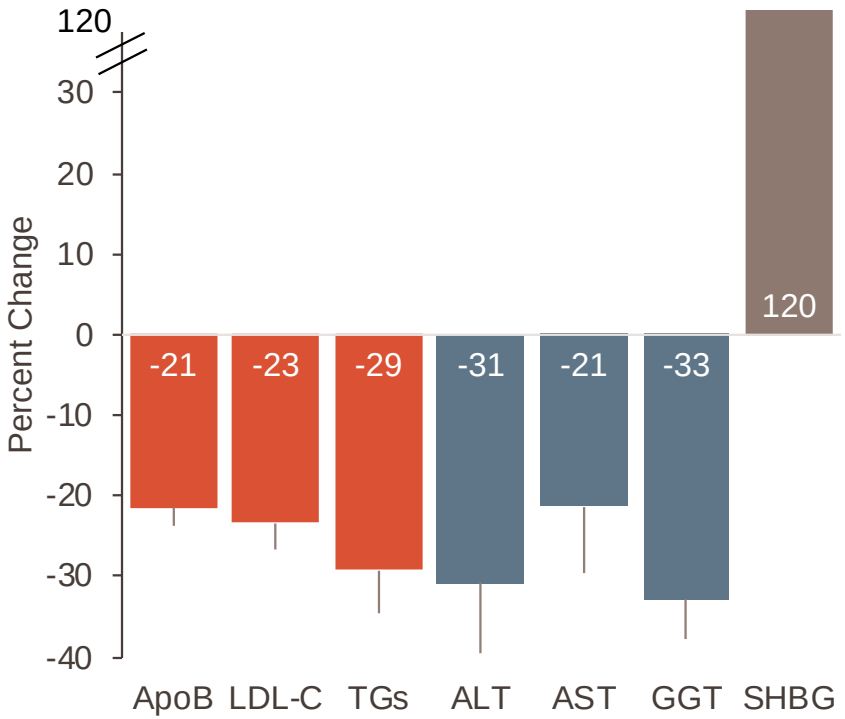
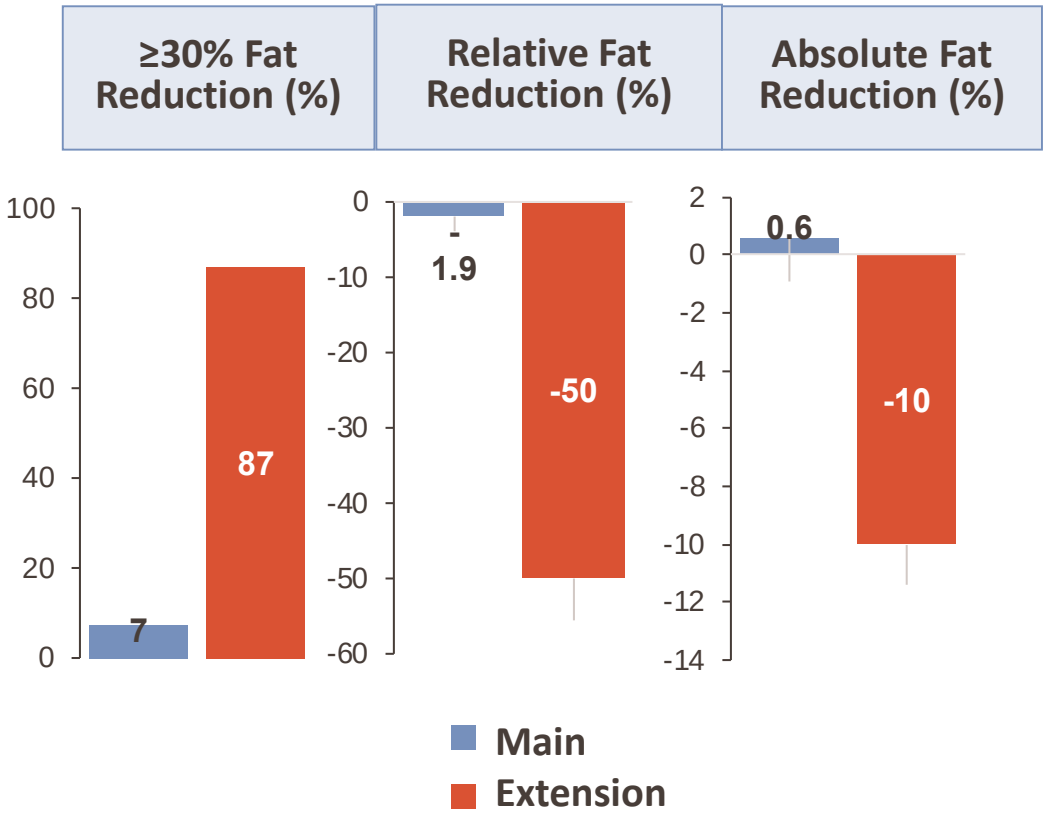
Extension Study of 36 Week Phase 2 Trial

Extension Study

- The Extension study includes 14 former placebo patients with persistently mildly to markedly elevated liver enzymes from the Main 36 Week study, ~ two thirds F2/F3
- Noninvasive end points, only
- To optimize exposure, all patients in the Extension study received 80 or 100 mg per day of MGL-3196, a higher average dose than in the 36 Week study to move all patients into the “high exposure” category
- Highly significant reduction in lipids including LDL-C, ApoB and triglycerides
- Well tolerated, few AEs, improvement in liver enzymes from baseline



Extension Study: Reduction in Liver Fat on MRI-PDFF



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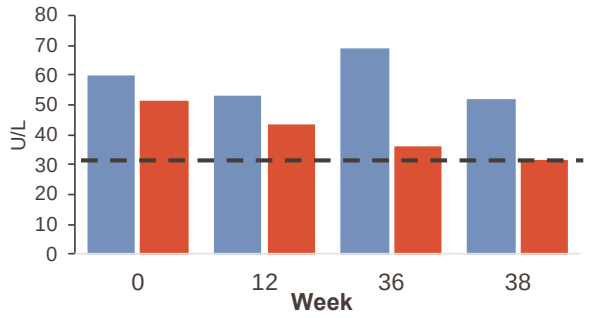
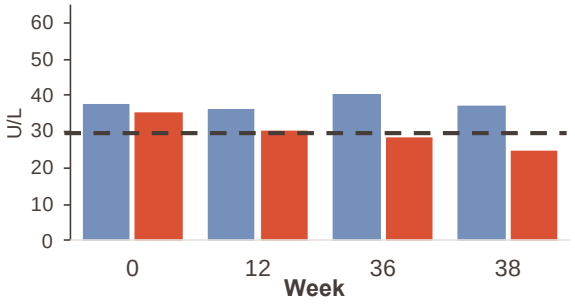
Week 36: Liver Enzymes

ALT



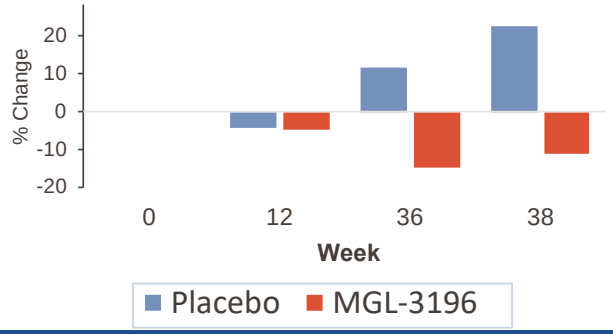
- Week 36, 40% reduction in ALT in patients with elevated baseline (p=0.01), and all MGL-3196 relative to placebo patients (p=0.002)
- At Week 36, 60% of MGL-3196 patients with ALT <30 vs 37% of placebo (p=0.03)

AST



- Week 36, statistically significant AST reduction in MGL-3196 vs placebo (% change and absolute change) p=0.002

GGT



- Week 36, statistically significant GGT reduction MGL-3196 vs placebo (% change and absolute change) p=0.002

Statistically significant reductions in ALT, AST and GGT versus placebo; no change in bilirubin or alkaline phosphatase

Baseline elevated ALT =45 male, 30 female. GGT shown as % change from baseline, females and males have different normal GGT ranges

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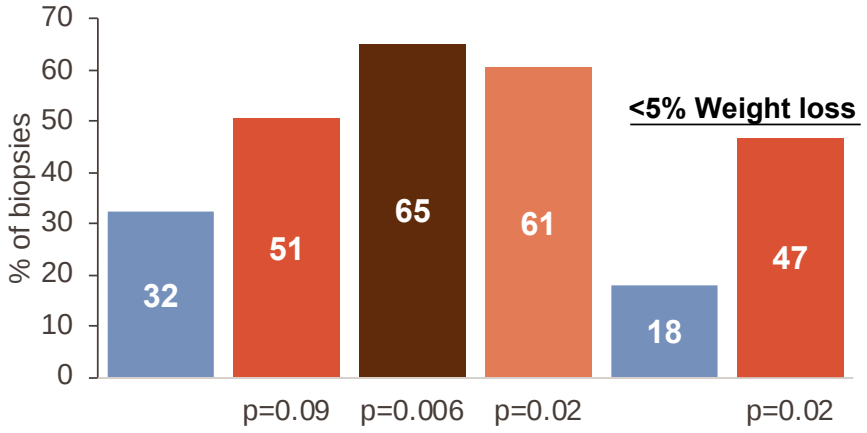
Week 36: NASH Liver Biopsy Endpoints

2-Point NAS Reduction

with at least a 1-pt reduction in ballooning or inflammation

(% of liver biopsies)

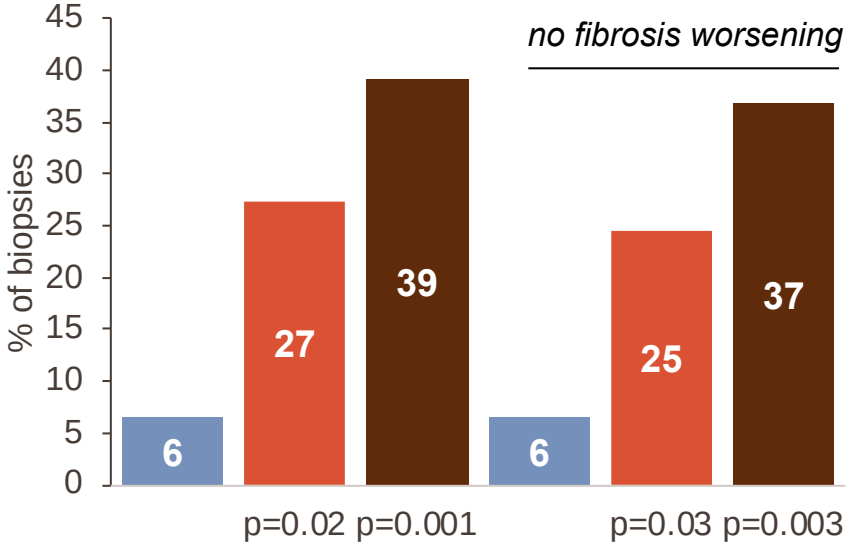


2-pt reduction in NAS in placebo patients was correlated with body weight loss

NASH Resolution

ballooning=0, inflammation =0, 1 with at least 2-point reduction in NAS

(% of liver biopsies)



- **Placebo**
- **MGL-3196** (all)
- **MGL-3196** (high exp)
- **MGL-3196, MRI responder**

In MGL-3196 treated patients with NASH resolution, 50% had fibrosis resolution (F=0)

MRI Responder; ≥ 30% fat reduction on Week 12 MRI-PDFF High Exp,, n=44; 2-pt NAS reduction; MGL-3196, n=73, placebo n=34; NASH Resolution, prespecified endpoint: at least 2-pt reduction in NAS; ballooning=0, inflammation=0, 1, <9.5% weight loss;

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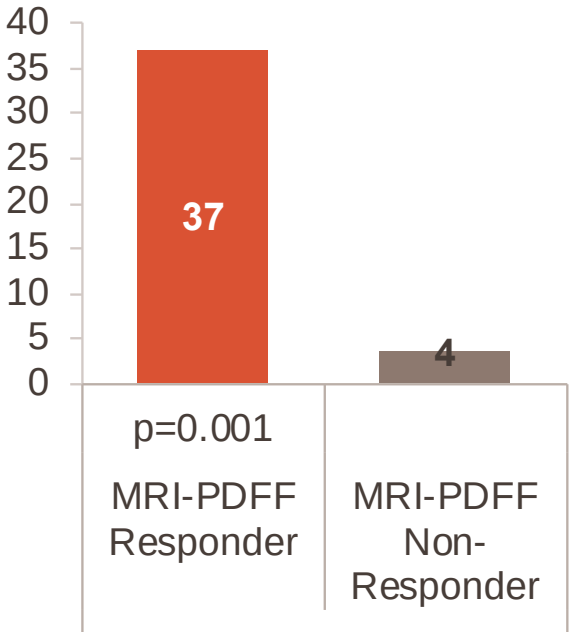
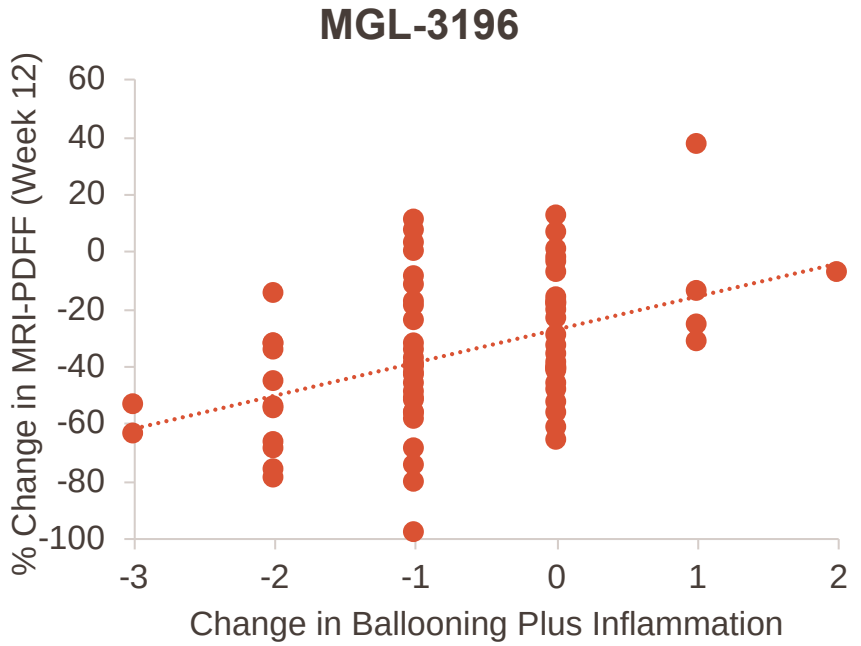
Correlation of Decrease in Hepatic Fat (MRI-PDFF) with Improvement in Ballooning and Inflammation on Liver Biopsy

NASH Resolution (%)
MGL-3196-treated



MRI-PDFF Week 12, % Relative Change: Correlation with Change in Ballooning Plus Inflammation Scores



- Patients who were not MRI-PDFF Responders (≥30% fat reduction) had a low rate of NASH resolution (*left panel*)
- In both MGL-3196 (correlation coefficient 0.42) (*right panel*) and placebo (correlation coefficient 0.58) % relative change in MRI-PDFF was correlated with reduction in ballooning plus inflammation scores on liver biopsy (steatosis score removed)

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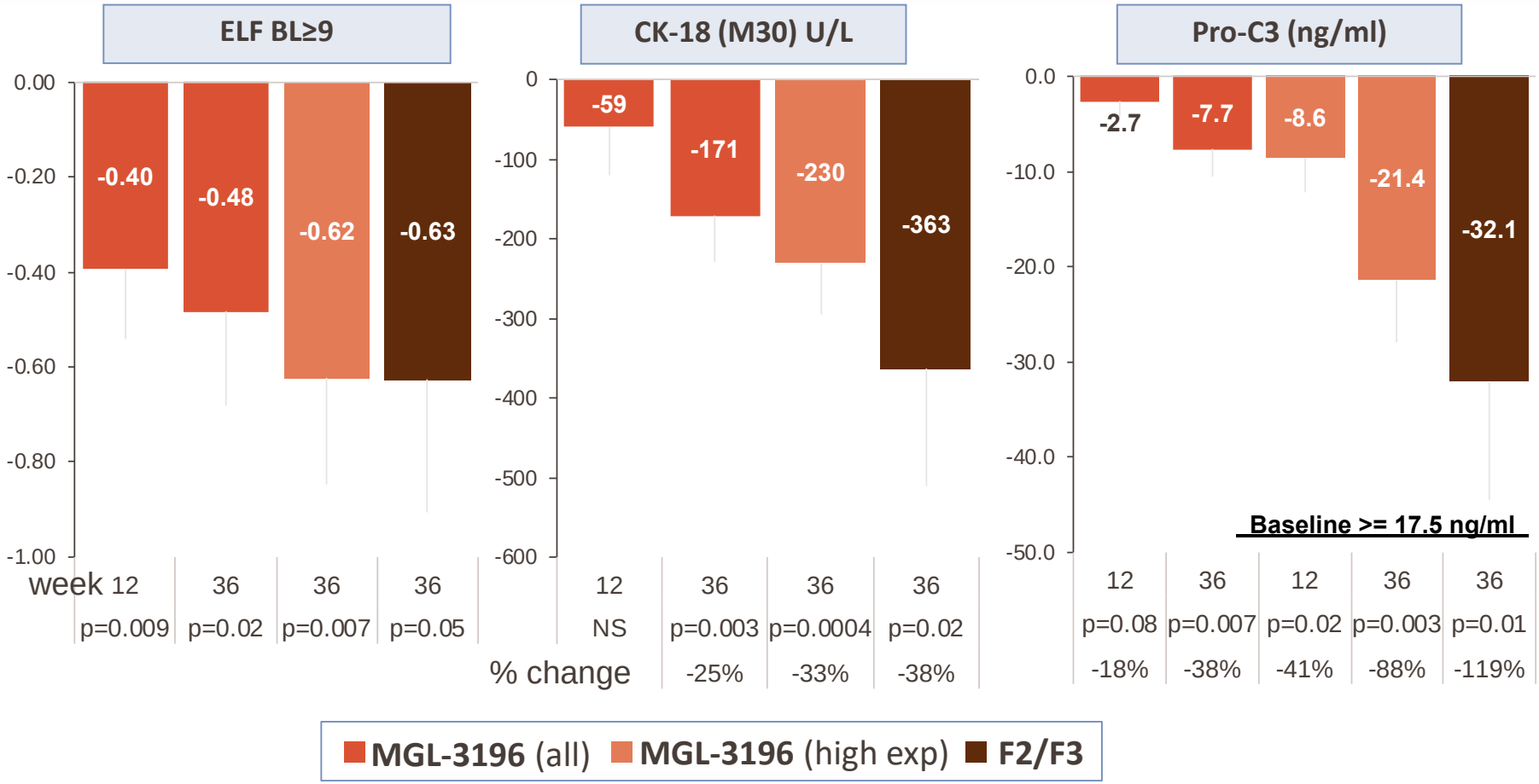
Week 36: Reduction of Fibrosis, Biomarkers



ELF, CK-18 and Pro-C3 scores, biomarkers correlated with liver fibrosis stage, were statistically significantly reduced in MGL-3196 treated, especially in patients with advanced fibrosis at baseline

BL, baseline; compared with placebo; all, placebo n=38; MGL-3196 n=78; ELF≥9 placebo n=21; MGL-3196 n=40; Pro-C3 BL≥17.5, placebo n=12; MGL-3196 n=29

*Liver Int. 2015 Feb;35(2):429-37; Journal of Hepatology 2013 vol. 59 j 236–242;

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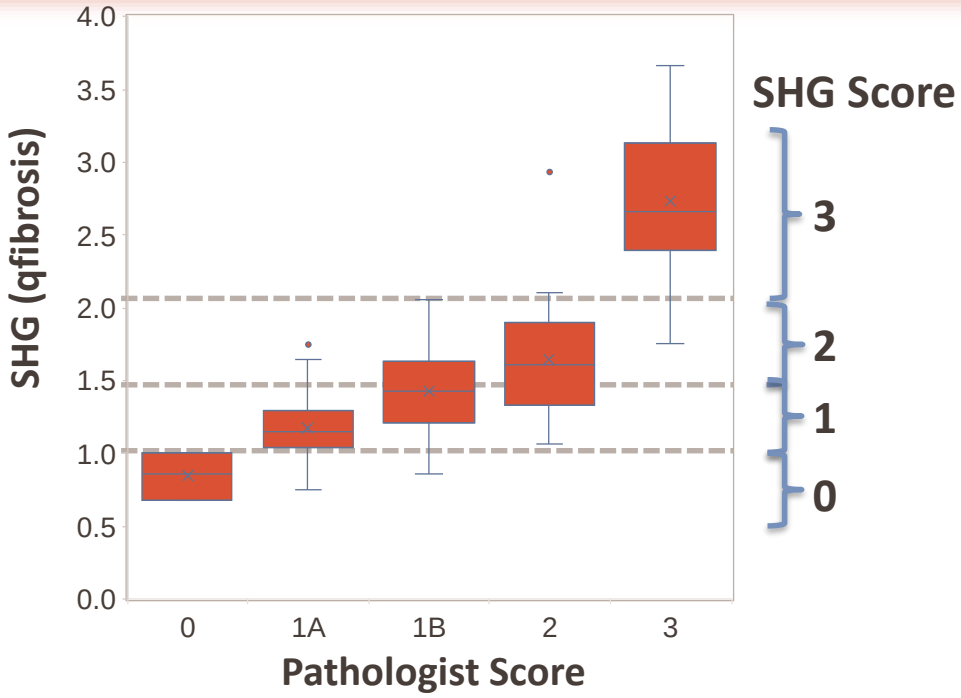
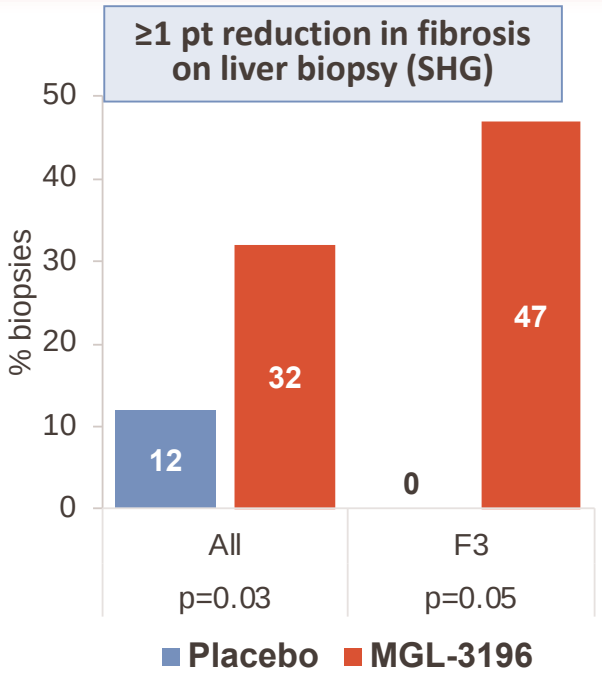
Week 36: Change in Fibrosis Score on Liver Biopsy





- Second Harmonic Generation (SHG) microscopy provides automated fully quantitative assessment of fibrosis on liver biopsy slides based on unique architectural features of collagen
- SHG score was generated and aligned with the pathologist baseline score (baseline, r=0.76), (*left panel*), blinded to treatment code
- Using SHG, MGL-3196 treated compared with placebo showed a statistically significant ≥1-pt reduction in fibrosis score at Week 36. Based on pathology score, fibrosis was reduced by ≥ 1 point in 29% of MGL-3196 treated patients vs. 23% in placebo

https://doi.org/10.1371/journal.pone.0199166

Week 36 pathology scores and treatment code were not provided to SHG readers.

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Safety and Additional Biomarkers

AEs

- AEs, mostly mild, a few moderate, balance between groups. Increase in MGL-3196 treated relative to placebo in loose stools, typically a single episode, only at the beginning of therapy
- No lab abnormalities or other AEs were increased in MGL-3196 compared with placebo patients
- 7 SAEs, distributed between placebo and drug-treated, all single occurrences, none related

Safety Biomarkers

- No effects on TSH, bone mineral density, heart rate, QTc, other CV biomarkers or diabetes biomarkers
- Small (<3%, not statistically significant) reduction in diastolic BP at Week 36 in MGL-3196 patients, consistent with reduced liver fat

Inflammation Biomarker

- Sustained statistically significant reduction in reverse T3
  - Reverse T3 is a marker of inflammation. Elevations in reverse T3 may be indicative of high hepatic thyroid hormone degradation, in NASH, potentially caused by activated stellate cells

Phase 3/4: MGL-3196 NASH Trial Design

Study Overview	
Drug	MGL-3196
Design	Blinded 2:1
Stage	Phase 3/4
Number of Patients	Phase 3: 900 Phase 4: up to 2000
Centers	~80, USA; EU
Treatment Duration	52 Weeks; 4.5 years

Study Details

Inclusion/Exclusion

- NASH on liver biopsy: NAS≥4, high risk F1, F2/3

Comparator/Arms

- MGL-3196 80 mg or Placebo, once daily

Primary Endpoint

- Phase 3: Liver biopsy at 52 weeks - resolution of NASH
- Phase 4: reduction in liver related events or progression to cirrhosis

Secondary Endpoints

- Reduction in atherogenic lipids
- Reduction of fibrosis
- 2-pt reduction in NAS

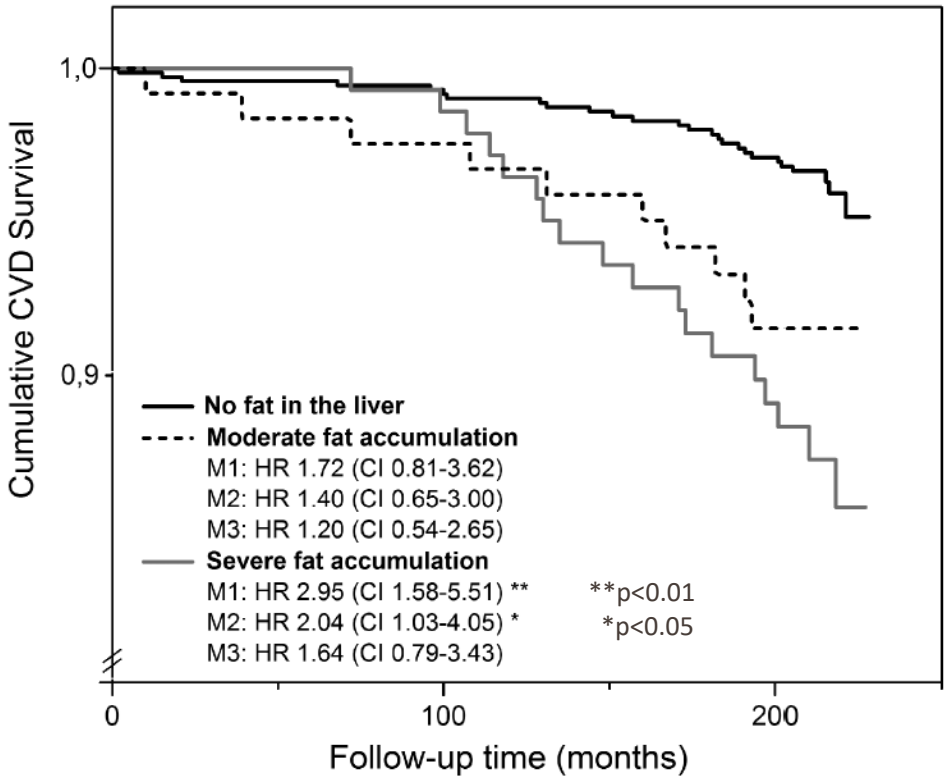
Exploratory

- Imaging MRI-PDFF
- NASH biomarkers

CV Risk in NASH and NAFLD

- Strong association between NAFLD and increased risk of CVD events and mortality
- Patients with NAFLD have a pro-atherogenic lipid profile:
  - Increased triglycerides
  - Increased apolipoprotein B
  - Higher concentration of small dense LDL
- Patients with NAFLD are at high risk for cardiovascular morbidity and mortality. Thus, aggressive modification of CVD risk factors is mandatory in all patients with NAFLD.

Fatty Liver Predicts Risk of CV Events



Pisto P et al. *BMJ Open* 2014;4:e004973. doi:10.1136/bmjopen-2014-004973

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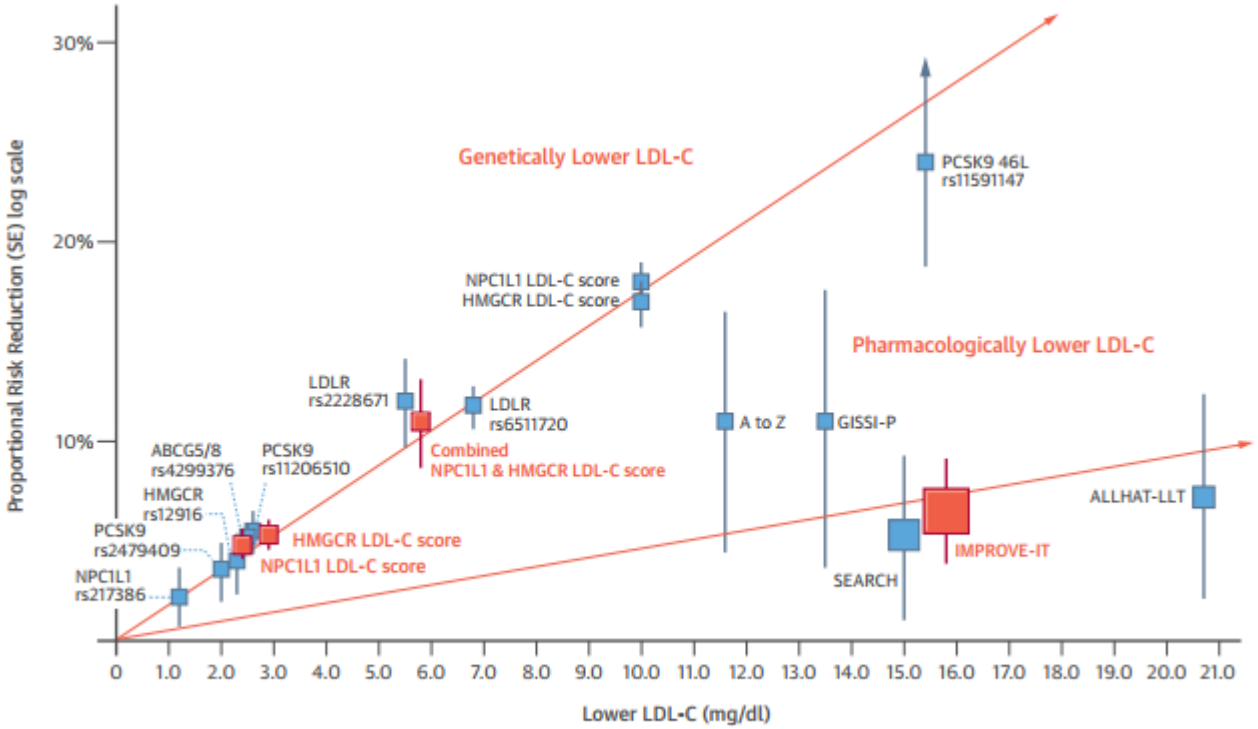
Genetic versus Therapeutic LDL-c Reduction



Ference, B.A. et al. J Am Coll Cardiol. 2015; 65(15):1552–61.

Key takeaways

- Lower LDL-C is better, use combination therapies to lower LDL-C as low as possible
- Start treatment of LDL early, patients with genetic predisposition to high LDL-C have life-time risk

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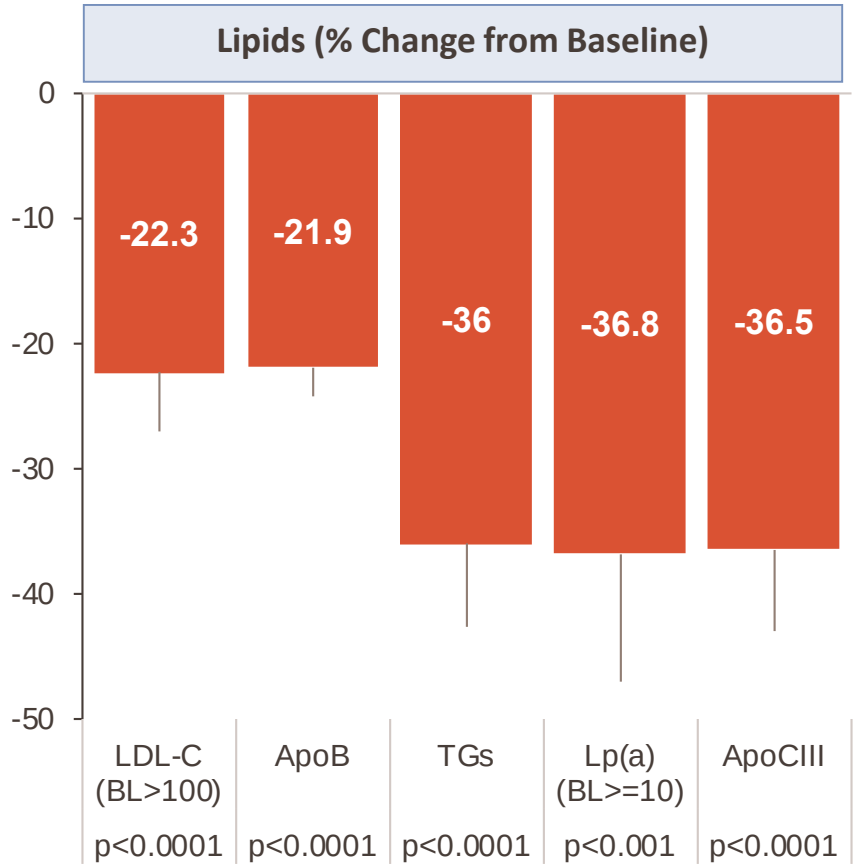
MGL-3196: Lipid Effects in NASH

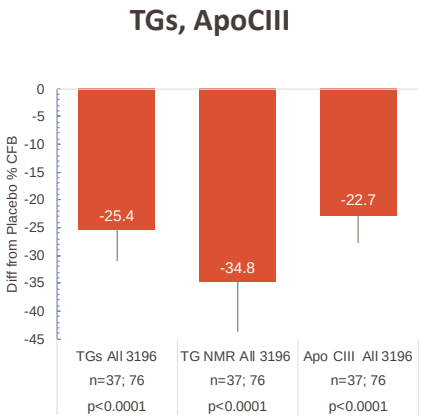


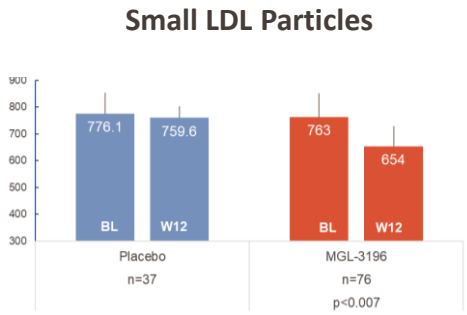
- ApoB is lowered by MGL-3196 about as much as LDL-c is lowered, a unique feature of this mechanism
- ApoCIII was robustly lowered
- Magnitude of triglyceride reduction equivalent or better than other therapeutics
- These effects have the potential to provide clinical benefit to both early and late NASH patients, who all are at increased CV risk and who die most frequently of CV disease

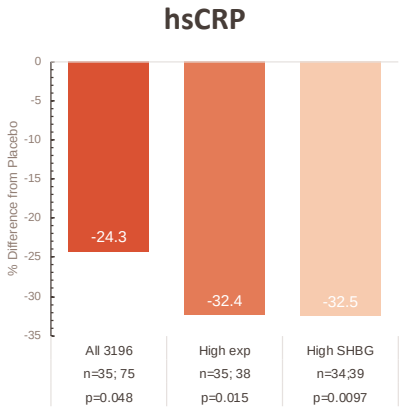
MGL-3196: Lipid Effects in FH

- MGL-3196 statistically significantly lowers LDL-c and other atherogenic lipids in patients with HeFH, a difficult to treat genetic dyslipidemia, including Lp(a)
- Lp(a) reduction appears greater than other known mechanisms
- MGL-3196 is most effective in patients intolerant to high intensity statins, lowering LDL-c 28.5%
- Unlike other mechanisms, ApoB and LDL-c reduction are similar, suggesting that MGL-3196 may directly lower ApoB, a better marker of atherogenicity than LDL

MGL-3196: Lipid Effects in FH







- MGL-3196 reduces triglycerides, VLDL and LDL-particles, particularly small LDL particles which are highly atherogenic
- ApoCIII reduction is likely an important mechanism by which MGL-3196 lowers TGs
- MGL-3196 reduces hsCRP, an important inflammatory marker predictive of CV risk

MGL-3196: Potential of a Dyslipidemia Indication in NASH/NAFLD

- MGL-3196 is the only NASH therapeutic able to lower lipids, consistent with regulatory approval for dyslipidemia; an also reduces fatty liver, an independent CV risk factor
- Significant dyslipidemia opportunity exists in early NASH / NAFLD (>30M people in the US) and diabetes populations (~70% have dyslipidemia)
  - Potential target population includes early NASH / NAFLD patients not eligible for most NASH clinical trials or NASH drugs in development
  - 50% to 67% of diabetics on statins do not reach their LDL-c target and also have elevated triglycerides; CV outcome studies consistently show that lower LDL-c/ApoB leads to better CV disease risk reduction: “lower is better”
- Possibility of regulatory approval based on LDL-c (and ApoB) reduction, with a post-approval Phase 4 clinical trial demonstrating CV disease benefit
  - Reduction of ApoB, Lp(a), ApoCIII/triglycerides, and liver fat in addition to CV benefit conferred by LDL-c lowering

MGL-3196: Potential of a Dyslipidemia Indication in NASH/NAFLD

A lipid indication, if approved, would allow treatment of early NASH / NAFLD patients based on reduction of LDL-cholesterol/ApoB lowering (no liver biopsy requirement)

Phase 3: MGL-3196 Dyslipidemia Trial

Study Overview	
Drug	MGL-3196
Design	2:1
Stage	Phase 3
Number of Patients	2000
Centers	USA, Europe, ROW
Treatment Duration	12 months

Study Details

Inclusion/Exclusion

- NASH/NAFLD, metabolic syndrome, diabetics, primary dyslipidemia patients not at target on current lipid therapy

Comparator/Arms

- MGL-3196 80 mg or Placebo, once daily

Primary Endpoint

- LDL cholesterol/Apo B lowering

Key Secondary Endpoints

- TGs, Lp(a), ApoCIII, hsCRP lowering
- Safety

Catalysts: Our Expectations for Development Timing

2016 | **2017** | **2018+**

Completed Milestones:

- ✓ Completion of long-term toxicology studies for MGL-3196
- ✓ Completion of Phase 1 trial of MGL-3196 dosed with statins for NASH
- ✓ Initiation of Phase 2 trial of MGL-3196 for NASH
- ✓ Initiation of 12-week Phase 2 trial of MGL-3196 for HeFH
- ✓ Positive topline 12-week data from Phase 2 trial of MGL-3196 for NASH
- ✓ Positive topline data from Phase 2 trial of MGL-3196 for HeFH
- ✓ 36-week topline liver biopsy data from Phase 2 trial of MGL-3196 for NASH

Upcoming Catalysts:

- End-of-Phase 2 FDA meeting (NASH)
- Phase 3 initiation in NASH 1Q19- CRO selected, API and tablet formulation ready
- Potential initiation of Phase 3 dyslipidemia study in 1H 2019

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