Mail Stop 4720

September 3, 2009

Robert Forrester
Interim President and Chief Executive Officer
CombinatoRx, Incorporated
245 First Street, Third Floor
Cambridge, Massachusetts 02142

Re: CombinatoRx, Incorporated
Registration Statement on Form S-4
Filed August 7, 2009
File No. 333-161146
Annual Report on Form 10-K
Filed March 16, 2009
File No. 000-51171

Dear Mr. Forrester:

We have reviewed your filings and have the following comments. Where indicated, we think you should revise your document in response to these comments. If you disagree, we will consider your explanation as to why our comment is inapplicable or a revision is unnecessary. Please be as detailed as necessary in your explanation. In some of our comments, we may ask you to provide us with information so we may better understand your disclosure. After reviewing this information, we may raise additional comments.

Please understand that the purpose of our review process is to assist you in your compliance with the applicable disclosure requirements and to enhance the overall disclosure in your filing. We look forward to working with you in these respects. We welcome any questions you may have about our comments or any other aspect of our review. Feel free to call us at the telephone numbers listed at the end of this letter.

Registration Statement on Form S-4

General

1. It does not appear that you have fully complied with the disclosure requirements of Form S-4 regarding information concerning either the registrant or the company being acquired. For example, we note that you have omitted certain disclosure with respect to the registrant, including "Selected Financial Data" and "Quantitative and Quantitative Disclosure about Market Risk." We also note that you have omitted disclosure with respect to Neuromed, including "Selected Financial Data." As a smaller reporting company, the registrant must provide all of the information required by, and in accordance with, Item 14 of Form S-4. Refer to General Instruction B.1.a.(ii). With respect to Neuromed, the required disclosure is governed by Item 17 of Form S-4. Refer to General Instruction C.1.c. of Form S-4. Please revise your Form S-4 accordingly and provide the omitted information with your amendment. This also applies to all of the disclosure required by Item 18(a)(7)(i) through (iii), including disclosure concerning related persons with respect to each person who will serve as a director or executive officer of the surviving company.

2. We note your pending request for confidential treatment in connection with portions of certain exhibits to your registration statement. We are currently processing this request and will issue comments to you in a separate letter that will be forthcoming. Please be advised that we will not consider requests for acceleration of the effective date of the registration statement on Form S-4 until all issues with respect to the confidential treatment request have been resolved and a final disposition is given.

3. Please note that you are required to file with the Commission any written instructions, scripts, and outlines that will be used by any person that solicit proxies on behalf of the company through personal interviews, or telephone, and all other soliciting material that will be furnished to the security holders of the company.

4. Please note that where we provide examples to illustrate what we mean by our comments, they are examples and not complete lists. If our comments are applicable to portions of the filing that we have not cited as examples, please make the appropriate changes in accordance with our comments.

5. In light of the significant repetition of certain disclosures throughout the registration statement, please be advised that one or more of our comments may be applicable to multiple sections of the S-4. Please ensure that any revision you make to the registration statement in response to our comments is applied throughout the S-4 as necessary to maintain the consistency of your disclosures.

Questions and Answers about the Merger, page 2

General

6. Please include a question and response concerning who the principal stockholders of the combined company will be after the merger is consummated and their respective percentages of ownership.

Q: What is the Neuromed special equity incentive plan…, page 3

7. We note that, pursuant to the special equity incentive plan, certain officers and directors of Neuromed will be granted the right to receive restricted stock unit awards such that the shares underlying such awards represent "not more than an aggregate of 1.5%" of the deemed outstanding shares of common stock of the combined company. Please explain how the number of underlying shares is determined, how this number adjusts and the circumstances under which these former officers and directors will be entitled to the top-most aggregate percentage of 1.5%. In addition, please specify the officer and directors who will receive these grants.

Summary, page 14

8. Please avoid repeating information in your summary that you have already included in the Q&A. For this purpose, you should consider the Summary and Q&A to be constitute a single section of your prospectus. If necessary, you may wish to remove information from your Q&A that you discuss in the Summary. Please review and revise your entire Q&A and Summary with this comment in mind.

Risk Factors, page 31

General

9. Please include a risk factor discussing competitive pressures within your industry that reflects the issues discussed on pages 186-187.

"Ownership of CombinatRx common stock may be highly concentrated . . .," page 34

10. Please revise this risk factor to include details about the ownership of your common stock post-merger, including the identities of the individuals or entities who will have concentrated ownership and their percentages of ownership.

"We expect to incur significant costs in connection with the merger . . .," page 34

11. To the extent practicable, please estimate the transaction costs you have incurred to date and expect to incur in connection with the merger.

"Failure to retain key employees . . .," page 34

12. Please revise this risk factor to name the key employees to which you refer.

"We may experience significant delays in obtaining FDA approval of Exalgo . . .," page 37

13. Information in this risk factor appears to be duplicative of the content in the risk factor immediately preceding it. Please condense these risk factors to avoid redundancy in this section.

"The active pharmaceutical ingredients in CombinatoRx combination product candidates . . .," page 41

14. This risk factor is duplicative of the one immediately preceding it. Please condense the risk factors to avoid redundancy in this section.

"Because we have limited manufacturing experience, we depend on third-party manufacturers . . .," page 45

15. This risk factor and the one immediately preceding it could be combined, as there is considerable overlap in the respective discussions. Please condense them into one risk factor or provide us with an explanation as to why you feel they represent two separate risks.

"If we are not able to retain CombinatoRx's and Neuromed's current senior management team . . .," page 48

16. This risk factor could be combined with the one on page 31 entitled "Failure to retain key employees . . .," as there is considerable overlap between them. Please condense them into one risk factor or provide us with an explanation as to why you feel they represent two separate risks.

"The regulatory approval process is costly and lengthy . . .," page 50

17. This risk factor is duplicative of the first two under the heading "Risks Relating to Our Business." Please condense these risk factors to avoid redundancy in this section.

"Litigation or third-party claims of intellectual property infringement could require substantial time and money . . .," page 55

18. This risk factor could be combined with the one on page 48 entitled "We may be required to spend substantial time and money litigating . . .," as there is considerable overlap between them. Please condense them into one risk factor or provide us with an explanation as to why you feel they represent two separate risks.

"A sale of all or a portion of the CombinatoRx common stock held by CombinatoRx's largest shareholder . . .," page 58

19. This risk factor could be combined with the one on page 33 entitled "Future sales of common stock by existing CombinatoRx and Neuromed stockholders . . .," as there is considerable overlap between them. Please condense them into one risk factor or provide us with an explanation as to why you feel they represent two separate risks.

The Merger, page 69

General Description of the Merger, page 69

20. We refer to the table on page 70 that illustrates how the percentage of your shares to be distributed to former Neuromed stockholders fluctuates depending on the date of FDA approval of Exalgo. Please provide a footnote explaining how the percentage of shares underlying restricted stock awards to former Neuromed officers and directors is calculated in relation to the percentages for current Neuromed stockholders.

Allocation of Merger Consideration Among Neuromed US Stockholders, page 70

21. In your discussion of the Series F preference amount, please explain why the value of shares of the combined company to be distributed to the holders of Series F redeemable preferred at the closing and the value of these holders' shares subject to escrow will be 85% and 70%, respectively, of the volume-weighted average of the closing prices. You should also explain the effect on the number of shares to be received by valuing the shares at less than 100% of their volume-weighted average.

Background of the Merger, page 73

22. Please provide us supplementally with copies of any non-public information — documents, financial forecasts, projections and presentations — used by you and Neuromed in the merger negotiations and all the schedules and attachments to the

merger agreement that were not filed with the registration statement. We may have additional comments.

23. You state that Neuromed engaged in discussion with six entities other than CombinatoRx regarding a potential merger or sale transaction during the period from June 2008 through April 2009. Of the entities that opted to pursue further discussions with Neuromed, please provide additional information about the parties' negotiations and, to the extent you are aware of them, include the reasons the parties chose to discontinue the discussions.

24. Please revise your description of some of the preliminary meetings and merger negotiations to ensure that you consistently identify all of the directors, executive officers, counsel, and affiliates who were present at the various meetings or who participated in conference calls, etc. As an example, you should identify which board members were in attendance at the meetings of your board on November 12 and 17, 2008. Alternatively, if there were any board members not present at any of these meetings, you may provide this disclosure instead.

25. In addition, please revise this section as necessary to describe in greater detail the nature and substance of the deliberations conducted at the various meetings, what conclusions were drawn and what actions, if any, were resolved to be taken as a result, either formally or informally. The disclosure should provide both your and Neuromed's stockholders with an understanding of how, when and why the terms of the proposed transaction evolved during the course of these discussions. If the board received updates or considered various courses of action, these should be fleshed out.

26. Please disclose whether, at any of the meetings described, your board also discussed the potential adverse effects of a combination with Neuromed. If so, please disclose the nature of those discussions. If not, please disclose why not and disclose when discussions regarding potential adverse effects took place.

27. Please briefly describe the preliminary efficacy and safety results from the Phase 2 clinical trial of Synavive that was announced by you on October 6, 2008 and the results of the further analysis of the Synavive knee osteoarthritis data that were discussed at the October 23, 2008 and November 12, 2008 board meetings. In addition, please explain the relationship between the results of the Synavive analysis and the board's consideration, and consummation, of the organizational restructuring and recommendations to reduce headcount and preserve capital.

CombinatoRx's Reasons for the Merger, page 86

28. The list of uncertainties and risks considered by the your board must include all material considerations, yet the preface to the list and the last bullet of the list suggest there may be other risks associated with the combined company and the merger transaction that you have neglected to include here. Please revise to include all such material risks that were considered by the board or, alternatively, make clear that the disclosure of the material risks is an exhaustive list.

Interests of CombinatoRx's Executive Officers and Directors in the Merger, page 89

29. Please disclose the basis of Mr. Forrester's one-time $693,000 payment, including the governing agreement, the method of calculating the amount and the specific conditions upon which Mr. Forrester is entitled to such payment.

Opinion of CombinatoRx's Financial Advisor, page 90

30. Please supplementally provide us with copies of any materials prepared by Wedbush Morgan in connection with its fairness opinion, including, among other things, any "board books," drafts of fairness opinions provided to the board of directors, and any summaries of presentations made to the board of directors. We may have further comments on your disclosure once we have had the opportunity to review these materials.

31. Please disclose the total fees paid by you to Wedbush Morgan in connection with the preparation of this opinion and any other fees paid by you to this bank over the course of this fiscal year.

32. Please revise the second full paragraph under "Summary of Analyses" on page 92 to state that the summaries describe all analyses and examinations that Wedbush deems material to the opinion. As written, the sentence could suggest that only some of the material analyses and examinations are discussed.

33. With respect to the "Discounted Cash Flow Analysis," please disclose the basis for the assumed EBITDA multiples of 5.9x, 6.9x and 7.9x.

34. Also, for the benefit of your shareholders who may not be accredited investors, please explain the significance of a discount rate and how Wedbush Morgan derived the range of 30% to 50%. If this is a customary discount rate spectrum used for similarly situated companies in the biopharmaceutical industry, please state such.

Neuromed's Reasons for the Merger, page 94

35. On page 96, you state that one of the risks identified by Neuromed in deliberating on the merger included the substantial expenses to be incurred in connection with, and liabilities of CombinatoRx to be assumed following, the merger. Please describe the liabilities to which you refer.

36. The preface to the list of uncertainties and risks considered by the Neuromed board on page 96, and the last bullet of the list, suggest there may be other risks associated with the combined company and the merger transaction that you have neglected to include. However, you must include all material uncertainties and risks considered by the Neuromed board. Accordingly, please revise to include all such material risks that were considered by the board or, alternatively, make clear that the current disclosure of the material risks is an exhaustive list.

Interests of Neuromed's Executive Officers and Directors in the Merger, page 97

37. Please quantify the number of shares underlying the outstanding Neuromed stock options and, if practicable, the volume weighted exercise price of the options that will be accelerated in full in connection with the merger.

Opinion of Neuromed's Financial Advisor, page 97

38. Please supplementally provide us with copies of any materials prepared by Evans & Evans in connection with its fairness opinion, including, among other things, any "board books," draft of fairness opinions provided to the board of directors, and any summaries of presentations made to the board of directors. We may have further comments on your disclosure once we have had the opportunity to review these materials.

39. Please disclose the total fees paid by Neuromed to Evans & Evans, Inc. in connection with the preparation of this opinion and any other fees paid by it to this bank over the course of the fiscal year.

40. In the "Summary of Analyses" discussion beginning on page 101, please revise the second full paragraph to state that the summaries describe all analyses and examinations that Evans & Evans deems material to the opinion. As written, the sentence could suggest that only some of the material analyses and examinations are discussed.

41. In the "Guideline Public Company Analysis," please explain the criteria by which Evans & Evans selected the eight companies on page 102 for review and provide more specific information about the additional criteria, such as key financial ratios, by which it narrowed the list to four companies.

42. Also, please specify the MVIC/revenue multiple calculated by Evans & Evans for the four selected guideline companies and clarify how Evans & Evans derived the marketability discount of 12% that it applied to its valuation of CombinatoRx.

43. Please explain the method by which Evans & Evans weighted the two valuation approaches.

44. On page 103, please explain the "scenario-based" Discounted Cash Flow method employed by Evans & Evans in and describe the various scenarios considered and how these affected the analysis.

45. In addition, please disclose the source of the forecast debt-free cash flow applied by Evans & Evans and specify the risk-adjusted discount rate applied by Evans & Evans in its valuation of Neuromed.

46. Please disclose the range of values yielded for Neuromed as a result of the analysis undertaken by Evans & Evans.

47. Please explain the manner in which Evans & Evans considered the liquidity preference of the various classes of shares in its fairness analysis and how this impacted such analysis.

Material United States Federal Income Tax Consequences of the Merger, page 104

48. Please revise your disclosure to identify the name of the firm that delivered this tax opinion and provide a cross-reference to the short-form opinion included in your Exhibit Volume.

49. In this discussion, your counsel opines on the tax treatment of the merger under two different scenarios. In the first scenario, counsel opines that if the stock value of your common stock is equal to or greater than a certain price, the merger "should" qualify as a reorganization under Section 368(a) of the Internal Revenue Code. However, counsel must opine whether the merger will or will not qualify as a reorganization unless significant doubt exists under this scenario. Any equivocal language that undermines this opinion should be removed or changed to reflect this comment. Please revise this statement accordingly. If there is significant doubt as to the treatment of the merger in the first scenario, counsel must explain the reasons for this doubt and the degree of uncertainty in the

opinion and you should consider the necessity of risk factor and/or other appropriate disclosure setting forth the risks to investors.

50. Under the second scenario, where the stock value of your common stock is less than a certain price, counsel opines that it is unclear whether the merger will qualify as a reorganization. With respect to this scenario, the opinion must clearly state:

    a. that counsel is not able to opine on whether the merger will qualify as a reorganization;
    b. why counsel is not able to opine on that tax consequence if, for instance, the facts are currently unknown or the law is unclear and
    c. the possible outcomes and risks to investors of that tax consequence.

    In addition, you should consider the necessity of risk factor and/or other appropriate disclosure setting forth the risks to investors.

CombinatoRx's Business, page 165

51. In this discussion, you make certain statements without providing adequate support. In particular, you state that:

    a. "CombinatoRx is . . . pioneering the field of synergistic combination pharmaceuticals;" and

    b. "CombinatoRx uses . . . innovative drug discovery technology . . ."

    Please provide a basis for these statements or revise your disclosure to remove them. To the extent that this comment applies to similar statements in your "Summary" section, please revise that disclosure accordingly.

CombinatoRx Principal Stockholders, page 198

52. In your disclosure concerning your two beneficial stockholders who own greater than 5% of the outstanding shares, you do not identify the individual or individuals who exercise voting and/or dispositive power on behalf of these entities. Please revise your disclosure to include this information.

Neuromed's Business, page 201

Exalgo, page 201

53. With respect to Neuromed's June 2009 agreement with Mallinckrodt concerning the sale of sell all of the tangible and intangible assets associated with Exalgo, please clarify what is meant by "tiered" royalties. In addition, please disclose the potential range of royalty payments (for example, "low-single-digits" or "high-single-digits") and disclose the duration of these payments. If these are potentially indefinite, or if there is a termination date certain, please so state.

Neuromed Principal Stockholders, page 225

54. In your disclosure concerning Neuromed's 5% beneficial stockholders, you do not identify the individual or individuals who exercise voting and/or dispositive power on behalf of the investment funds affiliated with MPM Capital LLC and Growth Works Group. Please revise your disclosure to include this information.

Unaudited Pro Forma Condensed Combined Financial Information, page 277

55. Final clearance of the filing is pending the outcome of the determination of the accounting acquirer as detailed in your August 7, 2009 letter to Office of Chief Accountant.

56. Please revise the pro forma weighted average number of common shares to reflect the total shares issued that correlate to the preliminary estimated consideration transferred of $30,504.

Notes to Unaudited Pro Forma Condensed Combined Financial Statements

Note 4. Preliminary Estimate of Consideration Expected to be Transferred, page 284

57. Please disclose the calculation of the probability weighted assessment of the additional shares that could be issued to Neuromed shareholders that shows the probability assigned to each outcome.

Historical Financial Statements of CombinatoRx, Incorporated

For The Years Ended December 31, 2008

General

58. Please update the financial statements, including pro forma financial information, for CombinatoRx, Incorporated and Combined financial information of

Neuromed Pharmaceuticals, Inc. and Neuromed Pharmaceuticals Ltd in accordance with Rule 3-12 of Regulation S-X.

Consolidated Statements of Cash flows, page F-7

59. Please tell us why you have classified proceeds from landlord under tenant improvements within operating activities rather than financing activities. Please cite the authoritative literature used to reach your conclusion.

Historical Combined Financial Statements of Neuromed Pharmaceuticals, Inc. and Neuromed Pharmaceuticals Ltd

For The Years Ended December 31, 2008

Combined Statements of Operations, page F-42

60. Please revise this statement to include the line items "Accretion to redemption value of redeemable convertible preferred stock" and "Net Loss Attributable To Common Shareholders". Refer to SAB.T.3C and SAB.T.6B.

61. Please revise this statement to include Loss Per Share disclosures in accordance with SFAS 128 including Loss Per Share attributable to Common Shareholders.

Notes To Combined Financial Statements

3. Significant Accounting Policies

(O) Net Loss Per Common Share, page F-51

62. Please expand your Accounting Policy for Earnings (Loss) Per Share to include a detail the basis of your computations and quantify and describe anti-dilutive securities not included in your calculations.

9. Collaboration Agreements and Commitments, page F-65

(b) ALZA Agreement, page F-65

63. Your discussion of the agreement with ALZA includes references to payments that you will potentially make related to achievement of milestones and royalties. Please assess whether these milestone payments and royalties meet the criteria of a purchase obligation and if these milestone payments and royalties should be shown in the contractual obligations table under Item 303(a)(5) of Regulation S-K. Include explanatory footnotes to this table as necessary to provide the essential data needed to understand the timing and amount of your specified

contractual obligations as well as those obligations that have been excluded from the table. If as a result of that assessment, you do not include these payments in the table, please expand your liquidity and capital resources disclosures to discuss the amount and timing of event milestone and royalty commitments that are reasonably likely to be paid. Please refer to Section IV of Financial 72, section IV.

* * *

As appropriate, please amend your registration statement in response to these comments. You may wish to provide us with marked copies of the amendment to expedite our review. Please furnish a cover letter with your amendment that keys your responses to our comments and provides any requested information. Detailed cover letters greatly facilitate our review. Please understand that we may have additional comments after reviewing your amendment and responses to our comments.

We urge all persons who are responsible for the accuracy and adequacy of the disclosure in the filing to be certain that the filing includes all information required under the Securities Act of 1933 and that they have provided all information investors require for an informed investment decision. Since the company and its management are in possession of all facts relating to a company's disclosure, they are responsible for the accuracy and adequacy of the disclosures they have made.

Notwithstanding our comments, in the event the company requests acceleration of the effective date of the pending registration statement, it should furnish a letter, at the time of such request, acknowledging that:

- should the Commission or the staff, acting pursuant to delegated authority, declare the filing effective, it does not foreclose the Commission from taking any action with respect to the filing;

- the action of the Commission or the staff, acting pursuant to delegated authority, in declaring the filing effective, does not relieve the company from its full responsibility for the adequacy and accuracy of the disclosure in the filing; and

- the company may not assert staff comments and the declaration of effectiveness as a defense in any proceeding initiated by the Commission or any person under the federal securities laws of the United States.

In addition, please be advised that the Division of Enforcement has access to all information you provide to the staff of the Division of Corporation Finance in connection with our review of your filing or in response to our comments on your filing.

We will consider a written request for acceleration of the effective date of the registration statement as confirmation of the fact that those requesting acceleration are aware of their respective responsibilities under the Securities Act of 1933 and the Securities Exchange Act of 1934 as they relate to the proposed public offering of the securities specified in the above registration statement. We will act on the request and, pursuant to delegated authority, grant acceleration of the effective date.

We direct your attention to Rules 460 and 461 regarding requesting acceleration of a registration statement. Please allow adequate time after the filing of any amendment for further review before submitting a request for acceleration. Please provide this request at least two business days in advance of the requested effective date.

You may contact James Peklenk at (202) 551-3661 if you have questions regarding comments on the financial statements and related matters. Please contact Scot Foley at (202) 551-3383 or me at (202) 551- 3715 with any other questions.

Sincerely,

Jeffrey Riedler
Assistant Director

cc: Stuart M. Cable, Esq.
Joseph L. Johnson III, Esq.
Art McGivern, Esq.
Goodwin Procter LLP
53 State Street
Boston, Massachusetts 02109