Axcella Reports Positive Top-Line Data from AXA1665-002 and Second Quarter Financial Results

August 5, 2020

- *Top-line data from AXA1665-002 show dose dependent improvements in markers of cognitive function and amino acid metabolism; both AXA1665 doses safe and well tolerated for 12 Weeks; plan to initiate Phase 2 clinical trial under IND in 1H 2021*
- *Reported positive top-line data for AXA1125, Axcella's NASH product candidate, with clinically relevant reductions in liver fat content, insulin resistance and fibroinflammation; plan to initiate Phase 2b clinical trial under IND in 1H 2021*
- *Completed follow-on equity offering, raising approximately $60 million in gross proceeds*
- *Company to hold conference call today at 8:30 a.m. ET*

CAMBRIDGE, Mass.--(BUSINESS WIRE)--Aug. 5, 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 reported positive top-line 12-week data from AXA1665-002, a placebo-controlled clinical study of AXA1665, and financial results for the second quarter ended June 30, 2020.

"The second quarter of 2020 was a time of significant accomplishment for Axcella," said Bill Hinshaw, President and Chief Executive Officer of Axcella. "This period was highlighted by positive top-line data from our AXA1125-003 clinical study, which served as another strong validator for our novel EMM platform. Preparations are now well underway for our engagement with the U.S. Food and Drug Administration (FDA) regarding our adult and pediatric NASH programs as we seek to finalize the design of our proposed Phase 2b clinical trial of AXA1125 and initiate enrollment in the first half of 2021. We are appreciative of the support from the investors that enabled us to bolster our balance sheet via a follow-on equity offering in May 2020."

"Today, we are pleased to share our AXA1665-002 top-line data that once again demonstrate safety, tolerability and activity across multiple biologies and, for the first time, show positive changes in neurocognitive measures. After additional data analyses and consultation with external medical experts, we plan to submit an IND and initiate a Phase 2 clinical trial of AXA1665 in patients with advanced liver disease. Ultimately, our goal is to provide a much-needed new treatment option for the many patients who have experienced an overt hepatic encephalopathy (OHE) event. We extend our sincere thanks to all of the subjects and investigators involved in AXA1665-002 for their participation in and commitment to this study, particularly in light of the ongoing global pandemic," Mr. Hinshaw concluded.

AXA1665-002 Top-Line Data

AXA1665-002 was a placebo-controlled, randomized clinical study that was designed to investigate the safety, tolerability and physiological impact of AXA1665, a proprietary composition of eight amino acids, in 60 subjects with mild (Child Pugh A) and moderate (Child Pugh B) hepatic insufficiency. Subjects in the study were randomized in a 2:2:1 ratio to receive either 29.4 g or 53.9 g of AXA1665 or a matched placebo in three divided doses per day for 12 weeks with a four-week follow up. In addition to safety and tolerability, the study evaluated plasma amino acid and ammonia levels as well as markers of neurocognition, muscle structure and function.

"We believe the data from the AXA1665-002 study show AXA1665's potential to address multiple fundamental dysregulations associated with cirrhosis and hepatic encephalopathy," said Manu Chakravarthy, M.D., Ph.D., Chief Medical Officer of Axcella. "This study replicated findings on amino acid metabolism from our previous short-term study, AXA1665-001, and we were pleased to see those effects sustained through 12 weeks. We also noted dose dependent, directionally consistent changes across all three psychometric tests that were utilized, which help to bolster our confidence in AXA1665's potential to reduce OHE events. We look forward to initiating a Phase 2 clinical trial to investigate this hypothesis and further evaluate this candidate's impact on measures of physical function and related patient reported outcomes in patients with advanced liver disease."

Key results from AXA1665-002 include:

- **Safety/Tolerability:** Both doses of AXA1665 were safe and well-tolerated. Rates of adverse events (AEs) were low, mostly unrelated to study product and generally mild or moderate. There were four serious adverse events reported in the study and two deaths (one due to complications of COVID-19; one due to a myocardial infarction during the study run-in period prior to dosing), none of which were determined to be related to AXA1665.

- **Neurocognitive Function:** Positive, dose dependent trends were observed in the AXA1665 arms across all three psychometric tests: Stroop EncephalApp, critical flicker frequency, and psychometric hepatic encephalopathy score (PHES). In PHES, a highly specific assessment to diagnose minimal hepatic encephalopathy (MHE), a statistically significant ($p < 0.05$) improvement of a clinically relevant magnitude was observed in the AXA1665 high dose arm vs. placebo. Additionally, the proportion of subjects achieving a clinically relevant threshold of PHES improvement was higher in the AXA1665 arms relative to placebo.

- **Amino Acid Metabolism:** A dose dependent and statistically significant ($p < 0.05$) percentage increase from baseline in

Fischer Ratio (FR; a measure of branched chain amino acids ÷ aromatic amino acids) was seen in the AXA1665 arms relative to placebo (low dose: 21%, high dose: 44%), which was sustained over 12 weeks. Observed changes in FR were accompanied by concomitant decreases in circulating aromatic amino acids (Phe and Tyr), which may suggest their incorporation into protein synthesis and an improved metabolic state. Published studies suggest that aromatic amino acids may contribute to impaired neurotransmission and have correlated lower FR with poor clinical outcomes in patients with cirrhosis and end-stage liver disease.

- **Ammonia Handling:** Despite the increased nitrogen load delivered via the amino acids in AXA1665, fasted plasma ammonia levels remained stable in the active arms over the 12-week dosing duration. In a subset of subjects with evidence of MHE at baseline as assessed by PHES, a mean reduction from baseline of approximately 7% in fasted plasma ammonia levels was observed in subjects receiving both doses of AXA1665 at week 12.

- **Muscle Structure and Function:** Key measures of muscle structure (e.g. lean mass) and function (e.g. gait speed, liver frailty index, or LFI) remained essentially stable in all groups from baseline to week 12. This observation may reflect the mild hepatic insufficiency and lack of overt sarcopenia in nearly all enrolled subjects at baseline. A higher proportion of subjects in the AXA1665 arms achieved a ≥0.3 absolute reduction in LFI (i.e. less frailty) versus placebo. Previous studies suggest that a ≥0.3 reduction in the LFI score may correlate with an improved ability to conduct activities of daily living in subjects with end-stage liver disease.

“Overt hepatic encephalopathy is a complex disease that involves dysregulation across multiple organ systems, including altered amino acids, elevated ammonia levels, dysregulated muscle metabolism, and cognitive dysfunction,” said Dr. Arun Sanyal, Professor of Medicine, Physiology and Molecular Pathology at Virginia Commonwealth University School of Medicine, and an investigator in AXA1665-002. “While previous approaches have focused on reducing ammonia load from the bowel alone, future approaches should incorporate the evolving knowledge of the role of other organs, such as muscle and the brain in the development of encephalopathy. I am encouraged by the multifactorial activity seen with AXA1665 in the 002 study and look forward to its continued investigation in a subsequent Phase 2 trial to evaluate AXA1665’s therapeutic potential to prevent OHE recurrence in advanced liver disease patients who are in dire need of new treatment options.”

Additional data will be discussed during the company’s conference call at 8:30 a.m. ET today and will be included in a presentation that will be posted to “Investors & News” section of Axcella’s website prior to the call. Details about how to access this conference call are included below.

Other Recent Developments

- **AXA1125 Top-Line Data:** Reported positive top-line data from AXA1125-003, a clinical study assessing the impact of AXA1125 and AXA1957 on safety, tolerability and physiology in subjects with non-alcoholic fatty liver disease (NAFLD). 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 both placebo and AXA1957, AXA1125 demonstrated larger and more consistent reductions in clinically relevant biomarkers, with a greater magnitude noted among subjects with type 2 diabetes.

- **AXA1665 Patents:** Announced the issuance of two key patents: U.S. Patent 10,682,325 and U.S. Patent 10,660,870. These are the first patents related to Axcella’s family of applications for AXA1665, the company’s product candidate for the reduction in risk of overt hepatic encephalopathy recurrence, covering both its composition and methods of use. These patents follow the issuance of composition and methods of use patents for Axcella’s other lead product candidate, AXA1125, in 2019.

- **Follow-On Stock Offering:** Axcella closed an underwritten public offering of an aggregate of 12,650,000 shares of its common stock, including the full exercise of the underwriters’ option to purchase additional shares. The gross proceeds of the offering, before deducting underwriting discounts and commissions and other estimated offering expenses payable by Axcella, were approximately $60.1 million.

- **Addition to Board of Directors:** The company also today announced that Chief Development Officer Shreeram Aradhye, M.D., will be stepping down from his full-time role to accept another opportunity and will be appointed to Axcella’s Board of Directors, effective on September 1, 2020. Dr. Aradhye has more than 20 years of pharmaceutical industry experience in clinical development and medical affairs, having previously served as Chief Medical Officer and Global Head, Medical Affairs for Novartis Pharmaceuticals. In previous roles at Novartis and Sandoz, he provided functional leadership for clinical development and medical affairs teams working on novel and biosimilar medicines across multiple indications, including multiple sclerosis, Alzheimer’s Disease, neuropathic pain, muscle disease and migraine.

- **Management Update:** Chief Medical Officer Manu Chakravarthy, M.D., Ph.D., has been promoted to Executive Vice President and will assume Dr. Aradhye’s day-to-day responsibilities. Additionally, Andrew Suchoff joined Axcella as Chief People Officer in June 2020. He is driving initiatives aimed at the company’s culture, talent, learning and development, employee engagement and compensation. Mr. Suchoff brings more than 20 years of human resources leadership experience to Axcella, having most recently served as Global Head of People Operations and Talent Development at Stallergenes Greer, a healthcare company with more than 1,200 employees and operations throughout the world.

Upcoming Planned Milestones

Liver Programs

- Q3 2020: Present AXA1125-003 data (late-breaker poster presentation) at The Digital International Liver Congress 2020 (EASL)
- 2H 2020: Engage with the FDA regarding the company's planned IND application for AXA1125, proposed Phase 2b clinical trial in adults and pediatric development program
- 1H 2021: Initiate a Phase 2b clinical trial of AXA1125 in adult NASH under an IND
- 1H 2021: Initiate a Phase 2 clinical trial of AXA1665 in patients with advanced liver disease (i.e. in cirrhotic subjects with at least one prior episode of OHE) under an IND

Blood Program

- Q4 2020: Report top-line data from Cohort 1 of AXA4010-001, a clinical study on safety, tolerability and blood physiology in subjects with sickle cell disease

Financial Results

R&D Expenses: Research and development expenses were $8.6 million and $9.3 million for the quarters ended June 30, 2020 and 2019, respectively. The change was primarily related to the completion of the company's AXA1125-003 clinical study.

G&A Expenses: General and administrative expenses were $4.6 million and $4.7 million for the quarters ended June 30, 2020 and 2019, respectively.

Net Loss: Net loss for the quarter ended June 30, 2020 was $13.9 million, or $0.48 per basic and diluted share. This compares with a net loss of $14.4 million, or $0.95 per basic and diluted share, for the quarter ended June 30, 2019.

Cash Position: Cash and cash equivalents at June 30, 2020 were $121.3 million, which compares with $92.1 million at December 31, 2019. The increase is primarily the result of net proceeds from the company's follow-on stock offering that was completed in May 2020.

Conference Call Reminder

Axcella will host a conference call today at 8:30 a.m. ET to discuss the top-line data from AXA1665-002 and other recent business updates. 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 section. 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 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 & 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 and the company's characterization of the results from its clinical studies and future clinical trials, including for AXA1125 and AXA1665, the design, status and timing of the company's ongoing clinical studies and planned IND-enabled clinical trials, the company's anticipated program milestones, including the timing of data readout from Cohort 1 of AXA4010-001, the subject and timing of the company's planned interactions with the

FDA on the AXA1665 and AXA1125 programs, including the potential timing of IND application submissions, the potential of the company's product candidates to impact health and/or disease, including AXA1125's potential in NASH and AXA1665 potential in OHE, and the importance of any intellectual rights granted to the company. 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 and planned interactions and submissions to FDA or other regulatory authorities 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 in our ongoing AXA4010-001 clinical study and potential delays in disclosure of the same, 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 IND submission and clinical trial initiation plans and timing, clinical trial design and target indications for AXA1125 and AXA1665, 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 in clinical studies or IND-enabled clinical trials, 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.

Axcella Health Inc.
Unaudited Condensed Consolidated Balance Sheets
(in thousands)

	June 30, 2020	December 31, 2019
Assets:		
Cash and cash equivalents	$121,326	$ 92,053
Other assets	3,222	2,306
Total assets	$124,548	$ 94,359
Liabilities and stockholders' equity:		
Liabilities	$ 31,585	$ 34,135
Stockholders' equity	92,963	60,224
Total liabilities and stockholders' equity	$124,548	$ 94,359

Axcella Health Inc.
Unaudited Condensed Consolidated Statements of Operations and Comprehensive Loss
(in thousands, except share and per share data)

	Three Months Ended June 30,		Six Months Ended June 30,	
	2020	2019	2020	2019
Operating expenses:				
Research and development	$ 8,565	$ 9,343	$ 18,900	$ 16,906
General and administrative	4,619	4,728	8,744	8,196
Total operating expenses	13,184	14,071	27,644	25,102
Loss from operations	(13,184)	(14,071)	(27,644)	(25,102)
Other income (expense), net	(708)	(376)	(1,257)	(918)
Net loss and comprehensive loss	$ (13,892)	$ (14,447)	$ (28,901)	$ (26,020)
Net loss per share, basic and diluted	$ (0.48)	$ (0.95)	$ (1.10)	$ (2.60)
Weighted average common shares outstanding, basic and diluted	29,202,367	15,230,815	26,195,591	10,032,202

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