NASDAQ: AXLA

Capitalizing on an Accelerated Path to Late-Stage Development

July 2021

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 AXA1665, AXA1125 and potential future EMM compositions, the potential for AXA1665 to reduce OHE events and improve the quality of life for cirrhotic patients, the potential for AXA1125 to serve as 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 planned Phase 2 clinical trial of AXA1665 and planned Phase 2b clinical trial 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 for AXA1125 and AXA1665, 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; the ability for the company to refinance its existing debt facility 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.

About Axcella's Development Model and Clinical Approach

EMMs have a fundamental role in biology and biological function. Using the Axcella Knowledge Base, Axcella designs and develops novel EMM compositions to engage identified biologies and pathways. Axcella then selects whether to evaluate a product candidate in a non-investigational new drug application (non-IND) clinical study under U.S. Food and Drug Administration regulations and guidance supporting research with food, or under an IND clinical trial. Axcella's non-IND clinical studies evaluate product candidates for safety, tolerability and effects on the normal structures and functions in humans, including in individuals with disease. The company's non-IND clinical studies include a substantial number of biomarkers that may inform biologies relevant to health but are not designed or intended to evaluate a product candidate's ability to diagnose, cure, mitigate, treat or prevent a disease or other health condition. These clinical studies are conducted at reputable medical centers following Good Clinical Practices (GCPs), including Institutional Review Board (IRB) approval, and utilize qualified investigators. Using a combination of data from these studies and/or other relevant information, the company decides whether to advance a product candidate's development as a therapeutic or supplement (independently or in partnership), or to terminate its development.

To date, Axcella has initially evaluated its product candidates as investigational food products in non-IND clinical studies. More recently, Axcella determined its lead compounds – AXA1665 and AXA1125 – to be therapeutic product candidates, meaning that their ongoing development will be conducted under IND to investigate their ability to treat diseases. As a result, the company will investigate the reduction in risk of recurrent OHE with AXA1665 and the treatment of NASH with AXA1125.

This presentation refers to Axcella's non-IND clinical studies as "clinical studies" and its IND clinical trials as "clinical trials."

What if…

We could now more effectively and safely treat complex, chronic diseases using oral, multi-targeted therapies composed of endogenous molecules?

Investment Highlights

Multiple shots on goal with significant room for upside

Enrolling AXA1665 Phase 2

Potential to Address Unmet Needs in OHE

Opportunity to improve standard of care in ~$1 billion and growing market with AXA1665[1,2]

Enrolling AXA1125 Phase 2b

Substantial NASH Market Opportunity

Aiming to be a first-line therapy in what is expected to be a multi-billion-dollar market with AXA1125[3]

Expanding Pipeline

Powerful Platform and Approach; Broad Applicability

Potential for EMM compositions to impact multiple areas with rapid clinical development paths

Cash runway into Q3 2022

Strong, experienced leadership team

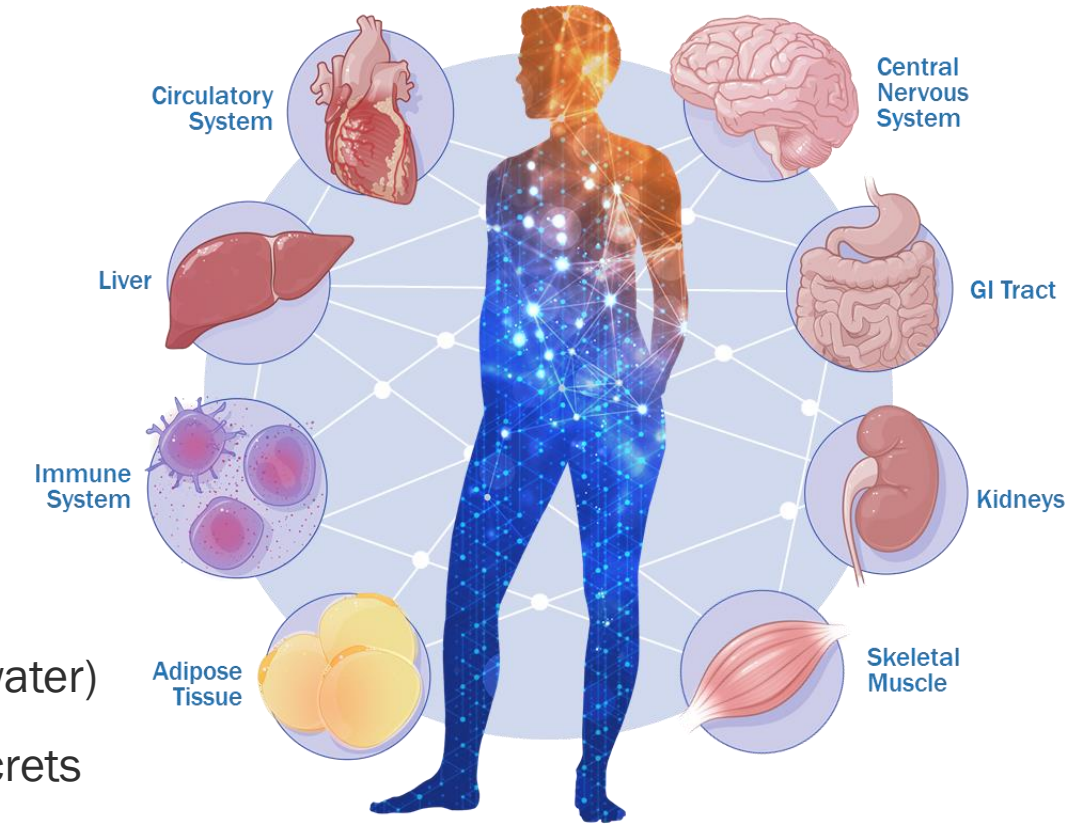
1. Company estimates based on Scaglione, S. et. al., J. Clin. Gastroenterol. (2015); HE Practice Guidelines by AASLD and EASL (2014); DelveInsight – HE Market Forecast (2019).
2. Based on currently marketed products only with potential for further expansion as new products come to market.
3. Company estimates based on Decision Resources Group (DRG) Non-alcoholic Steatohepatitis Landscape & Forecast.

Unlocking the Potential of Endogenous Metabolic Modulators (EMMs)

EMMs act as Master Regulators and Signaling Agents in human biology

Axcella's EMM Platform:

- Focused on amino acids and their derivatives; proven track record for clinical activity and safety/tolerability
- Utilize systems biology and machine learning to identify novel, multi-targeted compositions
- Potential to impact complex diseases in a multifactorial manner, working with the body's systems

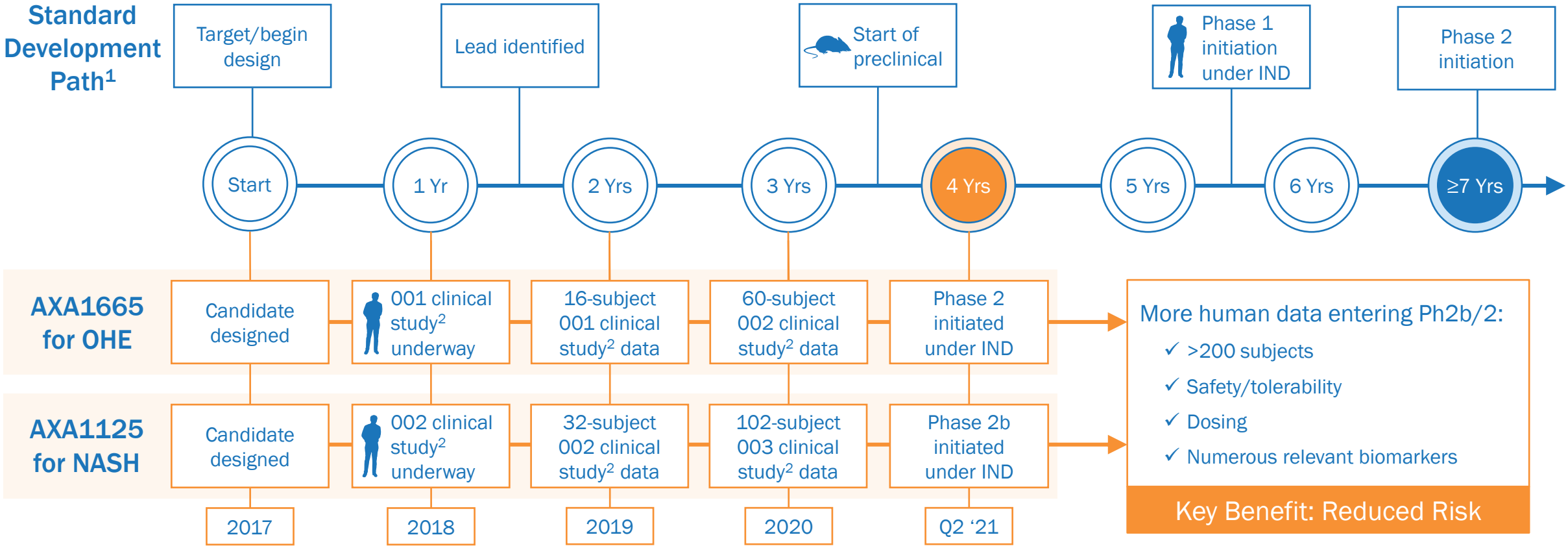


Axcella's Product Candidates:

- Administered orally (dry powder sachets mixed with 4-6 oz. of water)
- Protected by composition and method of use patents; trade secrets

Highly Informed, Rapid Paths to Later-Stage Clinical Trials

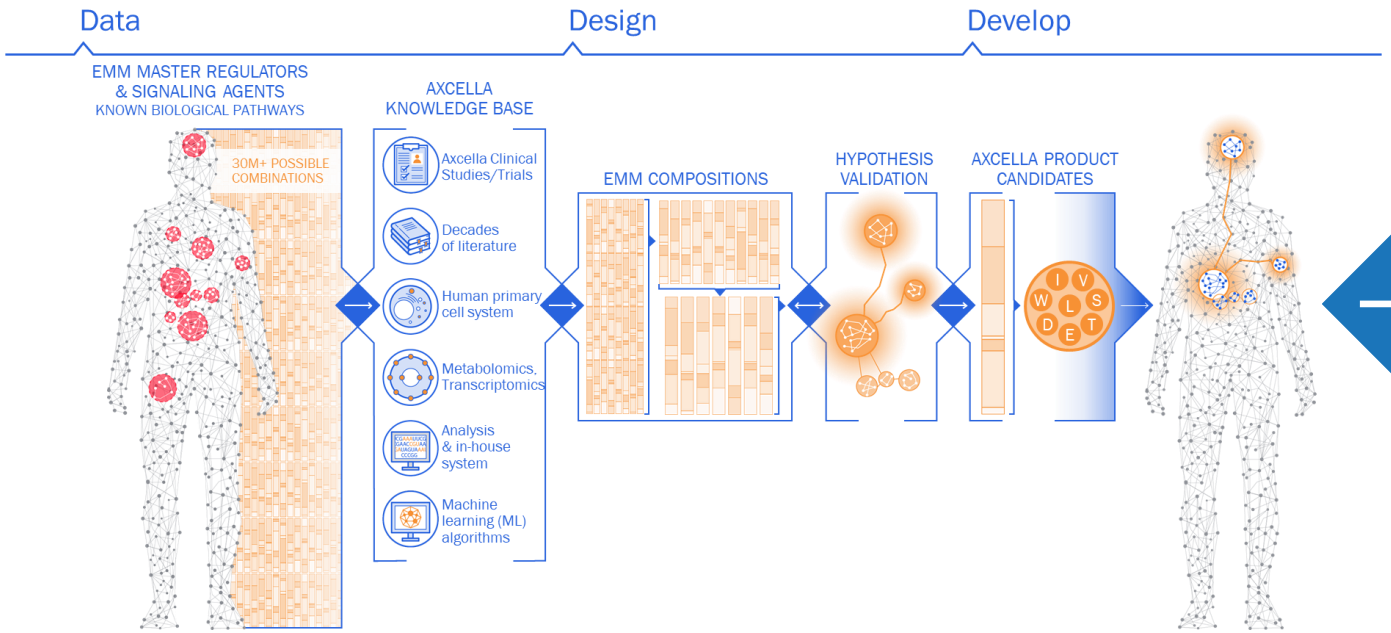
Extensive data from diseased human subjects generated in <4 years, helping to reduce program risk



1. Paul, S. M., et. al. Nature Reviews Drug Discovery (March 2010).
2. Non-IND clinical studies enrolling diseased human subjects. Please refer to slide 3 for further detail.

Timing of AXA1665 Phase 2 and AXA1125 Phase 2b clinical trials based on current expectations and subject to risks.

Potential for EMM Compositions in Many Areas



Initial Focus

- OHE
- NASH

Potential Applications

- Metabolism
- Mitochondrial
- Atrophy
- Inflammatory
- Immunology
- Neuroprotection

AXA1665

Potential Indication: Reduction in Risk of Recurrent Overt Hepatic Encephalopathy (OHE)

Status: Phase 2 Clinical Trial Ongoing

Overt Hepatic Encephalopathy (OHE)

A common, serious and complex manifestation of cirrhosis with substantial unmet needs

The Condition and Standards of Care:

- HE is a very common decline in brain function that occurs in cirrhotic patients
- Driven by a vicious cycle that includes reduced liver function, rising ammonia/aromatic amino acids and sarcopenia
- OHE, the most severe form of HE, can result in hospitalization, coma and eventually death
- Approved therapies (lactulose and rifaximin) challenged by limited mechanisms (ammonia scavengers), tolerability and compliance issues, OHE breakthrough events
- No effective treatments available for sarcopenia/frailty that results from cirrhosis

State of the Market:

- ~500,000 U.S. patients with minimal and overt hepatic encephalopathy[1]
- ~$1 billion annual U.S. market for OHE medications and growing[1,2]
- HE-related hospitalization costs exceed $7 billion annually and are rapidly growing[3]

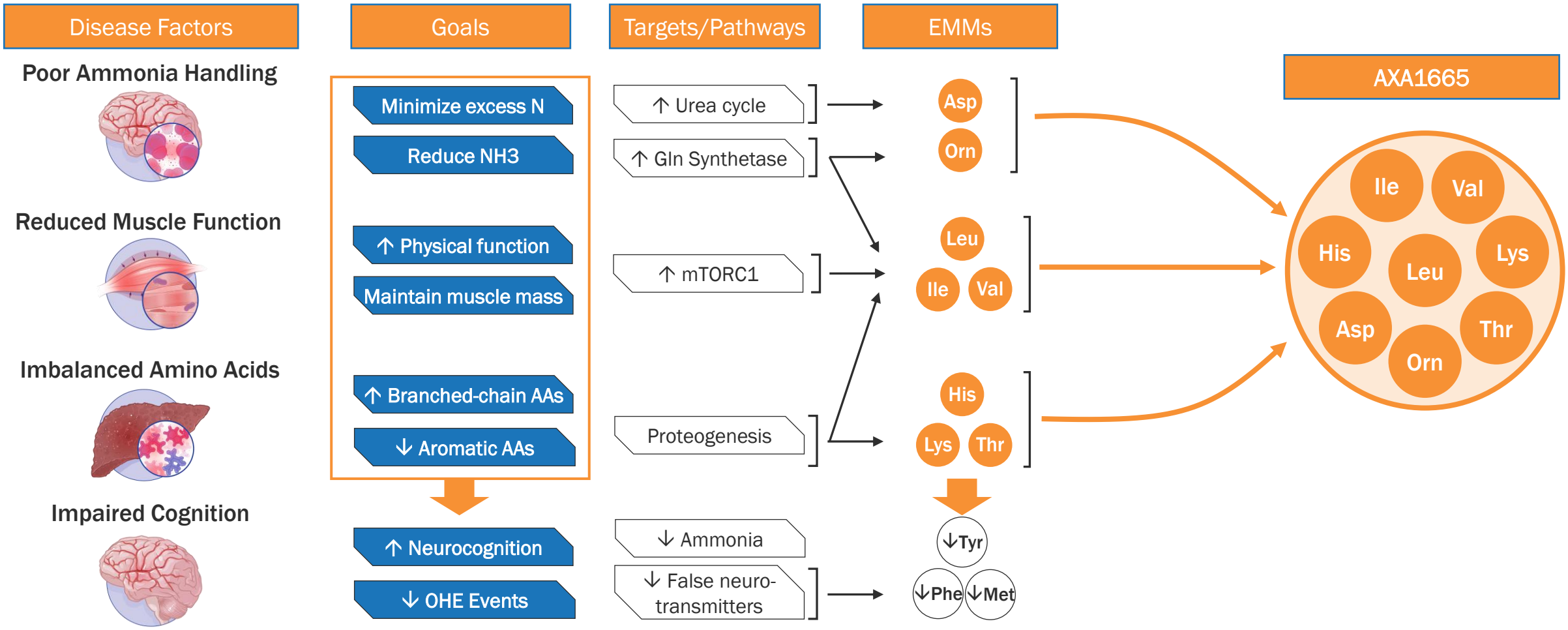
1. Company estimates based on Scaglione, S. et. al., J. Clin. Gastroenterol. (2015); HE Practice Guidelines by AASLD and EASL (2014); DelveInsight – HE Market Forecast (2019).
2. Based on currently marketed products only with potential for further expansion as new products come to market.
3. Flamm, S., Am J Manag Care (2018).

AXA1665: A Potential Comprehensive Treatment for OHE

- **Oral candidate with a multi-targeted mechanism** that goes well beyond today's ammonia-focused agents
- **Multifactorial effects observed** in ammonia, amino acid balance, muscle function and neurocognition
- **Modality utilizing inherently safe amino acids** substantially removes concerns about chronic use
- **Very well tolerated to date** with AE rates comparable to placebo
- **Potential to improve – and eventually become – the standard of care**

AXA1665 - A Potential Comprehensive OHE Therapy

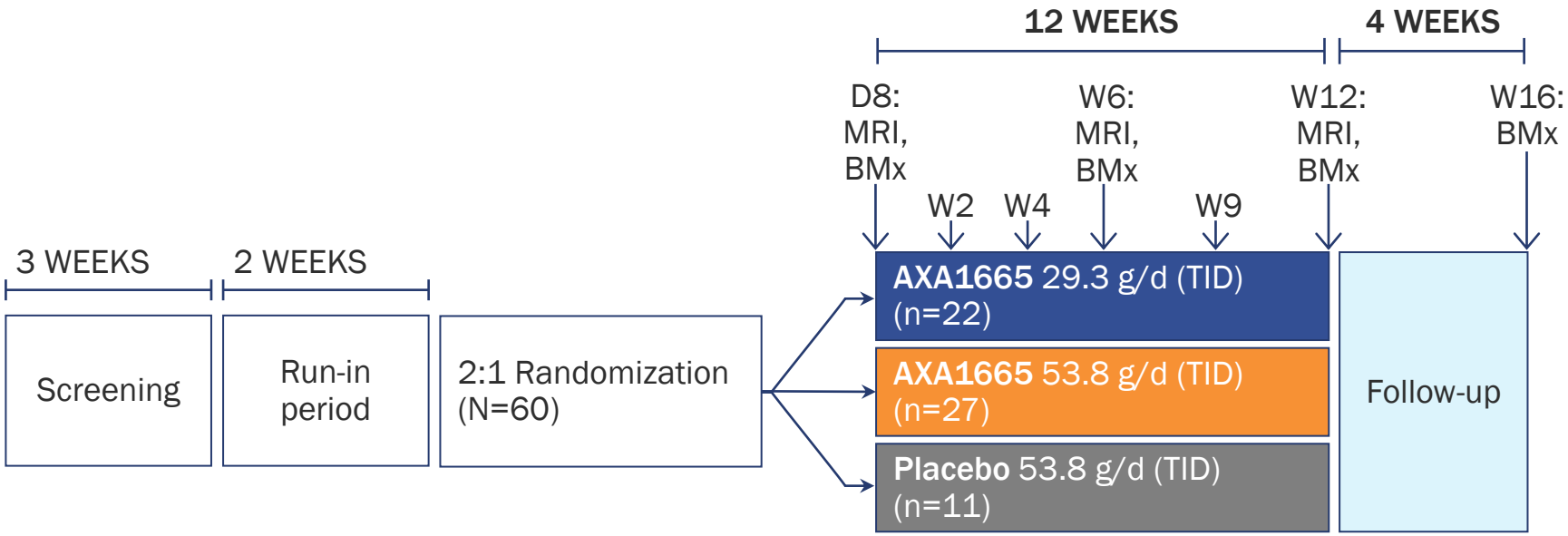
Designed to target multiple metabolic pathways; potential for multifactorial activity in cirrhosis



Hypothesized mechanisms depicted above.
Abbreviations: Asp, aspartate; Cit, citrulline; Gln, glutamine; Glu, glutamic acid; His, histidine; Ile, isoleucine; Leu, leucine; Lys, lysine; Met, methionine; mTORC1, mammalian target of rapamycin complex 1; NH3, ammonia; Orn, ornithine; Phe, phenylalanine; Thr, threonine; Tyr, tyrosine; Val, valine.

AXA1665-002: A 12-Week Placebo Controlled Study in Subjects with Mild and Moderate Hepatic Insufficiency

60 subjects enrolled and dosed for 12 weeks



KEY STUDY ELEMENTS[1]

Inclusions: Compensated cirrhosis without prior OHE; non-sarcopenic

Primary endpoint: Safety & tolerability (not powered for statistical significance)

Key structure-related assessments included those focused on body composition and muscle MRI; key function-related assessments included those focused on LFI, gait speed, psychometric tests

SAFETY/TOLERABILITY FINDINGS

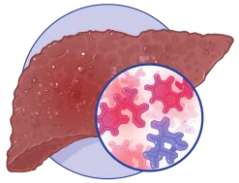
- AE rates from 36% to 50% in all arms; AEs generally mild/moderate and unrelated to study administration (no AE patterns/dose relationship)
- Five SAEs reported during administration period, none of which were attributed to AXA1665
- Two fatalities, neither attributed to AXA1665 (One myocardial infarction prior to dosing, one COVID-19)

1. Non-IND clinical study initiated prior to therapeutic development path decision. Please refer to slide 3 for further detail.
Abbreviation: BMx, biomarkers.

AXA1665-002: Improvement Noted in Key Biomarkers

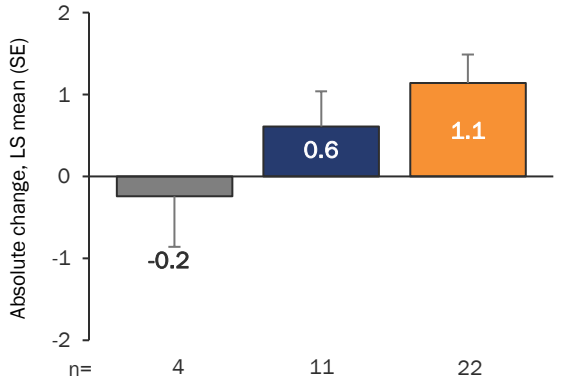
Data in a population with mostly mild hepatic insufficiency (Child A), without overt sarcopenia, but with MHE

Amino Acid Metabolism

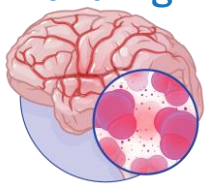


Change in Fischer Ratio Over Time[1]

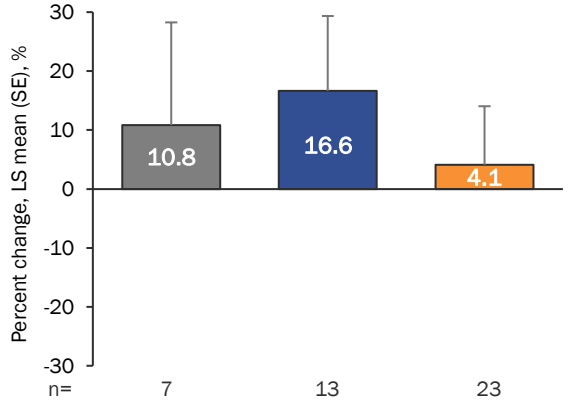
Change in Fischer Ratio



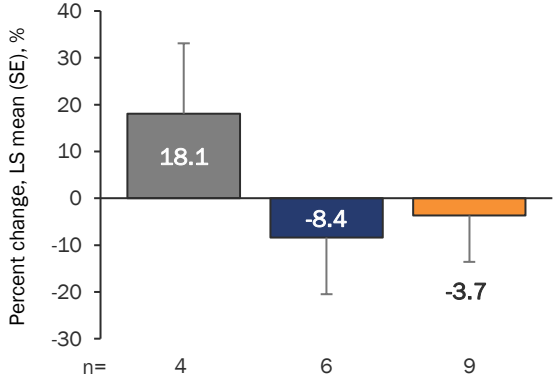
Ammonia Handling



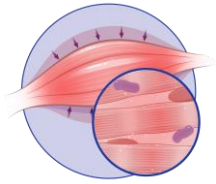
Ammonia Change in Safety Population



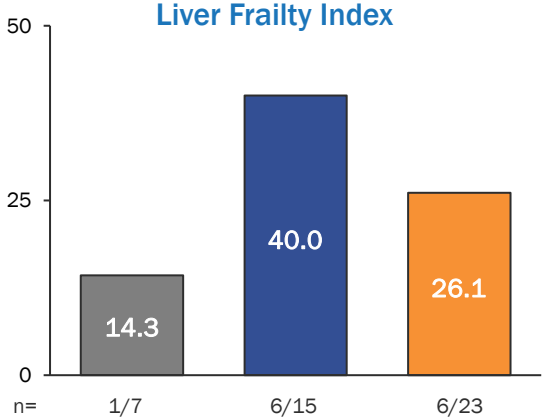
Ammonia Change in MHE Subpopulation



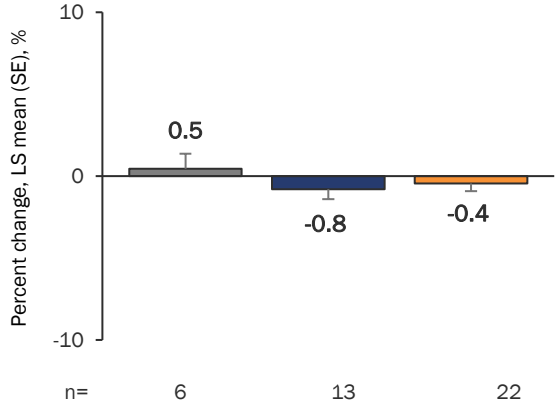
Muscle Metabolism



% of Subjects with ≥0.3 Reduction in Liver Frailty Index



Total Thigh Muscle Volume



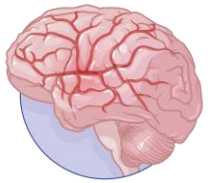
*p<0.05 vs. Placebo

Placebo | AXA1665 Low | AXA1665 High

1. 11, 22 and 27 subjects in placebo, AXA1665 low-dose, and AXA1665 high-dose arms, respectively, were included in the analysis; LS = Least-squares;

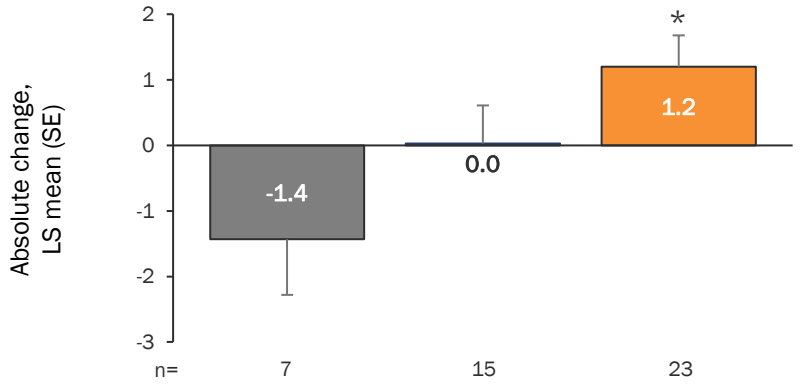
Dose Dependent Improvement Consistently Observed Across All Three Measures of Cognitive Function

Changes from baseline at week 12



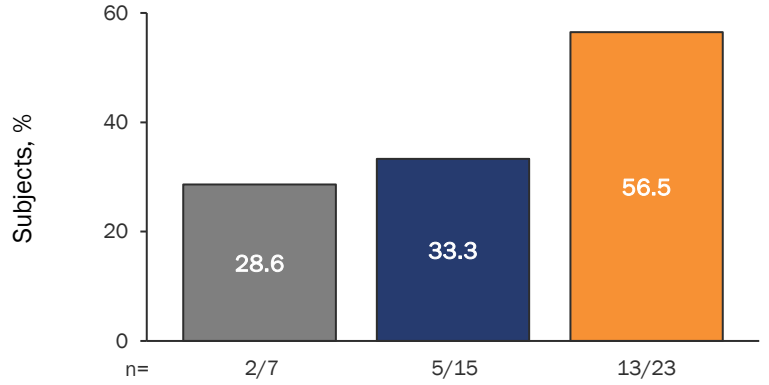
Cognitive Function

Psychometric Hepatic Encephalopathy Score (PHES)

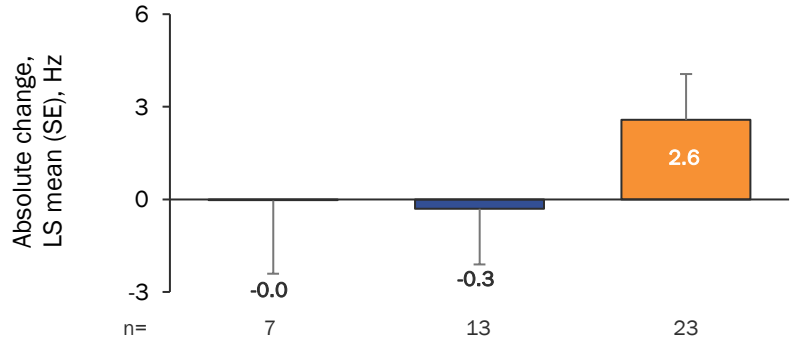


*p<0.01 vs. Placebo

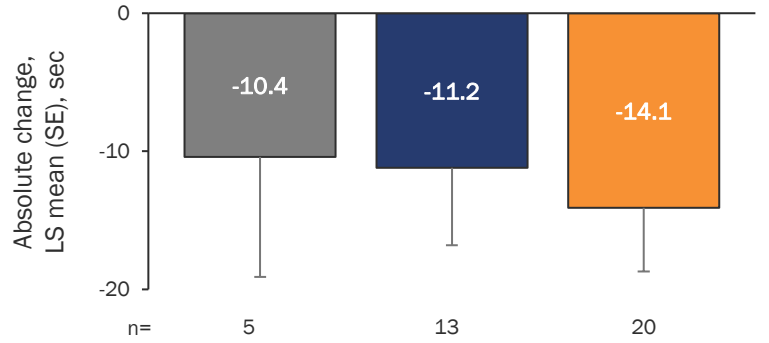
≥+2 change in PHES[1]



Critical Flicker Frequency (CFF)



Stroop Off+On Time

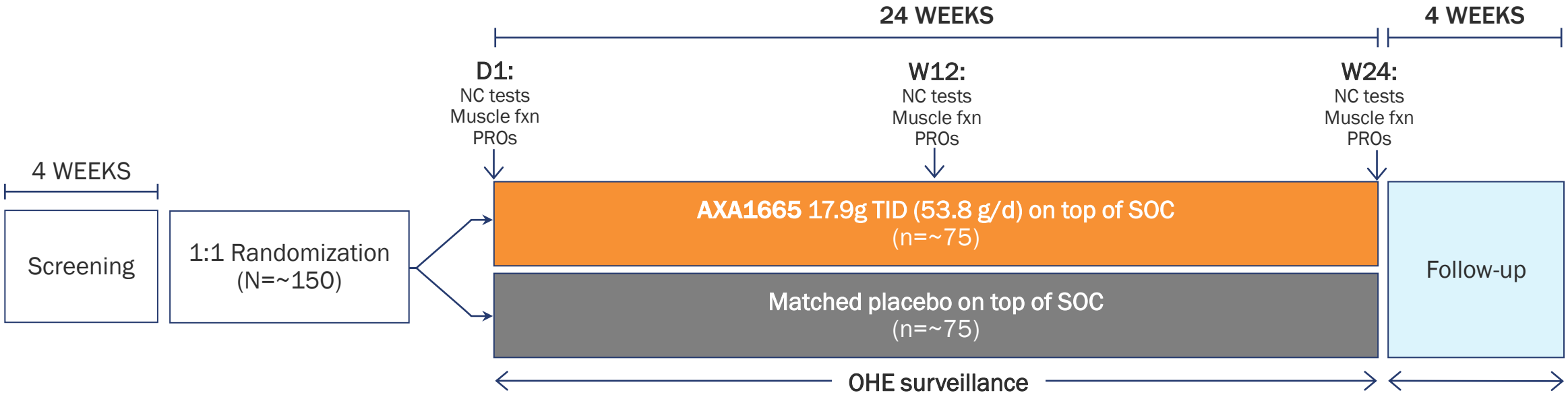


Placebo | AXA1665 Low | AXA1665 High

1. Considered to be a clinically relevant threshold based on PHES improvements ranging from 2.1 to 3.2 for lactulose, probiotics and LOLA in prior clinical trials. Singh, J, et al. Metab Brain Dis. 2017; Shavakhi, A, et al. J Res Med Sci. 2014; Varakanahalli, S, et al. Eur J Gastroenterol Hepatol (2018).

Phase 2 Clinical Trial Underway

Efficient design to measure PHES, OHE event rates, physical function, PROs



Core elements	Description
Design	• Randomized double blind, placebo-controlled study over 24 weeks
Study population	• Cirrhotic patients with at least 1 prior OHE event and with PHES ≤ –4 at screening with no active OHE at baseline • Stable OHE background therapy and stratified on rifaximin use
Primary endpoint	• Proportion of patients with ≥2 improvement in PHES from baseline to 24 weeks
Secondary and other endpoints	• Proportion of patients experiencing an OHE breakthrough event; time to first OHE breakthrough event, including time to hospitalization; changes in physical function; patient reported outcomes; ammonia, amino acid and inflammatory biomarkers

NC: neurocognitive; fxn: function; PROs: patient reported outcomes; SOC: standard of care (lactulose ± rifaximin)

AXA1125

Potential Indication: Non-Alcoholic Steatohepatitis (NASH)

Status: Phase 2b Clinical Trial Ongoing

Nonalcoholic Steatohepatitis (NASH)

A complex, chronic disease impacting up to 40 million Americans with no approved therapies

The Disease and Standard of Care:

- Progressive, chronic liver disease involving multiple drivers and pathways
- No NASH therapies approved in U.S.
- Comorbid population (T2D, heart disease, etc.) that already is on ~7 medications[1]
- Most drug candidates have single targets, leading to combination therapy development
  - Administration, safety tolerability challenges (injectables, lipids, pruritis, DDI, etc.)
  - Very limited pediatric development activity

State of the Market:

- Up to 40 million NASH patients in the U.S. alone and growing rapidly[2]
- Approximately 10% of U.S. children are estimated to have NASH[2]
- >40% of NASH patients also have type 2 diabetes (T2D)[3]
- Lifetime costs for all U.S. NASH patients exceeds $300 billion[2]

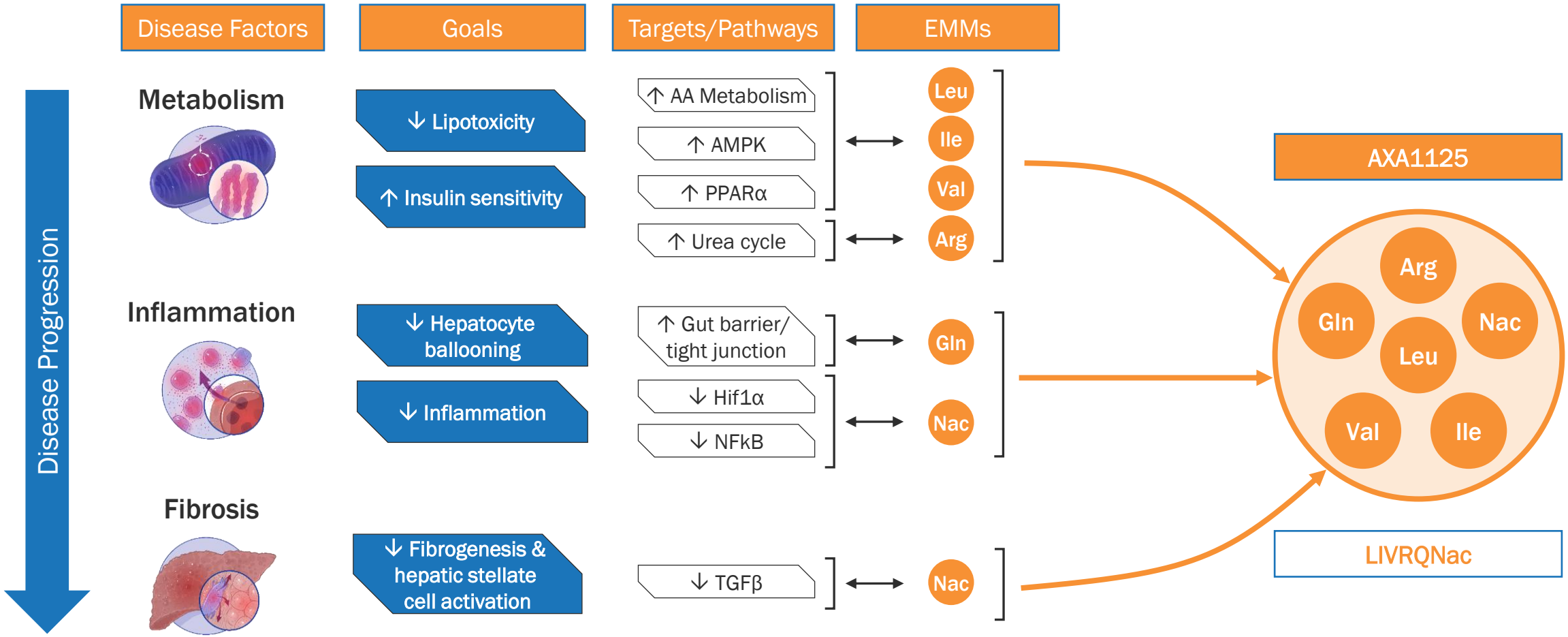
1. Desai, R. et al. Characterization of Polypharmacy in Patients with NAFLD. AASLD 2018
2. Global Liver Institute U.S. NASH Action Plan (Dec. 2020).
3. Younossi, Z. et al. Hepatology. Vol. 64, No. 1, 2016.

AXA1125: A Potential First-Line Treatment for NASH

- Oral candidate with a multi-targeted mechanism aimed at metabolism, inflammation and fibrosis pathways
- Data to date compare favorably with other oral agents, with enhanced activity in T2D
- Modality utilizing inherently safe amino acids substantially removes concerns about chronic use
- Very well tolerated to date with limited AE rates, no attributed SAEs and no impact on lipids or weight
- **Compelling candidate for first-line monotherapy, combo and pediatric use**

AXA1125 - Designed to Target Multiple Metabolic Pathways

Potential for multifactorial activity in NASH and compounding benefits over time

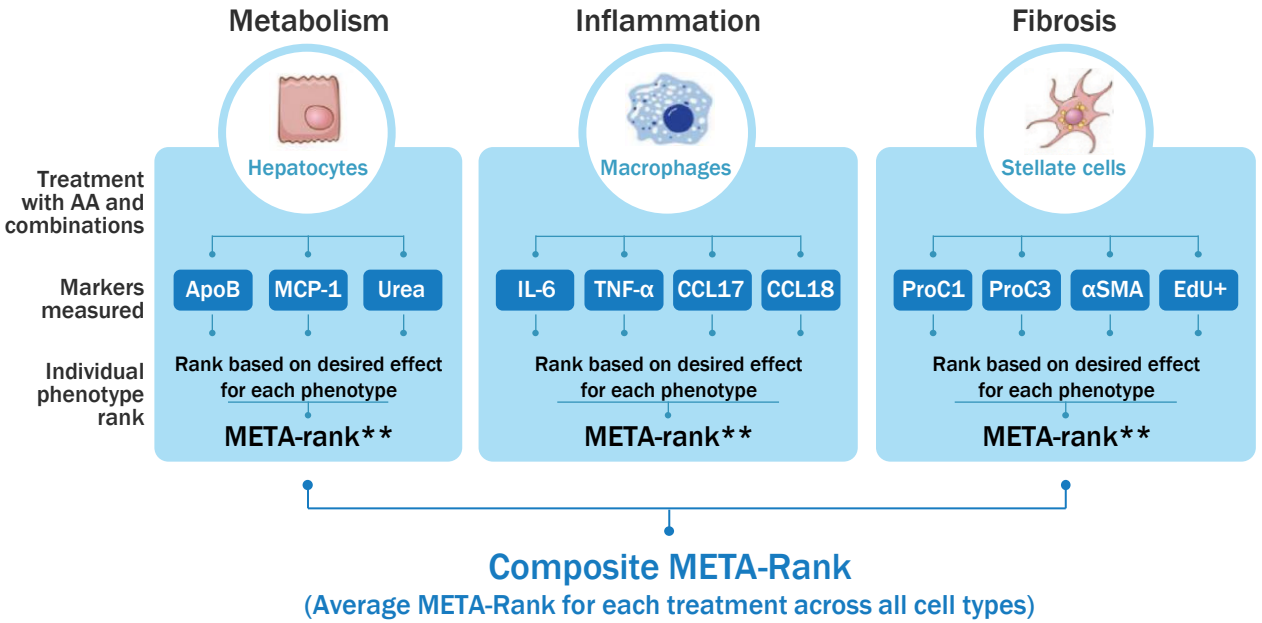


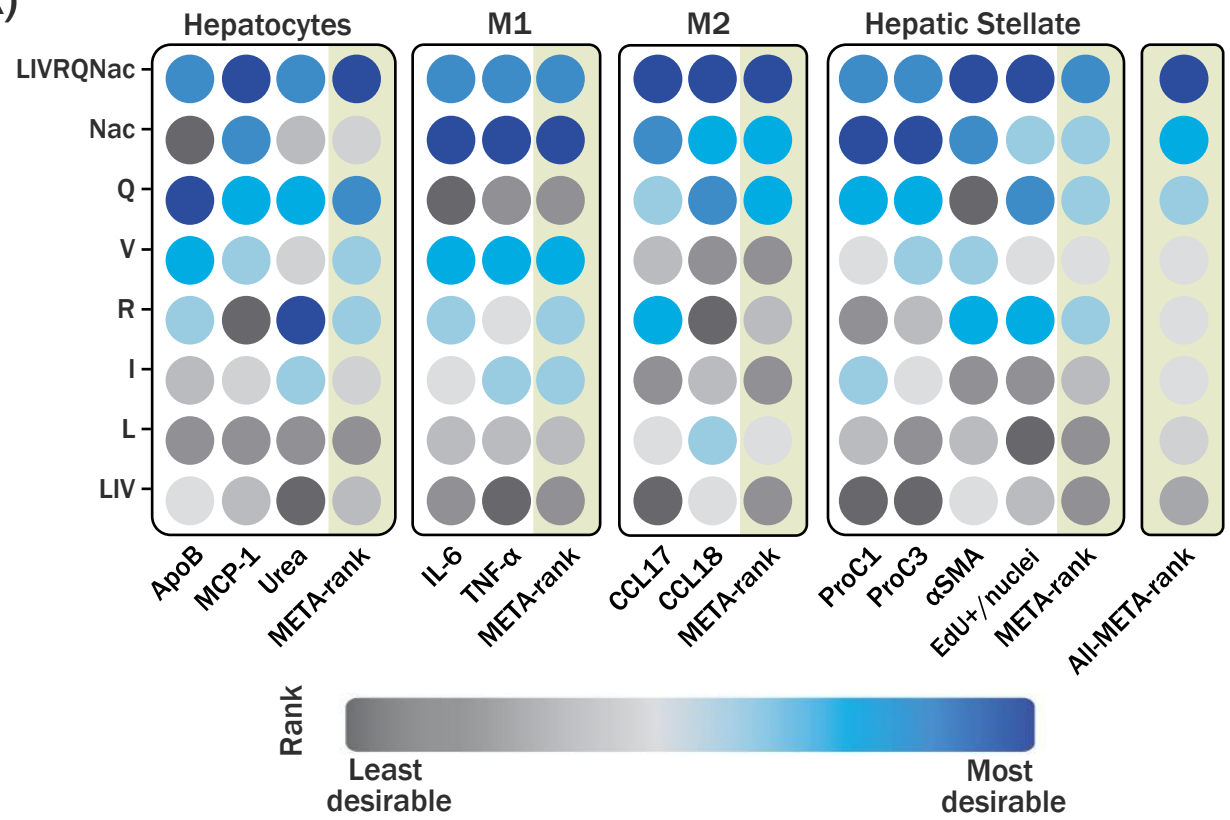
Hypothesized mechanisms depicted above.
AAs, amino acids; AMPK, AMP-activated protein kinase; Arg, arginine; Gln, glutamine; GSH, glutathione; Hif1α, hypoxia-inducible factor 1 alpha; GSH, glutathione; Ile, isoleucine; Leu, leucine; Nac, N-acetylcysteine; NASH, nonalcoholic steatohepatitis; NFκB, nuclear factor kappa-light-chain-enhancer of activated B cells; NH3, ammonia; NO, nitric oxide; PPARα, peroxisome proliferator-activated receptor alpha; ROS, reactive oxygen species; TGFβ, transforming growth factor beta; Val, valine.

Unique Impacts Across NASH Pathways in Cell Systems

LIVRQNac composition consistently outperforms its constituents in NASH META-rank

Multi-Objective Optimization Global Ranking (META-Rank)



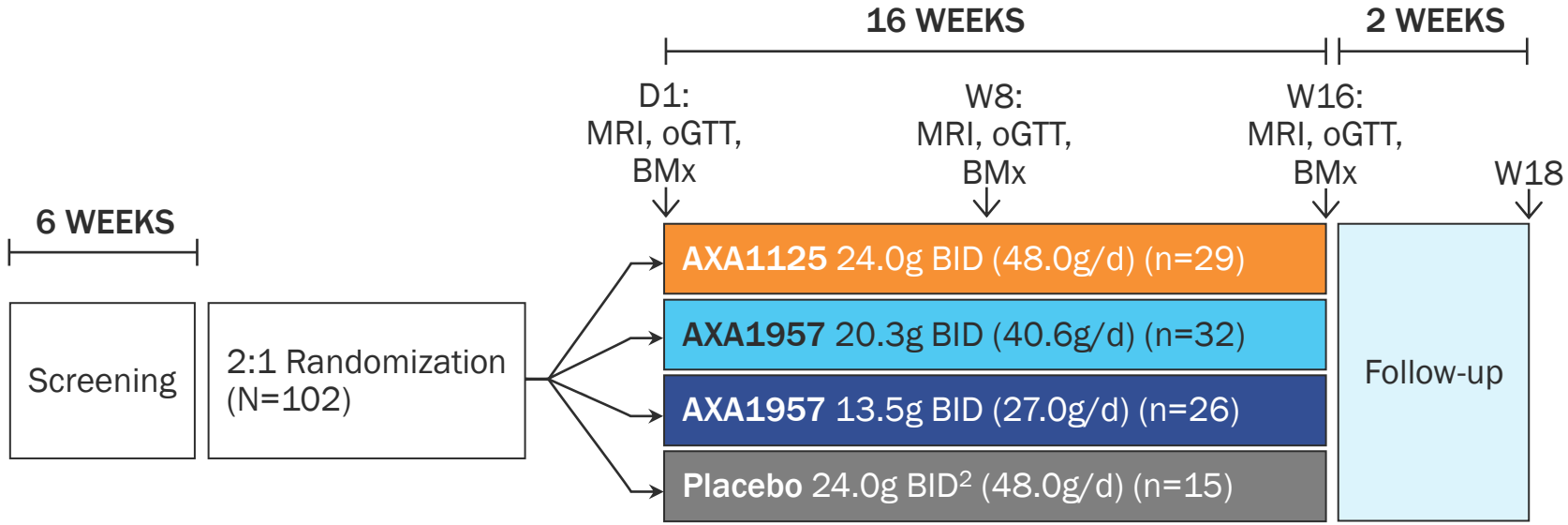


**Mean of the ranks for phenotypes measured in each cell type.
Ranking system: 1 is the most desirable and 9 is the least desirable.

αSMA, α-smooth muscle actin; AA, amino acid; ApoB, apolipoprotein B; CCL, C-C motif chemokine ligand; EdU, 5-ethynyl-2´-deoxyuridine; I, isoleucine; IL-4, interleukin 4; IL-6, interleukin 6; L, leucine; LIV, leucine/isoleucine/valine; LIVRQNac, 5 amino acids and N-acetylcysteine; LPS, lipopolysaccharide; M, macrophage; MCP-1, monocyte chemoattractant protein 1; Nac; N-acetylcysteine; Q, glutamine; ProC1, N-terminal type I collagen propeptide; ProC3, N-terminal type III collagen propeptide; R, arginine; sFFA, saturated free fatty acid; TGF-β, tumor growth factor-beta; TNF-α, tumor necrosis factor-alpha; V, valine.

Design of Our Most Recent Clinical Study: AXA1125-003

102 subjects enrolled and dosed in this 16-week clinical study



KEY STUDY ELEMENTS[1]

Inclusions: >10% fat by MRI-PDFF, cT1 >830 mSec

Stratified by T2D and non-diabetic subjects

Primary endpoint: Safety & tolerability (not powered for stat. sig.)

Key assessments: liver structure by MRI-PDFF and cT1; liver function by glucose, lipid homeostasis, inflammation, apoptosis and fibrosis BMx

SAFETY/TOLERABILITY FINDINGS

Most common findings were transient and self-resolving mild to moderate gastrointestinal AEs (mostly diarrhea)

Low rate of discontinuation due to AEs

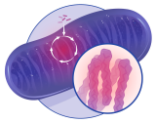
No effects on lipids or body weight

1. Non-IND clinical study initiated prior to therapeutic development path decision. Please refer to slide 3 for further detail.
2. Calorie-matched placebo control.

BID, 2 times a day; BMx, biomarkers; D, Day; cT1, corrected T1; IND, investigational new drug; MRI-PDFF, magnetic resonance imaging proton density fat fraction; oGTT, oral glucose tolerance test; T2D, type 2 diabetes; W, Week.

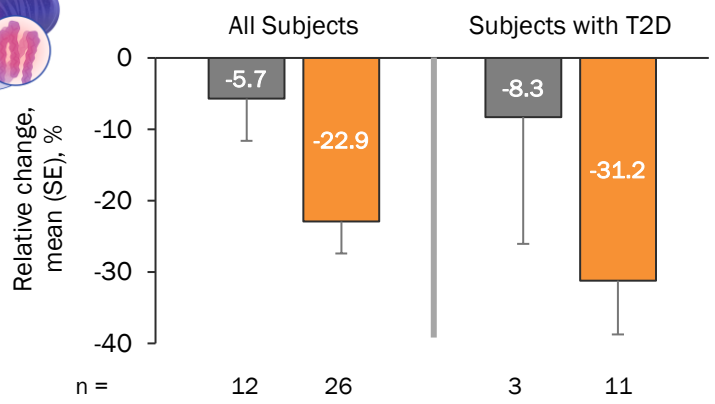
Reductions Noted in Key Biomarkers with AXA1125

Changes from baseline at week 16

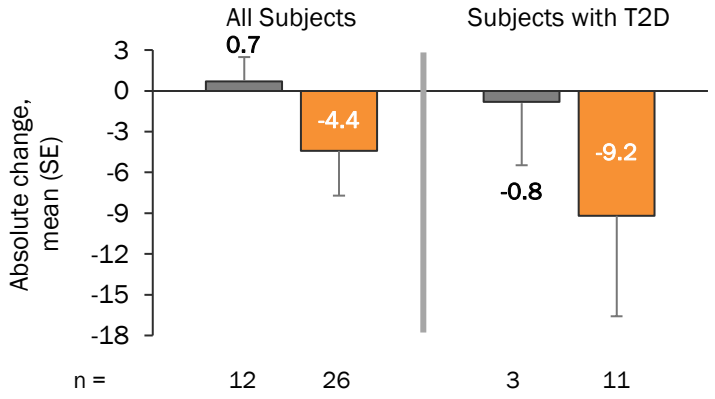


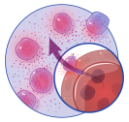
Metabolism

MRI-PDFF



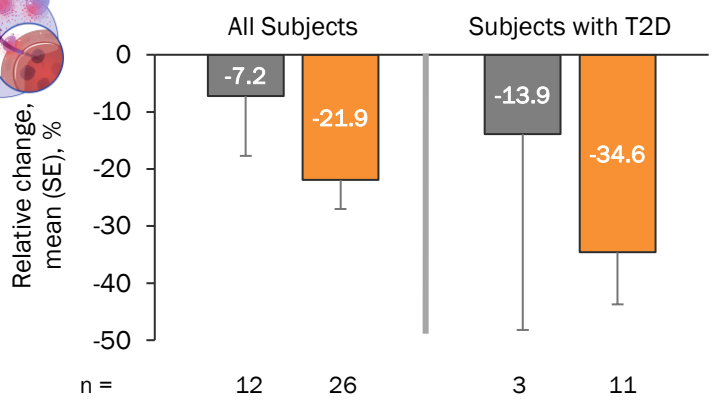
HOMA-IR



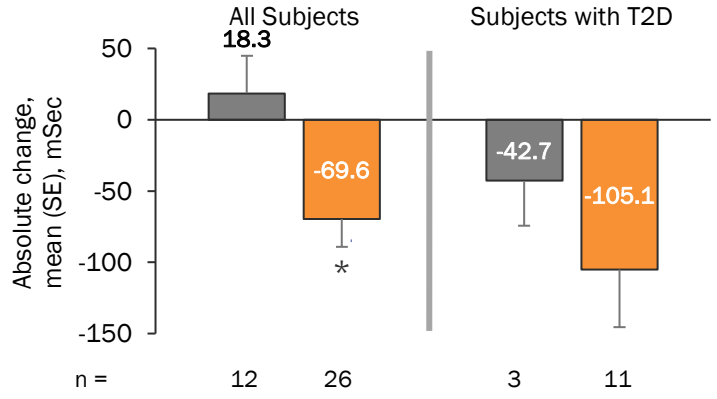


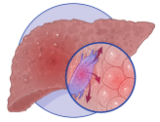
Inflammation

ALT



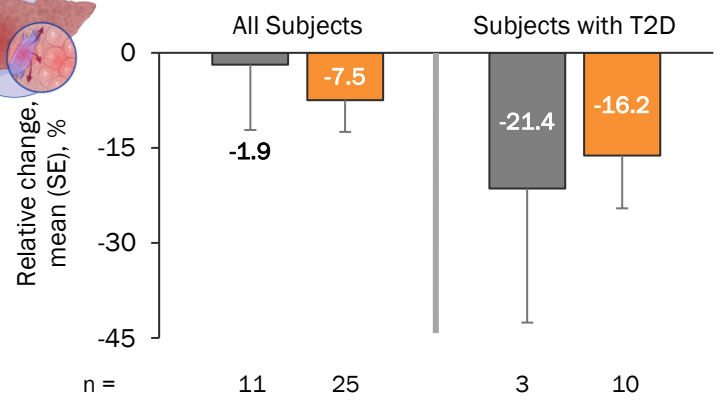
cT1



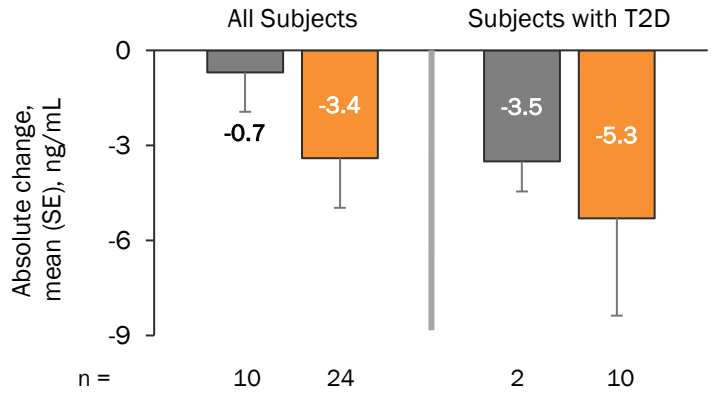


Fibrosis

FIB-4



ProC3



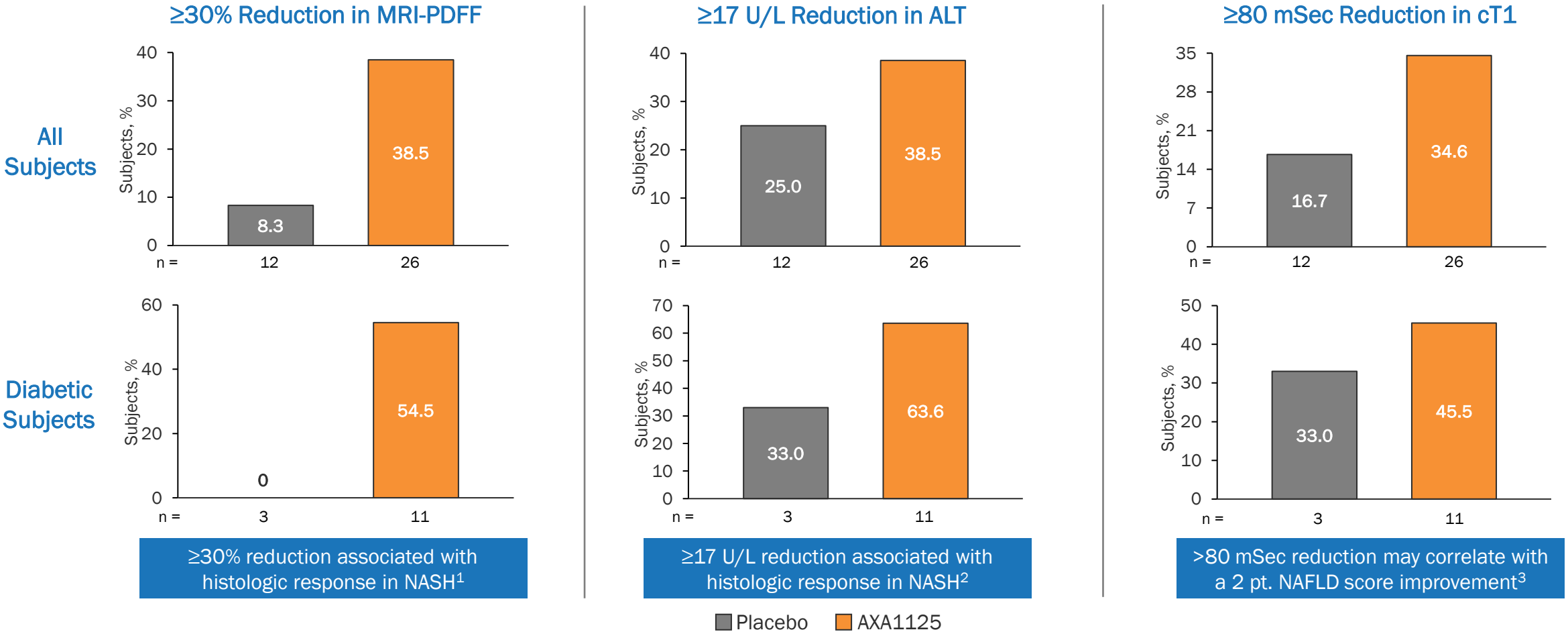
Placebo AXA1125

*p<0.05 versus placebo.

ALT, alanine aminotransferase; cT1, corrected T1; FIB-4, fibrosis 4; HOMA-IR, homeostasis model assessment of insulin resistance; MRI-PDFF, magnetic resonance imaging proton density fat fraction; ProC3, propeptide of type III collagen; SE, standard error; T2D, type 2 diabetes.

AXA1125: Meaningful Thresholds of Activity Achieved

Increasing evidence linking PDFF, ALT and cT1 with improved histological outcomes

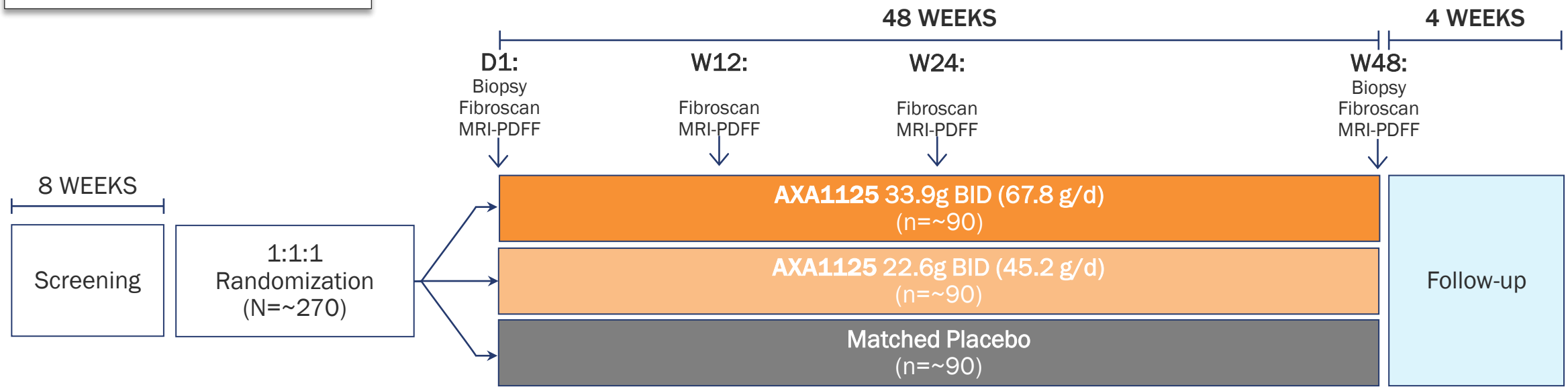


1. Loomba, R. et al. Hepatology (January 2020). 2. Loomba, R. et al. Gastroenterology (January 2019). 3. Dennis, A. et al. Frontiers in Endocrinology (November 2020).
ALT, alanine aminotransferase; cT1, corrected T1; MRI-PDFF, magnetic resonance imaging proton density fat fraction; NASH, nonalcoholic steatohepatitis; NAFLD, non-alcoholic fatty liver disease; SE, standard error.

EMMPACT℠ NASH CLINICAL TRIAL

Phase 2b Clinical Trial Underway

Interim analysis expected in mid-2022



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 diabetic status
Primary endpoint	• Biopsy-confirmed ≥2 point improvement in NAS
Secondary endpoints	• Biopsy-confirmed resolution of NASH without worsening of fibrosis • Biopsy-confirmed ≥1 stage improvement in fibrosis without worsening of NASH
Other endpoints	• Improvement in non-invasive markers, including MRI-PDFF, ALT and Fibroscan

Summary

Strategy Intended to Protect Axcella's First-Mover Advantages

PATENTING AREAS

Composition/Method of Use

- Liver
- Muscle
- Blood
- CNS

Platform-Focused

- Mechanistic and biological pathway uses

Formulation/Manufacturing

- Pharmaceutical-grade manufacturing
- Taste formulations

LEAD CANDIDATES

Composition and methods of use patents granted for AXA1125 and AXA1665; expirations in 2037 and 2038, respectively

TRADE SECRETS

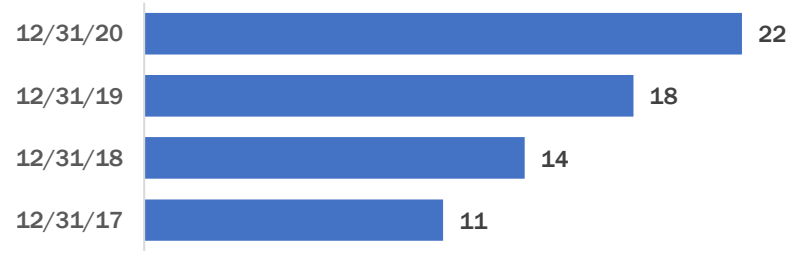
Leveraging extensive know how underlying research platform, EMM composition design and manufacturing

REGULATORY EXCLUSIVITY

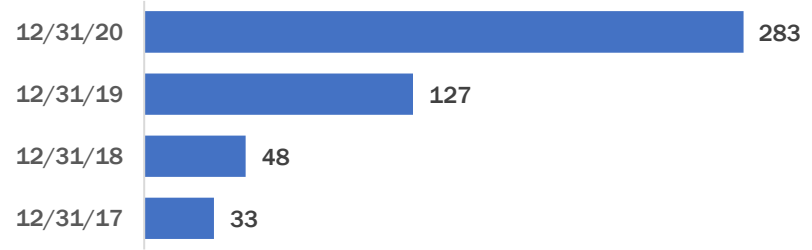
Plans to pursue regulatory exclusivity where available, particularly in U.S., Europe, Japan

PATENTS & APPLICATIONS

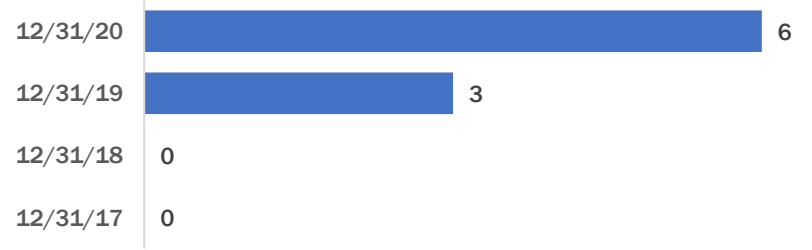
WORLDWIDE PATENT FAMILIES



WORLDWIDE PATENTS PENDING



U.S. PATENTS GRANTED/ALLOWED



Well Capitalized for Next Steps

$93 million in cash and marketable securities at March 31, providing runway into Q3 of 2022

(in thousands)	March 31, 2021
Assets:	
Cash and cash equivalents	$43,049
Marketable securities	49,909
Other assets	1,522
Total assets	**$94,480**
Liabilities and stockholders' equity:	
Liabilities	$32,822
Stockholders' equity	61,658
Total liabilities and stockholders' equity	**$94,480**

	Three Months Ended March 31,	
(in thousands, except share and per share data)	2021	2020
Operating expenses:		
Research and development	$10,240	$10,335
General and administrative	4,256	4,125
Total operating expenses	14,496	14,460
Loss from operations	(14,496)	(14,460)
Other income (expense), net	(693)	(549)
Net loss	$(15,189)	$(15,009)
Net loss per share, basic and diluted	$(0.40)	$(0.65)
Weighted average common shares outstanding, basic and diluted	**37,652,158**	**23,188,816**

Axcella's Experienced Leadership

Bill Hinshaw
President and CEO
NOVARTIS
Schering-Plough

Alison Schecter, MD
President, R&D
Baxalta SANOFI J&J

Paul Fehlner, PhD, JD
SVP and Chief Legal Officer
NOVARTIS
BAKER BOTTS LLP

Laurent Chardonnet
SVP and Chief Financial Officer
Incyte SANOFI

Virginia Dean
SVP and Chief People Officer
ARIAD TESARO

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Flagship Pioneering

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bluebird bio

Cristina Rondinone, PhD
Founder,
CMR Pharma Consulting

Shreeram Aradhye, MD
CMO
Dicerna Pharmaceuticals

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President and CEO
Axcella Health

Stephen Hoge, MD
President
Moderna Therapeutics

Catherine A. Sohn, PharmD
Adjunct Professor
University of California San Francisco

Greg Behar
CEO
Nestlé Health Science

Gary Pisano, PhD
Professor of Business
Harvard Business School

NASDAQ: AXLA

Thank You

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Cambridge, MA 02139

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Reference Materials

Axcella's EMM Platform and Therapeutic Approach

Use of Amino Acids as Therapeutics (*iScience*)

Combinatorial approach to EMMs (ICFSR)

AXA1665 for OHE

AXA1665-001 Data (*Clinical and Translational Gastroenterology*)

AXA1125 for NASH

Mechanism of Action (NASH-TAG 2021)

Nonclinical Findings (Nature's *Scientific Reports*)

AXA1125-003 All-Comer Data (EASL 2020 Late Breaker)

AXA1125-003 T2D Data (AASLD 2020)