Targacept's TC-5214 Achieves All Primary and Secondary Outcome Measures in Phase 2b Trial as Augmentation Treatment for Major Depressive Disorder

- High Statistical Significance Achieved on HAM-D Scale ($p < 0.0001$) in 265 Patients -

Winston-Salem, North Carolina, July 15, 2009—Targacept, Inc. (NASDAQ: TRGT) today announced positive top-line results from a double blind, placebo controlled, flexible dose Phase 2b clinical trial of TC-5214 as an augmentation (add-on) treatment for major depressive disorder, or MDD, in subjects who did not respond adequately to first-line treatment with citalopram alone. The result on the primary outcome measure for the trial, mean change between treatment (TC-5214 + citalopram) and placebo (placebo + citalopram) from baseline on the Hamilton Rating Scale for Depression-17, or HAM-D, was highly statistically significant in favor of TC-5214 ($p < 0.0001$) on an intent to treat basis. The results on all of the trial's secondary efficacy measures, including assessments of depression, irritability, disability, cognition, severity of illness and global improvement, were also highly statistically significant in favor of TC-5214 on an intent to treat basis.

"The magnitude and consistency of the effect of TC-5214 seen in this trial could represent a major breakthrough for patients with depression," said Dr. Madhukar H. Trivedi, Professor and the Director of the Mood Disorders Research Program and Clinic at the University of Texas Southwestern Medical Center at Dallas, one of the principal investigators for the trial and Co-Principal Investigator in the National Institute of Mental Health's large-scale STAR*D study. "It is particularly compelling that the superiority of TC-5214 as augmentation to citalopram over citalopram alone was first seen after only two weeks and grew steadily over the trial's last six weeks, culminating in remission for twice as many subjects in the TC-5214 group."

TC-5214 exhibited a favorable tolerability profile in the trial. The most frequent adverse events were headache, dizziness and constipation. There was no clinically significant difference between the dose groups in discontinuations due to adverse events. There was one serious adverse event in the trial considered by the investigators to be related to study drug (citalopram and/or TC-5214), a seizure experienced by a study subject.

"The strong results from this Phase 2b augmentation trial support the potential of TC-5214 to provide much needed help for the millions of depressed patients who do not respond adequately to currently available therapies," said Geoffrey C. Dunbar, M.D., Targacept's Vice President, Clinical Development and Regulatory Affairs. "This is the second time our clinical trials have shown antidepressant effects of this NNR mechanism. We are particularly enthusiastic about the finding in this study on irritability, which is a core symptom of MDD that is often difficult to treat."

Next Steps
Targacept plans to present detailed results from the Phase 2b trial of TC-5214 at the Society for Neuroscience meeting scheduled for October 2009 in Chicago, Illinois.

Targacept is active in discussions with multiple pharmaceutical companies with the goal of identifying a strategic partner to assist in the global development and planned commercialization of TC-5214. Targacept expects Phase 3 clinical development to be initiated in the second quarter of 2010, following planned discussions with FDA and production of clinical trial material.

Study Design
The Phase 2b trial of TC-5214 as an augmentation treatment for MDD was a two-phase study conducted at 20 sites in India and three sites in the United States. In the first phase, 579 subjects with MDD received first-line treatment with citalopram hydrobromide for eight weeks, 20mg daily for the first four weeks and 40mg daily for the next four weeks. Citalopram, an approved treatment for MDD marketed in the United States as Celexa®, is from the drug class known as selective serotonin reuptake inhibitors. At the end of the eight weeks, subjects whose Montgomery-Asberg Depression Rating Scale score had improved less than 50 percent and was no lower than 17 and whose Clinical Global Impression - Severity of Illness score was no lower than 4 were considered partial or non responders and randomized into the double blind second phase of the trial.

In the double blind second phase, subjects continued their citalopram treatment and also received either add-on TC-5214 or add-on placebo for an additional eight weeks. The daily dosage of TC-5214 was initially 2mg and could be increased at the discretion of the investigator to 4mg and to 8mg based on tolerability and therapeutic response. The primary outcome measure for the trial was mean change between treatment (TC-5214 + citalopram) and placebo (placebo + citalopram) from double blind baseline as measured by HAM-D at week 16. The intent to treat dataset included 265 subjects in the second phase.

About TC-5214
It is well known that depressive symptoms can result from an overstimulation of NNRs and other receptors in the brain that are activated by the neurotransmitter acetylcholine. Accordingly, compounds capable of inhibiting the activity of these overstimulated receptors may be expected to have antidepressant effects. TC-5214 is a nicotinic channel blocker that has unique properties in modulating the alpha4beta2 NNR subtype.

About Major Depressive Disorder
MDD is a serious mental illness characterized by one or more major depressive episodes. According to The National Institute of Mental Health, or NIMH, MDD is the leading cause of disability in the United States for people between the ages 15 and 44, and NIMH estimates that approximately 14.8 million American adults suffer from MDD.

In 2000, the total economic burden of treating depression in the United States was approximately $83.1 billion, with workplace costs, including missed days and lack of productivity due to illness, accounting for approximately 62% of the total economic

burden, treatment costs accounting for approximately 31% and suicide-related costs accounting for approximately 7%.[1]

The Sequenced Treatment Alternatives to Relieve Depression, or STAR*D, study undertaken by NIMH between 2001 and 2006 highlighted the inadequacy of currently available therapies for MDD. Approximately 63% of participants in the study did not achieve remission following initial treatment with citalopram alone. The study showed that augmentation therapies may be useful in the treatment of symptoms of depression that do not resolve with first-line treatment.[2]

About Targacept

Targacept is a clinical-stage biopharmaceutical company that discovers and develops NNR Therapeutics™, a new class of drugs for the treatment of central nervous system diseases and disorders. Targacept's product candidates selectively modulate neuronal nicotinic receptors that serve as key regulators of the nervous system to promote therapeutic effects and limit adverse side effects. Targacept has product candidates in development for major depressive disorder and resistant hypertension, attention deficit/hyperactivity disorder, Alzheimer's disease and cognitive dysfunction in schizophrenia, as well as multiple preclinical programs. Targacept also has a cognition-focused collaboration with AstraZeneca and a strategic alliance with GlaxoSmithKline. Targacept's news releases are available on its website at www.targacept.com.

Forward-Looking Statements

Statements in this press release that are not purely historical in nature constitute "forward-looking statements" made under the provisions of the Private Securities Litigation Reform Act of 1995. Forward-looking statements include, without limitation, statements regarding future development or commercialization of TC-5214, including the timing for initiation of Phase 3 clinical development, a strategic partnership with respect to TC-5214, the benefits that may be derived from TC-5214, or Targacept's plans, expectations or future operations, financial position, revenues, costs or expenses. Actual results may differ materially from those expressed or implied by forward-looking statements as a result of various important factors, including, without limitation, risks and uncertainties relating to: Targacept's ability to establish a strategic alliance, collaboration or licensing or other arrangement with respect to TC-5214 on favorable terms; Targacept's reliance on third parties for the manufacture of clinical trial material for future development of TC-5214; and the timing and success of submission, acceptance and approval of regulatory filings. These and other risks and uncertainties are described in greater detail under the heading "Risk Factors" in Targacept's most recent Annual Report on Form 10-K and in other filings that it makes with the Securities and Exchange Commission. As a result of the risks and uncertainties, the results or events indicated by

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[1]Michaud, McKenna, Begg, *et al.* The burden of disease and injury in the United States 1996. Population Health Metrics. 2006; 4:11.

[2]Rush, Trivedi, Wisniewski, *et al.* Acute and Longer-Term Outcomes in Depressed Outpatients Requiring One or Several Treatment Steps: A STAR*D Report. *American Journal of Psychiatry*. November 2006; 163:1905-1917.

the forward-looking statements may not occur. Targacept cautions you not to place undue reliance on any forward-looking statement.

In addition, any forward-looking statement in this press release represents Targacept's views only as of the date of this press release and should not be relied upon as representing its views as of any subsequent date. Targacept disclaims any obligation to update any forward-looking statement, except as required by applicable law.

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