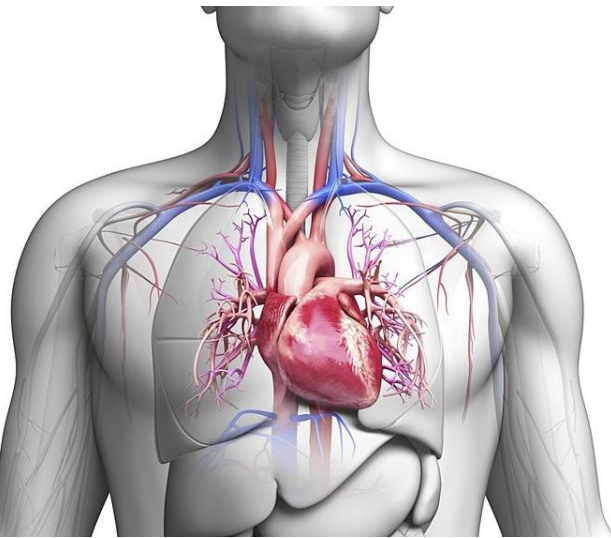
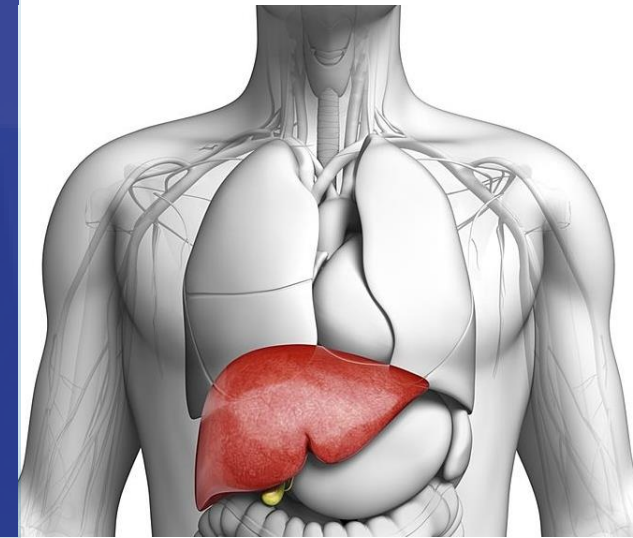


Gemphire *Therapeutics*



ADVANCING
CARDIOVASCULAR
AND
NASH
OPPORTUNITIES



CORPORATE PRESENTATION
March 2018

Safe Harbor Statement

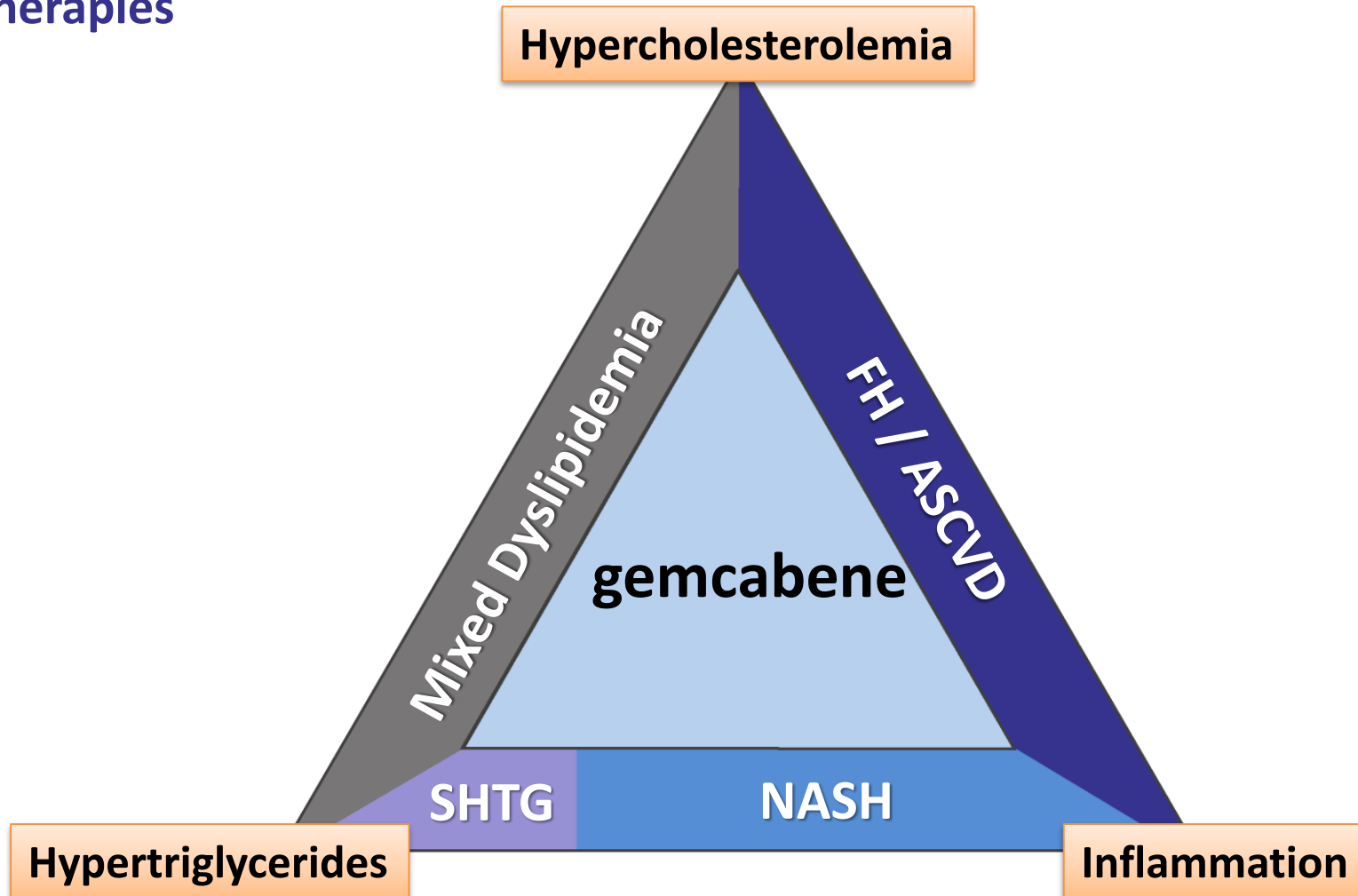
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Gemcabene Addresses Cardiometabolic Diseases

Once daily oral tablet observed to be a safe add-on to statins and other therapies



Gemcabene Pipeline and Clinical Plans

Multiple Value Drivers Expected in 2018

INDICATION		PH 1	PH 2	PH 3	NDA	ANTICIPATED MILESTONES
SHTG Severe Hypertriglyceridemia						Top-line data expected in 2Q 2018; Full data set expected 2H 2018
NAFLD/ NASH Non-alcoholic Fatty Liver Disease / Non-alcoholic Steatohepatitis	Adult					POC Programs Initiated; POC data expected 2H 2018; Full data set expected 1H 2019
	Pediatric					
HoFH Homozygous Familial Hypercholesterolemia						End of Phase 2 meetings with FDA; Plan to initiate P3 in FH 2H 2018
HeFH Heterozygous Familial Hypercholesterolemia						
ASCVD Atherosclerotic Cardiovascular Disease						

Gemcabene Pipeline in SHTG & NASH

Clinical Trial Results in 2018 and Early 2019

INDICATION		PH 1	PH 2	PH 3	NDA	ANTICIPATED MILESTONES	
SHTG Severe Hypertriglyceridemia							Top-line data expected 2Q '18; Full data set expected 2H '18
NAFLD/ NASH Non-alcoholic Fatty Liver Disease / Non-alcoholic Steatohepatitis	Adult (FPL)						<u>Both POC Programs Initiated</u> FPL POC data expected 2H '18
	Pediatric						Pediatric POC data expected Q1'19

Gemcabene: Keys to NAFLD/NASH Success



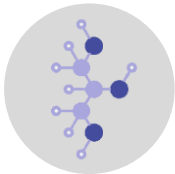
SAFETY

- Nearly 1,100 patients treated with gemcabene
- No muscle or liver toxicities in patients treated
- No drug interactions with statins or metformin



ATHEROGENIC PROFILE

- Significant LDL-C reduction as monotherapy and on top of statins
- Significant atherogenic burden with reductions in non-HDL-C, apoB and apoE



TRIGLYCERIDES

- Significant triglyceride reductions in hypertriglyceridemic patients
- For patients with TG \geq 200, GEM lowered TG 39%; TG \geq 500, GEM lowered TG 60%



INFLAMMATION

- Gemcabene has demonstrated over 40% reductions in hsCRP
- Significant TNF- α and IL-6 reduction in preclinical STAM™ Model



INSULIN SENSITIVITY

- Gemcabene demonstrated a doubling of the glucose disposal rate suggesting potential effects on insulin sensitivity

Epidemic of NAFLD and NASH in Children

Obesity is the Single Greatest Risk Factor for Pediatric NAFLD



- **NAFLD** is estimated to affect **7M** children in US
- **Pediatric NASH** estimated prevalence is **2M** children in US
- **38% of obese children have NAFLD;** 20% of children ages 12-19 are obese

24M

OVERWEIGHT OR
OBESE CHILDREN
(AGES 2-19)

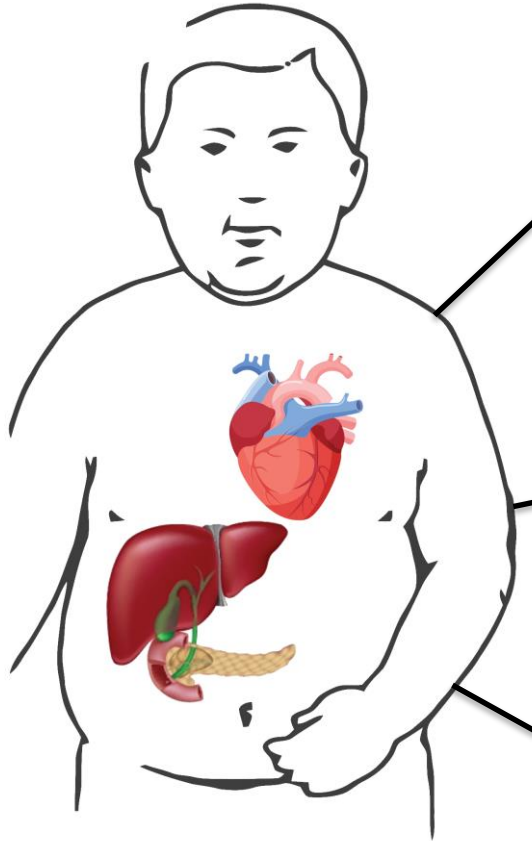
13M

OBESE
CHILDREN
(AGES 2-19)

Fussilo S, Rudolph B. Nonalcoholic fatty liver disease. Pediatrics in Review. 2015;36(5):198–206; The National Institute of Diabetes and Digestive and Kidney Diseases, 2016; Data derived from Health, United States, 2011 (NCHS); Schwimmer JB, Deutsch R, Kahen T, Lavine JE, Stanley C, and Behling C. Prevalence of fatty liver in children and adolescents. Pediatrics. 2006;118(4):1388–1393; CDC National Center for Health Statistics, FactStats – Overweight Prevalence, 2016; AHA Obesity Information, 2016.

Complications in Children with NAFLD/NASH

Premature Risk of Liver Transplant and Mortality



Dyslipidemia / Cardiovascular Disease

- Hypercholesterolemia, hypertriglyceridemia, low HDL
- Highly atherogenic lipid profile with more severe liver disease
- Left ventricular systolic and diastolic dysfunction
- Hypertension reported in about 20% - 30%

Cirrhosis / Hepatocellular Carcinoma

- 10% - 25% progress to advanced fibrosis/cirrhosis by 3rd-4th decade of life
- Pediatric NAFLD/NASH patients are more likely than adults to progress to decompensation (permanent liver damage)

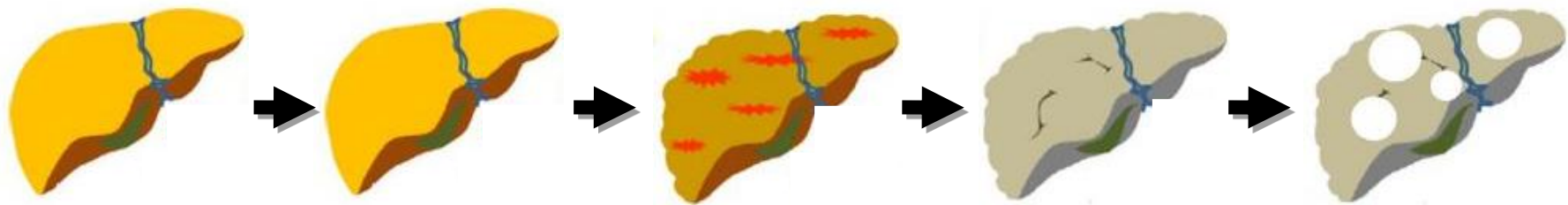
Diabetes

- An individual's risk of developing diabetes is increased approximately 5-fold if they have NAFLD
- Prevalence of prediabetes and diabetes are 23% and 6.5%, respectively

Pediatric NAFLD is associated with a 1,360% increase in mortality in the 20 years following diagnosis (13.6 SMR)

Selvakumar PKC, *Pediatr Clin North Am* 2017 Jun;64(3):659-675; *J Clin Gastroenterol* 2017; Hazlehurst J, *Metabolism*. 2016 Aug;65(8): 1096-1108.

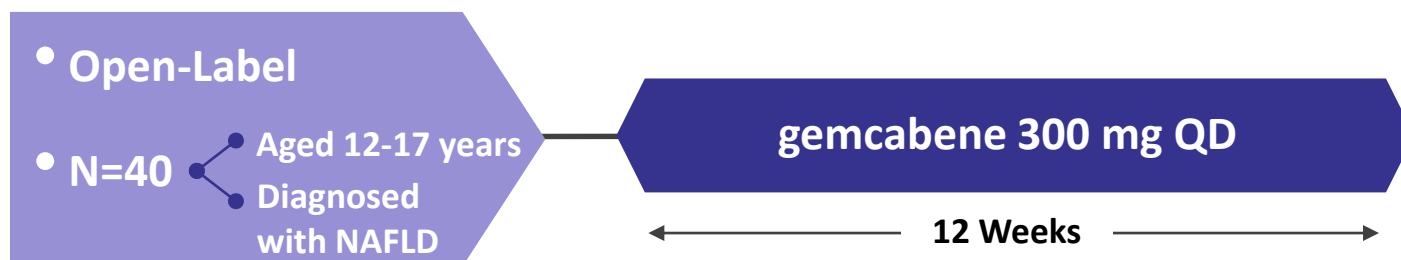
Gemcabene in NAFLD– Preventing Progression



NAFLD		NASH		Cirrhosis
Steatosis	Steatosis + Inflammation	Steatosis + Hepatocyte Injury (Ballooning)	Steatosis + Fibrosis	
gemcabene (Gemphire)			OCA (Intercept)	
MGL-3196 (Madrigal)			GR-MD-02 (Galectin)	
		cenicriviroc (Allergan/Tobira)		

Pediatric NAFLD Phase 2a Trial Design

GEM-IIT-601



Principal Investigator

- Miriam Vos, MD, MSPH, Emory University School of Medicine

Primary Endpoint:

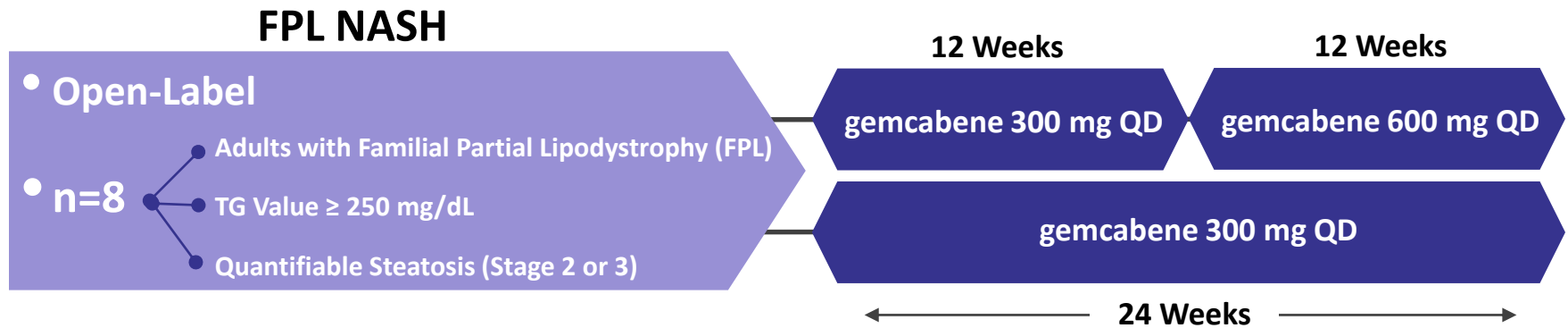
- % change in ALT from baseline to 12 weeks

Secondary Endpoints:

- Change in hepatic steatosis as measured by MRI-PDFF
- Change in liver inflammation and fibrosis (LIF) score by MRI Liver Multiscan
- Change in AST, insulin sensitivity, serum lipids (including TG), apolipoproteins, and inflammatory markers (including hsCRP)
- Safety and tolerability

Adult NASH POC Phase 2a Trial Design

Open-Label Trial Underway in Familial Partial Lipodystrophy (FPL) Patients



Principal Investigator

- Elif Oral, MD, University of Michigan

Primary Endpoint:

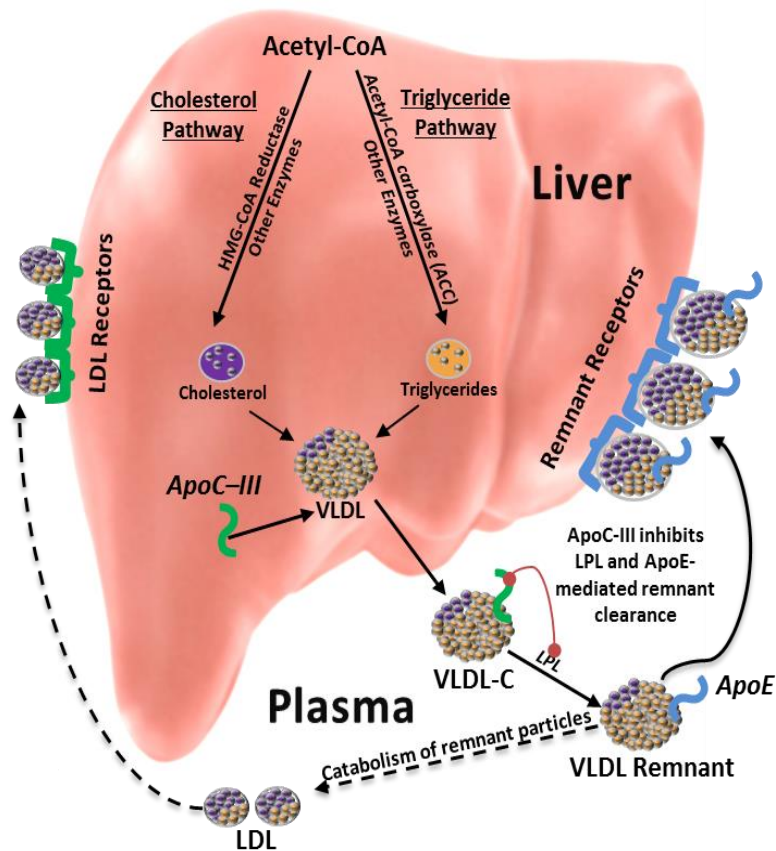
- % change in triglycerides (TG) from baseline to 12 weeks

Secondary Endpoints:

- Change in hepatic steatosis as measured by MRI-PDFF at 12 and 24 weeks
- Change in NAS (histology) at 24 weeks
- Change in AST, insulin sensitivity, serum lipids (including TG), apolipoproteins, and inflammatory markers (including hsCRP)
- Safety and tolerability

Gemcabene's Novel Dual Mechanism of Action

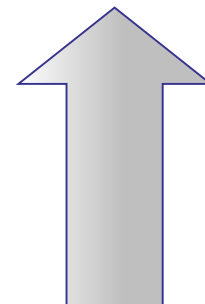
Complementary and Additive to Statin MOA Without DDI



Gemcabene further lowers LDL-C, non-HDL-C, Total-C, Triglycerides, ApoB, and hsCRP when added to background statin therapy, without showing DDI

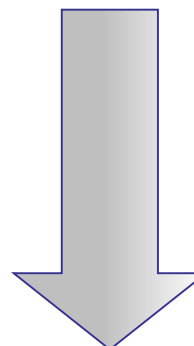
IMPROVES CLEARANCE

- Reduces ApoC-III gene expression and plasma ApoC-III protein levels
- Enhances VLDL-C clearance through increased affinity for the hepatic remnant receptor



REDUCES PRODUCTION

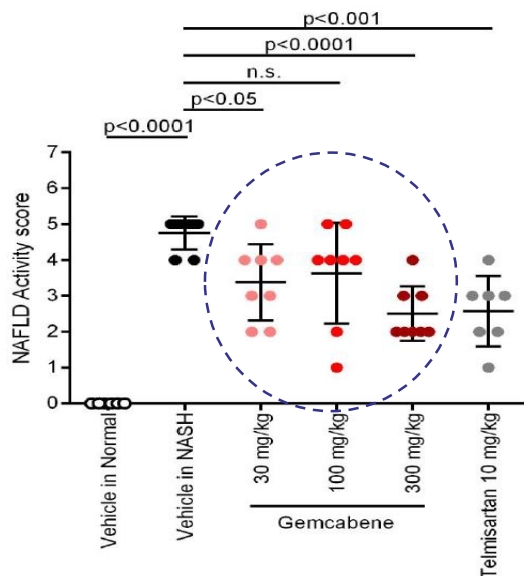
- Inhibits *de novo* synthesis of TGs and cholesterol in the liver
- TG effects due to inhibition of acetyl CoA carboxylase 1
- ↓VLDL-C particles leaves fewer apolipoproteins for catabolism to LDL-C



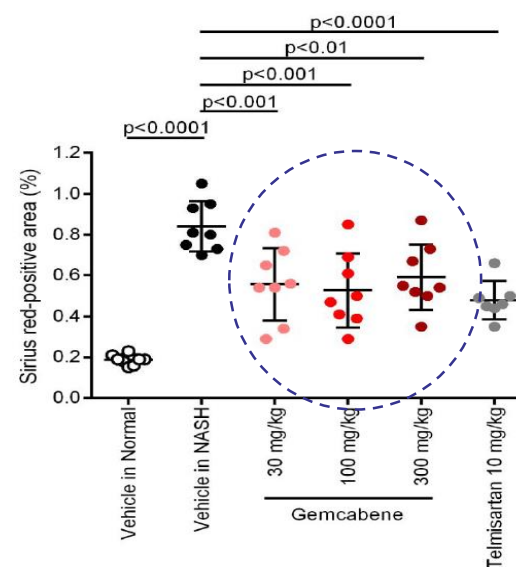
Gemcabene Improves NASH in Rodent Model

Gemcabene Lowers NAFLD Activity Score (NAS) and Fibrosis in STAM™ Model

↓ NAS Score¹ 25% to 48%



↓ Fibrosis ~33%



Gemcabene Comparable to Other Late Stage Compounds in STAM™ Model^{2,3,4}

TOBIRA'S CVC (CCR2/CCR5 INHIBITOR):
~23% to 30% improvement in NAS score
~60% reduction in fibrosis

INTERCEPT'S OCA (FXR AGONIST):
~23% improvement in NAS score

ENANTA'S EDP-305 (FXR AGONIST):
~30% improvement in NAS score

1. NAFLD Activity Score (NAS) composited comprised of steatosis, inflammation, & ballooning; 2. This comparison is for illustrative purposes as these were separate studies; 3. E. Lefebvre et al., The Liver Meeting AASLD, Abstract 30 presentation, 2013; 4. Enanta Pharmaceuticals Company Presentation, 2016

Gemcabene Has Been Shown to Improve Many Parameters in NASH

Lowered Activity of Inflammation & Lipid Metabolism Genes in STAM™ Model

Select Hepatic Gene Expression and Plasma Markers

Category	Gene Expression/ Plasma Markers	Vehicle in NASH	Gemcabene (300 mg/kg)
		(vs Vehicle in Normal)	(vs Vehicle in NASH)
Inflammation	<i>IL-6</i>	▲	▼
	<i>CRP</i>	--	▼
	<i>CCR2</i>	▲	▼
	<i>CCR5</i>	▲	▼
	<i>TNF-α</i>	▲	▼
	<i>MCP-1</i>	▲	▼
	<i>MIP-1β</i>	▲	▼
	<i>NF-kB</i>	▲	▼
Fibrosis	<i>TIMP-1</i>	▲	▼
	<i>MMP-2</i>	▲	▼
Lipid Metabolism	<i>ApoC-III</i>	▼	▼
	<i>SULF-2</i>	▲	▼
	<i>ADH4</i>	--	▼
	<i>ACC1</i>	--	▼

Key: -- No significant difference ▲ significant increase ▼ significant decrease

Summary

Gemcabene Provides Major Benefits for Cardiometabolic Patients including NASH

- Lowers LDL-C, Triglycerides and hsCRP
- Observed to be safe and effective in 1100 patients
- No observed DDI with statins and other drugs
- Oral, once daily, small molecule in-licensed from Pfizer
- Multidimensional MOA targets many underlying pathologies

Targeting Multiple Large Markets – 16-18M U.S. Patients

- Familial Hypercholesterolemia (FH: HoFH & HeFH) – 1.3M pts
- Severe Hypertriglyceridemia (SHTG) – 3M pts
- Fatty Liver Disease (NAFLD/NASH) – 6-8M pts
- High-risk cardiometabolic patients - 6.1M pts

Near Term Clinical Trial Catalysts including NASH POC Trials