Axcella Therapeutics Launches Clinical Program to Develop Treatment for Patients with Long COVID

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- *Potential to play leading role in addressing Long COVID fatigue and muscle weakness via AXA1125's mitochondrial and bioenergetic impact*
- *Phase 2a clinical trial to be initiated by researchers at Oxford University by year-end; top-line data readout anticipated by mid-2022*
- *Program to be discussed at Axcella's R&D Day today at 10 a.m. EDT*

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Oct. 26, 2021-- Axcella Therapeutics (Nasdaq: AXLA), a clinical-stage biotechnology company pioneering a new approach to treat complex diseases using multi-targeted endogenous metabolic modulator (EMM) compositions, today announced a new clinical program to investigate AXA1125 as a potential treatment for patients with Long COVID, a complex condition also known as Post COVID-19 Condition and Post-Acute Sequelae of COVID-19 (PASC). The United Kingdom's Medicines and Healthcare products Regulatory Agency (MHRA) accepted a Phase 2a clinical trial authorization (CTA) submission from Axcella on October 22, 2021.

Led by researchers at the Radcliffe Department of Medicine at the University of Oxford (U.K.), the clinical trial is planned to begin by the end of this year at the Oxford Centre for Clinical Magnetic Resonance Research, with top-line data expected by mid-2022. This new program is among the topics to be discussed at Axcella's R&D Day, which is taking place today beginning at 10 a.m. EDT.

More than 240 million cases of COVID-19 have been reported worldwide to date[1], and it is estimated that nearly a quarter of these people suffer from the virus's long-term effects [2]. These patients continue to experience a wide range of symptoms months after their initial diagnosis. Similar to many other conditions and diseases, mitochondrial dysfunction is increasingly being implicated as a key driver of Long COVID-induced fatigue, which is the most common symptom associated with the condition[3,4].

"Long COVID is having a truly devastating impact on countless people around the world, leaving many with a sense of hopelessness. It is widely recognized that mitochondrial dysfunction may contribute to the profound fatigue associated with this condition," said lead researcher Dr. Betty Raman, British Heart Foundation Oxford Centre of Research Excellence Clinical Transition Intermediate Fellow from Oxford University's Radcliffe Department of Medicine. "With no approved Long COVID therapies, the need for continued innovation is urgent. I am pleased to be leading an investigation of AXA1125 to understand its potential to restore cellular energetics and address patients' needs."

The Phase 2a trial will be a randomized, double-blind, placebo-controlled investigation to evaluate the efficacy and safety of AXA1125 in patients with exertional fatigue related to Long COVID. Approximately 40 patients will be enrolled and randomized evenly to receive either 67.8 grams per day of AXA1125 or a matched placebo in two divided doses for 28 days, with a one-week safety follow-up period.

"While Long COVID's enormous patient and socioeconomic burden has become readily apparent, its underlying pathophysiology is now emerging," said Dr. Alison Schecter, President of R&D at Axcella. "In two prior successful clinical studies and in preclinical models, AXA1125 has demonstrated an ability to restore mitochondrial function and improve energetic efficiency via increased fatty acid oxidation, restored cellular homeostasis, and reduced inflammation. This provides us with confidence about its potential to help the growing number of patients who are suffering from COVID's debilitating effects long after contracting the virus."

The trial's primary endpoint will assess the improvement of mitochondrial function within the skeletal muscle from baseline to Day 28 as measured by changes in phosphocreatine (PCr) recovery time via 31-phosphorus magnetic resonance spectroscopy (MRS). PCr recovery time is a well-established and highly sensitive measure that has been strongly correlated with a registrational endpoint (i.e., 6-minute walk test) in a number of other diseases in which fatigue and muscle weakness play a central role, including amyotrophic lateral sclerosis (ALS), Duchenne muscular dystrophy, and chronic kidney disease. Key secondary endpoints include lactate levels, a 6-minute walk test, fatigue scores, and safety and tolerability.

AXA1125 is also currently being investigated in patients with non-alcoholic steatohepatitis (NASH) in the EMMPACT Phase 2b clinical trial (NCT04880187). This global, placebo-controlled trial was initiated in the second quarter of 2021 and is enrolling approximately 270 subjects with biopsy-proven NASH for a 48-week treatment period. A second product candidate, AXA1665, is under investigation in patients with overt hepatic encephalopathy (OHE) in the EMMPOWER Phase 2 clinical trial (NCT04816916). This global, placebo-controlled trial, also initiated in the second quarter of 2021, is enrolling approximately 150 subjects with a history of OHE for a 24-week treatment period.

Bill Hinshaw, Axcella President and CEO, noted, "Today's announcement further demonstrates the power of our model and is the result of a confluence of events, including the ongoing global pandemic, new findings about Long COVID's manifestation and drivers, and Axcella's recent scientific, clinical, and regulatory successes with AXA1125. With the impending initiation of this Phase 2a trial and with EMMPOWER and EMMPACT already underway, we are positioned for multiple potentially transformational data readouts ahead."

Axcella R&D Day Today

Axcella's platform and each of its clinical programs will be discussed at the company's R&D Day, which takes place today, Tuesday, October 26, starting at 10:00 a.m. EDT. In addition to Axcella management, the event will feature presentations from the following physicians and key opinion leaders:

- Dr. Betty Raman, Radcliffe Department of Medicine, University of Oxford, United Kingdom (Topic: Long COVID)
- Dr. Stephen Harrison, Medical Director of Pinnacle Clinical Research, San Antonio, TX and Visiting Professor of

Hepatology, University of Oxford, United Kingdom (Topic: NASH)
- Dr. Eric Lawitz, VP, Scientific and Research Development, The Texas Liver Institute and Clinical Professor of Medicine, University of Texas Health San Antonio (Topic: OHE)
- Dr. Elliot Tapper, Director, Cirrhosis Program and Associate Professor of Medicine, University of Michigan (Topic: OHE)

A webcast of this event can be accessed by visiting the "Investors & News" section of the company's website, www.axcellatx.com. A webcast replay will be available for 90 days following the presentation.

Internet Posting of Information

Axcella uses its website, www.axcellatx.com, as a means of disclosing material nonpublic information and for complying with its disclosure obligations under Regulation FD. Such disclosures will be included on the company's website in the "Investors and News" section. Accordingly, investors should monitor this portion of the company's website, in addition to following its press releases, SEC filings and public conference calls and webcasts.

About Axcella Therapeutics (Nasdaq: AXLA)

Axcella is a clinical-stage biotechnology company pioneering a new approach to treat complex diseases using endogenous metabolic modulator (EMM) compositions. The company's product candidates are comprised of EMMs and derivatives that are engineered in distinct combinations and ratios to reset multiple biological pathways, improve cellular energetics, and restore homeostasis. Axcella's pipeline includes lead therapeutic candidates in Phase 2 development for the reduction in risk of overt hepatic encephalopathy (OHE) recurrence, the treatment of Long COVID, and the treatment of 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 the characteristics, competitive position and development potential of AXA1125 and AXA1665, the potential for these product candidates to address patients' unmet needs, and the timing of the company's clinical trial initiations and readouts. 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 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 AXA1665 and 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 AXA1665 and AXA1125, the clinical development and safety profile of AXA1665 and AXA1125 and their 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 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 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.

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[1] New York Times. https://www.nytimes.com/interactive/2021/world/covid-cases.html

[2] A Detailed Study of Patients with Long-Haul COVID, A FAIR Health White Paper, June 15, 2021

[3] Carfì A, et al. Persistent Symptoms in Patients After Acute COVID-19. JAMA. 2020

[4] Bindu D, et al. Redox imbalance links COVID-19 and myalgic encephalomyelitis/chronic fatigue syndrome. PNAS. Aug. 2021

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