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Cabaletta Bio®

# Cabaletta Bio Emerges Out of University of Pennsylvania to Develop CAAR T Cell Technology to Treat B Cell-mediated Autoimmune Diseases

*-- Signs exclusive license agreement and multi-year sponsored research agreementswith University of Pennsylvania*

*-- Completes $38 million Series A financing to advance lead asset, DSG3-CAART for mucosal pemphigus vulgaris, into clinical development*

RADNOR, Pa., Nov. 08, 2018 (GLOBE NEWSWIRE) -- Cabaletta Bio Inc., a biopharmaceutical company focused on the discovery and development of cellular therapies for B cell-mediated autoimmune diseases, has signed an exclusive license agreement and executed two multi-year sponsored research agreements with the University of Pennsylvania (Penn) for the discovery and development of engineered T cell therapy products for B cell-mediated autoimmune disease. The engineered T cell technology utilizes chimeric autoantibody receptors (CAARs) to bind and destroy only disease-causing B cells, while sparing the normal B cells which are essential for human health. In addition, the Company has entered into a master services agreement with Penn that will allow it to enter into agreements for scientific, clinical and manufacturing expertise to develop a first CAAR product for mucosal pemphigus vulgaris (mPV) based on compelling proof-of-concept data published in *Science* by the Penn research team. The Company's lead product is designed to selectively eradicate B cells that produce autoantibodies to desmoglein 3 (DSG3), which are necessary to cause mPV. The Company recently completed a $38 million Series A financing to advance this lead asset, DSG3-CAART, into clinical development.

"During the past 18 months, Cabaletta has advanced a series of CAAR T cell therapy products, licensed foundational intellectual property and assembled leading scientists, clinicians and experts in the discovery, development, manufacturing and regulatory approval of cell therapy products to accelerate development of highly specific CAAR T cell therapies that may offer a potential one-time cure for certain B cell-mediated autoimmune diseases," said Steven Nichtberger, M.D., co-founder, CEO and Chairman of Cabaletta Bio. "CAAR T cells are engineered T cells that build on the revolutionary chimeric antigen receptor (CAR) T cell technology developed at Penn, which is FDA approved for the treatment of certain B cell-mediated cancers. We believe the success of CAR T in B cell-mediated cancers reduces the risk profile of our CAAR T programs in B cell-mediated autoimmune diseases where chronic and broadly immunosuppressive therapies are typically used despite transient efficacy and significant adverse effects."

Cabaletta's foundational platform and lead asset are based on early work conducted at Penn by Michael Milone, M.D., Ph.D., and Aimee Payne, M.D., Ph.D., both of whom are co-founders of the Company.

Dr. Milone, Associate Professor of Pathology and Laboratory Medicine and member of the Center for Cellular Immunotherapy since inception at Penn, is a co-inventor of CTL019 (tisgenlecleucel, Kymriah®, Novartis), the first chimeric antigen receptor (CAR)-based T cell therapy to reach regulatory approval in the U.S. and Europe, as well as several new CAR T cell therapies for multiple myeloma and solid tumors that are currently in early phase clinical trials. Dr. Milone spent more than 15 years developing genetically-engineered T cell therapies including a post-doctoral fellowship with Dr. Carl June from 2004-2007. He now leads a team of translational researchers in the development of novel genetically engineered T cells for adoptive T cell immunotherapy.

“The work that we at Penn, and investigators at other organizations, have completed has clinically proven the value of CAR T therapies to treat other serious malignant diseases,” said Dr. Milone. “Through continued work at our institution, we have shown that this core platform can be slightly modified and directed toward B cell-mediated autoimmune diseases. Cabaletta was founded with the objective of expediting this important work and finding new and better solutions for patients who suffer from these debilitating diseases.”

Dr. Payne, the Albert M. Kligman Associate Professor of Dermatology and lead physician in the Autoimmune Blistering Clinic at Penn, is focused on understanding how autoimmunity occurs in pemphigus, the skin blistering B cell-mediated autoimmune disease that is the target of Cabaletta’s lead asset, DSG3-CAART, and developing novel targeted therapies for disease. Dr. Payne’s laboratory pioneered the CAAR T cell therapy concept for targeted depletion of autoreactive B cells and conducted the preclinical proof-of-concept work that demonstrated that DSG3 CAAR T cells could robustly control the disease in an animal model, which was published in *Science* (353: 179-184, 2016).

“Mucosal pemphigus vulgaris is a rare autoimmune disease that causes painful blisters on mucous membranes and increases risk of serious infections,” said Dr. Payne. “Current treatments, primarily immunosuppressants, are reasonably effective but can have very serious side effects. The highly targeted nature of CAAR T cells suggests that pathogenic B cells could be eliminated without impacting normal B cell function, a potentially ideal combination of efficacy and safety. We look forward to moving this program into the clinic in the near-term.”

Initial clinical trial activities for DSG3-CAART will be conducted with collaborators at Penn who have supported more than two dozen first-in-human clinical studies with novel cell and gene therapies. Manufacturing of DSG3-CAART for the trial is expected to be completed by the same organization at Penn that has manufactured cell therapy products for patients across two dozen cell and gene therapy protocols over the past decade.

In October 2018, Cabaletta completed its $38 million Series A financing led by 5AM Ventures, with participation from the founding investors Adage Capital Management, a second large U.S.-based, healthcare-focused investment fund and the University of Pennsylvania. The capital obtained from these financings will support preclinical and initial clinical activities for DSG3-CAART.

*Editor’s Note: Drs. Milone, Payne, and Nichtberger are all Penn faculty members and hold equity stakes in the Company, and the University of Pennsylvania is an equity holder and investor in the Company. In addition, both Penn and the inventors of the licensed technology may receive additional financial benefits under the license in the future.*

**About CAAR T Cell Therapy**
Chimeric autoantigen receptor (CAAR) T cells bind and destroy only disease-causing B cells, while sparing the normal B cells which are essential for human health. CAAR T cells are based on the revolutionary chimeric antigen receptor (CAR) T cell technology developed at the University of Pennsylvania that resulted in the first FDA-approved CAR T cell therapy. Rather than a CD19-targeting molecule, CAAR T cells express the autoantibody-targeted antigen on their surface. The 4-1BB co-stimulatory domain and the CD3-zeta signaling domain carry out the same activation and cytotoxic functions as in the CAR T setting. Thus, Cabaletta's CAARs direct the patient's T cells to kill only the self-reactive B cell population, potentially leading to complete and durable remission of disease while sparing all other B cell populations that provide beneficial immunity from infection.

**About Mucosal Pemphigus Vulgaris (mPV)**
Pemphigus vulgaris, an orphan disease, is a potentially fatal, chronic autoimmune disease characterized by the loss of adhesion between cells of the skin and mucous membranes. Pemphigus vulgaris is caused by specific pathogenic autoantibodies that target desmosomes, the major intercellular adhesion structures in the epidermis. Pemphigus vulgaris (PV) has two major clinical forms – mucosal PV (mPV), caused only by autoantibodies to the cell adhesion protein desmoglein (DSG) 3, and mucocutaneous PV (mcPV), caused by antibodies to DSG3 and DSG1. mPV comprises approximately 25% of the PV population and is characterized by painful blisters of the mucous membranes, including the mouth, nose, larynx, esophagus, eyes, genitals and other orifices. Mucocutaneous PV affects the other 75% of PV patients and has the additional involvement of skin blistering.

**About Cabaletta Bio**
Cabaletta Bio is a biopharmaceutical company focused on the discovery and development of cellular therapies for B cell-mediated autoimmune diseases. Cabaletta's therapeutic platform produces highly selective autologous chimeric autoantibody receptor (CAAR) T cells that bind and destroy only disease-causing B cells, while sparing healthy B cells which are essential for human health. Cabaletta has signed an exclusive licensing agreement and partnership with Penn focused on treating B cell-mediated autoimmune diseases with CAAR T cells. Cabaletta was founded by Dr. Michael Milone, Dr. Aimee Payne and Dr. Steven Nichtberger. Dr. Milone and Dr. Payne are physician/scientists at Penn and also serve as co-chairs of Cabaletta's Scientific Advisory Board. The Company's lead therapeutic program is a potential treatment for a prototypical B cell-mediated autoimmune disease, mucosal pemphigus vulgaris (mPV). mPV is a rare skin disorder that causes painful blisters and sores on mucous membranes such as the mouth, nose, throat, and genitals, leading to severe and sometimes debilitating and life-altering effects. For more information, visit www.cabalettabio.com.

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