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

DIVISION OF
CORPORATION FINANCE

Mail Stop 4720

May 27, 2016

Dinesh V. Patel, Ph.D.
President and Chief Executive Officer
Protagonist Therapeutics, Inc.
521 Cottonwood Drive, Suite 100
Milpitas, California 95035

Re: Protagonist Therapeutics, Inc.
Draft Registration Statement on Form S-1
Submitted May 3, 2016
CIK No. 0001377121

Dear Dr. Patel:

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.

Prospectus Summary, page 1

Overview, page 1

1. We note your statement that your primary focus is on developing drugs that "specifically target biological pathways that have been clinically validated through U.S. Food and Drug Administration (FDA) approved injectable antibody drugs." As currently drafted, this statement could imply that the FDA has approved, or will more easily approve, your products. Although your drugs may target certain pathways that have been used by other drugs, we note that your drug is still distinct from prior drugs that have been approved by the FDA. While it is appropriate to say that you are using a similar pathway to help guide your

development program, please revise your disclosure to remove any implication that your product candidates are more likely to receive FDA approval than others. Please also remove the statement that you have a "de-risked and differentiated competitive advantage." Please make similar revisions throughout your prospectus, including in your Business section, as necessary.

2. At first use, please define any significant scientific or technical terms in order for a lay investor to understand. As examples, please define the terms "integrin specific antagonist peptid," "hepcidin mimetic," and "cytokine."

3. Please tell us why you believe that your product candidates are "best-in-class" and "first-in-class."

4. The table of your pipeline product candidates on pages 2 and 82 should reflect the actual, and not the anticipated, status of your pipeline candidates as of the latest practicable date. The table currently suggests that PTG-100 has completed Phase 1 testing but your disclosure says that the Phase 1 testing is still ongoing. Similarly, the table suggests that both PTG-200 and PTG-300 have completed preclinical studies, when your disclosure states that both candidates are still in preclinical. Please also revise the table to reflect the difference in stages of PTG-200 and PTG-300, as the table currently indicates that they are equal. Finally, please remove the "undisclosed agonist" from the table. The table is intended to provide information about actual products. Unless an indication and a compound have been identified, the product is too preliminary for inclusion in the table.

5. We note your reference to Entyvio both here and in your business section. Please tell us whether you are using data from Entyvio as part of your IND submission and whether you have any agreements with the company to use this data. If you are not using this data, please clearly state what specifically you are using from Entyvio and how it impacts your development of PTG-100. In addition, please remove your statement that you can "de-risk" the development of PTG-100 by leveraging the regulatory path of Entyvio, and your statement on page 90 that your targeted approval for IBD has been "validated" by the 2014 FDA approval of Entyvio. Please also revise your disclosure throughout to remove any implication that the safety and efficacy results for Entyvio mean that you will have similar safety and efficacy results for PTG-100.

6. On page 94 your state that you utilized a liquid formulation in your Phase 1 clinical trial but will introduce a capsule formulation in your Phase 2b clinical trial. We note that you plan to conduct a bridging study to evaluate the bioavailability of the capsule formulation versus the liquid formulation. Your current disclosure states that you plan to file an IND by the end of the third quarter of 2016 for Phase 2b trials and that you plan to utilize a capsule formulation. Please tell us whether you will be able to rely on your Phase 1 results given that they were conducted using a liquid formulation and whether you are still on track to file an IND by the end of the third quarter.

7. In the first bullet point under "Risks Related to Our Business" please quantify your operating losses for the most recent fiscal year and your total accumulated deficit.

Risk Factors, page 12

8. We note that your restated certificate of incorporation includes an exclusive forum provision. Please add a risk factor to disclose that such a provision may limit a shareholder's ability to bring a claim in a judicial forum that it finds favorable for disputes, and may discourage lawsuits with respect to such claims against the company and its officers, directors or other employees.

Risks Related to Our Intellectual Property, page 37

9. The risk factors throughout this section suggest that you have multiple issued patents. However, we note that the disclosure on page 104 indicates that you only have one issued patent. Please revise your disclosure throughout this section to reflect this fact.

Management's Discussion and Analysis of Financial Condition and Results of Operations
Critical Accounting Policies and Estimates
Stock-Based Compensation, page 73

10. We may have additional comments on your accounting for equity issuances including stock compensation and beneficial conversion features. Once you have an estimated offering price, please provide us an analysis explaining the reasons for the differences between recent valuations of your common stock leading up to the IPO and the estimated offering price.

Contractual Obligations and Other Commitments, page 78

11. Please include in the table the milestone amounts due by type of event (i.e. development, regulatory, sales) under the Research Collaboration and License Agreement with Zealand Pharma A/S discussed under Material Agreements on page 102.

Business, page 81

PTG-100: An Oral α4β7 Integrin Antagonist, page 89

PTG-100's Pre-Clinical Proof-of-Concept Studies, page 91

12. Please expand your narrative discussion of Tables 1 and 2 to explain the meaning of all undefined scientific terms and measurements. Please also explain what the numeric results in the table indicate.

13. At first use, please provide a brief explanation of the abbreviation "nd" for a lay investor to understand.

14. At first use, please provide a brief explanation of the term "p-value" and how it is used to measure statistical significance. Please also explain the relevance of statistical significance to the FDA's evidentiary standards for drug approval.

PTG-100's Non-GLP and GLP Safety Pharmacology and Toxicology Studies, page 93

15. Please provide a brief explanation of the term "GLP" at first use.

PTG-100's Phase 1 Clinical Trial Overview, page 93

16. We note that you have initiated a Phase 1 clinical trial of PTG-100 in Australia following the submission and approval of a CTN. We also note your statements throughout the prospectus indicating that you intend to initially obtain marketing approval for PTG-100 in the United States. Please explain your reason for commencing clinical trials in Australia, rather than in the United States.

17. Please provide a brief explanation of what the results under the column labeled "AUC" in Table 5 indicate.

PTG-200's Pre-Clinical Proof-of-Concept Studies, page 96

18. Please expand your narrative discussion of Table 6 to explain the meaning of all undefined scientific terms and measurements. Please also explain what the numeric results in the table indicate.

19. Please expand your narrative discussion of Figure 8 to explain the results displayed in each graphic in more detail. For example, please provide a brief explanation of "macroscopic score," what it measures and what your results demonstrate.

Our Peptide Technology Platform, page 99

20. We note your statement that your "proprietary technology platform has been successfully applied to a diverse set of biological targets that has led to several pre-clinical and clinical-stage peptide-based NCEs…" Please revise this language to clearly indicate that you have only one clinical-stage product candidate at this point.

Material Agreements
Research Collaboration and License Agreement with Zealand Pharma A/S, page 102

21. We note that "the agreement continues in effect until [you] are no longer entitled to any financial benefit under the agreement." Please disclose the financial benefits that you are entitled to under this agreement.

22. Please disclose the royalty term under this agreement.

Competition, page 102

23. To the extent known, please disclose the stage of development of competing product candidates.

General

24. 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.

You may contact Tabatha McCullom at (202) 551-3658 or James Rosenberg at (202) 551-3679 if you have questions regarding comments on the financial statements and related matters. Please contact Christina Thomas at (202) 551-3577 or Erin Jaskot at (202) 551-3442 with any other questions.

Sincerely,

/s/ Erin K. Jaskot, *for*

Suzanne Hayes
Assistant Director
Office of Healthcare and Insurance

cc: Michael E. Tenta
Cooley LLP