GANNEX

A Member of the Ascletis Group

Corporate Presentation

A Biotech Dedicated to NASH

About Gannex

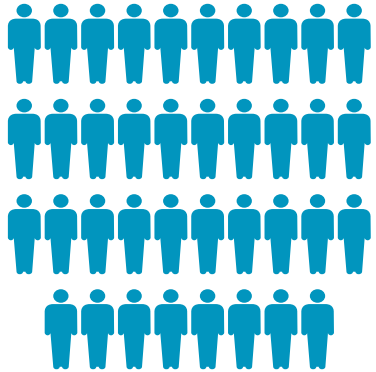
Gannex, a wholly-owned company of Ascletis, is dedicated to the R&D and commercialization of new drugs in the field of NASH. Gannex has three clinical stage drug candidates against three different targets – FASN, THRβ and FXR, and three fixed-dose combinations.

NAFLD and NASH Represent a Large and Growing Health Problem

- A large prospective study evaluated the prevalence and severity of NAFLD/NASH in an asymptomatic middle-aged population attending outpatient colonoscopy in the United States.

Middle-aged population (U.S.)

The prevalence of NAFLD is approximately 38%



The prevalence of NASH is approximately 14%

Significant liver fibrosis 5.9%

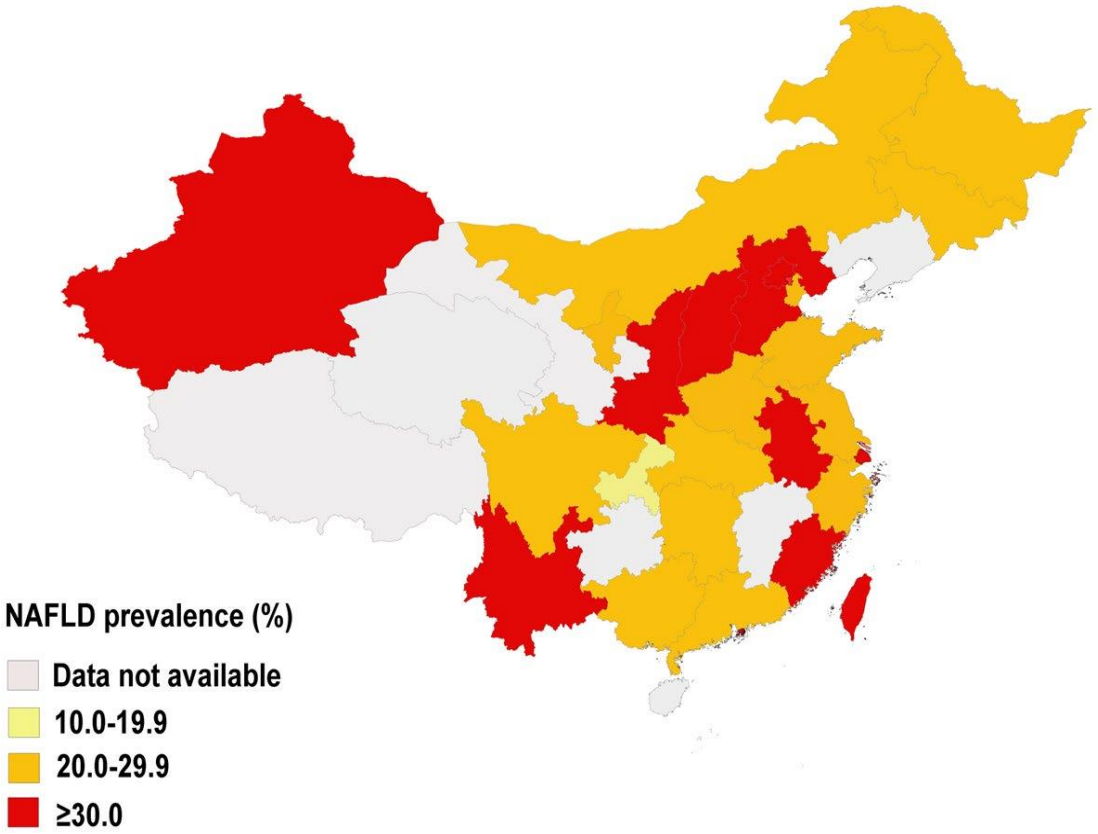
Bridging liver fibrosis 1.6%

Obesity and Diabetes are risk factors for progression to NASH

Source: Harrison S A, Gawrieh S, Roberts K, et al. Prospective evaluation of the prevalence of non-alcoholic fatty liver disease and steatohepatitis in a large middle-aged US cohort [J]. Journal of hepatology 2021, DOI: 10.1016/j.jhep.2021.02.034..

NAFLD and NASH Represent a Large and Growing Health Problem

- A large meta-analysis revealed that the prevalence of NAFLD in China was as high as **29.2%** from various perspectives.



NAFLD prevalence statistics in China

Highest NAFLD prevalence age group

- Age 50~59 (**32.9%**; 95% CI, 30.3-35.5)

Prevalence of NAFLD in people with obesity

- **51.6%**, 5 times higher than non-obese population (10.8%)

The prevalence of NAFLD in China is increasing rapidly

- 2008 ~ 2010 (25.4%) vs. 2015 ~ 2018 (32.3%)
- Twice as high as in Western countries, and already exceeds the average prevalence (29.2% vs. 25.2%)

Source: Zhou F, Zhou J, Wang W, et al. Unexpected Rapid Increase in the Burden of NAFLD in China From 2008 to 2018: A Systematic Review and Meta-Analysis [J]. Hepatology 2019, 70(4): 1119-33. DOI: 10.1002/hep.30702.

Significant Unmet Medical Needs for the Treatment of PBC

China

- The prevalence of PBC in China was 49.2 cases per 100,000 persons and as high as 155.8 cases per 100,000 in women older than 40 years old, indicating a total of 656,000 PBC patients in China, including 440,000 females over age 40.
- Ursodeoxycholic acid (UDCA) is the only drug approved in China for PBC to delay disease progression. However, approximately 40% PBC patients have inadequate responses to UDCA or have drug intolerance.

US/EU

- 120,000 PBC patients in the US in 2014.
- Obeticholic acid (Ocaliva) has been approved by US FDA for treatment of PBC in combination with UDCA in patients with inadequate responses to UDCA, or as monotherapy in patients with drug intolerance to UDCA.
- Ocaliva has significant side effects, including pruritus (63%) and fatigue (22%).

NASH/PBC Pipeline

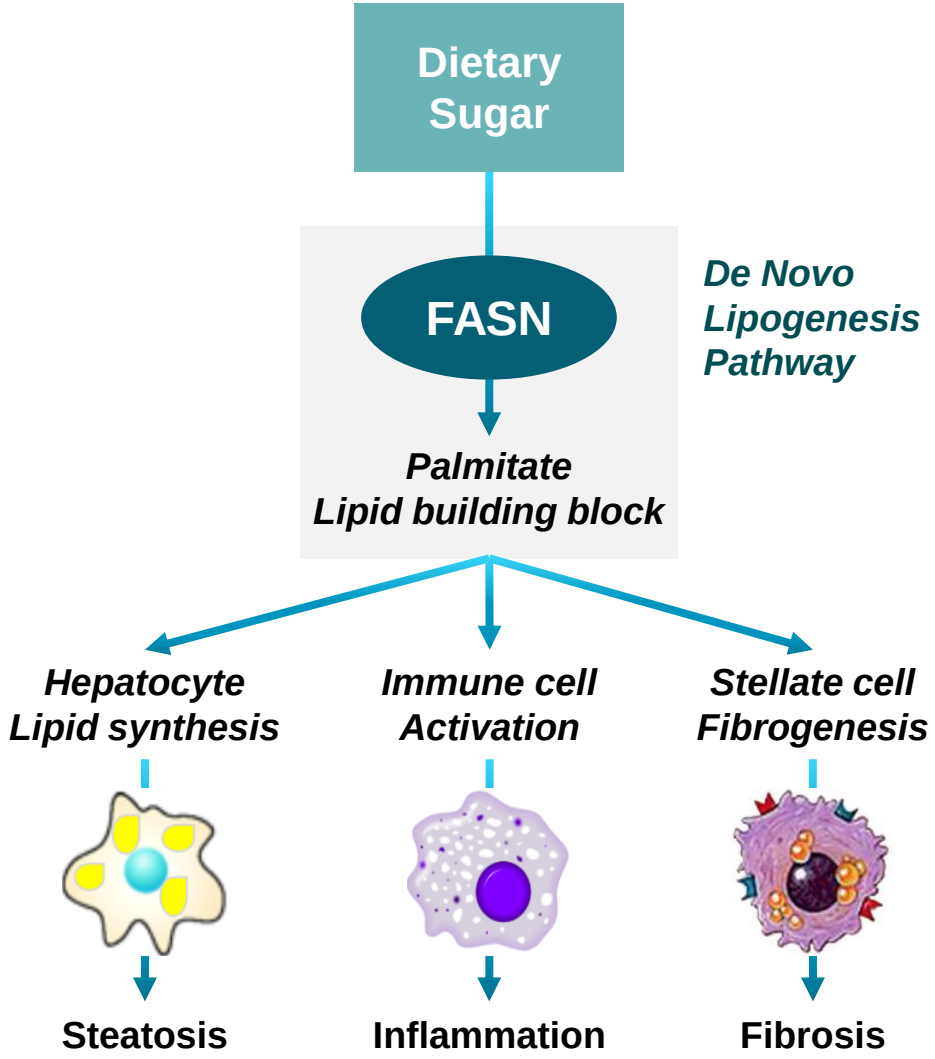
Target	Candidate	Commercial rights	Pre-IND	IND	Phase I	Phase IIa	Phase IIb	Phase III	Competitiveness
FASN	ASC40 (NASH)	Greater China[1]	***U.S. FDA Fast Track***						• First-in-class, inhibit de novo lipogenesis • US/CN phase II showed significant reduction of liver fat content, and minimal side effects compared to other NASH candidates
FXR	ASC42 (PBC)	Global							• No pruritus • CDE approval for Phase II/III clinical trials
THRβ	ASC41 (NASH)	Global							• Third-in-class globally, First-in-class in China • Triglyceride reduction >30% with 1mg per day dosing • No DDI with drugs commonly used by NASH patients
FXR	ASC42 (NASH)	Global	***U.S. FDA Fast Track***						• Potential Best-in-class, no pruritus or LDC-c elevation • Higher elevation of FGF-19, an FXR target engagement biomarker
THRβ + FXR	ASC43F FDC (NASH)	Global							• First-in-class, dual targets to THRβ and FXR
FASN + FXR	ASC44F FDC (NASH)	Global							• First-in-class, dual targets to FASN and FXR
FASN + THRβ	ASC45F FDC (NASH)	Global							• First-in-class, dual targets to THRβ and FASN

1. ASC40 is licensed from Sagimet Biosciences Inc. for the exclusive rights in the Greater China.

ASC40: First-in-Class Oral Fatty Acid Synthase (FASN) Inhibitor

FASN is an important rate-limiting step in intrahepatic fatty acid synthesis as well as De novo lipogenesis (DNL)

- Reduces steatosis by blocking DNL
- Reduces inflammation by decreasing cytokine secretion and Th17 differentiation
- Blunts fibrosis by reducing procollagen and profibrotic gene expression



Phase II U.S. Cohort: ASC40 Clinical Trial Design in NASH Patients

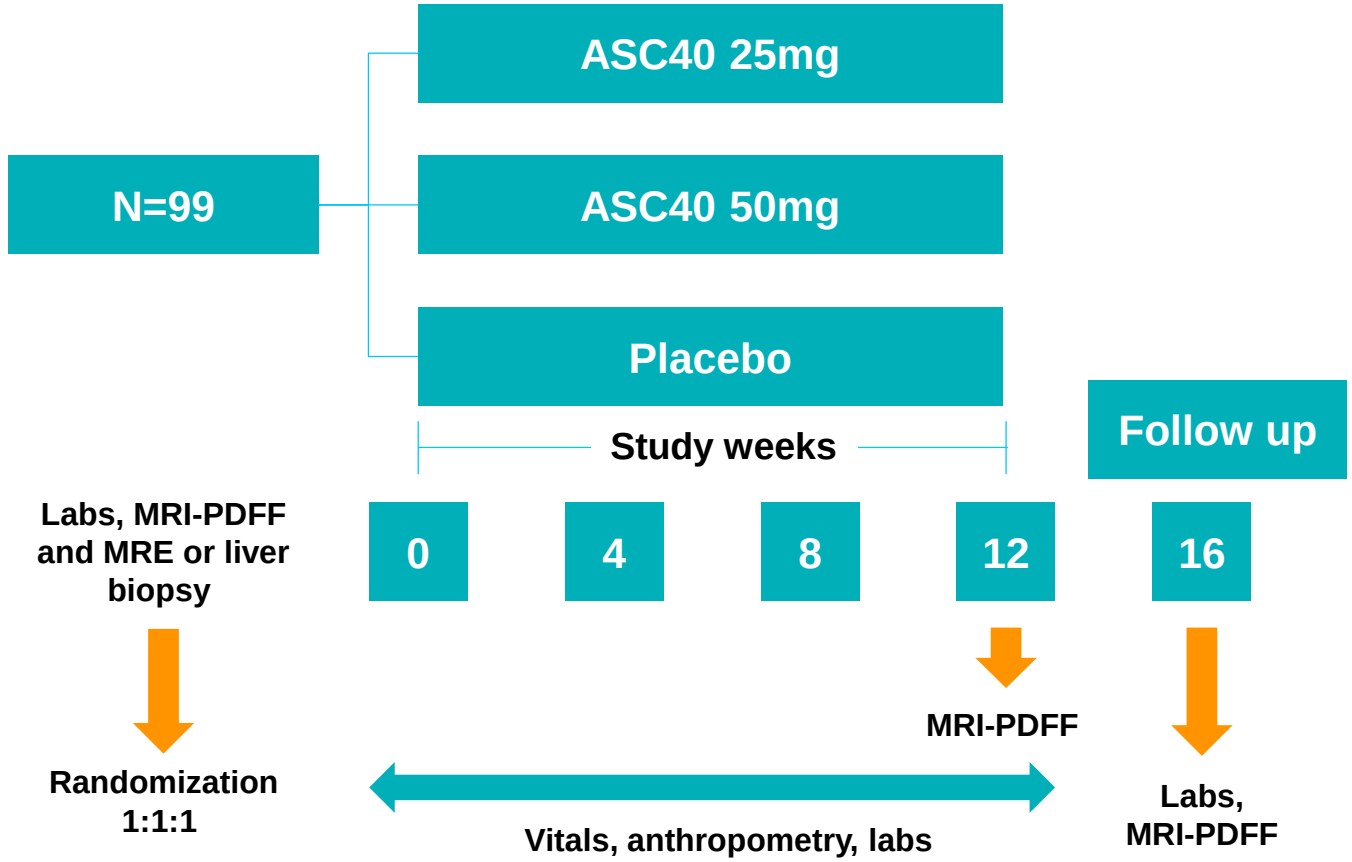
■ Multicenter, randomized, placebo-controlled trial 1:1:1 25mg:50mg:placebo (N=99)

Criteria

- Inclusion
  - ≥ 8% liver fat
  - MRE ≥ 2.5kPa or recent biopsy
- Exclusion
  - Evidence of cirrhosis
  - Other chronic liver disease

Endpoints

- Primary
  - Liver fat reduction by MRI-PDFF
  - Safety
- Secondary
  - % pts ≥30% reduction of liver fat
  - ALT, AST
  - Biomarkers

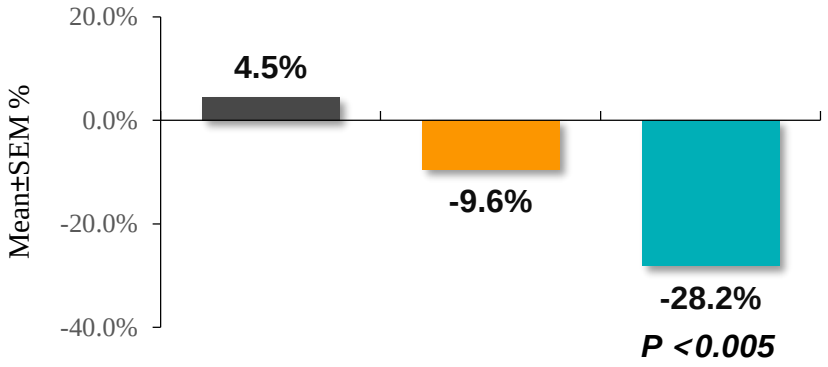


Source: Rohit Loomba et al. 2020,Hepatology 72;103.EASL 2020 Oral Presentation

Phase II U.S. Cohort: ASC40 Significantly Reduces Liver Fat Content

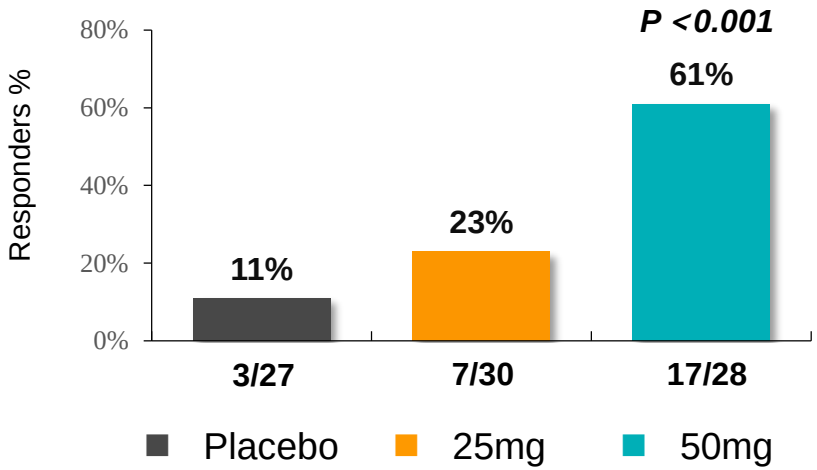
Mean relative liver fat reduction

MRI-PDFF at week 12

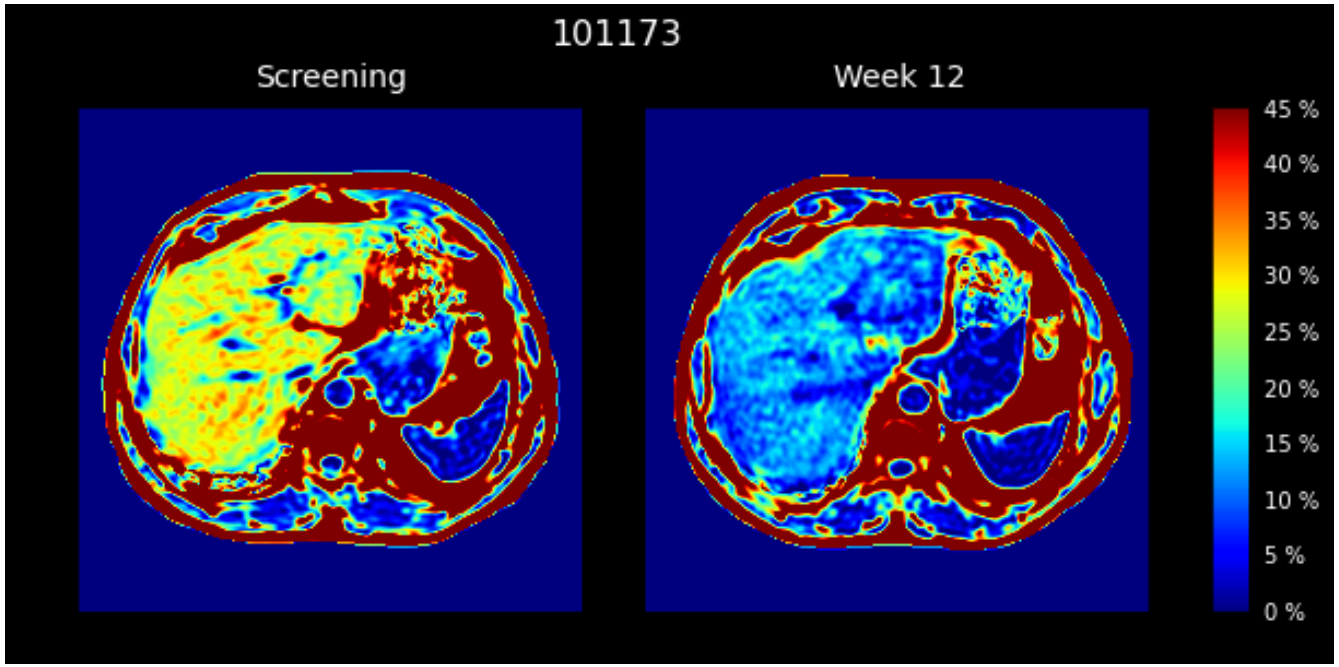


Responder frequency

Patients with ≥30% relative reduction



Significant reduction in liver fat content over 12 weeks of treatment

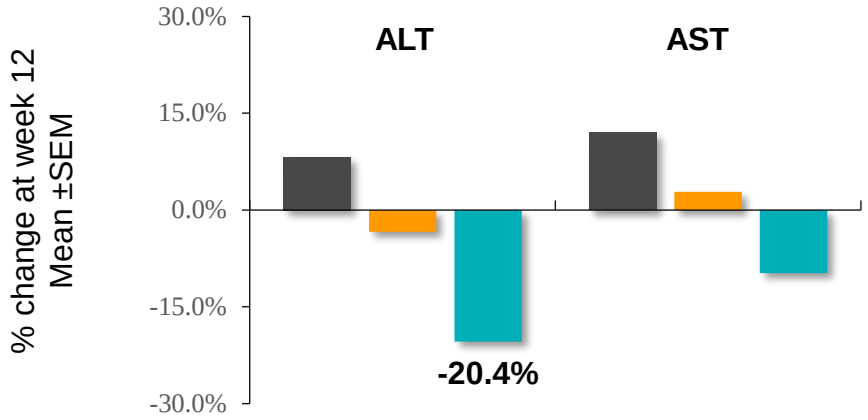


MRI-PDFF responders were defined as those with ≥ 30% MRI-PDFF decline relative to baseline

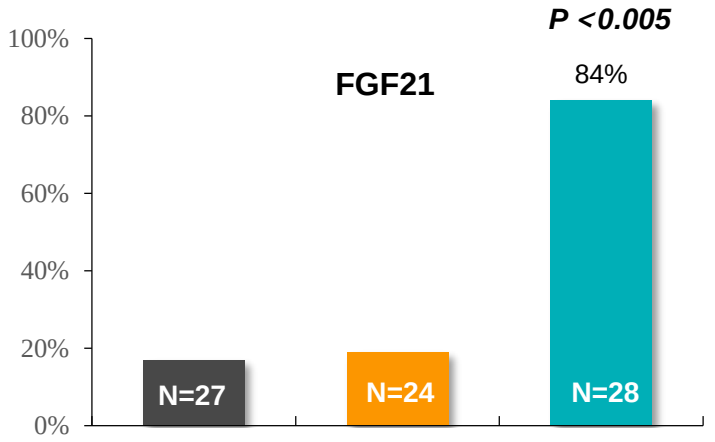
Source: Rohit Loomba et al. 2020, Gastroenterology & Hepatology 72;103AASLD 2020 Oral Presentation

Phase II U.S. Cohort: ASC40 Significantly Improves NASH-related Metrics

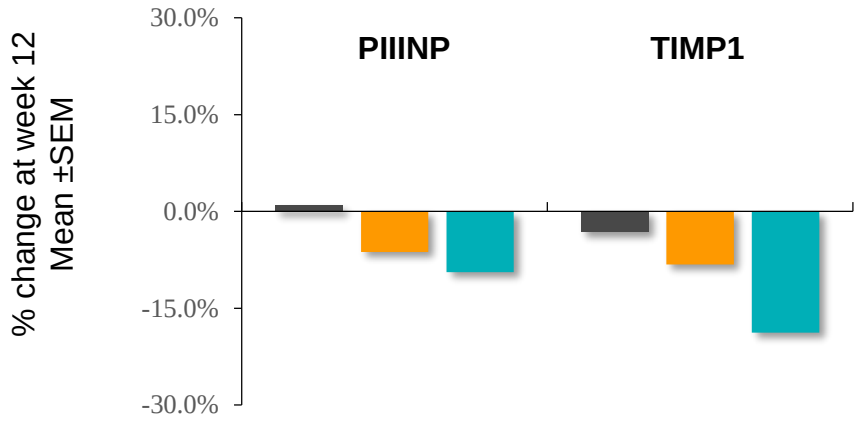
Dose-dependent response in reducing ALT/AST



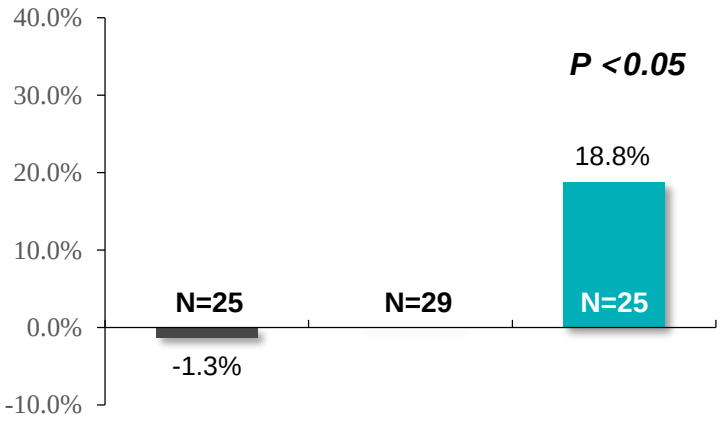
Improves markers of hepatic insulin sensitivity



Decreases fibrosis markers



Adiponectin



Placebo 25mg 50mg

Source: Rohit Loomba et al. 2020, Gastroenterology & Hepatology 72;103 AASLD 2020 Oral Presentation

Phase II ASC40 Compares Favorably With Other Phase II/III NASH Drugs

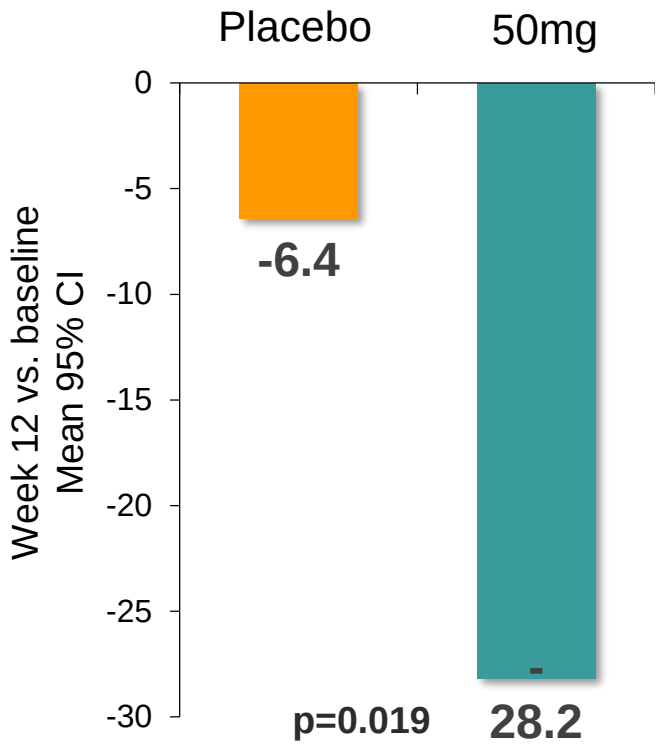
Drug Candidate	Company	Target	Dose	Weeks	≥ 30% liver fat reduction responder rate, %		Placebo adjusted ≥ 30% liver fat reduction responder rate, %	Safety
					Drug	Placebo		
ASC40[1]	Gannex /Sagimet	FASN	50 mg	12	60.7	11.1	49.6	minimal side effects
Firsocostat[2]	Gilead	ACC	20mg	12	47.8	15.4	32.4	TG ↑
Tropiflexor[3]	Novartis	FXR	200μg	12	64	20	44	LDL-C ↑, pruritus
Resmetirom[4]	Madrigal	THRβ	80mg	36	74.4	29.4	45	diarrhea, nausea

Non-head to head research

1、Rohit Loomba et al. 2020,Hepatology 72;103.EASL 2020 Oral Presentation
2、Eric J Lawitz et al. Clin Gastroenterol Hepatol. 2018 Dec;16(12):1983-1991
3、 Marcos Pedrosa et al. Contemp Clin Trials. 2020 Jan;88:105889.
4、Stephen A Harrison et al. Lancet. 2019 Nov 30;394(10213):2012-2024

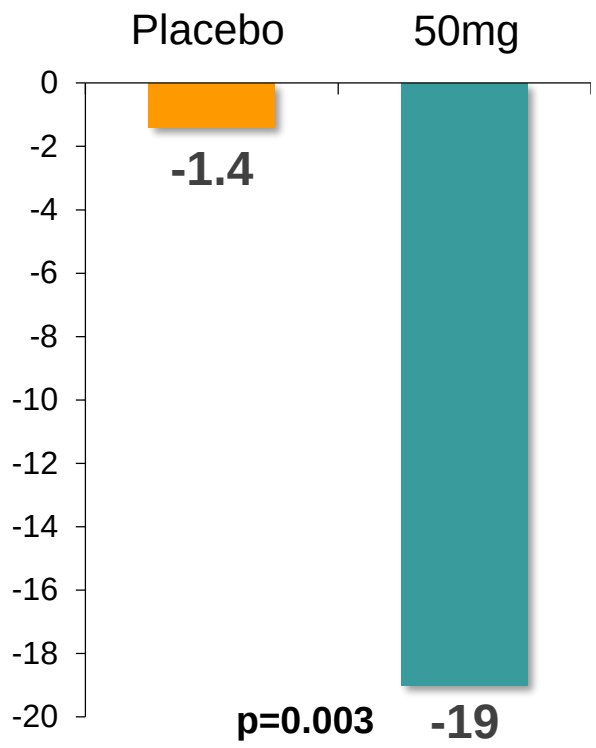
Phase II Combined U.S. & China Cohorts: ASC40 Reduces Liver Fat

Mean relative liver fat reduction
MRI-PDFF at week 12



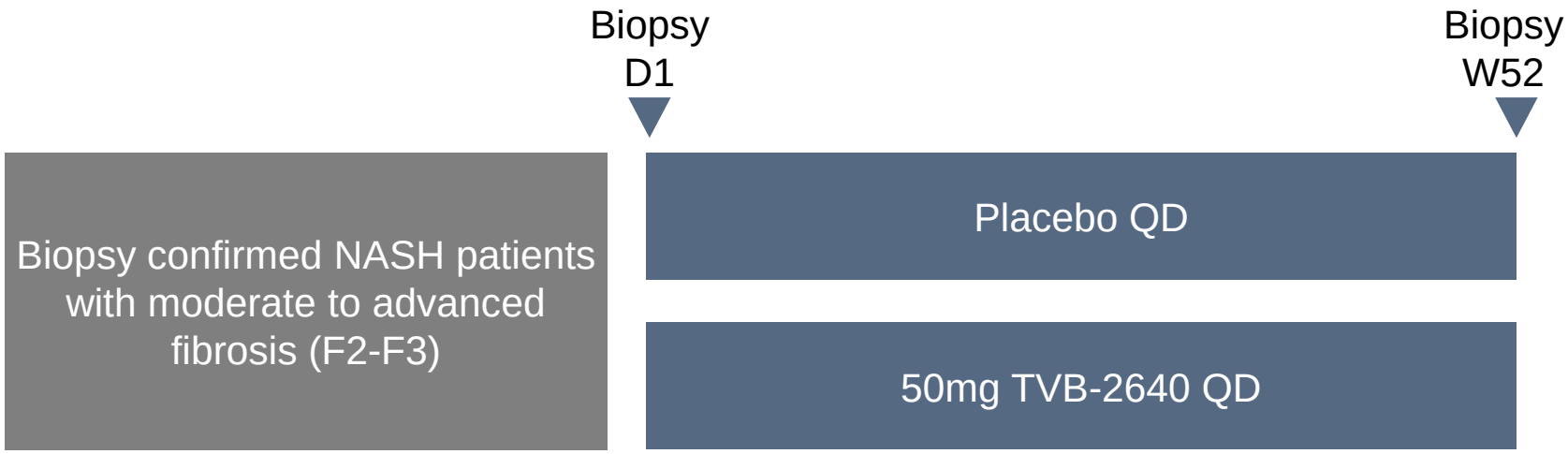
Mean absolute liver fat reduction
MRI-PDFF at week 12

Responder frequency
Patienct with ≥30% relative reduction



Source: *NOVEL, FIRST-IN-CLASS, FATTY ACID SYNTHASE (FASN) INHIBITOR TVB-2640 DEMONSTRATES ROBUST CLINICAL EFFICACY AND SAFETY IN A GLOBAL PHASE 2 RANDOMIZED PLACEBO-CONTROLLED NASH TRIAL (FASCINATE-1) CONDUCTED IN THE US AND CHINA 72th American Association for the Study of Liver Diseases (AASLD)& The Liver Meeting ®*, November 12-15, 2021. Virtual Conference.

ASC40 (TVB2640): US Phase IIb Study Design for NASH

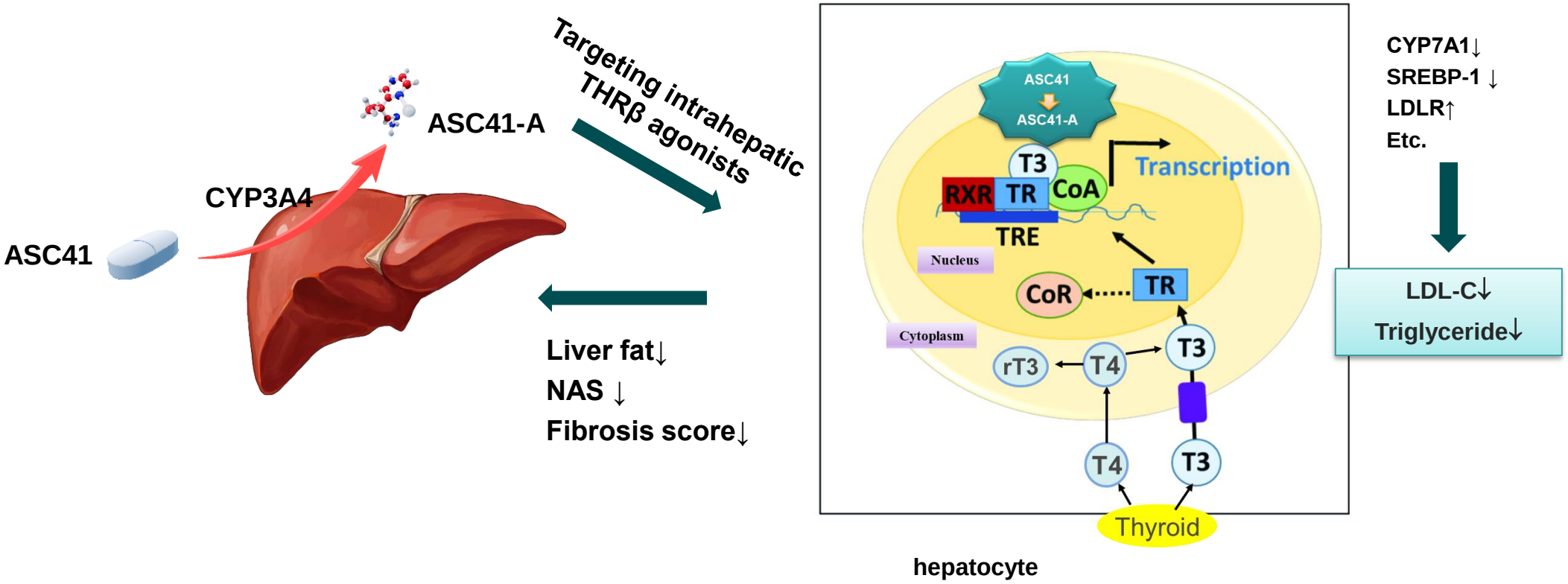


Primary efficacy endpoints:

1. *≥ 2-point improvement in NAS (Nonalcoholic fatty liver disease (NAFLD) Activity Score) that results from reduction of necro-inflammation (inflammation or ballooning), or*
2. *improvement in fibrosis.*

ASC41: A Liver Targeting Thyroid Hormone Receptor Beta (THRβ) Agonist

- ASC41 is a liver targeted small molecule which is converted to its active metabolite ASC41-A - a potent and selective THRβ agonist



Source: Gannex data

ASC41: Third-in-class THRβ Agonist in USA
First-in-class THRβ Agonist in China

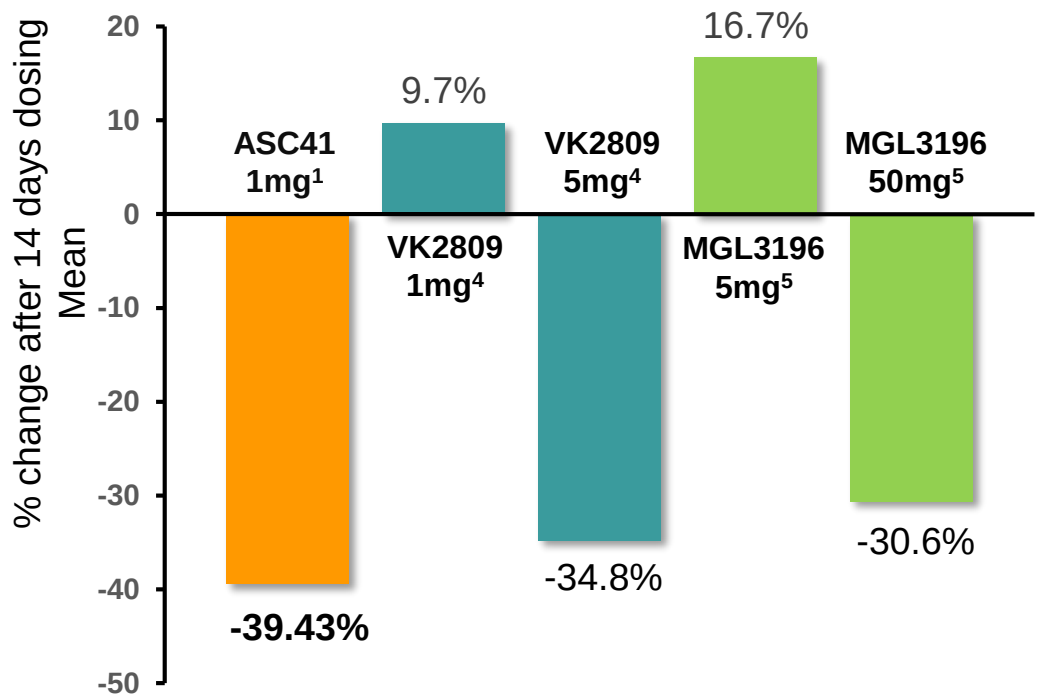
- In two NASH animal models, at 1/10 dose of MGL-3196, ASC41 demonstrated the same improvement of liver steatosis, inflammation and fibrosis.
- Commercially ready oral tablet formulation developed with in-house proprietary technology
- 2 Phase I studies completed
  - Single doses (1, 2, 5, 10, 20 mg) and 14 day multiple doses (1, 2, 5 mg) in 65 subjects with elevated LDL-C > 110 mg/dL
  - Food effect in 12 healthy subjects
- 1 Phase Ib study completed
  - 28 day, 10 mg in 20 overweight and obese subjects with elevated LDL-C > 110 mg/dL
- US Phase I study showed no significant drug-drug interactions between ASC41/ASC41-A and common used drugs in NASH patients such as antidepressants and statins
- Based on above studies, doses have been selected for Phase II trials in patients with NASH

Source: 1. PO1908. Significant Improvement of NAFLD Activity Scores and Liver Fibrosis by ASC41, a Selective THRβ Agonist, in HIgh Fat Diet Induced NASH SD Rats. Journal of Hepatology 2021 vol. 75(2) | S294–S803
2. PO1851. Significant lipid lowering by ASC41oral tablet, a liver targeted THRβ agonist, in a phase I randomized, double-blind, placebo controlled single- and multiple-ascending dose study. Journal of Hepatology 2021 vol. 75(2) | S294–S803

THRβ Differentiations: Gannex vs Viking and Madrigal

	Gannex ASC41[1]	Viking VK2809[2]	Madrigal MGL3196[3]
Oral formulation	Tablet, room temp storage, commercially ready	Capsule, refrigerated	Tablet, room temp storage, commercially ready
Dosing frequency	Once a day	Once every two days	Once a day
DDI	-	+	-
Human dose needed for > 30% TG reduction	1 mg	2.5 mg	50 mg

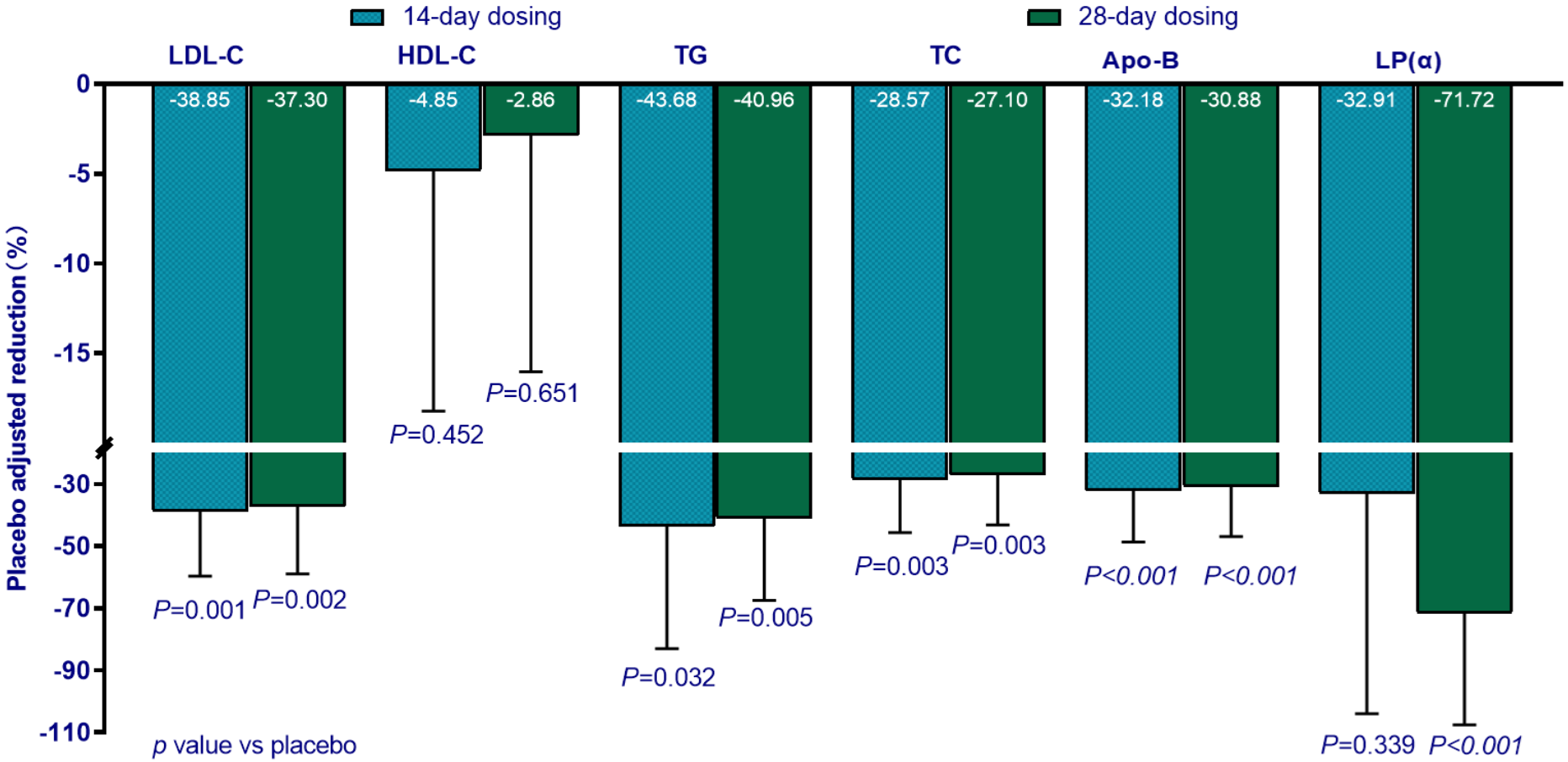
Placebo adjusted triglyceride reduction from baseline after 14 day dosing



1.EASL 2021 Abstract No. PO-1851 2.EASL2020 Abstract No. AS073. 3.Stephen A Harrison et al. Resmetirom (MGL-3196) for the treatment of non-alcoholic steatohepatitis: a multicentre, randomised, double-blind, placebo-controlled, phase 2 trial. www.thelancet.com Published online November 11, 2019 https://doi.org/10.1016/S0140-6736(19)32517-6 4 VK2809 data presented at the 2016 Meeting of the American College of Cardiology 5 Taub et al. Lipid lowering in healthy volunteers treated with multiple doses of MGL-3196, a liver-targeted thyroid hormone receptor-b agonist. Atherosclerosis 230 (2013) 373e380

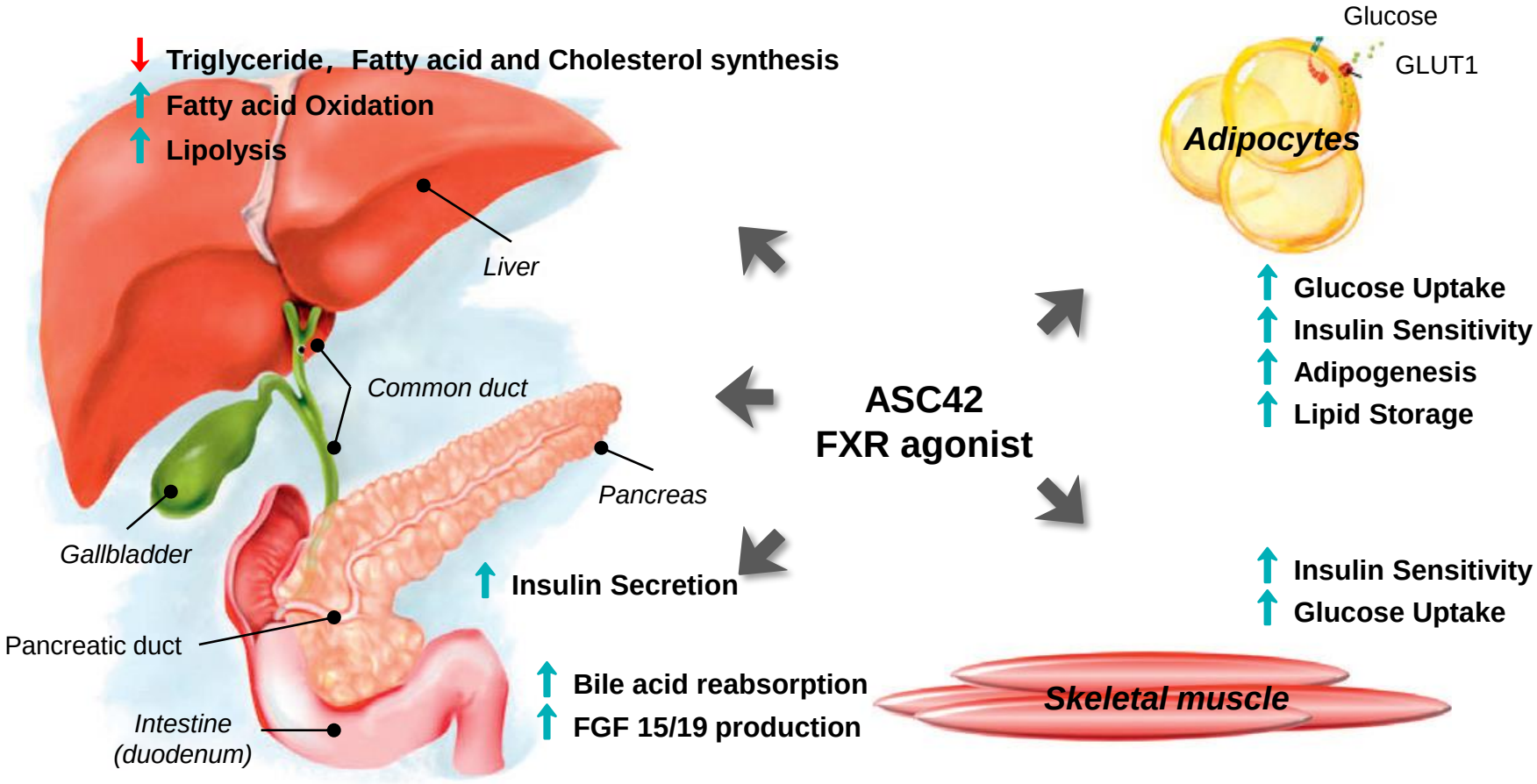
Positive Clinical Results in Overweight and Obese Subjects

Placebo-adjusted relative change (mean) from baseline after 14 or 28 days of once daily oral dosing of 10 mg ASC41 tablets in overweight and obese subjects



Source: A Phase Ib Study to Evaluate the Safety, Tolerability and Pharmacokinetics of ASC41, a THR-β Agonist, for 28-days in Overweight and Obese Subjects with Elevated LDL-C, a Population with Characteristics Of NAFLD. 72th American Association for the Study of Liver Diseases (AASLD)& The Liver Meeting ®, November 12-15, 2021. Virtual Conference.

ASC42: A Farnesoid X Receptor (FXR) Agonist



- Increased insulin sensitivity of adipocytes and skeletal muscle cells increases glucose uptake in peripheral tissues and increases energy consumption
- Reduced the synthesis of triglycerides, fatty acids and cholesterol in the liver, promoted liver fat decomposition and fatty acid oxidation

Source: Luciano Adorini et al. Farnesoid X receptor targeting to treat nonalcoholic steatohepatitis. Drug Discovery Today Volume 17, Numbers 17/18 September 2012

ASC42: A Novel Non-steroidal, Selective, Potent FXR Agonist

- Potentially best-in-class, **no pruritus** at human therapeutic doses
- U.S. FDA IND approval in Oct 2020
- U.S. FDA Fast Track Designation in Dec 2020
- U.S. Phase I trials completed
  - Single ascending doses and multiple ascending doses
  - Food effect
- Phase II/III clinical trials for PBC approved in Nov 2021 by China NMPA
- Oral tablet formulation developed with in-house proprietary technology and stable at room temperature

ASC42: Topline Results of the U.S. Phase I Trial

Dose（QD）	5mg	15mg
Incidence rate of pruritus during 14 days treatment (%)	0	0
LDL-C change from baseline on Day 14（%, Median）	-6.6	2.43
FGF19 on Day 14 versus baseline（%）	471	1780
C4 reduction on Day 14（%）	53	91
ALT change from baseline on Day 14（U/L, Median）	-1.0	-2.5

Source: ASC42, a Novel Non-steroidal FXR Agonist, Demonstrates a Normal Cholesterol Profile and Lack of Pruritus at Therapeutic Doses in a 14-day Phase I Randomized, Double-blind, Placebo Controlled Study in Healthy Volunteers. 72th American Association for the Study of Liver Diseases (AASLD)& The Liver Meeting ®, November 12-15, 2021. Virtual Conference.

FDC: Complementary among ASC40, ASC41 and ASC42

Treatment Goals	Monotherapy			FDC One-Pill, Once-a-Day		
	ASC40 FASN	ASC41 THRβ	ASC42 FXR	ASC43F THRβ + FXR	ASC44F FASN + FXR	ASC45F FASN + THRβ
Liver fat reduction	★★★	★★★	★★	★★★	★★★	★★★
Anti-inflammation	★★	★★	★★	★★	★★	★★
Anti-fibrosis	★★	★★	★★★	★★★	★★★	★★
Lowering LDL-C and TG		★★★		★★★		★★★

THANKS

GANNEX