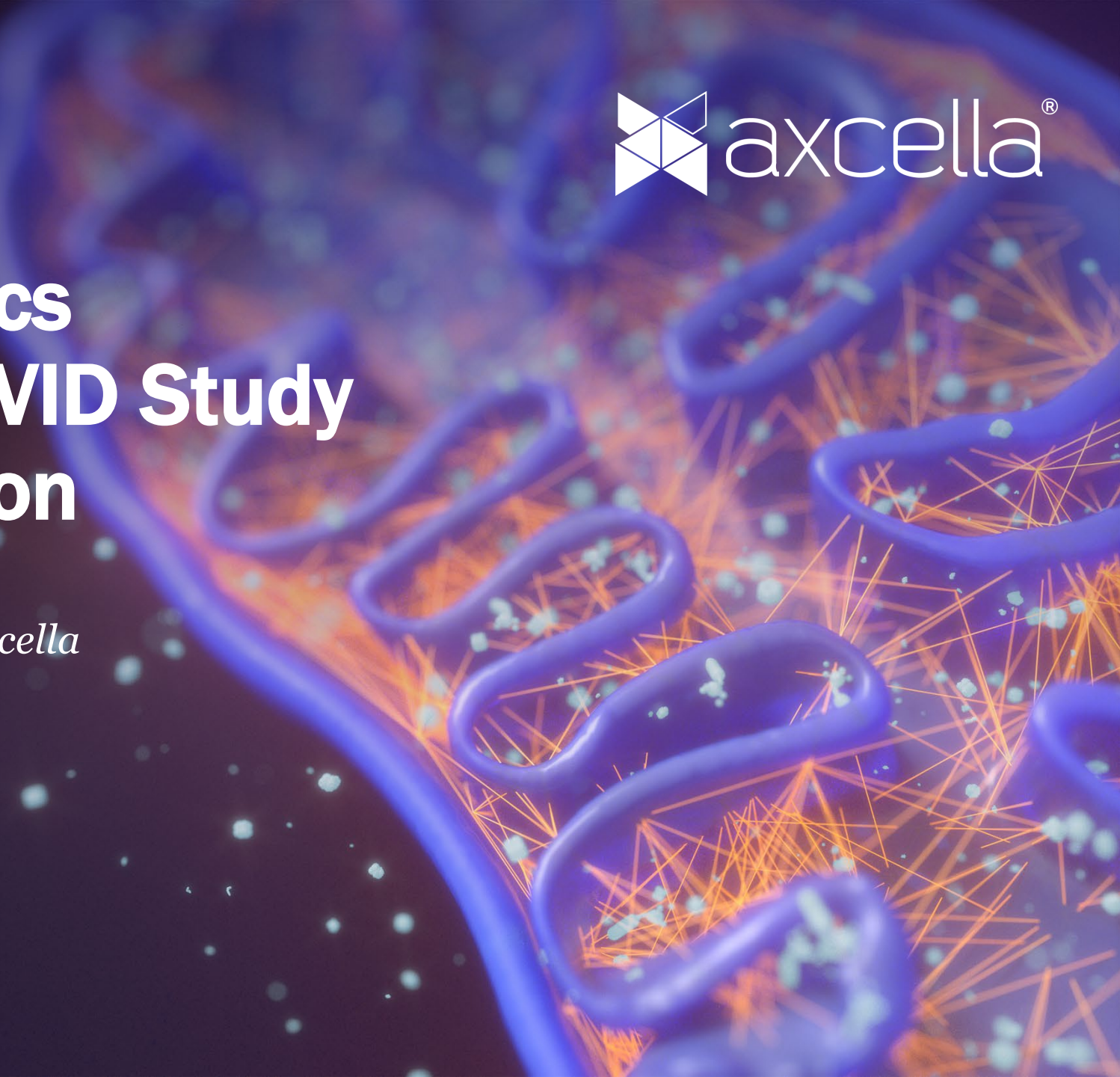
NASDAQ: AXLA

Axcella Therapeutics Phase 2A Long COVID Study Results Presentation

***Bill Hinshaw**, President and CEO, Axcella*

August 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 AXA1665, 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	Speaker
Introductory Remarks	5 min	8:00 am – 8:05 am	Bill Hinshaw
Clinical Trial Design and Protocol	10 min	8:05 am – 8:15 am	Dr. Raman
Clinical Trial Results	20 min	8:15 am – 8:35 am	Margaret Koziel
Patient Experience	5 min	8:35 am – 8:40 am	Dr. Raman
Mechanism of Disease & AXA1125	10 min	8:40 am – 8:50 am	Karim Azer
Independent 3rd Party Perspective	15 min	8:50 am – 9:05 am	Dr. Maley
Conclusion and Next Steps	5 min	9:05 am – 9:10 am	Bill Hinshaw
Q&A	20 min	9:10 am – 9:30 am	Bill, Margaret, Karim, Dr. Raman, Dr. Maley, Bob

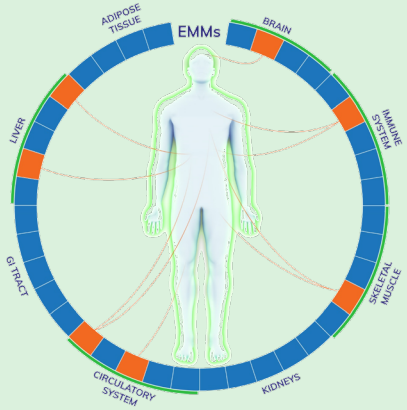
Dr. Betty Raman
Radcliffe Department of Medicine, Oxford University
Associate Professor of Cardiovascular Medicine

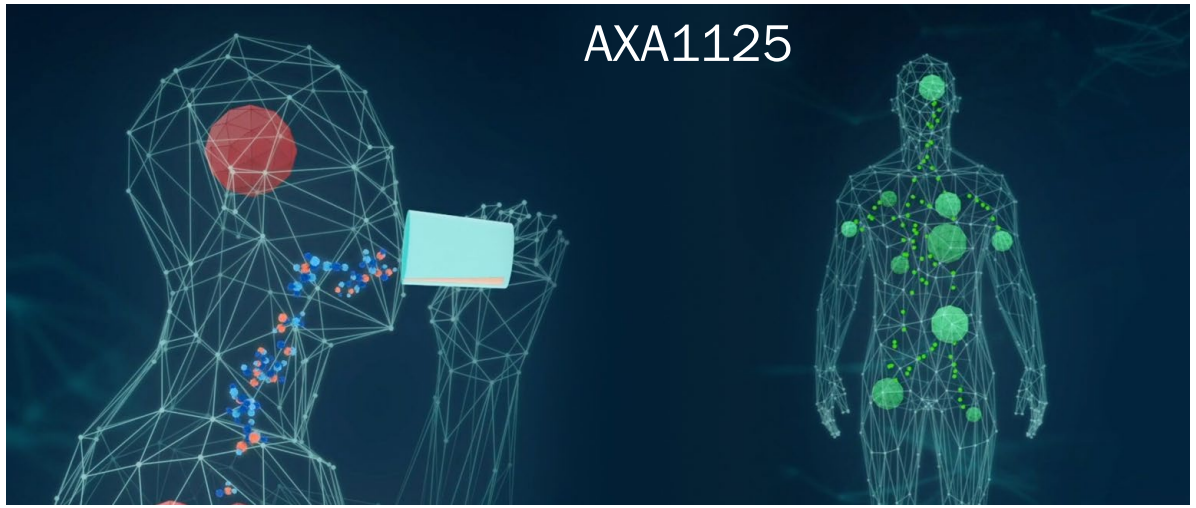
Dr. Jason Maley
Beth Israel Deaconess Medical Center
Director, BIDMC Critical Illness and COVID-19 Survivorship Program
Director of Quality, Pulmonary, Critical Care, and Sleep Medicine
Core Faculty, Center for Healthcare Delivery Science

World leader of multi-targeted therapies in complex diseases

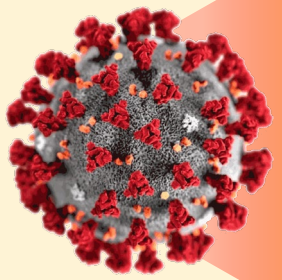
axcella®

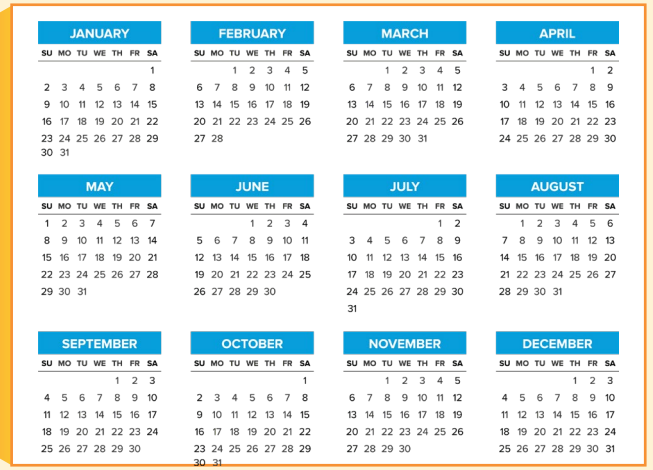
Endogenous Metabolic Modulators (EMMs)





Long COVID

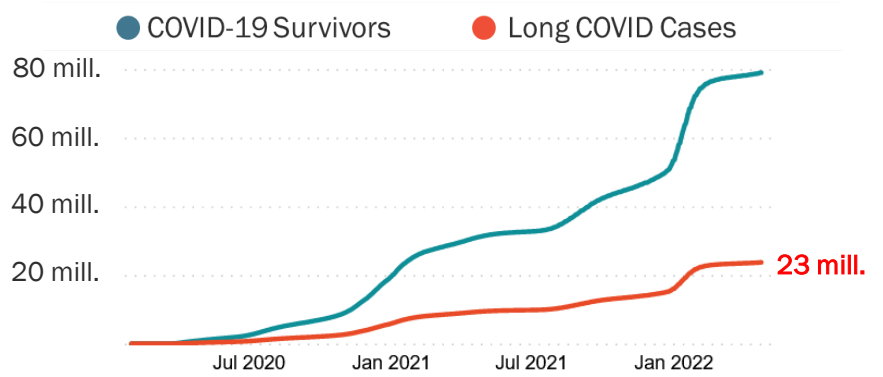




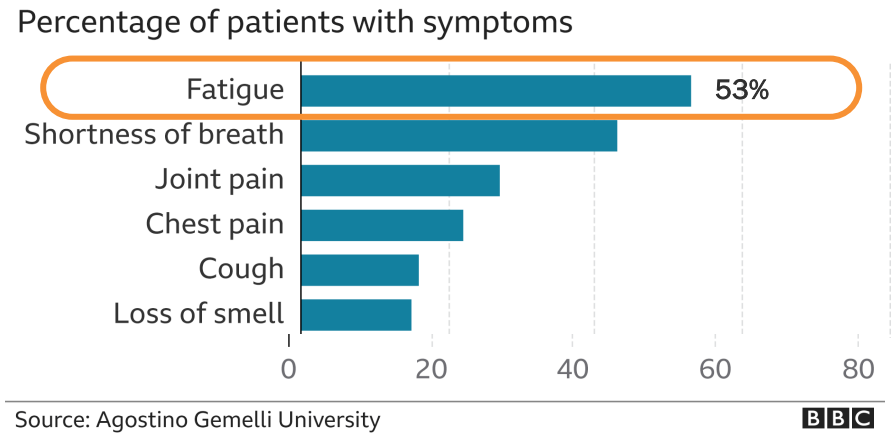
Long COVID: A Large and Still Emerging Public Health Crisis

- ~500M confirmed COVID-19 cases worldwide to date[1]
- 20-30% (100M-167M) of COVID patients report Long COVID symptoms[4]
- Susceptibility to Long COVID is not related to vaccination status, variant type, or severity of acute infection[5,6]
- Commonly reported symptoms include fatigue
- Estimated healthcare burden up to $40+ billion
- Growing Impact on the population:
  - 1 million Americans already out of work[3]
  - ~22% of UK work absences due to Long COVID

U.S. COVID Survivals and Long COVID Cases[2]



Most Common Long COVID Symptoms



1. WHO Coronavirus (COVID-19) Dashboard: https://covid19.who.int/
2. American Academy of Physical Medicine and Rehabilitation's "PASC Dashboard". PASC = Post-acute Sequelae of COVID-19. https://pascdashboard.aapmr.org/
3. Science & Tech Spotlight: Long COVID. (2022). Retrieved 29 July 2022, from https://www.gao.gov/products/gao-22-105666
4. Assessing the Global Burden of Post-COVID-19 Conditions. (2022). Retrieved 29 July 2022, from https://www.iqvia.com/insights/the-iqvia-institute/reports/assessing-the-global-burden-of-post-covid-19-conditions
5. Ayoubkhani D. (2022, May 6). Self-reported long COVID after infection with the Omicron variant in the UK. ONS.Gov.UK. https://www.ons.gov.uk/peoplepopulationandcommunity/healthandsocialcare/conditionsanddiseases/bulletins/selfreportedlongcovidafterinfectionwiththeomicronvariant/6may2022#prevalence-of-self-reported-long-covid-between-variants.
6. Antonelli, M., Penfold, R., Merino, J., Sudre, C., Molteni, E., Berry, S., Canas, L., Graham, M., Klaser, K., Modat, M., Murray, B., Kerfoot, E., Chen, L., Deng, J., Österdahl, M., Cheetham, N., Drew, D., Nguyen, L., Pujol, J., Hu, C., Selvachandran, S., Polidori, L., May, A., Wolf, J., Chan, A., Hammers, A., Duncan, E., Spector, T., Ourselin, S. and Steves, C., 2022. Risk factors and disease profile of post-vaccination SARS-CoV-2 infection in UK users of the COVID Symptom Study app: a prospective, community-based, nested, case-control study. The Lancet Infectious Diseases, 22(1), pp.43-55.

Very Limited Development and Axcella Leadership Opportunity

Very Few Trials in Long COVID and almost none in Fatigue And Growing Attention to this Public Health Crisis

THE WHITE HOUSE

BRIEFING ROOM

Memorandum on Addressing the Long-Term Effects of COVID-19

APRIL 05, 2022 • PRESIDENTIAL ACTIONS

MEMORANDUM FOR THE HEADS OF EXECUTIVE DEPARTMENTS AND AGENCIES

Axcella Leadership Opportunity

- Differentiated Profile
- Most Advanced Program
- Leadership Opportunity

Long COVID Overview

Betty Raman

British Heart Foundation Oxford Centre for Research Excellence Intermediate Transition Clinical Review Fellow

Associate Professor of Cardiovascular Medicine

Radcliffe Department of Medicine

University of Oxford

Long COVID/Post-Acute Sequelae of COVID-19

Betty Raman MBBS FRACP DPhil
Associate Professor of Cardiovascular Medicine
Radcliffe Department of Medicine
University of Oxford, United Kingdom
British Heart Foundation Oxford Centre of Research Excellence
Transition Intermediate Research Fellow
NIHR OXFORD BRC

Long COVID Overview

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Long COVID: UK Prevalence

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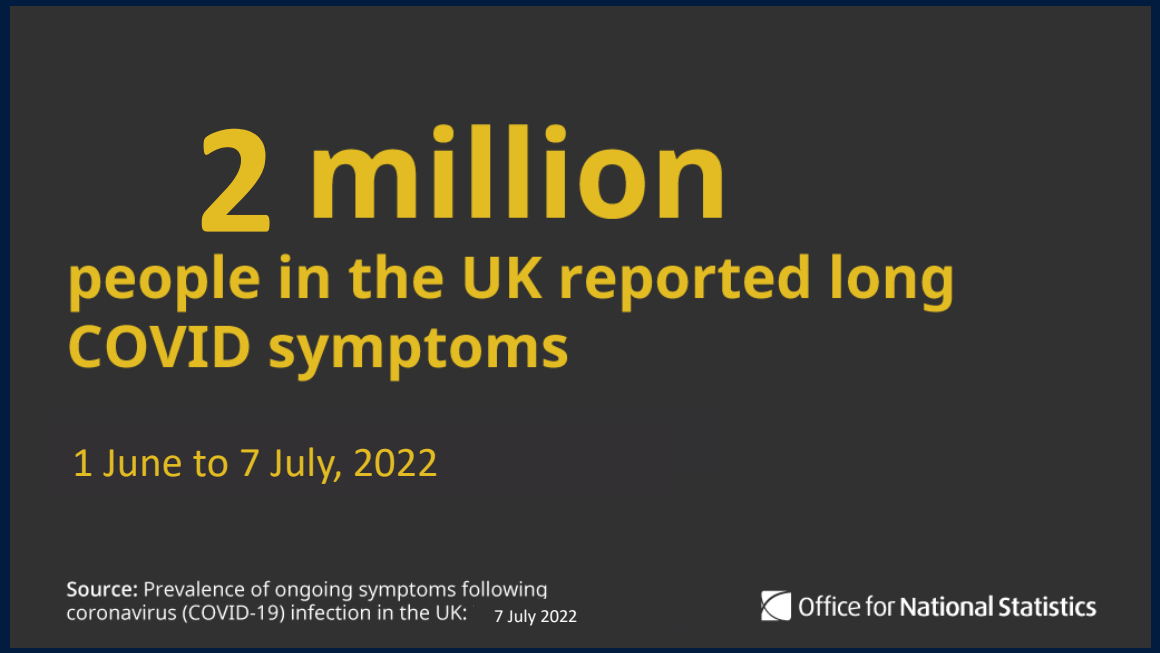
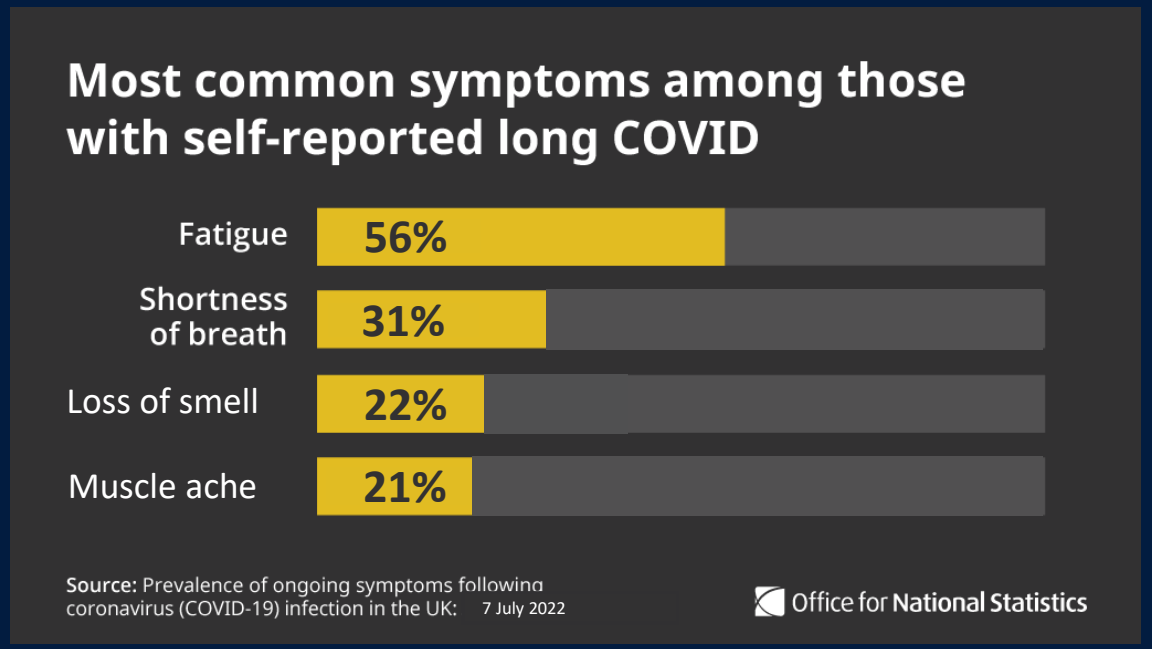




Source: https://www.ons.gov.uk/

Long COVID: Patient Journey

- “I have lost everything – my job, my life, my partner. Most of all I have lost myself. I want the old me back.” – P.L

Source:https://www.youtube.com/watch?v=IIeOoS_A4c8
Long COVID SOS support

Post-viral fatigue syndrome and myalgic encephalitis

- 1918 Spanish influenza
- 2003 SARS
- 2009 H1N1
- Ebola virus
- Ebstein Barr Virus
- Human Herpes Virus

CFS

No approved treatment for Long COVID or related disorders…..

Long COVID: Research in Oxford

UNIVERSITY OF OXFORD

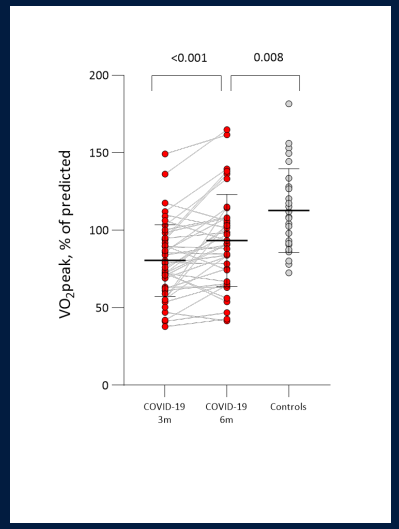
- C-MORE study – holistic multisystem study (Raman & Neubauer)
- Urgent Public Health Badging, NIHR-BHF COVID-19 Flagship status
- Impact on individuals
- 3 UK National post-COVID-19 studies – PHOSP-COVID, CONVALESCENCE, EXPLAIN study

C-MORE

Raman B et al, EClinicalMedicine, 2021

Long COVID: Insights from Oxford

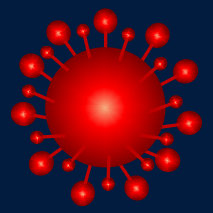
- Fatigue – most challenging and debilitating symptom experienced by patients
- Mitochondrial dysfunction highly likely – insights from CPET



Preserved breathing reserve
Normal O2 pulse
Normal cardiac function and volume
Early Anaerobic threshold[3]

Cassar. M et al, EClinicalMedicine, 2022

Mitochondrial dysfunction – COVID-19



SARS-CoV-2

Direct effects

Inhibit mitochondrial anti-viral signaling proteins (MAVS)[1]
Increased ROS[1,2,3]
Activation of inflammasomes → inflammation[1,2]
Muted interferon signaling
Release of mitokines[1]

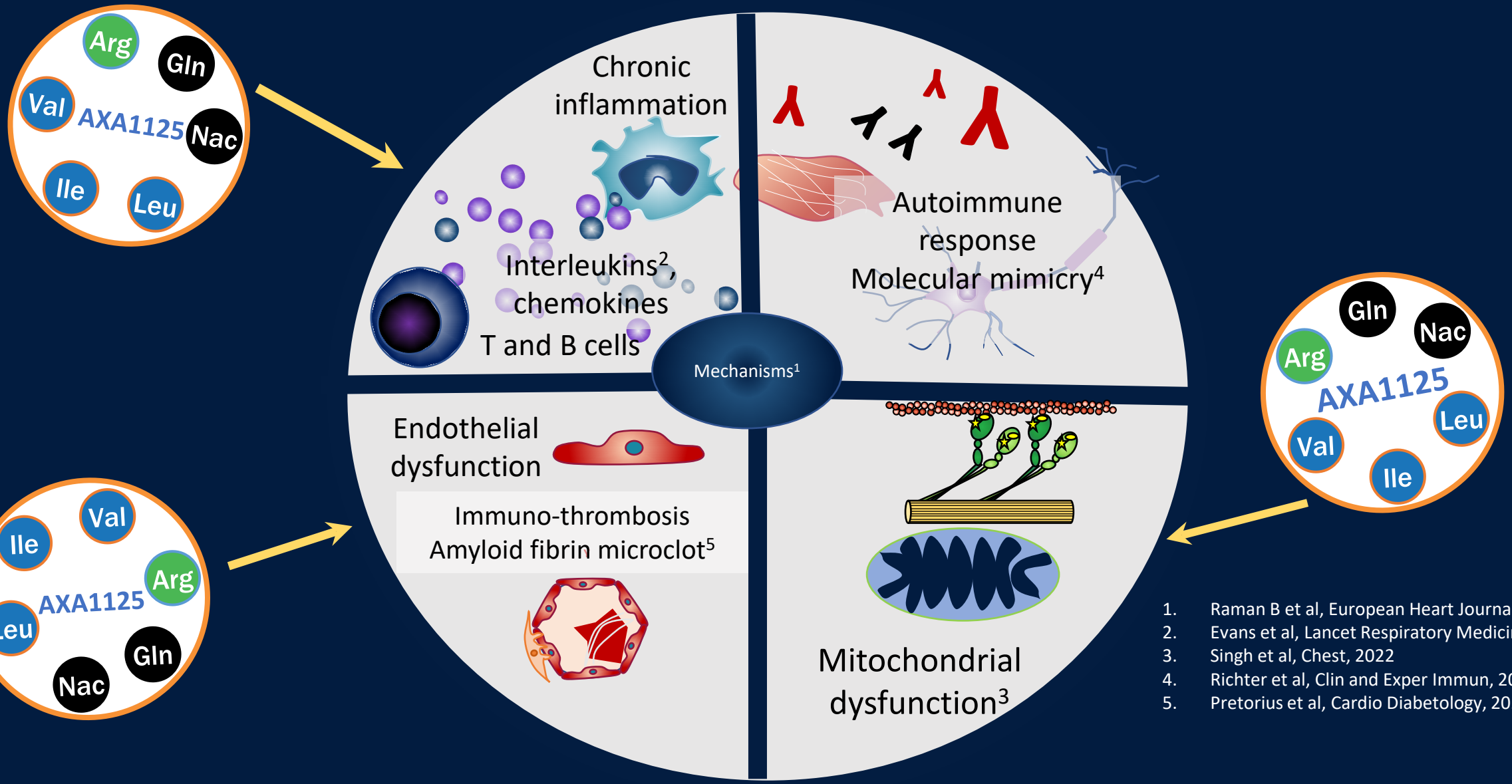
Indirect effects

ACE2 – activation of RAA[1]
Chronic inflammatory signalling

Chronic fatigue syndrome – **mitochondrial dysfunction**

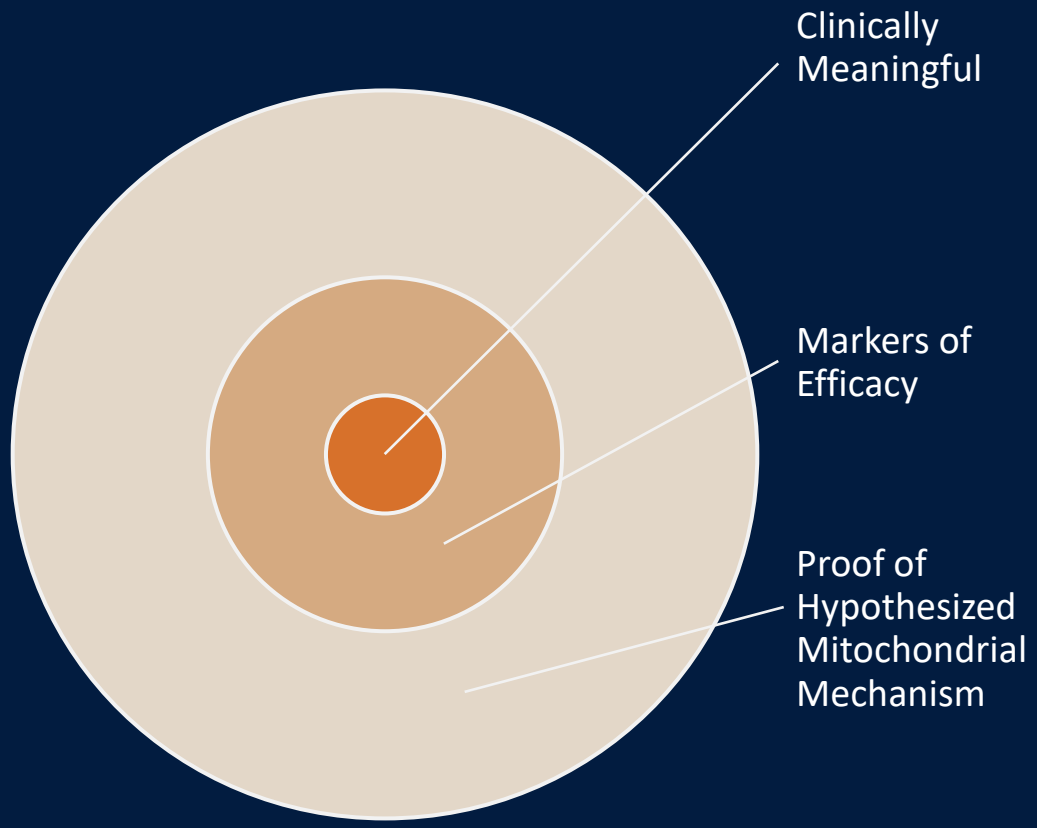
1. Singh et al, Am J Physiol Cell Physiol, 2020
2. Ajaz et al, Am J Physiol, 2020
3. Gibellini et al, EMBO Molecular Medicine, 2020
4. Cassar M et al, EClinicalMedicine, 2022

Potential mechanisms underlying Long COVID



1. Raman B et al, European Heart Journal, 2022
2. Evans et al, Lancet Respiratory Medicine, 2022
3. Singh et al, Chest, 2022
4. Richter et al, Clin and Exper Immun, 2022
5. Pretorius et al, Cardio Diabetology, 2021

Outcome measures of Clinical Efficacy



- **Chalder Fatigue Scale (CFQ-11): Validated in chronic fatigue score**
- **Includes both physical and mental subscales**
- **Six Minute Walk Test (6MWT)**

- Lactate Levels: used as measure of metabolic stress
- Biomarkers of inflammation

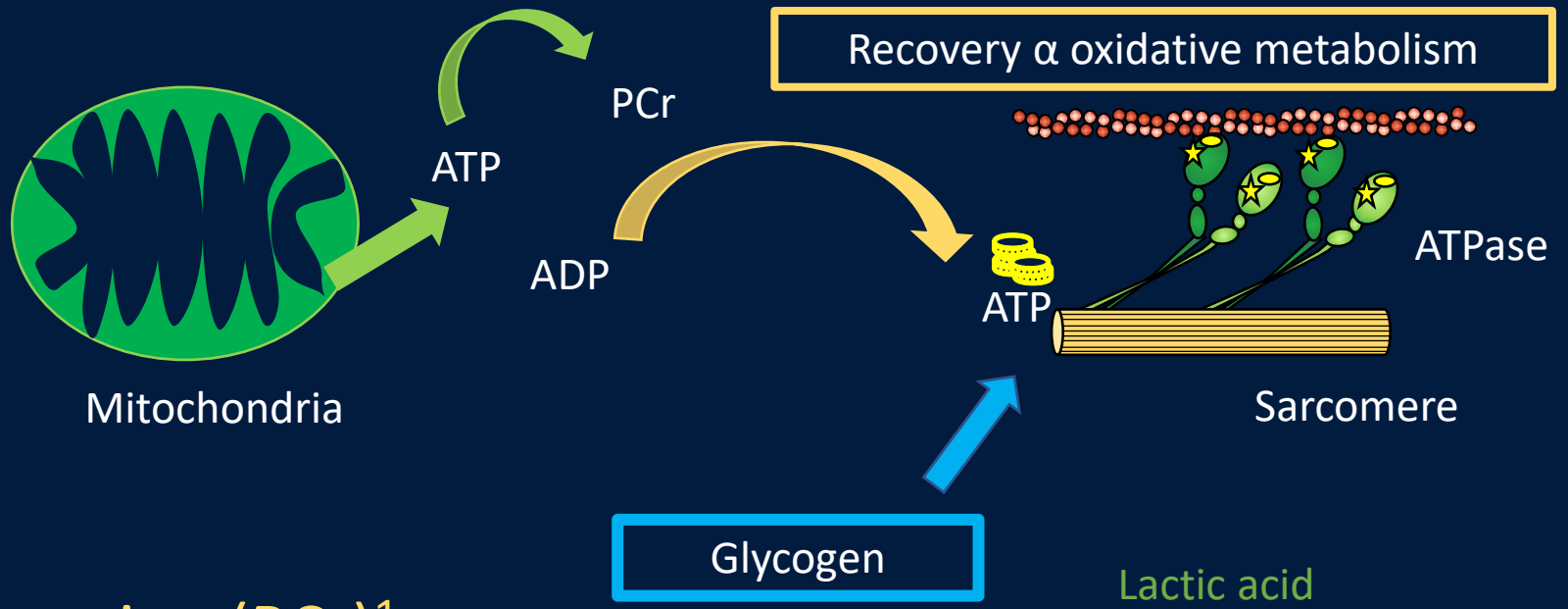
- Phosphocreatine Recovery Time (PCr, primary endpoint): measure of mitochondrial oxidative capacity
- Other measures in magnetic resonance spectroscopy, mitochondrial function

Chalder Fatigue Questionnaire

- Developed and validated for use in chronic fatigue syndrome/myalgic encephalomyelitis
- Assesses both physical and mental components of fatigue
- Standardized definitions to assess fatigue
- Two different scoring systems in use for the 11 questions
  - Bimodal (total 0-11)
  - Likert (total 0-33) (graded scoring for each question –0,1,2,3)

Do you have problems with tiredness?
Do you need to rest more?
Do you feel sleepy or drowsy?
Do you have problems starting things?
Do you lack energy?
Do you have less strength in your muscles?
Do you feel weak?
Do you have difficulty concentrating?
Do you make slips of the tongue when speaking?
Do you find it more difficult to find the correct word?
How is your memory?

Mitochondrial metabolism



- Phosphocreatine (PCr)[1]
- Anaerobic metabolism (glycolytic)
- Aerobic metabolism

PCr = Phosphocreatine

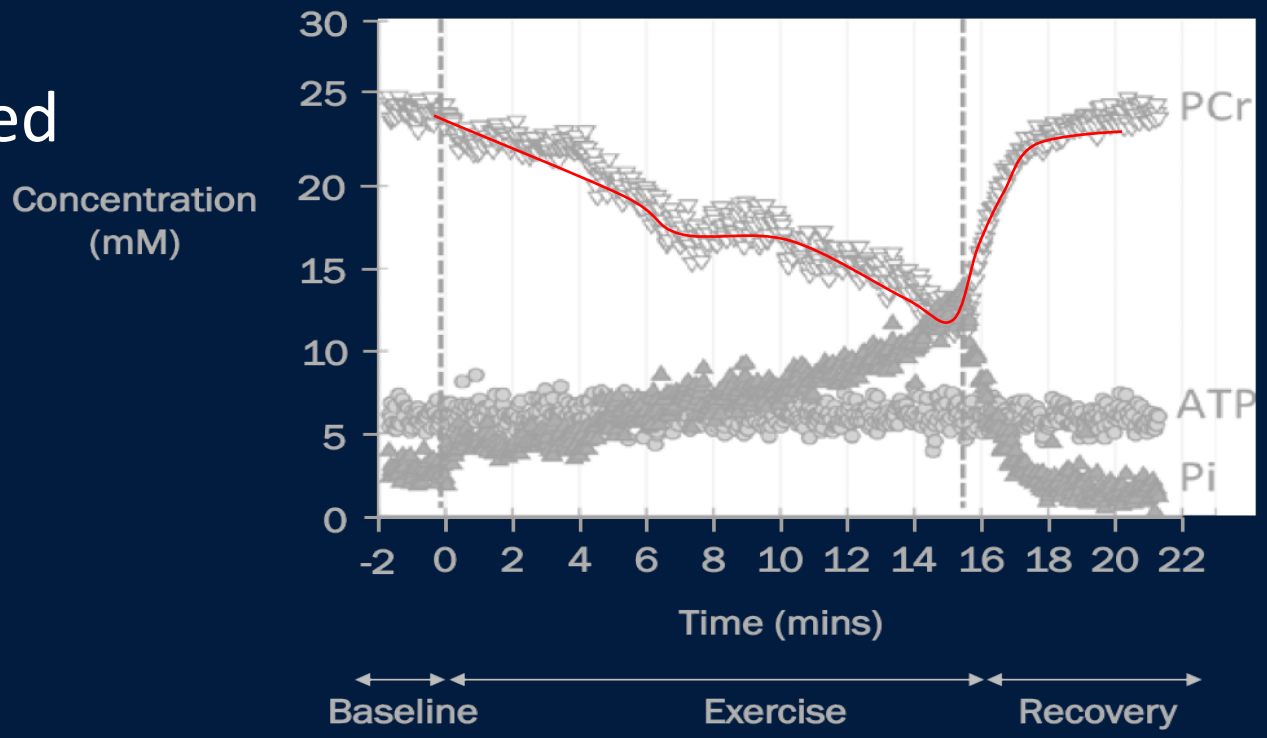
1. Chance et al,PNAS, 1981

PCr recovery time constant

- Normal recovery time constant

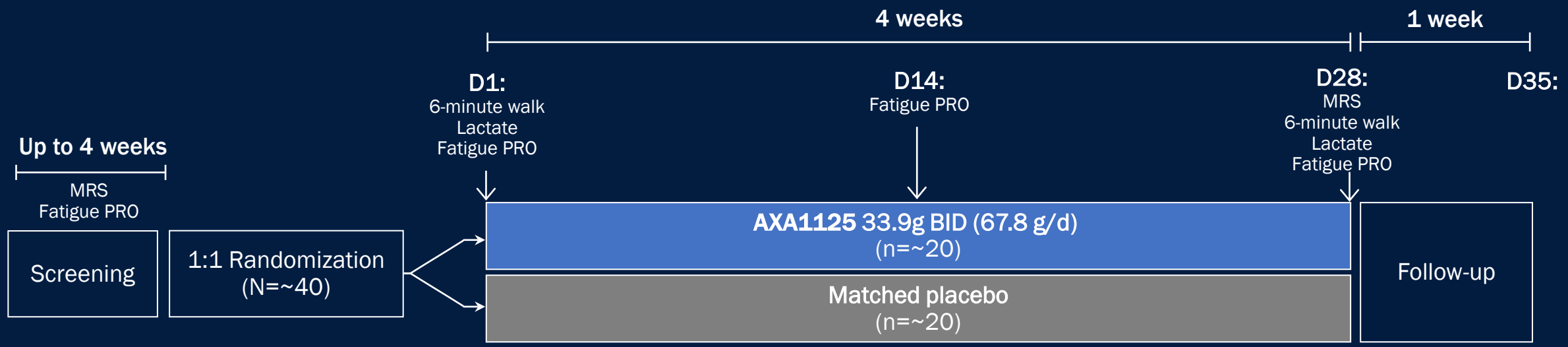
27±7 sec[1]; 31±7sec[2]; 32±3sec[3]

- > 50s is prolonged (>2SD of published norms)
- CFS studies – MRS abnormalities in fatigued patients[4]



1. Yoshida et al, Scand J Med Sci Sports., 2013
2. Šedivý et al, Med Phys, 2015
3. Scheuermann-Freestone et al, Circulation, 2003
4. McCully et al, Muscle & Nerve, 1996

Clinical Trial Study Design



Core elements	Description
Design	• Randomized double blind, placebo-controlled study over 28 days
Study population	• Including Long COVID patients (>12 weeks post PCR+) with fatigue-predominant symptoms/abnormalities: – PCr recovery time constant of >50 sec. – Chalder Fatigue bimodal score of >8 (very high level of fatigue) • Excluding patients with other potential drivers of fatigue and MRS abnormalities (vascular disease, diabetes, etc.)
Endpoints include	• Primary: PCr recovery time constant - Tau • 6-minute walk test • Lactate levels • Fatigue scores • Safety and tolerability

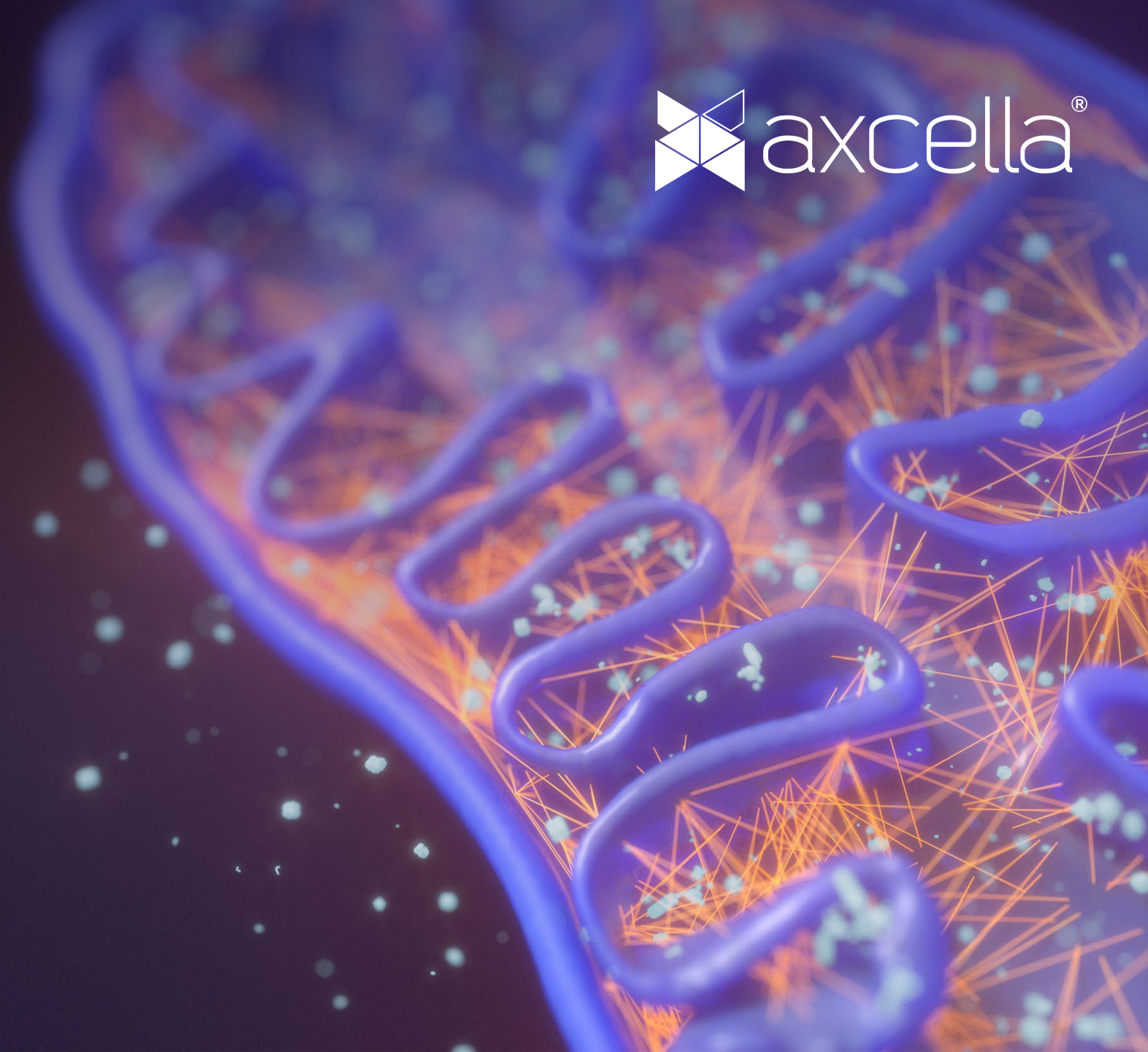
BID = twice daily; MRS = magnetic resonance spectroscopy; PCr = phosphocreatine; PRO = Patient Reported Outcomes

NASDAQ: AXLA

AXA1125 - 201 Top Line Data

Dr. Margaret Koziel

2 August 2022



Executive Summary

- AXA1125, compared to placebo, resulted in
  - Statistically significant improvements in fatigue as measured by CFQ-11
  - Improvements in both the physical and mental components of the fatigue scoring
  - Impressive clinical improvements in most patients treated
- AXA1125 responders had a statistically significant improvement in 6MWT
- In terms of measurement of PCr_{τ}, no differences at end of treatment
  - High variability means statistical demonstration of the difference very unlikely in this study size
  - Now shown as nonviable as a clinical trial endpoint
- There was a trend toward a reduction in peak lactate in those subjects who received AXA1125
- AXA1125 was safe and well tolerated in this study

CFQ-11, Chalder Fatigue Questionnaire 11 item scale; PCr_{τ}, phosphocreatine recovery rate time constant

AXA1125-201: Demographics

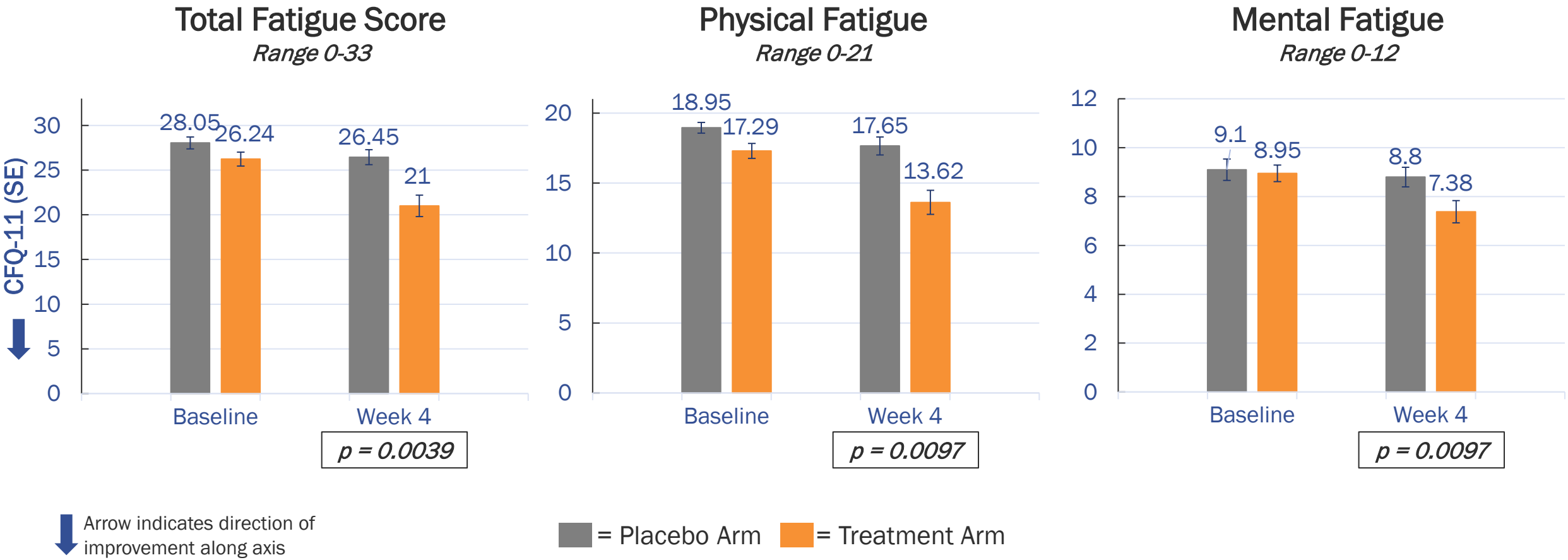
Demographics	Placebo (n=20)	AXA1125 (n=21)
Age, mean, years (SD)	43.6 (7.8)	43.6 (10.1)
Sex (% female)	15 (71.4)	13 (65.0)
Race	19/2 (90.5%) Caucasian 2/20 (9.5%) Asian	18/21 (90%) Caucasian 1/21 Asian (5%) Asian 1/21 (5%) Other
BMI, mean (SE)	26.42 (4.25)	26.38 (4.32)
CFQ-11, Total using bimodal (SE) (range 0-11)	10.50 (0.199)	10.48 (0.264)
CFQ-11, Total using Likert (SE) (range 0-33)	28.05 (0.663)	26.24 (0.783)
Percent predicted 6 minute walk test* (mean, SE)	86.82 (3.86)	82.41 (4.27)

All subjects completed all key assessments in the trial

*Based on calculated norm for age, gender, BMI; SD, standard error

There is a Statistically Significant Change in Fatigue Scores

Improvements seen in all scores using Likert scoring of CFQ-11



p-values from ANCOVA and represent LSM adjusting for differences in baseline

Subjects Taking AXA1125 Results in Greater Movement from Moderate/Severe to Mild in BOTH Physical & Mental Scales

Following tables map how patients shift from baseline to week 4

Physical Domain

Visit	Baseline Category	Post-Baseline Category	Placebo BID (n=20)	AXA1125 33.9g BID (n=21)
Baseline	Normal		0	0
	Mild		1 (5.0)	2 (9.5)
	Moderate/Severe		19 (95.0)	19 (90.5)
Week 4	Normal	Normal	0	0
		Mild	0	0
		Moderate/Severe	0	0
	Mild	Normal	0	2 (9.5)
		Mild	0	0
		Moderate/Severe	1 (5.0)	0
	Moderate/Severe	Normal	0	1 (4.8)
		Mild	4 (20.0)	12 (57.1)
		Moderate/Severe	15 (75.0)	6 (28.6)

Mental Domain

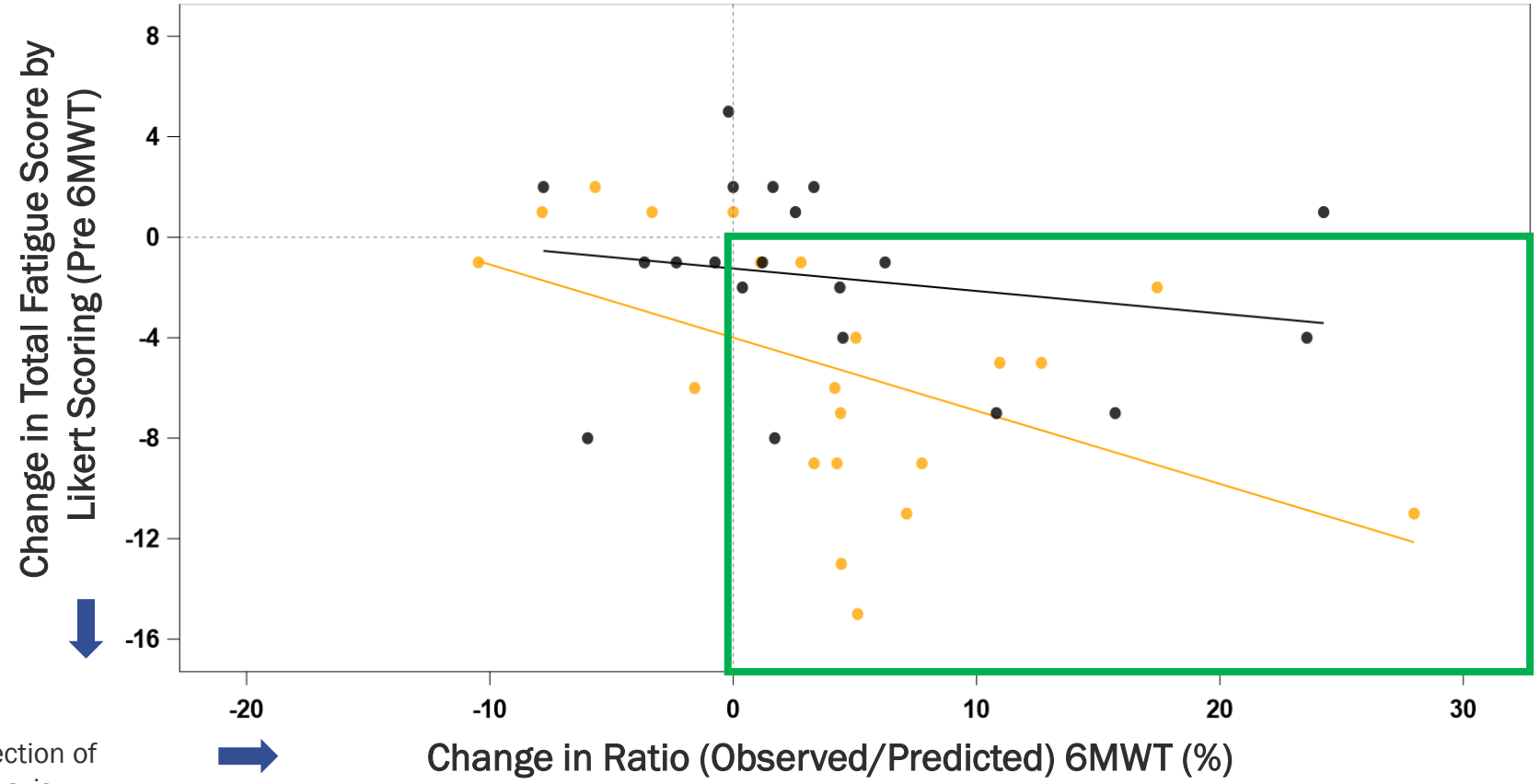
Visit	Baseline Category	Post-Baseline Category	Placebo BID (n=20)	AXA1125 33.9g BID (n=21)
Baseline	Normal		0	0
	Mild		4 (20.0)	2 (9.5)
	Moderate/Severe		16 (80.0)	19 (90.5)
Week 4	Normal	Normal	0	0
		Mild	0	0
		Moderate/Severe	0	0
	Mild	Normal	0	0
		Mild	3 (15.0)	2 (9.5)
		Moderate/Severe	1 (5.0)	0
	Moderate/Severe	Normal	0	0
		Mild	1 (5.0)	7 (33.3)
		Moderate/Severe	15 (75.0)	12 (57.1)

Physical scale: Normal, 0-9; Mild, 10-15; Moderate severe, ≥16 Mental scale: Normal, 0-3; Mild, 4-7; Moderate/severe, ≥8 Note denominator based on total in arm for percent

AXA1125 responders had statistically significant improvements and were able to walk farther

This effect only seen in subjects who received AXA1125

Correlation of 6MWT and improvement in fatigue



Arrow indicates direction of improvement along axis

Spearman Correlation Coefficient (p-value)

- AXA1125 33.9g BID: -0.621 (0.0027)
- Placebo BID: -0.271 (0.2487)

No Change in Phosphocreatine recovery rate time constant (PCr_τ)

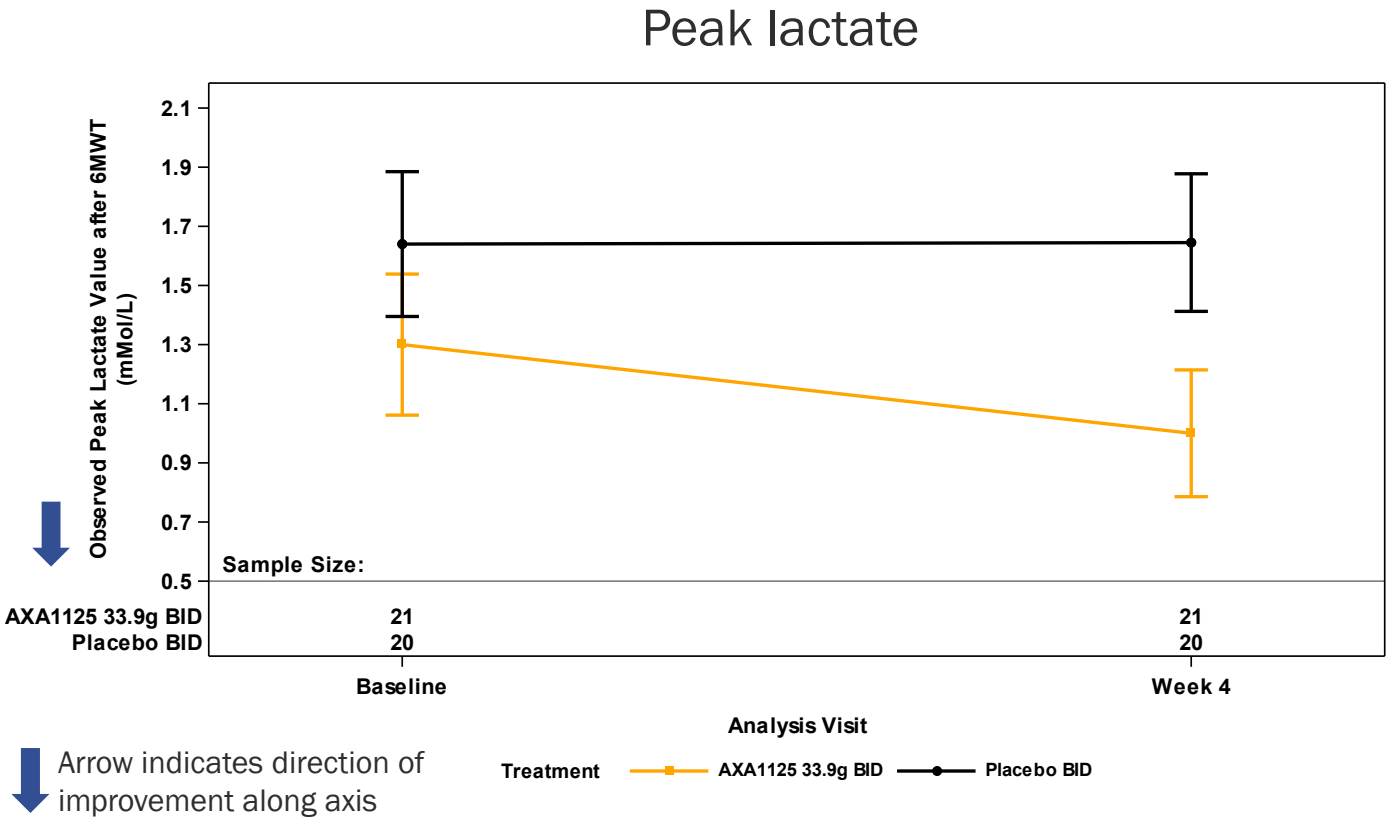
Much greater than expected variation in baseline – makes PCr_τ not useful as a clinical trial endpoint

- Unexpected large variation at baseline
  - Overall mean 92.46 S (SD 35.3)
  - Higher degree of variability than seen in other diseases
- No difference in change from baseline in PCr_τ between AXA and placebo
  - Statistical difference would require large sample size to detect planned 10S delta (250-500 subjects) or large delta (30S) between groups
- There was a correlation between improvements in fatigue and improvement in PCr_τ

PCR_τ, phosphocreatine recovery rate time constant. Rousell et al Biochimica Biophysica Acta 2000

AXA1125 Patients Showed A Trend Toward Improving Lactate Levels

- Baseline assumption that peak lactate would be high (> 3 mMol/L)
- Trend toward difference in model estimated mean (LSM) when accounting for difference in baseline –0.42 (p = 0.073, 2-sided)
- No correlation of change in lactate with measures of fatigue



AUC, area under the curve.

AXA1125 was safe and well tolerated in this study

TEAE s (Treatment Emergent Adverse Events)	Placebo (n=20)	AXA1125 (n=21)
Subjects with at least one TEAE	4 (20.0%)	11 (52.4%)
Subjects with at least one serious TEAE	0 (0.0%)	0 (0.0%)
Subjects with TEAE leading to withdrawal of study drug	0 (0.0%)	0 (0.0%)
Subjects with TEAE leading to death	0 (0.0%)	0 (0.0%)
Subjects with TEAE by worst severity grade		
– Grade 1	2 (10.0%)	10 (47.6%)
– Grade 2	2 (10.0%)	0 (0.0%)
– Grade 3	0 (0.0%)	1 (4.8%) (Syncope in MR)
Subjects with TEAE by worst relationship to study drug		
– Related	2 (10.0%)	6 (28.6%)
– Not related	2 (10.0%)	5 (23.8%)
TEAE seen in 2 or more subjects in either arm		
– Diarrhea	0 (0.0%)	3 (14.3%) (1 related)
– Abdominal distension	2 (10.0%)	0 (0.0%)
– Nausea	0 (0.0%)	2 (9.5%) (1 related)

. TEAE, treatment emergent adverse events.

Conclusion

- AXA1125, compared to placebo, resulted in:
  - Statistically significant improvements in fatigue as measured by CFQ-11
  - Improvements in both the physical and mental components of the fatigue scoring
  - Impressive improvements in Fatigue
- AXA1125 responders had a statistically significant improvement in 6MWT
- In terms of measurement of PCr_{τ}, no differences at end of treatment
  - High variability means statistical demonstration of the difference very unlikely in this study size
- There was a trend toward a reduction in peak lactate in those subjects who received AXA1125
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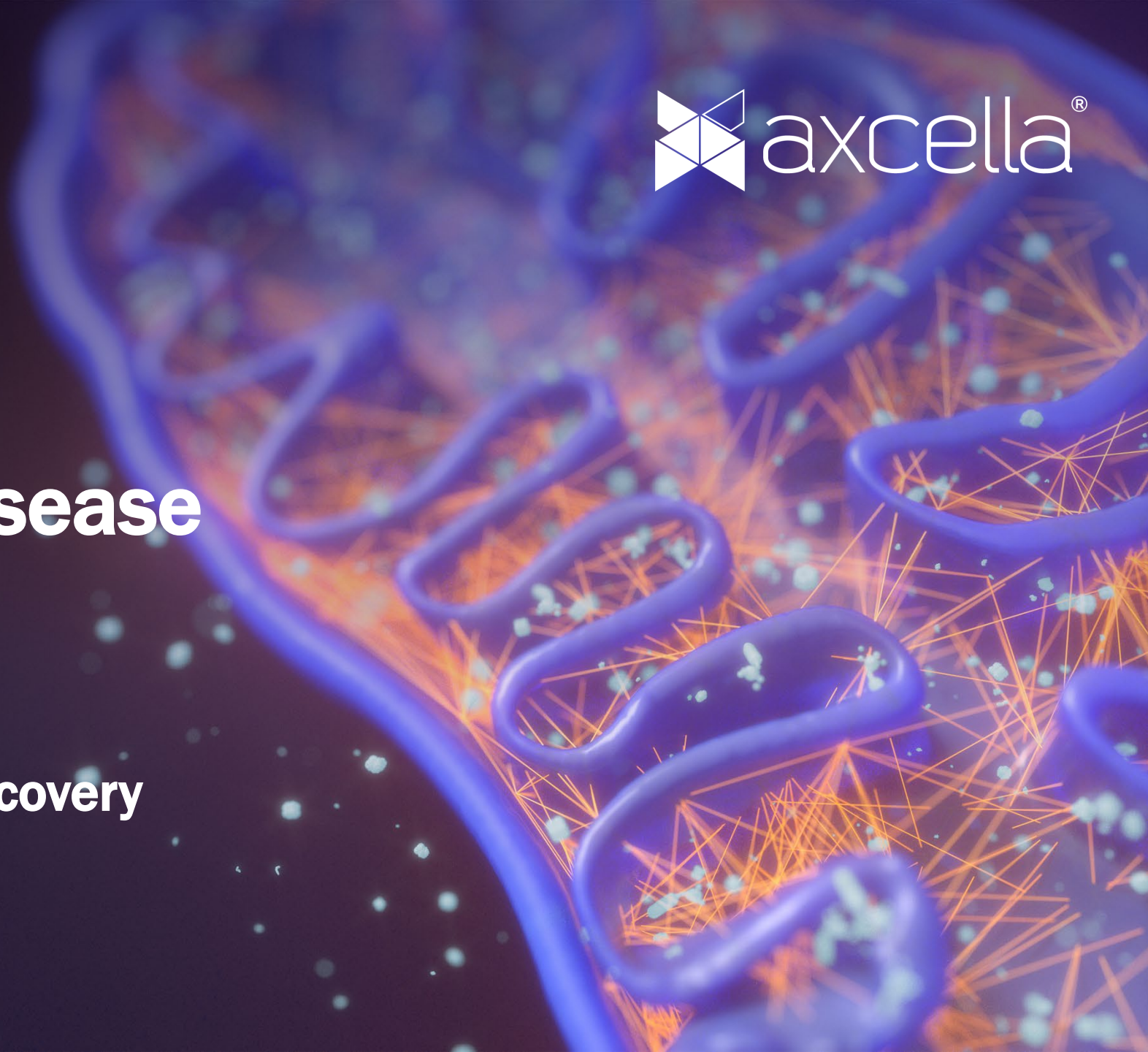
CFQ-11, Chalder Fatigue Questionnaire 11 item scale; PCr_{τ}, phosphocreatine recovery rate time constant

Long COVID: Patient Journey

- “I have lost everything – my job, my life, my partner. Most of all I have lost myself. I want the old me back.” – P.L

Source:https://www.youtube.com/watch?v=IIeOoS_A4c8
Long COVID SOS support

NASDAQ: AXLA



Mechanism of Disease & AXA1125

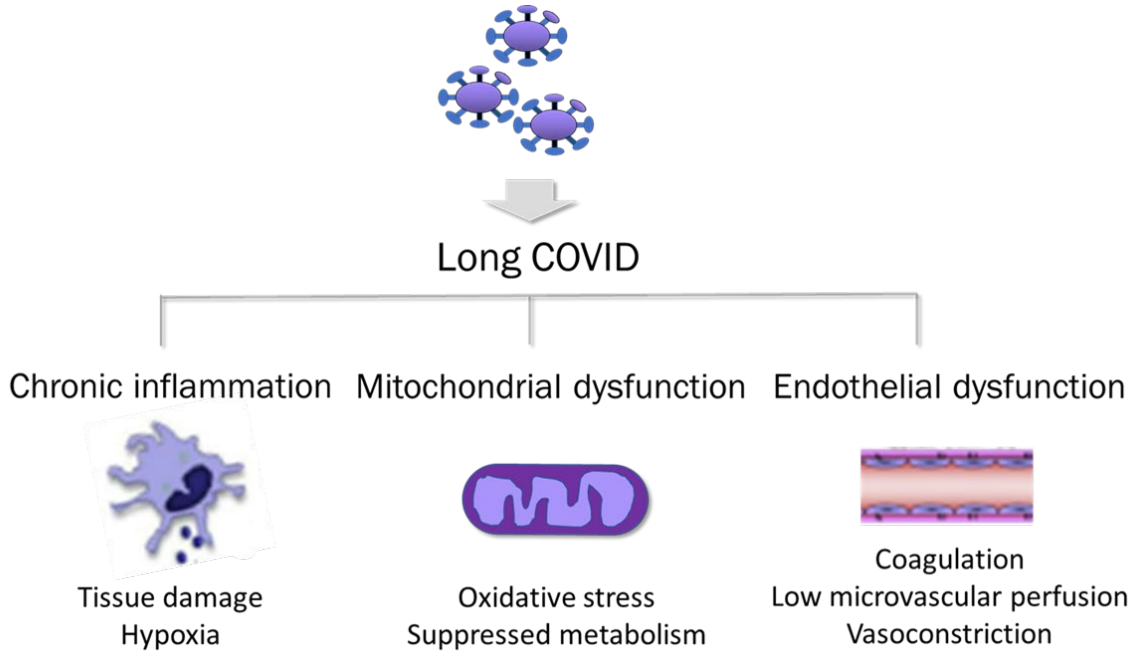
Karim Azer, PhD
VP, Head of Platform & Discovery

2 August, 2022

COVID-19 Hijacks Mitochondrial Metabolism, Dysregulates Vascular System and Leads to Chronic Inflammation in Long Covid

Building on a Foundation of AXA1125 Multi-Targeted Activity

- Vascular environment dysfunction, pro-inflammatory state, and suppressed mitochondrial metabolism are implicated in LC
  - Data supported through clinical registries and long covid literature
- AXA1125's multi-targeted MOA in NASH has
  - shown improvements in mitochondrial metabolism and inflammation
  - Provided the rationale and data to study its potential in Long Covid



AXA1125 Targets Key Environment, Inflammation and Metabolism Biologies in Long Covid

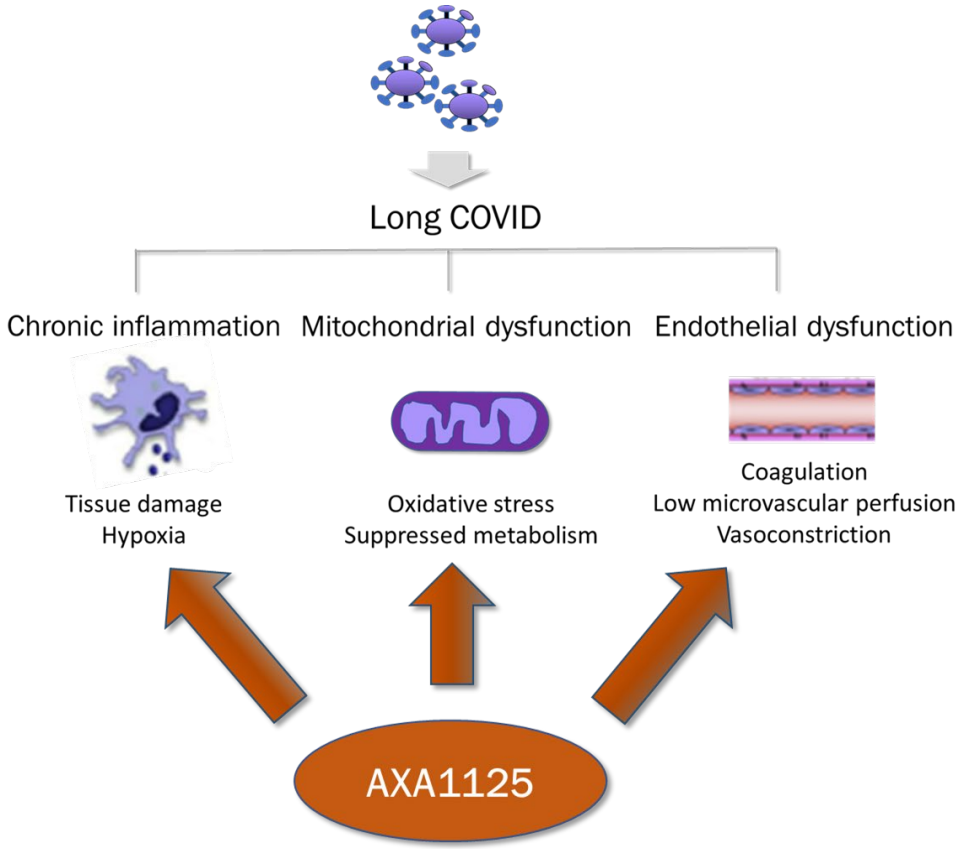
Key Hypotheses for Multi-Targeted Effect of AXA1125 Use in Long COVID

- AXA1125 multi-targeted MOA is proposed to improve vascular environment, inflammation, and mitochondrial metabolism.

- Improvement in markers of vascular environment
  - Dysregulated tissue environment in LC

- Improvement in oxidative stress and inflammation
  - Pro-inflammatory state persists from acute setting
  - Increased oxidative stress and reduced antioxidant availability

- Improvement in markers of metabolism and mitochondrial function
  - Dysregulated environment impacts high energy demand organs and limits function



Key MOA Takeaways from AXA1125 in Long Covid Fatigue

Multi-Targeted Impact on Improving Vascular Environment, Inflammation, and Mitochondrial Metabolism

Disease MOA	Biological Impact	Improved Clinical Treatment Response Biomarker(s) in LC	MOA Concordance from NASH Studies	Preliminary evidence in Pre-clinical Models
Vascular Environment Dysfunction	Dysregulated endothelial function, coagulation, reduced micro-vascular perfusion, reduced inflammation	✓ Biomarkers of vascular function	✓ Improved vascular marker	✓ Improved markers of endothelial function, inflammation and coagulation
Oxidative Stress, pro-inflammatory state	Reduced antioxidant availability, increased ROS and inflammation	✓ Biomarkers of inflammation and oxidative stress	✓ Reduced inflammation	✓ Decreased inflammatory and cytokine secretion
Mitochondrial Metabolism & Bioenergetics	Dysregulated lipid oxidation, insulin resistance, Increased glycolysis	✓ Mitochondrial metabolism and inflammation biomarkers e.g. **Lactate, FGF21**	✓ Improved fatty acid oxidation, lipid metabolism	✓ Increased fatty acid oxidation; decreased activation of HIF-1α pathway

AXA1125 Multi-Targeted MOA Restores Key Biologies Implicated in LC Fatigue Patients

- Vascular environment dysfunction, inflammation and suppressed metabolism are implicated in LC patients and reported in clinical registries
  - suppressed mitochondrial metabolism impacts high demand organs e.g. skeletal muscle
- AXA1125 restores key markers of vascular environment function, inflammation, and metabolism, as supported by Phase2a clinical and biomarker data
  - Building on a foundation of MOA from our NASH studies and pre-clinical models
- The proposed multi-targeted MOA of AXA1125 on both the tissue environment and on cell metabolism and energetics addresses key reported dysregulated biologies in patients suffering from LC fatigue

Long COVID Fatigue: Background and Trial Discussion

Jason H Maley, MD, MS

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Director, Critical Illness and COVID-19 Survivorship Program

Co-Chair, American Academy of PM&R Long COVID Clinic Collaborative

Co-Investigator, NIH Researching COVID to Enhance Recovery (RECOVER) Initiative

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BIDMC CRITICAL ILLNESS AND COVID-19 SURVIVORSHIP PROGRAM

HARVARD MEDICAL SCHOOL

Beth Israel Lahey Health
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Conflicts of Interest

I was not involved in the design, conduct, or reporting of this Phase 2a clinical trial. Following this trial, I began work as a scientific advisor on the topic of long COVID for Axcella.

38-year-old man, engineer, triathlete, COVID-19 in December 2020

- Initial illness managed at home, **felt it was a "mild cold,"** did not require hospitalization and symptoms resolved by day 4 of illness
- 8 weeks later: **severe physical and mental exhaustion** after an average day of work, had to stop working, can not walk around for more than 15 mins without having to lie down for hours
- "I keep making errors at work that are scary, completely lose train of thought, and am napping constantly"
- 6 months later, with supportive care and cognitive rehabilitation, remains on disability due to fatigue impacting physical and cognitive function

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BIDMC
CRITICAL ILLNESS AND
COVID-19 SURVIVORSHIP
PROGRAM

- **6-8 month wait list**, over 1000 patients seen at our clinic, same or longer wait around the country at 100+ long COVID clinics
- **No existing** physical or cognitive fatigue treatments targeting biology of long COVID
- Continue to see new patients with severe long COVID symptoms who were **infected in 2020**
- Daily messages from around the country from patients desperate for treatment

- Measure progress in **small steps every 4-6 months**, with many patients experiencing ongoing symptoms 2+ years from infection
- **Recovery from prolonged, severe fatigue in 1 month is exceptional**, not seen in the setting of our clinics
- Anticipate ongoing **pressing need for treatment indefinitely** – long COVID continues to occur in fully vaccinated people
- Patients with **chronic post-viral fatigue (ME/CFS) from other causes** now contacting our clinic for help as well

Characterizing Long COVID Fatigue

EMERGING EVIDENCE	CLINICAL CHARACTERISTICS
Impaired oxygen extraction during exercise	Exhaustion after minimal physical activity
Prolonged post-infectious inflammation	Post-exertional malaise
Immune Dysregulation	Impairs function at work and home
Mitochondrial Impairment	Accompanying cognitive impairment
	Non-restorative sleep

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My Key Takeaways from Trial

- **Patient-reported outcome** – Chalder Fatigue Scale (CFQ-11) – is the outcome that matters to patients and clinicians
- Clinically significant improvement in physical and cognitive domains
- Physical performance (6MWT) improved among those responsive to treatment

do you have problems with tiredness?
do you need to rest more?
do you feel sleepy or drowsy?
do you have problems starting things?
do you lack energy?
do you have less strength in your muscles?
do you feel weak?
do you have difficulties concentrating?
do you make slips of the tongue when speaking?
do you find it more difficult to find the right word?
how is your memory?

What would this mean to patients and to me

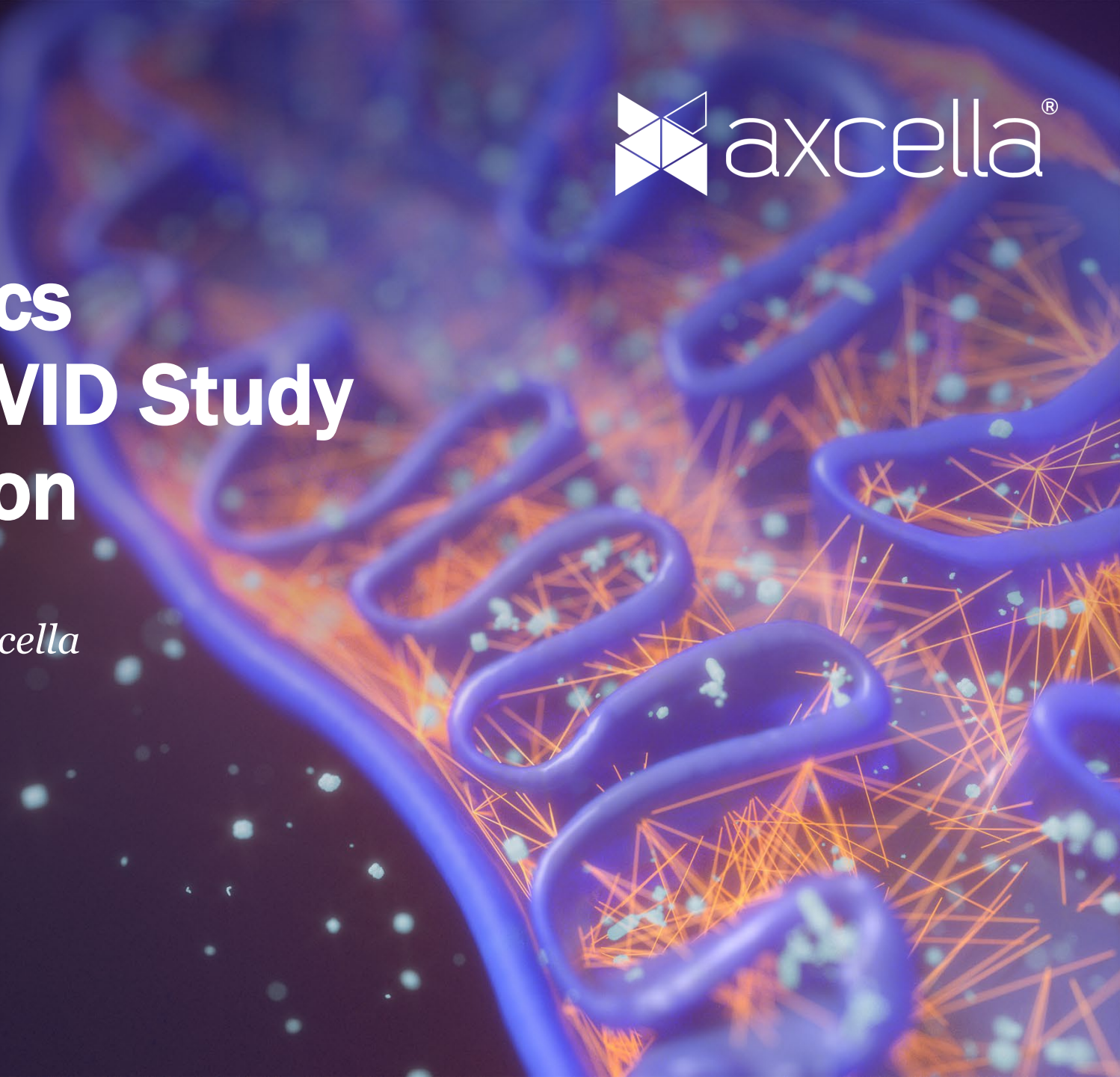
- **First fatigue therapy addressing underlying biology** – no current treatment for fatigue
- Cannot overstate **urgency** for treatments among patients and clinicians
- Ability to **return to work**, maintain income, **participate in home life**
- Return of **cognitive function**: memory, thinking, concentration, speech

NASDAQ: AXLA

Axcella Therapeutics Phase 2A Long COVID Study Results Presentation

***Bill Hinshaw**, President and CEO, Axcella*

August 2022



Milestone Rich Time

Program	Update	Timing	
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	
AXA1125 for NASH	Phase 2b Interim Data	Q3 2022	
	Scientific Communication	2H 2022	

Milestone timing based on current expectations and subject to change.
* Assumes positive Phase 2a data readout.

In Summary

- AXA1125 Demonstrated Highly Statistically Significant and Clinically Relevant Results
- COVID infections are continuing
- Long COVID will continue to be a major public health crisis
- Patients need options and treatment, not just observation
- Next Steps including Regulatory Engagement and Clinical Plans
- Axcella is leading in Long COVID therapeutics

Milestone timing based on current expectations and subject to change.
* Assumes positive Phase 2a data readout.

Q&A

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