GANNEX

A Member of the Ascletis Group

Corporate Presentation

A Biotech Dedicated to NASH

About Gannex

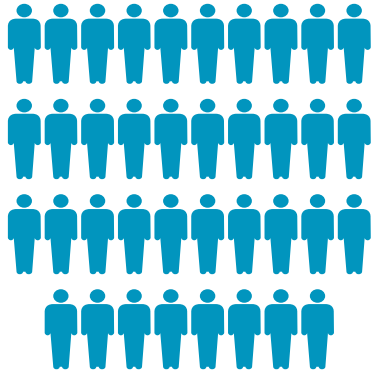
Gannex, a wholly-owned company of Ascletis, is dedicated to the R&D and commercialization of new drugs in the field of NASH. Gannex has three clinical stage drug candidates against three different targets – FASN, THR-β and FXR, and three combination therapies.

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%



Significant liver fibrosis 5.9%

Bridging liver fibrosis 1.6%

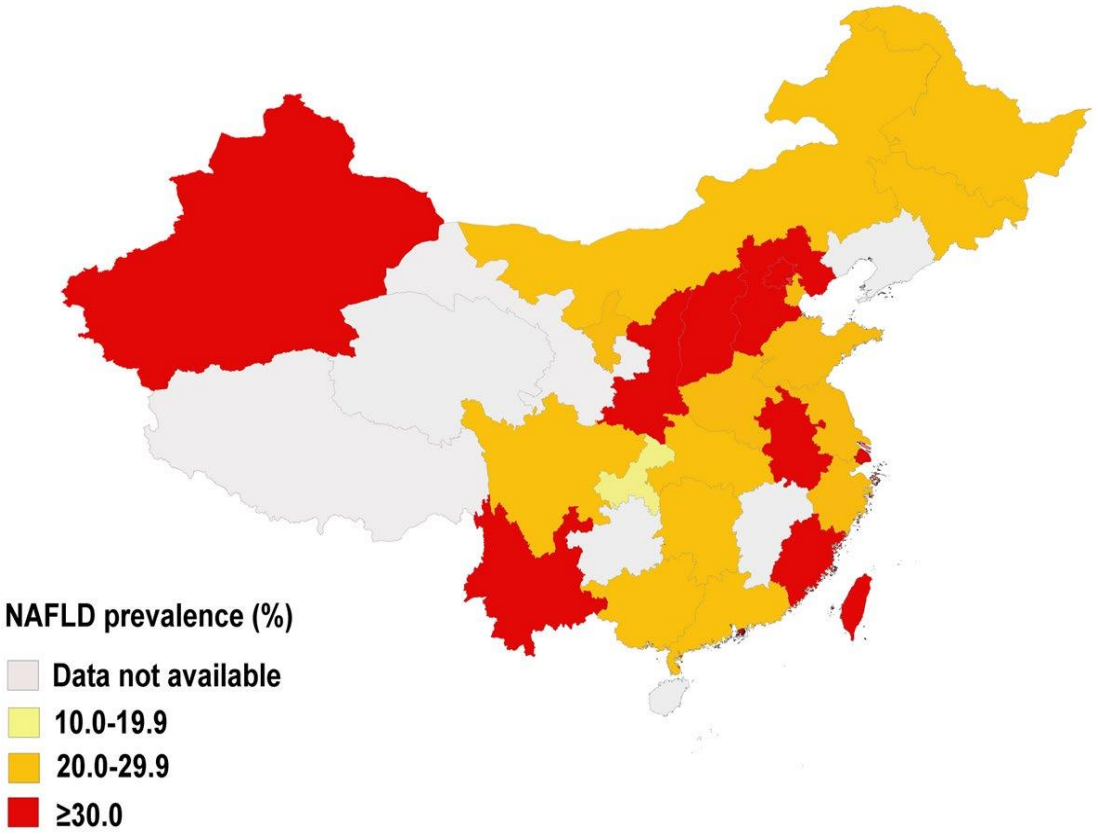
The prevalence of NASH is approximately 14%

Obesity and Diabetes are risk factors for progression to NASH

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%)

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.

NASH Pipeline: Single Agent and Combo Therapies

Target	Drug Candidates	Commercial Rights	Pre-IND	IND	Phase I	Phase IIa	Phase IIb/III
FASN	ASC40	Greater China[1]			*U.S. FDA Fast Track*		
THR-β	ASC41	Global					
FXR	ASC42	Global		*U.S. FDA Fast Track*			
THR-β + FXR	ASC43F One-Pill, Once-a-Day FDC	Global					
FASN + FXR	ASC44F One-Pill, Once-a-Day FDC	Global[1]					
FASN + THR-β	ASC45F One-Pill, Once-a-Day FDC	Global[1]					

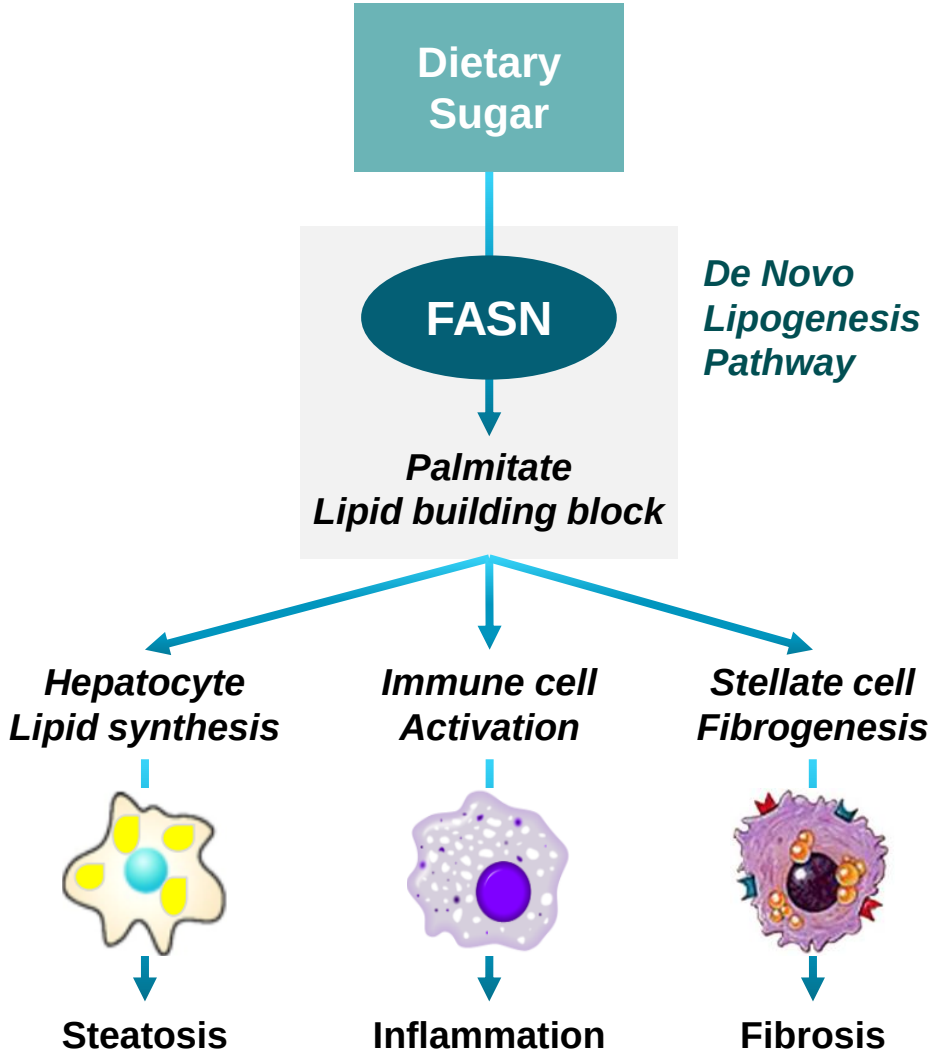
Notes: 1. ASC40 is licensed from Sagimet Biosciences Inc. (“Sagimet”) (previously known as 3-V Biosciences, Inc.) for the exclusive rights in the Greater China.

FASN: Fatty Acid Synthase THR-β: Thyroid Hormone Receptor Beta FXR: Farnesoid X Receptor FDC: Fixed Dose Combination

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

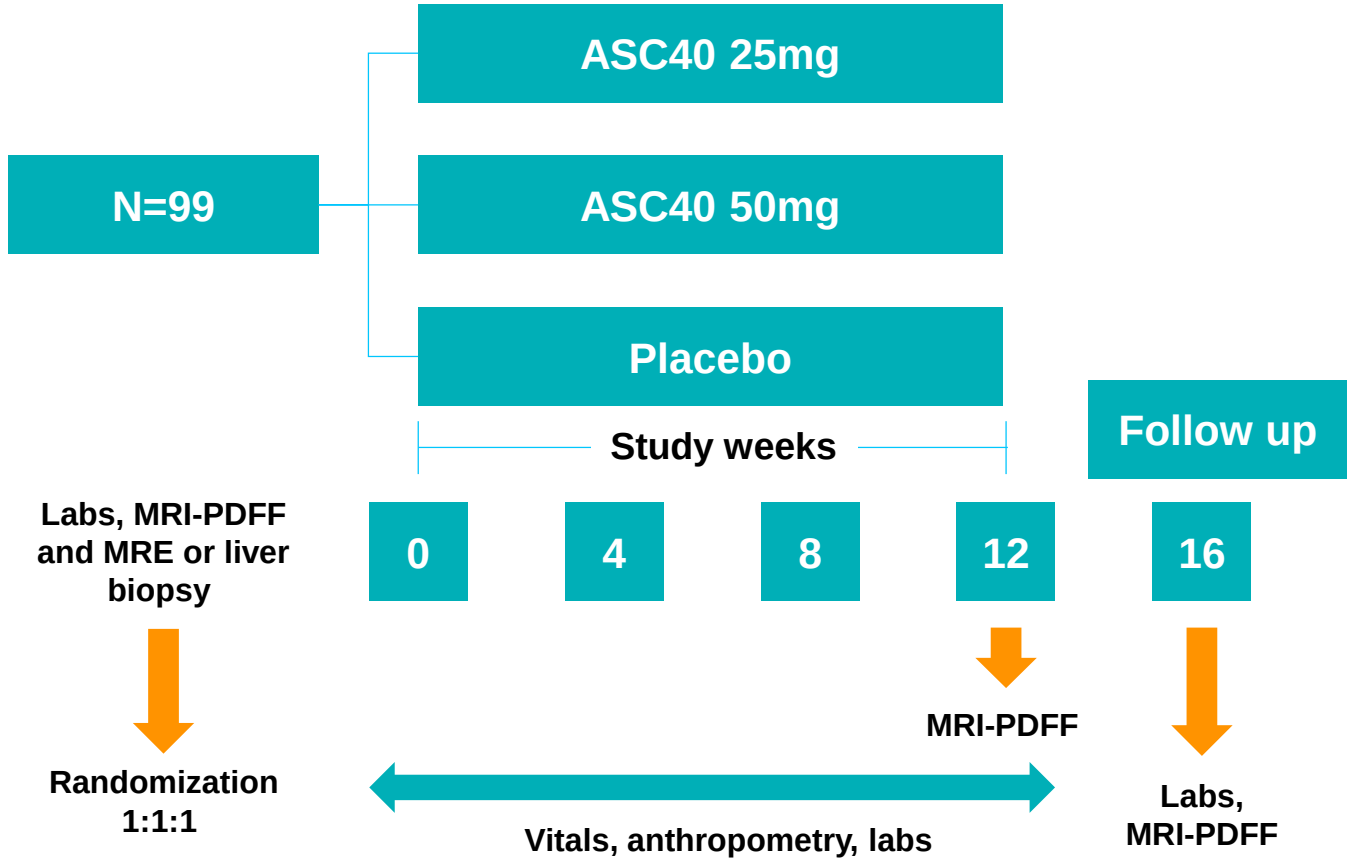
Multicenter, randomized, placebo-controlled trial 1:1:1 25mg:50mg:placebo (N=99)

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

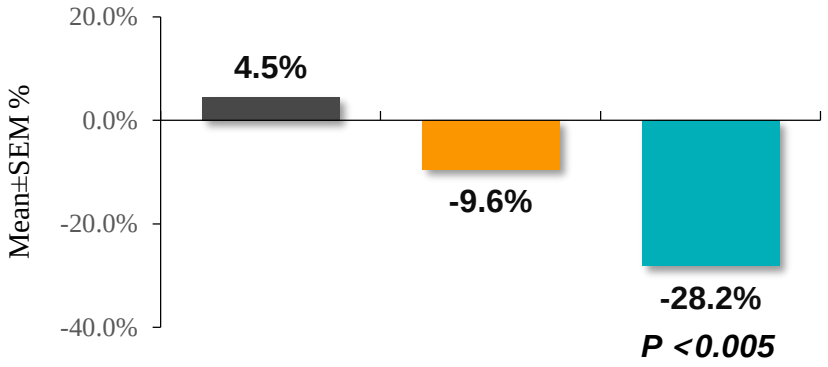


Rohit Loomba et al. 2020, Hepatology 72;103. EASL 2020 Oral Presentation

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

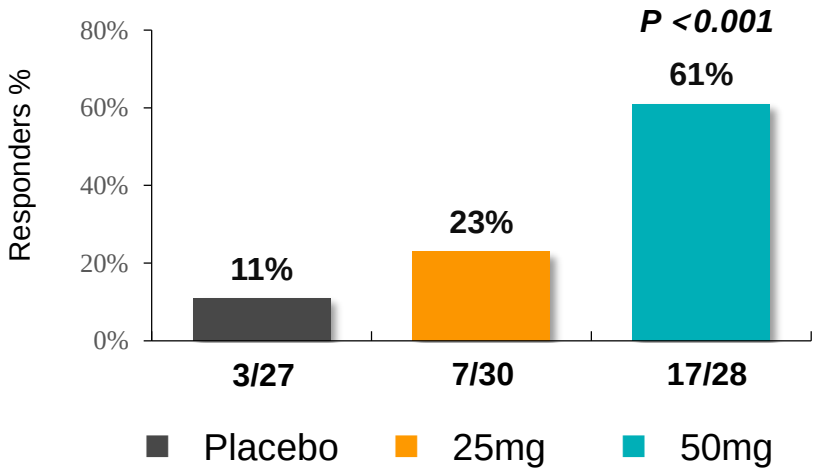
Mean relative liver fat reduction

MRI-PDFF at week 12

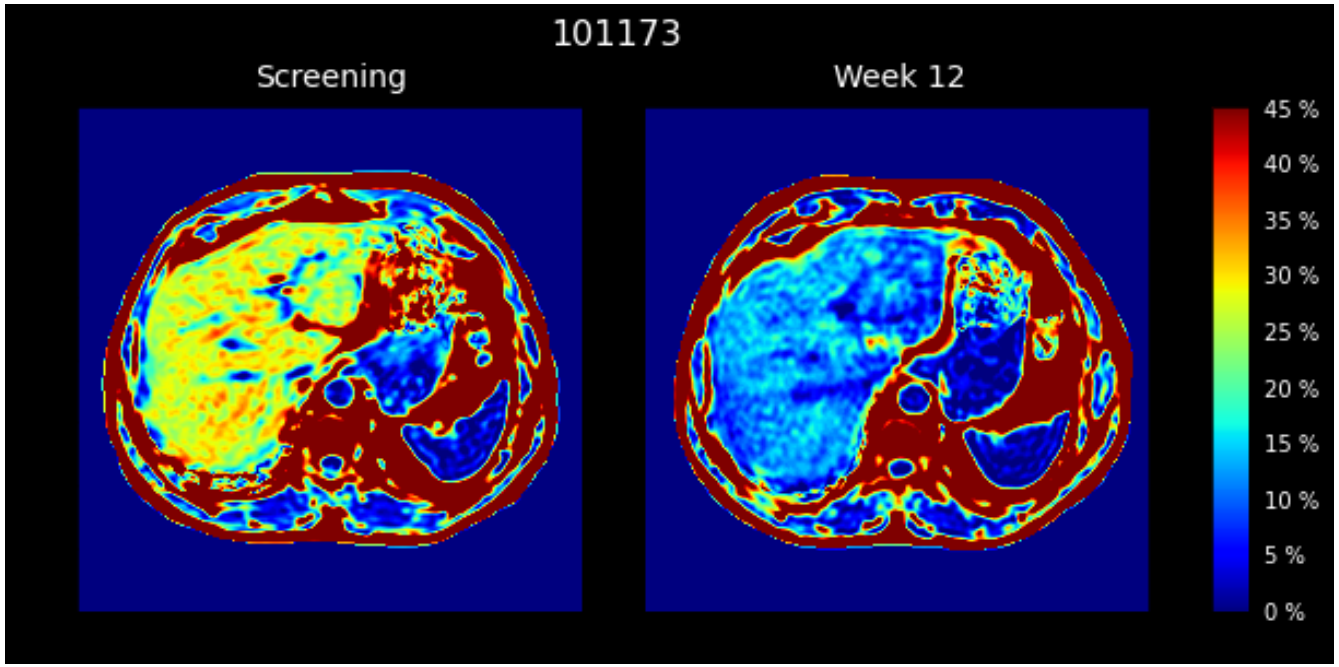


Responder frequency

Patients with ≥30% relative reduction



Significant reduction in liver fat content over 12 weeks of treatment

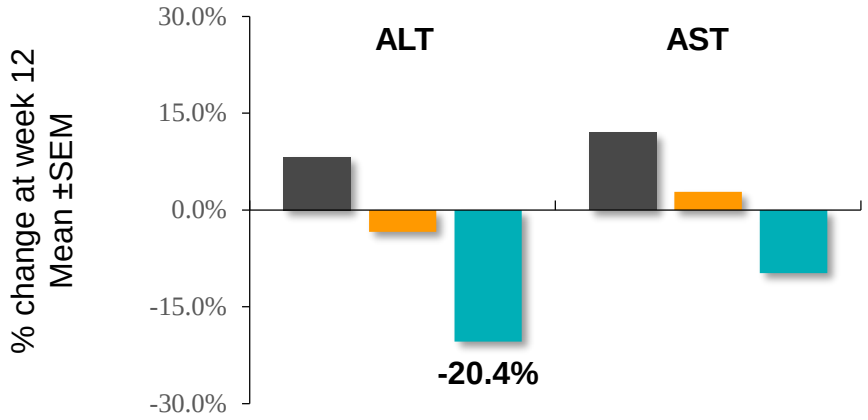


MRI-PDFF responders were defined as those with ≥ 30% MRI-PDFF decline relative to baseline

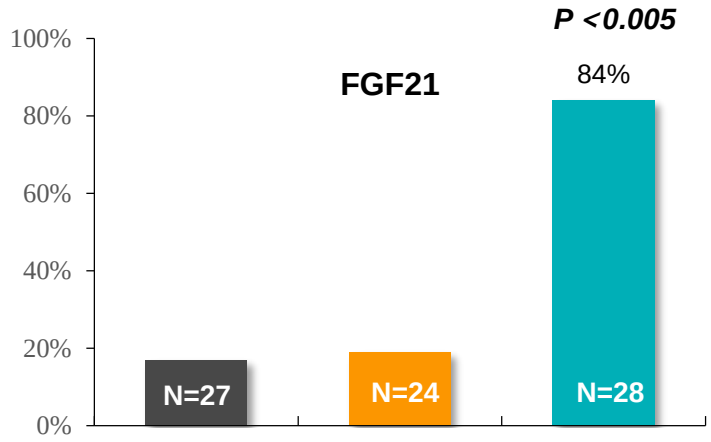
Rohit Loomba et al. 2020, Gastroenterology & Hepatology 72;103AASLD 2020 Oral Presentation

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

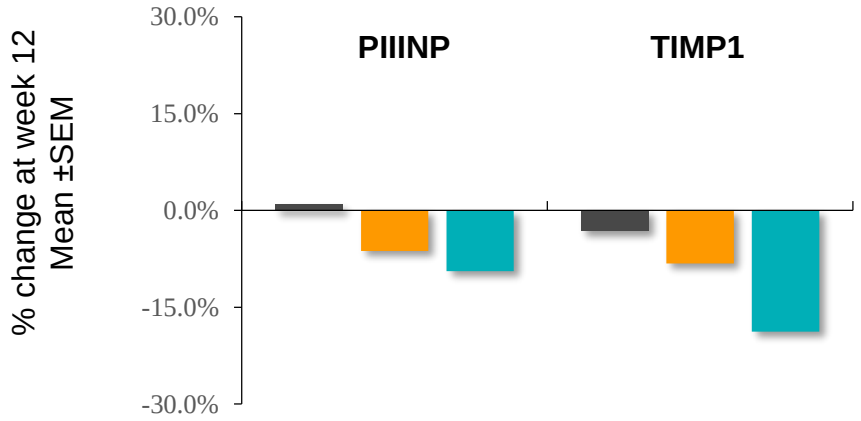
Dose-dependent response in reducing ALT/AST



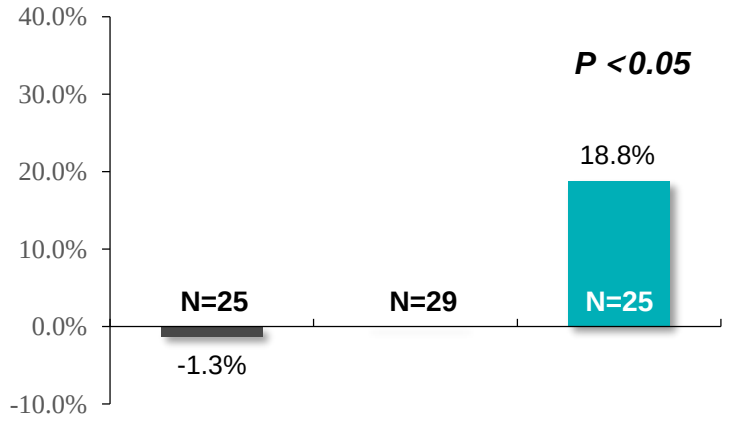
Improves markers of hepatic insunlin sensitivity



Decreases fibrosis markers



Adiponectin



Placebo 25mg 50mg

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	THR-β	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

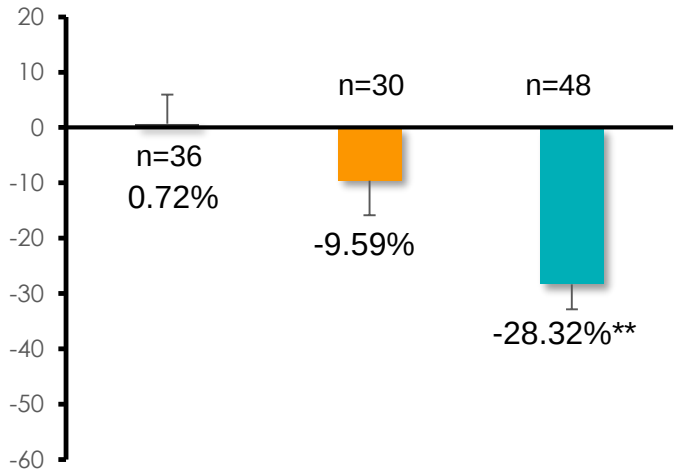
Phase II China Cohort: ASC40 Clinical Trial in NASH Patients

Phase II, multicenter, randomized, placebo-controlled trial 2:1 50mg:placebo (N=30)

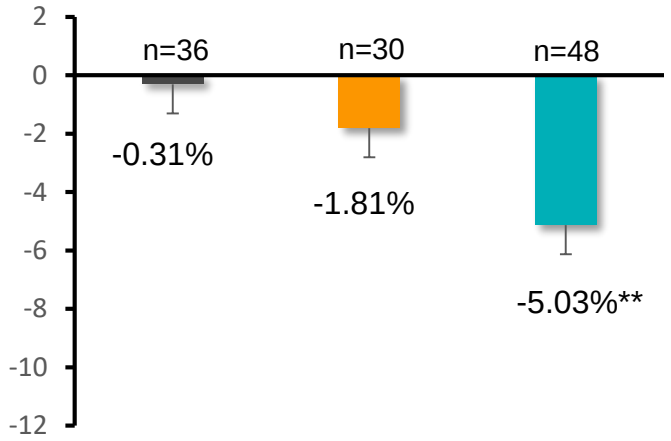
- ASC40 meaningfully reduced liver fat, the primary efficacy endpoint of this trial, with a 50% responder rate (patients achieving ≥30% reduction)
- ASC40 showed a statistically significant decrease in ALT by 29.8% (*P*=0.0499) (mean decrease of 33 U/L at week 12)
  - Indicates reduction of liver inflammation
- In 63% of patients on ASC40, ALT decreased by17 U/L or greater, which has been shown to correlate with liver biopsy response in NASH patients
- ASC40 was well tolerated with no serious adverse events. All treatment emergent adverse events were grade 1 or 2 and there were no statistically significant changes in serum triglycerides
- Data from the China cohort are consistent with those of the U.S. cohort, previously reported at the AASLD Liver Meeting in November 2020
- Based on the positive Phase II data, doses for the Phase IIb/III NASH trial in China have been selected

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

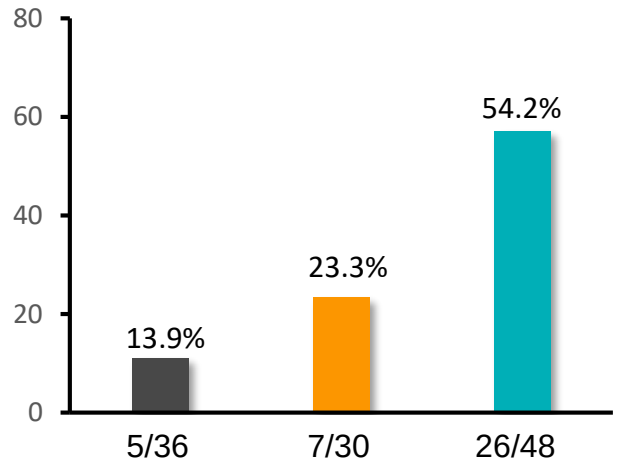
Mean relative liver fat reduction
MRI-PDFF at week 12



Mean absolute liver fat reduction
MRI-PDFF at week 12



Responder frequency
Patienct with ≥30% relative reduction

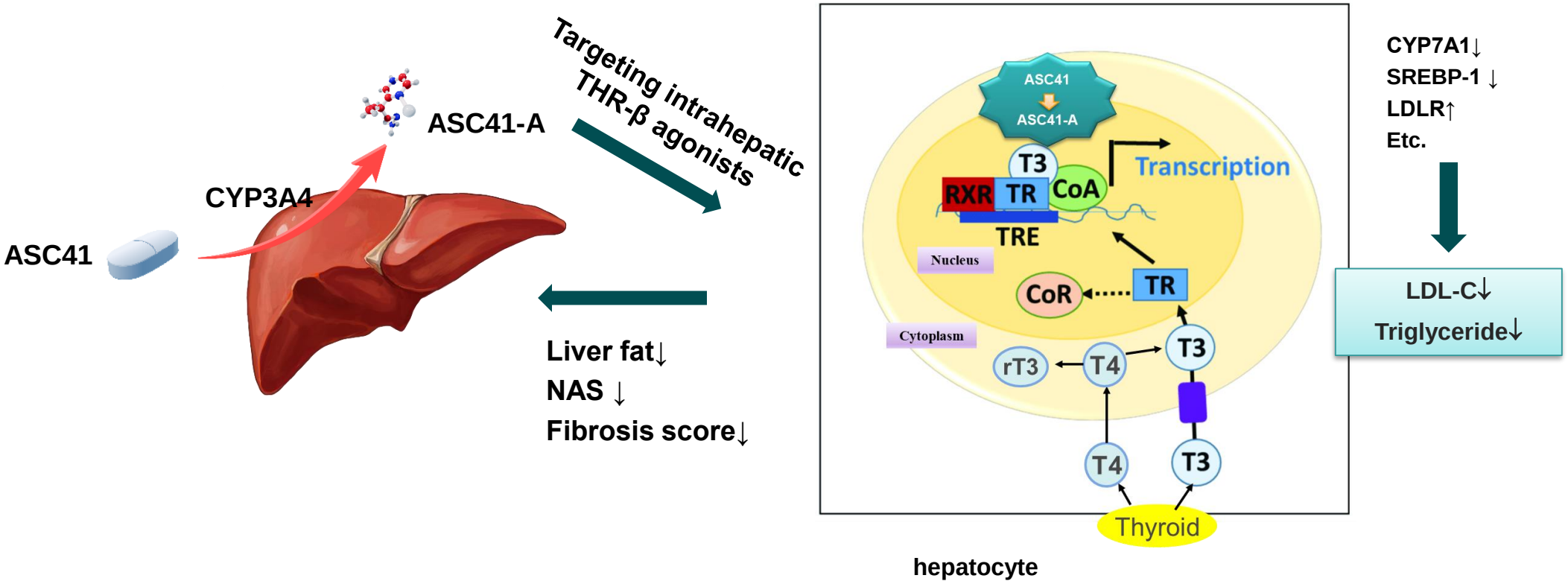


Placebo **25mg** **50mg**

p<0.05,p<0.01 Mean ± SEM LSM difference versus placebo for liver fat.Common risk difference for responder frequence*

ASC41: A Liver Targeting Thyroid Hormone Receptor Beta (THR-β) Agonist

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



Gannex data

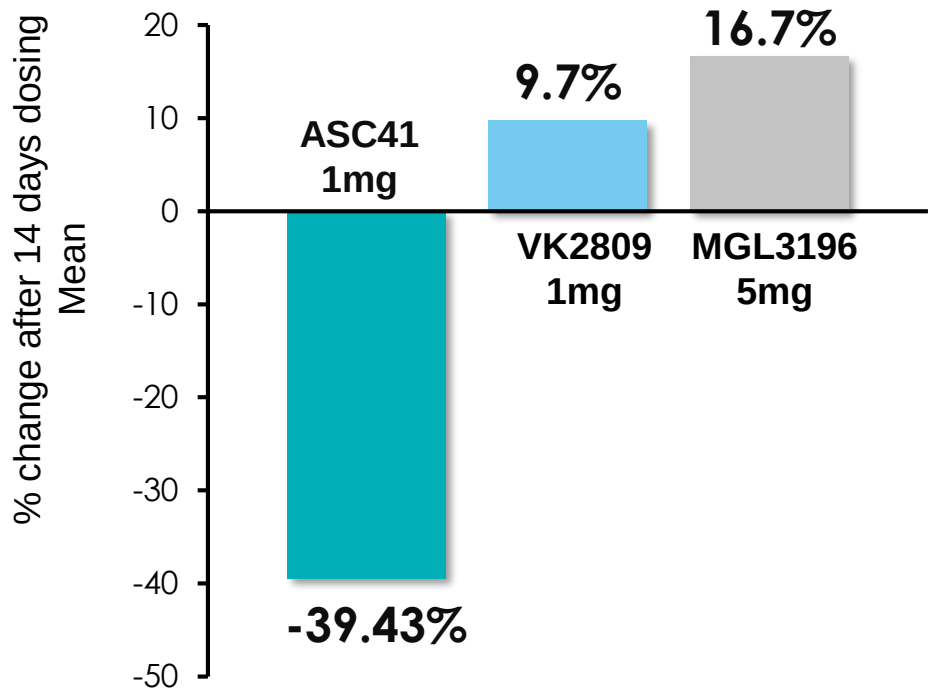
ASC41: Currently a Third-in-class THR-β Agonist in USA First-in-class in China

- In two NASH animal models, at 1/10th dose of MGL-3196, ASC41 demonstrated the same improvement in 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
- U.S. IND approved Feb 2021
- 1 Phase Ⅰb study completed
  - 28 day, 10 mg in 20 overweight and obese subjects with elevated LDL-C > 110 mg/dL
- Based on above studies, doses have been selected for Phase II trials in patients with NASH

THR-β 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
Human dose needed for > 30% TG reduction	1 mg	2.5 mg	50 mg

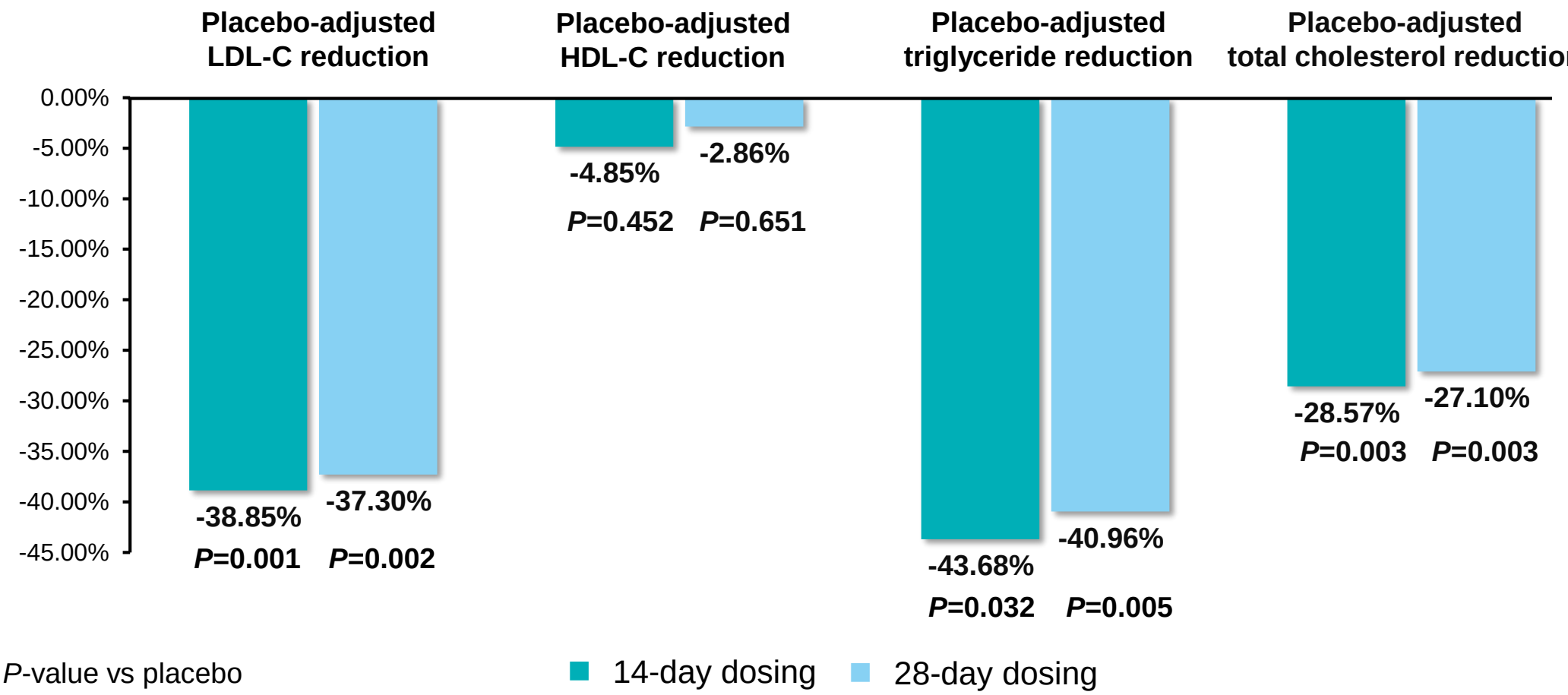
Placebo adjusted triglyceride reduction from baseline after 14 day dosing



1.Gannex data 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

Positive Clinical Results in Overweight and Obese Subjects

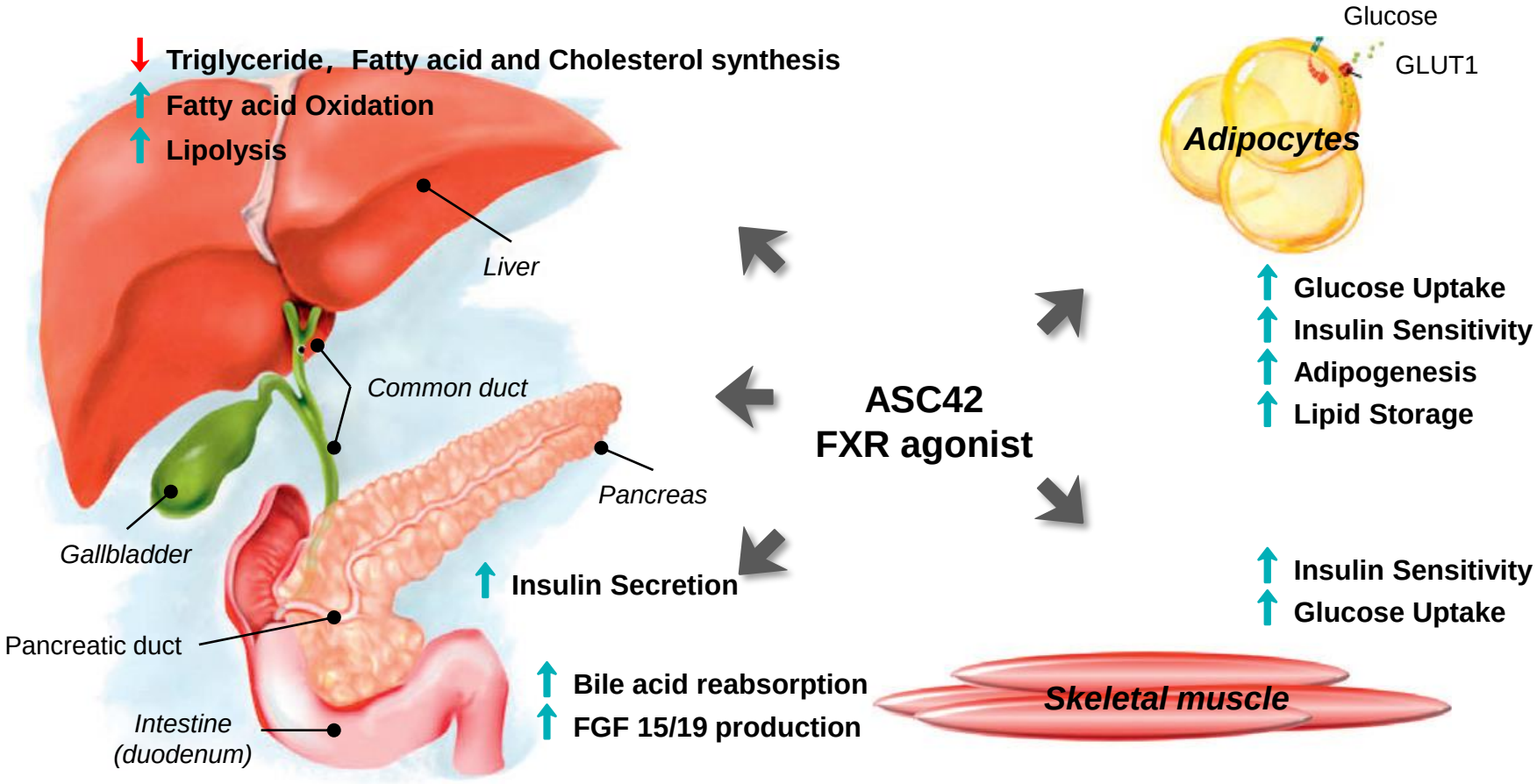
Placebo-adjusted relative change (mean) from baseline after 14 or 28 days of once daily oral dosing of 10 mg ASC41 tablets in overweight and obese subjects



P-value vs placebo

Gannex data

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

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
- Oral tablet formulation developed with in-house proprietary technology and stable at room temperature

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

- No pruritus observed during 14-day treatment of the once-daily human therapeutic dose of 15 mg.
- FXR target engagement biomarker FGF19 increased 1632% on Day 14 of treatment with 15 mg, once-daily
- FXR target engagement biomarker C4 decreased 93% on Day 14 of treatment with 15 mg, once-daily
- Mean LDL-C values remained within the normal range during 14-day, once daily treatment with 15 mg
- There were no treatment-emergent ALT and AST elevations during 14-day, once daily treatment with 15 mg
- Doses selected for Phase II trial in patients with NASH, which will be initiated by the end of 2021

Combo Therapies: Synergies among ASC40, ASC41 and ASC42

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

THANKS

GANNEX