# Axcella Announces Initiation of EMMPACT℠ Phase 2b Clinical Trial of AXA1125

May 11, 2021

- *Initial clinical sites activated and patient screening underway*
- *Potential for AXA1125 to serve as a first-line therapy for patients with nonalcoholic steatohepatitis (NASH)*

CAMBRIDGE, Mass.--(BUSINESS WIRE)--May 11, 2021-- Axcella (Nasdaq: AXLA), a clinical-stage biotechnology company pioneering a new approach to treat complex diseases and improve health using endogenous metabolic modulator (EMM) compositions, today announced that it has activated initial clinical sites and begun patient screening for its EMMPACT Phase 2b clinical trial of AXA1125, the company's multi-targeted oral product candidate for the treatment of NASH.

"NASH is the quintessential complex disease, involving the dysregulation of numerous biological pathways and impacting an enormous, heterogenous global population," said Stephen A. Harrison, M.D., Medical Director of Pinnacle Clinical Research in San Antonio, TX, visiting professor of Hepatology at the University of Oxford, UK and the principal investigator of EMMPACT. "These factors have confounded many physicians and drug developers in the past. Given its multi-modal mechanism, the activity and tolerability seen in past clinical studies and the presumed safety of its underlying amino acids, AXA1125 holds the potential to serve as an ideal first-line NASH agent. We are excited to have EMMPACT underway and are eager to gauge AXA1125's histological impact."

Axcella has branded this global trial EMMPACT based on the potential for AXA1125, an EMM composition, to deliver meaningful, multifactorial clinical benefits to patients with NASH. This randomized, double-blind, placebo-controlled, multi-center investigation will evaluate the efficacy and safety of AXA1125 in patients with biopsy-confirmed F2/F3 NASH. Approximately 270 patients will be enrolled and randomized 1:1:1 to receive either 45.2 or 67.8 grams per day of AXA1125 or a matched placebo in two divided doses for 48 weeks, with a four-week safety follow-up period. Patients will be stratified based on the presence or absence of type 2 diabetes.

"The initiation of EMMPACT is the latest in a series of exciting recent milestones for Axcella and comes just one month after clearing our IND application for AXA1125, which is a testament to our team's strong preparation and execution as well as our investigators' interest and engagement," said Bill Hinshaw, President and Chief Executive Officer of Axcella. "I am confident in our ability to extend our successful track record and rapidly enroll this clinical trial."

EMMPACT will be conducted globally across more than 70 clinical sites with a primary endpoint assessing the proportion of patients with a biopsy-confirmed ≥2 point improvement in NAFLD Activity Score (NAS) after the 48-week treatment period. Secondary endpoints will include the proportion of patients achieving biopsy-confirmed resolution of NASH without worsening of fibrosis and the proportion of patients achieving a ≥1 stage improvement in fibrosis without worsening of NASH. A range of non-invasive biomarkers, including MRI-PDFF and Fibroscan, will be utilized for additional endpoints and an interim analysis in the trial.

"In two consecutive clinical studies of AXA1125 in subjects with presumed NASH, meaningful improvements were seen in non-invasive measures of hepatic fat, insulin resistance, inflammation and fibrosis," said Alison Schecter, M.D., President of R&D at Axcella. "We expect EMMPACT to provide robust insights on AXA1125's dose response, longer-term effects, histological impact and potential differentiation in type 2 diabetics that can be leveraged to expand our development efforts."

Additional trial information can be found on https://clinicaltrials.gov/ via the identifier NCT04880187.

**About AXA1125 and Nonalcoholic Steatohepatitis (NASH)**

NASH is the most severe form of fatty liver disease and is driven by multifactorial systemic dysregulation of pathways associated with metabolism, inflammation and fibrosis. If left untreated, this disease may ultimately lead to life-threatening conditions such as cirrhosis or liver cancer, requiring liver transplant. According to the Global Liver Institute's U.S. NASH Action Plan published in December 2020, up to 40 million people in the U.S. alone are living with NASH and approximately 10% of U.S. children are afflicted with this disease. Incidence is expected to continue increasing in parallel with the obesity and type 2 diabetes epidemics. Currently, there are no approved drug therapies for NASH in the United States.

AXA1125, Axcella's product candidate for treatment of NASH, is a composition of six amino acids and derivatives that is designed to target multiple metabolic pathways known to affect the pathogenesis of fatty liver disease. In prior clinical studies, this oral product candidate has been safe, well tolerated and has demonstrated the potential to reduce liver fat, inflammation and fibrosis with a safe and well tolerated profile while avoiding an impact on lipids and weight. AXA1125 is now in Phase 2b development.

**About Endogenous Metabolic Modulators (EMMs)**

EMMs are a broad family of naturally occurring molecules, including amino acids, that regulate human metabolism. Axcella is developing a range of novel product candidates that are comprised of multiple EMMs engineered in distinct combinations and ratios to simultaneously impact multiple metabolic pathways to modify the underlying causes of various complex diseases and improve health.

**About Axcella's Clinical Studies**

Each of the clinical investigations that the company has completed to date have been conducted as non-investigational new drug application (IND)

clinical studies under U.S. Food and Drug Administration regulations and guidance supporting research with food. These studies evaluate product candidates for safety, tolerability and effects on the normal structures and functions in humans, including in individuals with disease. They are not designed or intended to evaluate a product candidate's ability to diagnose, cure, mitigate, treat or prevent a disease. If Axcella decides to further develop a product candidate as a potential therapeutic, as is the case with AXA1665 and AXA1125, any subsequent clinical studies will be conducted under an IND.

**Internet Posting of Information**

Axcella uses its website, www.axcellahealth.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**

Axcella is a clinical-stage biotechnology company pioneering a new approach to treat complex diseases and improve health using endogenous metabolic modulator (EMM) compositions. The company's product candidates are comprised of EMMs and their derivatives that are engineered in distinct combinations and ratios to simultaneously impact multiple biological pathways. Axcella's pipeline includes lead therapeutic candidates for non-alcoholic steatohepatitis (NASH) and the reduction in risk of overt hepatic encephalopathy (OHE) recurrence. For more information, please visit www.axcellahealth.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, the potential for AXA1125 to serve as a first-line NASH agent, the company's ability to rapidly enroll its clinical trials, and the company's ability to address other complex diseases 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 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 IND-enabled 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 planned clinical trial of AXA1125, other potential impacts of COVID-19 on the company's business and financial results, including with respect to the company's 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 initiation 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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