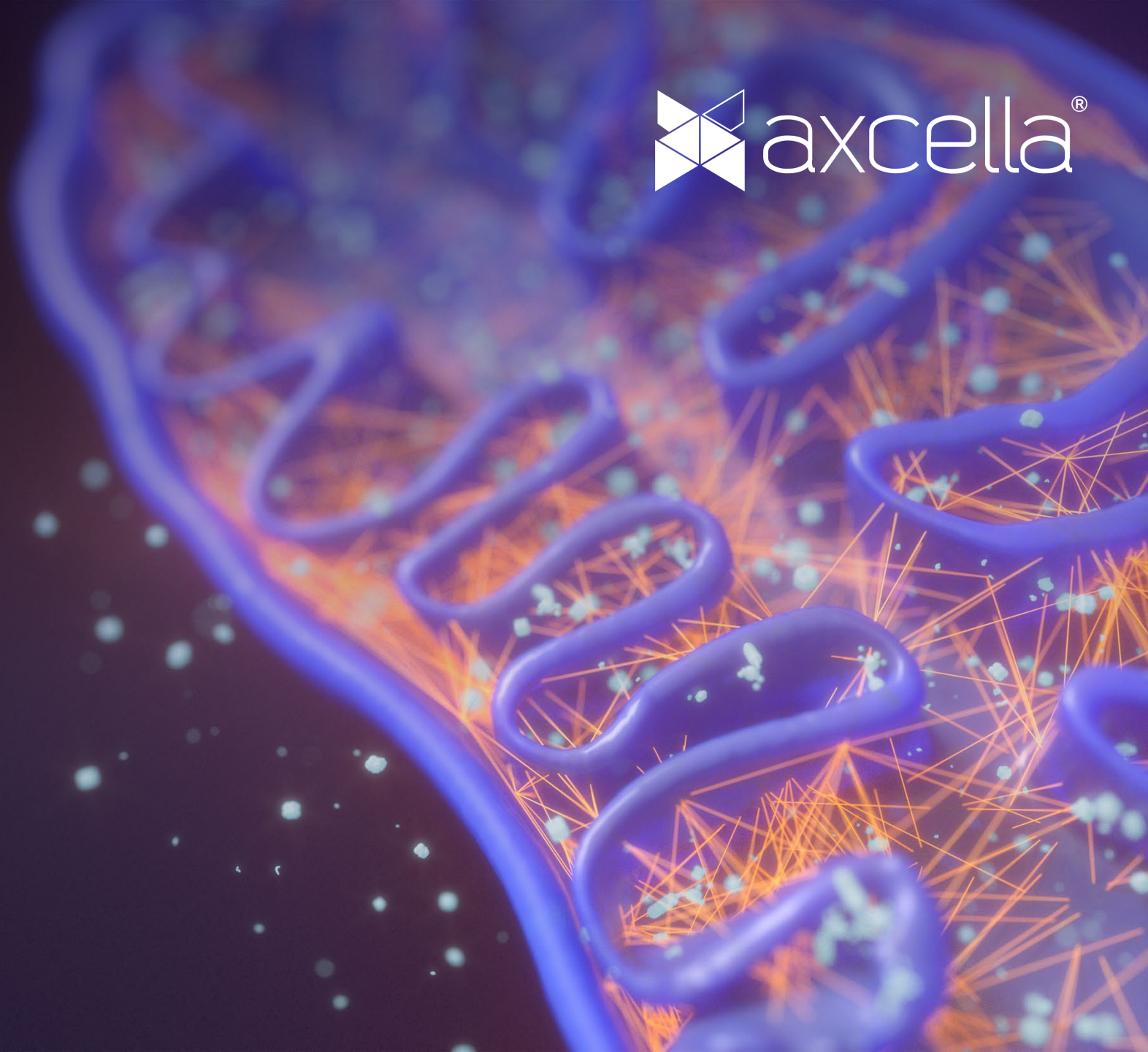
NASDAQ: AXLA

AXA1125-101 Interim Analysis



September 29, 2022

Forward-Looking Statements

This presentation contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, statements regarding the characteristics, competitive position and development potential of AXA1125 and potential future EMM compositions, the potential for AXA1125 to serve as a treatment for Long COVID and a first-line NASH monotherapy for adult and pediatric patients and be used in combination with other agents if required, the design, status and timing of the company's Phase 2a and Phase 2b clinical trials of AXA1125, the intended results of the company's strategy and approach, the size and growth potential of the markets for the company's product candidates, the company's intellectual property position, the company's cash runway and the company's ability to address other complex diseases and conditions utilizing EMM compositions. The words "may," "will," "could," "would," "should," "expect," "plan," "anticipate," "intend," "believe," "estimate," "predict," "project," "potential," "continue," "target" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. Any forward-looking statements in this presentation are based on management's current expectations and beliefs and are subject to a number of risks, uncertainties and important factors that may cause actual events or results to differ materially from those expressed or implied by any forward-looking statements contained in this presentation, including, without limitation, those related to the potential impact of COVID-19 or other events on our ability to conduct and complete ongoing or planned clinical studies and clinical trials and planned submissions to FDA or other regulatory authorities in a timely manner or at all due to patient or principal investigator recruitment or availability challenges, clinical trial site shutdowns or other interruptions and potential limitations on the quality, completeness and interpretability of data we are able to collect in our clinical studies and potential delays in disclosure of the same; other potential impacts of COVID-19 or other events on our business and financial results, including with respect to our ability to raise additional capital and operational disruptions or delays, changes in law, regulations, or interpretations and enforcement of regulatory guidance; clinical trial initiation plans and timing, clinical trial design and target indication(s) for AXA1125, the clinical development and safety profile of our product candidates and their health or therapeutic potential; whether and when, if at all, our product candidates will receive approval from the FDA or other comparable regulatory authorities, and for which, if any, indications; competition from other biotechnology companies; past results from clinical studies not being representative of future results and other risks identified in our SEC filings, including Axcella's Annual Report on Form 10-K, Quarterly Report on Form 10-Q and subsequent filings with the SEC. The company cautions you not to place undue reliance on any forward-looking statements, which speak only as of the date they are made. Axcella disclaims any obligation to publicly update or revise any such statements to reflect any change in expectations or in events, conditions or circumstances on which any such statements may be based, or that may affect the likelihood that actual results will differ from those set forth in the forward-looking statements. Any forward-looking statements contained in this presentation represent our views only as of the date hereof and should not be relied upon as representing its views as of any subsequent date.

Today's Agenda

Agenda	Length	Time	Speakers
Introductory Remarks	10 min	8:00 am – 8:10 am	Bill Hinshaw
Clinical Trial Design & Results	20 min	8:10 am – 8:30 am	Margaret Koziel
Mechanism of AXA1125	10 min	8:30 am – 8:40 am	Karim Azer
Clinical Relevance and Landscape	15 min	8:40 am – 8:55 am	Dr. Harrison
Closing Remarks	5 min	8:55 am – 9:00 am	Bill Hinshaw
Q&A	15 min	9:00 am – 9:15 am	Bill, Margaret, Karim, Dr. Harrison, Bob

Dr. Stephen Harrison
Medical Director for Pinnacle Clinical Research
President of Summit Clinical Research

Multi-Targeted Therapeutics to Restore Homeostasis

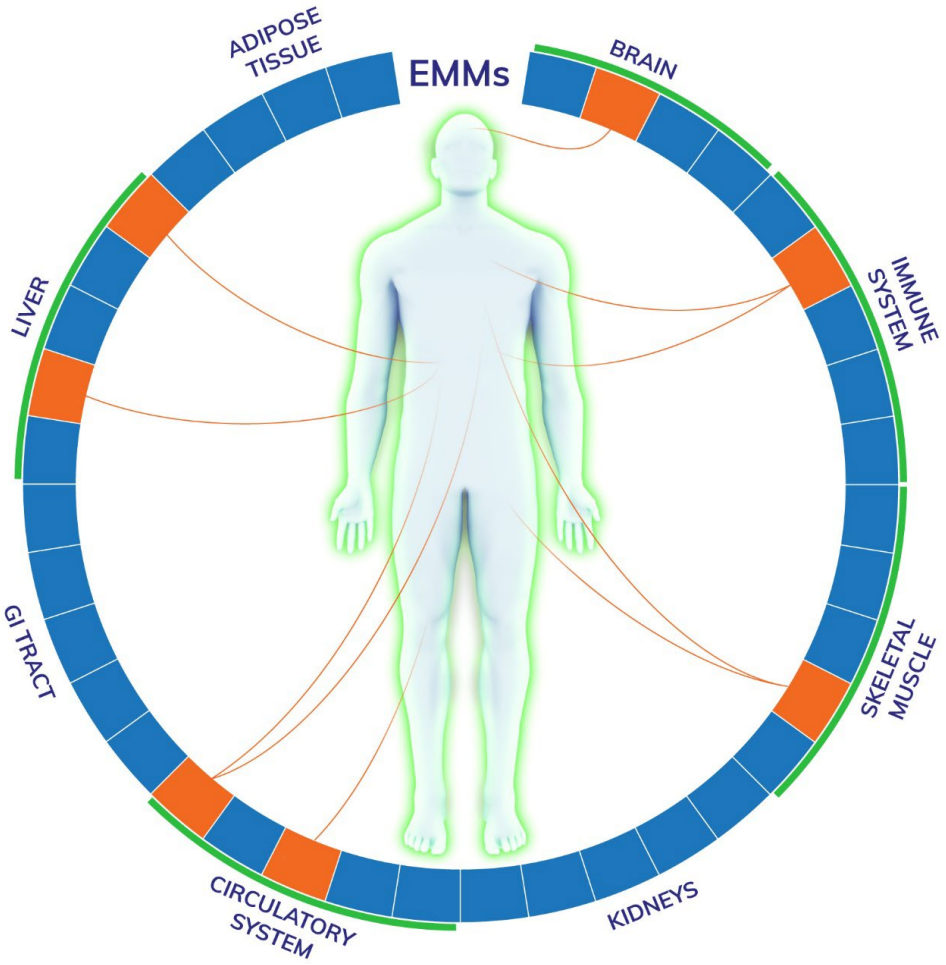
Leveraging Endogenous Metabolic Modulator (EMM) compositions to treat complex medical conditions

- Complex conditions are driven by dysregulation in multiple biological pathways, limiting the effect of single-targeted therapies

- Amino acid-based therapeutics can be safely used to:
  - Regulate key signaling pathways
  - Restore mitochondrial function
  - Shift substrate/redox balance to restore homeostasis

- Potential therapeutic benefits include:
  - Enhancing muscle function
  - Correcting metabolism
  - Decreasing inflammation
  - Improving neurocognition
  - Rebalancing IEMs
  - Reducing fibrosis

Axcella's clinical data demonstrate the potential to harness the power of EMMs to tackle complex chronic conditions

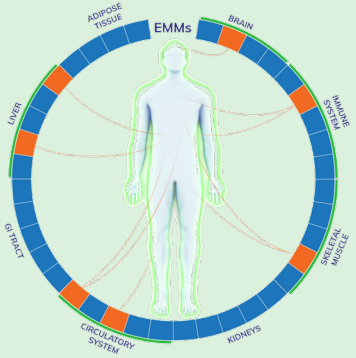


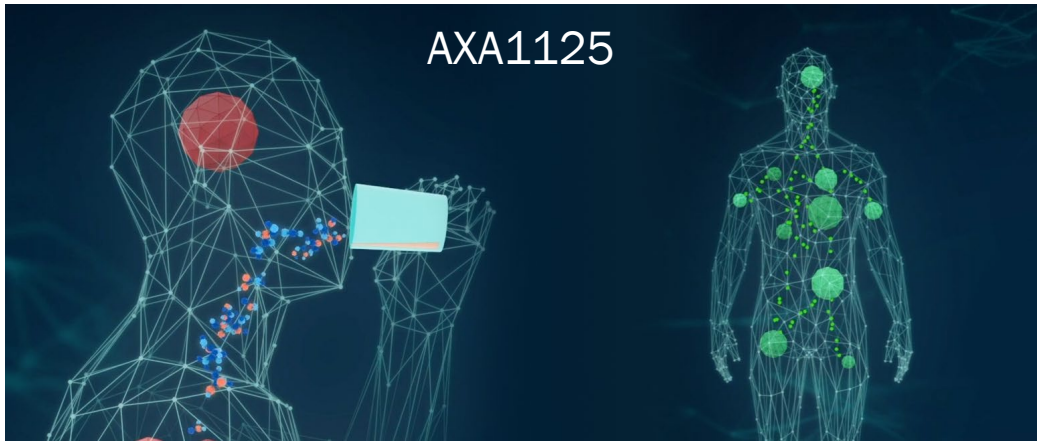
IEM = Inborn Errors of Metabolism

World leader of multi-targeted therapies in complex diseases

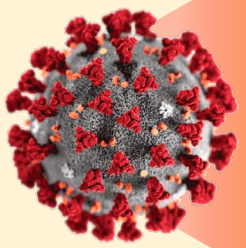
axcella®

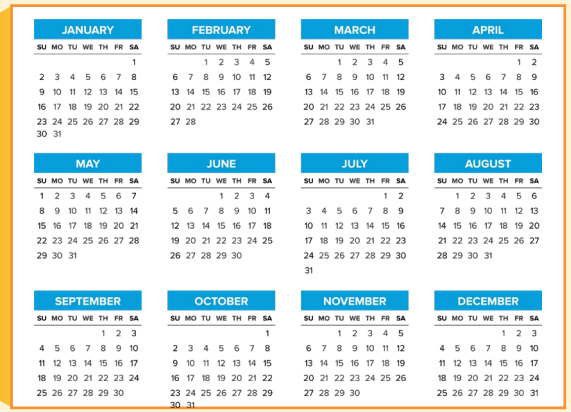
Endogenous Metabolic Modulators (EMMs)



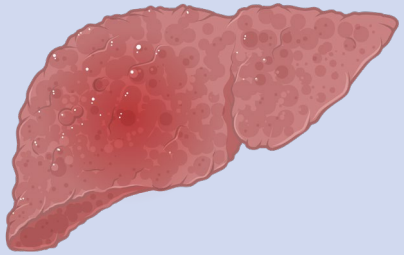


Long COVID





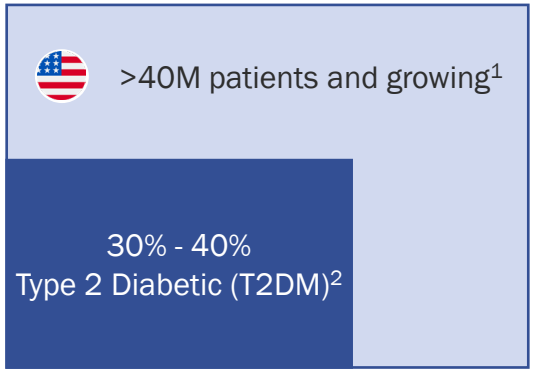
Non-Alcoholic Steatohepatitis (NASH)



NASH is a Complex Disease, Affecting Millions

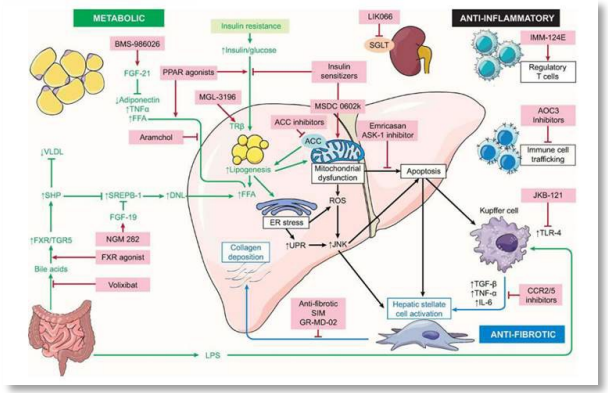
Given the Complexity of NASH, treatment options with different profiles will be required to adequately address broad patient population

State of the NASH Market



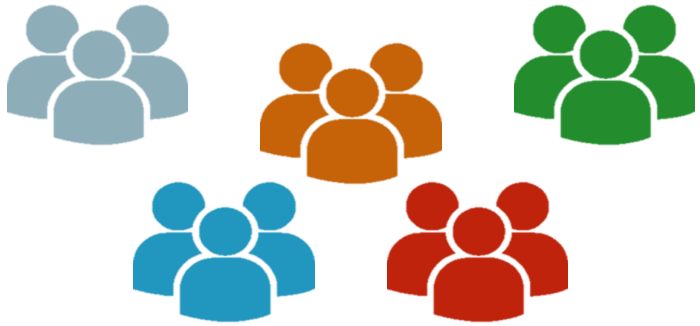
- Expected to be the leading liver transplant cause this year
- U.S. market expected to reach at least $8 billion by 2027[3]
- Approximately 10% of U.S. children are estimated to have NASH[1]
- No Approved Therapies

Complexity of NASH



- NASH disease pathogenesis involves many interacting pathways
- Due to complexity of disease, single targeted mechanisms have limitations

Need for Options

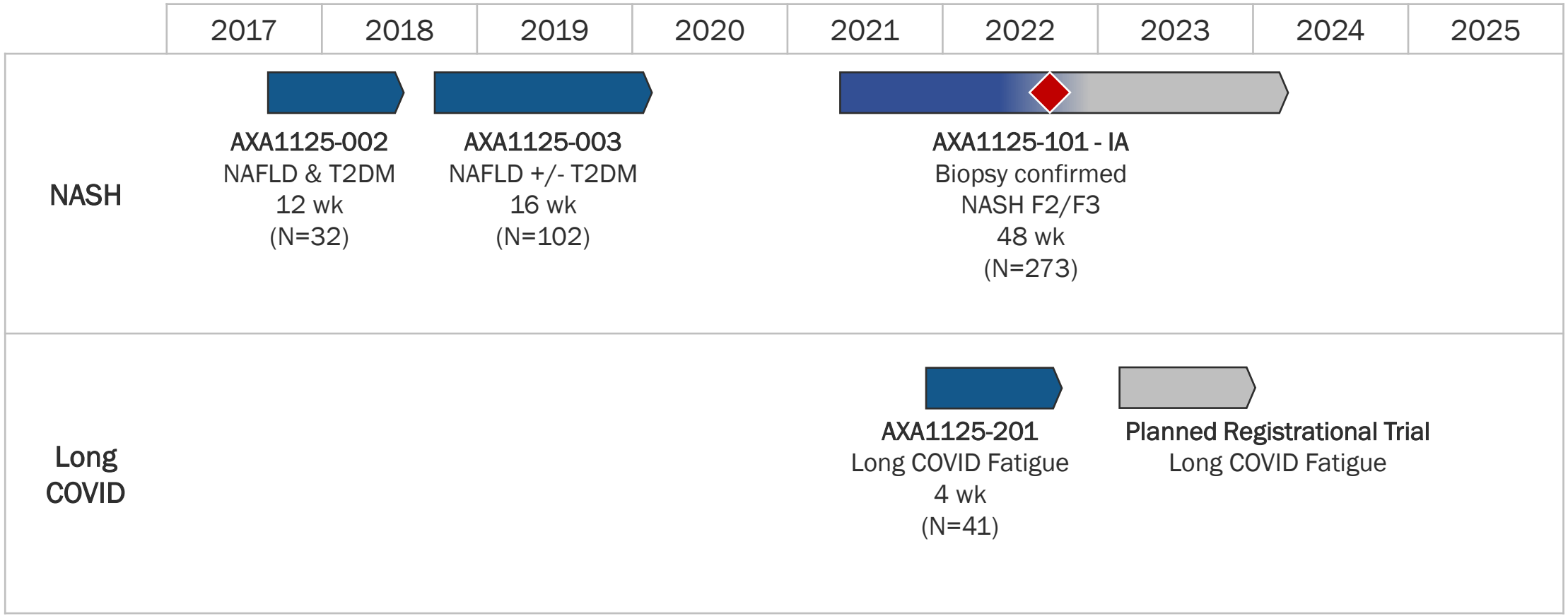


- Heterogeneous patient population
- Very limited pediatric development activity
- Combination/Add-on Therapies an area of focus

1. Global Liver Institute U.S. NASH Action Plan (Dec. 2020).
2. Cusi K. *Diabetologia*. 2016;59:1112-20.
3. Company estimates based on Decision Resources Group (DRG). Non-alcoholic Steatohepatitis Landscape & Forecast. DRG.

AXA1125 Has Demonstrated Positive Data Across Multiple Trials

AXA1125 has been studied in 4 clinical trials between NASH and Long COVID indications



F2/F3= stages of NASH fibrosis; NAFLD=non-alcoholic fatty disease; N=number of subjects; T2DM=type 2 diabetes mellitus; wk=weeks

AXA1125-101 Key Results of Interim Analysis

AXA1125 continues to demonstrate real biological impact and effect in NASH subjects

1. Significant Improvement in Liver Stiffness at 24 weeks

2. Reproduced Improvements in Liver Fat and Inflammation[1]

3. Demonstrates Potential 1st line Safety and Tolerability Profile

1. Harrison SA, et al. *Am J Gastroenterol*. 2021:116;2399-2409.

AXA1125: A Differentiated Product with a Potential Frontline Profile

Elements Supporting a Frontline Profile: AXA1125

Potential Additional AXA1125 Differentiators:

- Type 2 Diabetics
- Planning for pediatric development
- Amenable to combination

MoA = mechanism of action.

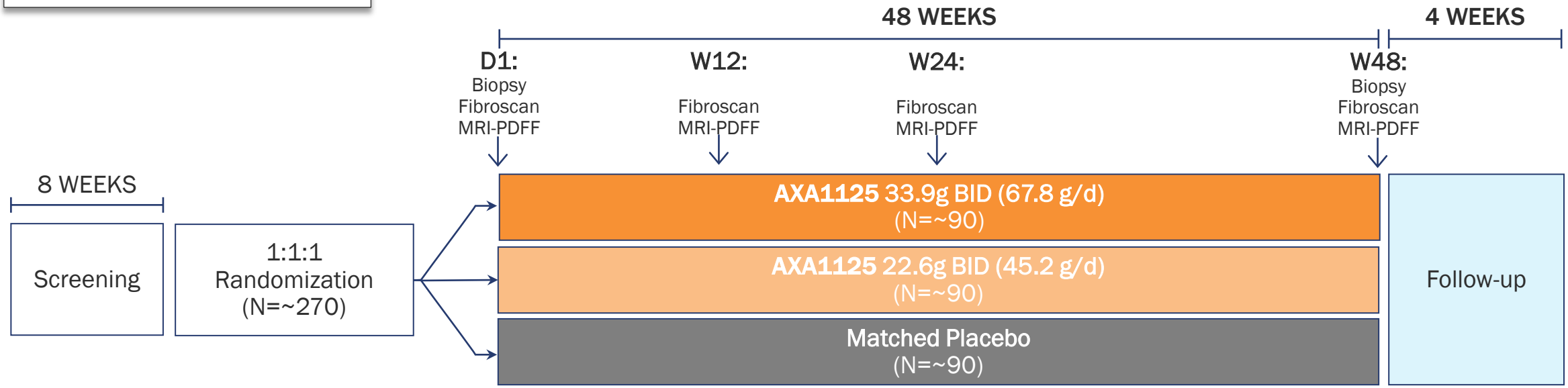
Clinical Trial Design & Results

Dr. Margaret Koziel

Chief Medical Officer

Phase 2b Clinical Trial Underway

Preplanned interim analysis when 30 subjects/arm reached week 12

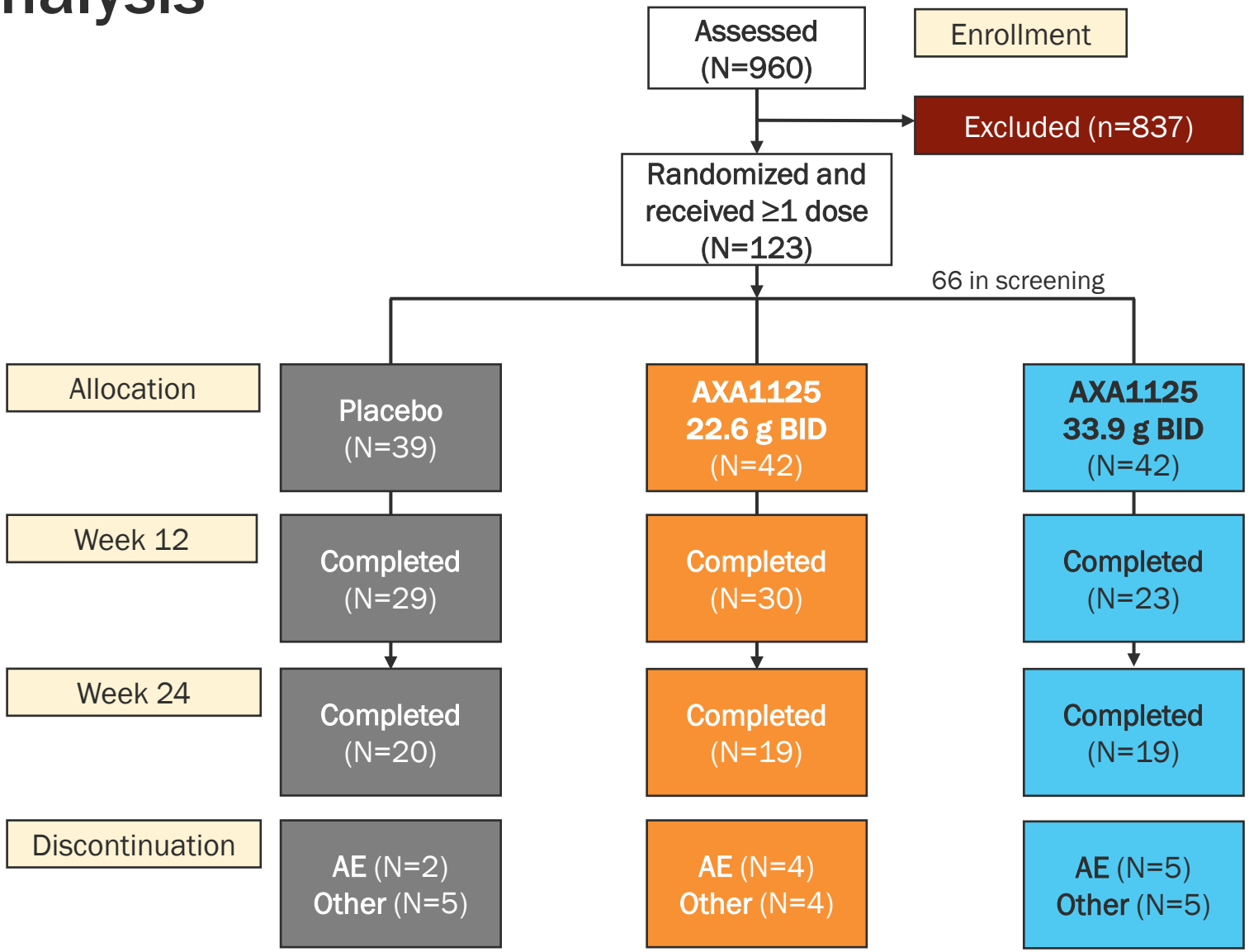


Core elements	Description
Design	• Randomized, double-blind, placebo-controlled, dose-ranging study over 48 weeks
Study population	• Biopsy-proven F2/F3 NASH with NAS≥4 • Stratification by type 2 diabetes status
Preplanned IA on secondary endpoints	• Improvement in non-invasive markers, including MRI-PDFF, ALT and Fibroscan

ALT=alanine aminotransferase; BID=twice a day; D=day; IA=interim analysis; MRI-PDFF=magnetic resonance imaging of the hepatis proton density fat fraction; N=number of subjects; NAS=NAFLD Activity Score.

Subject Flow and Data Analysis

- 123 subjects randomized and received at least one dose
- 82 subjects completed the study through week 12
- 58 subjects completed the study through week 24
- Few subjects discontinued due to AEs



BID=twice a day; AE=adverse events; N=Number of Subjects

Patient Demographics and Baseline Metrics

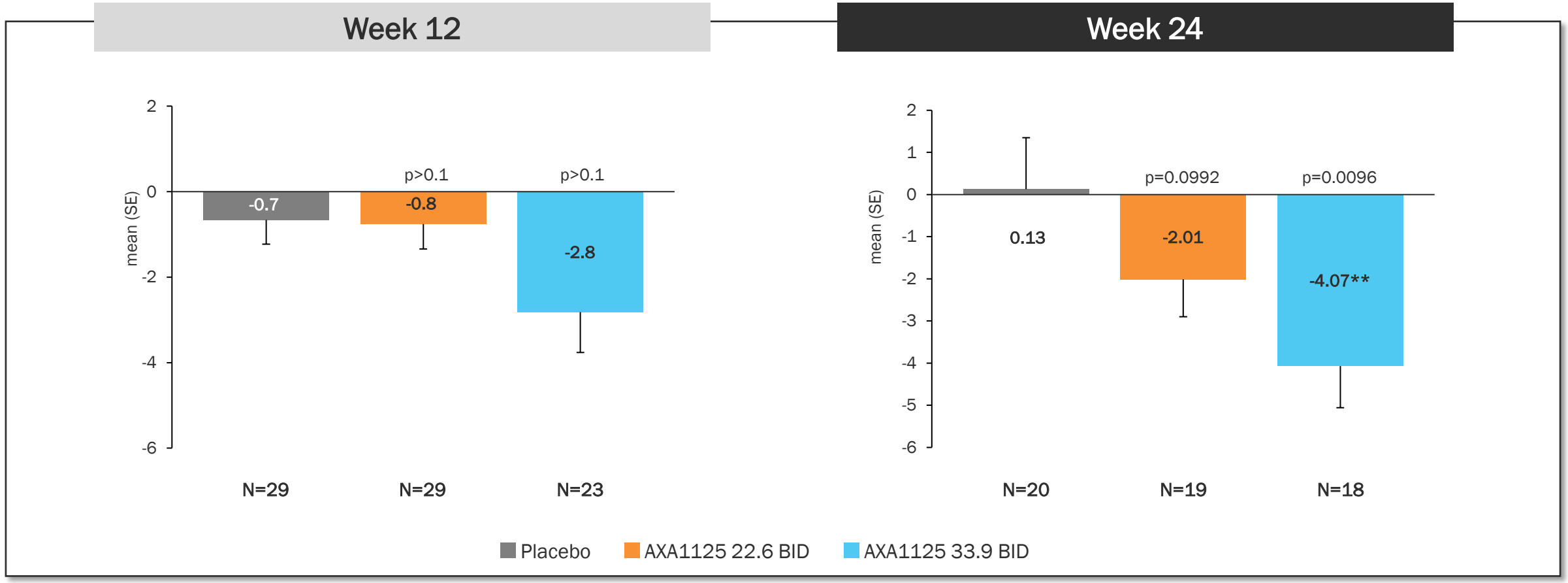
Baseline Demographic/Metric	Placebo (N=39)	AXA1125 22.6 BID (N=42)	AXA1125 33.9 BID (N=42)
Mean age in years (SD)	57.8 (9.8)	55.8 (13.5)	56.2 (12.4)
Sex			
Male, n (%)	12 (30.8)	10 (23.8)	19 (45.2)
Female, n (%)	27 (69.2)	32 (76.2)	23 (54.8)
Mean Body Mass Index, kg/m^2 (SD)	37.86 (7.78)	36.02 (7.08)	37.15 (7.29)
With Type 2 Diabetes, n (%)	22 (56.4)	24 (57.1)	24 (57.1)
Metabolism			
Mean Liver Fat Content by MRI-PDFF, % (SD)	18.991 (7.885)	18.300 (7.547)	20.026 (7.541)
Mean HOMA-IR	13.561 (10.977)	12.455 (10.097)	12.244 (9.460)
HbA1c, % (SD)	6.79 (1.05)	6.43 (1.00)	6.49 (1.05)
Inflammation			
Mean ALT (U/L) (SD)	58.6 (34.3)	51.5 (24.2)	54.1 (36.3)
Fibrosis			
Mean Fibroscan score (kPa) (SD)	13.29 (6.72)	11.40 (3.47)	14.80 (6.63)
Mean Fib-4 (SD)	1.48 (0.65)	1.24 (0.58)	1.32 (0.65)
Mean ELF (SD)	9.966 (0.716)	9.636 (0.843)	10.012 (0.859)

ALT=alanine aminotransferase; BID= twice a day; ELF=enhanced liver fibrosis; Fib-4=Fibrosis-4; HbA1c=hemoglobin A1C; HOMA IR=homeostatic measure of insulin resistance; kPa=kilopascals; MRI-PDFF=magnetic resonance imaging of the hepatis proton density fat fraction; SD=standard deviation

Effects on Non-Invasive Measures

Significant Improvements in Liver Stiffness as Measured by FibroScan

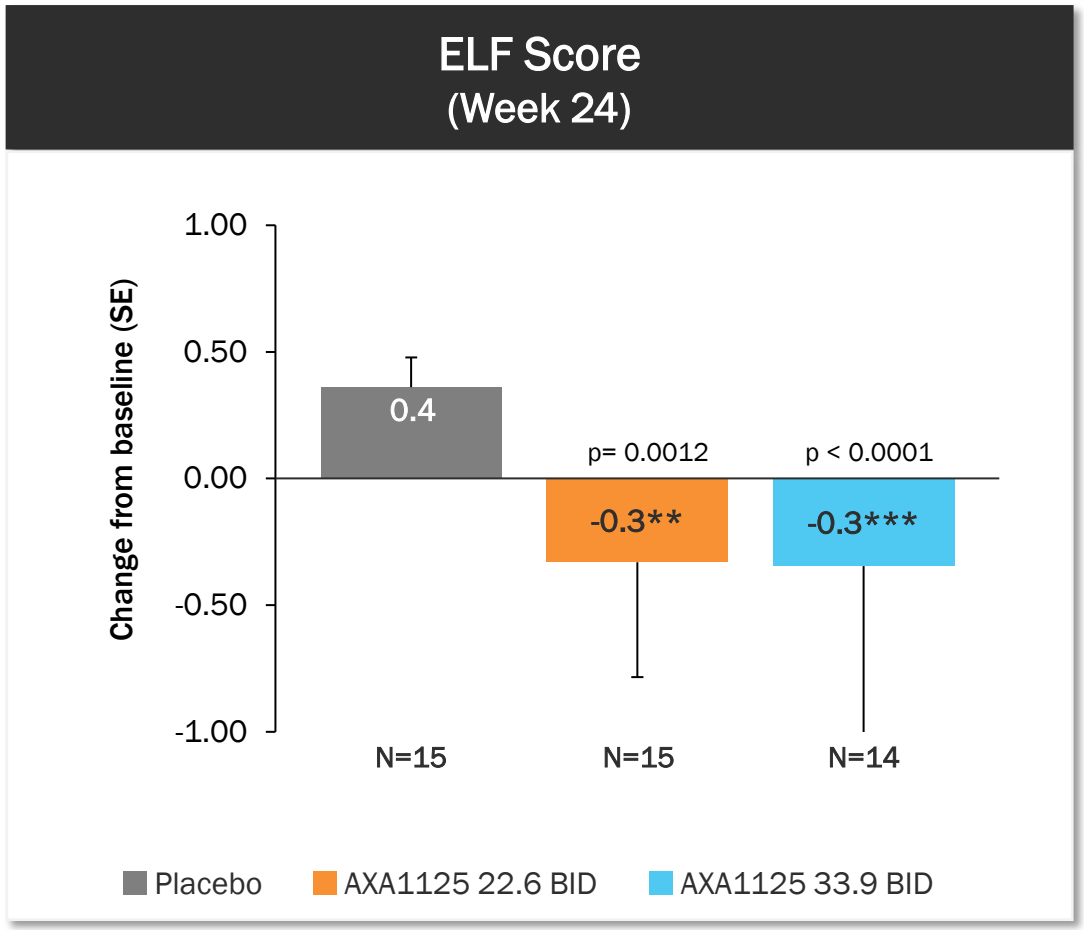
Consistent with prior data on fibrosis markers at week 16

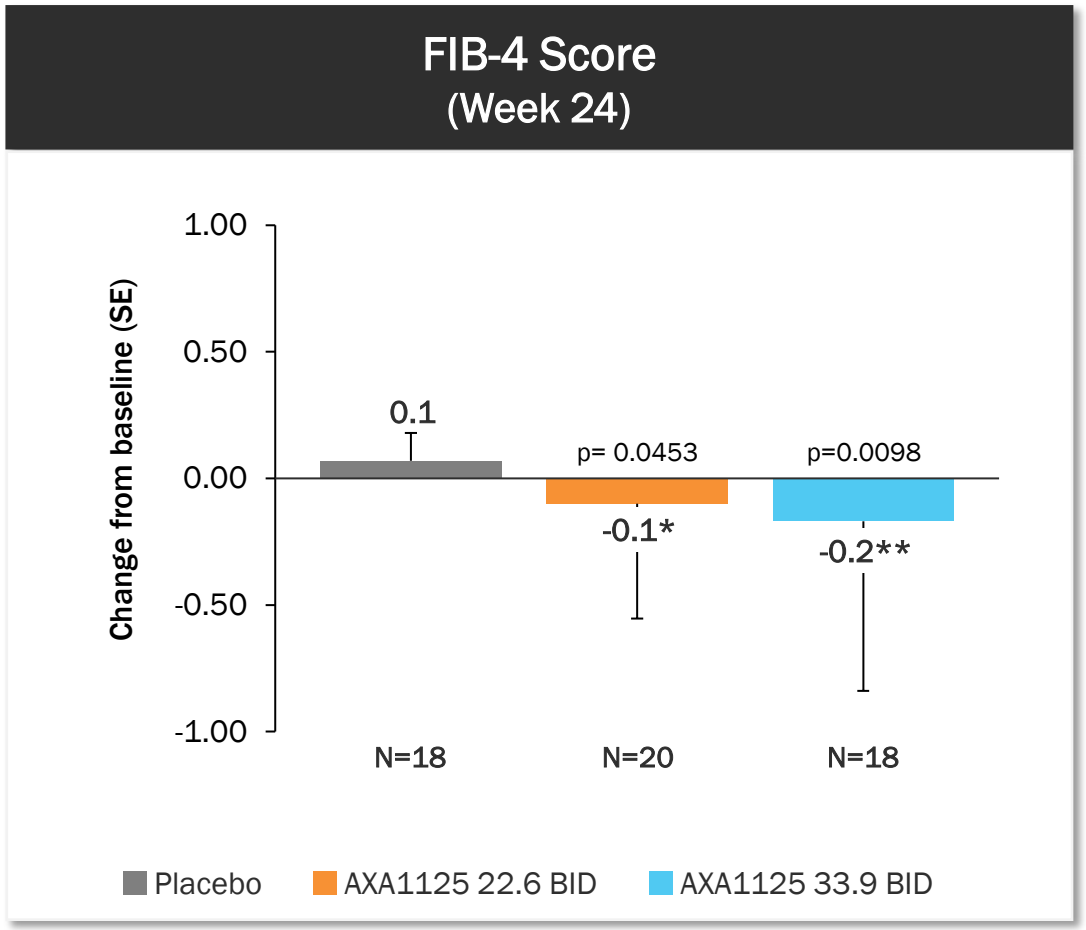


*p<0.05, **p<0.01, ***p<0.001, versus placebo; P values derived using mixed models approach. BID=twice a day; LSM=liver stiffness measurement; kPa=kilo pascals; SE=standard error; N=Number of Subjects

Blood Biomarkers Provide Further Evidence of Effect on Fibrosis

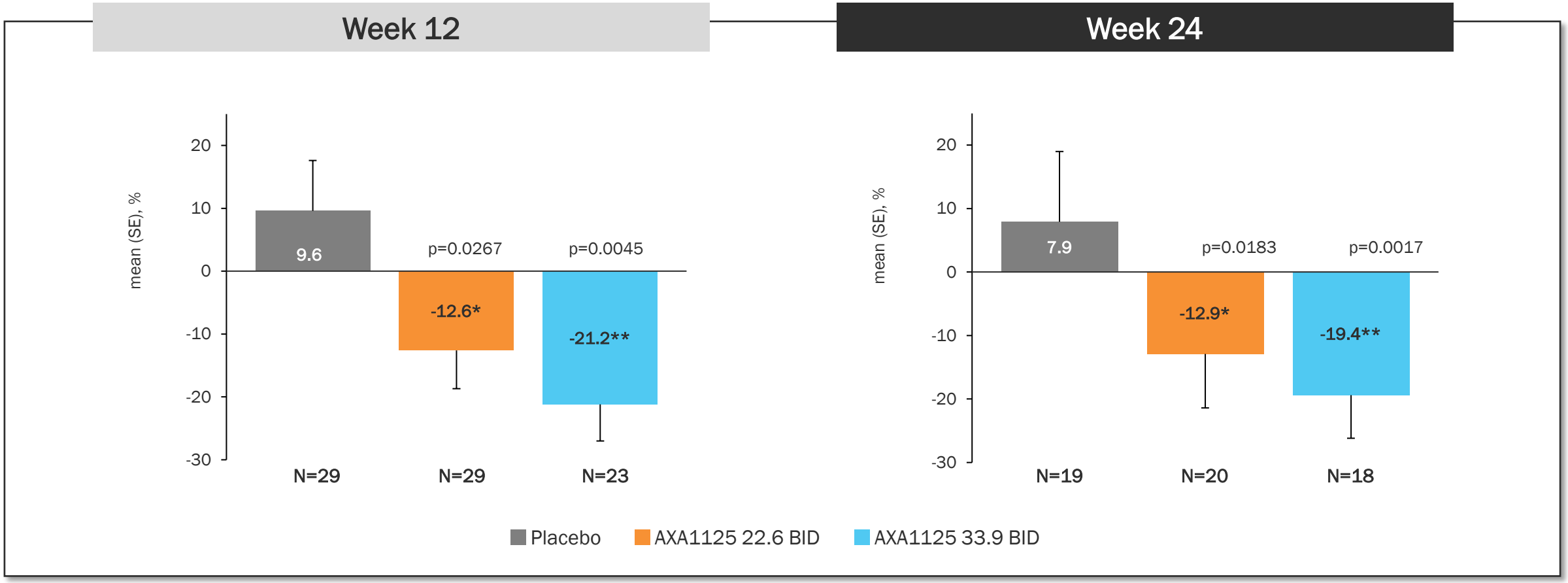
Statistically significant changes seen as early as week 12





*p<0.05, **p<0.01, ***p<0.001, versus placebo; p values derived using mixed models approach. BID=twice daily; N=Number of Subjects; SE=standard error

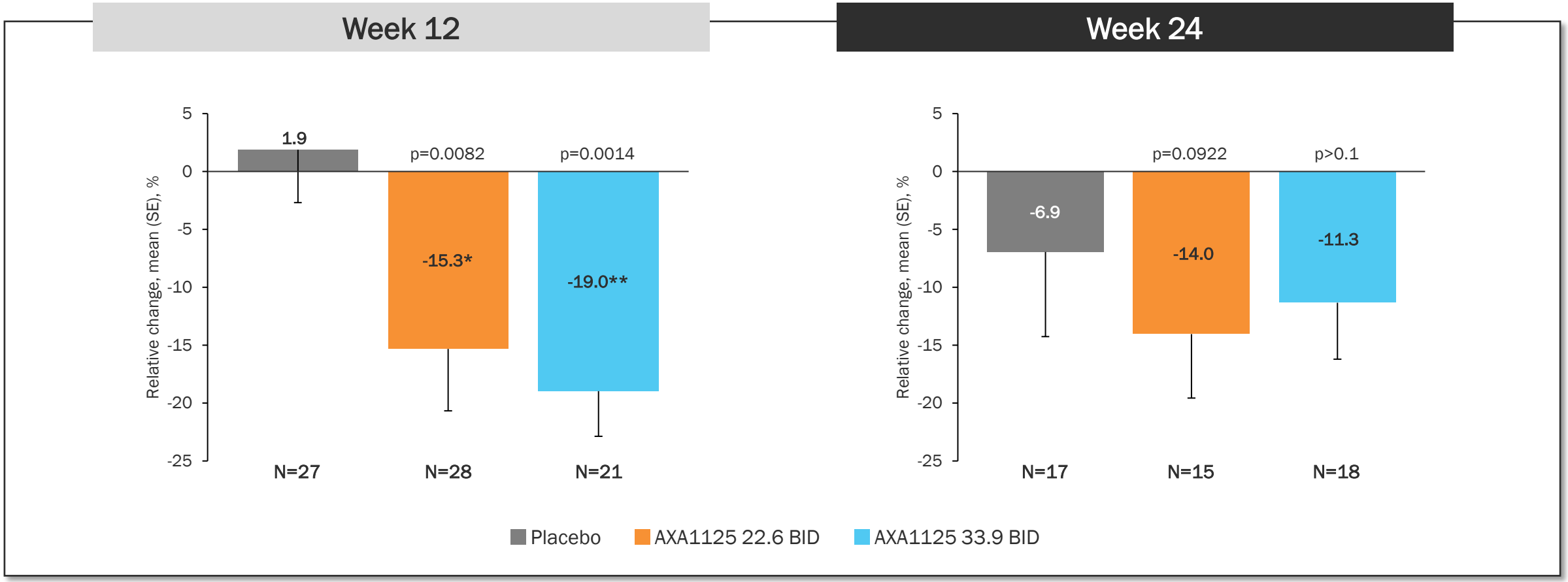
Improvements in ALT (Relative Change)



*p<0.05, **p<0.01, ***p<0.001, versus placebo ; p values derived using mixed models approach. BID=twice daily; LSM=liver stiffness measurement; kPa=kilo pascals; SE=standard error; N=Number of Subjects

MRI-PDFF – Relative Change from Baseline

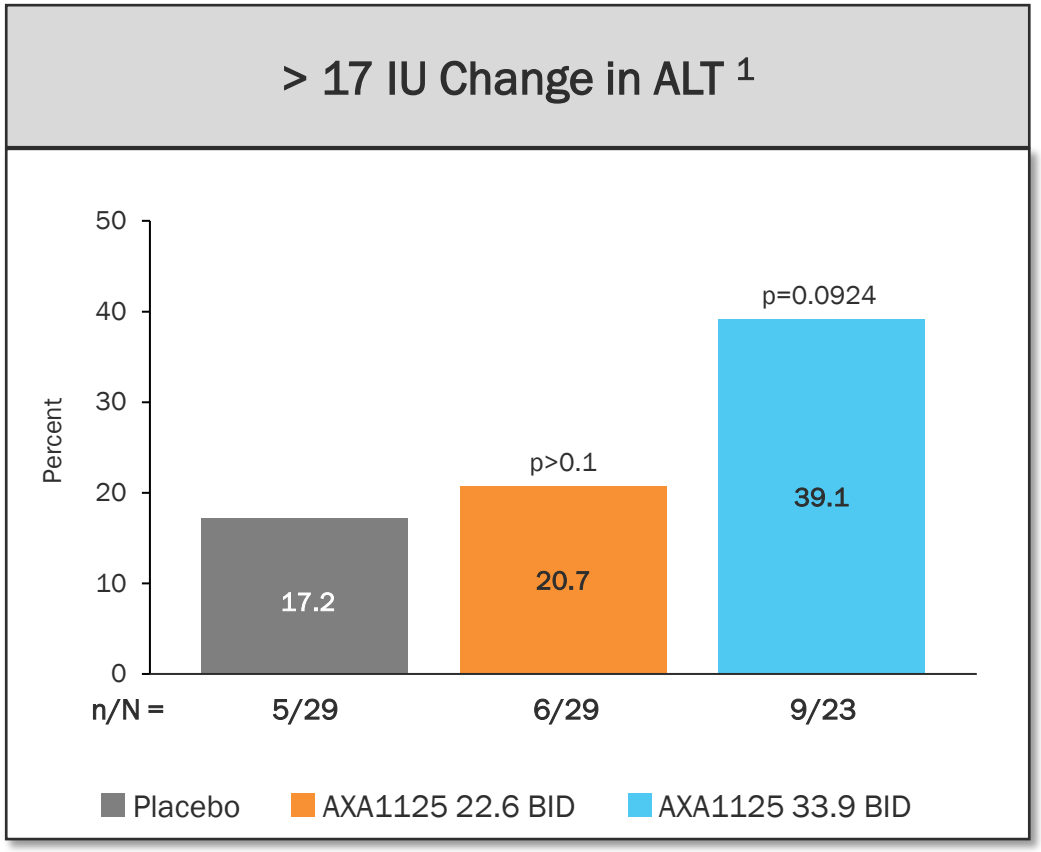
Statistically significant effects at week 12 in relative change from baseline in MRI-PDFF

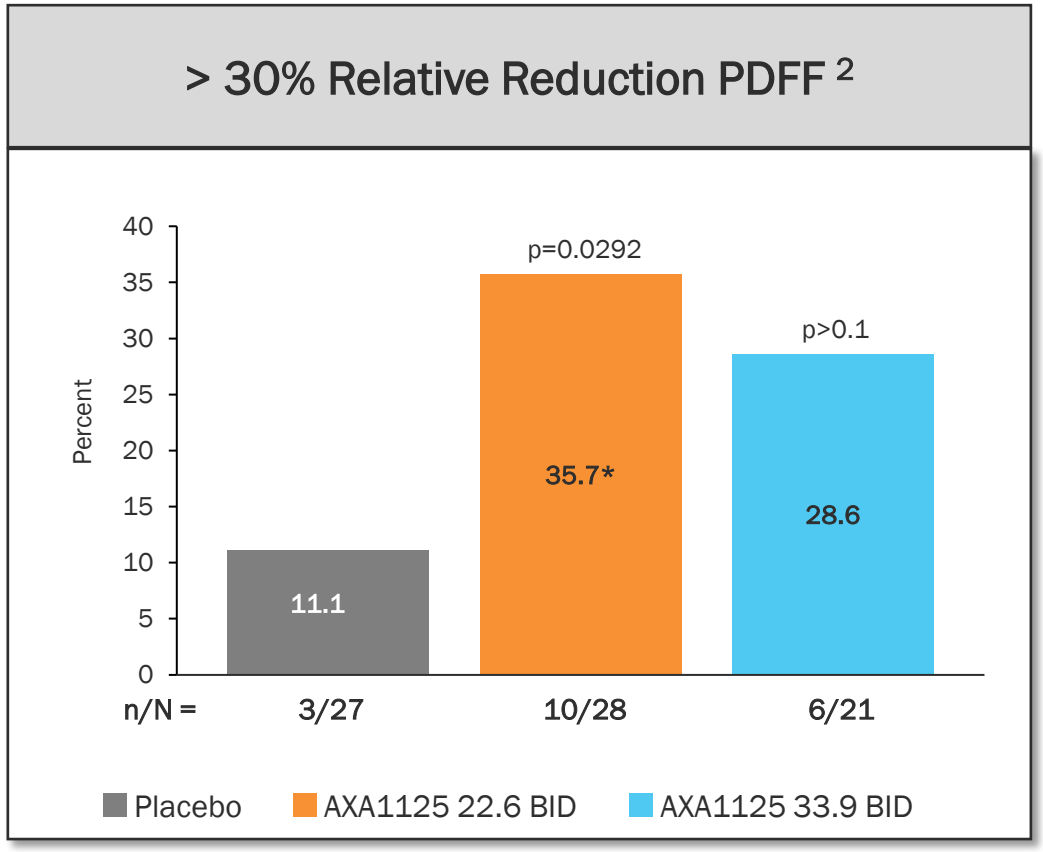


N = the number of subjects of each treatment arm in the specified category at each visit
*p<0.05, **p<0.01, ***p<0.001, versus placebo ; p values derived using mixed models approach. BID=twice daily; MRI-PDFF, magnetic resonance image proton density fat fraction

Proportion Achieving Benchmark Criteria at Week 12

These thresholds have been associated with histologic improvements in NASH clinical trials





n = the number of subjects who met criteria; N= the number of subjects with a post baseline visit
P values using Cochran-Mantel Haenszel test vs placebo *, p< 0.05. 1. Loomba R., et al. *Hepatology* . 2020;72:1219-29. 2. Loomba R., et al. *Gastroenterology* . 2019;156:1219-29

Safety

Safety Interim Analysis

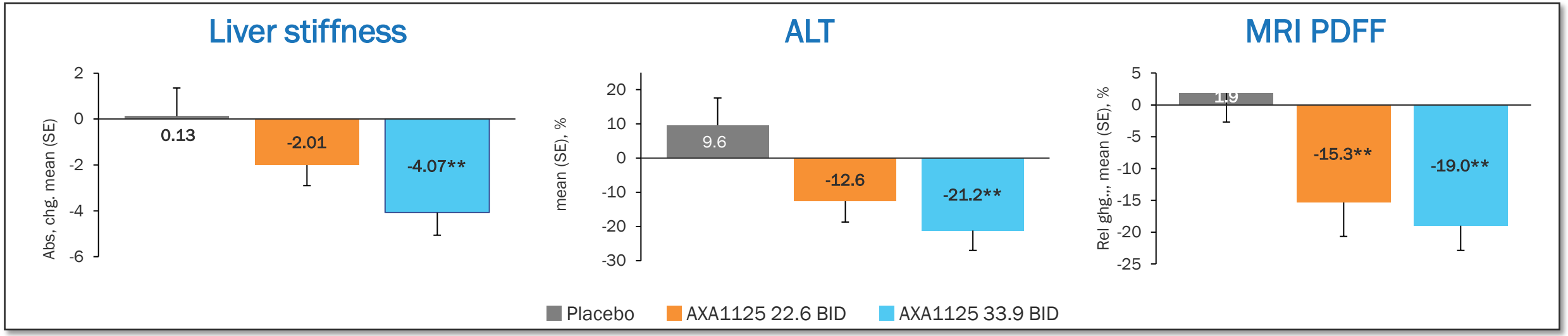
Safety and Tolerability Remains Favorable Based on the Blinded Review

	Placebo N=39 (%)	AXA1125 22.6 g BID N=42 (%)	AXA1125 33.9 g BID N=42 (%)
Subjects with ≥ 1 TEAE	28 (71.8)	28 (66.7)	30 (71.4)
Related TEAE	17 (43.6)	12 (28.6)	18 (42.9)
Maximum Severity, N (% of subjects)			
Grade 1	12 (30.8)	12 (28.6)	11 (26.2)
Grade 2	15 (38.5)	14 (33.3)	15 (35.7)
Grade 3	1 (2.6)	1 (2.4)	4 (9.5)
Grade 4	0	0	0
Grade 5	0	1 (2.4)	0
SAE	1 (2.6%)	1 (2.4%)	4 (4.8%)
Related SAE	0	0	0

- Most frequent TEAEs are gastrointestinal
- All SAEs and the death unrelated to study product
- No safety or tolerability signals of concern were observed; confirmed by an independent unblinded DMC review

Safety based on what subject received on day 1 of dosing. DMC, independent data monitoring committee; SAE, serious adverse event; TEAEs, treatment emergent adverse events

Summary of Results From this Interim Analysis



- Significant effects on liver stiffness comparable to or better than other agents in ph2b/3
- Continued demonstration of effects on relevant pathways of NASH biology
- Observed safety and tolerability pattern consistent with high safety margin
- Both doses are active, and effects consistent in overall population and T2DM
- Results position AXA1125 to be potential first line treatment in NASH

AXA1125 Mechanism of Action

Karim Azer, PhD

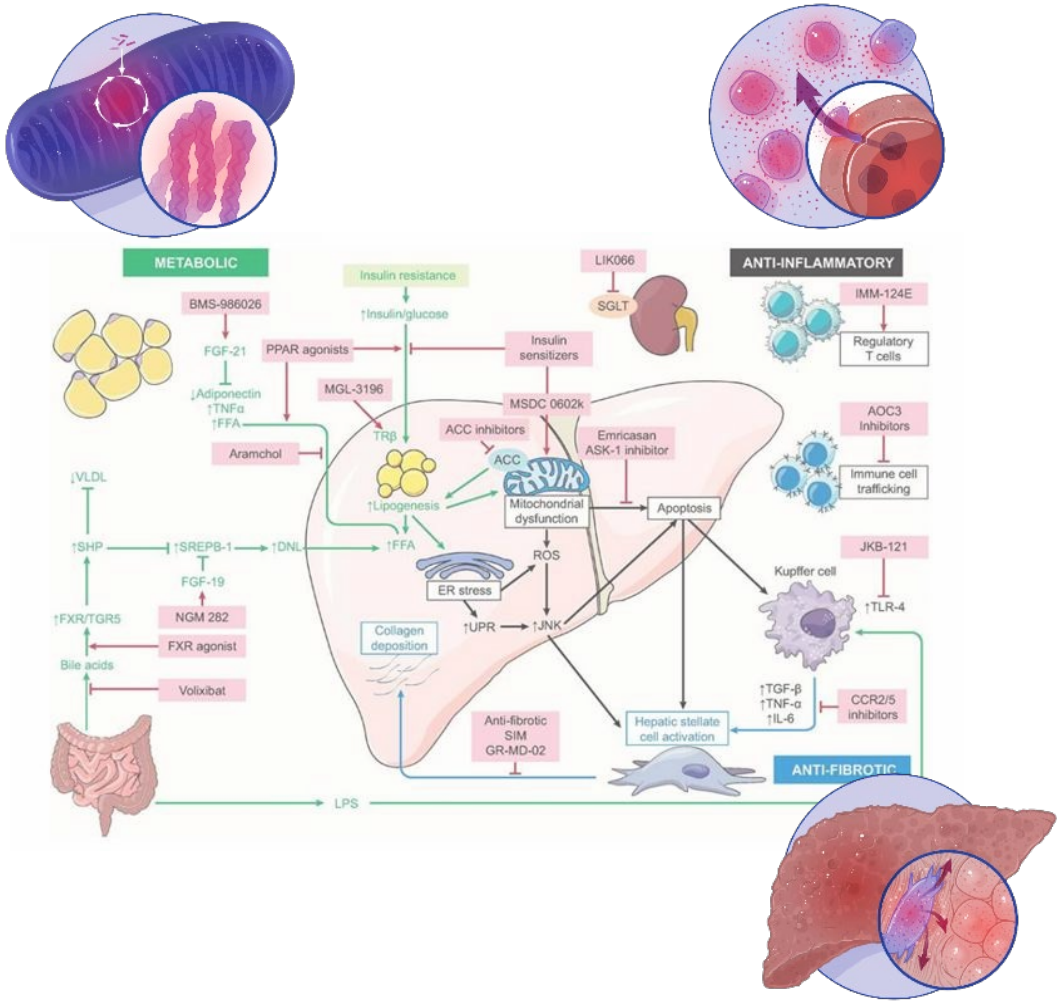
VP of Platform and Discovery

NASH is a Complex Disease with Pleiotropic Disease Pathways

AXA1125 is Multi-Targeted by Design Against Key Pathways across NASH Disease Drivers

Metabolism

Single Targets	AXA1125
• GLP-1	
• SCD1	↑ AA Metabolism
• FGF21	↑ AMPK
• THR-β	↑ PPARα
• PPAR	↑ Urea cycle
• FXR	



Inflammation

Single Targets	AXA1125
• Cyclophilin	↑ Gut barrier/ tight junction
• CCR2/5	↓ Hif1α
	↓ NFkB

Fibrosis

Single Targets	AXA1125
• Galectin	↓ TGFβ
• JNK	
• ASK-1	

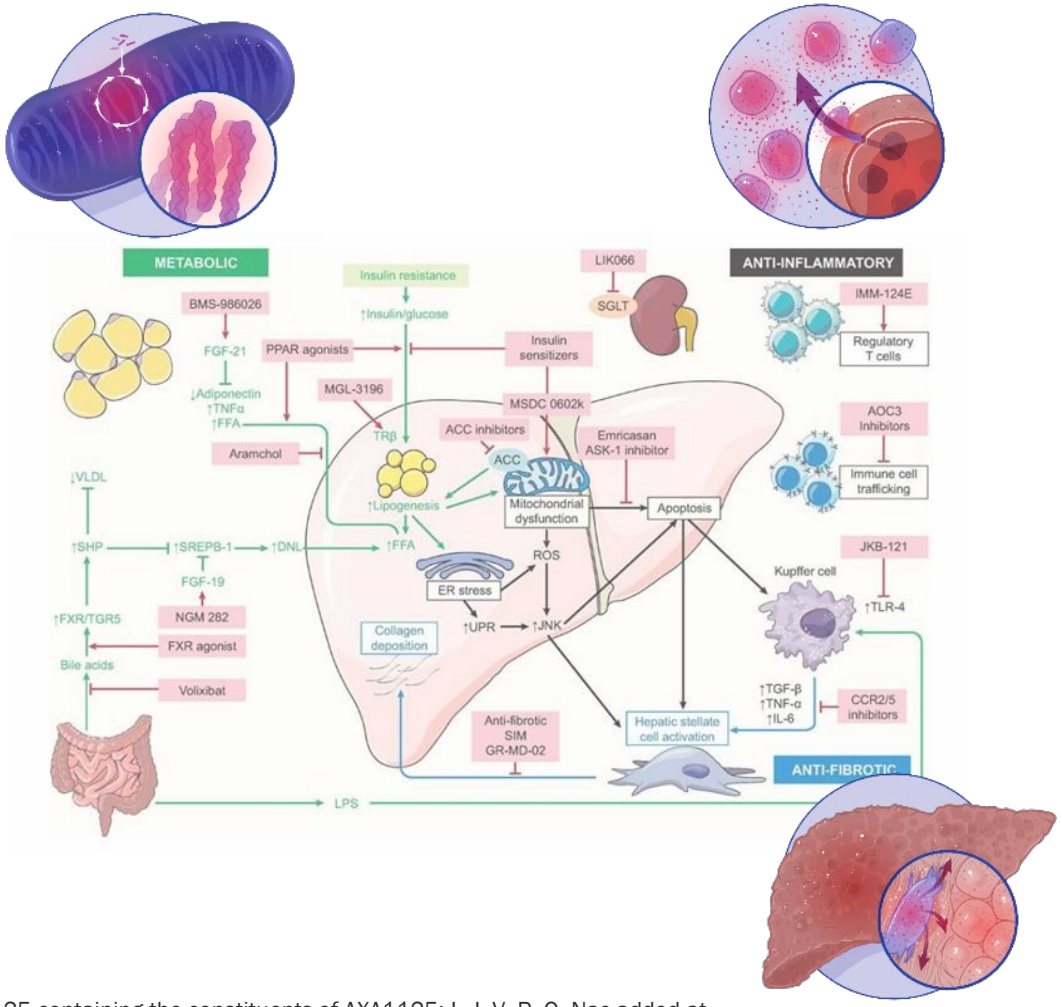
LIVRQNac (AXA1125)

NASH is a Complex Disease with Pleiotropic Disease Pathways

AXA1125 is Multi-Targeted by Design Against Key Pathways across NASH Disease Drivers

Metabolism

Single Targets	AXA1125
• GLP-1 • SCD1 • FGF21 • THR-β • PPAR • FXR	↑Fatty Acid Oxidation ↓Triglycerides



Inflammation

Single Targets	AXA1125
• Cyclophilin • CCR2/5	↓MCP-1 ↓ALT ↓TNF ↓IL-6

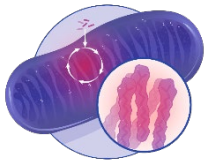
Fibrosis

Single Targets	AXA1125
• Galectin • JNK • ASK-1	↓ProC3 ↓αSMA ↓edu+ ↓HSP47

All studies conducted with LIVRQNac, a nonclinical form of AXA1125 containing the constituents of AXA1125: L, I, V, R, Q, Nac added at specified-fold concentrations above plasma (ex: 7.5×, 15×, 30×), where 1× concentration matches the mean physiological level found in human plasma (values published in the Human Metabolome Database [Wishart et al 2007])."

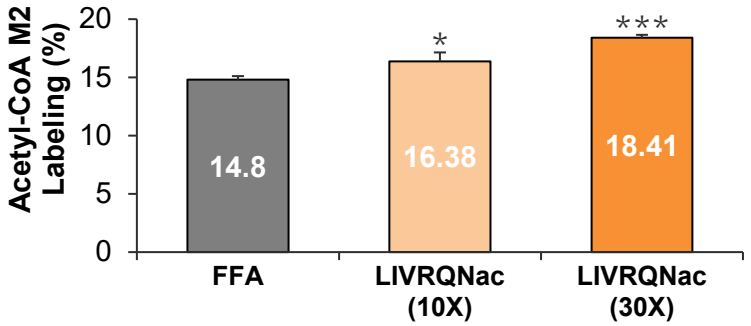
AXA1125 Improves Key Mitochondrial, Lipid and Energy Pathways Driving Reduced Liver Fat and Inflammation

Multi-targeted impact on Metabolism: Beta-Oxidation, Lipid and Bioenergetics

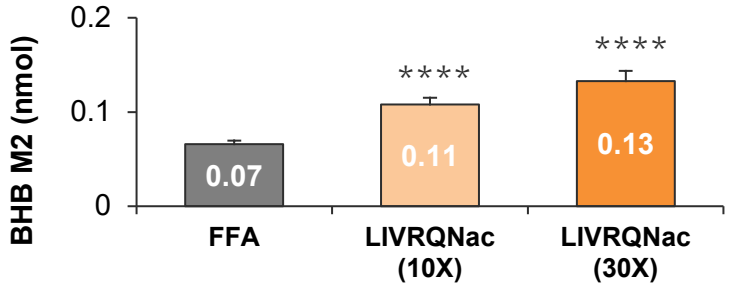


FAO Upregulation & Increased Ketones

↑ Acetyl-CoA M2



↑ BHB M2



*: p<0.05
**: p<0.01
***: p<0.001
****: p<0.0001
(Analysis of variance)

Improved Lipid & Bioenergetic Pathways

	Term	Dir	Score	FDR
1	Peroxisomal matrix	21	1.1e-13	3.7e-10
2	Electron transfer activity	10	2.4e-13	5.3e-10
3	Protein targeting to peroxisome	15	1.4e-11	1.8e-8
4	Fatty acid beta-oxidation	15	4.1e-10	3.1e-7
5	Tricarboxylic acid cycle	20	4.2e-9	0.0000025
6	Regulation of lipid metabolic process	2.5	1.4e-8	0.0000070
7	Electron transport chain	7.4	4.2e-8	0.000018
8	Cholesterol biosynthetic process	13	6.1e-8	0.000024
9	Cholesterol efflux	20	9.3e-8	0.000034
10	Cholesterol metabolic process	10	1.3e-7	0.000039

Lipid Metabolism | Energy Metabolism

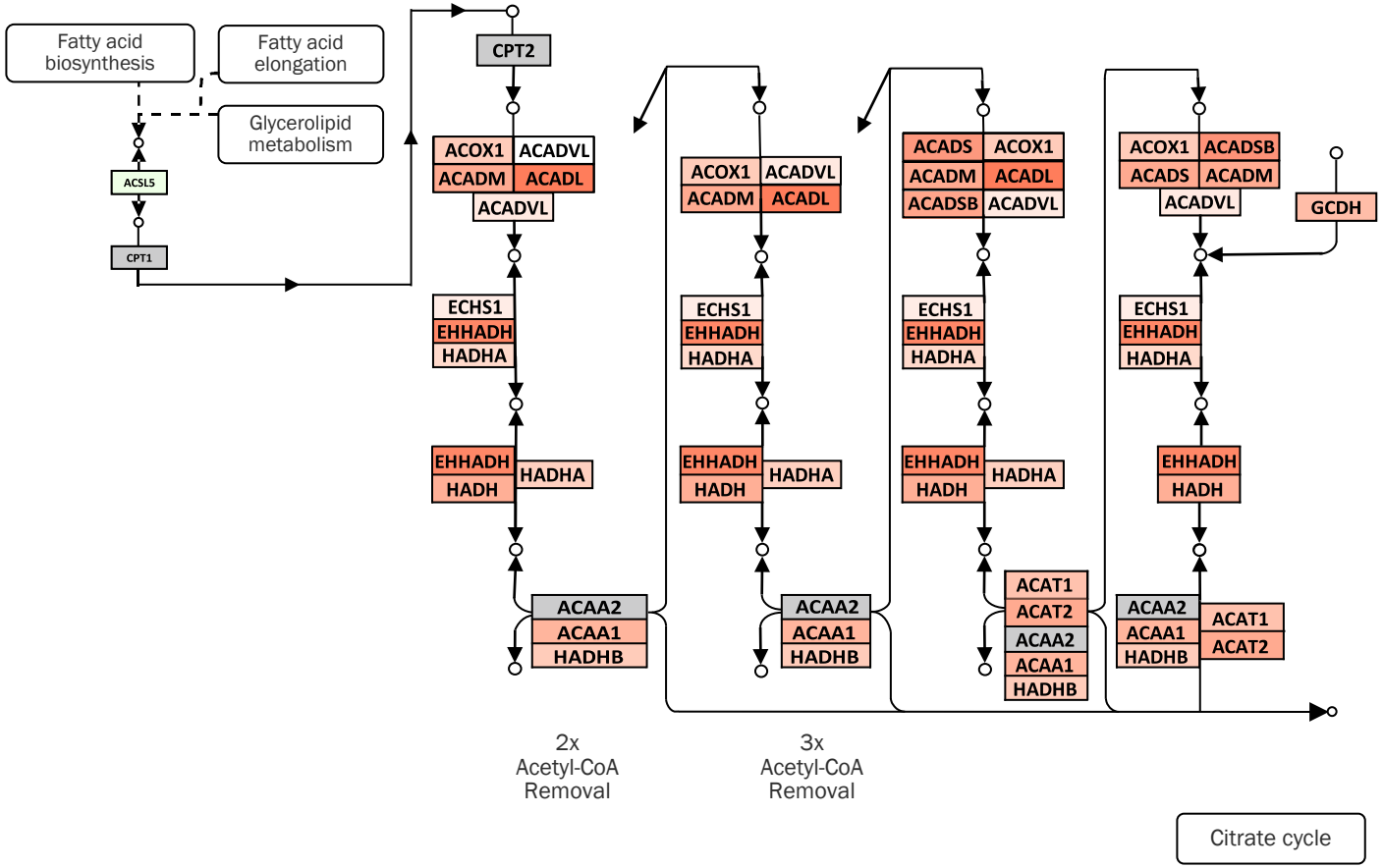
1. Russell et al. *EASL ILC2022* and *EASL NAFLD Summit*. 2022. Primary Human Hepatocytes were co-treated with 83uM:167uM palmitate:oleate and 1 ng/ml TNF-α to simulate conditions in NASH, and were exposed to the same conditions containing 83uM [U-^{13}C]palmitate label before analysis for tracer study. 167uM:333uM palmitate:oleate and 1 ng/ml TNF-α to simulate conditions in NASH, 30x LIVRQNac 48 hour co-treatment used for RNA-Seq.

AXA1125 Upregulates Fat Oxidation Genes and Pathway to Increase Consumption of Fatty Acids and Drive Liver Fat Reduction

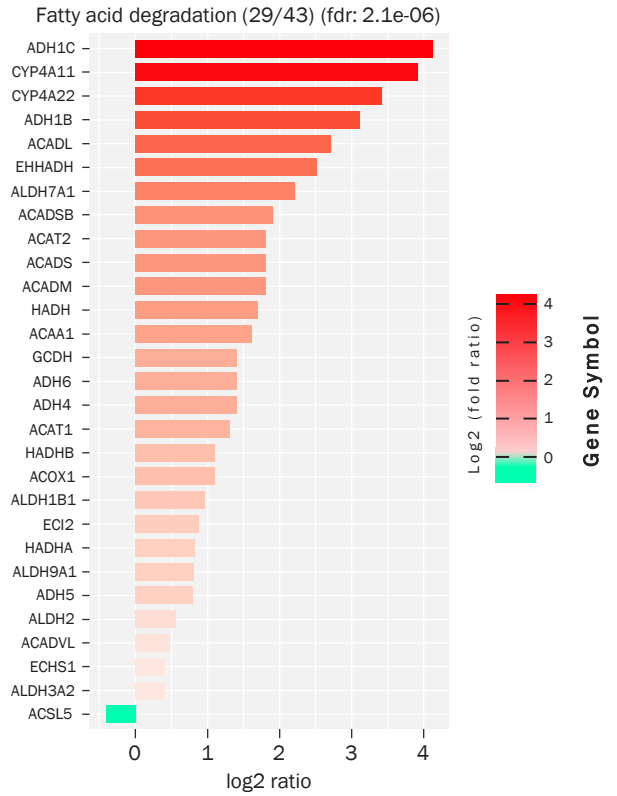
AXA1125 Regulates Mitochondrial Metabolism

Metabolism

Beta Oxidation Pathway Upregulated by AXA1125



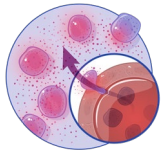
Beta Oxidation Genes Upregulated by AXA1125



Data derived Primary Human Hepatocyte (PHH) Lipotoxicity Model
Primary Human Hepatocytes were co-treated for 48 hours with 167uM:333uM palmitate:oleate and 1 ng/ml TNF-α to simulate conditions in NASH, 30x LIVRQNac, RNA was collected in triplicate for RNA-Seq

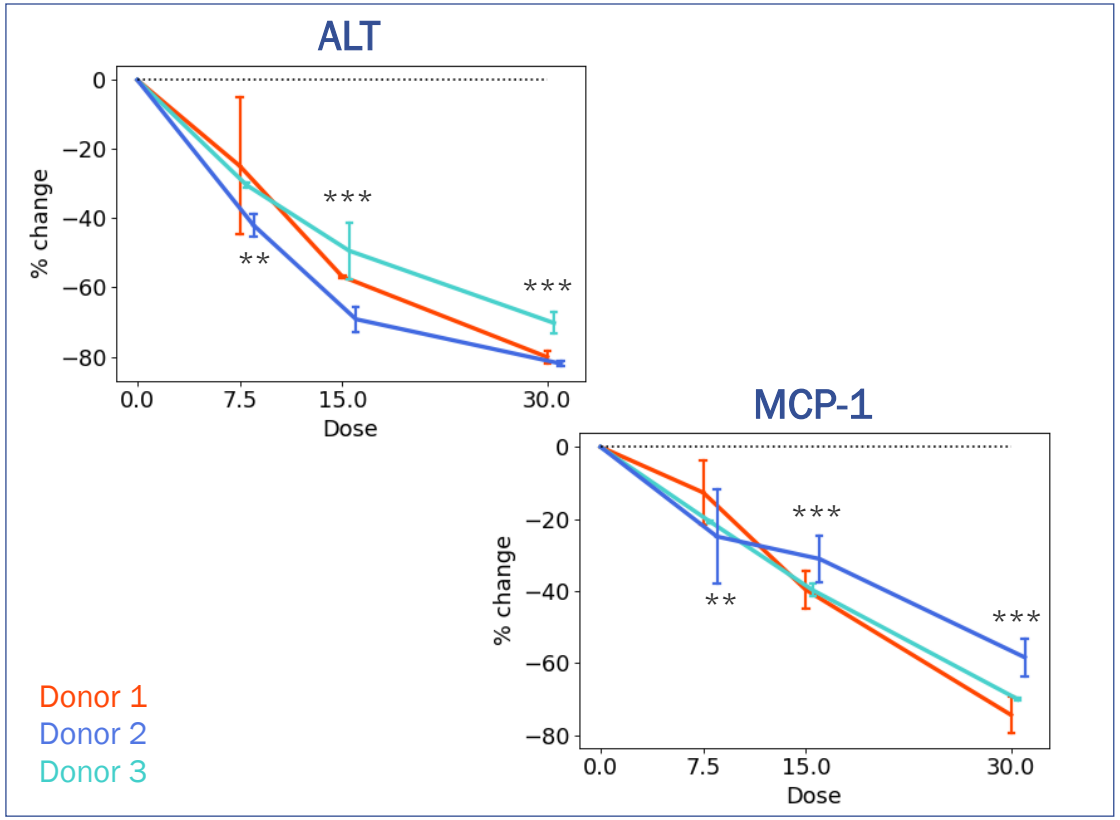
AXA1125 Decreases Hepatocyte Damage and Immune Cell Recruitment and Decreases Proinflammatory Cytokines

Multi-targeted impact on inflammation: Decreased Damage, Recruitment, Cytokines

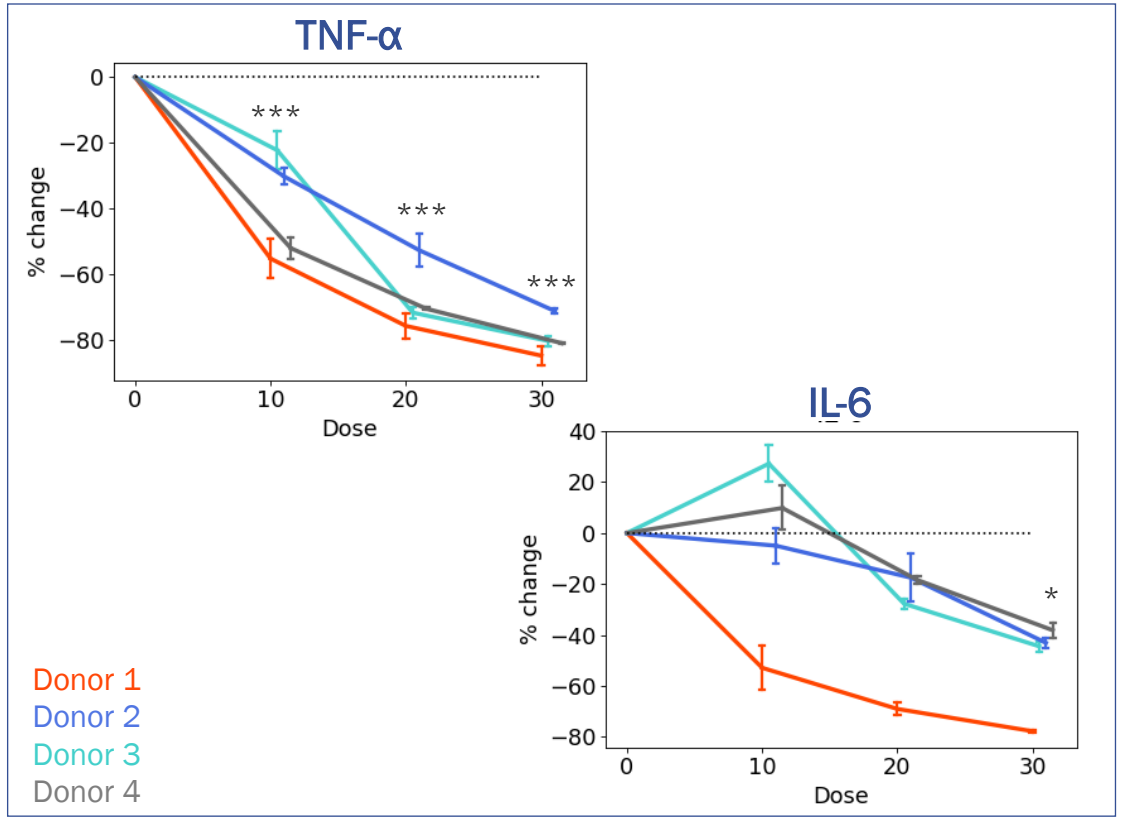


Inflammation

AXA1125 Decreases Hepatocyte Damage and Promotes Immune Recruitment

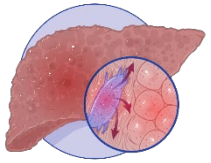


AXA1125 Decreases Macrophage Inflammatory Cytokines



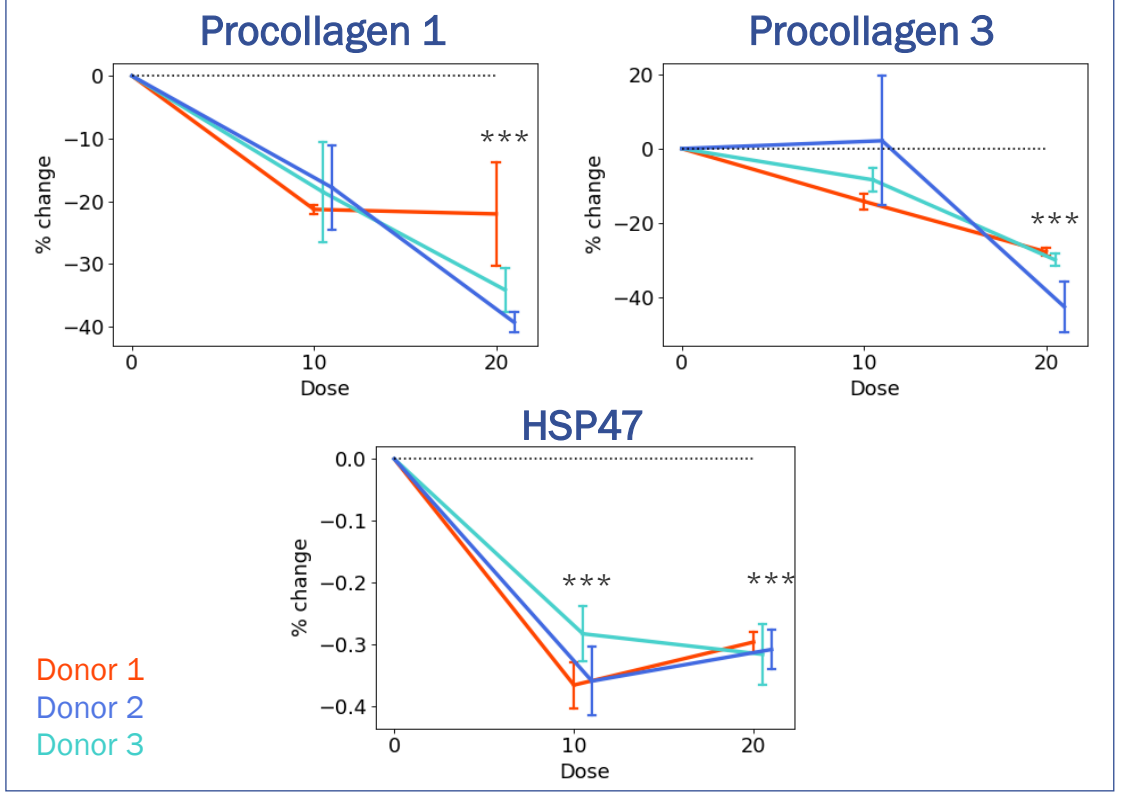
1. Daou et al. *Nat Sci Rep*. 2021. * p < 0.05, ** p < 0.01, *** p < 0.001, Data from Primary Human Hepatocytes (ALT, MCP-1) treated for 48 hours with 167uM:333uM palmitate:oleate and 1 ng/ml TNF-α to simulate conditions in NASH, data normalized to total protein; Data from Primary Human M1-polarized Macrophages (TNF-α, IL-6) pre-treated with LIVRQNac for 24 hours, then stimulated with 0.15ng/mL LPS for 24 hours, data not normalized to nuclei.

AXA1125 Decreases Fibrosis Activation, Proliferation, and Collagen Deposition

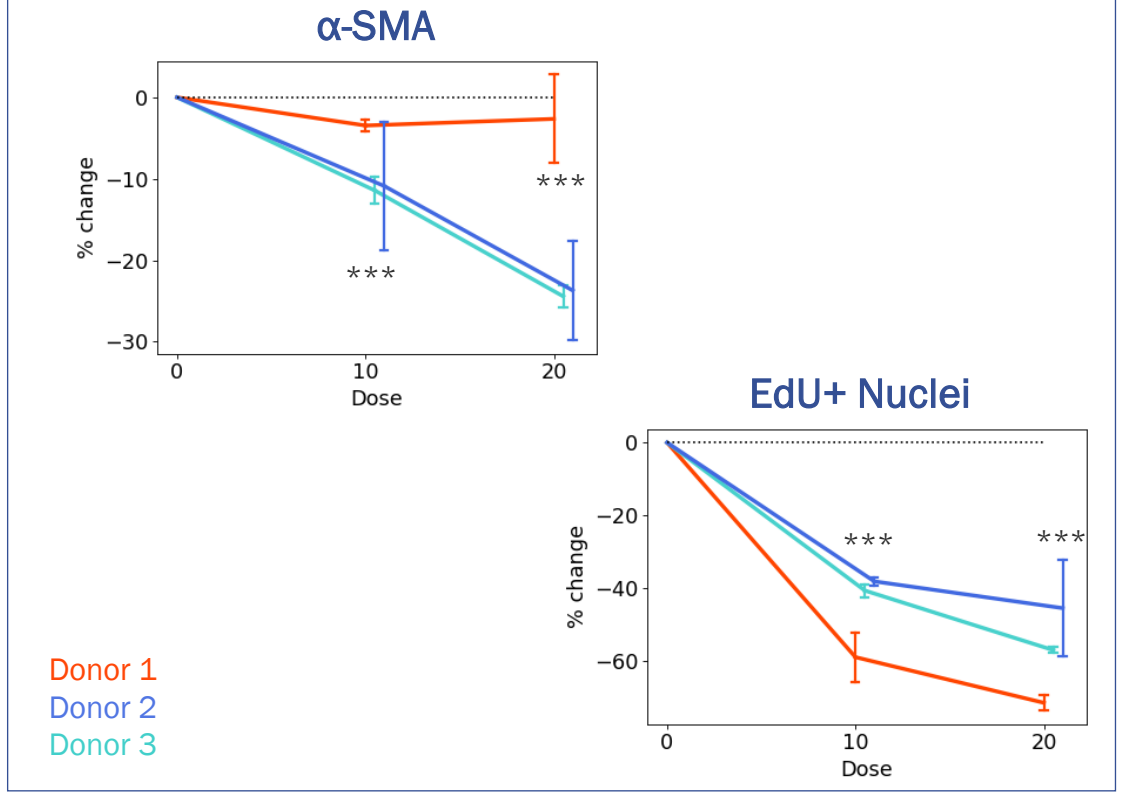


Multi-targeted impact on fibrosis improvement: Reduced Activation, Proliferation, Deposition

Decreases in Collagen Deposition Measured with AXA1125



Reduced Fibrogenic Activation & Proliferation



1. Daou et al. Nat Sci Rep. 2021. ***p < 0.001 versus TGF-β1, Data from Primary Human Hepatic Stellate Cells pre-treated with LIVRQNac for 24 hours, then stimulated with 3.3ng/ml TGF-β1 for 24 hours, EdU data normalized to nuclei, HSP47 expression normalized to GAPDH, other data not nuclei normalized.

Key MOA Takeaways

- NASH is a complex disease with metabolic, inflammatory and fibrotic dysregulations
- Combination therapy increases potential to impact multiple targets implicated in NASH
- AXA1125 is designed as a multi-targeted agent against key NASH dysregulations in distinct cellular targets
- Pre-clinical data demonstrates impact of AXA1125 effect on multiple cell types driving NASH fibrosis, inflammation and metabolic dysregulation
- Clinical data demonstrate the translation of AXA1125 MOA findings in patients

AXA1125 AND NASH TREATMENT LANDSCAPE

STEPHEN A. HARRISON, MD, COL (RET.), FAASLD

VISITING PROFESSOR OF HEPATOLOGY

RADCLIFFE DEPARTMENT OF MEDICINE, UNIVERSITY OF OXFORD

MEDICAL DIRECTOR, PINNACLE CLINICAL RESEARCH

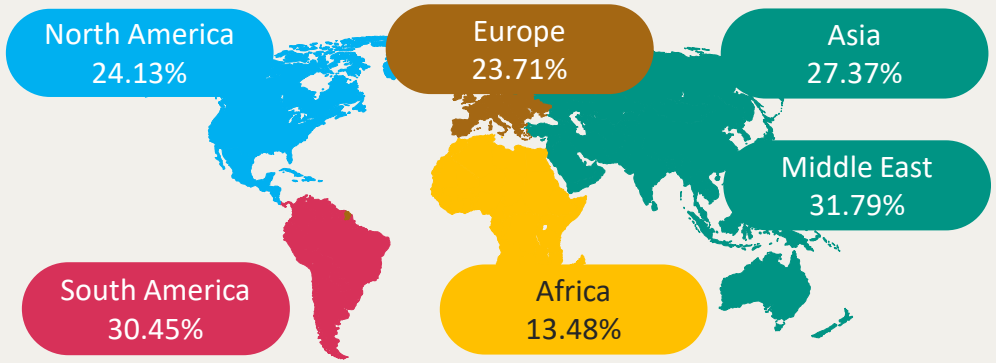
PRESIDENT, SUMMIT CLINICAL RESEARCH

PREVALENCE OF NAFLD AROUND THE WORLD

…is increasing in line with **obesity**, **type 2 diabetes** and **age**

…is about **25%** in the general population

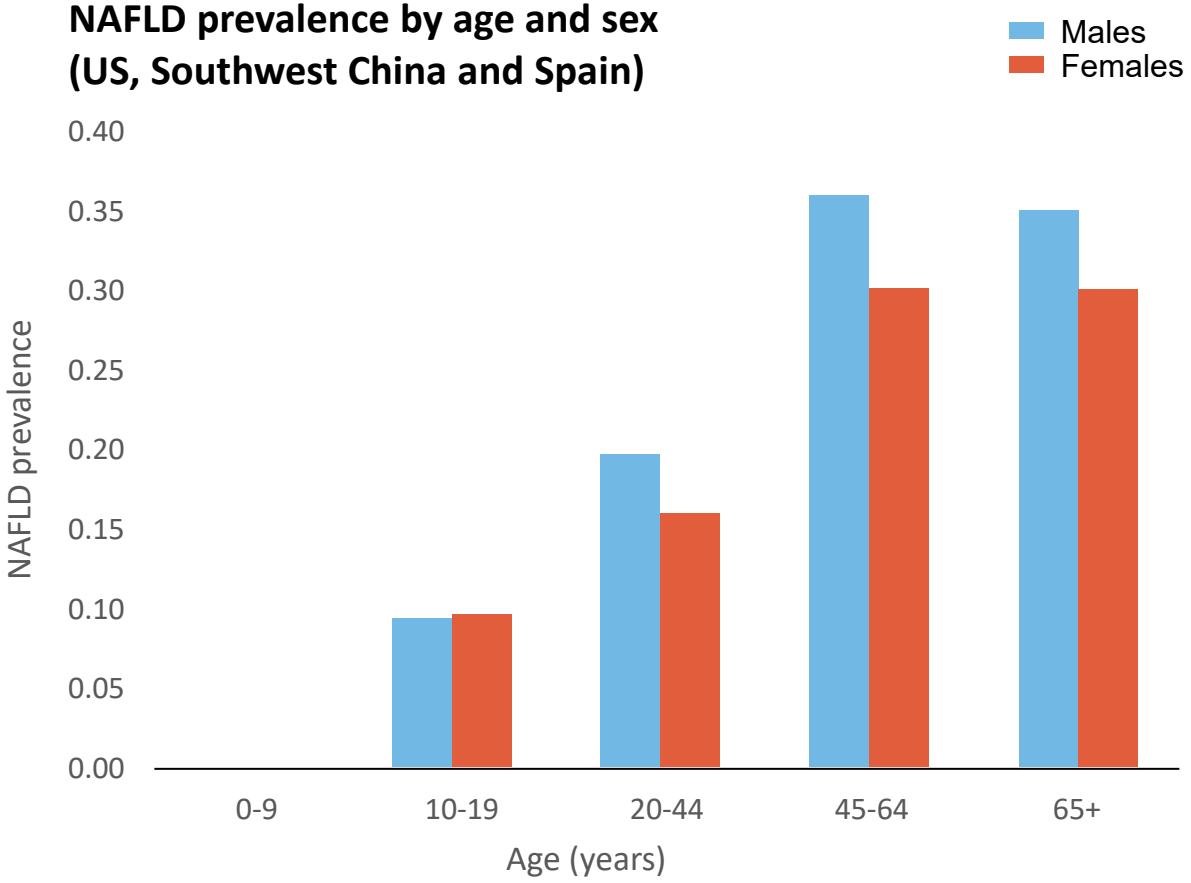
…varies across the **globe**



…varies across **ethnicities**
(Hispanics > non-Hispanic white > African Americans)

is higher in **urban** than rural population

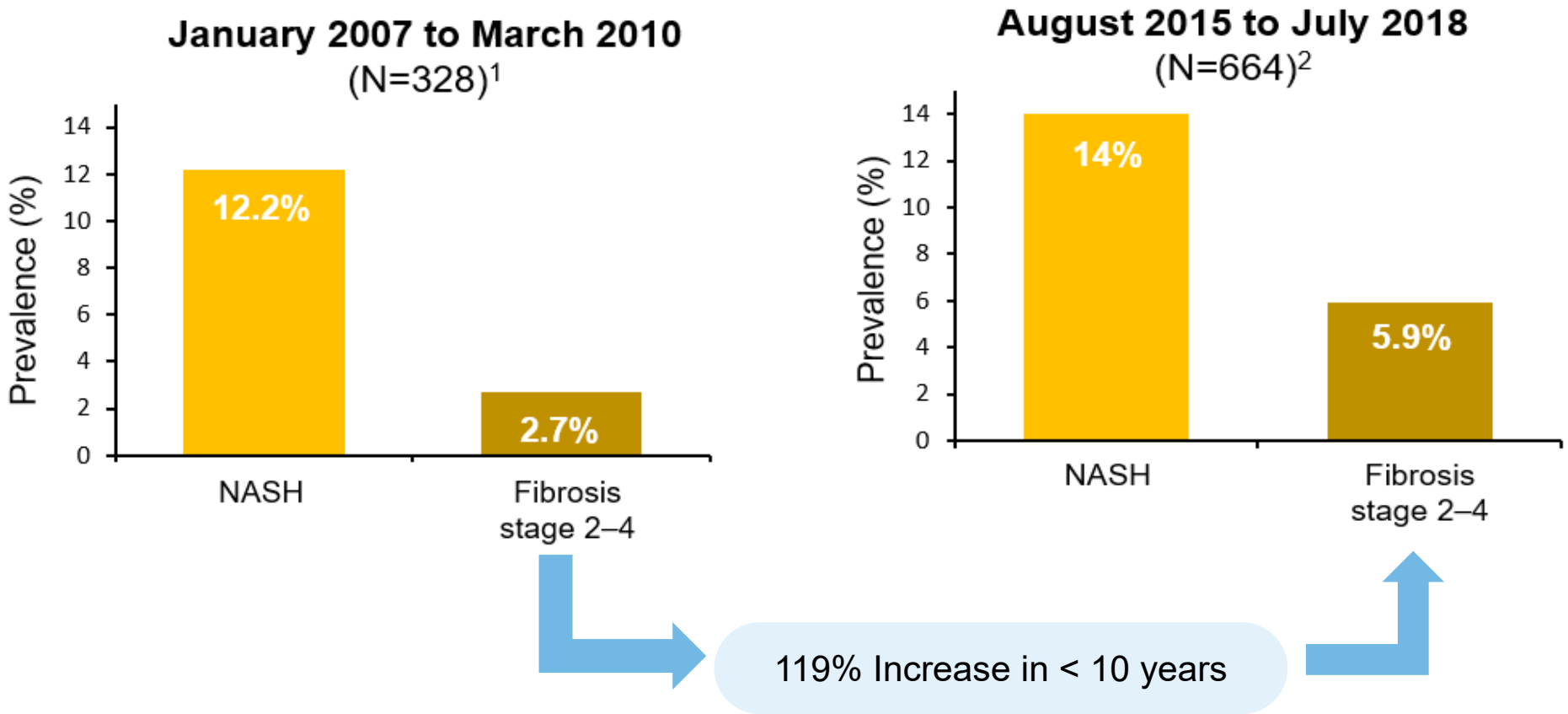
NAFLD prevalence by age and sex (US, Southwest China and Spain)



Younossi Z, et al. *Hepatology*. 2019;69(6):2672-2682; Younossi ZM et al. J *Hepatol.* 2019;70(3):531-544.

PREVALENCE OF NASH AMONG US MIDDLE-AGED COHORTS

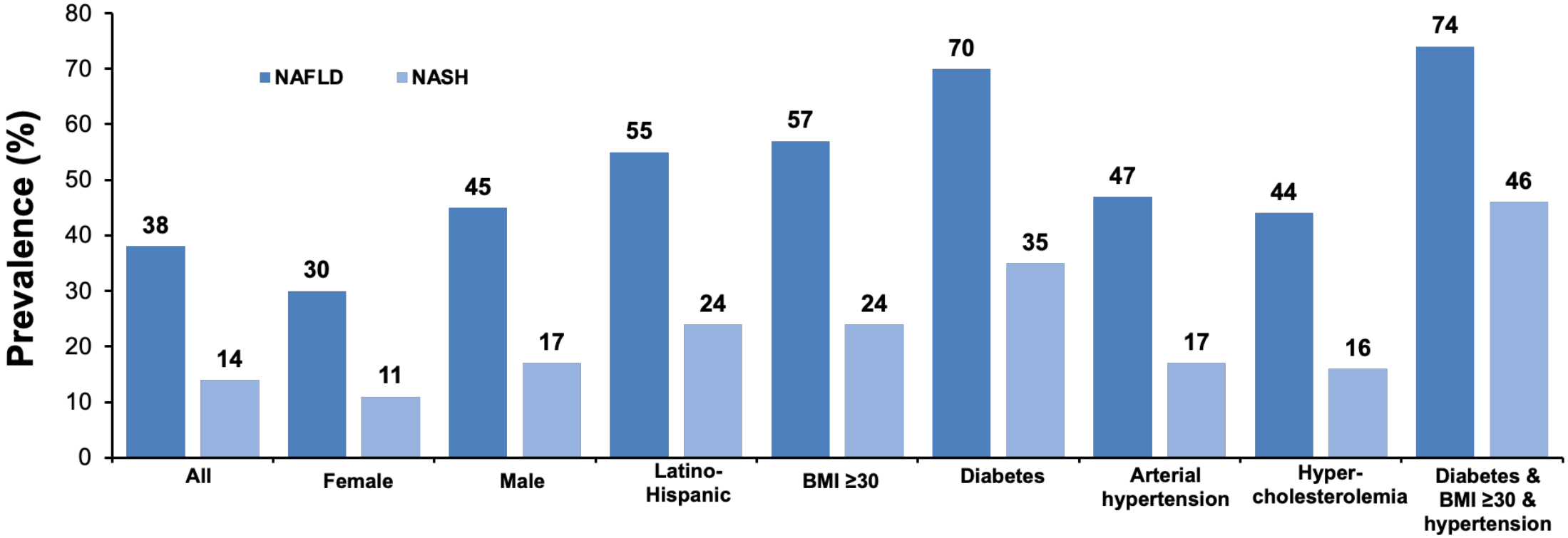
2 prospective NASH prevalence studies



NASH, non-alcoholic steatohepatitis.

1. Williams CD, et al. *Gastroenterology*. 2011;140:124–31; 2. Harrison SA, et al. *J Hepatol.* 2021;S0168-8278:00176-8.

NAFLD AND NASH PREVALENCE IN DIFFERENT GROUPS (US MIDDLE-AGED COHORT, N=664)

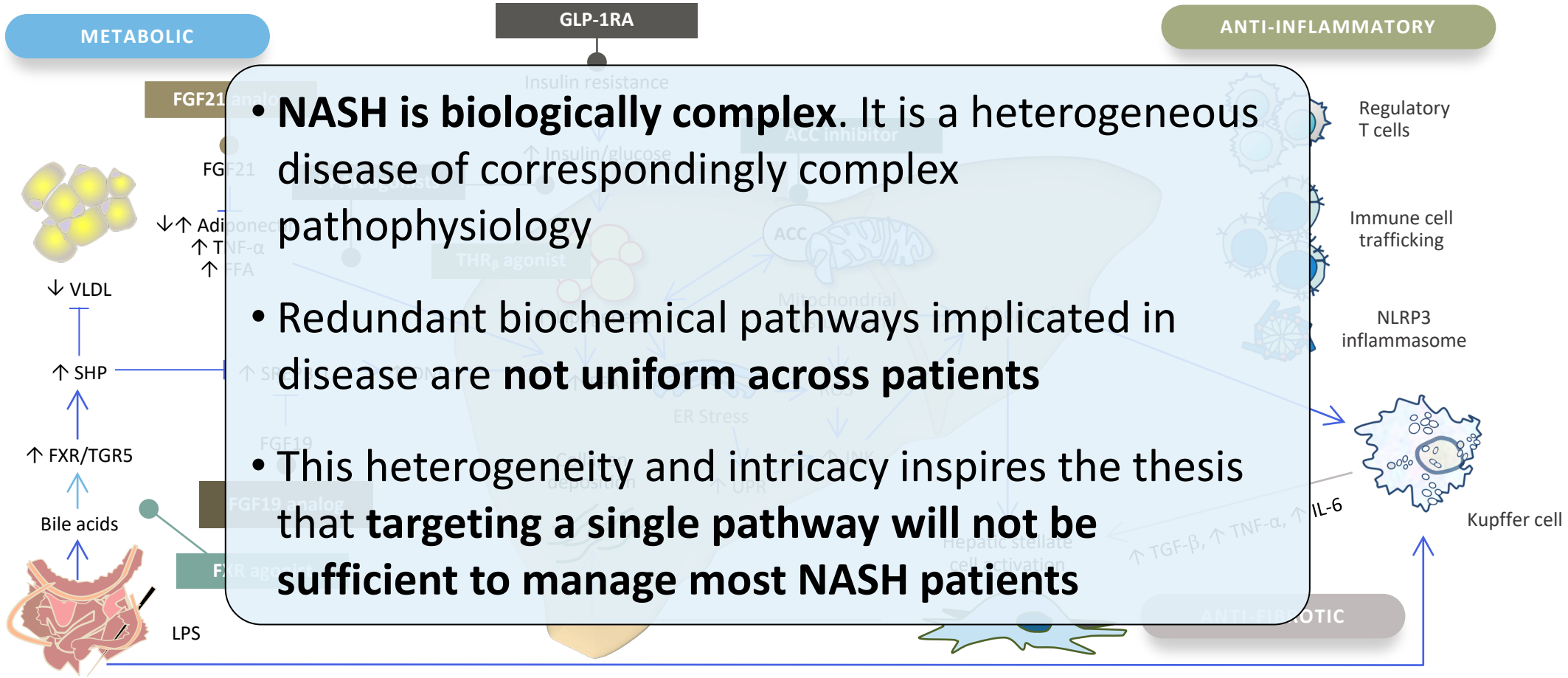


BMI measured in kg/m2

BMI, body mass index; NAFLD; non-alcoholic fatty liver disease; NASH, non-alcoholic steatohepatitis.

Harrison SA et al. *J Hepatol*. 2021;S0168-8278:00176-8.

NASH: POTENTIAL THERAPEUTIC TARGETS



- **NASH is biologically complex**. It is a heterogeneous disease of correspondingly complex pathophysiology
- Redundant biochemical pathways implicated in disease are **not uniform across patients**
- This heterogeneity and intricacy inspires the thesis that **targeting a single pathway will not be sufficient to manage most NASH patients**

See slides notes for abbreviations.
Adapted from: Konerman MA, et al. *J Hepatol.* 2018;68:362–375.

THE RISK/BENEFIT EQUATION CHANGES AS NASH PROGRESSES

F0 F1 F2 F3 F4

Liver Disease Progression

Safety First

Risk Tolerance

Key Physician Considerations

Agent needed to reduce liver fat and inflammation

Safety and tolerability are paramount as agent will likely be used chronically

Oral agents strongly preferred

Need to bring patients back from the brink ASAP

Willing to accept greater safety and tolerability risks

Injectables may be required

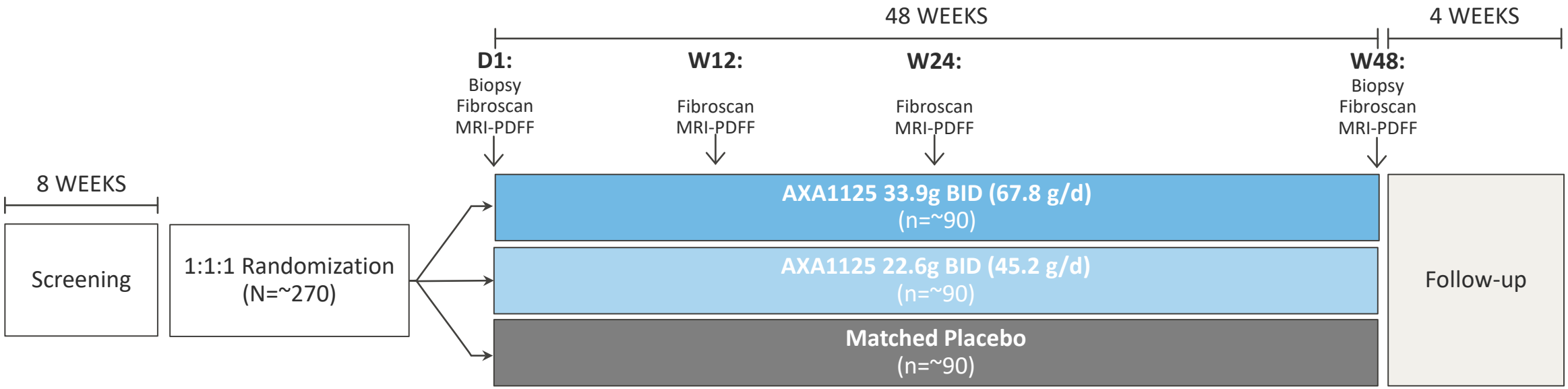
MULTIPLE OPTIONS TO ADDRESS A HETEROGENEOUS POPULATION

	Key Mechanisms	Candidates in Ph2/3 Development
Multi-Targeted	• EMMs • Combinations	• AXA1125 • Sema + cilo + firsocostat • Tropifexor + cenicriviroc
Anti-Fibrotic	• FXR • PPAR • Galectin protein inhibitors	• Belapectin • Lanifibranor • Tropifexor • Obeticholic acid
Anti-Hyperglycemics	• SCD-1 • THR-Beta • ACC Inhibitors • DGAT Inhibitors	• Aldafermin • Semaglutide • MK3655
Anti-Hyperlipidemics	• GLP-1 • MPC modulators • FGF • Insulin Receptors	• Aramchol • Resmetirom • VK2809
Anti-Inflammatory	• Toll-like receptors • AA3R agonist	• Secukinumab • JBK-122
Other	• AMPK • GHRF	• PXL770

NASH's complex pathophysiology demands development of a vast array of mechanisms and candidates

PHASE 2B CLINICAL TRIAL UNDERWAY

PREPLANNED INTERIM ANALYSIS WHEN 30 SUBJECTS/ARM REACHED WEEK 12



Core elements	Description
Design	• Randomized, double-blind, placebo-controlled, dose-ranging study over 48 weeks
Study population	• Biopsy-proven F2/F3 NASH with NAS≥4 • Stratification by type 2 diabetes status
Preplanned IA on secondary endpoints	• Improvement in non-invasive markers, including MRI-PDFF, ALT and Fibroscan

PATIENT DEMOGRAPHICS AND BASELINE METRICS

Baseline Demographic/Metric	Placebo (N=39)	AXA1125 22.6 BID (N=42)	AXA1125 33.9 BID (N=42)
Mean age in years (SD)	57.8 (9.8)	55.8 (13.5)	56.2 (12.4)
Sex			
Male (%)	12 (30.8)	10 (23.8)	19 (45.2)
Female (%)	27		3)
Mean Body Mass Index (kg/m^2) / (SD)	37.8		29)
With Type 2 Diabetes (%)	22		1)
Metabolism			
Mean Liver Fat Content by MRI-PDFF (SD)	18.99		541)
Mean HOMA-IR	13.56		460)
HbA1c (SD)	6.7		05)
Inflammation			
Mean ALT (U/L) (SD)	58.6 (34.3)	51.5 (24.2)	54.1 (36.3)
Fibrosis			
Mean Fibroscan score (kPa) (SD)	13.29 (6.72)	11.40 (3.47)	14.80 (6.63)
Mean Fib-4 (SD)	1.48 (0.65)	1.24 (0.58)	1.32 (0.65)
Mean ELF (SD)	9.966 (0.716)	9.636 (0.843)	10.012 (0.859)

This study population is reflective of a very active disease state with significant fibrosis

EFFECTS ON NON-INVASIVE MEASURES

DIFFERENT CONTEXT OF USE FOR NITs

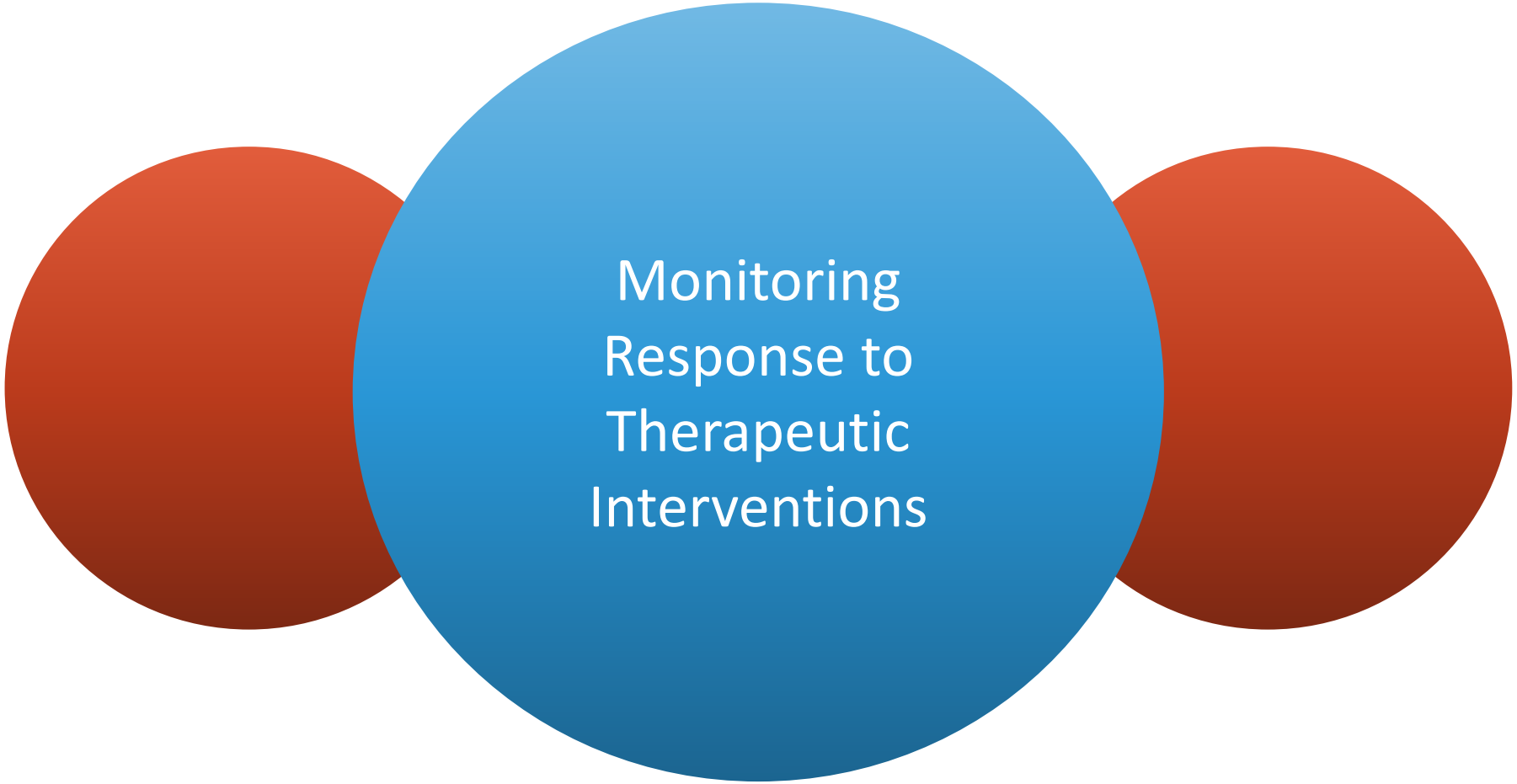
PINNACLE
CLINICAL RESEARCH

Diagnosis of at risk NASH

Monitoring Response to Therapeutic Interventions

Predicting Long-Term Outcomes

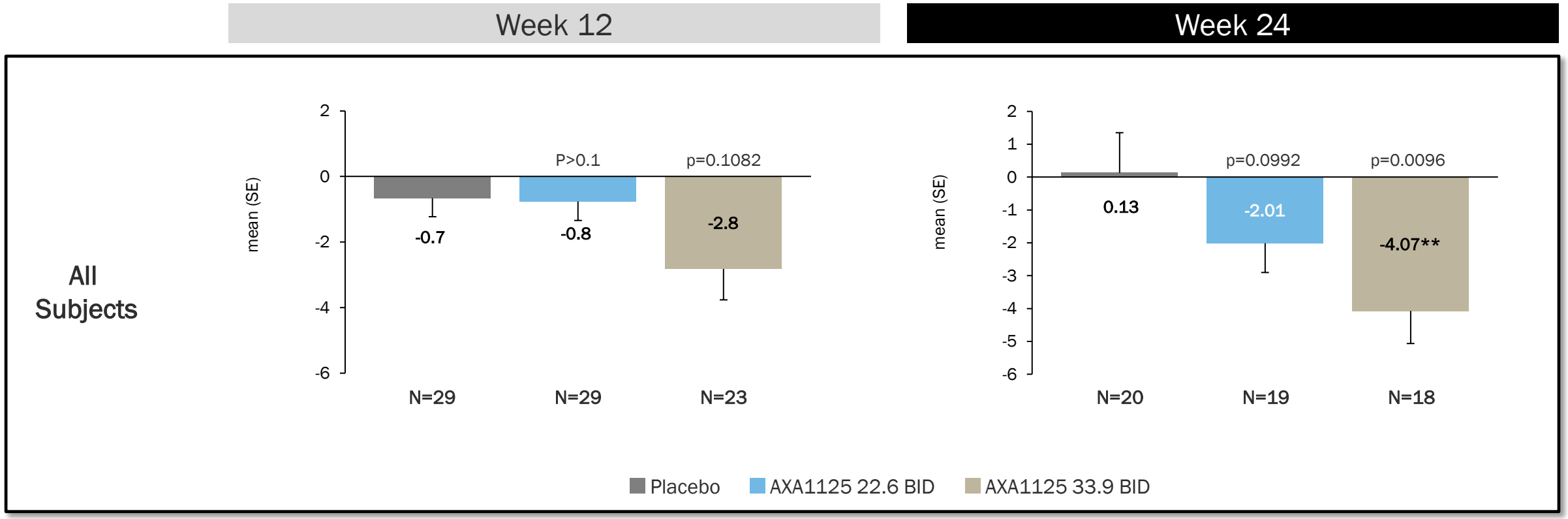
DIFFERENT CONTEXT OF USE FOR NITs



SIGNIFICANT IMPROVEMENTS IN LIVER STIFFNESS

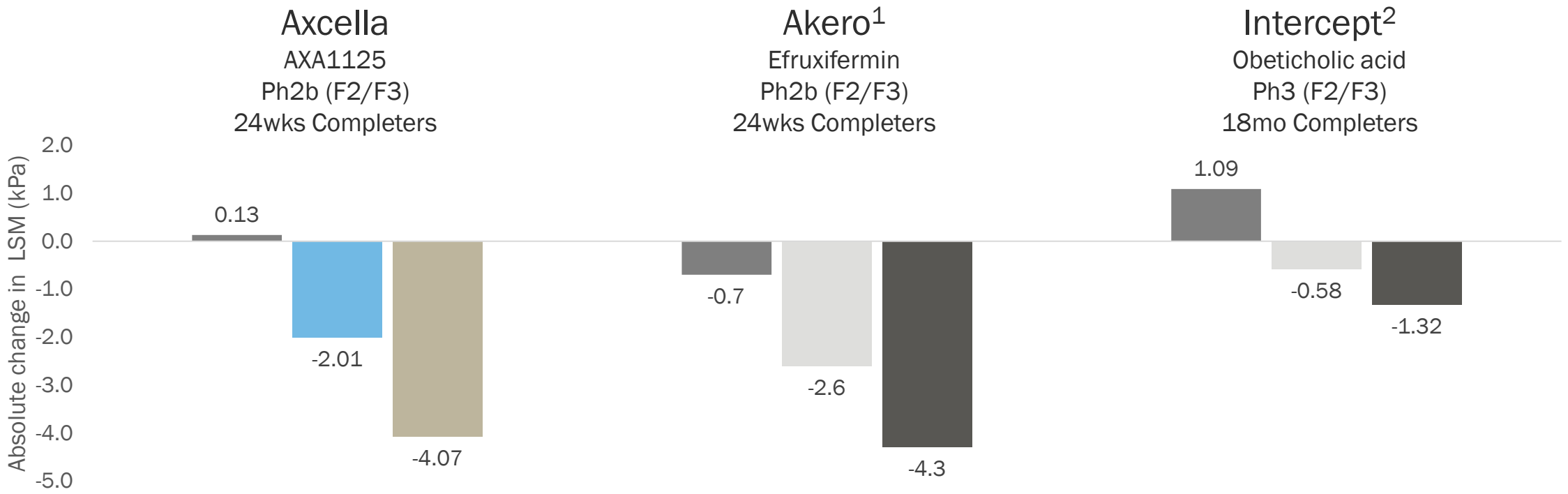
CONSISTENT WITH PRIOR DATA ON FIBROSIS MARKERS AT WEEK 16

PINNACLE CLINICAL RESEARCH



*p<0.05, **p<0.01, ***p<0.001, versus placebo; P values derived using mixed models approach. LSM, liver stiffness measurement; kPa, kilo pascals; SE, standard error

AXA1125 EFFECTS ON LIVER STIFFNESS IN COMPARABLE TO OTHER BEST IN CLASS AGENTS IN LATE DEVELOPMENT



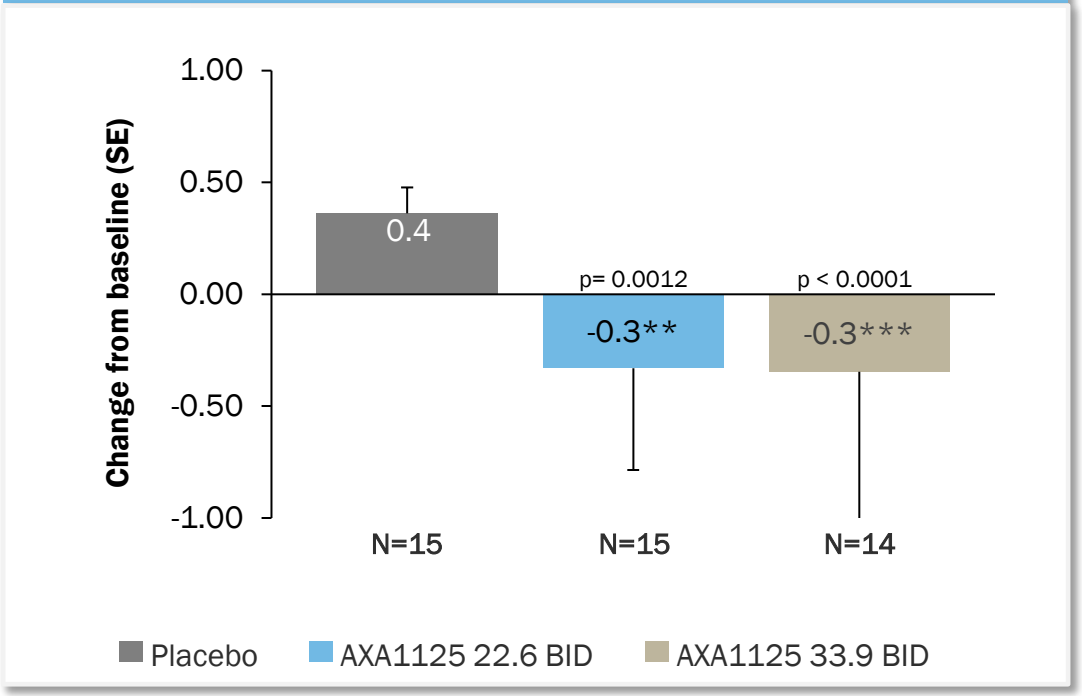
[1]Yale,C. (September 13, 2022). *Phase 2b HARMONY Study Results* [PowerPoint presentation]. Akero Phase 2B HARMONY Trial Data Presentation. https://ir.akerotx.com/static-files/b3cbfed1-3eee-49cf-8a10-cc75000855d5.
[2]Loomba, R et al. Obeticholic Acid Demonstrates Sustained Improvements at Month 24 in Transaminases and Non-Invasive Markers of Fibrosis: Results of a Post Hoc Analysis From the Interim Analysis of the REGENERATE Study. Poster presented at: European Association for the Study of the Liver; 27-29 August 2020; Virtual.
OLE = Open Label Extension

BLOOD BIOMARKERS PROVIDE FURTHER EVIDENCE OF EFFECT ON FIBROSIS

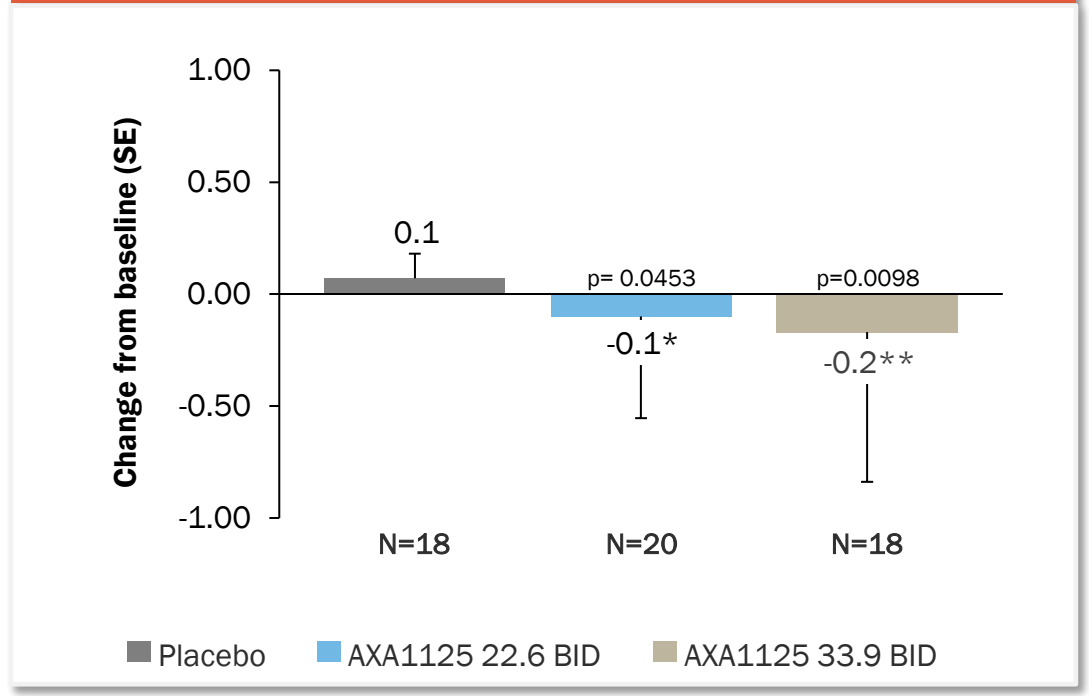
STATISTICALLY SIGNIFICANT CHANGES SEEN AS EARLY AS WEEK 12

PINNACLE
CLINICAL RESEARCH

ELF Score (Week 24)



FIB-4 Score (Week 24)



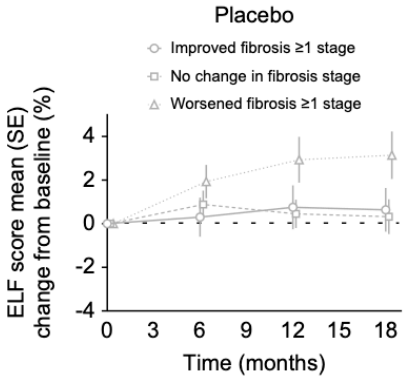
*p<0.05, **p<0.01, ***p<0.001, versus placebo; p values derived using mixed models approach. SE, standard error

ELF

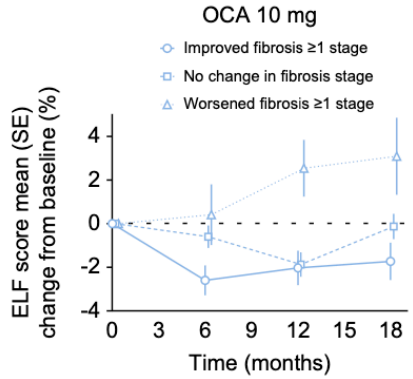
Monitoring Response to Therapeutic Interventions

EVIDENCE FROM REGENERATE TRIAL 18-MONTH INTERIM ANALYSIS – OBETICHOLIC ACID

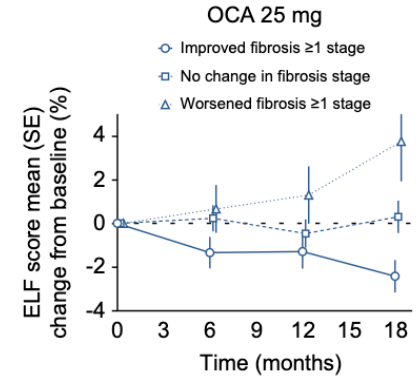
N=931



Improved, n =	60	59	57	58
No change, n =	137	137	134	127
Worsened, n =	52	52	53	50



Improved, n =	70	70	70	64
No change, n =	142	139	139	134
Worsened, n =	40	40	40	41



Improved, n =	89	88	88	86
No change, n =	118	117	117	114
Worsened, n =	32	33	33	31

- Patients with ≥1-stage fibrosis improvement had the greatest improvement in NITs, while patients with ≥1-stage fibrosis worsening typically showed no NIT improvement.
- AUROC values for each of these were suggestive of only weak association
- NIT improvements observed in REGENERATE are associated with fibrosis improvement at Month 18, individual NIT changes are not likely to be effective univariate clinical predictors of fibrosis improvement by Month 18.

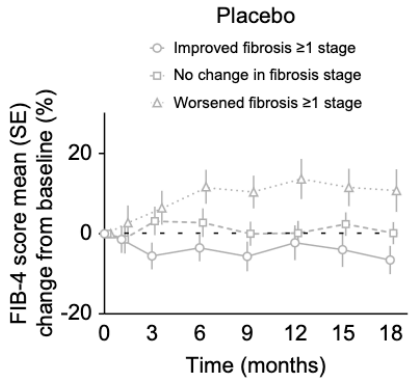
Rinella ME. Non-invasive evaluation of response to obeticholic acid in patients with NASH: Results from the REGENERATE study. J Hepatol. 2022 Mar;76(3):536-548

FIB-4

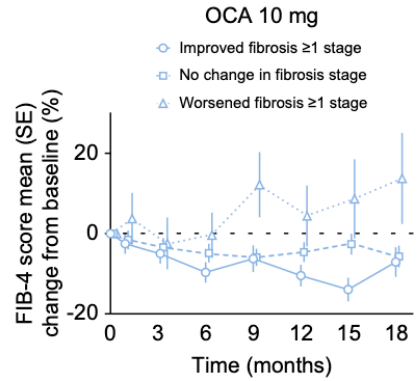
Monitoring Response to Therapeutic Interventions

EVIDENCE FROM REGENERATE TRIAL 18-MONTH INTERIM ANALYSIS – OBETICHOLIC ACID

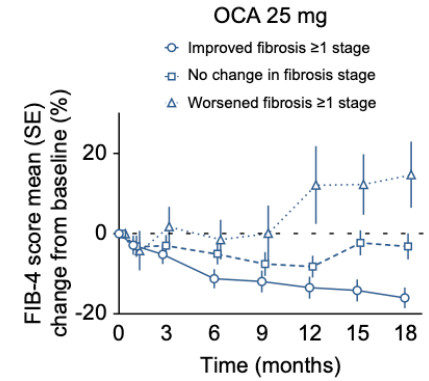
N=931



Improved, n =	60	58	60	58	57	59	57
No change, n =	148	146	146	143	141	143	136
Worsened, n =	55	53	53	54	52	54	51



Improved, n =	73	71	71	71	70	72	65
No change, n =	146	141	141	142	143	142	134
Worsened, n =	44	42	42	42	42	43	41



Improved, n =	93	90	91	91	91	89	90
No change, n =	124	123	123	123	121	120	119
Worsened, n =	34	34	34	34	34	33	31

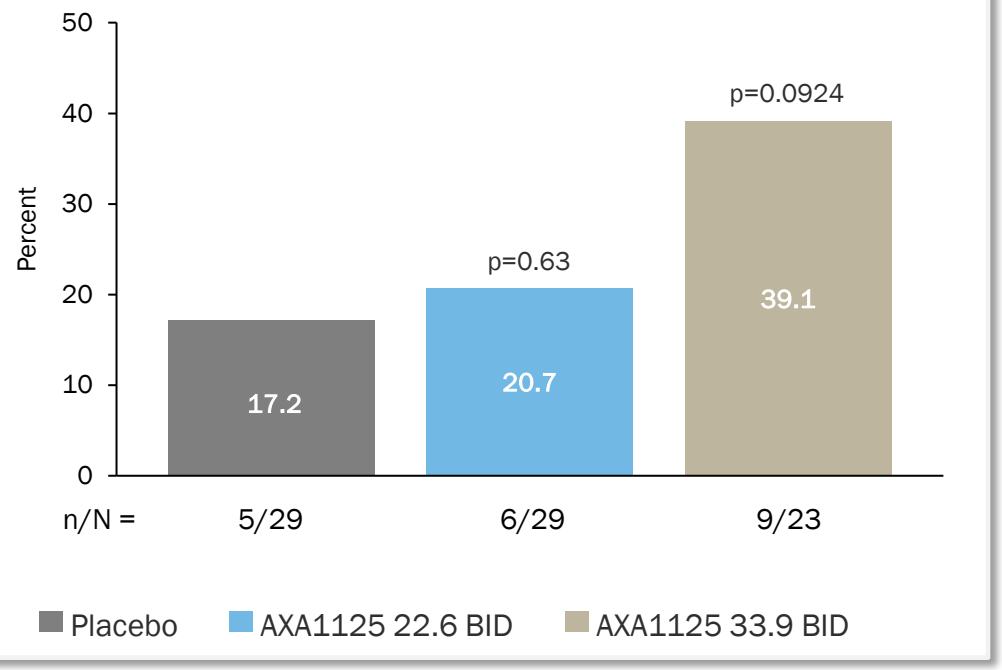
- Patients with ≥1-stage fibrosis improvement had the greatest improvement in NITs, while patients with ≥1-stage fibrosis worsening typically showed no NIT improvement.
- AUROC values for each of these were suggestive of only weak association
- NIT improvements observed in REGENERATE are associated with fibrosis improvement at Month 18, individual NIT changes are not likely to be effective univariate clinical predictors of fibrosis improvement by Month 18.

Rinella ME. Non-invasive evaluation of response to obeticholic acid in patients with NASH: Results from the REGENERATE study. J Hepatol. 2022 Mar;76(3):536-548

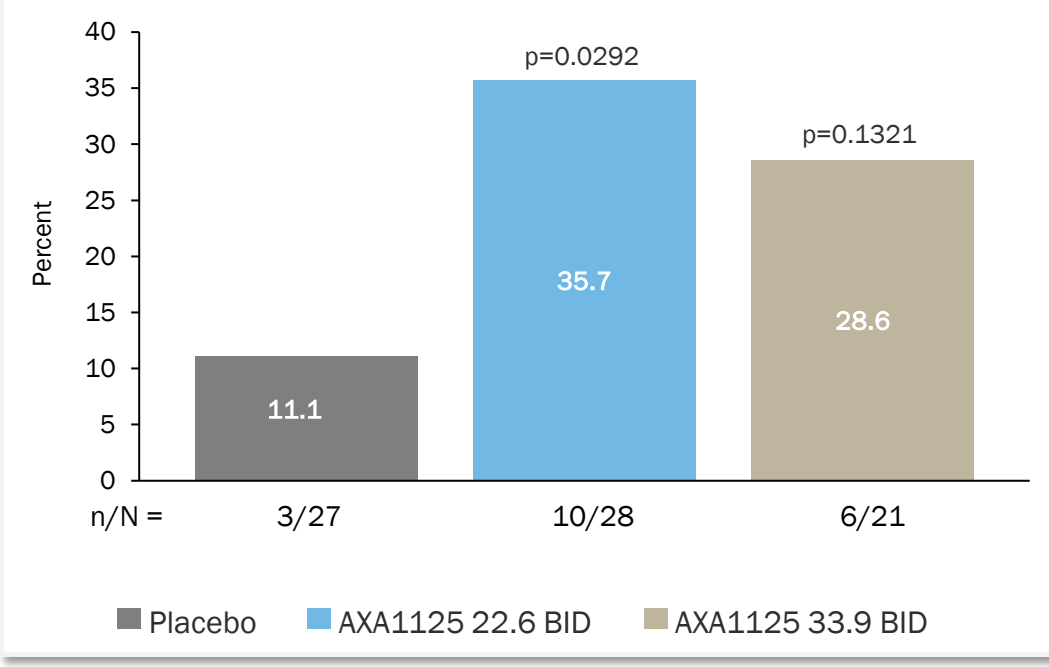
PROPORTION ACHIEVING BENCHMARK CRITERIA AT WEEK 12

PINNACLE
CLINICAL RESEARCH

> 17 IU change in ALT



> 30% rel reduction PDFF



n = the number of subjects who met criteria; N= the number of subjects with a post baseline visit; P values using Cochran-Mantel Haenszel test vs placebo

AXA1125 DEMONSTRATED SIMILAR RESULTS IN A PRIOR NASH CLINICAL STUDY

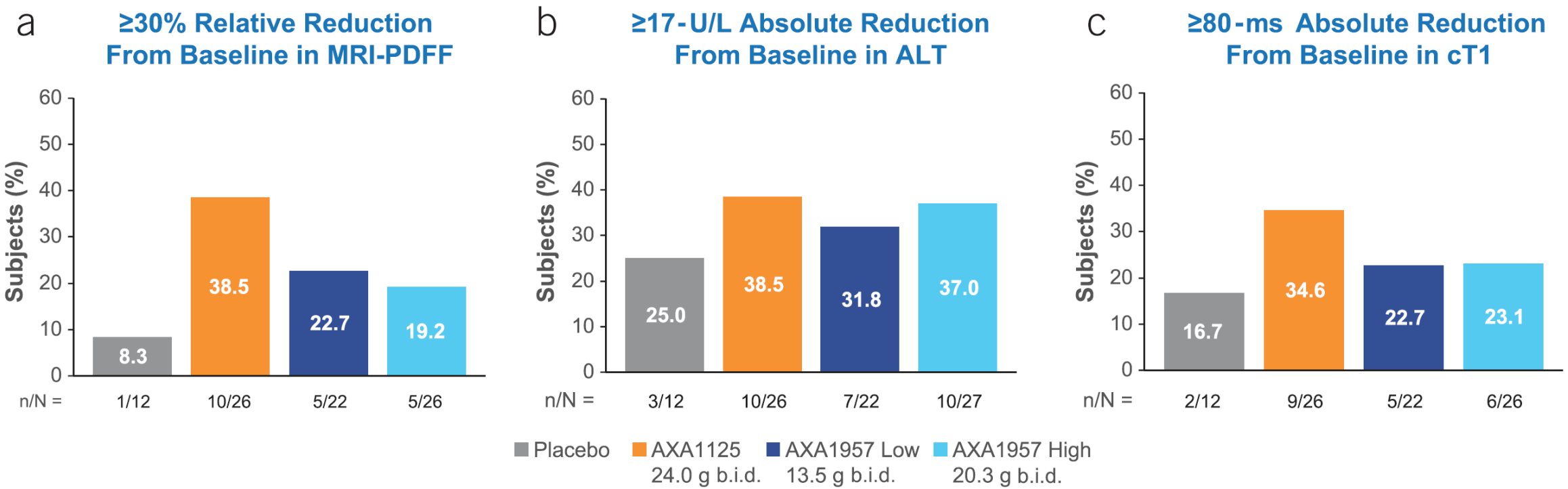


Figure 5. Proportion of subjects with clinically relevant thresholds of biologic activity (**a**, **b**, and **c**) in the overall safety population. ALT, alanine amino-transferase; cT1, corrected T1; MRI-PDFF, MRI-proton density fat fraction.

Harrison SA, Baum SJ, Gunn NT, Younes ZH, Kohli A, Patil R, Koziel MJ, Chera H, Zhao J, Chakravarthy MV. Safety, Tolerability, and Biologic Activity of AXA1125 and AXA1957 in Subjects With Nonalcoholic Fatty Liver Disease. Am J Gastroenterol. 2021 Dec 1;116(12):2399-2409. doi: 10.14309/ajg.0000000000001375. PMID: 34382947; PMCID: PMC8631161.

ALT

Monitoring Response to Therapeutic Interventions

EVIDENCE FROM FLINT 72-WEEK TRIAL OBETICHOLIC ACID

N=283

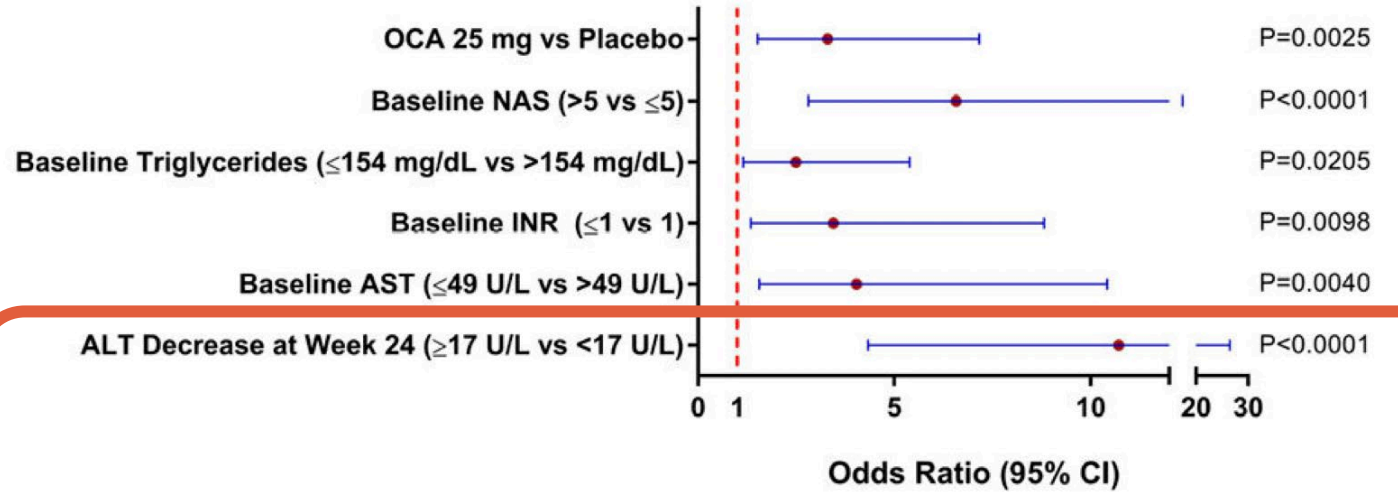


Figure 1. Forest Plot of Predictors of Histologic Response.

Plot shows the odds ratio and 95% CI for each of the selected predictors of responses, if the odds ratio is >1, the predictor is associated with higher odds of histological response. Significance of each of the selected predictors was assessed using a Wald Chi-Square test.

17 IU/L ALT decline was significantly associated with histologic markers of response

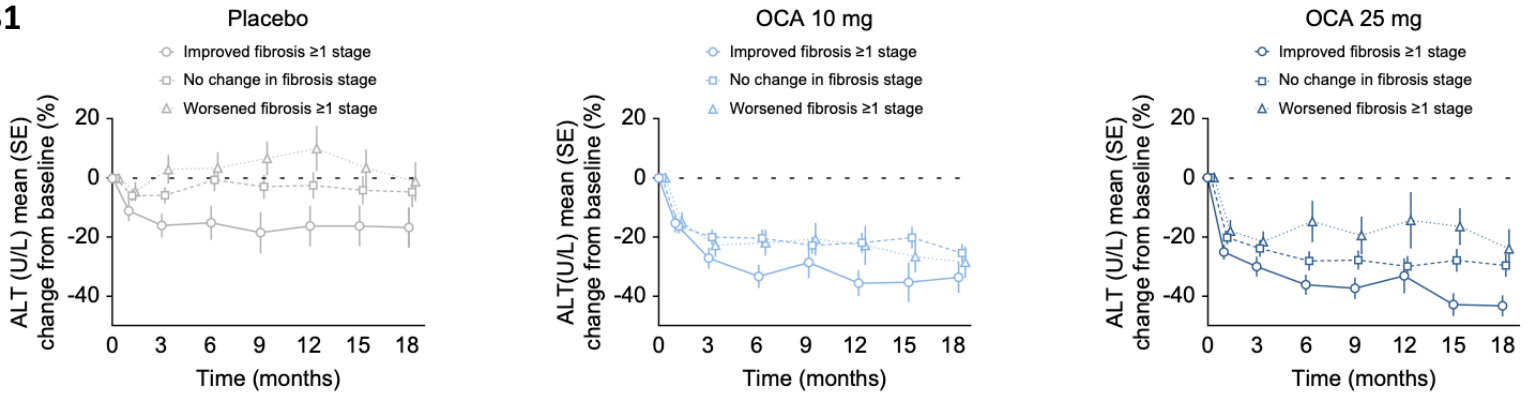
Loomba, Rohit et al. "Factors Associated With Histologic Response in Adult Patients With Nonalcoholic Steatohepatitis." *Gastroenterology*vol. 156,1 (2019): 88-95.e5.

ALT

Monitoring Response to Therapeutic Interventions

EVIDENCE FROM REGENERATE TRIAL 18-MONTH INTERIM ANALYSIS – OBETICHOLIC ACID

N=931



Improved, n =	60	58	60	59	58	59	57
No change, n =	146	148	147	146	144	143	139
Worsened, n =	55	55	53	54	54	55	52

Improved, n =	73	70	73	72	72	72	67
No change, n =	146	143	144	144	144	143	135
Worsened, n =	43	44	44	44	42	43	43

Improved, n =	92	92	92	92	91	92	90
No change, n =	124	124	124	123	123	121	119
Worsened, n =	34	34	34	34	34	33	31

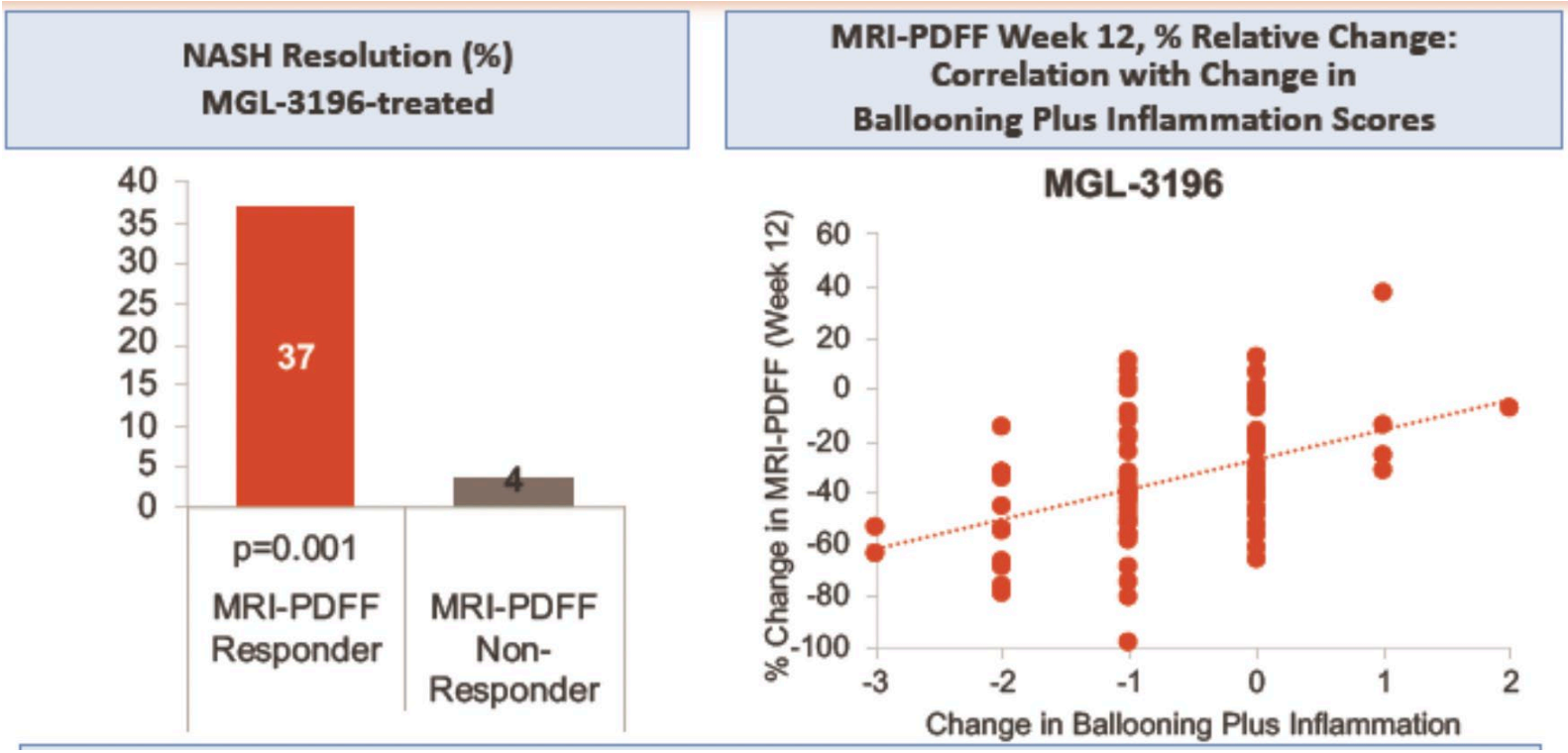
- Patients with ≥1-stage fibrosis improvement had the greatest improvement in NITs, while patients with ≥1-stage fibrosis worsening typically showed no NIT improvement.
- AUROC values for each of these were suggestive of only weak association
- NIT improvements observed in REGENERATE are associated with fibrosis improvement at Month 18, individual NIT changes are not likely to be effective univariate clinical predictors of fibrosis improvement by Month 18.

Rinella ME. Non-invasive evaluation of response to obeticholic acid in patients with NASH: Results from the REGENERATE study. J Hepatol. 2022 Mar;76(3):536-548

MRI-PDFF

Monitoring Response to Therapeutic Interventions

EVIDENCE FROM RESMETIROM 36-WEEK PH2 TRIAL



MRI Responders: ≥ 30% relative decline in LFC

Harrison SA In a placebo-controlled 36-week phase 2 trial, treatment with MGL-3196 compared to placebo results in significant reduc- tions in hepatic fat (MRI-PDFF), liver enzymes, fibrosis biomarkers, atherogenic lipids, and improvement in NASH on serial liver biopsy. Hepatology 2018;68:9A-10A.

MRI-PDFF

Monitoring Response to Therapeutic Interventions

≥30% RELATIVE DECLINE IN MRI-PDFF

Change in MRI-PDFF and Histologic Response in Patients with NASH: A Systematic Review and Meta-Analysis – 7 studies / 346 patients

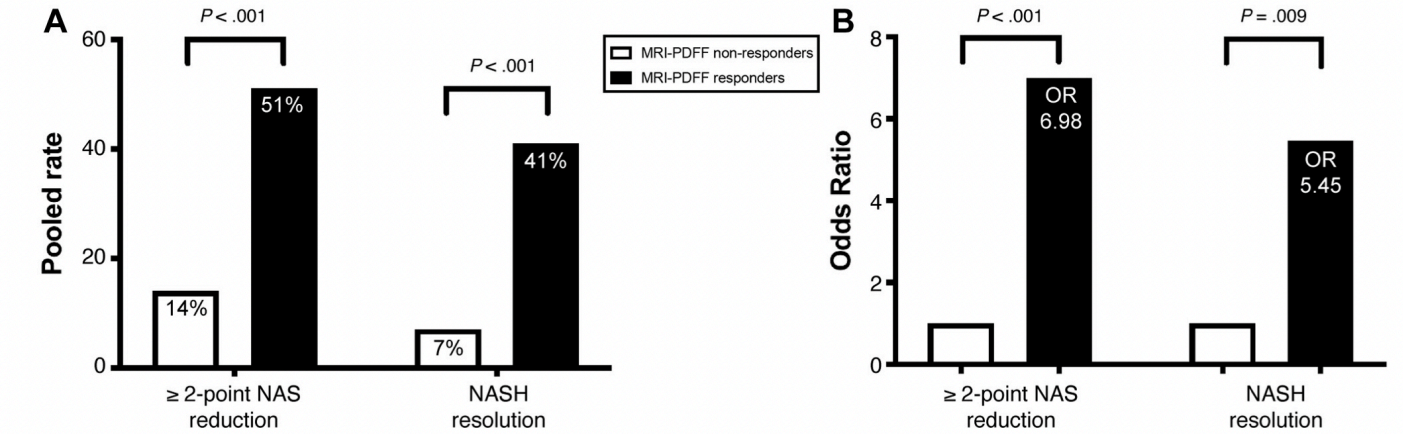


Figure 3. (*A*) The rate of 2-point improvement in NAS in MRI-PDFF responders vs nonresponders was 51% vs 15% ($P < .001$), and the rate of NASH resolution in MRI-PDFF responders vs nonresponders was 41% vs 7% ($P < .001$). (*B*) The odds of 2-point improvement in NAS in MRI-PDFF responders vs nonresponders was 6.98 (95% CI, 2.38–20.43; $P < .001$), and the odds of NASH resolution in MRI-PDFF responders vs nonresponders was 5.45 (95% CI, 1.53–19.46; $P < .009$).

"These results support the use of MRI- PDFF in non-invasive monitoring of treatment response in early-phase NASH clinical trials"

Stine JG, Munaganuru. Change in MRI-PDFF and Histologic Response in Patients With Nonalcoholic Steatohepatitis: A Systematic Review and Meta-Analysis. Clin Gastroenterol Hepatol. 2021 Nov.

SAFETY

SAFETY INTERIM ANALYSIS

SAFETY AND TOLERABILITY REMAINS FAVORABLE BASED ON THE BLINDED REVIEW

	Placebo N=39 (%)	AXA1125 22.6 BID N=42 (%)	AXA1125 33.9 BID N=42 (%)
Subjects with ≥ 1 TEAE	28 (71.8)	28 (66.7)	30 (71.4)
Related TEAE	17 (43.6)	12 (28.6)	18 (42.9)
Maximum Severity, n (% of subjects)			
Grade 1	12 (30.8)	12 (28.6)	11 (26.2)
Grade 2	15 (38.5)	14 (33.3)	15 (35.7)
Grade 3	1 (2.6)	1 (2.4)	4 (9.5)
Grade 4	0	0	0
Grade 5	0	1 (2.4)	0
SAE	1 (2.6%)	1 (2.4%)	4 (4.8%)
Related SAE	0	0	0

- Most frequent TEAEs are gastrointestinal
- All SAEs and the death unrelated to study product
- No safety or tolerability signals of concern were observed; confirmed by an independent unblinded DMC review

Safety based on what subject received on day 1 of dosing. DMC, independent data monitoring committee; SAE, serious adverse event; TEAEs, treatment emergent adverse events

SUMMARY

PINNACLE
CLINICAL RESEARCH

The current study is enrolling patients with significant NASH and fibrosis

AXA1125 appears safe and well tolerated

Oral formulation is key benefit

Non-invasive tests obtained at a relatively short time period in a subset of patients enrolled suggest a positive impact on disease activity and potentially fibrosis

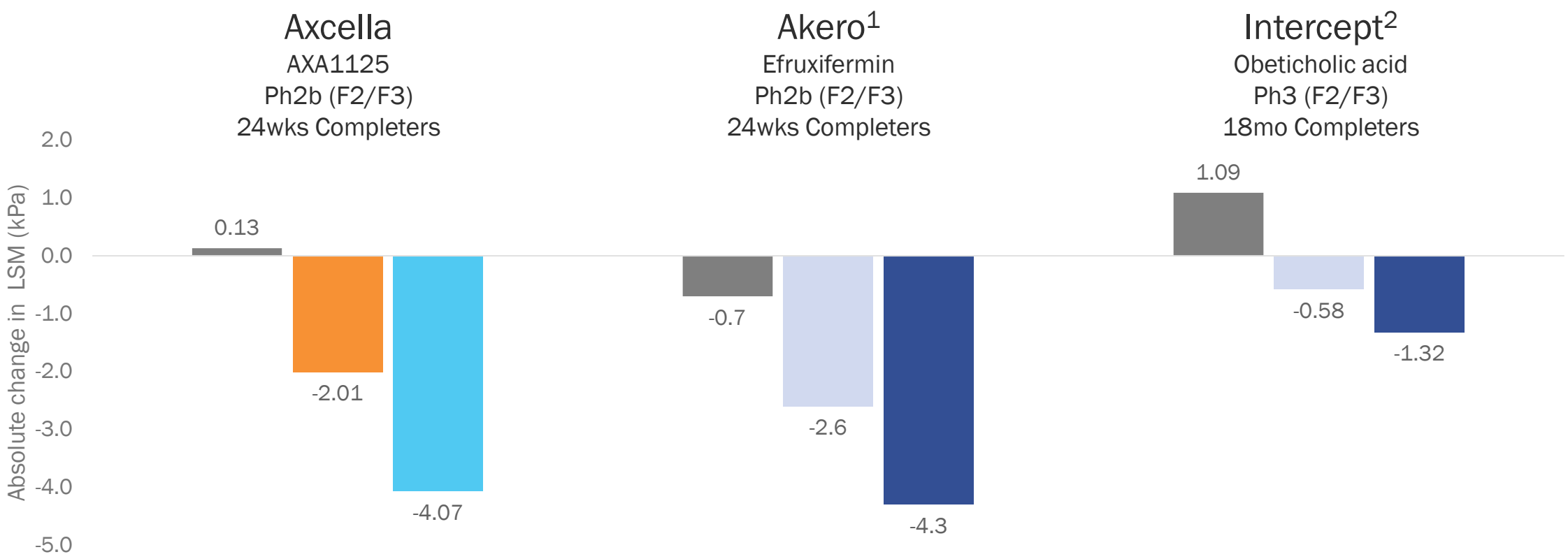
Potential for use as a monotherapy or as part of a combination therapy

Closing Remarks

Bill Hinshaw

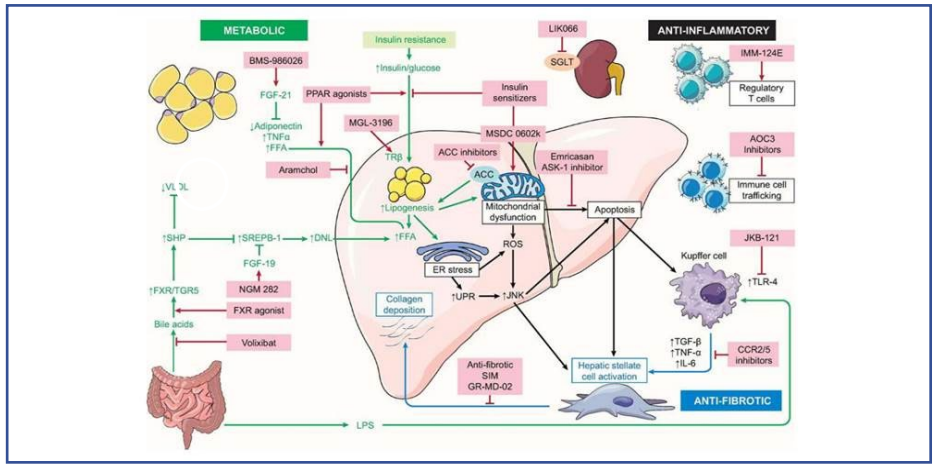
Chief Executive Officer

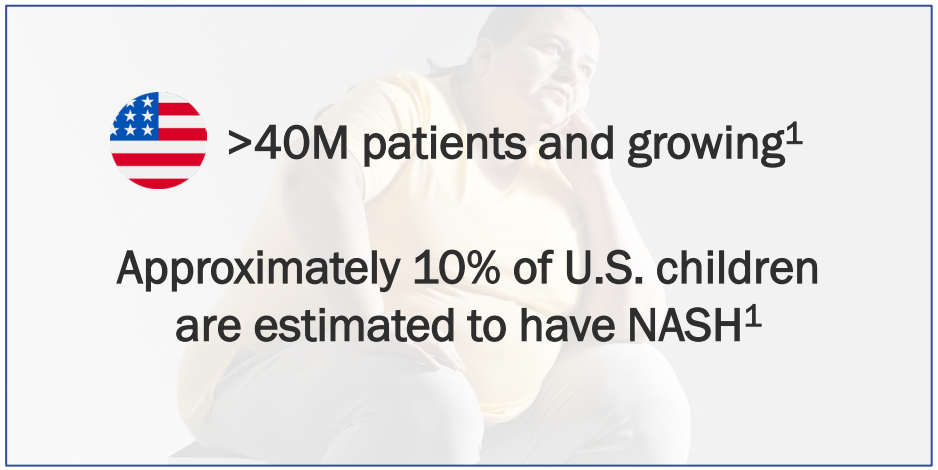
AXA1125 effects on liver stiffness are comparable to other best in class agents in late development



[1]Yale,C. (September 13, 2022). *Phase 2b HARMONY Study Results* [PowerPoint presentation]. Akero Phase 2B HARMONY Trial Data Presentation. https://ir.akerotx.com/static-files/b3cbfed1-3eee-49cf-8a10-cc75000855d5.
[2]Loomba, R et al. Obeticholic Acid Demonstrates Sustained Improvements at Month 24 in Transaminases and Non-Invasive Markers of Fibrosis: Results of a Post Hoc Analysis From the Interim Analysis of the REGENERATE Study. Poster presented at: European Association for the Study of the Liver; 27-29 August 2020; Virtual.

Conclusion





- NASH is a large complex disease with a high unmet need and **will require multiple strategies and products**
- AXA1125 demonstrated **best in field fibrotic measures** at 24 weeks
- AXA1125 continues to **demonstrate its direct multi-targeted effects** across metabolism, inflammation and fibrosis with both doses and in both populations
- Potential for **differentiation** in key populations
  - T2D, Adolescents, Combinations
- Well **positioned for 1st line** with attractive profile:
  - Multi-targeted activity, favorable tolerability and convenient dosing

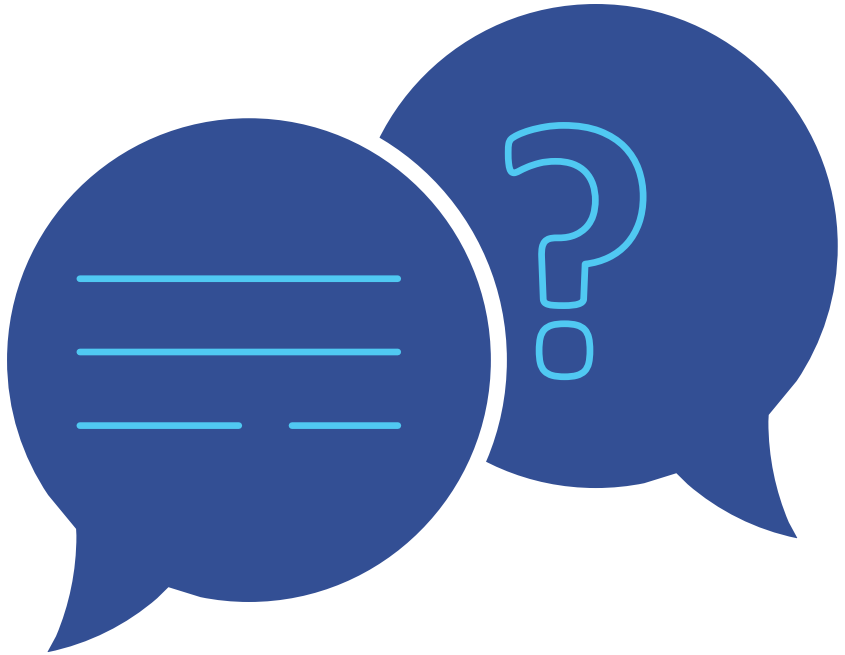
[1]Global Liver Institute U.S. NASH Action Plan (Dec. 2020)
Image sourced from: https://www.today.com/health/nonalcoholic-fatty-liver-disease-are-you-risk-t121855

Milestone Rich Time

Program	Update	Timing	
AXA1125 for NASH	Phase 2b Interim Data	Q3 2022	✓
	First Adolescent Subject Enrolled	Q4 2022	
	Scientific Communication	2H 2022	
	NASH Top-Line Data	1H 2024	
AXA1125 for Long COVID	Phase 2a Enrollment Completion	Q2 2022	✓
	Phase 2a Top-Line Data	Q3 2022	✓
	Regulatory Engagement	2H 2022	
	Scientific Communication	2H 2022	
	Next Trial Initiation	1H 2023	

Milestone timing based on current expectations and subject to change.

Q&A



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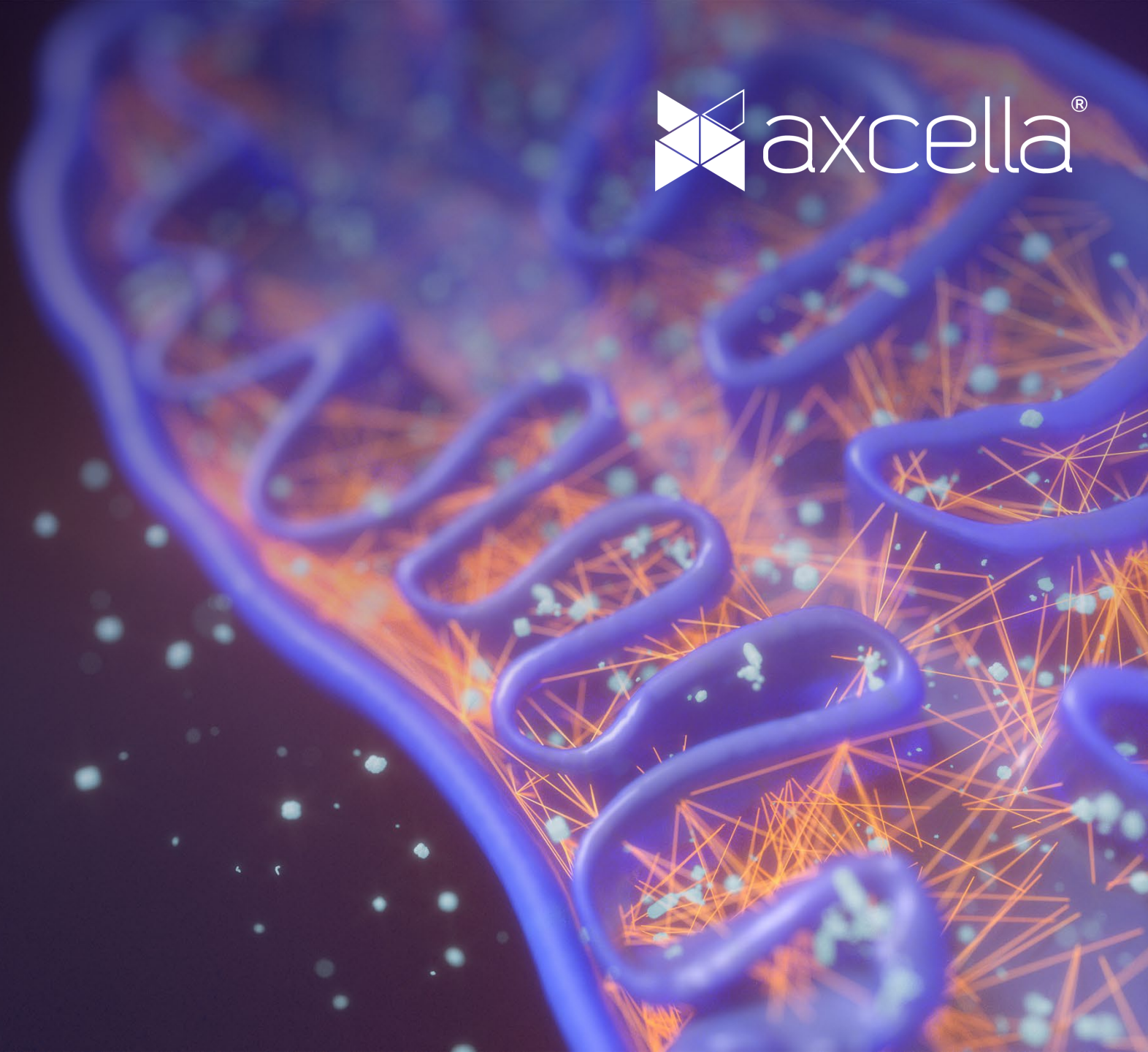
NASDAQ: AXLA

Thank You



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