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

DIVISION OF
CORPORATION FINANCE

January 17, 2013

Via E-mail
William Lis
President and Chief Executive Officer
Portola Pharmaceuticals, Inc.
207 E. Grand Avenue
South San Francisco, CA 94080

Re: Portola Pharmaceuticals, Inc.
Confidential Draft Registration Statement on Form S-1
Submitted December 21, 2012
CIK 0001269021

Dear Mr. Lis:

We have reviewed your confidential 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 confidential 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 confidential draft registration statement or filed registration statement, we may have additional comments.

FORM S-1
General

1. 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. Similarly, please supplementally provide us with any research reports about you that are published or distributed in reliance upon Section 2(a)(3) of the Securities Act of 1933 added by Section 105(a) of the Jumpstart Our Business Startups Act by any broker or dealer that is participating or will participate in your offering

2. We note that you have submitted a number of confidential treatment requests in relation to certain agreements you intend to file by amendment to the registration agreement. Please

note that you will be receiving comments to the confidential treatment requests under separate cover and that all confidential treatment issues must be resolved before we will consider a request for acceleration of the registration statement. Please file these agreements and all other exhibits as soon as possible.

3. Please note that when you file a pre-effective amendment containing pricing-related information, we may have additional comments. As you are likely aware, you must file this amendment prior to circulating the prospectus. Please note that when you file a pre-effective amendment that includes your price range, it must be bone fide. We interpret this to mean that your range may not exceed $2 if you price below $10 and 20% if you price above $10.

4. Please provide us proofs of all graphic, visual or photographic information you will provide in the printed prospectus prior to its use, for example in a preliminary prospectus. Please note that we may have comments regarding this material.

Prospectus Summary, page 1

5. You disclose that, if approved, you intend to commercialize Betrixaban and PRT4445 in the United States and possibly other major markets. We note that on pages 2, 89-90, and elsewhere throughout the filing, you provide an estimate of acute medically ill patients in the G7 countries for whom VTE prophylaxis was appropriate. We also note on pages 2, 90, and elsewhere throughout the filing, you provide estimates of the worldwide sales of enoxaparin for the use of acute medically ill patients. If true, please confirm that you intend to develop Betrixaban in all of the G7 countries and on a worldwide basis and consistently revise your disclosures. Alternatively, please revise your disclosure throughout the filing to limit your estimates to the markets in which you intend to develop Betrixaban. Similarly, based on your disclosure on pages 3, 84, and elsewhere throughout the filing, if true, please confirm that you intend to develop PRT4445 on a worldwide basis and consistently revise your disclosures. Alternatively, please revise your disclosure throughout the filing to limit your estimates to the markets in which you intend to develop PRT4445.

6. Please state whether the research you have performed and the discoveries you have made concerning Betrixaban provides conclusive evidence that there is substantial risk of VTE in acute medically ill patients with restricted mobility and whether your product candidate can demonstrate both safety and efficacy in extended duration VTE prophylaxis in acute medically ill patients both in the hospital and after discharge. If controversy remains in the scientific community as to any of your hypotheses, you should amend your disclosure to note this and to discuss any potential ramifications, particularly how these uncertainties cast doubt upon the possibility of developing Betrixaban. Any such controversy should also be addressed wherever else appropriate in your registration statement, including the relevant risk factors and your Business section. Similarly, please revise your disclosure

concerning PRT4445 and whether you have conclusive evidence that PRT4445is a universal reversal agent for all Factor Xa inhibitors.

7. On pages 2 and 84, we note that you provide one example of a study that demonstrated that the incidence of VTE-related death increased over several weeks after hospital discharge. Please revise your disclosure on pages 2 and 84 to disclose the number of trials that you are aware of on this topic and the range of the results from the studies. In addition, on page 86, please expand your disclosure to describe the results of each of the studies and each of the sponsors of the studies. Alternatively, please provide us with your analysis that the two studies summarized on page 86 adequately reflect the results of each of the trials that you are aware of on this topic. Please similarly revise your disclosure on page 93.

8. Please expand your disclose on page 2 to disclose that in March 2011 Merck chose to terminate your exclusive worldwide license and collaboration agreement for the development and commercialization of Betrixaban, effective September 30, 2011. To the extent you are aware, please also expand your Business section to disclose any material negative events, findings or results of Betrixaban or another competitive product that may have preceded this termination.

Our Strategy, page 4

9. Please expand your disclosure to clarify that PRT4445 has not yet been approved for an expedited development and approval process.

Risk Factors

Risks Related to the Development and Commercialization of our Product Candidates , page 14

"If clinical studies of our product candidates fail…" page 15

10. Please explain what is meant by the Phase 2 studies not being "sufficiently powered" to demonstrate statistically significant effectiveness.

11. This risk factor appears to disclose two different material risks. Accordingly, please revise your disclosure to discuss the risk of the FDA potentially requiring a second adequate and well-controlled clinical study in connection with your NDA for Betrixaban for extended duration VTE prophylaxis in acute medically ill patients even if you have positive results from your APEX study in a separately headed risk factor.

"If serious adverse side effects are identified…" page 17

12. Please expand your disclosure to disclose any known undesirable side effects or adverse effects that have been associated with your potential product candidates in addition to the

risk of life-threatening bleeding which all currently marketed inhibitors of Factor Xa carry.

13. We note that you disclose in this risk factor that a serious adverse effect has been identified for Betrixaban and this serious adverse effect caused a competitor's Factor Xa inhibitor to fail a Phase 3 trial for the indication you are pursuing. This appears to be a material risk that should be discussed in a separately headed risk factor. In addition, please expand your disclosure on page 5 to note this serious adverse effect.

"Delays in the enrollment of patients…" page 17

14. Please expand your disclosure in this risk factor and on page 98 to disclose the number of patients currently enrolled in your APEX study.

Risks Related to our Reliance on Third Parties, page 23

"We rely on third parties to conduct our clinical studies…" page 23

15. Please disclose here whether you are substantially dependent on any of the third parties that currently conduct your clinical development activities. If so, here and in the Business section, please identify the party, describe the material terms of any contract with such party and file any related agreements as exhibits to your filing.

"We intend to rely on third-party contract manufacturing…" page 24

16. Please disclose here whether you are substantially dependent on any third party manufacturers or single source suppliers for manufacture and supply of drug product for your clinical studies. If so, here and in the Business section, please identify the party, describe the material terms of any contract with such party and file any related agreements as exhibits to your filing.

Risks Related to the Operation of Our Business, page 27

"Requirements associated with being a public company will increase…" page 28

17. Please include in this risk factor an estimate of the annual compliance costs you will incur as a result of your reporting obligations as a public company.

"We are an emerging growth company…" page 29

18. As you did on page 5 of the Summary, please cite here the circumstances that would cause you to lose emerging growth company status earlier than five years.

Risks Related to Intellectual Property, page 30

"If we fail to comply with our obligations…" page 30

19. Please state whether you have to date materially complied with the terms of your intellectual property license agreements with third parties. State whether any third party has given you notice of non-compliance or its intent to terminate the agreement.

"Third parties may initiate legal proceedings…" page 32

20. Please expand your disclosure to explain the impact of the USPTO's decision to grant priority to U.S. Application No. 12/203,640 on your business and your licensed patent rights.

"We may be subject to claims that our employees have wrongfully used…" page 33

21. Please state how many employees total and how many of your executives are currently subject to non-disclosure agreements or related arrangements with prior employers.

Market, Industry and Other Data, page 47

22. We note that you engaged Navigant Consulting, Inc. to provide research services, estimates and forecasts which you have summarized and attributed throughout this registration statement. Pursuant to Section 7(a) of the Securities Act and Securities Act Rule 436, please file the consent of Navigant Consulting, Inc. for each attributed statement in this registration statement. See also Securities Act Rules CDI Question 233.02.

23. Please note that it is not appropriate to state or imply that you do not have liability for the statements in your registration statement. The statements "they do not guarantee the accuracy or completeness of such information," "we have not independently verified market and industry data" and "neither this research nor these definitions have been verified by any independent source" appear to imply that you are not taking liability for the industry, market and other data included in your registration statement. Please delete these statements or include a statement specifically accepting liability for these statements.

Use of Proceeds, page 48

24. Based on your planned use of net proceeds from this offering and your existing cash, cash equivalents and investments, please expand your disclosure to disclose the stage of development that you expect to achieve for PRT4445. For example, do you expect the above funding to be sufficient to complete your Phase 2 proof-of-concept study?

25. Please expand your disclosure to provide a brief outline of each material capital expenditure and quantify the approximate amount of funding that will be used to fund each expenditure.

Management's Discussion and Analysis of Financial Condition and Results of Operations
Critical Accounting Policies and Significant Judgments and Estimates

Stock-based Compensation, page 68

26. Please tell us the names of the peer companies that you consider similar to you and why you consider these companies similar to you. Please continue to update your disclosures in the table on page 70 for any grants or equity issuances up until the time of effectiveness of your registration statement. Please note that once your filing includes an estimated offering price we may have further comments on stock compensation as well as your capitalization and dilution tables.

Business, page 83

27. Please name the prior companies at which your management team played a central role in discovering, developing and commercializing therapeutics in the area of thrombosis.

28. Please describe any formal collaboration agreements or arrangements with the academic institutions you describe on page 83. Further, if any such collaboration agreements or arrangements are material to your business, please include the material terms in the Business section and file the agreements as exhibits to your filing.

29. Please state on page 83, as you do elsewhere in the Business section, the name of the company that produces enoxaparin and state its commercial name.

30. Although you discuss this concept in detail later on in the Business section, please explain on page 84 what is meant by low renal clearance.

Product Candidates
Betrixaban

Established and Novel Anticoagulants, page 90

31. Please clarify here which other entities are developing the other novel agents and who is conducting the multiple Phase 3 clinical trials.

32. Please disclose whether you believe that any of the other novel agents are also continuing to seek approval for prophylactic use in the acute medically ill patient population.

Betrixaban Clinical Experience, page 94

33. For each study, please disclose whether or not the results were statistically significant. If a study had a statistically significant result, please disclose each of the relevant p-values.

34. For each study, please disclose all of the adverse effects that were observed in connection with Betrixaban.

35. Please explain to us supplementally why, in the nineteen Phase I studies referenced in the chart on page 95, the regimen tested was a twice daily dosing. It appears that one of the advantages you repeatedly cite of Betrixaban is the long half-life and ability to have once daily dosing. Please explain this discrepancy.

PRT4445

PRT4445 Preclinical Results, page 101

36. We note that you state that you have developed substantial evidence supporting the safety, efficacy and rapid activity of PRT4445. It appears that the substantial evidence is from human plasma and animals models. Please revise your disclosure to so clarify.

PRT4445 Clinical Results and Development Strategy, page 102

37. For your Phase I study and the observations in your ongoing Phase 2 study, please disclose all of the adverse effects that were observed in connection with PRT4445.

Collaboration with BMS and Pfizer, page 103

38. Please expand your disclosure here and on page 108 to disclose the amounts paid to date, the aggregate development fees due to you, and the termination provisions of the agreement.

Collaboration and License Agreements

Millennium Agreements, page 107

39. Please disclose a range for the royalty payments, not to exceed ten percent, related to your November 2003 and August 2004 agreements. In addition, please disclose the termination provisions of your August 2004 agreement.

Merck Agreement, page 107

40. Please confirm that Merck has returned all rights to Betrixaban to you and that there are no material obligations remaining under this agreement.

Biogen Agreement, page 108

41. Please disclose a range for the royalty payments, not to exceed ten percent, related to this agreement and all the termination provisions of the agreement.

Astellas Agreement, page 108

42. Please disclose a range for the royalty payments related to this agreement, not to exceed ten percent, the remaining aggregate milestone payments due under the agreement and the termination provisions of the agreement.

Novartis Agreement, page 109

43. Please confirm that Merck has returned all rights to Elinogrel to you and that there are no material obligations remaining under this agreement.

Executive Compensation, page 128

44. Please expand your disclosure to provide your executive compensation disclosure for your fiscal year ended December 31, 2012.

Certain Relationships and Related Party Transactions

Agreements with Global Blood Therapeutics, Inc. and MyoKardia, Inc., page 139

45. Please explain to us supplementally why these two agreements were deemed not material to the company. Provide us with the approximate dollar value of each contract and any other material terms.

Principal Stockholders, page 140

46. Please update the principal stockholders table to the most recent practicable date.

Financial Statements
Notes to Financial Statements
6. Collaboration and License Agreements
Biogen Idec, Inc. F-20

47. Please disclose how you determined and allocated the amount of consideration to the various deliverables identified in the Biogen agreement. Provide also provide us the computation that supports the revenue recognition of $37.1 million upon delivery of the license.

48. You disclose that your agreement provides for additional payments of up to $508.5 million based on the achievement of certain development and regulatory events. Please revise your disclosure to include a description of the significant development and regulatory milestones and the related contingent consideration as required by ASC 605-28-50-2.b. and include the disclosures required by ASC 605-28-50-2.c. and d.

14. Net Income (Loss) and Pro Forma Net Income per Share Attributable to Common Stockholders, page F-33

49. Please provide us the computations used to determine the value of noncumulative dividends on preferred stock and undistributed earnings allocated to participating securities at December 31, 2011 and September 30, 2012.

Unaudited Interim Condensed Financial Statements
Notes to Unaudited Interim Condensed Financial Statements
11. Subsequent events, page F-55

50. Please disclose how you intend to account for the three-way agreement entered into with Bristol-Myers Squibb Company and Pfizer Inc.

If you intend to respond to these comments with an amended draft registration statement, please submit it and any associated correspondence in accordance with the guidance we provide in the Division's October 11, 2012 announcement on the SEC website at http://www.sec.gov/divisions/corpfin/cfannouncements/drsfilingprocedures101512.htm.

Please keep in mind that we may publicly post filing review correspondence in accordance with our December 1, 2011 policy (http://www.sec.gov/divisions/corpfin/cfannouncements/edgarcorrespondence.htm). If you intend to use Rule 83 (17 CFR 200.83) to request confidential treatment of information in the correspondence you submit on EDGAR, please properly mark that information in each of your confidential submissions to us so we do not repeat or refer to that information in our comment letters to you.

You may contact Ibolya Ignat at (202) 551-3656 or Gus Rodriguez at (202) 551-3752 if you have questions regarding comments on the financial statements and related matters. Please contact Nandini Acharya at (202) 551-3495 or Jennifer Riegel at (202) 551-3575 with any other questions.

Sincerely,

/s/ Jennifer Riegel for

Jeffrey Riedler
Assistant Director

Via E-mail

cc: Kenneth L Guernsey, Esq.
Sally A. Kay, Esq.
Cooley LLP
101 California Street, 5th Floor
San Francisco, CA 94111