[Letterhead of Targacept, Inc.]

December 11, 2007

Confidential Treatment Requested by Targacept, Inc.

Via EDGAR Submission

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

Attention: Jim B. Rosenberg, Senior Assistant Chief Accountant

Re: Targacept, Inc.
Form 10-K for the Year Ended December 31, 2006
Filed March 22, 2007
Form 10-Q for the Quarterly Period Ended September 30, 2007
Filed November 9, 2007
File No. 000-51173

Ladies and Gentlemen:

This letter is submitted in response to comments contained in the letter dated November 28, 2007 from Jim B. Rosenberg of the Staff (the "Staff") of the Securities and Exchange Commission (the "Commission") to Donald deBethizy, Chief Executive Officer and President of Targacept, Inc. (the "Company") regarding the Company's Form 10-K for the fiscal year ended December 31, 2006 (the "Form 10-K") and the Company's Form 10-Q for the quarterly period ended September 30, 2007 (the "Form 10-Q").

The comments and responses set forth below are keyed to the numbering of the comments and the headings used in the Staff's November 28, 2007 letter. Page numbers referred to in the responses below reference the applicable pages of the Form 10-K or Form 10-Q, as appropriate. Capitalized terms used but not otherwise defined herein have the meanings given them in the Form 10-K and Form 10-Q.

Form 10-K for the Year Ended December 31, 2006

Item 8. Financial Statements and Supplementary Data, page 75

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Comment 1: *Please tell us the facts and circumstances that determined the $20 million milestone to be (1) substantive; and (2) reasonable in relation to the effort expended, in accordance with your revenue recognition policy. As the $20 million milestone was paid to you merely upon AstraZeneca deciding to pursue development of AZD3480, tell us what consideration you gave to this milestone being in substance part of the "remaining $5 million of the initial fee" that was deferred.*

Response 1: As discussed below, the Company respectfully submits that each of the conditions of the Company's revenue recognition policy referenced by the Staff was satisfied with respect to the $20 million milestone received upon AstraZeneca's determination to proceed with further development of AZD3480 (sometimes referred to as TC-1734 or ispronicline).

The Company and AstraZeneca entered into their collaborative research and license agreement in December 2005, and the agreement became effective in January 2006. At the time of the agreement, the Company was conducting a Phase II clinical trial of AZD3480, the lead product candidate subject to the agreement, in age associated memory impairment, or AAMI, and it was understood by both parties that the Company would complete the AAMI trial independently. AAMI is a condition characterized by gradual memory loss or other cognitive impairment that generally occurs with normal aging.

Among other things, the terms of the agreement provided for:

- AstraZeneca to pay an initial fee of $10 million to the Company, which the Company allocated partially to the preclinical research collaboration described below and partially to license grants related to AZD3480;
- the Company and AstraZeneca to commence, upon effectiveness of the agreement, a preclinical research collaboration designed to identify and develop additional compounds that act on the same molecular target as AZD3480;
- AstraZeneca to conduct additional safety and product characterization studies of AZD3480 before making a determination whether to proceed with planned Phase II clinical trials to evaluate its efficacy in mild to moderate Alzheimer's disease and cognitive deficits in schizophrenia; and
- AstraZeneca to have the right, based on the results of AstraZeneca's additional safety and product characterization studies and all other available information with respect to AZD3480 (including the results of the Company's then-ongoing AAMI trial), to terminate the agreement by April 20, 2007 if it determined not to proceed with further development of AZD3480.

In December 2006, AstraZeneca communicated to the Company its determination to proceed with further development of AZD3480, triggering, among other things, a non-refundable $20 million milestone payment to the Company. The Company evaluated the accounting for the $20 million that it received from AstraZeneca under its revenue recognition policy, which provides that "revenue for non-refundable payments based on the achievement of research and development milestones is recognized as revenue when the milestones are achieved if all of the following conditions are met: (1) achievement of the milestone event was not reasonably assured at inception of the arrangement;

(2) substantive effort is involved to achieve the milestone event; and (3) the amount of the milestone payment appears reasonable in relation to the effort expended, the other milestone payments in the arrangement and the related risk associated with achievement of the milestone event."

The $20 million milestone payment clearly required substantive effort in order to be achieved. The Company received no funding from AstraZeneca to complete the then-ongoing AAMI trial and in fact completed the trial independently. In the trial, 193 subjects were enrolled and randomly assigned to one of two AZD3480 dose groups or to a placebo group. The Company completed the trial in March 2006 and achieved statistically significant results in favor of AZD3480 in one of the dose groups on all three of the trial's primary endpoints. In addition, AZD3480 was generally well tolerated in the trial as compared to placebo. The Company believes that these results provided AstraZeneca with strong evidence of the effects of AZD3480 in a cognitively-impaired population and contributed significantly to an overall profile that ultimately led to AstraZeneca's determination to proceed with further development of AZD3480 and not to terminate the agreement.

Moreover, AstraZeneca conducted additional safety and product characterization studies of AZD3480 at its own expense before making its determination to proceed with planned Phase II clinical trials. The safety and product characterization studies that AstraZeneca conducted consisted of:

- in vitro studies to assess whether AZD3480, when administered at a therapeutically relevant dose, activates a particular protein that can activate a particular enzyme known as CYP1A1;
- a clinical trial to characterize the cardiovascular effects of various doses of AZD3480 in persons who break down and eliminate, or metabolize, AZD3480 at varying rates;
- a single–dose study in dogs to further assess AZD3480's cardiovascular effects; and
- one or more clinical trials to evaluate the interaction and combined effects of AZD3480 with paroxetine, a known inhibitor of a key enzyme involved in AZD3480's primary metabolic pathway.

These studies collectively took most of 2006 to complete. Drug development is an inherently uncertain process and the likelihood of success of these particular studies was unknown. Unfavorable results from any one or more of them, or from the Company's AAMI trial, carried a significant risk of causing AstraZeneca to determine not to proceed with further development of AZD3480 and to terminate the agreement. Furthermore, AstraZeneca's willingness to invest its own financial resources to conduct the studies demonstrates its belief that the studies were required to substantiate the value of AZD3480 and support a determination to proceed with later-stage clinical trials and were therefore substantive.

AstraZeneca was required under the agreement to use commercially reasonable efforts to conduct its additional safety and product characterization studies during the period from effectiveness of the agreement until the date of its determination whether to proceed, but not later than April 20, 2007. The negotiated standard of diligence required for these studies demonstrates their import to AstraZeneca in support of whether to proceed with further development of AZD3480. Although AstraZeneca had to make a "decision" to proceed, its decision required the value that was

created (i.e., a milestone) by the results of such studies, as well as the Company's then-ongoing AAMI trial, over the period prior to its December 2006 determination rather than value that was known (or imminent) at the time of the agreement.

For all of the foregoing reasons, the Company believes that the $20 million milestone payment that it received upon AstraZeneca's determination to proceed with further development of AZD3480 was substantive.

In addition to being substantive, the amount of the $20 million milestone payment is, based on the research and development activities completed as described above, reasonable in relation to the effort expended. In essence, this payment corresponded to success in activities (the Company's AAMI trial and AstraZeneca's additional safety and product characterization studies) that provided sufficient additional support for AstraZeneca to invest resources in and proceed with two Phase II clinical trials (in mild to moderate Alzheimer's disease and cognitive deficits in schizophrenia, which are currently ongoing). For context, under the terms of the agreement, if the ongoing Phase II trials establish clinical proof of concept in either mild to moderate Alzheimer's disease or cognitive deficits in schizophrenia, the Company would be entitled to receive a [*******] milestone payment and, [*******] (which would [*******] if clinical proof of concept were established), another [*******] milestone payment. If AstraZeneca were also to [*******] of AZD3480 [*******], the Company would be entitled to receive an additional [*******] milestone payment. Taken together, these payments would total [*******] (or [*******] in the case of [*******]). Taking into account the relative effort that was expended and that would then have been expended, the reasonableness of the $20 million received by the Company based on activities to support proceeding with Phase II clinical trials is illustrated by comparison to the [*******] (or [*******]) that the Company would be entitled to receive based on [*******].

For the reasons described above, the Company considers the non-refundable $20 million milestone payment both (1) substantive and (2) reasonable in relation to the effort expended and, therefore, does not consider it to be in substance part of the "remaining $5 million of the initial fee." As additional support, in contrast to the $20 million milestone payment, the "remaining $5 million of the initial fee" constituted consideration for an exclusive license to patent rights covering AZD3480, as well as other related or useful intellectual property licenses. Accordingly, the Company is recognizing the $5 million as revenue over the development period of AZD3480, which is currently estimated to be five years from AstraZeneca's determination to proceed with further development. If, rather than electing to proceed with further development of AZD3480, AstraZeneca had instead terminated the agreement, the Company would have been required to pay AstraZeneca $5 million as compensation for an assignment of the data and any intellectual property generated in AstraZeneca's additional safety and product characterization studies, in which event the Company would have reduced its deferred revenue by $5 million.

Comment 2: *Please tell us why the maximum potential payment that may be received under your collaboration agreement with AstraZeneca AB of $249 million was not audited.*

Response 2: The Company was made aware by its independent registered public accounting firm that the disclosed amount of milestone payments for which the Company is eligible with respect to AZD3480 under the agreement with AstraZeneca had not been audited because the disclosure was forward looking and subject to future contingencies. Although the Company derived the amount based on the terms of the agreement and believed that the disclosure would provide users of the

financial statements with additional context regarding the scope of the agreement as related to AZD3480, neither the Company nor its independent registered public accounting firm believed that disclosure of the pro forma amount was necessary to fairly present the Company's financial position, operating results or cash flows for the periods reported. Consequently, in accordance with Statement of Auditing Standards (AU) section 508, paragraph 28, the Company's independent registered public accounting firm advised it to identify the amount as "unaudited." There was no disagreement between the Company and its independent registered public accounting firm regarding disclosure of the amount.

Form 10-Q for the Quarterly Period Ended September 30, 2007

4. Collaborative Research and License Agreements, page 10

AstraZeneca AB, page 10

Comment 3: *Please tell us, why under GAAP, you:*

- *deferred the preclinical research revenues prior to AstraZeneca's decision to pursue development of AZD3480; and*
- *recognized all the deferred amounts at the time of AstraZeneca's decision.*

Response 3: The Securities and Exchange Commission Staff Accounting Bulletin No. 101, *Revenue Recognition in Financial Statements*, as amended by Staff Accounting Bulletin No. 104, Revenue Recognition (*replacement of SAB 101*), Topic 13, requires an amount of revenue to be "fixed or determinable" in order to be recognized. Under the terms of the Company's agreement with AstraZeneca, if AstraZeneca had determined not to proceed with further development of AZD3480 following completion of its additional safety and product characterization studies (and the Company's then-ongoing AAMI trial) and terminated the agreement, the Company would have been obligated to refund all research fees that it had received from AstraZeneca during the period in which such studies were conducted. Because of the uncertain outcome of these studies, there was substantive risk that AstraZeneca would make a determination to terminate the agreement. As a result of the risk of refund, the amount of research fee revenue for the Company was neither fixed nor determinable until AstraZeneca made its determination not to terminate the agreement. As a result, all research fees received by the Company prior to AstraZeneca's determination were deferred. In December 2006, when AstraZeneca made its determination to continue the agreement, the deferred research fees became non-refundable and, accordingly, recognizable by the Company, as the research services had been performed and the related expenses incurred.

* * *

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. Thank you for your time and attention.

Sincerely,

/s/ Peter A. Zorn

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

cc: *Securities and Exchange Commission*
Ms. Kei Ino
Mr. Jim Atkinson

Targacept, Inc.
J. Donald deBethizy, Ph.D.