December 14, 2021

# Cabaletta Bio Reports Top-line Biologic Activity Data from Two Lowest Dose Cohorts in DesCAARTes™ Trial in Patients with Mucosal Pemphigus Vulgaris

PHILADELPHIA, Dec. 14, 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 reported top-line data on biologic activity from the two lowest dose cohorts in the DesCAARTes™ Phase 1 clinical trial of DSG3-CAART for the treatment of patients with mucosal Pemphigus Vulgaris (mPV).

As of December 12, 2021, six patients, comprising the two lowest dose cohorts (20 million and 100 million DSG3-CAART cells administered without lymphodepletion) had completed three to six months of follow-up for evaluation of DSG3-CAART biologic activity. Patients enrolled had persistent mild to moderate disease severity prior to infusion despite receiving or having received systemic medication for treatment of their mPV symptoms prior to enrollment. Parameters being used in the trial to evaluate potential biologic activity include persistence of DSG3-CAART, change in level of DSG3 autoantibodies, change in mPV therapy or need for new systemic rescue therapy, and change in disease activity (e.g., as assessed by Pemphigus Disease Area Index (PDAI) and Oral Disease Severity Score (ODSS)). Prior to infusion, disease activity scores improved in five of six participants in the absence of any protocol directed additions to baseline therapy. Of those five participants, one had a decline in DSG3 autoantibody levels ≥20% during that period. Top-line data on biologic activity among the first six participants in the lowest dose cohorts are:

- *In cohort A1, participants received 20 million DSG3-CAART cells:*
    - *Two of three participants had DSG3 autoantibody levels that rose ≥20% along with disease activity scores (e.g., PDAI and ODSS) that worsened within six months after DSG3-CAART infusion, with one of these participants receiving additional systemic medication. Both participants reduced or discontinued selected systemic therapies prior to DSG3-CAART infusion, as required by the protocol.*
    - *One of three participants had modest DSG3 autoantibody levels and mild disease activity at infusion and had a negative DSG3 level at six months along with disease activity scores of zero on both scales at six months with no systemic medications for mPV since DSG3-CAART infusion. As permitted by protocol, this participant was enrolled due to worsening symptoms despite receiving two different systemic therapies within 9 months of DSG3-CAART infusion. The systemic therapies may have impacted clinical scores and DSG3 levels, both of which improved between screening and infusion.*

- *In cohort A2, participants received 100 million DSG3-CAART cells:*
    - *Two of three participants maintained stable DSG3 autoantibody levels that have not persistently changed +/- 20% of pre-infusion levels through four months. Through the six month follow-up period, one of these patients maintained stable disease activity scores, while the other patient maintained stable scores initially before subsequently worsening. Both patients did not require any new systemic medications post-infusion through the entire follow-up period.*
    - *One of three participants had DSG3 autoantibody levels that rose ≥20% from pre-infusion levels despite stable disease activity scores with four months of follow-up. This participant subsequently received systemic medication to improve disease activity after DSG3-CAART infusion.*
- *DSG3-CAART persistence was not observed above the assay's threshold for quantification in any participant from the first two cohorts at three months post-infusion.*

Additional data on the initial cohorts in the DesCAARTes™ trial are anticipated to be presented at medical meetings and/or scientific sessions in 2022.

"As the first targeted cell therapy clinical trial for patients with a B cell-mediated autoimmune disease, the DesCAARTes™ trial was designed with patient safety as the top priority. By starting with these low-dose cohorts, we have been able to administer the product to autoimmune patients, with no dose-limiting toxicities or clinically relevant adverse events observed to date," reported David J. Chang, M.D., Chief Medical Officer of Cabaletta. "While clear signs of DSG3-CAART biologic activity were not observed to date in the two lowest cell dose cohorts, the emerging clinical and serological data in one of the six patients who has improved since DSG3-CAART infusion is notable. Patients in the fourth dosing cohort are currently being dosed with 2.5 billion cells, which is 25 and 125 fold greater than the two dose cohorts reported today. Based on communications with the U.S. Food and Drug Administration (FDA) dating to the first half of 2021, as well as the safety data reported from our first three dosing cohorts, we plan to expand the DesCAARTes™ trial to evaluate higher dose cohorts and consolidated dosing regimens and, subject to an IND amendment, an enhanced manufacturing process. Our engagements and interactions with patients, investigators, and advocacy groups have given us confidence that patients with mPV are highly interested in a deep, durable, and potentially curative therapy, and we look forward to advancing the trial to potentially identify an optimal dose regimen that maximizes the opportunity for patients to achieve those goals, while maintaining a favorable safety profile."

The first additional cohort in the dose escalation phase of the DesCAARTes™ trial is anticipated to be the A5 cohort, in which patients will receive between 5.0-7.5 billion DSG3-CAART cells with a consolidated fractionated infusion regimen including only two fractions – 30% followed by 70%. The planned enhanced manufacturing process aims to amplify the already present cell subtypes in the product in order to potentially improve product potency and trafficking to tissue where the target B cells reside.

"Based on the reported safety data from the first three cohorts, the observation of dose-dependent increases in persistence previously reported in Cohort A3 relative to the first two cohorts, and consultation with investigators, advisors, and the FDA, we now have the

opportunity to expand the trial to evaluate higher dose cohorts, consolidated dosing and, subject to an IND amendment, an enhanced manufacturing process," said Steven Nichtberger, M.D., Chief Executive Officer and Co-founder of Cabaletta. "With six sites activated and dosing underway in the fourth cohort at a dose of 2.5 billion DSG3-CAART cells, we anticipate reporting top-line biologic activity from the 500 million cell cohort A3 as well as 28-day safety data from the 2.5 billion cell cohort in the first quarter of 2022."

**About the DesCAARTes™ Clinical Trial**
Cabaletta's DesCAARTes™ Phase 1 trial is an open-label, multi-center study of DSG3-CAART in adults with mucosal-dominant pemphigus vulgaris (mPV). The trial is designed to evaluate the safety and tolerability of DSG3-CAART as well as to identify evidence of target engagement and early signs of efficacy. The study consists of three parts: 1) dose escalation to determine the maximum tolerated dose, 2) dose consolidation, and 3) cohort expansion at the final selected dose and schedule. The trial is expected to enroll approximately 33 patients across multiple clinical sites throughout the United States. Visit our website (DesCAARTes™ Phase 1 Trial) for more information.

**About Pemphigus Vulgaris**
mPV is a rare autoimmune blistering disease that is characterized by the loss of adhesion between cells of the skin or mucous membranes. mPV 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 (mcPV) 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'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 U.S. Food and Drug Administration (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.

**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, dose each dosing cohort in the intended manner and advance the trial as planned; the expected timing and significance around the announcement of top-line biologic activity from the 500 million cell cohort and 28-day safety for the fourth dose cohort in the first quarter of 2022; the expectation that Cabaletta Bio may improve outcomes for patients suffering from mPV; the effectiveness and timing of product candidates that Cabaletta 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 Cabaletta's pipeline portfolio; presentation of additional data at upcoming scientific conferences, and other preclinical data; the impact of COVID-19 on the timing, progress, interpretability of data, and results of ongoing or planned preclinical and clinical trials; and planned regulatory filings for Cabaletta's 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: the risk that signs of biologic activity may not inform long-term results; 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 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 the impact of public health epidemics affecting countries or regions in which Cabaletta has operations or does business, such as COVID-19; Cabaletta's ability to retain and recognize the intended incentives conferred by Orphan Drug Designation and Fast Track Designation for DSG3-CAART for the treatment of pemphigus vulgaris; 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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Source: Cabaletta Bio