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): December 9, 2023

COGENT BIOSCIENCES, INC.
(Exact name of registrant as specified in its charter)

Delaware	**001-38443**	**46-5308248**
(State or other jurisdiction of incorporation)	**(Commission File Number)**	**(I.R.S. Employer Identification No.)**

275 Wyman Street, 3rd Floor **Waltham, Massachusetts**	**02451**
(Address of principal executive offices)	**(Zip Code)**

Registrant's telephone number, including area code: (617) 945-5576

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, $0.001 Par Value	COGT	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 or Rule 12b-2 of the Securities Exchange Act of 1934.

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 8.01 Other Events

On December 9, 2023, Cogent Biosciences, Inc. (the "Company") announced positive initial data from the Company's ongoing Phase 2 SUMMIT clinical trial evaluating bezuclastinib in patients with nonadvanced systemic mastocytosis ("NonAdvSM") at the 65th American Society of Hematology ("ASH 2023") Annual Meeting & Exposition taking place December 9-12, 2023 in San Diego, CA. On December 11, 2023, the Company announced positive data from Part 1 of the Company's ongoing Phase 2 APEX clinical trial evaluating bezuclastinib in patients with advanced systemic mastocytosis ("AdvSM"), which data is also being presented at ASH 2023.

Phase 2 SUMMIT Trial

SUMMIT is a randomized, double-blind, placebo-controlled, global, multicenter, Phase 2 clinical trial of bezuclastinib in patients with NonAdvSM. Twenty patients in Part 1a were treated with either bezuclastinib or placebo plus best supportive care for all arms. The median age of patients at study entry was 50.5 years (ranging from 38-75 years). Patients were enrolled with the following sub-types: 18 patients with indolent systemic mastocytosis ("ISM") and two patients with smoldering systemic mastocytosis ("SSM"). One patient had received prior avapritinib.

Safety Data

Bezuclastinib demonstrated an encouraging safety and tolerability profile for patients dosed at both 100 mg and 200 mg QD. The majority of treatment emergent adverse events were low grade and reversible with no related serious adverse events, bleeding or cognitive impairment events reported. There were two dose reductions for fatigue and one patient discontinued treatment due to increased ALT. One patient with SSM was enrolled at a 400mg dose and following Grade 4 neutropenia was dose reduced to 200mg. Following completion of Part 1a patients received a median duration of treatment in the open label extension ("OLE") of 16 weeks. A consistent safety and tolerability profile was observed for patients starting bezuclastinib treatment following placebo.

Pharmacodynamic Data

Twenty patients enrolled in SUMMIT Part 1a were evaluated for signs of clinical activity within the first 12 weeks, including well-accepted biomarkers of disease burden.

- 100% of bezuclastinib patients achieved ≥50% reduction in serum tryptase levels vs. 0% of placebo patients
  - 90% (9/10) of bezuclastinib patients with elevated baseline serum tryptase (>20 ng/ml) achieved reduction below 20 ng/ml within 12 weeks
  - 67% (8/12) of patients with abnormal baseline serum tryptase (≥11.4ng/mL) achieved a normal tryptase value (<11.4ng/mL) after 12 weeks of bezuclastinib
- 100% of bezuclastinib patients with detectable baseline variant allele fraction ("VAF") achieved ≥50% reduction in KIT D816V VAF vs. 0% of placebo patients
- 100% of bezuclastinib patients with measurable baseline mast cell aggregates achieved ≥50% reduction in bone marrow mast cell burden vs. 14% of placebo patients

Patient Reported Outcomes ("PRO") Data

Twenty patients enrolled in SUMMIT Part 1a were evaluated for signs of clinical activity within the first 12 weeks across quality-of-life and/or symptomatic severity scales including Mast Cell Quality-of-Life ("MC-QoL"), Mastocytosis Activity Scale ("MAS"), Patient Global Impression of Severity ("PGIS") and Patient Global Impression of Change ("PGIC"). Additional patient assessments were made during the open-label extension using MC-QoL, PGIS and PGIC. In patients with completed questionnaires:

- By week 12, bezuclastinib patients showed a median best improvement of 37% on MC-QoL vs. 24% for placebo patients.
  - By week 20, bezuclastinib patients increased median best improvement to 57% on MC-QoL
  - Patients who crossed over from placebo to bezuclastinib, showed median best improvement on MC-QoL of 75% by week 8 of active treatment
- At week 12, bezuclastinib patients showed a 35% change from baseline on MAS vs. a 28% change from baseline for placebo

- For bezuclastinib patients treated at 100 mg QD, the MAS improvement from baseline at week 12 was 49%

- At week 12, 63% of bezculastinib patients showed a ≥1 point improvement on PGIS (5 point scale) compared with 0% of placebo patients
  - At week 20, this increased to 78% of bezuclastinib patients reporting ≥1 point improvement
  - 67% of patients who crossed over from placebo to bezuclastinib showed ≥1 point improvement on PGIS by week 8 of active treatment
- At week 12, 63% of bezuclastinib patients reported overall symptoms were "much better" to "very much better" on PGIC vs. 0% of placebo patients
  - At week 20, this increased to 78% of bezuclastinib patients
  - 43% of patients who crossed over from placebo to bezuclastinib reported symptoms were "much better" to "very much better" by week 8 of active treatment
  - By week 20, 100% of patients treated with bezuclastinib reported improved Dermatological and Pain symptoms, 75% of patients reported improvement in Fatigue, and 67% of patients reported improvement in Gastrointestinal symptoms

Phase 2 APEX Trial

APEX is a global, open-label, multi-center, two-part Phase 2 clinical trial in patients with AdvSM evaluating the safety, efficacy, pharmacokinetic, and pharmacodynamic profiles of bezuclastinib. As of the data cutoff date of September 25, 2023, 32 patients were treated in Part 1 at one of four dose levels (50 mg BID, 100 mg BID, 200 mg BID or 400 mg QD). The median age of patients at study entry was 68 years (ranging from 33-87 years). Patients were enrolled with the following sub-types: seven patients with aggressive systemic mastocytosis ("ASM"), 23 patients with systemic mastocytosis with associated hematologic neoplasm ("SM-AHN"), and two patients with mast cell leukemia ("MCL"). Five patients had received prior avapritinib and 10 patients had received prior midostaurin treatment.

Safety Data

As of the data cutoff date of September 25, 2023, bezuclastinib continues to demonstrate a differentiated safety and tolerability profile across doses. The majority of adverse events were low grade and reversible and there were no related cognitive impairment or bleeding events reported. Related serious adverse events were reported in four patients including Grade 4 thrombocytopenia, Grade 3 hypersensitivity (mediator flare), Grade 3 leishmaniasis, and Grade 3 drug induced liver injury in a patient who was subsequently found to have biliary tract outflow obstruction. Nine patients required dose reduction due to adverse events, six of whom were at the 400mg dose, and three patients discontinued due to adverse events.

Clinical Activity Data

As of the data cutoff date of September 25, 2023, 32 patients enrolled were evaluated for signs of clinical activity, 27 of whom were mIWG-MRT-ECNM evaluable. Patients without post baseline biomarker data were excluded from relevant analyses.

- 52% ORR (CR+CRh+PR) per mIWG-MRT-ECNM criteria, including 56% ORR for TKI-treatment-naïve patients
  - 100% of patients treated with 100 mg BID achieved PR or better and all remain on study
    - 150 mg QD optimized formulation dose selected for APEX Part 2 is expected to deliver patient exposures consistent with this cohort
- 75% ORR (CR+PR) per pure pathological response ("PPR") criteria, including 86% ORR for TKI-treatment-naïve patients
- Nearly all patients demonstrated a significant improvement in biomarkers associated with disease burden
  - 94% of patients achieved ≥50% reduction in serum tryptase levels
    - 100% of patients receiving ≥2 cycles achieved ≥50% reduction
    - 53% of patients achieved reduction of serum tryptase below 20 ng/mL
  - 93% of KITD816V-positive patients achieved ≥50% reduction in KIT D816V VAF
  - 97% of patients achieved a ≥50% reduction in bone marrow mast cell burden
    - 79% achieved complete clearance of mast cell aggregates by central review

Bezuclastinib Clinical Development

The Company completed enrollment in SUMMIT Part 1 and plans to initiate SUMMIT Part 2, a registration-directed, global, randomized placebo-controlled trial in the first half of 2024. In addition, the Company plans to present data from the completed SUMMIT Part 1 trial (1a and 1b), including all 54 patients enrolled across Part 1a and Part 1b, in the first quarter of 2024.

The Company continues to actively enroll Part 2 of the APEX trial, which is expected to include approximately 65 AdvSM patients and is on-track to complete enrollment by the end of 2024.

In Gastrointestinal Stromal Tumors ("GIST"), the Company continues to actively enroll patients in Part 2 of the Phase 3 registration-enabling PEAK trial and remains on track to complete enrollment by the end of 2024, with over 100 active sites globally.

Forward Looking Statements

This Current Report on Form 8-K contains forward-looking statements within the meaning of the Private Securities Litigation Reform Act of 1995, including, but not limited to, statements regarding: the potential for bezuclastinib's safety and tolerability profile to support chronic dosing for patients with NonAdvSM; plans for the Company to initiate Part 2 of SUMMIT in the first half of 2024 and present data from the completed SUMMIT Part 1 trial (1a and 1b), including all 54 patients enrolled across Part 1a and Part 1b, in the first quarter of 2024; the potential of bezuclastinib to become a new treatment option patients with AdvSM; the expectation for the Company to complete enrollment of approximately 65 patients in Part 2 of APEX by the end of 2024; that the 150 mg QD optimized formulation dose selected for APEX Part 2 is expected to deliver patient exposures consistent with the 100 mg BID Part 1 cohort; and plans to complete enrollment in PEAK by the end of 2024 with over 100 active sites globally. The use of words such as, but not limited to, "anticipate," "believe," "continue," "could," "estimate," "expect," "intend," "may," "might," "plan," "potential," "predict," "project," "should," "target," "will," or "would" and similar words expressions are intended to identify forward-looking statements. Forward-looking statements are neither historical facts nor assurances of future performance. Instead, they are based on the Company's current beliefs, expectations and assumptions regarding the future of the Company's business, future plans and strategies, the Company's clinical results, the rate of enrollment in the Company's clinical trials and other future conditions. New risks and uncertainties may emerge from time to time, and it is not possible to predict all risks and uncertainties. No representations or warranties (expressed or implied) are made about the accuracy of any such forward-looking statements. The Company may not actually achieve the forecasts or milestones disclosed in its forward-looking statements, and you should not place undue reliance on its forward-looking statements. Such forward-looking statements are subject to a number of material risks and uncertainties including but not limited to those set forth under the caption "Risk Factors" in the Company's most recent Annual Report on Form 10-K, Quarterly Report on Form 10-Q and subsequent filings made with the Securities and Exchange Commission. Any forward-looking statement speaks only as of the date on which it was made. Neither the Company, nor its affiliates, advisors or representatives, undertake any obligation to publicly update or revise any forward-looking statement, whether as result of new information, future events or otherwise, except as required by law. These forward-looking statements should not be relied upon as representing the Company's views as of any date subsequent to the date hereof.

SIGNATURES

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

Date: December 11, 2023

COGENT BIOSCIENCES, INC.

By: /s/ Evan Kearns
Evan Kearns
Chief Legal Officer