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

DIVISION OF
CORPORATION FINANCE

February 19, 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.
Amended No. 1 to
Confidential Draft Registration Statement on Form S-1
Submitted February 5, 2013
CIK 0001269021

Dear Mr. Lis:

We have reviewed your response letter and amended 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

Prospectus Summary, page 1

1. We have reviewed your response to prior comment 7. Please expand your disclosure on pages 2, 86 and 89 to identify the name of the studies referenced. In addition, on pages 2 and 86, you disclose that incidence of VTE-related death rose four-fold over several weeks after hospital discharge; however, on page 89, you disclose that the rate of VTE-related death for the 35-day period after hospital admission was a five-fold increase. Please revise your disclosure for consistency or explain the discrepancy.

Risks associated with our business, page 5

2. Please refer to our prior comment 13. Please include a bullet point on this page addressing the increased risk that your APEX trial for Betrixaban may fail to a potential risk of increased bleeding, as experienced by your competitors in similar clinical trials evaluating Factor Xa inhibitors for the same indication that you are pursing.

Risk Factors
Risks Related to the Development and Commercialization of our Product Candidates
"If clinical studies of our product candidates fail…" page 16

3. In response to prior comment 10, you disclose that the Phase 2 studies of Betrixaban did not include enough participants to demonstrate statistically significant effectiveness. Please expand your disclosure to state the number of participants in each Phase 2 trial and the number of participants that you believe is necessary to demonstrate statistically significant effectiveness.

"Delays in the enrollment of patients…" page 18

4. Please refer to our prior comment 14. It appears that the number of patients currently enrolled in your APEX study is material to investors, especially since you identify delays in enrollment as a potential risk factor. Please revise this risk factor and your Business section disclosure to include this information. It is unclear from your response how disclosure of this information would cause you competitive harm. Additionally, it does not appear that the inclusion of the number of patients currently enrolled would be misleading to investors and that potential investors would impart their own expectations regarding the pace at which enrollment might occur. You have made it clear that the study is unprecedented in size and scope for your company and that delay may occur. Given this context, it is even more significant to investors to know how many patients you have enrolled to date.

Market, Industry and Other Data, page 48

5. In response to prior comment 22, you state that you will be seeking confidential treatment of your original submission to redact all references to Navigant. Consistent with your filing obligations of under Section 106(a) of the Jumpstart Our Business Startups Act and Section 6 of the Securities Act of 1933, please advise us how you intend to request confidential treatment for the references to Navigant and when you intend to submit the redacted draft.

6. Please refer to our prior comment 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 statement "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 this statement or include a statement specifically accepting liability.

Business
Betrixaban
Betrixaban clinical experience, page 96

7. Please disclose that none of the results of your clinical trials have been statistically significant.

8. In addition to the side effects listed on page 97, you disclose on page 18 that subjects taking Betrixaban had an increased rate of gastrointestinal issues, such as diarrhea, nausea and vomiting. Please expand your disclosure here to also disclose these side effects.

PRT4445 Clinical Results and Development Strategy, page 104

Collaboration with BMS and Pfizer, page 105

9. Please refer to our prior comment 38. Please note that we believe that the termination provisions of a material agreement are material and required to be disclosed. Accordingly, please revise your disclosure to include the material terms of these provisions. Similarly, please disclose the aggregate development fees due to you. We are reviewing your related confidential treatment application and will evaluate your competitive harm analysis with respect to the amounts paid to date. We will issue any comments on the confidential treatment application separately.

Collaboration with Bayer and Janssen, page 105

10. Please file a copy of your agreement with Bayer and Janssen. Alternatively, please provide us with a detailed analysis which supports your belief that you are not substantially dependent on this agreement.

Collaboration and License Agreements, page 109

Millennium Agreements, page 109

11. Please refer to our prior comment 39. Please expand your disclosure to discuss the termination provisions of your August 2004 agreement.

Astellas Agreement, page 111

12. Please refer to our prior comment 42. Please disclose the remaining aggregate milestone payments due under the agreement.

Manufacturing, page 115

13. Please expand your disclosure in this section to describe your relationship with Hovione concerning the active pharmaceutical ingredient for Betrixaban.

Executive Compensation, page 131

14. We note your response to prior comment 44. Please revise the disclosure to include, in addition to the disclosure for fiscal year 2012, compensation paid during your fiscal year ended December 31, 2011 as was originally included in your draft registration statement. Please see Instruction 1 to Item 402(n) of Regulation S-K.

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 Jennifer Riegel at (202) 551-3575 with any other questions.

Sincerely,

/s/ Jennifer Riegel for

Jeffrey P. Riedler
Assistant Director

Via E-mail

cc: Kenneth L Guernsey, Esq.
Sally A. Kay, Esq.
Cooley LLP
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