Company Overview

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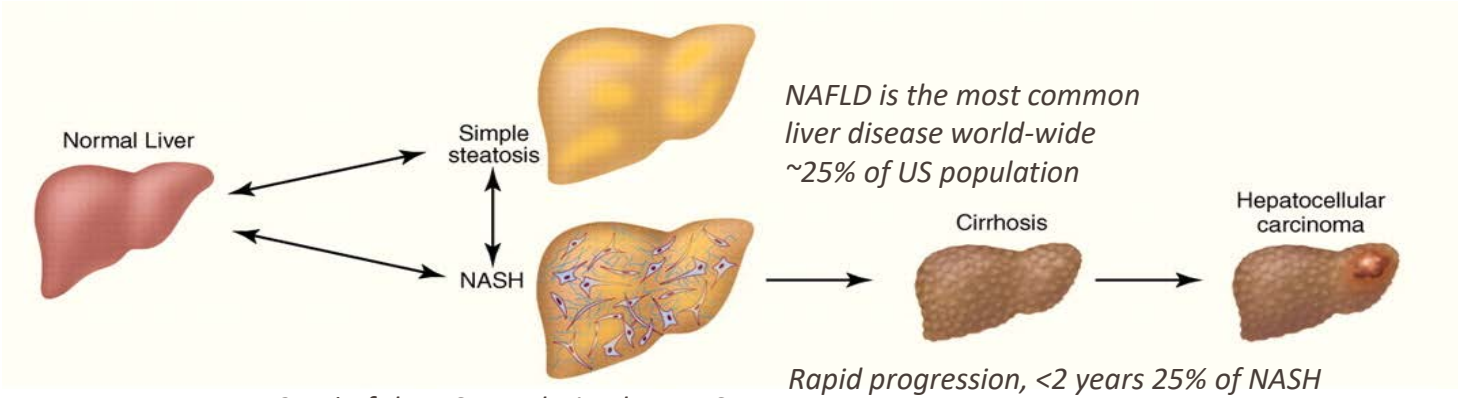
Unmet Need: Madrigal Aims to Treat Patients with NASH, a Large and Underserved Population

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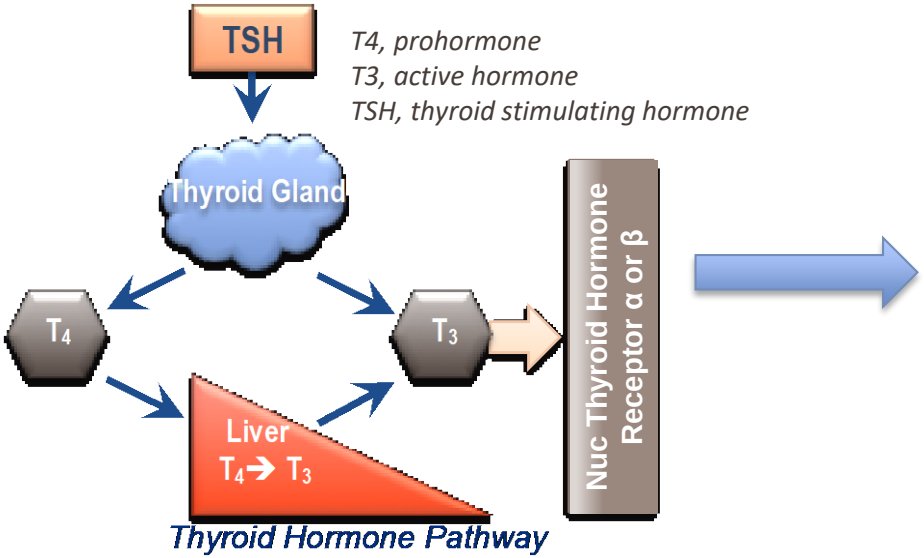
Mechanism of Action: The Importance of Liver THR-β in NASH

We believe that MGL-3196, a selective THR-β agonist, will treat the underlying disease in NASH patients



In humans, THR-β agonism:

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

No thyrotoxicosis (THR-α effect)

- Unlike other pathways which raise LDL-cholesterol (FXR, FGF-19) or triglycerides (ACC1 antagonist), THR-β agonism reduces both plasma triglycerides and LDL-cholesterol and may provide CV benefit to NASH patients

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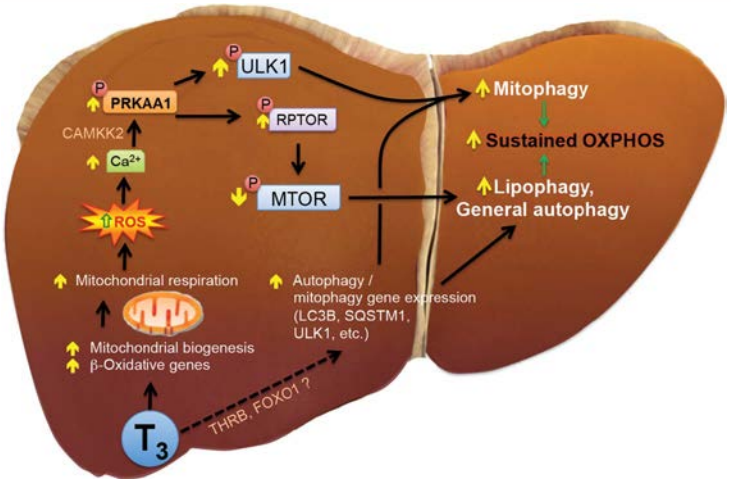
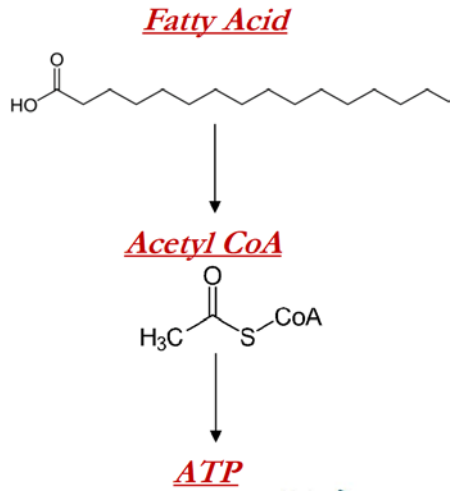
Lipotoxicity: THR-β Agonists May Reduce Lipotoxicity

- Most hepatic fat derives from external sources, particularly free fatty acids from adipocytes; in NASH, β-oxidation of liver lipids is reduced contributing to lipotoxicity
- THR-β agonists reduce liver fat through breakdown of fatty acids, and stimulate mitochondrial biogenesis in the NASH liver, thus, we believe, reducing lipotoxicity and improving liver function
- In human NASH, the liver has relatively low THR-β activity, exacerbating mitochondrial dysfunction and lipotoxicity
- We believe MGL-3196 has pleiotropic effects characteristic of an "ideal" NASH drug, with potential for addressing the underlying metabolic syndrome and hallmark features of NASH: steatosis/lipotoxicity, inflammation, ballooning, fibrosis (both directly and indirectly)
- Treating NASH, rather than fibrosis, is key to addressing the disease
  - Resolution of NASH, without reducing fibrosis, is an approvable endpoint
  - Recognition that liver fibrosis will decrease with time after NASH resolves (similar to reduction of fibrosis as the liver regenerates after cure of HCV)





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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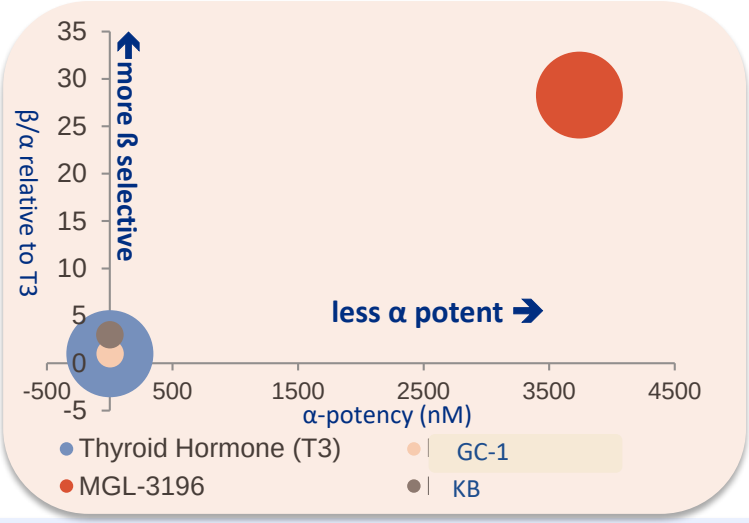
MGL-3196: A First-in-Class Liver-Directed THR- β Agonist

We believe MGL-3196 is the first bona fide THR-β selective molecule with key advantages over other companies' previous analogues

- Discovery of MGL-3196 and backups at Roche utilized a novel functional assay that went beyond what previous companies had done (simple receptor binding assay)
  - Earlier compounds from other companies, purported to be THR-β selective, show no functional selectivity in this assay and, like thyroid hormone, activate the THR-α receptor equally well as the β receptor

- *in vivo* data confirm MGL-3196's high liver uptake and preclinical safety
  - Avoids activity at the systemic THR-α receptor (increased heart rate, osteoporosis)
  - Unlike other company's earlier thyroid receptor agonists, no cartilage findings in chronic toxicology or liver enzyme increases in human studies
  - Tested in more than 180 subjects in Phase 1 studies and 150 patients in Phase 2 studies
  - Phase 2 dosing in humans includes 9 months of treatment in humans with NASH
  - MGL-3196 treated healthy volunteers and patients show normal central thyroid axis and vital signs



J Med Chem. 2014;57(10):3912-3923

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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

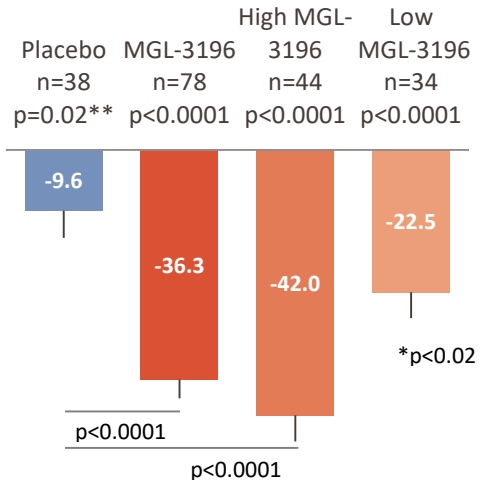
- Reduction of liver fat (MRI-PDFF) at 12 weeks

Secondary Endpoints

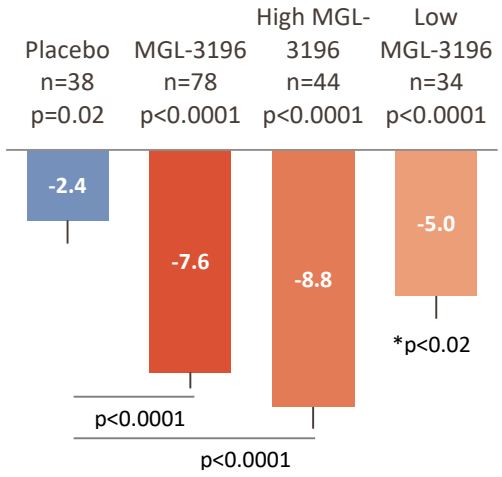
- NASH biomarkers and lipids at 12, 36 weeks
- Repeat MRI-PDFF at 36 weeks
- Liver biopsy at 36 weeks - reduction/resolution of NASH in patients on drug; reduction of fibrosis
- Ongoing extension study in a subset of patients who completed the Main 36 week study

Week 12: Primary Endpoint Achieved

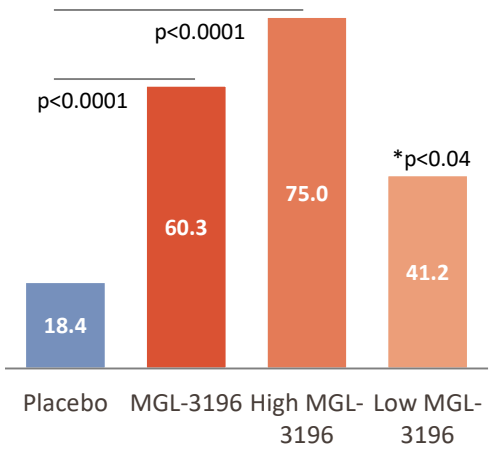
Relative Change in MRI-PDFF (%)



Absolute Change in MRI-PDFF



≥30% Fat Reduction (%)



- Highly significant relative change in MRI-PDFF (% change from baseline (median)) and absolute fat reduction
- Pre-specified high exposure MGL-3196 patients achieved a 75% response for ≥30% liver fat reduction
- No effect of MGL-3196 on body weight; 5 out of the 7 placebo patients who achieved ≥ 30% fat reduction lost ≥5% body weight

*compared with placebo
**within group p-value

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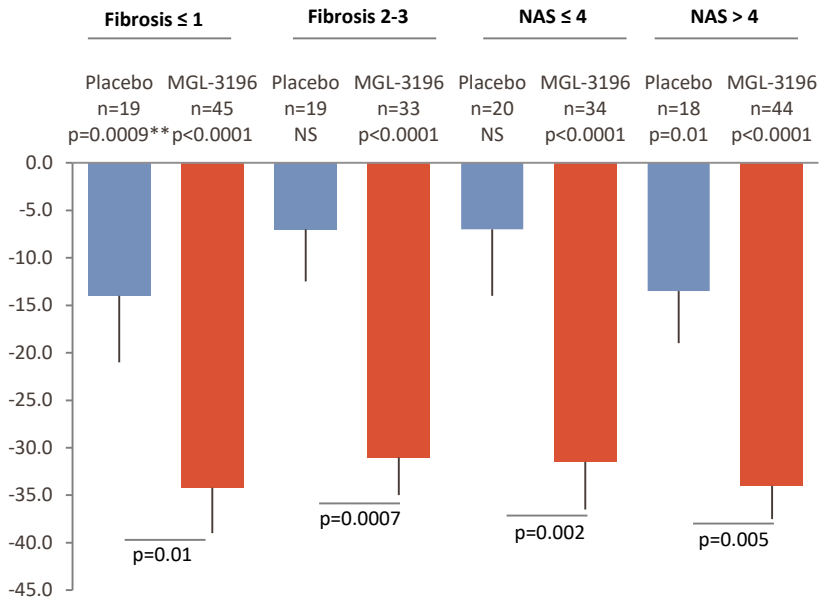
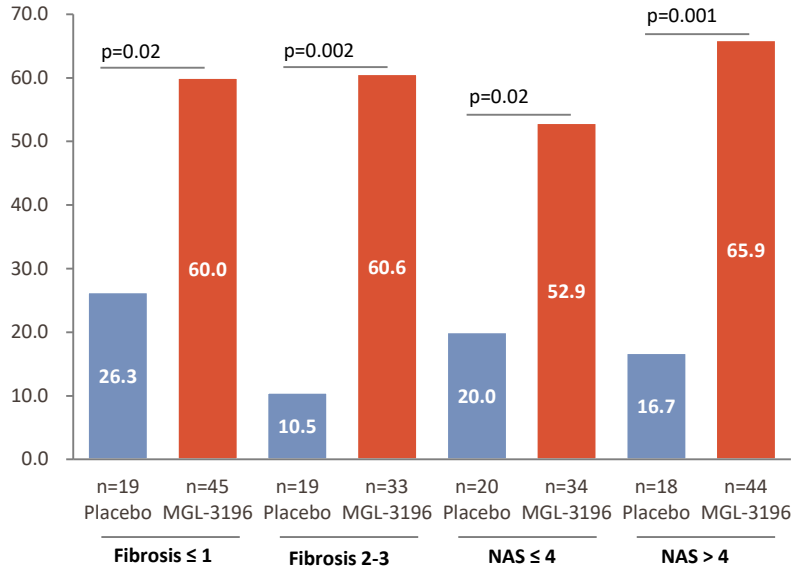
Week 12: Fat Reduction Relative to NAS / Fibrosis Stage

Relative Change in MRI-PDFF (%)



≥30% Fat Reduction (%)



MGL-3196 reduces liver fat effectively in both early and advanced NASH fibrosis

**within group p-value

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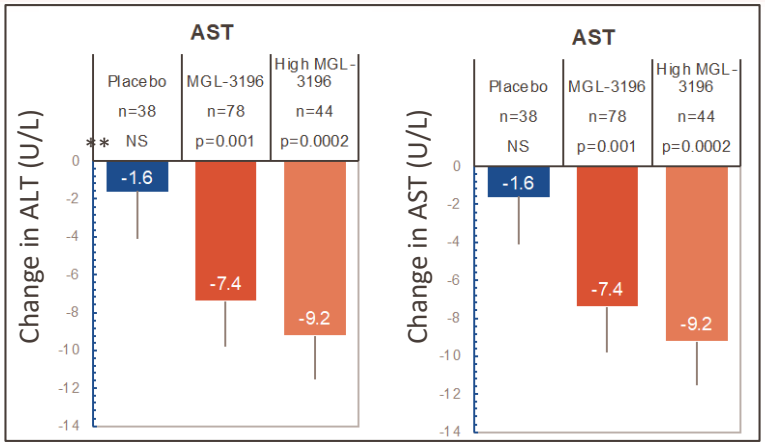
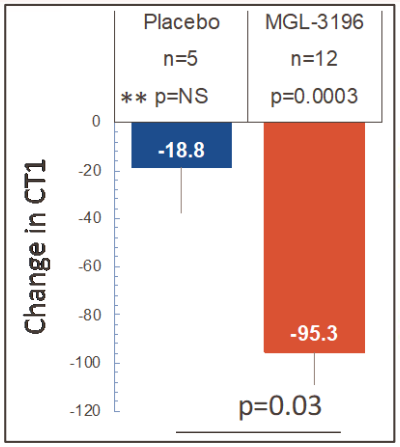
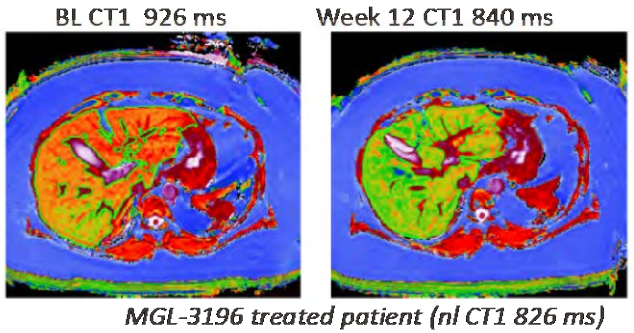
Phase 2: Reduction at Week 12 of Liver Enzymes and Markers of Inflammation, Fibrosis







MGL-3196 treated patient (nl CT1 826 ms)

- Decrease in liver enzymes is correlated with improvement in NASH on serial liver biopsy. Significant decrease in ALT, AST (within group MGL-3196); significant decrease in ALT (patients with ALT* elevations at baseline) and AST (p=0.04, 0.02, respectively) compared with placebo in high MGL-3196 patients
- Pro-C3 and ELF scores have been correlated with the liver fibrosis score on liver biopsy in NASH patients. MGL-3196 significantly decreases ELF and Pro-C3 (up to 40% relative to placebo) fibrosis biomarkers particularly in patients with > normal level at baseline reflective of more advanced baseline liver fibrosis
- Multiparametric MRI has been validated as a predictive test for NASH, and the CT1 predicts NAS on liver biopsy, particularly correlating with inflammation. Significant decrease in MGL-3196 treated patients.
- Significant decrease in reverse T3 (p<0.0001), an inflammatory biomarker that is relatively increased in patients with NASH, particularly advanced NASH

**within group p-value

*Baseline ALT, >=45 males; >=30 females

doi: 10.1210/en.2014-1302) Clinical Gastroenterology and Hepatology 2018;16:123–131

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Phase 2: MGL-3196 Achieved Key NASH Liver Biopsy Endpoints at 36 Weeks

	MGL-3196	MGL-3196 MRI-PDFF Responders[1]	Placebo
36 Week Biopsy Results (Secondary Endpoints)			
Number of patients[2]	73	46	34
≥ 2 Point Decrease in NAS	56% p=0.02	70% p=0.001	32%
NASH Resolution	27% p=0.02	39% p=0.001	6%

- Sustained, highly statistically significant ($p<0.0001$) reduction in liver fat compared with placebo on Week 36 MRI-PDFF; mean fat reduction MGL-3196 37%; placebo, 8.9%
- Sustained, statistically significant reductions in low-density lipoprotein cholesterol (LDL-C), ApoB, triglycerides, and lipoprotein(a)
- Well-tolerated: mostly mild and a few moderate AEs, generally balanced between drug treated and placebo
  - An increase in incidence of transient mild diarrhea in MGL-3196-treated compared with placebo, often a single episode, occurring only early in the course of treatment
  - 7 reported SAEs all unrelated to drug; 5 in MGL-3196-treated, 2 placebo (2-1 randomization)

Phase 2 liver biopsy results demonstrate the potential for MGL-3196 to show a clear benefit in patients with NASH, including both reduction and resolution of NASH and improvement in multiple atherogenic lipids

[1] MGL-3196 MRI-PDFF Responders = MGL-3196 treated patients with >=30% relative fat reduction on Week 12 MRI-PDFF.
[2] Includes only patients with base line and end-of-study liver biopsies. Does not include one patient whose end-of-study liver biopsy was deemed inadequate.

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Phase 2: MGL-3196 Achieved Key Endpoints at 36 Weeks

Positive Signals on Fibrosis

- Statistically significant reductions in fibrosis biomarkers in MGL-3196 treated vs placebo
- On liver biopsy, fibrosis was reduced by ≥ 1 point in 29% of MGL-3196 treated patients vs. 23% in placebo
- Of the MGL-3196 treated patients that achieved NASH resolution, 50% also achieved fibrosis resolution
- All MGL-3196 treated patients that achieved NASH resolution also achieved a statistically significantly fibrosis decrease relative to placebo patients

Reductions in Liver Enzyme Levels

- Statistically significant reductions in liver enzymes relative to placebo, with reductions of greater magnitude with longer duration of MGL-3196 treatment
- Statistically significantly more MGL-3196 treated than placebo patients had normalization of ALT

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

FH: Phase 2 HeFH Clinical Trial Read Out in 2018

Study Overview	
Drug	MGL-3196
Design	2:1
Stage	Phase 2
Number of Patients	116
Centers	13, Europe
Treatment Duration	12 weeks

Study Details

Inclusion/Exclusion

- HeFH on maximally tolerated statins (typically high dose), ezetimibe

Comparator/Arms

- MGL-3196 60 mg, 100 mg or Placebo, once daily

Primary Endpoint

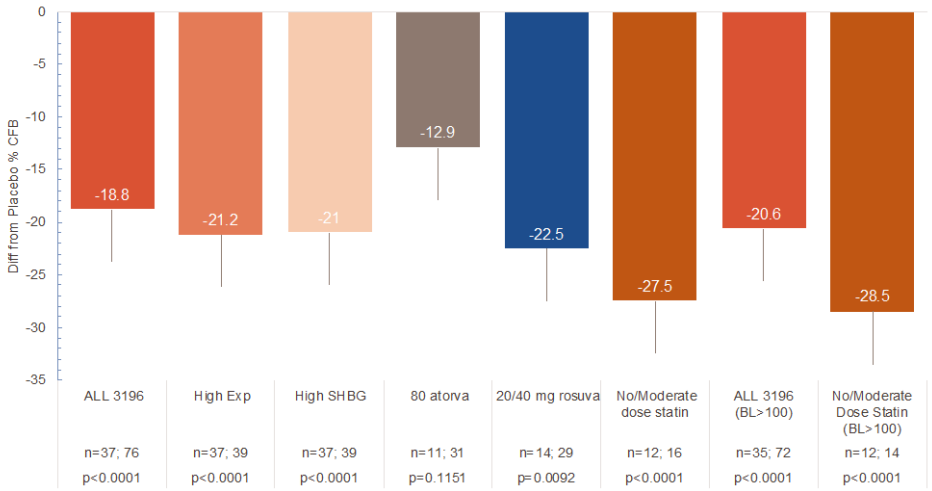
- LDL cholesterol lowering

Secondary Endpoints

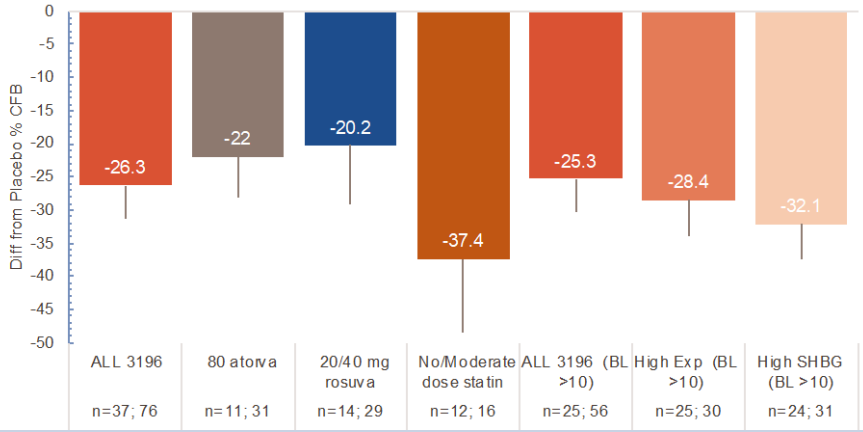
- TGs, Lp(a), ApoB lowering
- Safety

HeFH Phase 2 Study: MGL-3196 Effects on Lipids

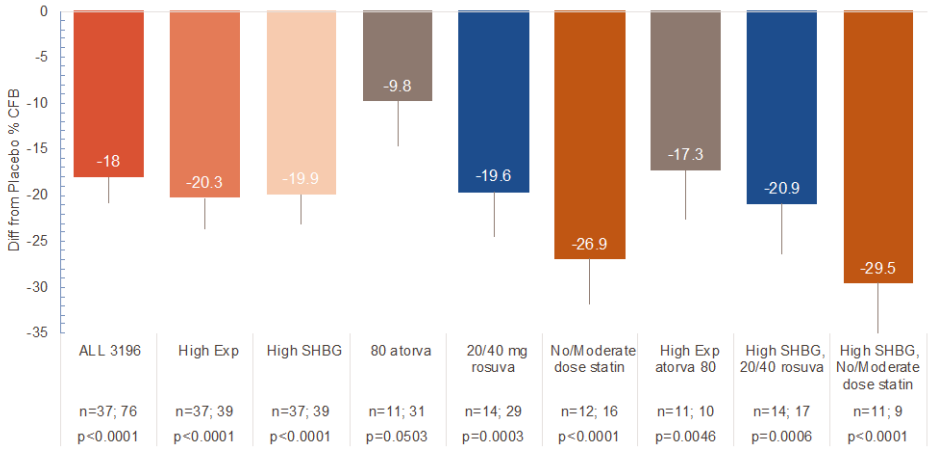
LDL Cholesterol



Lp(a)



Apolipoprotein B



- 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

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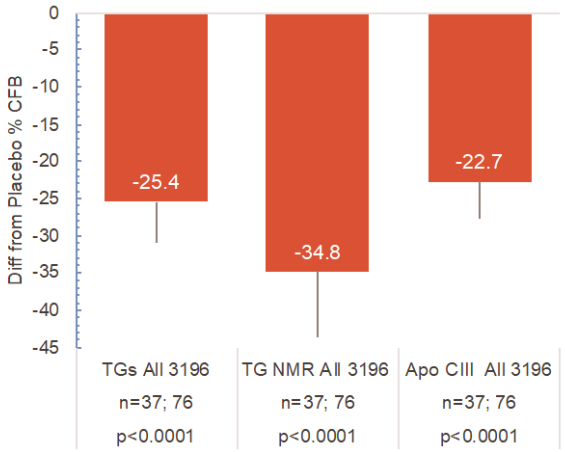
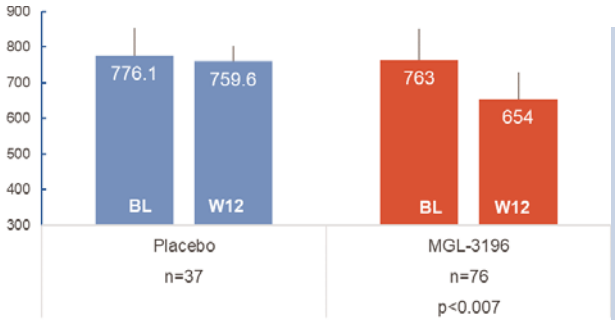
HeFH Phase 2 Study: Effects on Lipids, Lipid Particles, hsCRP

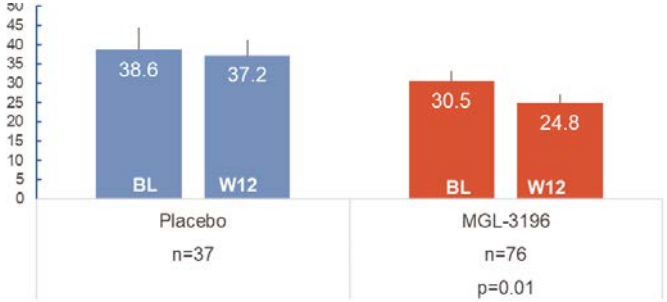
TGs, ApoCIII



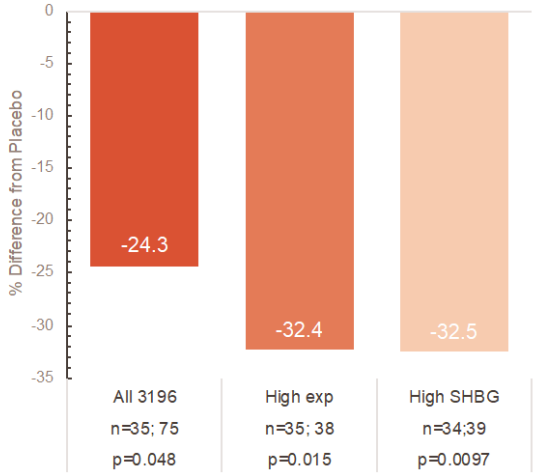
Small LDL Particles



VLDL Particles



hsCRP



- 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
- The effect to reduce multiple atherogenic lipids makes MGL-3196 an excellent candidate to lower CHD risk in NAFLD/NASH, diabetics and mild to severely statin intolerant patients

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Dyslipidemia Opportunity

- MGL-3196 clinical results suggest potential cardio-protective profile on top of statins
- Significant dyslipidemia opportunity exists in early NASH/NAFLD (>30M people in US), diabetes and mixed dyslipidemia populations
  - Elevated CV risk leads to recommended lipid lowering therapy in patients with Type 2 diabetes, metabolic syndrome, hypertension, primary dyslipidemias
  - Fatty liver, even without NASH, is associated with increased CV risk
  - Both primary and secondary (existing atherosclerotic CV disease) prevention possible
  - 50% - 67% of diabetics on statins do not reach their LDL target; CV outcome studies consistently show that lower LDL leads to better risk reduction: “lower is better”
  - Potential population includes early NASH / NAFLD patients not eligible for most NASH clinical trials or NASH drugs in development
- Lipid indication, if approved, would allow treatment of early NASH / NAFLD patients based on reduction of LDL-cholesterol/ApoB lowering (no liver biopsy requirement)
- Possibility of regulatory approval based on LDL (and ApoB) reduction, with post-approval Phase 4 clinical trial demonstrating CV benefit

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:

- AASLD plenary presentation, NASH Phase 2 results
- End-of-Phase 2 FDA meeting (NASH)
- Phase 3 initiation in NASH 4Q 18-1Q19- CRO selected, API and tablet formulation ready
- Potential initiation of Phase 3 dyslipidemia study in 1H 2019

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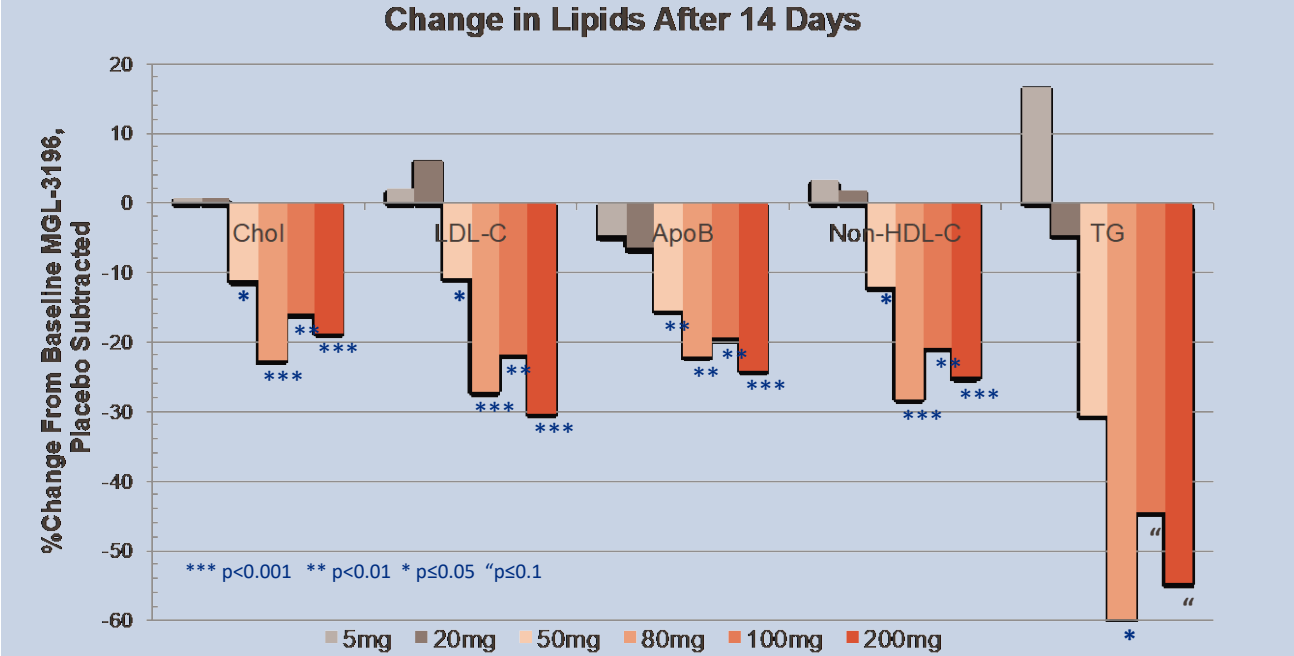
4. Seasoned Management Team
5. Well-Financed with $490M of Cash & Securities at June 30, 2018

Appendix:

Additional Material

Phase 1: Robust LDL and Triglyceride Lowering Established in 14 Day Multiple Ascending Dose Study



Change from Baseline (CFB) by mean % CFB calculated for each individual subject 24h after 14th dose; baseline value obtained just prior to first dose; ApoB, apolipoprotein B; Chol, total cholesterol; LDL-C, LDL cholesterol directly measured; Non-HDL-C, non-HDL cholesterol; TG, triglycerides (median %CFB)

- Six dose cohorts, 36 total healthy volunteers dosed daily with MGL-3196 (5, 20, 50, 80, 100, or 200 mg) and 12 with placebo for 14 days
- Healthy volunteers with slightly elevated LDL cholesterol (> 110 mg/dL)
- Well-tolerated, appeared safe at all doses tested
- No effect on vital signs, heart rate, central thyroid axis, or liver enzymes

Once daily oral treatment led to highly statistically significant and dose-dependent up to ~30% reduction of apolipoprotein B (ApoB), total, LDL, non-HDL cholesterol; Strong trends in triglyceride reduction up to 60%; Near maximal effect at 80 mg dose

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THR-β Agonism: Potential Anti-Fibrotic Actions

- Treating NASH, rather than fibrosis, is key to addressing the disease
  - Resolution of NASH, without reducing fibrosis, is an approvable endpoint
  - Recognition that liver fibrosis will decrease with time after NASH resolves (similar to reduction of fibrosis as the liver regenerates after cure of HCV)
- THR-β, the operative receptor in hepatocytes, may ameliorate lipotoxicity and resultant local inflammation which lead to hepatocyte dysregulation and apoptosis. These perturbations lead to a profibrotic environment through:
  - Ongoing inflammation
  - Production by the dysregulated / damaged / dying hepatocytes of profibrotic factors, with TGF-β among the most important
- THR-β may have direct anti-fibrotic effects
  - Thyroid hormone receptor agonism has been shown to dampen inflammation in vivo and to inhibit TGF-β signaling in cell culture and in vivo
  - In animal models of liver fibrosis, the extent of fibrosis is decreased by thyroid hormone administration and increased if thyroid hormone receptors are knocked out

PNAS 113: 3451, 2016

MGL-3196: Agonism of Hepatic THR-β

- In livers of euthyroid individuals T3 induces about half the maximal transcriptional activity of THR-beta
- MGL-3196 can further beneficially increase this transcriptional activity as we have shown in euthyroid animal models and humans.
- Interestingly, systemic hypothyroidism, at the level of the thyroid gland itself, leads to increases in plasma lipids (LDL-C and triglycerides) and increases the risk of nonalcoholic fatty liver disease.
- In fact, actual NASH is at least twice as common in hypothyroid individuals as in the general population.
- Further, liver-specific hypothyroidism is present in human NASH, caused by degradation of thyroid hormone (increased deiodinase 3 produced by stellate and inflammatory cells) in the NASH liver
  - In a vicious cycle this liver-specific hypothyroidism increases as NASH progresses
  - Thus, MGL-3196, which is not affected by deiodinases, can increase transcriptional activity over an even broader range than in the non-NASH euthyroid state
  - With MGL-3196-induced resolution of NASH, with the concomitant decrease in numbers and level of activation of stellate cells, normalization of hepatic thyroid function should occur.