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

DIVISION OF
CORPORATION FINANCE

December 19, 2023

Amit Etkin
Chief Executive Officer
Alto Neuroscience, Inc.
369 South San Antonio Road
Los Altos, CA 94022

Re: Alto Neuroscience, Inc.
Draft Registration Statement on Form S-1
Submitted November 22, 2023
CIK No. 0001999480

Dear Amit Etkin:

We have reviewed your draft registration statement and have the following comments.

Please respond to this letter by providing the requested information and either submitting an amended draft registration statement or publicly filing your registration statement on EDGAR. If you do not believe a comment applies to your facts and circumstances or do not believe an amendment is appropriate, please tell us why in your response.

After reviewing the information you provide in response to this letter and your amended draft registration statement or filed registration statement, we may have additional comments.

Draft Registration Statement on Form S-1 Submitted November 22, 2023

Prospectus Summary
Overview, page 1

1. Here and throughout the registration statement, please revise to disclose how you define "late-stage" or remove statements that any of your product candidates are in "late-stage" clinical trials, as these statements may imply that your products are farther along in the development process than they actually are.

2. We note that a key element of your strategy is to build and expand your pipeline of product candidates, including through your "differentiated biomarker-based approach" that relies heavily on insights derived from your proprietary Precision Psychiatry Platform (the "Platform"). Here and where appropriate throughout the prospectus, please expand your discussion of your Platform to describe how it was built and how it grows. For instance, discuss the scope of your data repository and explain whether lines of data are

added through third-party data sets or libraries. Also, address the "scalable" nature of your Platform. To the extent that the scalability of the Platform is currently aspirational, please so state.

3. Please balance your discussion of your Platform and biomarkers-based approach to matching potential drug responders with therapeutic product candidates. Explain that such approach is unproven and disclose, if true, that you anticipate that you will be required to develop and obtain FDA approval of a companion diagnostic for such therapeutic product candidates. Disclose whether or not you have had any conversations with or received any input from the FDA to date regarding the use of your Platform and/or your biomarkers-based approach to product development, and if so, describe the outcome of such discussions.

4. We note your statements of belief that your Platform-driven approach to developing therapeutics will enable you to improve upon the high failure rates of late-stage clinical trials and improve your product candidates' probability of clinical success. Please balance these and other statements in your Summary by prominently highlighting that:
   - your Platform is unproven and clinical evidence to support your approach is preliminary and limited at this time;
   - there can be no guarantee that your candidates will have an increased chance of approval.

   Make conforming revisions throughout, including in the Business section, as appropriate.

5. We note disclosure in the prospectus summary, in the section beginning on page 125, and in other places throughout the prospectus regarding your pursuit of a strategy to match patients to the right medication "quickly" or to quickly find patient populations more likely to respond to a particular product candidate. Please revise these and any similar disclosures throughout the prospectus to remove any implication that you will be successful in obtaining necessary regulatory approvals or commercializing your product candidates in a rapid or accelerated manner, as such statements are speculative given your current stage of development. You may state, if true, that your goal is to develop drug candidates more efficiently than current industry standards.

6. We note your disclosure at the end of the second paragraph on page 1 that you estimate one or both of two independent biomarkers are present in approximately three-quarters of the overall MDD population. We also note your disclosure in the table on page 2 that 30%-60% of patients are likely to be biomarker positive. Please revise your disclosure so that investors can better understand how to reconcile these different percentages.

Our Pipeline, page 3

7. It appears that your current pipeline consists of clinical-stage assets that have been acquired or in-licensed, and that in certain cases the originators of such candidates progressed your candidates through certain phases of clinical development. Please add footnotes to your pipeline table to show which columns relate to work conducted by the company and which, if any, relate to the work of third parties. Also, as appropriate, please

disclose where third party clinical trials were conducted and discuss any interaction the company has had with the FDA regarding its ability to rely on such trial data in the event any trials were not conducted in the United States.

8. To the extent that your product candidates were previously known by different names prior to being acquired or in-licensed by your company, please revise your disclosure to include these names.

9. We note that you disclose the potential timing of clinical trials you expect to initiate without addressing whether you have active INDs for your clinical-stage candidates in each indication you are studying. Please revise to clarify. If you do not have active INDs for each candidate and indication, please disclose when you plan to submit INDs.

10. With respect to your study of ALTO-100 for PTSD:
    - Please remove the reference in the pipeline table, and any other similar references throughout the prospectus, to ALTO-100 for PTSD being "Phase 2b/3 ready" to remove any implication that the FDA has signed off on a registrational trial for any of your product candidates in any indication.
    - If true, include a footnote to the table disclosing, as you have on page 4, that your plans to continue study of ALTO-100 for PTSD are dependent upon generating positive Phase 2b data from the ongoing trial of ALTO-100 for patients with MDD. Clarify that there is no guarantee that the results from the ongoing trial will be positive.

11. Please revise the narrative disclosure supporting the pipeline table appearing on pages 3 and 100 to support your statement that each of ALTO-101, ALTO-203 and ALTO-202 are "Phase 2 ready." In this regard, we note that it is unclear from your disclosure whether you have active INDs for your product candidates in the indications you state you are currently pursuing.

ALTO-101, page 5

12. Please revise this section to explain, if true, that ALTO-101 is being developed as a combination product due its patch formulation. Explain the implications of combination product status with respect to the regulatory approval process. Disclose whether or not you have had any conversations with or received any input from the FDA to date regarding the patch formulation of ALTO-101, and if so, describe the outcome of such discussions.

Other Pipeline Programs, page 5

13. We note that the prospectus contains minimal discussion of your ALTO-202 program, and as such, it is not clear why this program is sufficiently material to your current operations to warrant being highlighted in the pipeline table appearing on pages 3 and 100. To the extent that ALTO-202 is currently material to your business, please expand your

disclosure here and in your Business section to provide a more fulsome discussion of that program, including a description of development activities you have conducted to date, relevant clinical work conducted or in process, and the remaining steps to develop and commercialize the product. In this regard, your disclosure concerning clinical work should support the positioning of the progress arrow in your pipeline table.

Risk Factor Summary, page 6

14. We note your disclosure on page 145 that you have reformulated ALTO-101 in a transdermal patch formulation, as well as your disclosure on page 162 regarding the regulation of patch formulations of drugs as combination products in the United States. If material, please add summary risk and risk factor disclosure discussing any risks or challenges related to your development of ALTO-101 and/or the approval process if the FDA may consider ALTO-101 to be a drug/device combination product.

15. Consistent with your disclosure on page 153, please revise your summary risk and risk factor disclosure where appropriate to highlight that issued patents covering the composition of ALTO-100, one of your lead product candidates, are due to retire in 2024 and patents covering the method of its manufacturing are due to expire in 2030.

16. We note your disclosure on page 148 with respect to the license agreement with Stanford University that your rights under the Licensed Patents are exclusive until December 2029, at which time it will become non-exclusive, and that your rights under the Licensed Technology are non-exclusive. Please include related disclosure in your risk factor summary and risk factor disclosure.

Our amended and restated certificate of incorporation will provide..., page 82

17. Since you state that the exclusive forum provision will apply to claims under the Securities Act, please revise here and in the Choice of Forum section on page 211 to state that investors cannot waive compliance with the federal securities laws and the rules and regulations thereunder. In that regard, we note that Section 22 of the Securities Act creates concurrent jurisdiction for federal and state courts over all suits brought to enforce any duty or liability created by the Securities Act or the rules and regulations thereunder.

Capitalization, page 93

18. Please revise to include your term loan as shown on your September 30, 2023 balance sheet at F-35 as part of your capitalization table. Also revise to double-underline your cash and cash equivalent balance so it is clear that cash and cash equivalent is not part of your total capitalization.

Business
Our Team, page 123

19. We note the references to your "scientific advisory board." If material, please include disclosure in the appropriate section or sections of your prospectus that:
    - Describes the role or function of your scientific advisory board;
    - Describes the composition of such board; and
    - Describes the material provisions of any advisory contracts between advisory board members and the Company, including how such board members are compensated. In this regard, we note disclosure on page 69 that seemingly indicates that you have entered into advisory agreements with certain physicians who are paid, in part, in the form of stock or stock options.

Our Differentiated Approach and Capabilities, page 125

20. You state: "We believe developing product candidates for biomarker-characterized patient populations and likely drug responders could improve efficacy within such populations, enabling us to conduct smaller more cost-efficient trials without sacrificing statistical power." Please place this and any similar statements in context by disclosing that the FDA or other regulatory authorities may disagree with your clinical trial designs and interpretation of data or may not permit you to reduce the number of patients required. Please also revise to clarify whether the FDA has permitted you to reduce the number of patients in your currently active trials.

Methodical Approach to Curate Product Candidates, page 126

21. Conclusions regarding the safety or efficacy of your drug candidates are solely within the authority of the FDA and comparable regulatory bodies. As such, please remove or revise the following statement on page 126, and any similar statements throughout: "We have focused on acquiring or in-licensing novel chemical entities with favorable safety results, clear biological rationale, and preliminary pharmacodynamic data indicative of potential efficacy in biomarker-characterized patient groups."

Our Approach to Biomarker Discovery and Managing Development Risk, page 128

22. You state that to power your biomarker approach, you run larger trials than typical Phase 1 or Phase 2a trials for CNS product candidates. Revise to provide examples of the size of completed Phase 1 or Phase 2a trials you have conducted for your product candidates as well as the "typical" size of such trials for CNS product candidates.

23. Please revise the graphic on page 128 as follows:
    - Define references to "bio +," "bio -," and "PBO; and
    - In right-most column labeled "Phase 2B/3," please revise the reference to "establish efficacy in Bio +" and to "Efficacy: Drug > PBO in Bio+" to remove any implication that your process for discovery and development will demonstrate the efficacy of any of your product candidates. In this regard, we note that determinations of efficacy are solely within the authority of the FDA or equivalent foreign regulator.

2) Biomarker Validation - "Test" Data, page 129

24. You state: "We believe the independent prospective validation not only directly demonstrates the robustness of the biomarkers we identify, but also increases the probability of success for our pivotal clinical development plan, representing substantially more knowledge about a product candidate than is typical at that stage of CNS drug development." Please explain what you mean by "pivotal clinical development plan" and explain the basis for your belief. Where appropriate, disclose whether or not you have discussed your clinical study plans and designs with the FDA, and if so, describe the outcome of such discussions.

Our Product Candidates
ALTO-100
Data from Prior ALTO-100 Clinical Trials in MDD, page 130

25. Please revise this section to explain who completed the multiple preclinical models of ALTO-100 referenced on page 132. Also, please identify the "originator" that studied ALTO-100 in two previous clinical trials for patients with MDD, when such trials were completed, and disclose the primary and secondary endpoints of such studies as well as the results as they relate to those endpoints.

ALTO-101, page 143

26. You state on page 143 that ALTO-101 has been studied across multiple Phase 1 trials, in which the product candidate demonstrated human brain penetration and was well tolerated. Please revise to clarify the number of such prior Phase 1 trials conducted by third parties, and when such trials were conducted.

ALTO-101 Phase 1 Clinical Data, page 144

27. It appears based on your disclosure that prior to your acquisition of ALTO-101, this product candidate was studied in a human positron emission tomography study and a total of nine Phase 1 trials involving healthy subjects and Parkinson's disease patients. Please revise to explain whether you intend to rely on such prior PET study and Phase 1 clinical trial data to support your trial design for your intended Phase 2 proof-of-concept trial in which you plan to evaluate ALTO-101 for patients with cognitive impairment associated with schizophrenia, or CIAS.

28. Please revise your graphics on page 145, and any other tables or graphics throughout your filing where appropriate, to ensure that the text in each, including subscript or other notations are clearly legible.

29. We note that you are collaborating with MedRX to reformulate ALTO-101 from its initial oral delivery method and are currently conducting a second Phase 1 trial in healthy human subjects studying transdermally delivered ALTO-101. You state on page 145 that you observed successful transdermal drug delivery at the desired concentrations in mini-

pig studies. Please revise to present more detailed information regarding these animal studies, such as the number of animal models used, the number of tests conducted, the range of results or effects observed in these tests and how such results were measured. Alternatively, explain to us why this disclosure would not be material.

ALTO-203, page 146

30. Please revise this section to:
- Identify the "originator" that studied ALTO-203 in prior Phase 1 trials, disclose the number of prior Phase 1 trials conducted, disclose the indication(s) for which ALTO-203 was studied in such trials, and when such trials were conducted.
- Revise to present more detailed information regarding the originator's preclinical study of dopamine release with ALTO-203 referenced on page 147, such as the date(s) of the studies, scope and size, dosage and duration, and the range of results or effects observed in these tests and how such results were measured. Alternatively, explain to us why this disclosure would not be material.
- Explain whether you intend to rely on the originator's preclinical and/or prior Phase 1 clinical trial data to support your trial design for your intended Phase 2 proof-of-concept trial in which you plan to evaluate ALTO-203 for patients with MDD and higher levels of anhedonia.

License and Other Agreements, page 148

31. We note your disclosure that unless terminated earlier, the license agreements with Sanofi, Cerecor and MedRx will expire with respect to each licensed product, on a country-by-country basis, upon the expiration of a Royalty Term. Here and in the section beginning on page 101, please revise to clarify when the patents underlying such Royalty Terms are expected to expire. Likewise, revise to clarify when the patents underlying the royalty term under the Teva Asset Purchase Agreement are expected to expire.

License Agreement with Sanofi, page 149

32. We note your disclosure that if you achieve regulatory approval for one or more Licensed Products, you will owe Sanofi certain commercial milestone payments for the achievement of specified levels of aggregate, annual worldwide net sales of all Licensed Products, up to an aggregate amount in the "very low triple digit millions for all Licensed Products." Please quantify the potential aggregate payments for commercial milestones.

Teva Asset Purchase Agreement, page 151

33. We note your disclosure that if you successfully achieve regulatory approval, then beginning with first commercial sale, on a Product-by-Product and country-by-country basis, you will be required pay Teva tiered royalties on worldwide annual net sales of Products at percentages ranging from the mid-single-digit to the very low-double-digits. Please revise your description of this royalty range so that the upper bound of the range is

more specific.

Product Candidate Patent Portfolio, page 153

34. Please include a discussion of the patents and patent applications related to ALTO-202, including whether such patents or patent applications cover composition of matter of ALTO-202.

ALTO-101, page 154

35. Please disclose the jurisdiction in which you co-own one pending foreign priority patent application with MedRx that is directed to an ALTO-101 formulation.

Principal Stockholders, page 203

36. Please revise your disclosure to identify the natural person(s) who have sole or shared voting or investment power for the securities beneficially owned by entities affiliated with Aperion Investment Group Ltd., entities affiliated with Lightswitch Capital, and Alpha Wave Venutres II, LP.

Notes to the Audited Consolidated Financial Statements
9. Asset Purchase and License Agreements, page F-19

37. For each agreement, including the MedRx agreement entered into in September 2023, please revise to separately disclose the milestone payments the company may be required to make, broken down by the nature of the milestone such as development, regulatory, and commercial. Also, please quantify the annual license fee you will be required to pay under the Stanford license agreement.

Unaudited Condensed Consolidated Financial Statements as of and for the Nine Months Ended September 30, 2023 and 2022
Note 2. Summary of Significant Accounting Policies and Basis of Presentation
6. Stock Based Plans, page F-46

38. Once you have an estimated offering price or range, please explain to us how you determined the fair value of the common stock underlying your equity issuances and the reasons for any differences between the recent valuations of your common stock leading up to the IPO and the estimated offering price. This information will help facilitate our review of your accounting for equity issuances. Please discuss with the staff how to submit your response.

General

39. 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, have presented or expect to present to potential investors in reliance on Section 5(d) of the

Securities Act, whether or not they retain copies of the communications.

Please contact Li Xiao at 202-551-4391 or Mary Mast at 202-551-3613 if you have questions regarding comments on the financial statements and related matters. Please contact Lauren Hamill at 303-844-1008 or Tim Buchmiller at 202-551-3635 with any other questions.

Sincerely,

Division of Corporation Finance
Office of Life Sciences

cc: Divakar Gupta