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September 6, 2019

Ms. Julia Griffith
Mr. Dietrich King
Office of Healthcare and Insurance
Division of Corporation Finance
Securities and Exchange Commission
100 F Street, N.E.
Washington, D.C. 20549

Re: Cabaletta Bio, Inc.
Draft Registration Statement on Form S-1
Submitted August 2, 2019
CIK No. 0001759138

Dear Ms. Griffith and Mr. King:

This letter is confidentially submitted on behalf of Cabaletta Bio, Inc. (the "**Company**") in response to comments of the staff of the Division of Corporation Finance (the "**Staff**") of the U.S. Securities and Exchange Commission (the "**Commission**") with respect to the Company's Draft Registration Statement on Form S-1 confidentially submitted on August 2, 2019 (the "**Draft Registration Statement**"), as set forth in the Staff's letter dated August 28, 2019 to Steven Nichtberger, the Company's Chief Executive Officer (the "**Comment Letter**"). The Company is concurrently confidentially submitting Amendment No. 1 to the Registration Statement ("**Amendment No. 1**"), which includes changes to reflect responses to the Staff's comments and other updates.

For reference purposes, the text of the Comment Letter has been reproduced and italicized herein with responses below each numbered comment. Unless otherwise indicated, page references in the descriptions of the Staff's comments refer to the Draft Registration Statement, and page references in the responses refer to Amendment No. 1. All capitalized terms used and not otherwise defined herein shall have the meanings set forth in Amendment No. 1.

The responses provided herein are based upon information provided to Goodwin Procter LLP by the Company. In addition to confidentially submitting this letter via EDGAR, we are sending via Federal Express four (4) copies of each of this letter and Amendment No. 1 (marked to show changes from the Draft Registration Statement).

Draft Registration Statement on Form S-1 filed August 2, 2019

Prospectus Summary, page 1

1. *Please revise the disclosure in the first paragraph of the Overview to clarify what you mean by"IND-ready."*

   RESPONSE: The Company respectfully acknowledges the Staff's comment and has revised the disclosure on page 1 of Amendment No. 1 to remove the phrase "IND-ready."

Pipeline, page 2

2. *We note your disclosure regarding "in vivo evidence of efficacy and safety in an animal model..." We also note other examples of statements regarding safety and efficacy on pages 3, 117, 119, and 124. Since none of your product candidates has received FDA approval, please revise your disclosure regarding safety and efficacy in the summary and throughout your prospectus to clarify this point.*

   RESPONSE: The Company's respectfully acknowledges the Staff's comment and has revised the disclosure on pages 2, 3, 29, 30, 116-118, 123, 127, 129, and 137 of Amendment No. 1 to clarify this point.

3. *We note your statement on page 13 that you are early in your development efforts and have not initiated clinical trials for any product candidates. Please expand the table on page 2 to include more information about the progress of the company's pre-clinical trials, and to clarify in the table that no products are past the phase of IND enabling studies. In addition, please include columns for Phase 1, 2 and 3 testing that are equally prominent with the pre-clinical columns, and clarify that these columns refer to clinical testing. In this regard, our concern is that potential investors see a balanced graphical presentation of where you are in the drug development process, and that the table adequately depict, if true, that you have not yet filed an IND application for any product. Please make conforming changes in the Business section as well.*

   RESPONSE: The Company respectfully acknowledges the Staff's comment and has revised the table on pages 2, 110 and 119 of Amendment No. 1.

Implications of Being an Emerging Growth Company, page 7

4. *Please supplementally provide us with copies of all written communications, as defined in Rule 405 under the Securities Act, that you, or anyone authorized to do so on your behalf, present to potential investors in reliance on Section 5(d) of the Securities Act, whether or not they retain copies of the communications.*

   RESPONSE: The Company respectfully advises the Staff that it will provide the Staff, on a confidential basis under separate cover, copies of all written communications presented to potential investors in reliance on Section 5(d) of the Securities Act, whether or not they retain copies of such communications.

Risk Factors, page 12

5. *We note that there are references to foreign regulators and foreign markets throughout the Risk Factors and other sections of your prospectus. Please revise to explain what non-U.S. markets, if any, you plan to enter, and what steps you have taken to attain the necessary regulatory approvals.*

RESPONSE: The Company respectfully acknowledges the Staff's comment and has removed references to foreign regulators and foreign markets throughout the Risk Factors and other sections of Amendment No. 1.

6. *Please provide us with a basis for your statement on page 21 that although clinical trials for cell-based therapies have historically included "a lymphodepleting chemotherapeutic regime to condition the patient prior to infusion [with CAR T-cell based therapies]," and that such infusions have resulted in neurotoxicity and other serious side effects, you believe that the use of CAR T cell therapies without preconditioning will avoid neurotoxicity or other side effects. We note your statement that "Based on evidence from other CAR T cell clinical trials demonstrating clinical activity without prior conditioning and the levels of certain cytokines that promote T cell expansion in the patients we are treating relative to cancer patients, as well as data from engineered T cell therapy in the setting of HIV without conditioning, we believe that CAAR T cell therapy may be functional in our autoimmune target patient populations without preconditioning regimens. Based on preclinical studies where DSG3-CAART is combined with stimulatory DSG3 antibodies, we observed these antibodies generate a modest level of cytokine activity that is an order of magnitude less than what was observed when DSG3- CAART engaged with target B cells. We believe this data indicates the presence of soluble DSG3 antibodies could stimulate DSG3-CAART expansion and potentially facilitate engraftment. This information coupled with the risks associated with certain lymphodepleting regimens used for preconditioning, we believe exposing autoimmune patients to these regimens without data to support the benefit is difficult to justify." Please expand your disclosure to include references to the specific studies on which you base your beliefs, and clarify the reasons for your belief that preconditioning is not necessary for your product candidate.*

RESPONSE: The Company respectfully acknowledges the Staff's comment and has revised the disclosure on pages 20 and 21 of Amendment No. 1 to provide greater detail as to the reasons for the Company's belief that a preconditioning regimen is not necessary for its product candidates and its plan to initiate its Phase 1 clinical trial of DSG3-CAART without a preconditioning regimen. In particular, the Company's belief is based on evidence that CAR T cells are functional in the absence of preconditioning, evidence of long-term persistence of engineered T cell therapy in the setting of HIV patients without preconditioning, the profile of the patients that the Company plans to dose in its planned Phase 1 clinical trial, and the fact that, unlike CARs used in oncology, the Company's CAARs are designed to target antibodies rather than tumor antigens. The revised disclosure on pages 20 and 21 of Amendment No. 1 also includes references to the specific studies on which the Company's beliefs are based.

To assist the Staff in its review of the revised disclosure, the Company supplementally advises the Staff that its CAAR T cells, which are being designed to treat patients with autoimmune diseases, differ from CAR T cells used in oncology in a number of ways that lead the Company to believe that CAAR T cell therapy may be functional in its

autoimmune target patient populations without preconditioning regimens. The mechanisms by which preconditioning increase engraftment and activity of T cell-based therapies in humans are currently poorly understood. In certain oncology patients, it is believed that a lymphodepleting preconditioning regimen can deplete populations of suppressive host immune cells within the tumor microenvironment and reduce competition for stimulatory, or homeostatic, cytokines capable of driving T cell expansion. When lymphodepleting regimens are used in these patients, it appears that CAR T cell expansion and activity is more significant and the likelihood of tumor cell escape, leading to a resistant cancer, is lowered. By contrast, in the autoimmune patient population, a target cell microenvironment does not exist to be modified by lymphodepletion. In addition, lymphodepletion may actually lead to an exacerbation of autoimmune and autoimmune like conditions due to the T cell regeneration process referred to as homeostatic proliferation, in which T cells can be stimulated in part by self-antigens.

7. *We note your disclosure on page 80 and on page 184 that your exclusive forum provision does not apply to actions arising under the Securities Act or the Exchange Act. Please also ensure that the exclusive forum provision in the bylaws (as effective on the closing of the offering) states this clearly, or tell us how you will inform investors in future filings that the provision does not apply to any actions arising under the Securities Act or Exchange Act.*

RESPONSE: The Company acknowledges the Staff's comment and respectfully advises the Staff that, following the closing of the offering, it intends to file a Form 8-K pursuant to Item 5.03 that will contain a summary of the Company's amended and restatedby-laws (the "**By-laws**"). Such summary will inform investors that the exclusive forum provision contained in the By-laws does not apply to any actions arising under the Securities Act or Exchange Act. The Company will file both the By-laws and its as filed Amended and Restated Certificate of Incorporation as exhibits to the Form 8-K.

8. *Please refer to the Risk Factor on page 36 which states that you expect to grow the size of your organization by expanding your employee base. Please explain, here and in the Use of Proceeds section on page 84, what portion of the proceeds of this offering you plan to spend on this endeavor, how long you expect that application of proceeds to last, or what additional source of funds you expect to use in growing your employee base.*

RESPONSE: The Company respectfully acknowledges the Staff's comment and will respond in a subsequent amendment to the Draft Registration Statement when it has more information regarding the size of the offering.

9. *Please revise your risk factor disclosure to address more specifically the fact that 88.7% of the company will be held by the current stockholders following the offering, and detail*

more clearly the dilutive impact on investors in this offering that the conversion of outstanding convertible notes, convertible preferred stock, and the exercise of outstanding stock options would have, or tell us why you believe this is not a material risk.

RESPONSE: The Company acknowledges the Staff's comment and has revised the disclosure on page 74 of Amendment No. 1 to detail the dilutive impact on investors in this offering of the conversion of outstanding convertible preferred stock and the exercise of outstanding stock options. The Company respectfully advises the Staff that the disclosure on page 74 of the Draft Registration Statement reflects that 88.7% of the Company's voting stock is held by its executive officers, directors and 5% stockholders prior to the offering, and the Company has revised its disclosure in Amendment No. 1 to reflect that a subsequent amendment will provide further detail on the percentage of the Company's voting stock to be held by such stockholders following completion of the offering.

Use of Proceeds, page 84

10. *Please revise to clarify whether you believe the net proceeds will be sufficient to complete the Phase 1 clinical trials for your four product candidates, and if not, how far into those trials you expect the proceeds to last.*

RESPONSE: The Company respectfully acknowledges the Staff's comment and will respond in a subsequent amendment to the Draft Registration Statement when it has more information about the size of the offering.

Management's Discussion and Analysis of Financial Condition and Results of Operations Components of Operating Results

Research and Development, page 95

11. *Please quantify the research and development expenses by types of costs incurred for each of the periods presented.*

RESPONSE: The Company respectfully acknowledges the Staff's comment and has revised the disclosure on pages 96 and 97 of Amendment No. 1 to quantify the research and development expenses by types of costs incurred for each of the periods presented.

Critical Accounting Policies and Significant Judgements and Estimates Stock-Based Compensation, page 103

12. *Once you have an estimated offering price or range, please explain to us the reasons for any differences between the recent valuations of your common stock leading up to the initial public offering and the estimated offering price. This information will help facilitate our review of your accounting for equity issuances including stock compensation and beneficial conversion features.*

RESPONSE: The Company respectfully acknowledges the Staff's comment and will supplementally provide the requested information once the estimated offering price or range has been determined.

Financial Statements

Statements of Operations, page F-4

13. *Please provide us your computation of weighted-average number of shares used in computing net loss per share for all periods presented. Also, tell us your consideration of disclosing in the financial statements how you determined weighted-average number of shares used in computing net loss per share.*

RESPONSE: The Company respectfully acknowledges the Staff's comment and has provided below a summarized computation of its weighted-average number of shares used in computing net loss per share for all periods presented. Further, the Company advises the Staff that it has revised the disclosure regarding the Company's calculation of basic and diluted net loss per share attributable to common stockholders on pages F-10, F-32 and F-33 in Amendment No. 1.

Cabaletta Bio, Inc.
Weighted Average Number of Shares Outstanding Calculation
For the Period from Inception to December 31, 2017

Date	Description	Shares	Cumulative Outstanding (excluding unvested)	Weighted Percent	Weighted Average Outstanding
04/03/17	Inception	—	—	51%	—
08/22/17	Issuance of common shares	4,183,250	4,183,250	34%	1,409,740
11/22/17	Vesting of common shares	204,187	4,387,437	15%	642,848
					2,052,588

Cabaletta Bio, Inc.
Weighted Average Number of Shares Outstanding Calculation
For the Year Ended December 31, 2018

Date	Description	Shares	Cumulative Outstanding (excluding unvested)	Weighted Percent	Weighted Average Outstanding
12/31/17	Shares outstanding at 12/31/17	4,387,437	4,387,437	13%	576,978
02/17/18	Vesting of common shares	3,156	4,390,593	1%	60,145
02/22/18	Vesting of common shares	204,187	4,594,780	20%	893,779
05/04/18	Amendment of vesting terms (1)	(3,130,874)	1,463,906	4%	52,139
05/17/18	Vesting of common shares	3,156	1,467,062	25%	369,780
08/17/18	Vesting of common shares	3,156	1,470,218	15%	217,512
10/10/18	Issuance of common shares	721,978	2,192,196	10%	228,229
11/17/18	Vesting of common shares	3,156	2,195,352	12%	264,645
					2,663,207

(1) As disclosed in Note 8 to the financial statements for the year ended December 31, 2018, in May 2018, 4,356,000 shares of common stock previously issued to the Founders were modified to include vesting provisions that require continued service to the Company. As a result, those unvested shares have been excluded from outstanding common stock in the computation of weighted-average shares outstanding and considered pursuant to the application of the two-class method described in ASC 260-10-45-61A. The reduction of 3,130,874 shares shown above represents the previously vested shares which became unvested upon modification.

Notes to the Financial Statements

6. Commitments and Contingencies

Operating Lease Agreement, page F-14

14. *Please tell us how you recognize rental expense for leases in which the rent varies from year to year.*

RESPONSE: The Company respectfully advises the Staff that it recognizes rental expense for leases in which the rent varies fromyear to year on a straight-line basis over the term of the respective lease agreement.

The Regents of the University of California, page F-15

15. *Please quantify the obligation you are committed to fund. If no such amount is defined in the contract, disclose the estimate of such obligations and whether there is a limit to such obligations.*

RESPONSE: The Company respectfully advises the Staff that the Company considers such obligation to be immaterial to the Company's financial statements prepared in conformity with GAAP, and further considers the amount of such obligation to be negotiated, competitively harmful information that is not material to an investment decision. The Company has therefore omitted the quantity of this obligation from its financial statements and has redacted it from the copy of the agreement filed as Exhibit 10.11 to Amendment No. 1 pursuant to the provisions of Rule 406 of the Securities Act and Regulation S-K, Item 601(10)(iv).

General

16. *Please provide us mockups of any pages that include any additional pictures or graphics to be presented, including any accompanying captions. Please keep in mind, in scheduling your printing and distribution of the preliminary prospectus, that we may have comments after our review of these materials.*

RESPONSE: The Company respectfully acknowledges the Staff's comment and informs the Staff that it has included an additional graphic on page 120 of Amendment No. 1. The Company informs the Staff that it does not intend to include any additional graphical materials or artwork in its prospectus.

* * * * *

Should you have any further comments or questions with regard to the foregoing, please contact the undersigned at (617)570-1021.

Sincerely,

/s/ Michael J. Minahan

Michael J. Minahan, Esq.

Enclosures:

cc: Steven Nichtberger, *Cabaletta Bio, Inc.*
Anup Marda, *Cabaletta Bio, Inc.*
Mitchell S. Bloom, *Goodwin Procter LLP*
Patrick O'Brien, *Ropes & Gray LLP*
Benjamin Kozik, *Ropes & Gray LLP*