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 8, 2024

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** **(Address of principal executive offices)**	**02451** **(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 8, 2024, Cogent Biosciences, Inc. (the "Company") announced positive updated data from the Company's ongoing Phase 2 APEX clinical trial evaluating bezuclastinib in patients with advanced systemic mastocytosis ("AdvSM") at the 66th American Society of Hematology ("ASH 2024") Annual Meeting & Exposition taking place December 7-10, 2024 in San Diego, CA. On December 9, 2024, the Company announced positive updated clinical data from the Company's ongoing Phase 2 SUMMIT clinical trial evaluating bezuclastinib in patients with nonadvanced systemic mastocytosis ("NonAdvSM"), which data is also being presented at ASH 2024.

Phase 2 APEX Trial

Patient Demographics

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. Thirty-two 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). Earlier this year, the Company announced APEX Part 2 would be conducted at the optimized 150mg QD dose, which closely matches the exposure from 100 mg BID dose in APEX Part 1. 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.

Clinical Activity Data

As of the data cutoff date of October 11, 2024, 32 patients enrolled were evaluated for signs of clinical activity, 27 of whom were mIWG-MRT-ECNM evaluable. Clinical activity analyzed across dose levels and focused on 100 mg BID cohort showed:

- 52% ORR (CR+CRh+PR+CI) per mIWG-MRT-ECNM criteria, including 61% ORR for TKI-treatment-naïve patients
    - 83% ORR for patients treated at 100 mg BID dose cohort
- 88% ORR (CR+PR) per pure pathological response ("PPR") criteria
    - 100% ORR for patients treated at 100 mg BID dose cohort
- Median time to achieve response was 2.2 months and median duration of response has not yet been reached
    - Median PFS was not yet reached at median follow-up of 20 months; PFS rate at 24 months was 82%

Pharmacodynamic Data

Nearly all patients demonstrated a significant improvement in biomarkers associated with disease burden. Patients without post baseline biomarker data were excluded from relevant analyses.

- 94% of patients achieved ≥50% reduction in serum tryptase levels
    - 100% of patients receiving ≥2 cycles achieved ≥50% reduction
    - 66% of patients achieved reduction of serum tryptase below 20 ng/mL
- 93% of KITD816V-positive patients achieved ≥50% reduction in KIT D816V variant allele fraction ("VAF")
- 100% of evaluable patients achieved a ≥50% reduction in bone marrow mast cell burden
    - 83% achieved complete clearance of mast cell aggregates by central review

Safety Data

As of the data cutoff date of October 11, 2024, bezuclastinib continues to demonstrate a differentiated safety and tolerability profile across doses. The majority of hematological adverse events were low grade and reversible. There have been no new treatment related serious adverse events or discontinuations reported since ASH 2023. Due to confounding medical issues, one patient previously reported with DILI has been reassessed and reported as a Grade 4 gamma-glutamyl transferase ("GGT") elevation case. Twelve patients required dose reduction, eight of whom were treated at a 400 mg daily dose.

Bezuclastinib in Systemic Mastocytosis

The Company is actively enrolling patients into APEX Part 2 which is anticipated to complete enrollment in Q1 2025 with top-line results expected in mid-2025.

Phase 2 SUMMIT Trial

Patient Demographics

SUMMIT is a registration-directed, randomized, double-blind, placebo-controlled, global, multicenter, clinical trial of bezuclastinib in patients with NonAdvSM. In SUMMIT Part 1, patients received bezuclastinib or placebo for a 12-week period to determine the recommended dose for use in the pivotal portion of the trial, SUMMIT Part 2. Earlier this year, the Company announced that the recommended go-forward dose was selected at once-daily 100 mg. After the initial 12-week period, all patients were given the opportunity to receive bezuclastinib in the SUMMIT Open Label Extension ("OLE"). The clinical results presented at ASH 2024 focus on 27 patients in the OLE who were treated with the once-daily 100 mg dose of bezuclastinib. The median age of patients at study entry was 52 years (ranging from 36-76 years). One patient had received prior avapritinib.

Patient Reported Outcomes ("PRO") Data

SUMMIT patients were evaluated for signs of clinical activity over 24 weeks using multiple PRO measures, including the Mastocytosis Symptom Severity Daily Diary ("MS2D2") and the Mastocytosis Quality-of-Life ("MC-QoL") scale. Updated clinical data presented at ASH 2024 show:

- 56% mean improvement in Total Symptom Score ("TSS") at 24 weeks
- 76% of patients demonstrated >50% reduction from baseline in MS2D2 TSS with 88% of patients exceeding 30% reduction from baseline after 24 weeks
- 49% mean improvement in MC-QoL Total Score at 24 weeks

At 24 weeks of treatment, 31% of patients have already reduced or discontinued best supportive care ("BSC") medications.

Pharmacodynamic Data

Bezuclastinib showed rapid, deep, and sustained reductions in serum tryptase over the course of 24 weeks of treatment including:

- 89% of patients had ≥50% decrease in serum tryptase levels by four weeks of treatment
- 95% of patients with baseline tryptase ≥20ng/mL achieved <20ng/mL by week 24
- 84% of patients with baseline serum tryptase ≥11.4ng/ml achieved <11.4ng/mL by week 24

Safety Data

As of the data cutoff, August 29, 2024, the median duration of bezuclastinib treatment was 56 weeks for patients in the active arm and 40 weeks for placebo patients who crossed over to the OLE. The majority of treatment emergent adverse events were low grade and reversible with no treatment-related bleeding or cognitive impairment events reported. The most common treatment related adverse events were hair discoloration and transaminase elevations. All patients experiencing elevated transaminases were asymptomatic and reversible: five patients resolved without any dose modifications and remain on study; two patients resolved with dose reduction and remain on study, one of whom re-escalated to original dose; and two patients resolved following discontinuation, one of whom was presented previously at ASH 2023. There were no other discontinuations due to adverse events.

SUMMIT Enrollment Update

The Company also announced on December 9, 2024 that enrollment in the registration-directed SUMMIT Part 2 study is now complete. In the nine months between February and October 2024, 265 NonAdvSM patients were screened for SUMMIT Part 2 at 70 clinical sites, concentrated predominantly in the U.S. and Western Europe. More than 90% of these patients were naïve to KIT inhibitor therapy. A total of 179 patients were enrolled and top-line results from the trial are expected in July 2025.

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 expectation for the Company to complete enrollment for APEX Part 2 in Q1 2025 and to have top-line data in mid-2025; and the Company's expectation to present top-line results from SUMMIT Part 2 in July 2025. 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 9, 2024

COGENT BIOSCIENCES, INC.

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