Axcella Announces AXA1125's IND Clearance for the Treatment of NASH

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- *Multi-targeted oral candidate with the potential to be a first-line treatment option for adult and pediatric patients with NASH*
- *Phase 2b clinical trial in adults expected to begin in Q2*

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Apr. 13, 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 achieved a key milestone with U.S. Food and Drug Administration (FDA) clearance of an Investigational New Drug (IND) application for AXA1125, enabling the company to proceed directly into a Phase 2b clinical trial. AXA1125 is Axcella's multi-targeted oral product candidate for nonalcoholic steatohepatitis (NASH), a chronic and progressive liver disease impacting up to 40 million people in the U.S. alone.

"This IND follows close on the heels of AXA1665's IND clearance earlier this year, ushering in an exciting new era for Axcella as we seek to tackle a variety of complex diseases and address important unmet needs for patients utilizing multi-targeted EMM compositions," said Bill Hinshaw, President and Chief Executive Officer of Axcella. "I am pleased by our team's strong execution in completing two robust FDA submissions and readying us for the start of our highly efficient, later-stage clinical trials."

Axcella expects to initiate its Phase 2b clinical trial in the second quarter of 2021. This randomized, double-blind, placebo-controlled, multi-center trial will evaluate the efficacy, safety and tolerability of AXA1125 in adult 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 trial 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.

"AXA1125 leverages a mechanism that engages multiple pathophysiologic pathways involved in the development of NASH using a modality with well-precedented safety, which is particularly important given the many comorbidities associated with this chronic disease," said Alison Schecter, M.D., President of R&D at Axcella. "In past clinical studies, compelling activity has been seen with AXA1125 across a range of non-invasive biomarkers, with enhanced effects in type 2 diabetics. Our goal in the Phase 2b is to affirm AXA1125's impact via histology and further strengthen its profile as a compelling candidate for first-line treatment in NASH."

The upcoming Phase 2b clinical trial follows two earlier non-IND clinical studies in which reductions were seen with AXA1125 in key measures of hepatic fat, insulin resistance, inflammation and fibrosis with a safe and well tolerated profile. Presentations containing those findings can be found by visiting https://axcellahealth.com/publications/.

About AXA1125 and Nonalcoholic Steatohepatitis (NASH)

NASH is the most severe form of non-alcoholic fatty liver disease (NAFLD). This chronic, complex disease is associated with significant morbidity and mortality globally, and it is estimated to impact up to 40 million Americans, including up to 10% of American children. Despite its severity and increasing prevalence, there are currently no approved therapies for NASH in the United States.

AXA1125, Axcella's NASH product candidate, is a composition of six amino acids and derivatives that is designed to target multiple metabolic pathways involved in NASH's progression from metabolism to inflammation to fibrosis. In prior clinical studies, this oral product candidate has been safe and well tolerated and has demonstrated clinically meaningful reductions in a range of well-accepted, non-invasive NASH biomarkers, with the most pronounced activity noted in subjects with type 2 diabetes. AXA1125 is now entering Phase 2b development in adults with NASH. Axcella also plans to investigate AXA1125 in pediatric NASH.

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 company's clinical studies to date are or 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 were not designed or intended to evaluate a product candidate's ability to diagnose, cure, mitigate, treat or prevent a disease. INDs were recently cleared for Axcella's lead product candidates, AXA1665 and AXA1125, allowing for the investigation of these candidates' efficacy, safety and tolerability in subsequent clinical trials.

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 design, status and timing of the company's planned Phase 2b clinical trial of AXA1125, 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 our 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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