October 15, 2021

Cabaletta Bio Announces Presentation of Preclinical Data Supporting PLA2R-CAART as a Potential Precision Therapy for Antigen-Specific B Cell Depletion in PLA2R Membranous Nephropathy at ASN Kidney Week 2021

– Chimeric AutoAntibody Receptor (CAAR) T cells specifically recognized and eliminated anti-PLA2R antibody-expressing B cells in vitro –

– Membrane proteome arrays screened with PLA2R CAAR candidates did not identify off-target interactions –

– Pre-IND interaction with the Food and Drug Administration (FDA) is planned for later this year for PLA2R-CAART preclinical candidate –

PHILADELPHIA, Oct. 15, 2021 (GLOBE NEWSWIRE) -- Cabaletta Bio, Inc. (Nasdaq: CABA), a clinical-stage biotechnology company focused on the discovery and development of engineered T cell therapies for patients with B cell-mediated autoimmune diseases, today announced that data from *in vitro* studies supporting the early preclinical validation of PLA2R-Chimeric AutoAntibody Receptor T (CAART) cell candidates will be presented at ASN Kidney Week 2021. The data will be presented as an oral abstract by Aimee Payne, M.D., Ph.D., Professor of Dermatology at the University of Pennsylvania's Perelman School of Medicine and co-chair of the Scientific Advisory Board and co-founder at Cabaletta Bio at the American Society of Nephrology (ASN) Kidney Week 2021 being held virtually from November 4-7, 2021.

"Current therapeutic strategies for PLA2R membranous nephropathy patients include generalized immune suppression, including B cell depletion with rituximab, which often requires repeat treatments and may cause serious infections in certain patients. Building on the platform for CAART product candidates that are more advanced in development, including DSG3-CAART and MuSK-CAART, we aim to develop a highly specific therapy that provides safety, efficacy, and durability for patients suffering from this autoimmune disease," said Dr. Payne "This initial preclinical data is promising, as it demonstrates the *in vitro* function of PLA2R-CAART cells against autoantibody-binding epitopes relevant to pathogenic B cells from patients with primary membranous nephropathy, with no evidence of off-target interactions."

For this study, the Payne Laboratory generated multiple CAARs comprised of the PLA2R epitopes targeted by autoantibodies in PLA2R membranous nephropathy patients, as an extracellular decoy on the surface of T cells. These CAARs were observed to direct specific

cytolysis of B cells expressing each of the anti-PLA2R autoantibodies tested. The data suggest that PLA2R-CAAR T cell therapy has the potential to target pathogenic B cells expressing autoantibodies against PLA2R while sparing healthy B cells, which could provide a novel precision therapeutic approach for patients with PLA2R membranous nephropathy. Membrane proteome arrays screened against leading PLA2R CAAR candidates did not identify any off-target interactions.

“These discovery and early preclinical studies conducted by our co-founder Dr. Aimee Payne and colleagues at the University of Pennsylvania are a meaningful step for Cabaletta Bio, as they further support the breadth of the CABA™ platform for patients with B cell-mediated autoimmune diseases and high unmet clinical need,” said Gwendolyn Binder, Ph.D., EVP Science and Technology at Cabaletta Bio. “These data provide the scientific rationale to commit our lead PLA2R-CAART candidate to preclinical development for patients with PLA2R membranous nephropathy.”

Oral Abstract Presentation Details	
Title	Chimeric autoantibody receptor (CAAR) T cells as a precision therapy for antigen-specific B cell depletion in PLA2R membranous nephropathy
Abstract Number	FR-OR32
Session	Glomerular Diseases: Antibodies, Complement, and Inflammatory Mediators
Session Date/Time	Fri, Nov 5, 4:30 PM - 6:00 PM PDT
Format	Pre-recorded, virtual with live Q&A after presentation

PLA2R-CAART is one of seven CAAR T programs that have emerged from the Cabaletta Approach to selective B cell Ablation (CABA™) platform. Cabaletta’s lead product candidate, DSG3-CAART, is currently being evaluated in the DesCAARTes™ Phase 1 clinical trial as a potential treatment for patients with mucosal pemphigus vulgaris (mPV). The lead preclinical product candidate, MuSK-CAART, is designed as a potential treatment for patients with MuSK-associated myasthenia gravis, with an IND submission planned by the end of 2021. Cabaletta has four additional discovery programs derived from the CABA™ platform.

About Membranous Nephropathy
Primary membranous nephropathy (MN) is a B cell-mediated autoimmune disease that affects the kidneys. Approximately 70-80% of the 15,000 primary MN patients in the U.S. have autoantibodies directed to the phospholipase A2 receptor (PLA2R) on kidney podocytes. Since the discovery of these anti-PLA2R autoantibodies in 2009, evidence has shown that these autoantibodies accumulate as immune deposits in the glomeruli of the kidney and damage the filtration barrier, leading to nephrotic syndrome as characterized by proteinuria as well as risk for progression to kidney failure and dialysis and potential need for transplant. Immunosuppressive therapies are commonly used, but high unmet need remains as a significant fraction of patients either relapse or fail to respond or experience risk of serious infection following treatment with immunosuppressive agents.

About CAAR T Cell Therapy
Chimeric AutoAntibody Receptor (CAAR) T cells are designed to selectively bind and eliminate only disease-causing B cells, while sparing the normal B cells that are essential for human health. CAAR T cells are based on the chimeric antigen receptor (CAR) T cell

technology. While CAR T cells typically contain a CD19-targeting molecule, CAAR T cells express an autoantibody-targeted antigen on their surface. The co-stimulatory domain and the signaling domain of both a CAR T cell and a CAAR T cell carry out the same activation and cytotoxic functions. Thus, Cabaletta's CAARs are designed to direct the patient's T cells to kill only the pathogenic cells that express disease-causing autoantibodies on their surface, potentially leading to complete and durable remission of disease while sparing all other B cell populations that provide beneficial immunity from infection.

About Cabaletta Bio
Cabaletta Bio is a clinical-stage biotechnology company focused on the discovery and development of engineered T cell therapies, and exploring their potential to provide a deep and durable, perhaps curative, treatment, for patients with B cell-mediated autoimmune diseases. The Cabaletta Approach to selective B cell Ablation (CABA™) platform, in combination with Cabaletta's proprietary technology, utilizes CAAR T cells that are designed to selectively bind and eliminate only specific autoantibody-producing B cells while sparing normal antibody-producing B cells, which are essential for human health. The Company's lead product candidate, DSG3-CAART, is being evaluated in the DesCAARTes™ phase 1 clinical trial as a potential treatment for patients with mucosal pemphigus vulgaris, a prototypical B cell-mediated autoimmune disease. The FDA granted Fast Track Designation for DSG3-CAART in May 2020. For more information about the DesCAARTes™ Phase 1 clinical trial, please visit our website (DesCAARTes™ Phase 1 Trial). The Company's lead preclinical product candidate, MuSK-CAART, is in IND-enabling studies and is designed as a potential treatment for patients with MuSK-associated myasthenia gravis. For more information, visit www.cabalettabio.com.

University of Pennsylvania Financial Disclosure
Dr. Payne is a Penn faculty member, scientific collaborator, key advisor, and co-founder of Cabaletta Bio. As such, she holds an equity stake in the Company, her laboratory at Penn receives sponsored research funding from Cabaletta Bio, and as an inventor of the licensed technology she may receive additional future financial benefits under licenses granted by Penn to Cabaletta Bio. The University of Pennsylvania may also receive future financial benefit under licenses it has granted to Cabaletta Bio.

Forward-Looking Statements
This press release contains "forward-looking statements" of Cabaletta Bio within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including without limitation, express or implied statements regarding expectations regarding the progress and results of its DesCAARTes™ Phase 1 trial, including Cabaletta Bio's ability to enroll the requisite number of patients; the expectations regarding the preliminary results from *in vitro* data in anti-PLA2R antibody-expressing B cells; the timing of Cabaletta's planned initiation of investigational new drug (IND) enabling studies for MuSK-CAART; the effectiveness and timing of additional product candidates and discovery programs that Cabaletta may develop from the CABA™ platform, including in collaboration with academic partners; the safety, efficacy and tolerability of DSG3-CAART for the treatment of mPV, MuSK-CAART for the treatment of MuSK-associated myasthenia gravis, and PLA2R-CAART for the treatment of PLA2R membranous nephropathy; the impact of preclinical data on the future development of CAAR T therapies in Cabaletta's pipeline portfolio; expectations of the potential impact of COVID-19 on strategy, future operations, and the timing of Cabaletta's clinical trials, including the potential impacts on its DesCAARTes™ Phase 1 trial; and

statements regarding regulatory filings regarding its development programs.

Any forward-looking statements in this press release are based on management's current expectations and beliefs of future events, and are subject to a number of risks and uncertainties that could cause actual results to differ materially and adversely from those set forth in or implied by such forward-looking statements. These risks and uncertainties include, but are not limited to: Cabaletta Bio's ability to demonstrate sufficient evidence of safety, efficacy and tolerability in its preclinical and clinical trials of DSG3-CAART, MuSK-CAART and PLA2R-CAART; risks related to clinical trial site activation or enrollment rates that are lower than expected; risks related to unexpected safety or efficacy data observed during clinical studies; risks related to our planned regulatory submissions and developments; risks related to the impact of public health epidemics affecting countries or regions in which we have operations or do business, such as COVID-19; risks related to Cabaletta's ability to protect and maintain its intellectual property position; uncertainties related to the initiation and conduct of studies and other development requirements for its product candidates; and the risk that the results of preclinical studies or clinical studies will not be predictive of future results in connection with future studies. For a discussion of these and other risks and uncertainties, and other important factors, any of which could cause Cabaletta's actual results to differ from those contained in the forward-looking statements, see the section entitled "Risk Factors" in Cabaletta's most recent annual report on Form 10-K as well as discussions of potential risks, uncertainties, and other important factors in Cabaletta's other filings with the Securities and Exchange Commission. All information in this press release is as of the date of the release, and Cabaletta undertakes no duty to update this information unless required by law.

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