Axcella Announces Positive Interim Data from Phase 2b EMMPACT Study of AXA1125 in Nonalcoholic Steatohepatitis (NASH)

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Subjects enrolled with biopsy confirmed NASH experienced clinically and statistically significant improvements in liver stiffness as measured by FibroScan, a non-invasive measure of liver fibrosis

Subjects with NASH experienced clinically and statistically significant improvements in alanine aminotransferase (ALT), a measure of liver cell inflammation, at both dose levels of AXA1125

Findings demonstrate improvement in hepatic fat as measured by MRI-PDFF

AXA1125 continues to demonstrate a safe and well tolerated profile

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

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Sep. 29, 2022-- 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 reported interim results from their ongoing global Phase 2b randomized, double-blind, placebo-controlled, dose ranging EMMPACT study to evaluate the safety, tolerability, and efficacy of AXA1125 for the treatment of NASH. These interim results report findings regarding the effects of AXA1125 administration on selected outcome measures after 12- and 24-weeks of treatment.

This interim analysis was preplanned to be conducted when enrollment reached 30% of the target of 270 subjects with biopsy confirmed stage 2 or 3 NASH across all trial arms. Data from this ongoing blinded study included 82 subjects at week 12 and 58 subjects at week 24; approximately half of the subjects have type 2 diabetes mellitus (T2DM). In addition to effects on hepatic fat and ALT, previously reported in 2 other studies, this study also included vibration controlled transient elastography (FibroScan), a widely accepted and accessible non-invasive test (NIT) that assesses both liver fat and stiffness. Specifically, the study examines liver stiffness, changes of which have been correlated with improvements in liver fibrosis and outcomes in clinical studies. Study participants were randomized 1:1:1 to receive either a placebo or 22.6g or 33.9g of AXA1125 twice daily.

At 24-weeks there were statistically significant improvements in the liver stiffness measurement (LSM) compared to placebo in the high dose arm for all subjects. Absolute changes in LSM were 0.13, -2.01, and -4.07 kilopascals (kPa) in the placebo, low dose and high dose arms, respectively (p= 0.0992 and 0.0096 for the low and high dose, respectively, compared to placebo). These results were supported by statistically significant improvements in other NITs of liver fibrosis: ELF and FIB-4. Statistically significant improvements in ALT were seen at both weeks 12 and 24 in all subjects (placebo-adjusted difference of -28.61% (p=0.0183) and -36.3% (p=0.0017) for the low and high doses, respectively). All subjects experienced significantly greater changes from baseline in MRI-PDFF at 12-weeks compared to the change from baseline in the placebo group (placebo adjusted difference of -18.98% (p=0.0082) and -21.24% (p=0.0014) for the low and high doses, respectively). Numerical trends of improvement relative to placebo in PDFF were seen at week 24 but these were not statistically significant in the small number of subjects. Overall, these positive results confirm AXA1125's multi-targeted impact, a differentiated approach to directly and simultaneously targeting multiple pathways that are dysregulated in NASH. Consistent with previous results, AXA1125 was found to be very safe and well-tolerated in this study. Both dose levels are active and will be continued. Consistent with prior clinical trials, T2DM showed results comparable to non-diabetics.

"We find the results from this 12- and 24-week interim analysis to be extremely encouraging," commented Axcella CEO Bill Hinshaw. "They indicate that administration of AXA1125 over 24-weeks leads to statistically significant improvements compared to placebo in biomarkers for metabolism, inflammation and fibrosis, underscoring its multi-targeted efficacy. Given AXA1125's market leading safety and tolerability profile, and its oral dosing, these findings position AXA1125 as an attractive candidate for first line treatment of NASH. We look forward to the continuation of the trial and gathering the data from the complete patient population. We expect to report the topline, 48-week biopsy results in the first half of 2024."

Dr. Margret Koziel, Chief Medical Officer of Axcella remarked that, "The positive change in liver stiffness at 24-weeks at both dose levels suggests that AXA1125 administration is correlated with improvement in fibrosis, which is the major histologic finding associated with liver disease mortality. This, in concert with effects on hepatic fat and inflammation, provides significant confidence in our ability to demonstrate improvements in liver histology at the end of this study." NASH expert, Dr. Stephen Harrison, added: "I find these results to be very promising. NASH is a complex condition that must be addressed by modulating multiple pathways. Axcella's multi-targeted approach is well-suited to playing an important role in addressing the challenges posed by the condition, and these preliminary results offer further support for this therapeutic strategy. Moreover, AXA1125 has a very favorable risk-benefit profile given its impact on disease activity and its high level of safety, creating an opportunity for a frontline treatment option in NASH."

Internet Posting of Information

Axcella uses the "Investors and News" section of its website, www.axcellatx.com, as a means of disclosing material nonpublic information, to communicate with investors and the public, and for complying with its disclosure obligations under Regulation FD. Such disclosures include, but may not be limited to, investor presentations and FAQs, Securities and Exchange Commission filings, press releases, and public conference calls and webcasts. The information that we post on our website could be deemed to be material information. As a result, we encourage investors, the media and others interested to review the information that we post there on a regular basis. The contents of our website shall not be deemed incorporated by reference in any filing under the Securities Act of 1933, as amended.

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 restore cellular homeostasis in multiple key biological pathways and improve cellular energetic efficiency. Axcella's pipeline includes lead therapeutic candidates in Phase 2 development for the treatment of Long COVID and 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, the potential for AXA1125 to serve as a first-line treatment option. 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 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 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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