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Cabaletta Bio®

Cabaletta Bio Announces Publication of Comprehensive Preclinical Study Results for DSG3-CAART in Pemphigus Vulgaris

- *DSG3-CAART achieved autoantibody elimination and resolution of blisters in active immune mouse model of pemphigus vulgaris*
- *Soluble autoantibodies demonstrated potential to enhance DSG3-CAART efficacy and did not demonstrate off-target toxicity*
- *DesCAARTes™ Phase 1 clinical trial actively recruiting patients*

PHILADELPHIA, Aug. 25, 2020 (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 comprehensive preclinical study results evaluating DSG3-CAART (Desmoglein 3 chimeric autoantibody receptor T cells), its lead product candidate for patients with mucosal pemphigus vulgaris (mPV), were published in *The Journal of Clinical Investigation*. The manuscript, titled “Antigen-specific B-cell depletion for precision therapy of mucosal pemphigus vulgaris,” includes the preclinical data that enabled the DSG3-CAART IND submission and opening of the DesCAARTes™ clinical trial. The paper can be accessed online at: https://www.jci.org/articles/view/138416/pdf.

The preclinical studies, conducted at the Perelman School of Medicine at the University of Pennsylvania and led by the laboratory of Aimee Payne, MD, PhD, assessed the potential toxicity and specific target engagement of DSG3-CAART in inducing antigen-specific B cell depletion. *In vitro* results of DSG3-CAART demonstrated specific killing of anti-DSG3 B cell receptor (BCR) expressing cell lines, as well as killing of desmoglein 3 (DSG3) specific B cells from patients with pemphigus vulgaris (PV) while sparing normal B cells. No off-target cytotoxic interactions were detected, and no DSG3-CAART activity against known binding partners to DSG3 was detected. Together the data demonstrate specific anti-DSG3 BCR killing along with a lack of on-target and off-target toxicity for DSG3-CAART.

In vivo studies included use of an active immune PV model, characterized by a PV clinical phenotype, including skin blistering and physiologic anti-DSG3 IgG levels. In these mice, DSG3-CAART reduced serum levels of pathogenic anti-DSG3 antibodies, as well as tissue bound antibodies in the epithelium, a hallmark of PV disease. Clinical and histologic resolution of blisters was observed in DSG3-CAART treated animals.

The potential impact of anti-DSG3 antibodies on DSG3-CAART toxicity and target engagement was also evaluated. The researchers studied whether anti-DSG3 antibodies could serve as a “cytotoxic bridge” enabling DSG3-CAART to kill cells which express antibody receptors on their surface, and no such cross reactivity was detected. Building on prior evidence that DSG3-CAART function is not meaningfully inhibited by anti-DSG3 antibodies, and that proliferation of DSG3-CAART in response to polyclonal PV serum IgG is observed (as previously reported in the 2016 publication in *Science*), the recently published

studies demonstrated functional activation of DSG3 CAAR T cells in response to anti-DSG3 antibodies. This may improve the potential efficacy of DSG3-CAART in targeting rare B cells. The potential risk for CRS or other inflammatory responses resulting from DSG3-CAART interaction with soluble anti-DSG3 autoantibodies post-infusion is being mitigated in the DesCAARTes™ Phase 1 trial design through a conservative fractionated-dose approach where increasing fractions of the target dose are infused, enabling for safety monitoring between infusions while preserving the opportunity for the patient to receive a full dose.

“We believe these comprehensive preclinical data for DSG3-CAART, published in The Journal of Clinical Investigation, support our approach to develop a durable, potentially curative, treatment for patients with mucosal pemphigus vulgaris,” said Steven Nichtberger, M.D., Chief Executive Officer and co-founder of Cabaletta. “CAAR T cells represent a precision therapy approach designed to eliminate the underlying cause of B cell-mediated autoimmune diseases. The data also inform development of the multiple additional CAAR T therapies for B cell-mediated diseases that are in our pipeline.”

The safety and tolerability of DSG3-CAART in targeting pathogenic B cells in patients with mPV is currently being evaluated in the DesCAARTes™ clinical trial, which recently started recruiting. The FDA granted Fast Track Designation to DSG3-CAART in May 2020.

About Pemphigus Vulgaris
PV is a rare autoimmune blistering disease that is characterized by the loss of adhesion between cells of the skin or mucous membranes. PV is caused by the production of autoantibodies that disrupt structural proteins within the skin and/or mucosa that connect with other proteins to enable the skin and/or mucosal cells to connect with each other. The autoantibodies can target DSG3 and/or desmoglein 1 (DSG1), which are primarily expressed in the mucosal membranes and skin, respectively. mPV is characterized by autoantibodies against DSG3 only whereas mucocutaneous PV is characterized by autoantibodies against DSG3 and DSG1.

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 Bio’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 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 Chimeric AutoAntibody Receptor (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 see www.clinicaltrials.gov. 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.

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 the safety, effectiveness and timing of product candidates that Cabaletta Bio may develop, including in collaboration with academic partners; the safety, efficacy and tolerability of DSG3-CAART for the treatment of mPV; the impact of preclinical data on the future development of CAAR T therapies in our pipeline portfolio; expectations regarding the intended incentives conferred by Fast Track Designation for DSG3-CAART for the treatment of mPV; expectations of the potential impact of COVID-19 on strategy, future operations, and the timing of its clinical trials, including the potential impacts on enrollment and initiation of 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; 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; Cabaletta's ability to retain and recognize the intended incentives conferred by Fast Track Designation for DSG3-CAART for the treatment of PV; 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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