Axcella Announces FDA IND Clearance Supporting Regulatory Path to Registration of AXA1125 for Long COVID Fatigue

February 15, 2023

Phase 2b/3 study may proceed under U.S. Investigational New Drug application

Study design now accepted by U.S. and U.K. regulatory authorities

Axcella to present at Long COVID forum co-sponsored by BIO and Solve M.E.

Axcella to host a conference call February 16 at 8:00 a.m. ET; To register, click here

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Feb. 15, 2023-- 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 announced its Investigational New Drug (IND) application to initiate a phase 2b/3 trial in the U.S. for AXA1125 in the treatment of Long COVID Fatigue has been cleared by the U.S. Food and Drug Administration (FDA). The company reported that it had received regulatory guidance from the FDA, supporting a trial that is designed to serve as the registration trial for patients with Long COVID Fatigue. The study design now has acceptance from both the U.S. and U.K. regulatory authorities. Last month, the company announced a regulatory path to registration of AXA1125 in the treatment of Long COVID Fatigue, and that it had received regulatory guidance from The Medicines and Healthcare products Regulatory Agency (MHRA), the U.K.'s regulatory agency, supporting a single trial that could serve as the registration trial for patients with Long COVID Fatigue.

The guidance from the FDA and the MHRA follows the company's submission of materials to both regulatory agencies including 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. The study found that subjects who received AXA1125 experienced clinically and statistically significant improvement in mental (p=0.0097) and physical (p=0.0097) fatigue scores compared to placebo subjects. Consistent with the Ph2a trial, the Ph2b/3 trial will enroll participants who have had fatigue for at least 12 weeks after COVID-19 infection. The primary endpoint will utilize the same patient reported outcome tool, the Chalder Fatigue Questionnaire (CFQ-11), to measure improvements in fatigue. Additional endpoints will evaluate improvements in physical function, quality of life, and ability to return to work. Participants will receive either placebo or AXA1125 for three months.

"We're excited to now have the regulatory clearance from both the U.S. and U.K. authorities to advance our Long COVID program into a trial that can lead to registration," said Bill Hinshaw, CEO of Axcella. "The guidance from the FDA demonstrates continued progress, following the MHRA milestone a few weeks ago, providing clear next steps in this important, ongoing, and as-yet untreated disease. There are millions of people around the world suffering from Long COVID Fatigue who are without options. Axcella has the leading program in the field, and this regulatory feedback provides the next step in developing a potential Long COVID Fatigue treatment."

"We are pleased to obtain FDA clearance for this phase 2b/3 study, following our positive feedback from the MHRA," said Margaret Koziel, M.D., Chief Medical Officer of Axcella. "Both on an individual and a societal level, the impact of Long COVID on the ability to have a full and productive life is significant, and we hope to offer a solution to these patients."

Dr. Koziel will be presenting at a forum on February 21 that will bring hundreds of stakeholders together to discuss how the government and private industry can foster greater and more urgent public-private engagement on treatments for Long COVID. The forum is co-sponsored by the Biotechnology Innovation Organization (BIO) and SOLVE M.E., a non-profit organization that serves as a catalyst for critical research into diagnostics, treatments, and cures for myalgic encephalomyelitis/chronic fatigue syndrome (ME/CFS), Long COVID and other post-infectious diseases. Axcella will make a presentation at the forum to discuss its novel approach to treating Long COVID Fatigue and its promising clinical data.

"Treatment with AXA1125 resulted in statistically significant improvement in mental and physical fatigue scores, compared to placebo, in a well-designed and carefully conducted randomized controlled trial," added Jason Maley, M.D., Director of the Beth Israel Deaconess Medical Center COVID-19 Survivorship Program. "I'm eager to see AXA1125 move into a phase 2b/3 study. This work is important to help patients with Long COVID who commonly experience debilitating daily fatigue."

"There remains an urgent need for treatment developed specifically for the millions of patients suffering from Long COVID Fatigue, a disease that is having a devastating health and economic impact," said Oved Amitay, Chief Executive Officer of Solve M.E. Amitay, who also is the co-founder of the Long COVID Alliance, a network of patient-advocates, scientists, disease experts, and drug developers focused on educating policy makers and accelerating research into post-viral illnesses, added, "I am looking forward to the conversation at the BIO and SOLVE forum, where I expect multiple stake-holders to continue to advance progress for Long COVID patients."

Long COVID is a persistent and growing long-term consequence of the pandemic, affecting an estimated one hundred million patients worldwide, with fatigue as the most commonly reported symptom. Recent estimates indicate that 15-20% of Americans with COVID have persisting health issues,[i] up to four million Americans are out of work due to Long COVID symptoms, and that Long COVID has contributed to approximately $1 trillion in lost earnings and $544 billion in increased medical spending.[ii]

Investor Conference Call Information
Axcella will host a live conference call and webcast at 8:00 a.m. ET on Thursday, February 16, 2023. Participants include Bill Hinshaw, Dr. Margaret Koziel, and Dr. Jason Maley. To access the live conference call, please dial 844-808-7139 (domestic) or 412-902-0127 (international) and refer to "Axcella Health." A webcast of the call will also be available under "Events and Presentations" in the Investors section of the Axcella Health website at https://ir.axcellatx.com/. The archived webcast will be available on Axcella's website approximately two hours after the conference call and will be

available for 90 days following the call.

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 reset multiple biological pathways, improve cellular energetics, and restore homeostasis. Axcella's pipeline includes lead therapeutic candidates for the treatment of Long COVID, NASH, and the reduction in risk of OHE recurrence. 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 potential utility of AXA1125 as a treatment of Long COVID and the Company's anticipated regulatory pathway for AXA1125 and the timing and potential success thereof. 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 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 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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[i] Bull-Otterson L, Baca S, Saydah S, et al. Post–COVID Conditions Among Adult COVID-19 Survivors Aged 18–64 and ≥65 Years — United States, March 2020–November 2021. MMWR Morb Mortal Wkly Rep 2022;71:713–717. DOI: http://dx.doi.org/10.15585/mmwr.mm7121e1external icon

[ii] Bach K. New data shows long Covid is keeping as many as 4 million people out of work. Brookings Institute. August 24, 2022. https://www.brookings.edu/research/new-data-shows-long-covid-is-keeping-as-many-as-4-million-people-out-of-work/#footnote-3

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