Axcella Announces IND Clearance for AXA1665, Program Updates and 2021 Milestones

January 11, 2021

- *AXA1665 Phase 2 trial initiation planned for Q2*
- *AXA1125 Phase 2b trial initiation planned for Q2*
- *Company decides not to expand enrollment in AXA4010-001 following cohort 1 readout*
- *Pipeline expansion opportunities to be announced in 2021*

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Jan. 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 clearance of the company's first investigational new drug (IND) filing and provided an update on its product candidates, research and development activities and expected milestones for 2021.

"The year 2020 was a time of tremendous accomplishment for Axcella as we reported positive data for our lead candidates, AXA1665 and AXA1125, and prepared for their later stage clinical trials," said Bill Hinshaw, President and Chief Executive Officer of Axcella. "We are excited to begin 2021 by announcing the clearance of our first investigational new drug (IND) filing, which enables us to advance AXA1665 into Phase 2 with a wealth of clinical data just four years after this candidate was designed. This validates our accelerated, highly informed development approach, which enables us to de-risk candidates and maximize our resources. As we enter what we expect to be a momentous 2021, our attention is firmly focused on clinical trial execution for our lead candidates and the expansion of our EMM composition pipeline."

AXA1665 Program Update

Axcella announced today that its IND application has been cleared by the U.S. Food and Drug Administration (FDA) for AXA1665, the company's oral product candidate for the reduction in risk of recurrent overt hepatic encephalopathy (OHE). In the second quarter of 2021, Axcella plans to initiate a Phase 2 trial of AXA1665.

The Phase 2 trial will be a randomized, double-blind, placebo-controlled, multi-center study evaluating the efficacy and safety of AXA1665 in patients who have experienced at least one prior OHE event and have neurocognitive dysfunction at screening. Approximately 150 patients on either lactulose ± rifaximin (stratified by rifaximin use) will be enrolled and randomized 1:1 to receive either 53.8 grams per day of AXA1665 or a calorie-matched placebo in three divided doses for 24 weeks, with a two-week safety follow-up period.

The trial will be conducted globally with the primary endpoint assessing change in the psychometric hepatic encephalopathy score (PHES) after 24 weeks of treatment. Secondary endpoints will include the proportion of patients experiencing an OHE breakthrough event; time to first OHE breakthrough event, including time to hospitalization; changes in physical function; and patient-reported outcomes. Other endpoints include measures of circulating ammonia, amino acids, and inflammation-related markers.

"Over the course of the past few years, we have advanced AXA1665 from initial concept and design through two clinical studies enrolling more than 70 subjects with liver disease, demonstrating its multifactorial therapeutic potential," said Manu Chakravarthy, M.D., Ph.D., Chief Medical Officer of Axcella. "We are excited to now initiate a global Phase 2 clinical trial assessing AXA1665's efficacy in patients with OHE. Ultimately, our goal is to bring a new multi-targeted oral treatment option that improves upon today's standard of care for OHE patients and more comprehensively addresses their unmet needs."

In 2020, Axcella reported positive top-line data from AXA1665-002. In this clinical study, AXA1665 was observed to be well tolerated with a strong safety profile. Dose-dependent changes were noted across measures of amino acid metabolism and neurocognition over 12 weeks in subjects with mild and moderate hepatic insufficiency. These included statistically-significant ($p < 0.05$) improvements in the Fischer Ratio and the psychometric hepatic encephalopathy score (PHES) in the AXA1665 high dose arm vs. placebo. Additionally, clinically-relevant trends were seen in certain measures of nitrogen/ammonia handling and physical function in the AXA1665 arms versus placebo.

AXA1125 Program Update

Axcella completed a successful Type B pre-IND meeting with the FDA in late 2020 and is now working actively on its IND application for AXA1125, the company's oral product candidate for nonalcoholic steatohepatitis (NASH). Subject to FDA clearance, Axcella plans to proceed directly into a 48-week placebo-controlled Phase 2b paired biopsy clinical trial enrolling adult patients with biopsy-proven NASH, with the primary endpoint based on liver histology. This trial is expected to be initiated in the second quarter of 2021.

In 2020, Axcella reported positive top-line data from AXA1125-003. In this clinical study, AXA1125 was observed to be well tolerated with a strong safety profile in subjects with presumed NASH. Additionally, sustained reductions versus placebo over 16 weeks were noted in virtually all key biomarkers of metabolism, inflammation and fibrosis, including MRI-PDFF, HOMA-IR, ALT and ProC3. Among subjects with type 2 diabetes enrolled in the study, reductions in most biomarkers were even greater versus placebo. Based on AXA1125's multi-targeted design and these data, Axcella believes this candidate holds the potential to serve as a first-line NASH monotherapy for both adult and pediatric patients and may be used in combination with other agents if required.

AXA4010 Program Update

AXA4010 has been under investigation in an open label pilot clinical study, AXA4010-001. An initial cohort of nine subjects with sickle cell disease (SCD) was enrolled and received AXA4010 in two 26-gram doses per day for up to 12 weeks. This first cohort was intended to allow the company to a) efficiently assess this candidate's safety, tolerability and effects on blood structure and function, including red blood cell metabolism/hemolysis, inflammation and vascular function/adhesion, and b) decide whether to expand enrollment to additional cohorts.

Clinical data from this first cohort were recently received. Most of the reported adverse events, including all serious adverse events, were considered to be associated with underlying disease. Five subjects reported mild to moderate gastrointestinal events (diarrhea and nausea) that were considered to be possibly related to AXA4010. Biomarker data from this cohort suggest activity in targeted biologies, including generally positive trends in markers related to inflammation. Other markers related to hemolysis and vascular adhesion demonstrated greater variability. Based on the totality of the findings to date, Axcella has decided not to expand enrollment in the AXA4010-001 study.

R&D Update

Axcella sees the potential to develop a range of EMM compositions for a variety of diseases and conditions, including those related to metabolism, muscle atrophy, mitochondrial biology, neuroprotection, inflammation and immunology. The company has characterized approximately 75 potential therapeutic applications for EMMs and is now applying platform advances and program learnings to assess pipeline expansion opportunities.

Axcella plans to provide an update on its research and development activities and share details about opportunities it has identified for pipeline expansion later in 2021. As demonstrated with AXA1125 and AXA1665, the company sees the opportunity for rapid, efficient and highly informed clinical development for its future product candidates.

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 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 trials 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 AXA1665, AXA1125 and potential future EMM compositions, the potential for AXA1665 to reduce OHE events and improve the quality of life for cirrhotic patients, the potential for AXA1125 to serve as a first-line NASH monotherapy for both adult and pediatric patients and be used in combination with other agents if required, the design, status and timing of the company's planned Phase 2 clinical trial of AXA1665 and planned Phased 2b clinical trial of AXA1125, the timing and outcome of IND application submissions, the intended results of the company's strategy and approach and the company's ability to address other complex diseases and conditions 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 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 trials of AXA1665 and 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 initiation plans and timing, clinical trial design and target indications for AXA1665 and AXA1125, the clinical development and safety profile of AXA1665 and 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.

View source version on businesswire.com: https://www.businesswire.com/news/home/20210111005285/en/

Company Contact
Jason Fredette
jfredette@axcellahealth.com
(857) 320-2236

Source: Axcella