NASDAQ: AXLA

AXA1665-002 Top-Line Data

August 5, 2020

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 the company's EMM product candidates, including for AXA1125 and AXA1665, the design, status and timing of the company's ongoing clinical studies and planned IND-enabled clinical trials, the company's anticipated program milestones, the subject and timing of the company's planned interactions with the FDA on the AXA1665 and AXA1125 programs, including potential timing of IND application submissions, and the potential of the company's product candidates to impact health and/or disease, including AXA1125's potential in NASH and AXA1665's potential in OHE. 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 on the company's ability to conduct and complete its ongoing or planned clinical studies and IND enabled clinical trials and planned interactions and 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 AXA1665-002 and AXA4010-001 clinical studies and potential delays in disclosure of the same, other potential impacts of COVID-19 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, whether data readouts and/or FDA feedback support our IND submission and clinical trial initiation plans and timing, clinical trial design and target indication for AXA1125 and AXA1665, the clinical development and safety profile of the company's product candidates and their health or therapeutic potential, whether and when, if at all, the company's 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 the company's 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 the company's views only as of the date hereof and should not be relied upon as representing its views as of any subsequent date. The company explicitly disclaims any obligation to update any forward-looking statements.

About Axcella's Development Model and Clinical Approach

EMMs have a fundamental role in biology and 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. They 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 terminate its development.

To date, Axcella has evaluated its current product candidates as investigational food products in non-IND clinical studies. Axcella has determined its lead compounds – AXA1665 and AXA1125 – to be therapeutic product candidates, meaning that pending and subject to final data readouts from non-IND clinical studies and FDA feedback, any future development of these product candidates will be under IND clinical trials. These IND clinical trials would therefore be designed to evaluate each product candidate's ability to diagnose, cure, mitigate, treat or prevent targeted diseases. The company's current plans are to target OHE with AXA1665 and NASH with AXA1125 in IND clinical trials.

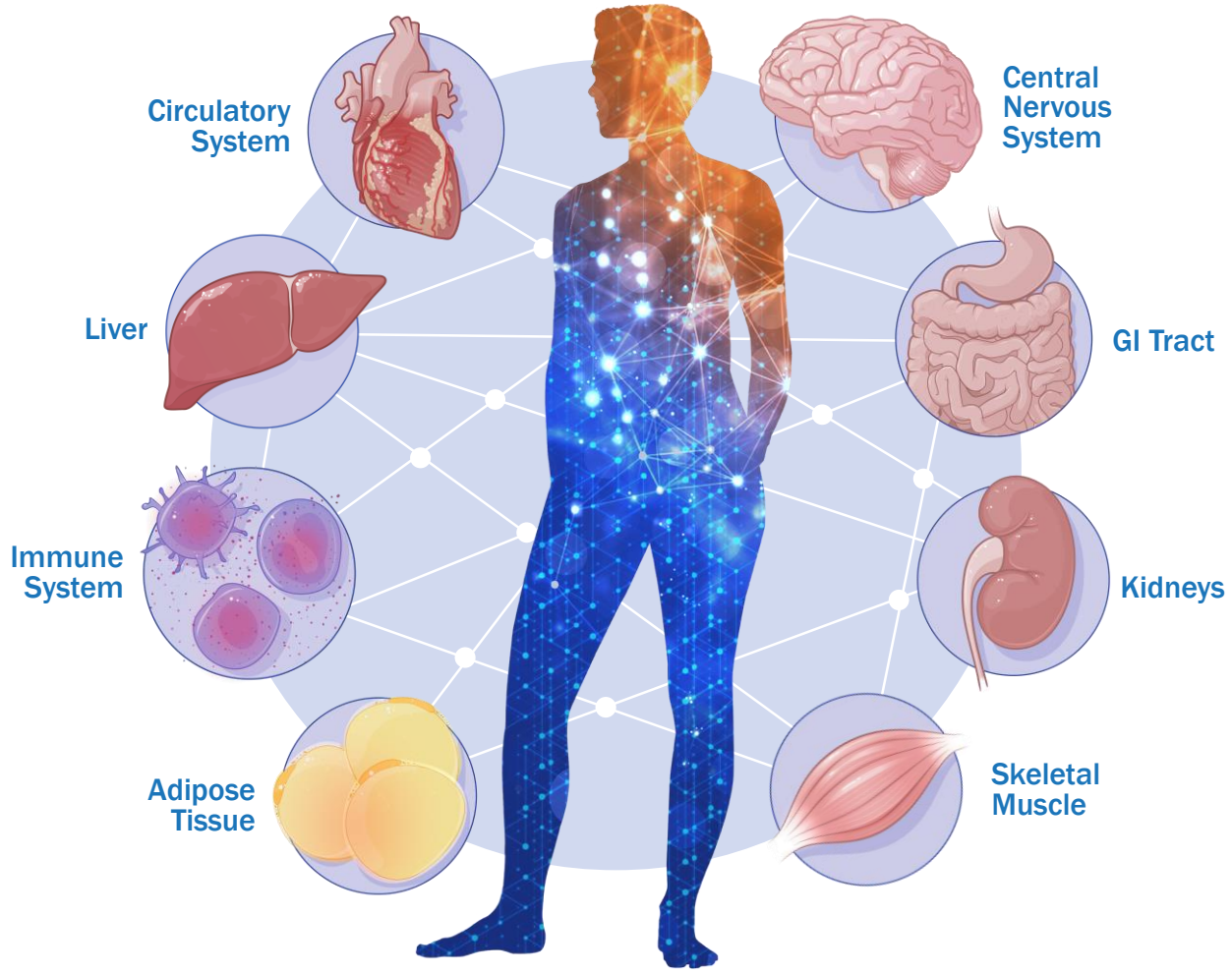
In the future, if Axcella decides to pursue therapeutic development for a new product candidate, it will initiate clinical development under an IND-enabled trial.

This presentation refers to Axcella's non-IND clinical studies as "Clinical Studies" and its planned IND-enabled clinical trials as "Clinical Trials."

Axcella's Focus: Endogenous Metabolic Modulators (EMMs)

EMMs Act as Signaling Agents and Master Regulators in Human Biology

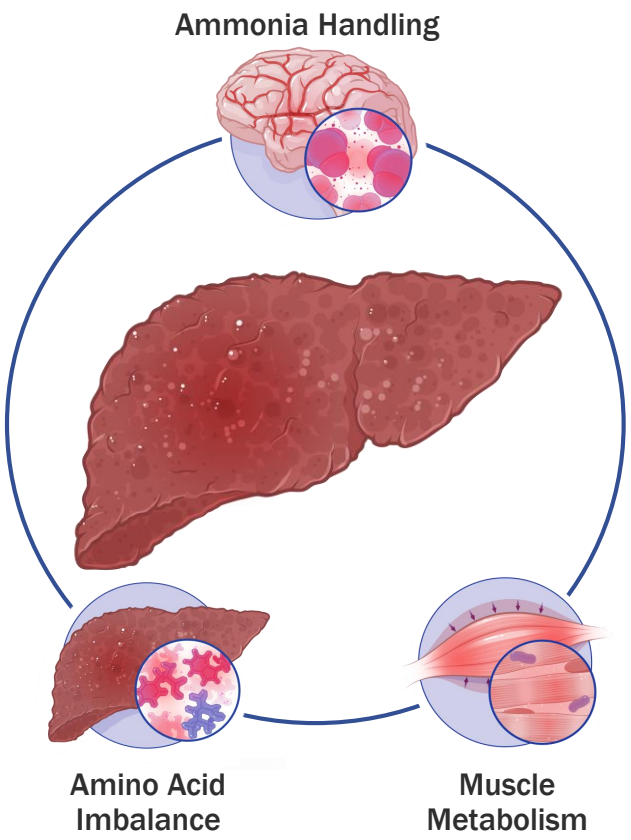
- EMMs, including amino acids, are well established agents used to support health
- Single EMMs and simple EMM combinations have been approved as treatments for various diseases
- Leveraging advances in machine learning and systems biology, Axcella is developing novel EMM compositions that:
  - Include up to 10 amino acids and derivatives
  - Are designed to affect multiple biological pathways simultaneously
  - Have disease-modifying potential



Overt Hepatic Encephalopathy

A complex disease with unmet need that would benefit from a multifactorial intervention

Key Processes Involved in HE



Unmet Needs:

- Limited use of existing treatments: rifaximin and lactulose due in part to tolerability/compliance
- Existing treatments do not adequately address other disease drivers such as muscle wasting
- Continued need to improve neurocognition and reduce OHE episodes

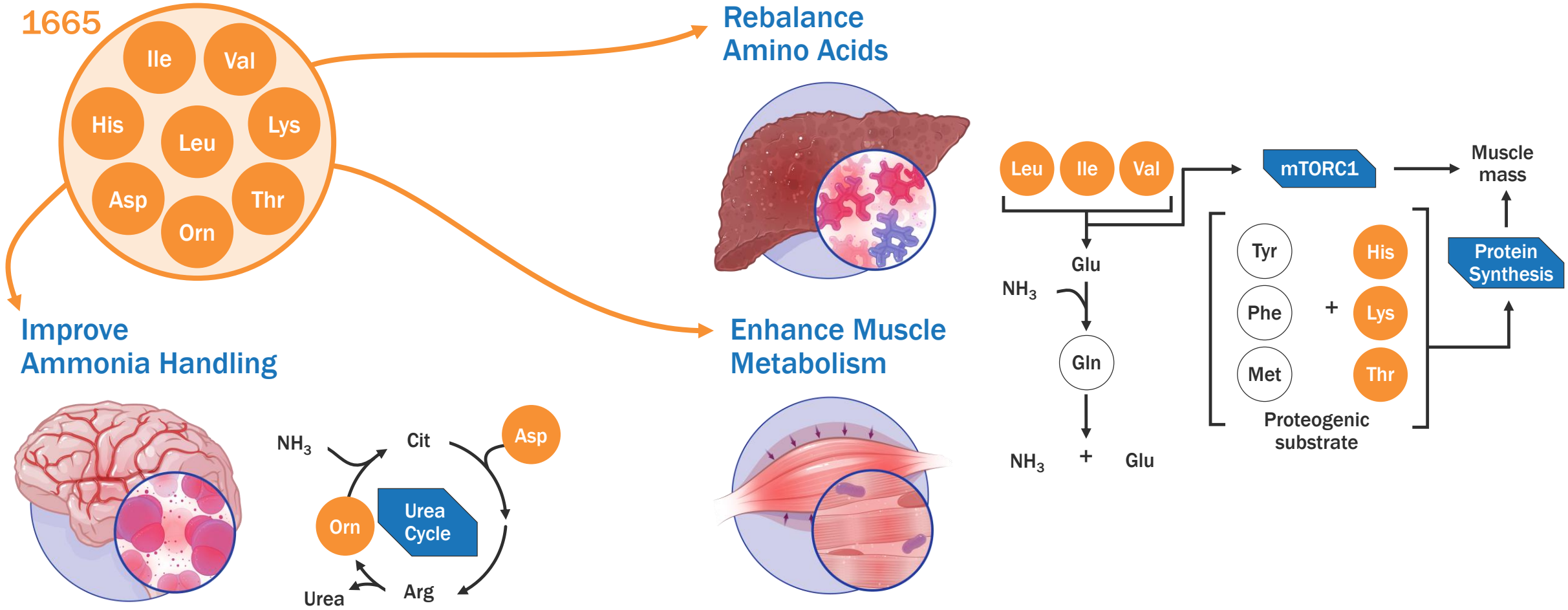
Market Potential[1]:

- ~500,000 U.S. patients with covert and overt hepatic encephalopathy
- ~$1 billion U.S. market and growing[2]

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.

AXA1665 – Hypothesized Mechanism

Designed to target multiple metabolic pathways implicated in pathogenesis of HE and muscle wasting in cirrhosis

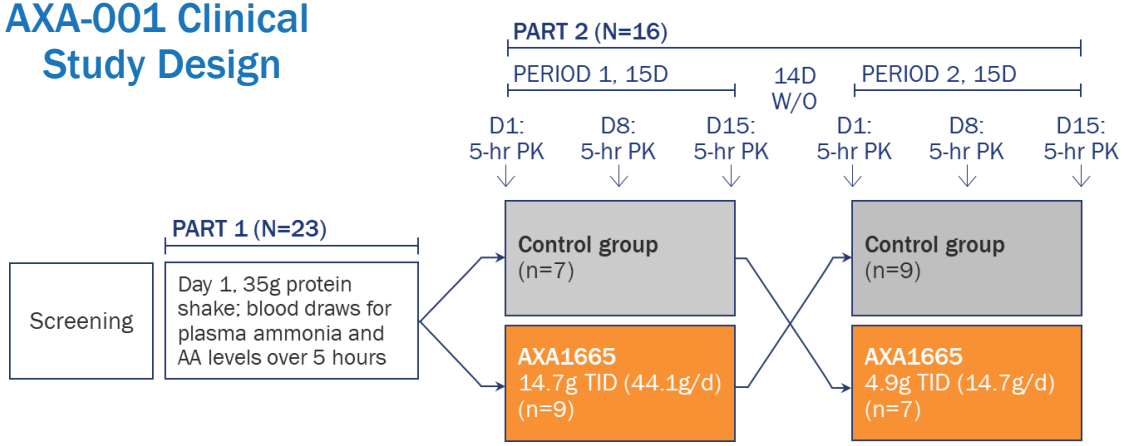


Abbreviations: Asp, aspartate; Cit, citrulline; Gln, glutamine; Glu, glutamic acid; His, histidine; Ile, isoleucine; Leu, leucine; Lys, lysine; Met, methionine; mTORC1, mammalian target of rapamycin complex 1; NAC, N-acetylcysteine; NH3, ammonia; Orn, ornithine; Phe, phenylalanine; Thr, threonine; Tyr,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

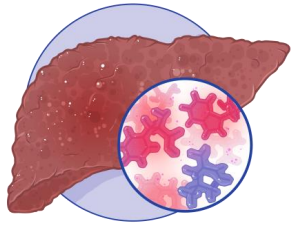
AXA1665-001: Initial Proof of Biological Activity in Child A & B Subjects

Dose-dependent changes seen in multiple measures in short-term, highly controlled study

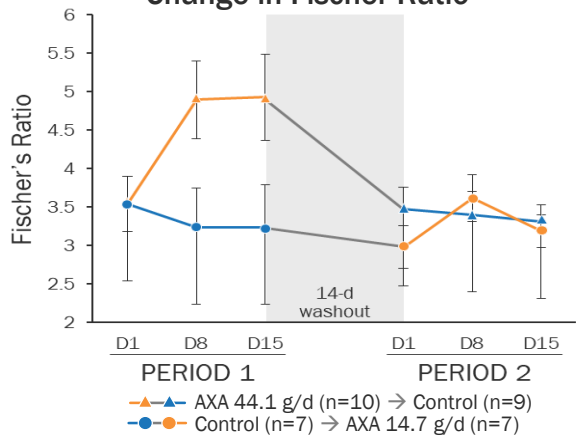
AXA-001 Clinical Study Design



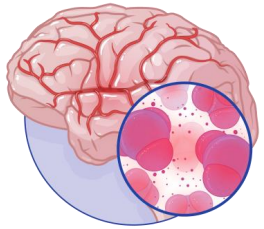
Amino Acid Imbalance



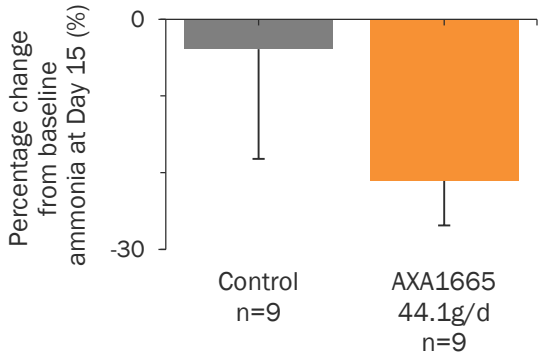
Change in Fischer Ratio[2]



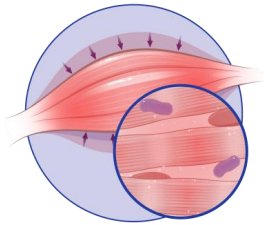
Ammonia Handling



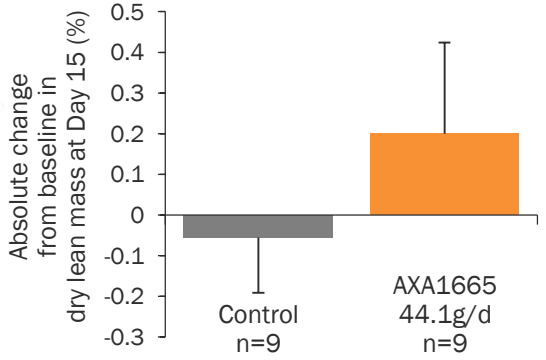
Change in ammonia



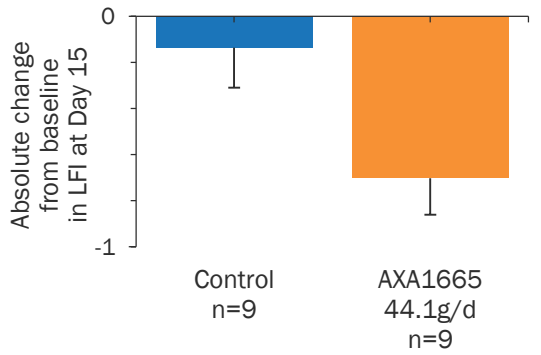
Muscle Metabolism



Dry lean mass
Period 1: Day 15 vs Day 1



Liver frailty index[1]
Period 1 of Part 2: Day 15 vs Day 1



1. Composite of hand grip strength, chair stands and balance; LFI predicts mortality in end-stage liver disease (ESLD).
2. Change in the basal (fasted) FR over time in both Periods 1 and 2 of Part 2. Data represent mean ± SE; Control (n=7) → AXA 14.7g/d (n=7); AXA 44.1g/d (n=10)→ Control (n=9).

Abbreviations: BFM, body fat mass; LBM, lean body mass; LFI, liver frailty index.

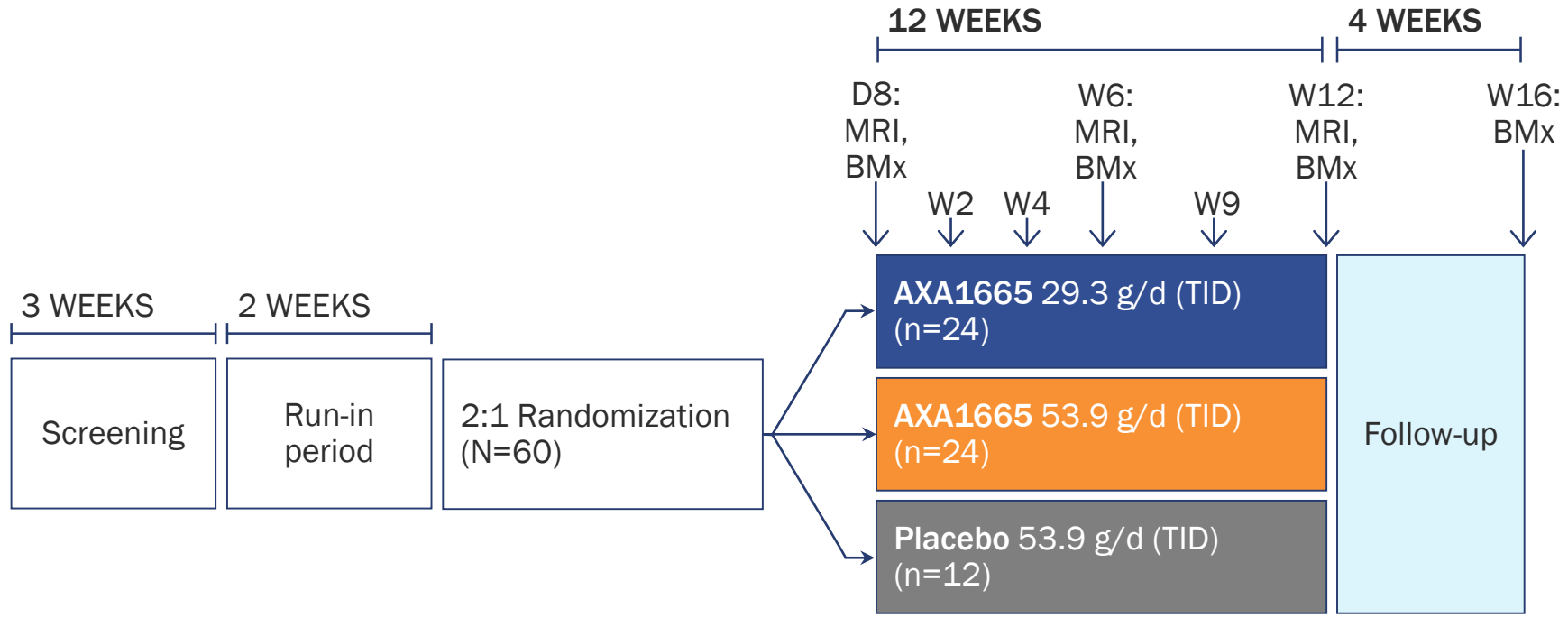
AXA1665-002: A 12-Week Placebo Controlled Study in Subjects with Mild (Child A) and Moderate (Child B) Hepatic Insufficiency

NCT04147936

AXA1665-002 STUDY DESIGN[2]

12-week (with a four-week follow-up), randomized placebo-controlled, Clinical Study to assess:

- Safety, tolerability
- *Structure:* Body composition, muscle MRI
- *Function:* LFI, gait speed, psychometric tests



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

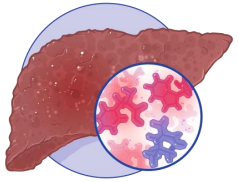
Demographics Suggest Population with Mostly Mild Hepatic Insufficiency (Child A), Without Overt Sarcopenia, but with MHE

Baseline Demographic/Metric	Placebo (n=11)	AXA1665 29.3 g (n=22)	AXA1665 59.3 g (n=27)
Age, years	58.0 (14.4)	58.5 (11.6)	59.0 (9.3)
Sex			
Male, n (%)	6 (54.5)	8 (36.4)	9 (33.3)
Female, n (%)	5 (45.5)	14 (63.6)	18 (66.7)
Body weight (kg)	107.2 (26.5)	86.9 (17.1)	85.2 (16.6)
BMI (kg/m^2)	37.7 (8.2)	31.9 (7.1)	32.3 (6.5)
Child Pugh Status			
CPC-A, n (%)	10 (90.9)	21 (95.5)	25 (92.6)
CPC-B, n (%)	1 (9.1)	1 (4.5)	2 (7.4)
MELD-Na score	10.2 (4.3)	9.2 (2.5)	9.0 (1.8)
Ammonia (µmol/L)	46.8 (19.4)	41.5 (21.7)	35.8 (17.0)
L3 Skeletal Muscle Index (cm^2/m^2)	57.4 (12.2)	51.1 (12.1)	51.1 (13.4)
Liver Frailty Index	3.9 (0.4)	3.9 (0.3)	4.0 (0.3)
Stroop EncephalApp Off+On Time (sec)	182.4 (52.0)	187.4 (49.6)	186.2 (45.1)
Psychometric Hepatic Encephalopathy Score (PHES)	-3 (2.2)	-4 (3.7)	-4 (3.6)
Minimal Hepatic Encephalopathy (by Stroop and PHES), n (%)	4 (36.4)	9 (40.9)	9 (33.3)

All values are mean (SD) unless otherwise noted.

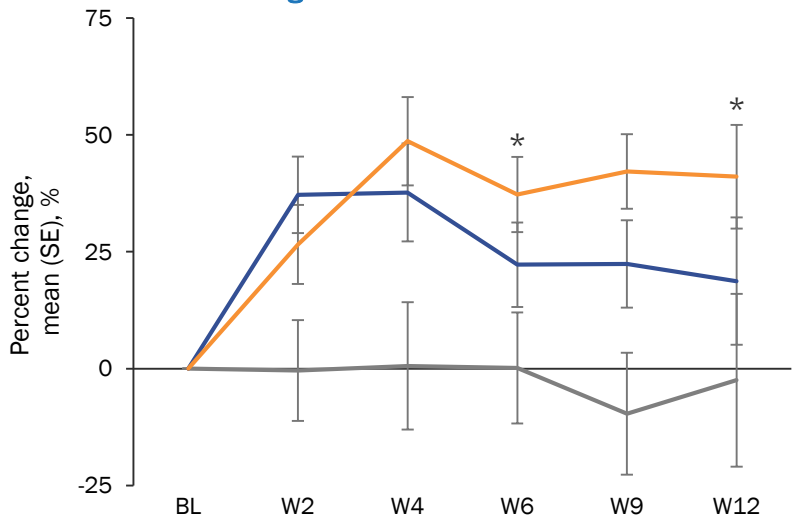
Dose Dependent Improvements in Amino Acid Metabolism

Changes in Fischer Ratio from baseline over and at week 12



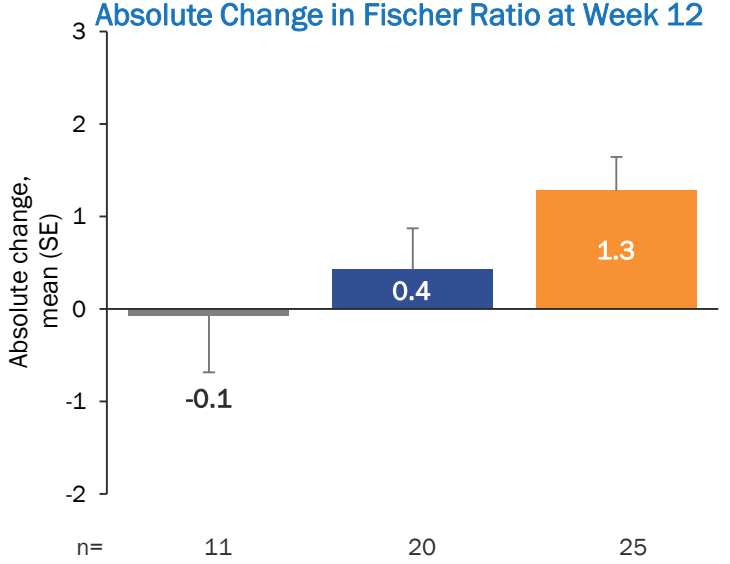
Amino Acid Metabolism

Change in Fischer Ratio Over Time[1]



*p<0.05 vs. Placebo

Absolute Change in Fischer Ratio at Week 12



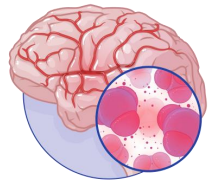
Placebo AXA1665 Low AXA1665 High

- Increase in FR was driven by both an increase in circulating branched chain amino acids and a decrease in aromatic amino acids, Phe and Tyr, which may contribute to impaired neurotransmission[2,3]
- A low FR is correlated with poor clinical outcomes and mortality in patients with end-stage liver disease[4]

1. 11, 20 and 25 subjects in placebo, AXA1665 low, and AXA1665 high, respectively, were included in the analysis. 2. Fischer, JE and Baldessarini, RJ. Lancet. 1971. 3. Bernardini, P and Fischer, JE. Ann Rev Nutr. 1982.
4. Kinny-Koster, B, et al. PLoS One. 2016.

Fasted Plasma Ammonia Levels Stable Despite Added Nitrogen in AXA1665 Arms; Greater Reductions Observed in MHE Subgroup

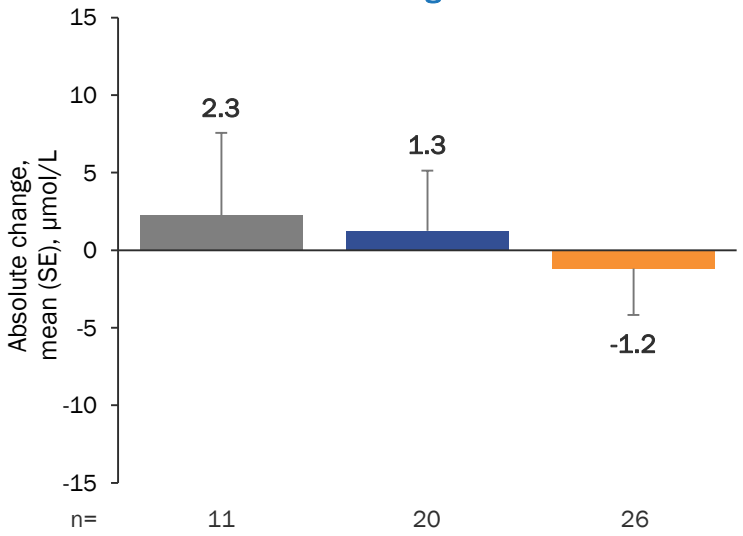
Changes from baseline at week 12



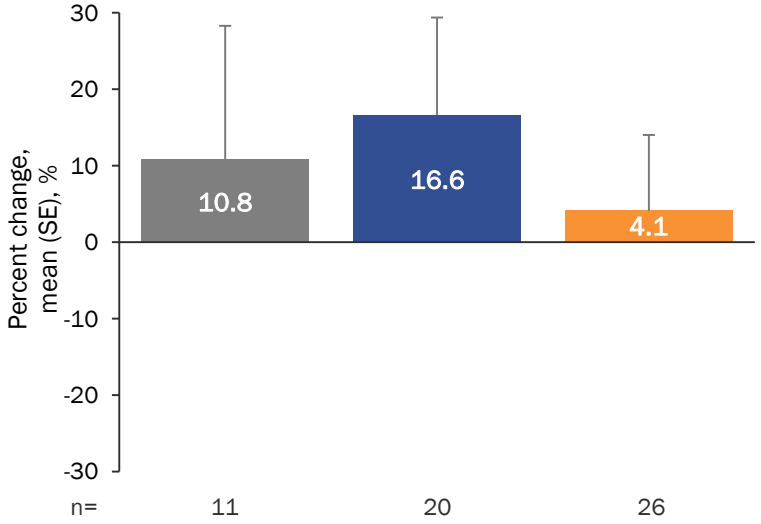
Ammonia Handling

Overall Safety Cohort

Absolute Change in Ammonia

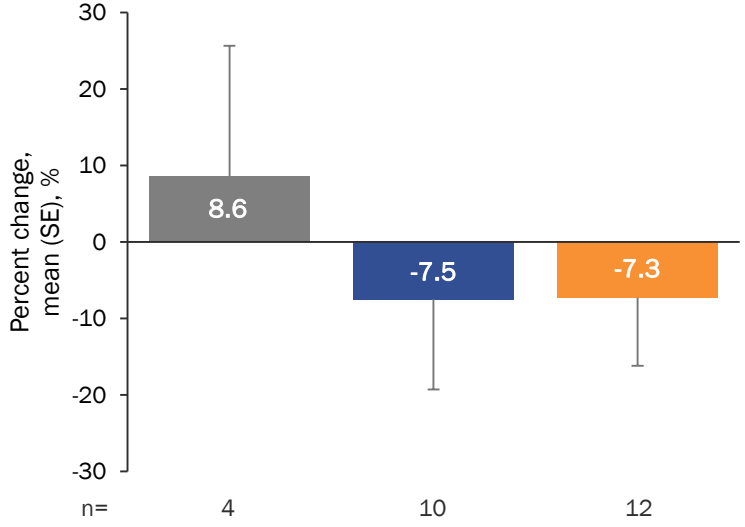


Percent Change in Ammonia



Subgroup with Baseline MHE

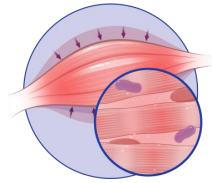
Percent Change in Ammonia



Placebo AXA1665 Low AXA1665 High

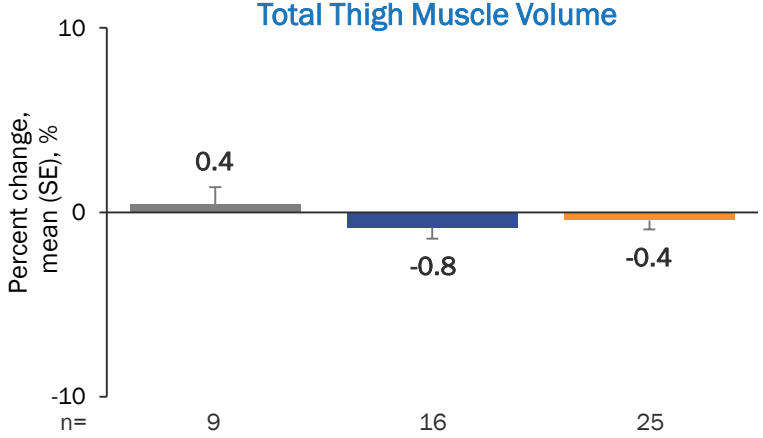
In This Non-Sarcopenic Population, Measures of Muscle Structure and Function Remained Stable Across Groups

Changes from baseline at week 12

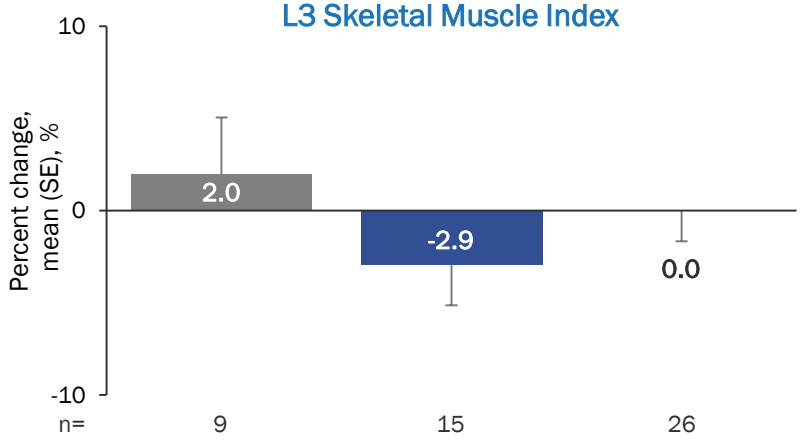


Muscle Metabolism

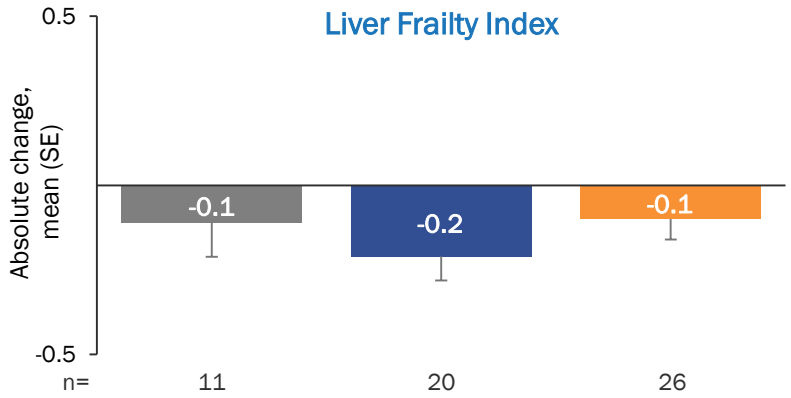
Total Thigh Muscle Volume



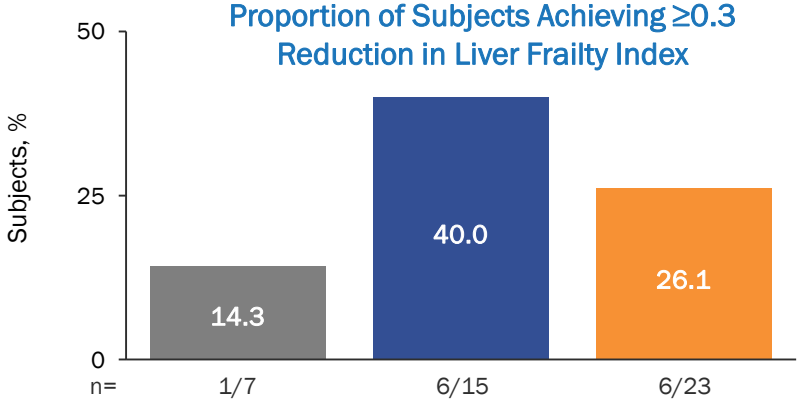
L3 Skeletal Muscle Index



Liver Frailty Index



Proportion of Subjects Achieving ≥0.3 Reduction in Liver Frailty Index



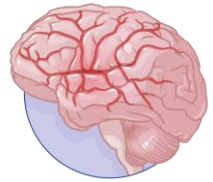
Previous studies suggest that a ≥0.3 reduction in the Liver Frailty Index score may correlate with an improved ability to conduct activities of daily living in subjects with end-stage liver disease[1,2]

TTMV measurement CV = 0.8-1.5%; L3 SMI intrasubject SD = 3 cm^2/m^2.
1. Lai, JC, et al. J Hepatol. 2020; 2. Kardashian, AA, et al. Hepatology. 2020

Placebo AXA1665 Low AXA1665 High

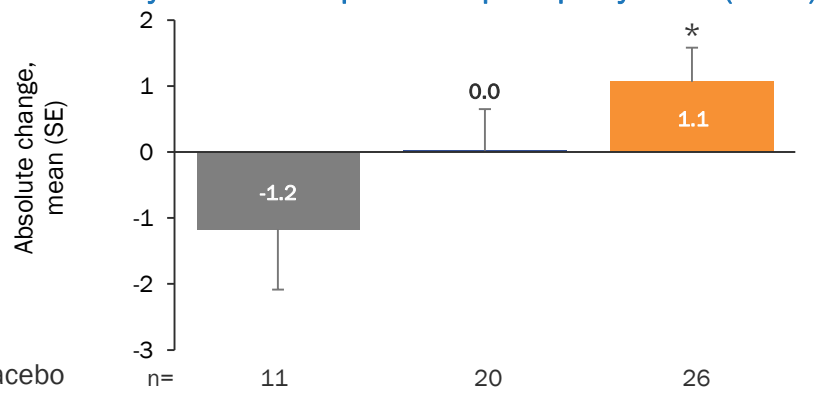
Dose Dependent Improvement Consistently Observed Across All Three Measures of Cognitive Function

Changes from baseline at week 12



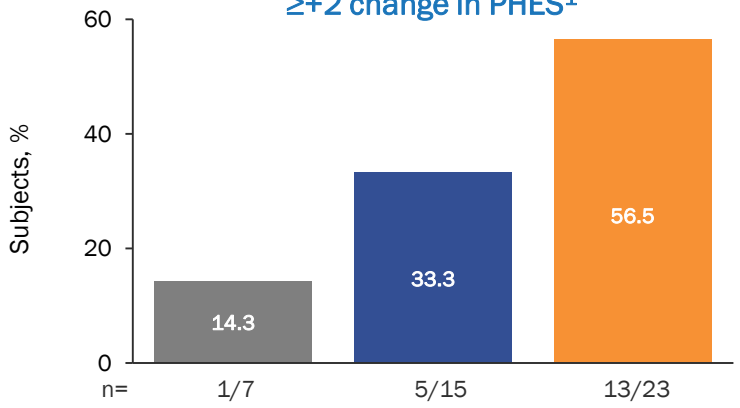
Cognitive Function

Psychometric Hepatic Encephalopathy Score (PHES)

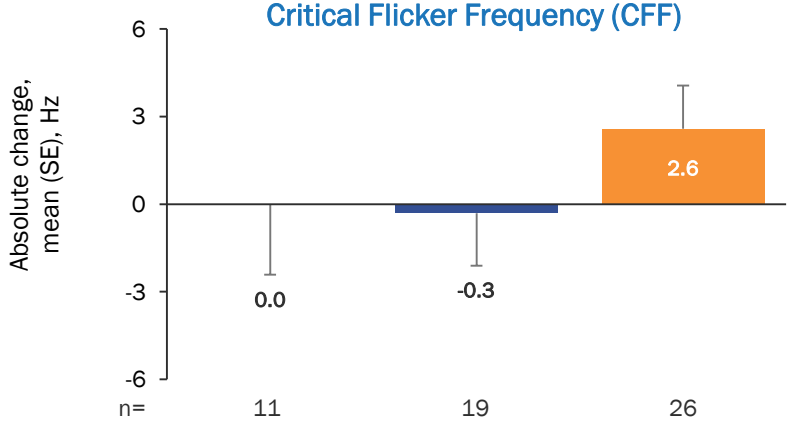


*p<0.05 vs. Placebo

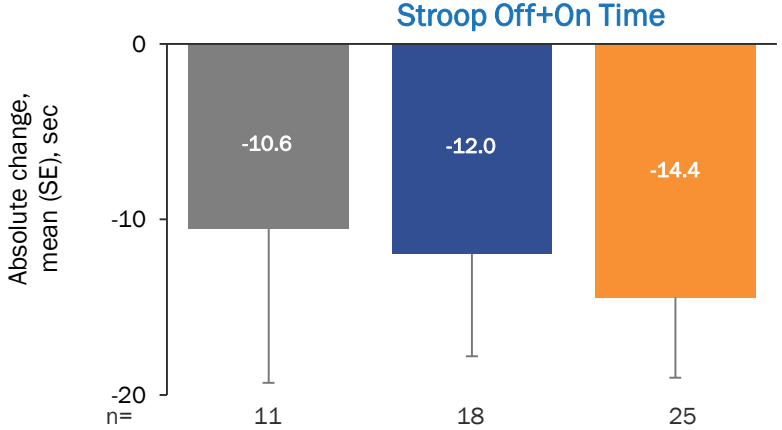
≥+2 change in PHES[1]



Critical Flicker Frequency (CFF)



Stroop Off+On Time



Statistically significant change in overall PHES, and higher proportion of subjects in AXA1665 arms vs. placebo achieved a clinically relevant[1] threshold of improvement in PHES

Placebo AXA1665 Low AXA1665 High

1. Based on PHES improvements ranging from 2.1 to 3.2 for lactulose, probiotics and LOLA in prior clinical studies.
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.

AXA1665 was Well Tolerated with Low Adverse Event Rates

Subjects with product-emergent adverse events (PEAEs), n (%)[1]	Placebo (n=11)	AXA1665 Low (n=22)	AXA1665 High (n=27)
All PEAEs	4 (36.4)	8 (36.4)	10 (37.0)
All PEAEs reported in ≥10% for any arm:			
All Gastrointestinal Events	1 (9.1)	2 (9.1)	4 (14.8)
All Infections	1 (9.1)	1 (4.5)	4 (14.8)

- AEs were generally mild to moderate and mostly unrelated to study administration
- Four discontinuations due to AEs, all in the low dose arm
- Four SAEs reported (two in placebo and two in AXA1665 low dose) and two fatalities (one COVID-19 complication; one myocardial infarction prior to dosing), all assessed as unrelated to study product administration

1. Safety based on what subject received on day 1 of dosing. Subjects counted only once if they had more than one event reported during the product administration period.

Summary

- Further evidence of our ability to design multi-targeted EMM compositions that impact multiple biologies and have been safe and well tolerated to date
- Positive, dose dependent trends across measures of neurocognition; statistical significance in PHES
- Dose dependent and statistically significant increases in measures of amino acid metabolism
- Stable fasted plasma ammonia levels despite AXA1665's nitrogen load; 7% reductions seen in subgroup with minimal hepatic encephalopathy
- In this non-sarcopenic population, muscle mass and function stable; higher proportion of subjects in AXA1665 arms reached clinically relevant LFI reduction (≥0.3)
- Further data analyses underway; plan to bring AXA1665 forward in a Phase 2 clinical trial under IND in patients with advanced liver disease

Our thanks to the subjects and investigators who participated in AXA1665-002

axcella

Participating Sites:

Catalina Research Institute, LLC
Montclair, CA

Orange County Research Center
Tustin, CA

Panax Clinical Research
Miami Lakes, FL

OMEGA Research Maitland, LCC
Orlando, FL

Avita Clinical Research
Tampa, FL

Atlanta Center for Medical Research
Atlanta, GA

Delta Research Partners
Bastrop, LA

Texas Liver Institute
San Antonio, TX

Virginia Commonwealth University
Richmond, VA