Axcella Announces Positive Top-Line Data from AXA1125-003 Clinical Study Showing Multifactorial Activity in Adult Subjects with NAFLD

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- *Clinically relevant reductions in liver fat content, insulin resistance and fibroinflammation markers observed with AXA1125 along with favorable tolerability, supporting its potential to be a first-line NASH therapy*
- *Greater activity in key markers seen among subjects with type 2 diabetes receiving AXA1125*
- *Company plans to engage with FDA regarding IND submission for AXA1125, proposed Phase 2b clinical trial in adult NASH and pediatric development program*
- *Conference call to be held today at 8:30 a.m. ET*

CAMBRIDGE, Mass.--(BUSINESS WIRE)--May 6, 2020-- Axcella (Nasdaq: AXLA), a clinical-stage biotechnology company focused on leveraging endogenous metabolic modulators (EMMs) to pioneer a new approach for treating complex diseases and improving health, today announced positive top-line data from AXA1125-003.

AXA1125-003 is a placebo-controlled, randomized, multi-arm clinical study assessing the impact of AXA1125 and AXA1957 on safety, tolerability and effects on structures and functions of the liver, as measured by a comprehensive panel of imaging and soluble biomarkers related to metabolism, inflammation and fibrosis. Both of these distinct product candidates are proprietary compositions of amino acids and derivatives that have been designed to support liver health. In this non-IND study, 102 adult non-alcoholic fatty liver disease (NAFLD) subjects with presumed nonalcoholic steatohepatitis (NASH), based on inclusion criteria, were enrolled and dosed in a 2:2:2:1 ratio to receive AXA1125, one of two AXA1957 doses, or placebo administered twice daily for 16 weeks. Study subjects were stratified based on the presence or absence of type 2 diabetes.

Results from the study showed that AXA1125 and AXA1957 were generally well-tolerated, with sustained reductions noted for both product candidates versus placebo in key biomarkers of metabolism, inflammation and fibrosis over 16 weeks. Overall, as compared to placebo, AXA1125 demonstrated larger and more consistent reductions in clinically relevant biomarkers than AXA1957. Among subjects receiving AXA1125, 39% achieved a ≥30% relative reduction in liver fat content (MRI-PDFF), 39% achieved a ≥17 U/L reduction in alanine aminotransaminase (ALT), and 35% achieved a ≥80 mSec reduction in corrected T1 (cT1). Among the 11 subjects with type 2 diabetes receiving AXA1125, a greater proportion achieved each of these thresholds. Emerging evidence suggests that these thresholds of activity increase the likelihood of histopathological improvement in NASH subjects. Notably, the above results were seen without impacting mean body weight or serum lipids.

Manu Chakravarthy, M.D., Ph.D., Chief Medical Officer of Axcella, said, “In AXA1125-003, we were seeking to evaluate safety and tolerability while also determining what differential responses may be seen from AXA1125 and AXA1957 across markers of metabolism, inflammation and fibrosis. It is gratifying that multifactorial activity and a favorable tolerability profile were noted for AXA1125 in this multi-arm, placebo-controlled randomized study, which replicates findings from our previous clinical study in subjects with NAFLD and type 2 diabetes. We believe that these data, coupled with AXA1125’s oral route of administration and favorable tolerability profile to date, reinforce its potential to meaningfully improve the lives of patients with NASH.”

“These data indicate that AXA1125 holds the potential to be a first-line therapy in NASH, with impressive, concordant metabolism, inflammation and fibrosis activity as well as a favorable tolerability profile with no meaningful changes to serum lipids and body weight,” 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 AXA1125-003. “Additionally, in the majority of subjects with type 2 diabetes receiving AXA1125, clinically relevant thresholds of activity were observed in non-invasive tests that suggest a higher probability of positive outcomes histopathologically. This is a potential differentiator and is particularly encouraging given that nearly 40% of the NASH population is diabetic and the disease is known to be more severe in these patients.”

Select Measures of Relevance at 16 Weeks

Measure	Placebo	AXA1125	AXA1957 Low	AXA1957 High
Subjects dosed	15	29	26	32
Mean relative reduction in liver fat content (MRI-PDFF)	-6%	-23%	-20%	-8%
Subjects with ≥30% relative reduction in liver fat content	8%	39%	23%	19%
Mean relative reduction in ALT	-7%	-22%	-19%	-21%
Subjects with ≥17 U/L reduction in ALT	25%	39%	32%	37%
Subjects with ≥80 mSec reduction in cT1	17%	35%	23%	23%
Mean absolute change in proC3 (ng/mL)	-0.7	-3.4	-3.1	-4.1

** Mean values and percentages above only include subjects for whom data was available at the week 16 timepoint.*

AXA1125 and AXA1957 were both generally well tolerated in the study. The adverse events (AEs) experienced in ≥10% of subjects were gastrointestinal (diarrhea, nausea, reduced appetite) and upper respiratory infection. Gastrointestinal AEs were generally mild and transient, self-resolving in two to three weeks on average. Two serious adverse events were reported, both of which were determined to be unrelated to study product administration.

"The findings from this clinical study further validate the strength of our EMM platform and its ability to identify product candidates with the potential to address complex diseases in a multi-targeted manner," said Bill Hinshaw, President and Chief Executive Officer of Axcella. "Given the strength and consistency of data on AXA1125, we have selected it as our product candidate for NASH and have decided that we will not reinitiate our AXA1957-002 pediatric study, which had recently been suspended due to COVID-19. In the months ahead, we plan to engage with the U.S. Food and Drug Administration (FDA) to discuss our investigational new drug (IND) application for AXA1125, proposed Phase 2b clinical trial in adults and pediatric development program. We give our thanks to the many subjects and investigators who participated in AXA1125-003 and will continue working diligently toward our goal of providing them with an effective and safe treatment option."

Conference Call Information

Axcella will host a conference call today at 8:30 a.m. ET to discuss the top-line data from AXA1125-003. The conference call webcast and accompanying slides will be made available shortly before the start of the call on the company's website at www.axcellahealth.com in the Investors & News. To access the call via telephone, please dial (866) 652-5200 (U.S. toll free) or (412) 317-6060 (international) five minutes prior to the start time. For those unable to listen in live, a webcast archive will be available on the company's website for 30 days following the call.

About Endogenous Metabolic Modulators (EMMs)

EMMs are a broad family of 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 root causes of various complex diseases and improve health.

About Axcella's Clinical Studies

Each of the company's clinical studies to date, including AXA1125-003, 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 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 such portions 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 focused on leveraging endogenous metabolic modulators (EMMs) to pioneer a new approach for treating complex diseases and improving health. 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. Additional muscle- and blood-related programs are in earlier-stage development. 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 the company's EMM product candidates, including AXA1125, the design, status and timing of the company's ongoing clinical studies and planned IND-enabled clinical trials, including with respect to the company's planned adult and pediatric clinical trials for AXA1125, the subject and timing of the company's interactions with the FDA, including with respect to an IND application, Phase 2b clinical trial in adults and pediatric development plans for AXA1125, and the potential of the company's product candidates to impact health and/or disease, including AXA1125's potential in NASH. 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 planned 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 we are able to collect, other potential impacts of COVID-19 on our business and financial results, including with respect to our ability to raise additional capital and operational disruptions or delays, , changes in law, regulations, or interpretations and enforcement of regulatory guidance, whether data readouts and/or FDA feedback support our planned timing for an IND filing, clinical trial design and target indication for AXA1125, the clinical development and safety profile of the company's product candidates and their health or therapeutic potential, whether and when, if at all, the company's product candidates will receive approval from the FDA or other comparable regulatory authorities, and for which, if any, indications, competition from other biotechnology companies, past results from clinical studies not being representative of future results, 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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