

[Letterhead of Targacept, Inc.]

September 23, 2010

Via EDGAR Submission

Securities and Exchange Commission
Division of Corporation Finance
100 F Street, N.E.
Washington, D.C. 20549

Attention: Mr. Jeffrey Riedler, Assistant Director

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

Ladies and Gentlemen:

This letter is submitted in response to comments contained in the letter dated September 13, 2010 from Jeffrey Riedler of the Staff (the "Staff") of the Securities and Exchange Commission (the "Commission") to J. Donald deBethizy, Chief Executive Officer and President of Targacept, Inc. (the "Company"), regarding the Company's Annual Report on Form 10-K for the fiscal year ended December 31, 2009 (the "2009 Form 10-K") and the Company's Definitive Proxy Statement filed on April 16, 2010 (the "Proxy Statement").

The comments and responses set forth below are keyed to the numbering of the comments and the headings used in the Staff's September 13, 2010 letter. Page numbers referred to in the responses below reference the applicable pages of the 2009 Form 10-K or Proxy Statement, as appropriate. Capitalized terms used but not otherwise defined herein have the meanings given them in the 2009 Form 10-K or Proxy Statement, as the case may be.

Form 10-K

License Agreements, page 23

Comment 1: *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.*

Response 1: The Company proposes to include the following disclosure in its Annual Report on Form 10-K for the fiscal year ending December 31, 2010 (the "2010 Form 10-K") in place of the corresponding bullet points (the first and second) under the heading "License Agreements — University of South Florida Research Foundation" on page 23 of the 2009 Form 10-K, with the remainder of the disclosure under that heading currently expected to remain substantially unchanged.

“• an annual license fee of \$50,000 until we or AstraZeneca or any future sublicensee files an NDA or foreign equivalent for use of a product subject to the license to treat a neuropsychiatric disease or disorder;

• an annual fee of \$20,000 to maintain our right of first refusal to acquire rights under the licensed patents and patent applications beyond the scope of our current license;”

Comment 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.*

Response 2: The Company proposes to include the following disclosure in its 2010 Form 10-K in place of the corresponding bullet points (the first and fourth) under the heading "License Agreements — Yale University" on pages 23 and 24 of the 2009 Form 10-K, with the remainder of the disclosure under that heading currently expected to remain substantially unchanged.

“• an issuance fee of \$50,000 that is conditional upon the issuance of a licensed patent in the United States that meets specified conditions;

...

• a specified percentage of other amounts received from any sublicensee of the licensed patent rights, if the applicable sublicense is not combined with a license to other patent rights owned or licensed by us that cover compounds or their therapeutic use in humans or with an agreement by us to collaborate to discover, research, develop or commercialize compounds or products for therapeutic use in humans. Because our sublicense to AstraZeneca under our 2009 agreement with AstraZeneca is combined with both a license to other patent rights and an agreement by us to co-develop TC-5214 as a treatment for major depressive disorder, no other amounts received from AstraZeneca under the agreement give rise to any payment obligation to Yale.”

The Company submits to the Staff supplementally that the specific percentage of “other” amounts that may be received by the Company from a sublicensee of the licensed patent rights and payable to Yale is not material because the only current sublicensee is AstraZeneca and, based on the terms of the Company’s 2009 agreement with AstraZeneca as noted above, the obligation should not apply to other amounts received from AstraZeneca. Moreover, the specific percentage constitutes confidential commercial information that is covered by a Commission Order Granting Confidential Treatment dated June 1, 2007 (File No. 0-51173 — CF#20030), the disclosure of which would cause the Company competitive harm by disadvantaging the Company in negotiations with potential future licensors, licensees or other collaborators.

Definitive Proxy Statement

The Board’s Role in Risk Oversight, page 15

Comment 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.*

Response 3: Pursuant to Item 402(s) of Regulation S-K, disclosure is required “[t]o the extent that risks arising from the registrant’s compensation policies and practices for its employees are reasonably likely to have a material adverse effect on the registrant.” The Company concluded that there were no risks meeting that standard and, accordingly, that no disclosure in response to Item 402(s) of Regulation S-K was necessary.

To reach such conclusion, the Compensation Committee of the Company’s Board of Directors considered the Company’s compensation programs, policies and practices as set forth under the heading “Executive Compensation — Compensation Discussion and Analysis” on pages 21-31 of the Proxy Statement and, specifically, the three elements of the Company’s compensation program utilized historically – base salary, annual cash incentive awards and stock options. In particular, the Compensation Committee met with the Company’s chief executive officer and general counsel to discuss whether any of these elements encouraged unnecessary or inappropriate risk taking or individual short-term enrichment at the expense of the Company’s long-term success. The consensus from that meeting was that only the annual cash incentive awards — because they are earned based substantially on the achievement of performance objectives that are pre-determined by the Compensation Committee at or around the beginning of a year, any of which could, at least theoretically, become during the year no longer in the best interest of the Company — could potentially present the risk contemplated by Item 402(s) of Regulation S-K. However, the Company does not believe that risk meets the standard requiring disclosure under Item 402(s) of Regulation S-K. Moreover, the Company believes that the discretion retained by the Compensation Committee to react to changing circumstances during a particular year eliminates any risk that might otherwise exist. As noted on page 28 of the Proxy Statement, “The Compensation Committee believes that the discretion that it retains to modify any performance objective during the year or to credit any performance objective that may not have been met for a particular reason (such as, for example, a strategic change that occurs during the year . . .) eliminates any risk that may be associated with a change in circumstances.”

Comment 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.

Response 4: The Company confirms that its proxy statement in connection with its 2011 annual meeting of stockholders will include the specific weight assigned to each performance objective used to determine the amount of the annual cash incentive bonus payable to its named executive officers for 2010, unless it has a reasoned basis to determine that the specific weights meet the standard for exclusion from disclosure set forth in Instruction 4 to Item 402(b) of Regulation S-K. If the Company does not disclose in its proxy statement in connection with its 2011 annual meeting of stockholders the weight assigned to one or more of its performance objectives in reliance on Instruction 4, the Company undertakes to provide the weight(s) to the Staff supplementally upon request.

The Company believes that the specific weights assigned to the performance objectives for any particular completed year may constitute confidential commercial information, the disclosure of which would result in competitive harm to the Company. For example, with respect to any particular performance objective, disclosure of the assigned weight could unfairly assist the Company's competitors by providing guidance for their own activities that would otherwise be confidential as to the relative strategic importance of specific Company research and development or other business initiatives or as to prioritization of Company resources or therapeutic focus, either of which could allow a competitor to modify its strategies to compete more effectively with the Company. In addition, disclosure of the weight assigned to any particular performance objective could adversely impact the Company's relationships with its strategic partners or collaborators, who may based on the assigned weights perceive that the particular product candidate or research program in which they are interested is inappropriately valued by the Company relative to other initiatives or that the Company is not sufficiently committed to their interest. As a result, such disclosure could damage important relationships, in extreme circumstances potentially even lead to litigation and hamper the Company in its efforts to secure similar arrangements in the future, any of which would constitute competitive harm to the Company.

Closing

The Company acknowledges that it is the view of the Commission that: (i) the Company is responsible for the adequacy and accuracy of the disclosure in the above-referenced filings; (ii) Staff comments or changes to disclosure in response to Staff comments do not foreclose the Commission from taking any action with respect to the above-referenced filings; and (iii) 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.

We hope that the above responses will be acceptable to the Staff. If you have any questions regarding the foregoing, please do not hesitate to call me at (336) 480-2115.

Sincerely,

/s/ Peter A. Zorn
Senior Vice President, Legal Affairs and General Counsel

cc: *Securities and Exchange Commission*
Mr. Bryan Pitko
Ms. Suzanne Hayes
Targacept, Inc.
J. Donald deBethizy, Ph.D.