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

Date of Report (Date of earliest event reported): February 1, 2024

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 February 1, 2024, Cabaletta Bio, Inc. (the "Company") issued a Press Release announcing that the U.S. Food and Drug Administration (the "FDA") granted Orphan Drug Designation to CABA-201, a 4-1BB-containing fully human CD19-CAR T cell investigational therapy, for the treatment of idiopathic inflammatory myopathies (IIM, or myositis) (the "Press Release"). A copy of the Press Release is attached hereto as Exhibit 99.1 to this Current Report on Form 8-K.

The information contained in Item 7.01 of this Current Report on Form8-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 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 or the Exchange Act, except as shall be expressly set forth by specific reference in such filing.

Item 8.01 Other Events.

On February 1, 2024, the Company issued the Press Release announcing that the FDA has granted Orphan Drug Designation toCABA-201, a 4-1BB-containing fully human CD19-CAR T cell investigational therapy, for the treatment of idiopathic inflammatory myopathies (IIM, or myositis). CABA-201 is in development as a potential treatment for autoimmune diseases driven by B cells. Four RESET™ (REstoring SElf-Tolerance) Phase 1/2 trials are advancing for the evaluation of CABA-201 across multiple autoimmune conditions, including the Phase 1/2 RESET-Myositis™ trial.

The RESET-Myositis™ trial is a Phase 1/2 open-label study ofCABA-201 in subjects with active idiopathic inflammatory myopathy (IIM, or myositis), including the subtypes of dermatomyositis (DM), anti-synthetase syndrome (ASyS) and immune-mediated necrotizing myopathy (IMNM). Subjects will receive a one-time infusion of CABA-201 at a dose of 1 x 10^6 cells/kg, preceded by a standard preconditioning regimen of fludarabine and cyclophosphamide. Key inclusion criteria include patients between ages 18 to 65 (inclusive), evidence of active disease and disease activity despite prior or current treatment with standard of care treatments. Key exclusion criteria include cancer-associated myositis, significant lung or cardiac impairment, treatment with a B cell depleting agent within the prior approximately six months or treatment with a biologic agent within the prior approximately three months. As part of Cabaletta's CARTA (Chimeric Antigen Receptor T cells for Autoimmunity) strategy, this trial is intended to evaluate the potential ability of CABA-201 to transiently, but fully, eliminate B cells, potentially enabling durable remissions via a "reset" of the immune system.

CABA-201 is designed to deeply and transiently deplete CD19-positive B cells following a one-time infusion, which may enable an "immune system reset" with the potential for durable remission off therapy in patients with autoimmune diseases. To date, Cabaletta has received clearance from the FDA for Investigational New Drug (IND) applications for CABA-201 in multiple autoimmune conditions including systemic lupus erythematosus (SLE), myositis, systemic sclerosis (SSc) and generalized myasthenia gravis (gMG). Cabaletta is conducting four Phase 1/2 clinical trials with a total of nine cohorts that can advance simultaneously, employing a similar parallel cohort design and starting dose of 1 x 10^6 cells/kg without a dose escalation requirement.

Myositis refers to a group of autoimmune diseases characterized by inflammation and muscle weakness. In some cases, myositis may also affect other organs and systems in the body, such as the lungs, heart, or skin. Myositis is classified into several subtypes based on the underlying immune mechanisms and clinical characteristics. Although the pathogenesis of myositis is not well understood, there are several subtypes thought to be driven by B cells, including dermatomyositis (DM), anti-synthetase syndrome (ASyS) and immune-mediated necrotizing myopathy (IMNM). These three subtypes impact approximately 66,000 patients in the US alone, and typically affect middle-aged individuals, particularly women. All three subtypes can lead to severe functional impairment and may be life-threatening. Current treatment typically involves medications to suppress the immune system and/or chronic intensive therapies such as intravenous immunoglobulin, or IVIg. Despite these therapies, a significant portion of myositis patients have disease that remains refractory to existing medications.

Forward-Looking Statements

The information under this Item 8.01 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 its expectations regarding: Cabaletta's ability to retain and recognize and its expectations around the intended incentives conferred by Orphan Drug Designation for CABA-201 for the treatment of idiopathic inflammatory myopathies; Cabaletta's ability to retain and recognize the intended incentives conferred by Fast Track Designations for CABA-201 in multiple autoimmune diseases; Cabaletta's expectations around the potential success and therapeutic benefits of CABA-201, including its belief that CABA-201 may enable an "immune system reset" and provide deep and durable responses in patients across an increasing number of autoimmune diseases; Cabaletta's belief that it is making meaningful progress toward the development and potential launch of the first targeted, and perhaps curative, cellular therapies for patients with autoimmune diseases; the Company's advancement of separate Phase 1/2 clinical trials of CABA-201 in patients with SLE, myositis, SSc and gMG; Cabaletta's ability to leverage its research and translational insights; and the Company's expectations for the efficiency of the trial design for its Phase 1/2 clinical trials of CABA-201.

Any forward-looking statements in this Item 8.01 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: risks related to regulatory filings and potential clearance; 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 CABA-201; the risk that the results observed with the similarly-designed construct employed in the recent academic publications, including due to the dosing regimen, 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 and public health crises; 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 filings with the Securities and Exchange Commission. All information in this Item 8.01 is as of the date of this Current Report on Form 8-K, 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 February 1, 2024, 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: February 1, 2024

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

Cabaletta Bio®

Cabaletta Bio Announces FDA Granted Orphan Drug Designation to CABA-201 for Treatment of Myositis

PHILADELPHIA, Feb. 1, 2024 — 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 the U.S. Food and Drug Administration (FDA) has granted Orphan Drug Designation (ODD) to CABA-201, a 4-1BB-containing fully human CD19-CAR T cell investigational therapy, for the treatment of idiopathic inflammatory myopathies (IIM, or myositis). CABA-201 is in development as a potential treatment for autoimmune diseases driven by B cells. Four RESET™ (REstoring SElf-Tolerance) Phase 1/2 trials are advancing for the evaluation of CABA-201 across multiple autoimmune conditions, including the Phase 1/2 RESET-Myositis™ trial.

"Myositis, believed to be driven by B cells, is a severe and potentially fatal autoimmune disease for which no curative therapy exists. Current treatment options provide modest efficacy, with a significant portion of diagnosed patients having an inadequate response to treatment, thus, there is a clear need for innovative medicines that can meaningfully change the treatment paradigm," said David J. Chang, M.D., Chief Medical Officer of Cabaletta. "CABA-201 is designed to deeply and transiently deplete CD19-positive B cells, which may enable an immune system reset, and has the potential to deliver durable remission off therapy in patients diagnosed with myositis and other autoimmune diseases where B cells play a role. Orphan Drug Designation is an important recognition for investigational therapies for rare diseases and provides us with potentially valuable benefits as we seek to make a difference in the lives of patients and develop the first targeted, and potentially curative, cell therapy for patients with autoimmune diseases."

The FDA grants Orphan Drug Designation to drugs or biologics intended to treat or prevent rare diseases or conditions that affect fewer than 200,000 individuals in the United States. This designation qualifies Cabaletta for certain incentives, which may include partial tax credit for clinical trial expenditures, waived user fees and potential eligibility for seven years of marketing exclusivity.

About the RESET-Myositis™ Trial

The RESET-Myositis™ trial is a Phase 1/2 open-label study of CABA-201 in subjects with active idiopathic inflammatory myopathy (IIM, or myositis), including the subtypes of dermatomyositis (DM), anti-synthetase syndrome (ASyS) and immune-mediated necrotizing myopathy (IMNM). Subjects will receive a one-time infusion of CABA-201 at a dose of 1 x 10^6 cells/kg, preceded by a standard preconditioning regimen of fludarabine and cyclophosphamide. Key inclusion criteria include patients between ages 18 to 65 (inclusive), evidence of active disease and disease activity despite prior or current treatment with standard of care treatments. Key exclusion criteria include cancer-associated myositis, significant lung or cardiac impairment, treatment with a B cell depleting agent within the prior approximately six months or treatment with a biologic agent within the prior approximately three months. As part of Cabaletta's CARTA (Chimeric Antigen Receptor T cells for Autoimmunity) strategy, this trial is intended to evaluate the potential ability of CABA-201 to transiently, but fully, eliminate B cells, potentially enabling durable remissions via a "reset" of the immune system.

About CABA-201

CABA-201 is designed to deeply and transiently deplete CD19-positive B cells following a one-time infusion, which may enable an "immune system reset" with the potential for durable remission off therapy in patients with autoimmune diseases. To date, Cabaletta has received clearance from the FDA for Investigational New Drug (IND) applications for CABA-201 in multiple autoimmune conditions including systemic lupus erythematosus (SLE), myositis, systemic sclerosis (SSc) and generalized myasthenia gravis (gMG). Cabaletta is conducting four Phase 1/2 clinical trials with a total of nine cohorts that can advance simultaneously, employing a similar parallel cohort design and starting dose of 1 x 10^6 cells/kg without a dose escalation requirement.

About Myositis

Myositis refers to a group of autoimmune diseases characterized by inflammation and muscle weakness. In some cases, myositis may also affect other organs and systems in the body, such as the lungs, heart, or skin. Myositis is classified into several subtypes based on the underlying immune mechanisms and clinical characteristics. Although the pathogenesis of myositis is not well understood, there are several subtypes thought to be driven by B cells, including dermatomyositis (DM), anti-synthetase syndrome (ASyS) and immune-mediated necrotizing myopathy (IMNM). These three subtypes impact approximately 66,000 patients in the US alone, and typically affect middle-aged individuals, particularly women. All three subtypes can lead to severe functional impairment and may be life-threatening. Current treatment typically involves medications to suppress the immune system and/or chronic intensive therapies such as intravenous immunoglobulin, or IVIg. Despite these therapies, a significant portion of myositis patients have disease that remains refractory to existing medications.

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 the RESET™ (REstoring SElf-Tolerance) clinical trials in systemic lupus erythematosus, myositis, systemic sclerosis and generalized myasthenia gravis, 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 is designed to develop potentially curative therapies that offer deep and durable responses 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: Cabaletta's ability to retain and recognize and its expectations around the intended incentives conferred by Orphan Drug Designation for CABA-201 for the treatment of idiopathic inflammatory myopathies; Cabaletta's ability to retain and recognize the intended incentives conferred by Fast Track Designations for CABA-201 in multiple autoimmune diseases; Cabaletta's expectations around the potential success and therapeutic benefits of CABA-201, including its belief that CABA-201 may enable an "immune

system reset" and provide deep and durable responses in patients across an increasing number of autoimmune diseases; Cabaletta's belief that it is making meaningful progress toward the development and potential launch of the first targeted, and perhaps curative, cellular therapies for patients with autoimmune diseases; the Company's advancement of separate Phase 1/2 clinical trials of CABA-201 in patients with SLE, myositis, SSc and gMG; Cabaletta's ability to leverage its research and translational insights; and the Company's expectations for the efficiency of the trial design for its Phase 1/2 clinical trials of CABA-201.

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