

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

September 13, 2010

J. Donald deBethizy Chief Executive Officer and President Targacept, Inc. 200 East First Street, Suite 300 Winston-Salem, North Carolina 27101

Re: Targacept, Inc.

Form 10-K for the Fiscal Year Ended December 31, 2009

Filed March 11, 2010 File No. 000-51173

Definitive Proxy Statement Filed April 16, 2010

Dear Dr. deBethizy

We have reviewed your above referenced filings 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 within ten business days by providing the requested information, or by advising us when you will provide the requested response. If you do not believe our comments apply to your facts and circumstances, please tell us why in your response.

After reviewing the information you provide in response to these comments, we may have additional comments.

Form 10-K

License Agreements, page 23

- We note that you have entered into an exclusive license agreement with the University of South Florida Research Foundation in relation to TC-5214. Please provide proposed disclosure to be included in your Form 10-K for 2010 which includes the following information:
 - The annual license fee that must be paid until an NDA is filed for use of a product subject to the license to treat a neuropsychiatric disease or disorder; and
 - The annual license fee that must be paid to maintain a right of first refusal for license patents and applications beyond the scope of the current license.

J. Donald deBethizy Targacept, Inc. September 13, 2010 Page 2

- 2. We note that you have entered into an exclusive license agreement with Yale University in relation to TC-5214. Please provide proposed disclosure to be included in your Form 10-K for 2010 which includes the following information:
 - The issuance fee that must be paid upon the issuance of a licensed patent in the United States; and
 - The percentage of other amounts received from AstraZeneca or any other sublicensee of the licensed patent rights under the circumstances identified in your disclosure.

Definitive Proxy Statement

The Board's Role in Risk Oversight, page 15

3. We note that you have not included any disclosure in response to Item 402(s) of Regulation S-K. Please advise us of the basis for your conclusion that disclosure is not necessary and describe the process you undertook to reach that conclusion.

Cash Incentive Bonus, page 27

4. We note that performance objectives under your cash incentive bonus plan are ascribed a percentage weight totaling 135% in the aggregate. Please confirm that your Proxy Statement for 2010 will include the specific individual weighting for each performance objective used to determine the incentive compensation award for your Named Executive Officers.

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 the information the Securities Exchange Act of 1934 and all applicable Exchange Act rules require. 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.

In responding to our comments, please provide a written statement from the company acknowledging that:

- the company is responsible for the adequacy and accuracy of the disclosure in the filing;
- staff comments or changes to disclosure in response to staff comments do not foreclose the Commission from taking any action with respect to the filing; and
- the company may not assert staff comments as a defense in any proceeding initiated by the Commission or any person under the federal securities laws of the United States.

J. Donald deBethizy Targacept, Inc. September 13, 2010 Page 3

Please contact Bryan Pitko at (202) 551-3203 or Suzanne Hayes at (202) 551-3675 if you have any questions. In this regard, please also feel free to contact me at (202) 551-3715.

Sincerely,

Jeffrey Riedler Assistant Director