



Axcella Announces Highly Promising Results from Phase 2a Placebo Controlled Clinical Trial for Long COVID

August 2, 2022

Subjects with Long COVID receiving AXA1125 experienced a clinically and statistically significant improvement in mental ($p=0.0097$) and physical ($p=0.0097$) fatigue scores compared to placebo subjects

Responders to AXA1125 demonstrated significantly improved scores during a 6 minute walk test

No emergent adverse events (AEs) or serious adverse events (SAEs) occurred

Regulatory meetings are planned to discuss a path to registration trial

Axcella to host a conference call today at 8:00 a.m. ET; To register, click [here](#)

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Aug. 2, 2022-- Axcella Therapeutics (Nasdaq: AXLA), a clinical-stage biotechnology company pioneering novel approaches to treating complex diseases using multi-targeted endogenous metabolic modulator (EMM) compositions, today reported topline results from the Phase 2a randomized, double-blind, placebo-controlled investigation to evaluate the efficacy and safety of AXA1125 in patients with fatigue related to Long COVID.

Long COVID is a persistent and growing challenge of the pandemic, affecting an estimated one hundred million patients worldwide with fatigue as the most common symptom reported. The recent Congressional subcommittee on Long COVID stated that one million Americans have been pushed out of work due to Long COVID. Additionally, it was stated that Long COVID contributed to approximately \$1 trillion in lost earnings and \$529 billion in increased medical spending.

We believe effective treatment of this complex and often debilitating disease requires addressing the underlying dysregulation of multiple biological pathways. Given the lack of therapeutic options for Long COVID patients and based on our understanding of AXA1125's positive impact on mitochondrial function, bioenergetics, and inflammation, Axcella conducted a placebo-controlled interventional study in collaboration with clinical researchers at University of Oxford as an exploratory trial to test the hypothesis that administration of AXA1125 could ameliorate fatigue symptoms of Long COVID. Bill Hinshaw, CEO of Axcella, remarked, "At Axcella, once we understood we had a potential Long COVID intervention we acted rapidly to test the hypothesis that we could address the high and growing need that exists for patients living with debilitating Long COVID fatigue. We are delighted to report that we have meaningful clinical results as well as an increased understanding on the best endpoints for future, potentially registrational studies and look forward to engaging with the regulatory authorities around the next steps in clinical development."

Since established endpoints for Long COVID do not exist, the study incorporated multiple endpoints for prioritization, selection, and use in a future registration trial to assess the effects of AXA1125 compared to placebo in subjects with moderate to severe fatigue. Safety and tolerability were also studied.

In the study, 41 subjects were enrolled and randomized to receive either 67.8 grams per day of AXA1125 (N=21) or a matched placebo (N=20) in two divided doses for 28 days, with a one-week safety follow-up period. All 41 subjects who started the study remained in the study to completion. Endpoints included phosphocreatine recovery time (PCr_T) following moderate exercise as assessed by 31P-magnetic resonance spectroscopy (MRS), which was included to assess mitochondrial function, and most importantly, clinically relevant endpoints including self-reported mental and physical fatigue as assessed by the Chalder Fatigue Questionnaire (CFQ-11), 6 minute walk test (6MWT) as well as serum lactate levels. The CFQ-11 is a validated patient reported outcome measure of fatigue that has been used in measuring patient impact in fatigue states such as chronic fatigue syndrome.

Subjects who received AXA1125 had improvements in measures of mental and physical fatigue that were both highly statistically significant and clinically relevant compared to those who received placebo. Mean changes in total, physical and mental scores in the CFQ-11 versus placebo were -4.30 ($p=0.0039$), -2.94 ($p=0.0097$) and -1.32 ($p=0.0097$), respectively. Clinically meaningful shifts in the severity of physical and mental fatigue were also noted in subjects who received AXA1125 compared to those who received placebo. There was a statistically significant correlation of improvement in fatigue score and greater distance achieved in the 6MWT ($p=0.0027$), an objective measure of physical ability, only observed in subjects who received AXA1125.

Baseline PCr_T among all subjects was significantly higher and had a higher degree of inter-subject variability (92.46 Seconds \pm 35.3 Seconds) than previously reported in the literature. These findings support the hypothesis that there is significant mitochondrial dysfunction in these patients but limits the utility of this parameter in a clinical trial. There was no significant difference on the primary outcome measure of PCr_T following moderate exercise between subjects receiving AXA1125 and placebo. There was a notable trend toward significant improvement in serum lactate levels after a 6MWT in AXA1125 subjects ($p=0.0730$). AXA1125 was safe and well tolerated with no significant adverse events reported by study subjects.

"The statistically significant improvement in reported mental and physical fatigue among study participants receiving AXA1125 is a very encouraging finding for Long COVID patients, who often experience extreme and constant fatigue throughout their day," said study leader, Dr. Betty Raman, Associate Professor of Cardiovascular Medicine at the Radcliffe Department of Medicine, University of Oxford.

Karim Azer PhD, Axcella's VP, Platform and Discovery stated, "The results of this trial encourage us to further evaluate the multi-targeted effects of AXA1125 on mitochondrial and related biomarkers to advance our understanding of the benefits AXA1125 delivers to Long COVID patients. Preliminary analysis including mitochondrial, inflammatory, and endothelial environment biomarker work provides additional data strengthening the

core rationale for AXA-1125's compelling clinical benefits."

Dr. Jason Maley, Director of Beth Israel Deaconess Medical Center Critical Illness and COVID-19 Survivorship Program, remarked that, "This is the first pharmaceutical agent to demonstrate improved outcomes for patients with Long COVID in a randomized controlled trial and suggests that AXA1125 may play an important part in the long-term treatment of these patients as they seek to return to the life they had before the infection. On behalf of the innumerable patients urgently seeking therapies for the debilitating symptoms of Long COVID, I am excited to see the continued development of AXA1125."

Conference Call Information

Register for the call by clicking [here](#).

A live webcast of the call, as well as a replay, will be available on the Events and Presentations section on the Company's website:

<https://ir.axcellatx.com/events-and-presentations>.

Internet Posting of Information

Axcella uses the "Investors and News" section of its website, www.axcellatx.com, as a means of disclosing material nonpublic information, to communicate with investors and the public, and for complying with its disclosure obligations under Regulation FD. Such disclosures include, but may not be limited to, investor presentations and FAQs, Securities and Exchange Commission filings, press releases, and public conference calls and webcasts. The information that we post on our website could be deemed to be material information. As a result, we encourage investors, the media and others interested to review the information that we post there on a regular basis. The contents of our website shall not be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended.

About Axcella Therapeutics (Nasdaq: AXLA)

Axcella is a clinical-stage biotechnology company pioneering a new approach to treat complex diseases using compositions of endogenous metabolic modulators (EMMs). The company's product candidates are comprised of EMMs and derivatives that are engineered in distinct combinations and ratios to restore cellular homeostasis in multiple key biological pathways and improve cellular energetic efficiency. Axcella's pipeline includes lead therapeutic candidates in Phase 2 development for the treatment of Long COVID and non-alcoholic steatohepatitis (NASH). The company's unique model allows for the evaluation of its EMM compositions through non-IND clinical studies or IND clinical trials. For more information, please visit www.axcellatx.com.

Forward-Looking Statements

This press release contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including, without limitation, statements regarding interest that may ensue in the Company's product candidates or securities following announcement of the Company's recent clinical trial results and the timing of the Company's clinical trial data readouts and next steps for its clinical programs, including a potential registration trial of AXA1125 for the treatment of Long COVID. 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 press release 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 press release, including, without limitation, those related to the belief that mitochondrial dysfunction is a key driver of Long COVID induced fatigue, potential impact of COVID-19 on the Company's ability to conduct and complete its ongoing or planned clinical studies and clinical trials 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 the Company is able to collect in its clinical trials of AXA1125, other potential impacts of COVID-19 on the Company's business and financial results, including with respect to its ability to raise additional capital and operational disruptions or delays, changes in law, regulations, or interpretations and enforcement of regulatory guidance, whether data readouts support the Company's clinical trial plans and timing, clinical trial design and target indications for AXA1125, the clinical development and safety profile of AXA1125 and its therapeutic potential, whether and when, if at all, the Company's product candidates will receive approval from the FDA or other comparable regulatory authorities, potential competition from other biopharma companies in the Company's target indications, and other risks identified in the company's SEC filings, including Axcella's Annual Report on Form 10-K, Quarterly Reports 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 press release 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.

Dr. Maley receives compensation as a consultant for the Company.

View source version on [businesswire.com](https://www.businesswire.com/news/home/20220802005461/en): <https://www.businesswire.com/news/home/20220802005461/en>

Company

Ashley Robinson

arr@lifesciadvisors.com

(617) 430-7577

Source: Axcella Therapeutics