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

DIVISION OF
CORPORATION FINANCE

June 25, 2021

James Porter
Chief Executive Officer
Nuvalent, Inc.
One Broadway, 14th Floor
Cambridge, MA 02142

Re: Nuvalent, Inc.
Draft Registration Statement on Form S-1
Submitted May 28, 2021
CIK No. 0001861560

Dear Dr. Porter:

We have reviewed your draft registration statement and have the following comments. In some of our comments, we may ask you to provide us with information so we may better understand your disclosure.

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 our comments apply 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 these comments and your amended draft registration statement or filed registration statement, we may have additional comments.

Draft Registration Statement on Form S-1 submitted May 28, 2021

Overview, page 1

1. Please revise this opening paragraph to explain that your operations are preclinical.

2. Please clarify the meaning and significance of scientific or technical terms the first time they are used in order to ensure that lay readers will understand the disclosure. For example, please briefly explain the meaning of kinase targets, ROS1-positive and ALK-positive cancers, brain metastasis, as well as the significance of optimizing brain penetrance and solvent-front mutations.

3. We refer to your disclosure that your therapeutic programs are focused on certain clinically proven kinase targets. Please revise to clarify that such kinase targets have been developed and clinically proven by third parties, and to the extent known, please identify such third parties.

4. Please remove all references to "Phase 1/2" clinical trials throughout the prospectus and instead reference either phase 1, 2, or 3 distinctly or tell us the basis for your belief that have been approved to conduct a Phase 1/2 trial.

5. We note your statement on pages 3, 118, 130 and elsewhere in the prospectus that your lead product candidates are “potential best-in-class product candidate[s].” The term “best-in-class” suggests that the product candidates are effective and likely to be approved as a therapy for the treatment of NSCLC and other advanced cancers. Given the early stage of development of NVL-520 and NVL-655, it is not appropriate to suggest that this product is likely to be effective or receive regulatory approval. Please delete these references throughout your registration statement.

Our pipeline of novel, highly selective kinase inhibitor product candidates, page 3

6. Please revise your pipeline table on pages 3 and 117 to include separate columns for Phase 2 and 3 trials.

Our team, page 4

7. We note that you identify certain entities as investors in your company on page 5; however, some do not appear to be among your principal stockholders as disclosed on page 196. If material, please expand your disclosure to describe the nature of each named entity's investment in you and explain to us why including this information is appropriate. Please also explain in your response your plans to update investors about any changes these entities make with respect to their investments in the company.

Our Strategy, page 5

8. We note your disclosure under the first bullet point on pages 5 and 120 that you plan to “rapidly advance” your two lead product candidates (NVL-520 and NVL-655) through clinical development and regulatory approval. Please revise these statements and any similar disclosure to remove any implication that you will be successful in advancing your product candidates in a rapid or accelerated manner as such statements are speculative.

Risks associated with our business, page 6

9. Please add a bullet highlighting the risks related to the concentration of ownership of your common stock, as discussed on page 81. Please include in this bullet and in the corresponding risk factor beginning on page 81 a discussion of the number of your executive officers and directors who are affiliated with your principal stockholders.

Use of Proceeds, page 92

10. Please revise your disclosure to indicate how far the proceeds from the offering will allow you to proceed with continued development of each program referenced.

Management's Discussion and Analysis of Financial Condition and Results of Operations
Critical accounting policies and significant judgments and estimates
Stock-based compensation, page 112

11. Once you have an estimated offering price range, please explain to us the reasons for any differences between recent valuations of your common stock leading up to the planned offering and the midpoint of your estimated offering price range. This information will facilitate our review of your accounting for stock compensation and beneficial conversion features. Please discuss with the Staff how to submit your response.

Our solution: NVL-520, a ROS1-selective inhibitor, page 129

12. On page 129 and elsewhere you discuss your observation of NVL-520 to be a "potent, highly selective, and brain-penetrant ROS1 inhibitor." As safety and efficacy determinations are solely within the FDA's authority and they continue to be evaluated throughout all phases of clinical trials, please remove these and any similar references in your prospectus. You may present objective data resulting from your pre-clinical trials without including conclusions related to efficacy.

13. We note your comparison of NVL-520 and NVL-655 to other inhibitors on pages 130 and 140. As you have not conducted head-to-head clinical trials, please tell us why you believe it is appropriate to include these comparisons. Include in your response whether you expect to be able to rely on this data to support an application for marketing approval from the FDA or comparable regulatory body for commercialization of NVL-520 and NVL-655.

Preclinical results, page 130

14. For each of the preclinical trials discussed in this section and your preclinical results discussion starting on page 140, please revise to clarify scope, size, and design; whether the studies were powered to show statistical significance; and revise your characterizations of the pre-clinical trials to discuss the data, rather than drawing conclusions from the results. Please also explain the different color coding used in Figure 7, as well as Figure 15 and Figure 16.

Competitors, page 147

15. We refer to your disclosure on page 148 that there are no approved therapies for second-line treatment of ROS1-positive NSCLC and that your NVL-520 product candidate has a differentiated profile compared to TRK treatments. Please expand your disclosure to discuss how your NVL-520 is differentiated from other first-line treatments that do not appear to be TRK-based, such as crizotinib and entrectinib.

16. You disclose on page 149 that while there are five currently approved ALK inhibitors for the treatment of NSCLC, none have been approved for third-line treatment for NSCLC. Please clarify if any ALK inhibitors have been approved as second-line treatments and also expand your disclosure, where applicable, relating to the differences in the first, second and third-line treatments and the criteria used in their approval process.

Intellectual Property, page 149

17. Please disclose the expected expiration and applicable jurisdiction of the patent applications for your ROS1, ALK and ErbB programs.

Agreements with our stockholders, page 194

18. We note your disclosure of your revenue sharing agreements with Deerfield and Dr. Matthew Shair. Please expand your disclosure to include the termination provisions, when the last-to-expire patent is scheduled to expire, the aggregate future milestone payments to be paid and the amounts of any upfront fees, as applicable. Please also include similar disclosure in the Business section.

General

19. Please provide us with supplemental 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 you retained, or intend to retain, copies of those communications.

You may contact Franklin Wyman at 202-551-3660 or Kevin Vaughn at 202-551-3494 if you have questions regarding comments on the financial statements and related matters. Please contact Jane Park at 202-551-7439 or Jeffrey Gabor at 202-551-2544 with any other questions.

Sincerely,

Division of Corporation Finance
Office of Life Sciences

cc: Sarah Ashfaq