UNITED STATES
SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 8-K

CURRENT REPORT
Pursuant to Section 13 or 15(d)
of The Securities Exchange Act of 1934

May 2, 2023
Date of Report (Date of earliest event reported)

CABALETTA BIO, INC.
(Exact name of Registrant as Specified in its Charter)

Delaware	**001-39103**	**82-1685768**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

2929 Arch Street, Suite 600, Philadelphia, PA	**19104**
(Address of principal executive offices)	**(Zip Code)**

(267) 759-3100
(Registrant's telephone number, including area code)

Not Applicable
(Former name or former address, if changed since last report)

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

☐ Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)

☐ Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)

☐ Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))

☐ Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))

Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	**Trading Symbol(s)**	**Name of Each Exchange on Which Registered**
Common Stock, par value $0.00001 per share	CABA	The Nasdaq Global Select Market

Indicate by check mark whether the registrant is an emerging growth company as defined in Rule 405 of the Securities Act of 1933 (§230.405 of this chapter) or Rule 12b-2 of the Securities Exchange Act of 1934 (§240.12b-2 of this chapter).

Emerging growth company ☒

If an emerging growth company, indicate by check mark if the registrant has elected not to use the extended transition period for complying with any new or revised financial accounting standards provided pursuant to Section 13(a) of the Exchange Act. ☐

Item 7.01 Regulation FD Disclosure.

On May 2, 2023, Cabaletta Bio, Inc. (the "Company") issued a Press Release announcing that Samik Basu, M.D., Chief Scientific Officer at the Company, will deliver an invited, oral presentation titled "CD 19 CAR T-cells for SLE" as part of the session titled "Immune Effector Cells: 2023 and Beyond!" on Tuesday, May 16, 2023, at 11:05 a.m. PT at the upcoming American Society of Gene and Cell Therapy ("ASGCT") 26th Annual Meeting, which is being held at the Los Angeles Convention Center in Los Angeles, CA from May 16-20, 2023 ("ASGCT Annual Meeting"). A copy of the press release is attached hereto as Exhibit 99.1 and is incorporated by reference into this Item 7.01 of this Current Report on Form 8-K.

The information contained in Item 7.01 of this Current Report on Form 8-K, including Exhibit 99.1 attached hereto, is being furnished and shall not be deemed to be "filed" for the purposes of Section 18 of the Securities Exchange Act of 1934, as amended (the "Exchange Act"), or otherwise subject to the liabilities of that section and shall not be incorporated by reference in any filing under the Securities Act of 1933, as amended, or the Exchange Act, except as shall be expressly set forth by specific reference in such filing.

Item 8.01 Other Events.

On May 2, 2023, two abstracts providing (i) new preclinical data for CABA-201, a 4-1BB-containing fully human CD19-CAR T cell investigational therapy, and (ii) updated clinical and translational data from the ongoing DesCAARTes™ trial for DSG3-CAART in adults with mucosal-dominant pemphigus vulgaris (mPV) were published at the ASGCT's website. The abstracts have been selected for poster presentations at the upcoming ASGCT Annual Meeting as further detailed in Item 7.01 of this Current Report on Form 8-K.

The accepted abstracts are as follows:

- **Preclinical Specificity and Activity of CABA-201, a Fully Human 4-1BB Containing CD19 CAR T Therapy for Treatment-Resistant Autoimmune Disease**: Over 4% of the world population is estimated to live with autoimmune disease. Treatment typically requires systemic immunosuppressive therapy that have associated toxicities and are not curative. There is increasing evidence that B cells play a central role in disease pathogenesis, based upon responsiveness to B cell depletion by antibody-based therapeutics; however, responses are typically transient due to the incomplete depletion of B cells in secondary lymphoid tissue. Chimeric antigen receptor (CAR) T cells are a novel gene-engineered cellular immunotherapy where a synthetic T cell receptor is expressed to redirect the T cell to a desired target. Several B cell targeted CD19 CAR T cell products have led to durable remissions of B cell leukemias and lymphomas; three have been approved by regulators globally, each of which utilizes the murine derived CD19 scFv binding domain FMC63. Data from numerous studies have established the ability of these products to deeply deplete B cells. An early proof of concept pilot study evaluating the safety and efficacy of an FMC63-41BB-CD3z CAR T cell product, analogous to one of the approved therapies, in 5 patients with treatment refractory systemic lupus erythematosus suggests the potential to achieve rapid, deep and durable drug-free remissions. We designed a new CD19 CAR T product (CABA-201) containing a clinically de-risked (NCT05091541) fully human CD19 binder (IC78), to minimize immune mediated interference with activity. In addition, the construct utilizes the same 41BB costimulatory domain used in the pilot study above, which is reported to have a reduced incidence and severity of cytokine release syndrome (CRS) and immune effector cell-associated neurotoxicity syndrome (ICANS) in oncology patients. Preclinical studies were conducted to explore the specificity and activity of CABA-201 compared to the specificity and activity of the FMC63-41BB-CD3z construct using the same cell production method. CABA-201 demonstrated comparable cytotoxic activity to FMC63 CAR T cells against $CD19^+$ Nalm6 cells in vitro, and comparable in vivo potency was observed in a dose ranging study in the NSG-Nalm6 tumor model. No evidence of off-target cytotoxic activity of CABA-201 was identified against a panel of selected primary human cells, and no off-target binding against IC78 was detected in a membrane proteome array, or in clinical studies evaluating IC78 in a tandem CAR formation. CABA-201 generated from primary T cells from multiple autoimmune disease patients showed robust CAR surface expression and effective elimination of target autologous $CD19^+$ B cells in vitro. Together, these data support the safety and activity of CABA-201, and provide a clinically relevant benchmark for dose related potency in clinical studies planned for initiation later this year.
- **Correlative Findings Following DSG3-CAART Infusion with and without Combination Preconditioning Therapy in Patients with Pemphigus Vulgaris (DesCAARTes™ Study)**: Mucosal-dominant pemphigus vulgaris (mPV) is a painful autoimmune blistering disease mediated by anti-desmoglein 3 autoantibodies (anti-DSG3 Ab). The current standard of care for mPV includes broadly immunosuppressive therapies that have risks of serious or

life threatening infection. We are evaluating the safety and activity of a novel cellular therapy consisting of gene-modified autologous T cells (DSG3-CAART) engineered to eliminate DSG3 reactive B cells in mPV. We previously reported on the translational and clinical data from mPV subjects receiving escalating doses of DSG3-CAART ranging from 1 x 10^5 to 7.5x10^9 transduced cells without preconditioning (NCT04422912). Manufactured DSG3-CAART eliminated target cell lines in vitro and were comprised of a mixture of effector and memory cells. DSG3-CAART cells were detected in the blood of all subjects within the first 29 days post-infusion with a dose dependent increase in peak persistence and persistence AUC for the first 29 days (AUC_{29d}), which reached a plateau at a dose of 2.5x10^9 DSG3-CAART cells. Here, we expand on those findings by including subjects who received combination therapy consisting of intravenous immune globulin (IVIG) to reduce potentially neutralizing autoantibodies and cyclophosphamide to reduce leukocytes followed by an infusion of 2.5x10^9 DSG3-CAART cells. Both peak persistence and persistence AUC_{29d} were further elevated in subjects receiving the combination therapy than those subjects receiving DSG3-CAART alone. Although persisting cells were predominantly of the central memory or stem cell memory phenotype in both groups, initial data from combination therapy subjects suggest that persisting DSG3-CAART cells exhibited signs of increased activation, including increased HLA-DR expression on DSG3-CAART cells, that were not observed in the DSG3-CAART cells in non-combination therapy subjects. Furthermore, in subjects receiving combination therapy, transient (< 2 weeks) leukopenia and neutropenia were observed but without lymphopenia. These data suggest that combination therapy with IVIG and cyclophosphamide enhances DSG3-CAART persistence and activation and support continued exploration of DSG3-CAART for mPV patients.

Forward-Looking Statements

This 8-K contains “forward-looking statements” of the Company within the meaning of the Private Securities Litigation Reform Act of 1995, as amended, including without limitation, express or implied statements regarding expectations regarding: its ability to grow its autoimmune-focused pipeline; the potential role of B cells in disease pathogenesis; its expectations around the potential success and therapeutic benefits of CABA-201 and the DSG3-CAART product candidate, including the significance of its preclinical data, DSG3-CAART’s initial data from the combination therapy study, and its safety, activity and tolerability profile to date, and its ability to identify a clinically relevant benchmark for dose related potency for CABA-201; the significance of preclinical data on CABA-201 and clinical and translational data on DSG3-CAART; the Company’s business plans and objectives, including clinical development plans, clinical trial initiation for CABA-201 and anticipated regulatory interactions; and the ability to accelerate its pipeline and develop meaningful therapies for patients.

Any forward-looking statements in this 8-K 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 or persistence may not inform long-term results; the Company’s ability to demonstrate sufficient evidence of safety, efficacy and tolerability in its preclinical studies and clinical trials of DSG3-CAART and CABA-201; the risk that the results observed with the similarly-designed construct employed in the recent *Nature Medicine* publication are not indicative of the results we seek to achieve with CABA-201; 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 volatile market and economic conditions; risks related to the impact of public health epidemics affecting countries or regions in which the Company has operations or does business, such as COVID-19; the Company’s ability to retain and recognize the intended incentives conferred by Orphan Drug Designation and Fast Track Designation for its product candidates, as applicable; risks related to the Company’s ability to protect and maintain its intellectual property position; risks related to fostering and maintaining successful relationships with the Company’s collaboration and manufacturing partners; uncertainties related to the initiation and conduct of studies and other development requirements for its product candidates; the risk that any one or more of the Company’s product candidates will not be successfully developed and/or commercialized; and the risk that the initial or interim 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 the Company’s actual results to differ from those contained in the forward-looking statements, see the section entitled “Risk Factors” in the Company’s most recent annual report on Form 10-K as well as discussions of potential risks, uncertainties, and other important factors in the Company’s other filings with the Securities and Exchange Commission. All information in this 8-K is as of the date hereof, and the Company undertakes no duty to update this information unless required by law.

Item 9.01 Financial Statements and Exhibits.

(d) Exhibits

99.1	Press Release issued by the registrant on May 2, 2023, furnished herewith.
104	Cover Page Interactive Data File (embedded within the Inline XBRL Document).

SIGNATURE

Pursuant to the requirements of the Securities Exchange Act of 1934, as amended, the registrant has duly caused this report to be signed on its behalf by the undersigned, hereunto duly authorized.

CABALETTA BIO, INC.

Date: May 2, 2023

By: /s/ Steven Nichtberger
Steven Nichtberger, M.D.
President and Chief Executive Officer

Cabaletta Bio®

Cabaletta Bio to Present at the American Society of Gene and Cell Therapy 26th Annual Meeting

PHILADELPHIA, May 2, 2023 — Cabaletta Bio, Inc. (Nasdaq: CABA), a clinical-stage biotechnology company focused on developing and launching the first curative targeted cell therapies for patients with autoimmune diseases, today announced that Samik Basu, M.D., Chief Scientific Officer at Cabaletta Bio, will deliver an invited, oral presentation titled "CD 19 CAR T-cells for SLE" as part of the session titled "Immune Effector Cells: 2023 and Beyond!" on Tuesday, May 16, 2023, at 11:05 a.m. PT at the upcoming American Society of Gene and Cell Therapy (ASGCT) 26th Annual Meeting, which is being held at the Los Angeles Convention Center in Los Angeles, CA from May 16-20, 2023. In addition, new preclinical data for CABA-201, a 4-1BB-containing fully human CD19-CAR T cell investigational therapy, and updated clinical and translational data from the ongoing DesCAARTes™ trial for DSG3-CAART in adults with mucosal-dominant pemphigus vulgaris (mPV) will be presented in poster presentations.

Details of the poster presentations are as follows:

Title: Preclinical Specificity and Activity of CABA-201, a Fully Human 4-1BB Containing CD19 CAR T Therapy for Treatment-Resistant Autoimmune Disease

Abstract Number: 1418

Date and Time: Friday, May 19, 2023, 12:00 p.m. – 2:00 p.m. PT

Presenter: Jinmin Lee, Ph.D., Associate Director, Preclinical Research and Jason Peng, Ph.D., Senior Scientist at Cabaletta Bio

Title: Correlative Findings Following DSG3-CAART Infusion with and without Combination Preconditioning Therapy in Patients with Pemphigus Vulgaris (DesCAARTes™ Study)

Abstract Number: 1138

Date and Time: Thursday, May 18, 2023, 12:00 p.m. – 2:00 p.m. PT

Presenter: Jenell Volkov, Ph.D., Director, Translational Medicine and Daniel Nunez, Ph.D., Associate Director, Computational Biology at Cabaletta Bio

Additional information, including the accepted abstracts, can be accessed on the ASGCT website. Presentation materials will be made available on the Posters & Publications section of the Company's website following the event.

About CAR T Cell Therapy

Chimeric Antigen Receptor (CAR) T cells are designed to achieve transient depletion of all B cells following a single treatment by using T cells engineered to express an antibody fragment that recognizes a B cell receptor expressed on the surface of all B cells, which is designed to allow for the complete elimination of B cells that contribute to disease with subsequent repopulation by healthy naïve B cells. This approach offers the potential for durable and complete clinical responses through an immune system reset without the need for chronic immunosuppression in patients with autoimmune diseases.

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 CD 19-targeting molecule, CAAR T cells express an autoantibody-targeted antigen on their surface. Theco-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 (Nasdaq: CABA) is a clinical-stage biotechnology company focused on the discovery and development of engineered T cell therapies that have the potential to provide a deep and durable, perhaps curative, treatment for patients with autoimmune diseases. The CABA™ platform encompasses two strategies: the CARTA (Chimeric Antigen Receptor T cells for Autoimmunity) strategy, with CABA-201, a 4-1BB-containing fully human CD19-CAR T, as the lead product candidate being evaluated in lupus nephritis and systemic lupus erythematosus without renal involvement, and the CAART (Chimeric AutoAntibody Receptor T cells) strategy, with multiple clinical-stage candidates, including DSG3-CAART for mucosal pemphigus vulgaris and MuSK-CAART for MuSK myasthenia gravis. The expanding CABA™ platform may offer potentially curative therapies for patients with a broad range of autoimmune diseases. Cabaletta Bio's headquarters and labs are located in Philadelphia, PA.

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: Cabaletta's ability to grow its autoimmune-focused pipeline; the significance of preclinical data on CABA-201 and clinical and translational data on DSG3-CAART, including potential therapeutic benefits; the Company's business plans and objectives, including clinical development plans and anticipated regulatory interactions; Cabaletta Bio's expectations around the potential success and therapeutic benefits of CABA-201, DSG3-CAART, and MuSK-CAART, including its belief that its candidates may enable an "immune system reset" and provide deep and durable responses for patients with autoimmune diseases; and the ability to accelerate Cabaletta's pipeline and develop meaningful therapies for patients.

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 or persistence may not inform long-term results; Cabaletta's ability to demonstrate sufficient evidence of safety, efficacy and tolerability in its preclinical studies and clinical trials of DSG3-CAART, MuSK-CAART and CABA-201; the risk that the results observed with the similarly-designed construct employed in the recent*Nature Medicine* publication are not indicative of the results we seek to achieve withCABA-201; 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 volatile market and economic conditions; 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 its product candidates, as applicable; risks related to Cabaletta's ability to protect and maintain its intellectual property position; risks related to fostering and maintaining successful relationships with Cabaletta's collaboration and manufacturing partners; uncertainties related to the initiation and conduct of studies and other development requirements for its product candidates; the risk that any one or more of Cabaletta's product candidates will not be successfully developed and/or commercialized; and the risk that the initial or interim 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 and subsequent 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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