

---

---

**UNITED STATES  
SECURITIES AND EXCHANGE COMMISSION**  
Washington, D.C. 20549

---

**FORM 8-K**

---

**CURRENT REPORT**

**Pursuant to Section 13 or 15(d) of the Securities Exchange Act of 1934**

**Date of Report (Date of earliest event reported): October 15, 2009**

---

**TARGACEPT, INC.**

(Exact name of registrant as specified in its charter)

---

**Delaware**  
(State or other jurisdiction  
of incorporation)

**000-51173**  
(Commission File Number)

**56-2020050**  
(IRS Employer  
Identification No.)

**200 East First Street, Suite 300**  
**Winston-Salem, North Carolina**  
(Address of principal executive offices)

**27101**  
(Zip Code)

**(336) 480-2100**  
Registrant's telephone number, including area code

---

Check the appropriate box below if the Form 8-K filing is intended to simultaneously satisfy the filing obligation of the registrant under any of the following provisions:

- Written communications pursuant to Rule 425 under the Securities Act (17 CFR 230.425)
  - Soliciting material pursuant to Rule 14a-12 under the Exchange Act (17 CFR 240.14a-12)
  - Pre-commencement communications pursuant to Rule 14d-2(b) under the Exchange Act (17 CFR 240.14d-2(b))
  - Pre-commencement communications pursuant to Rule 13e-4(c) under the Exchange Act (17 CFR 240.13e-4(c))
- 
-

**Item 8.01. Other Events.**

On October 15, 2009, Geoffrey C. Dunbar, M.D., Vice President, Clinical Development and Regulatory Affairs of Targacept, Inc. ("Targacept"), presented data from Targacept's completed Phase 2b clinical trial of TC-5214 as an augmentation treatment for major depressive disorder at the Nicotinic Acetylcholine Receptors as Therapeutic Targets Symposium (the "Symposium"), a satellite meeting of the 39th annual meeting of the Society for Neuroscience. The slide presentation made at the Symposium by Dr. Dunbar is attached to this Current Report on Form 8-K as Exhibit 99.1. A related press release issued by Targacept is attached to this Current Report on Form 8-K as Exhibit 99.2.

**Item 9.01. Financial Statements and Exhibits.**

(d) Exhibits

The following exhibits are filed with this report:

<u>Exhibit Number</u>	<u>Description</u>
99.1	Slide presentation made at the Nicotinic Acetylcholine Receptors as Therapeutic Targets Symposium on October 15, 2009
99.2	Press release dated October 15, 2009

**SIGNATURES**

Pursuant to the requirements of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned hereunto duly authorized.

**TARGACEPT, INC.**

Date: October 15, 2009

/s/ PETER A. ZORN

---

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

**EXHIBIT INDEX**

Exhibit Number

Description

99.1	Slide presentation made at the Nicotinic Acetylcholine Receptors as Therapeutic Targets Symposium on October 15, 2009
99.2	Press release dated October 15, 2009



***Positive effects of the nicotinic channel blocker ~~bTC-5214~~ as augmentation treatment in patients with major depressive disorder who are inadequate responders to a first-line SSR***

Geoffrey C. Dunbar, M.D.  
*Targacept*

# Cautionary Note re: Forward-Looking Statements



This presentation includes “forward-looking statements” made under the provisions of the Private Securities Litigation Reform Act of 1995. Forward-looking statements include, without limitation, statements that are not purely historical in nature regarding: the progress, scope or duration of the development of TC-5214, such as the size, design, conduct or objective of any clinical trial of TC-5214, the timing for initiation or completion of or availability of results from any clinical trial of TC-5214 or for submission or approval of any regulatory filing regarding TC-5214, or the indication(s) for which TC-5214 may be developed; the benefits that may be derived from TC-5214; or our plans, expectations, objectives, prospects or future operations, financial position, revenues, costs or expenses. The words “may,” “will,” “could,” “would,” “should,” “expect,” “intend,” “plan,” “anticipate,” “believe,” “estimate,” “predict,” “project,” “potential,” “continue,” “ongoing,” “scheduled” and similar expressions are intended to identify forward-looking statements. Actual results, performance or experience may differ materially from those expressed or implied by any forward-looking statement as a result of various important factors, including our critical accounting policies and the risks and uncertainties described under the heading “Risk Factors” in our most recent Annual Report on Form 10-K, in our subsequent Quarterly Reports on Form 10-Q and in other filings that we make with the Securities and Exchange Commission. As a result of the risks and uncertainties, the results or events indicated by the forward-looking statements may not occur.

All forward-looking statements speak only as of the date this presentation is made and should not be relied upon as representing our views as of any date after this presentation is made. We specifically disclaim any obligation to update any forward-looking statement, except as required by applicable law.

# Large Unmet Medical Need for Depressed Patients not Responding Adequately to First-line Antidepressants



## STAR★D

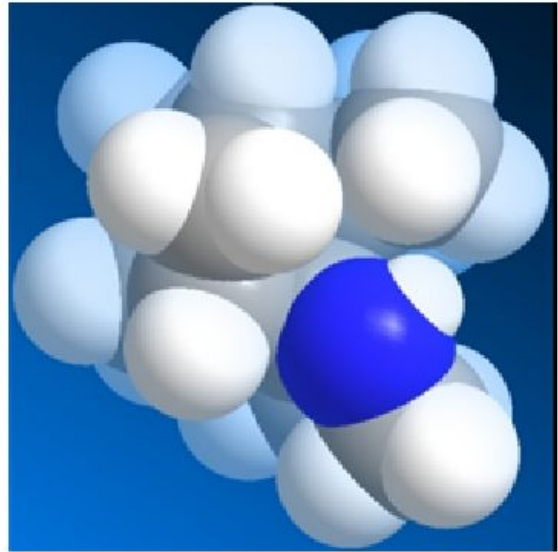
Sequenced Treatment Alternatives to Relieve Depression

- STAR★D study (Funded by NIMH – studied 3,671 “real world” patients)
  - **Step 1:** Tested effectiveness of first-line treatments for remission
    - Only 36.8% (QIDS<sup>1</sup>) patients in remission after 12 weeks of treatment with citalopram
  - **Step 2:** Tested switching vs. augmentation to achieve remission
    - Switch – 27% (QIDS<sup>1</sup>) and 21% (HAM-D<sup>2</sup>)
    - Augment – 35% (QIDS<sup>1</sup>) and 30% (HAM-D<sup>3</sup>)
- **The results suggest that augmentation may be more effective than switching**

<sup>1</sup> Rush et al., *Am. J. Psychiatry* 163:1905-17 (2006) <sup>2</sup> Rush et al., *N Engl J Med.* 354:1231-42 (2006)

<sup>3</sup> Trivedi et al., *N Engl J Med.* 354:1243-52 (2006)

- Mecamylamine demonstrated antidepressant effects as augmentation treatment in inadequate responders to citalopram (2007)
- TC-5214 is the S-(+) enantiomer of mecamylamine
- TC-5214 is a nicotinic channel blocker that has unique properties in modulating different forms of the  $\alpha 4\beta 2$  NNR
- TC-5214 has exhibited an overall profile superior to mecamylamine in preclinical models of depression and anxiety



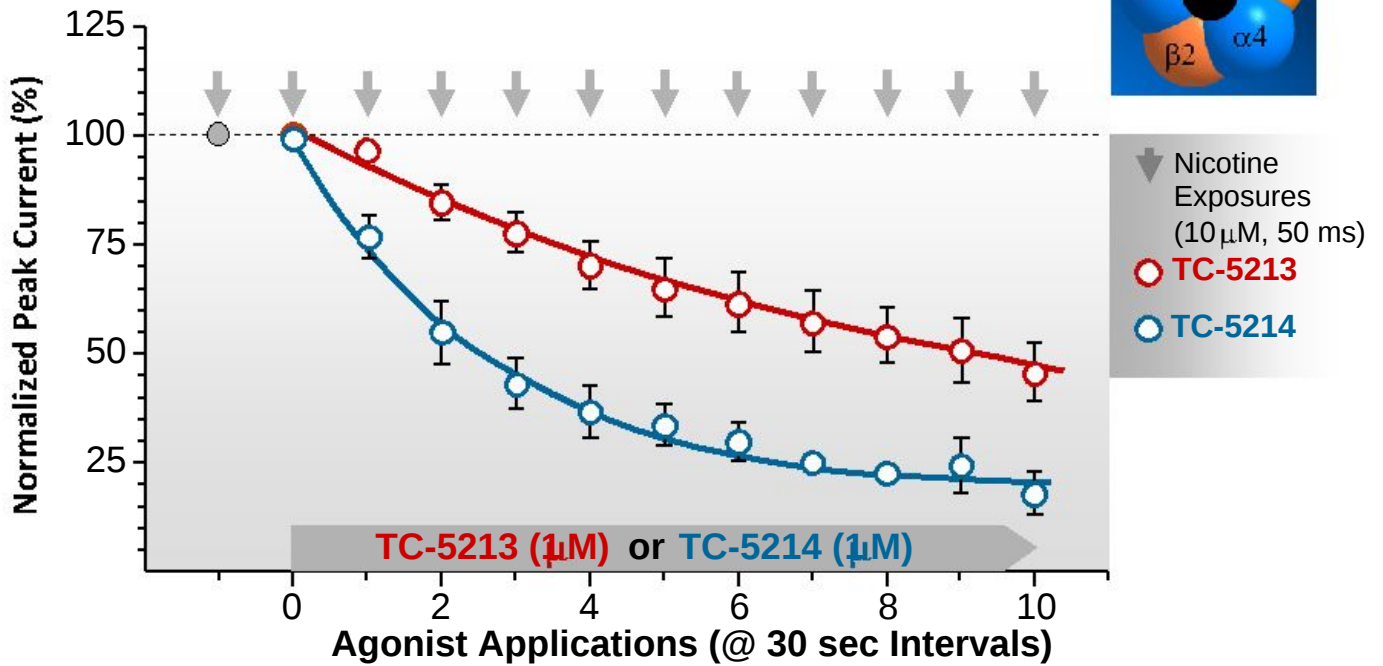
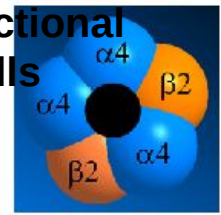
**TC-5214**



# TC-5214 is a More Effective Non-competitive Inhibitor of $\alpha 4 \beta 2$ NNR than TC-5213



## Use-Dependent Effects of Enantiomers on Functional Activation of $\alpha 4 \beta 2$ by Nicotine in SH-EP1 Cells

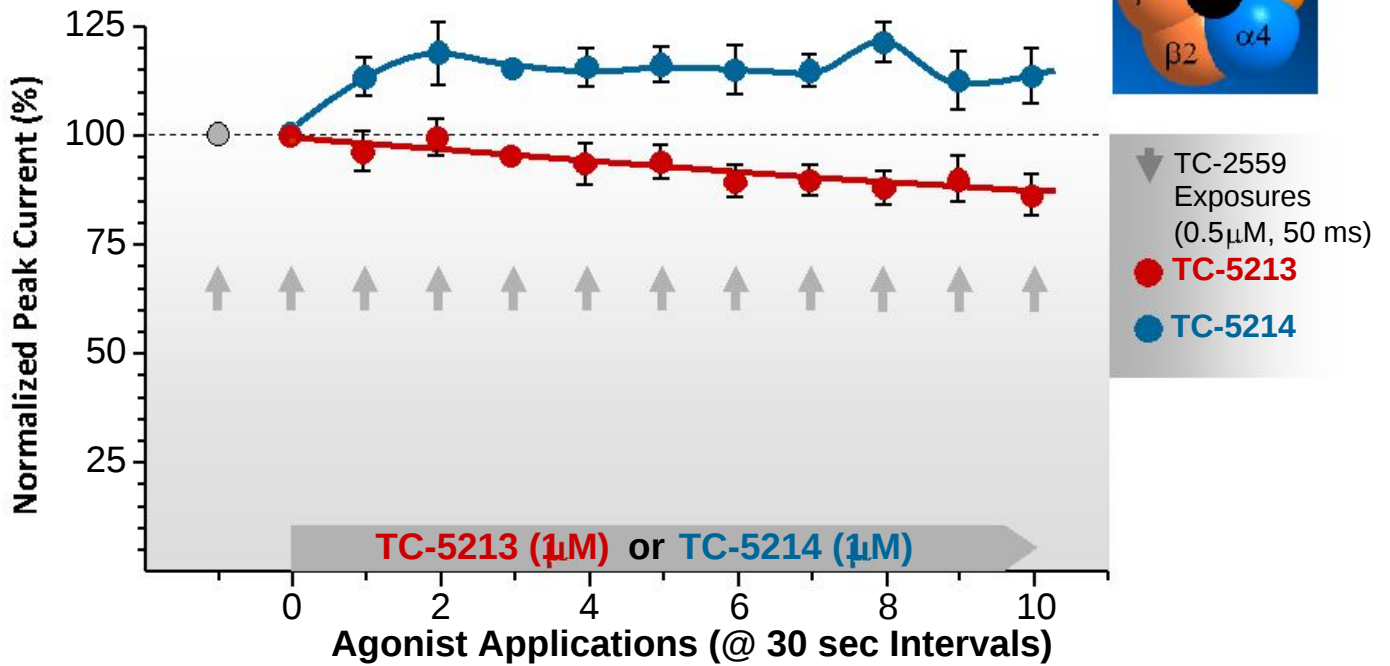


From Fedorov et al., *JPEB* 28: 525-32 (2009)

# TC-5214 Enhances and TC-5213 Blocks Activation of HS $\alpha_4\beta_2$ NNRs



## Use-Dependent Effects of Enantiomers on Functional Activation of HS $\alpha_4\beta_2$ by TC-2559 in SH-EP Cells



From Fedorov et al., *JPEB* 28: 525-32 (2009)

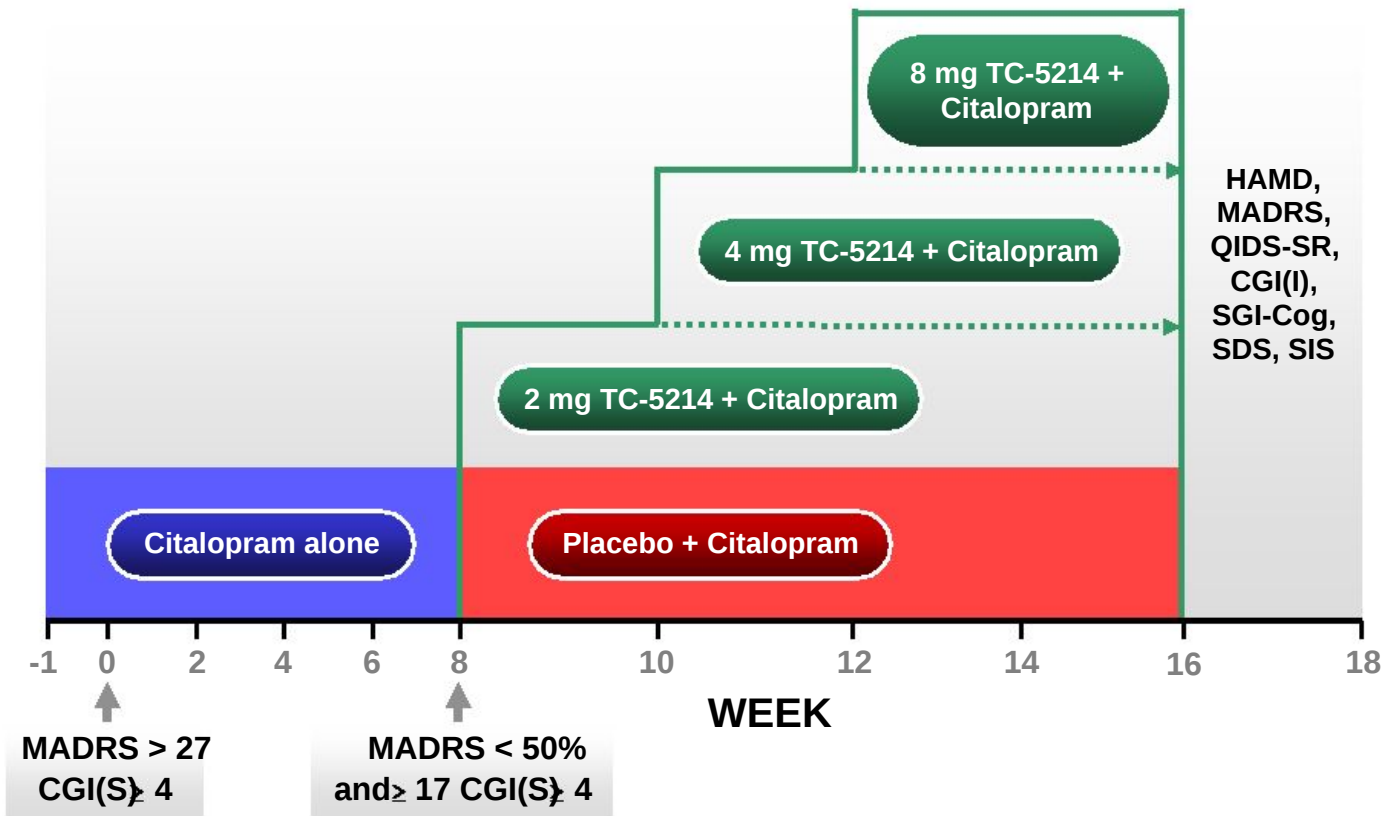


***TC-5214 Phase 2b Augmentation Study  
in Major Depressive Disorder***

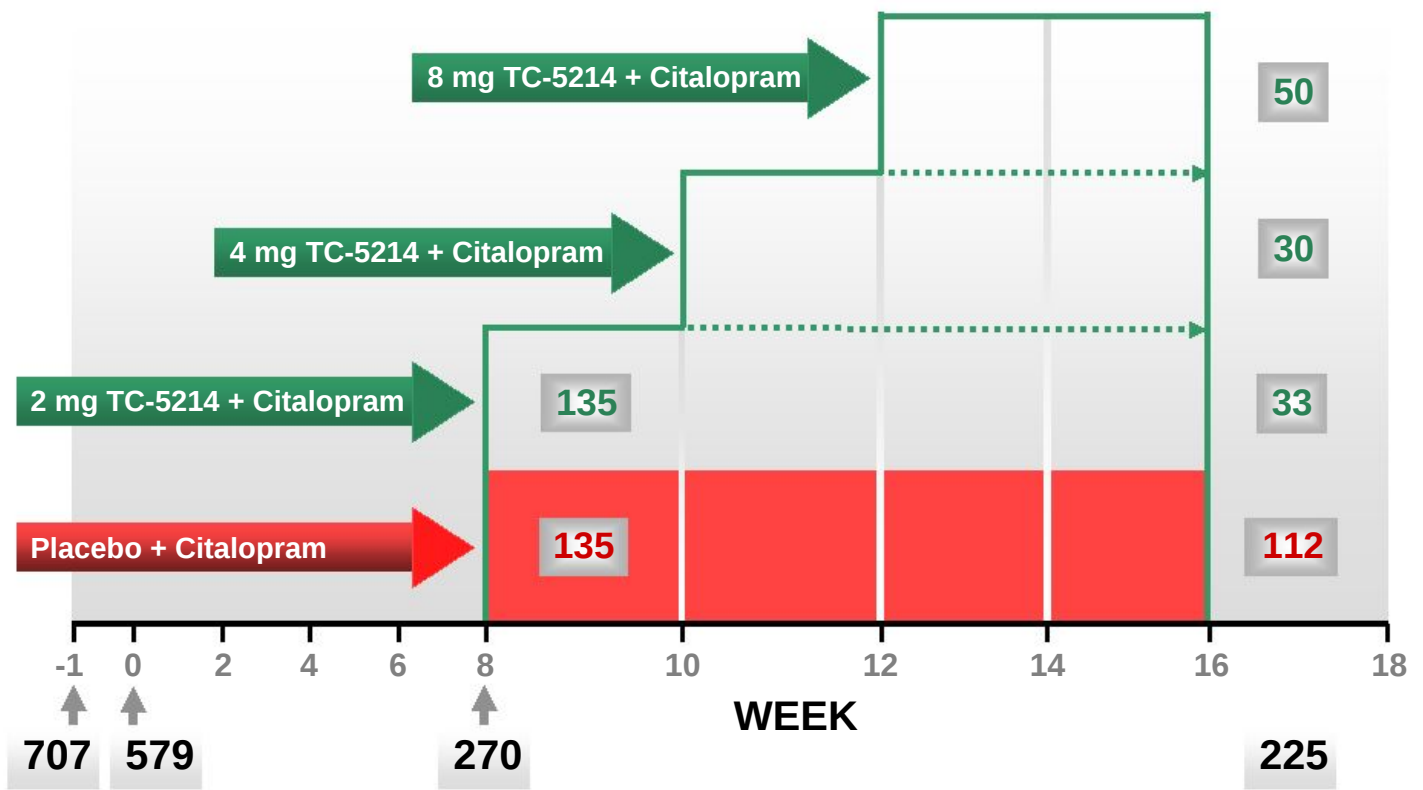
- Male or female subjects aged 18 – 70 yrs
- DSM IV criteria for MDD
- MADRS score > 27; CGI-SI
- No other uncontrolled medical condition
- No clinically meaningful abnormalities in biochemistry, vital signs or ECG

- 23 Sites: USA (3) and India (20)
- Citalopram (20mg then 40 mg) given for 8 weeks
- Subjects with MADRS change  $< 50\%$ , MADRS and CGI-S  $\geq 4$  were considered inadequate responders
- Randomized to double-blind augmentation with TC-5214 or placebo (citalopram dose unchanged) for further 8 weeks
- TC-5214 given as flexible dose of  $\rightarrow 24 \rightarrow 8\text{mg}$  (1  $\rightarrow$  2  $\rightarrow$  4 mg b.i.d.) depending on tolerability and inadequate response

# Trial Design



# Subject Progression During Trial



# Baseline Demographics of Randomized Subjects (N=270)



Variable	Placebo + citalopram (N=135)	TC-5214 + citalopram (N=135)	Total (N=270)
<b>Age (Mean) (Yrs)</b>	35.5	35.6	35.55
<b>Asian</b>	126 (93%)	125 (93%)	251 (93%)
<b>Hispanic</b>	6 (5%)	6 (4%)	12 (4%)
<b>White</b>	3 (2%)	4 (3%)	7 (3%)
<b>Male</b>	67 (50%)	66 (49%)	133 (49%)
<b>Female</b>	68 (50%)	69 (51%)	137 (51%)
<b>Weight (Mean) (kg)</b>	59.9	61.4	60.6
<b>Height (Mean) (cm)</b>	162.9	163.0	162.95
<b>BMI (Mean) (kg/m<sup>2</sup>)</b>	22.6	23.1	22.8
<b>Education</b>			
< HS/SS	51 (38%)	56 (41%)	107 (40%)
HS/SS	53 (39%)	53 (39%)	106 (39%)
College	23 (17%)	21 (16%)	44 (16%)
MS/PhD	8 (6%)	5 (4%)	13 (5%)
<b>MADRS (sd)</b>	<b>29.8 (5.6)</b>	<b>30.0 (5.25)</b>	--



# Subject Disposition ITT Population (N = 265)



Disposition	Placebo + citalopram (N = 132)	TC-5214 + citalopram (N = 133)	Total (N = 265)
<b>*ITT Subjects in Double Blind Phase</b>	132 (100%)	133 (100%)	265 (100%)
<b>Completed</b>	112 (85%)	113 (85%)	225 (85%)
<b>Prematurely Withdrawn</b>	20 (15%)	20 (15%)	40 (15%)
<b>Primary Reason for Withdrawal</b>			
Adverse event	<b>1 (1%)</b>	<b>1 (1%)</b>	<b>2 (1%)</b>
Consent withdrawn	<b>7 (5%)</b>	<b>5 (4%)</b>	<b>12 (5%)</b>
Lost to follow up	<b>5 (4%)</b>	<b>8 (6%)</b>	<b>13 (5%)</b>
Other	<b>5 (4%)</b>	<b>4 (3%)</b>	<b>9 (3%)</b>
Positive drug screening/pregnancy test	<b>1 (1%)</b>		<b>1 (0%)</b>
Protocol deviation	<b>1 (1%)</b>	<b>2 (2%)</b>	<b>3 (1%)</b>

\* 270 Subjects were randomized to drug (135) and placebo (135) but five subjects had no post-baseline assessment making them ineligible to be categorized as ITT as defined in protocol

# TC-5214 Treatment-Emergent Serious Adverse Events (SAEs) (n=2)



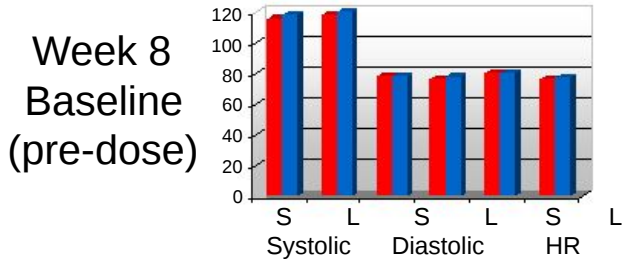
- Not drug related:
  - Heavy menstruation in 51 year old female: End of study
    - Peri-menopausal state
    - 4 weeks of menstrual bleeding and  $Hb 8.9$  gm/dL on last day of study drug;  $Hb 5.5$  gm/dL on follow-up visit
    - Treated with blood transfusion and hysterectomy
  
- Drug related:
  - Seizure -50 year old male: Day 4 of citalopram + TC-5214 treatment
    - Event not seen by medical personnel and reported inconsistently by relatives
    - Citalopram alone carries 0.3% chance of seizure (1 in 300)
    - TC-5214 is anticonvulsant in pre-clinical models

# TC-5214 Well Tolerated: Most Common Adverse Events

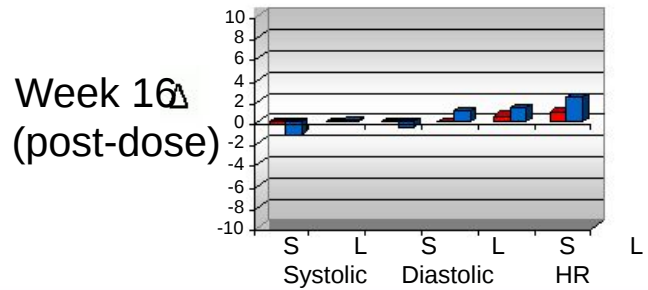
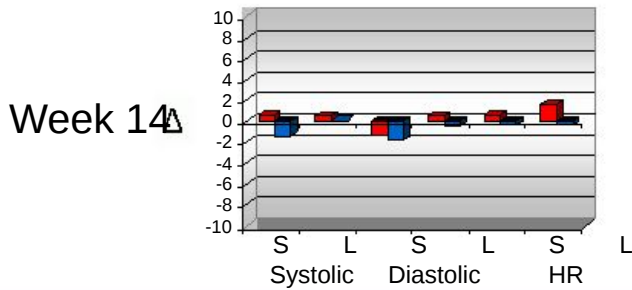
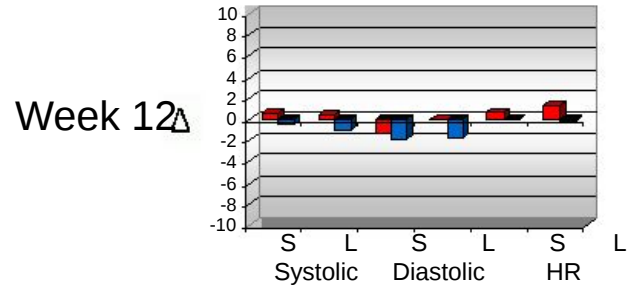
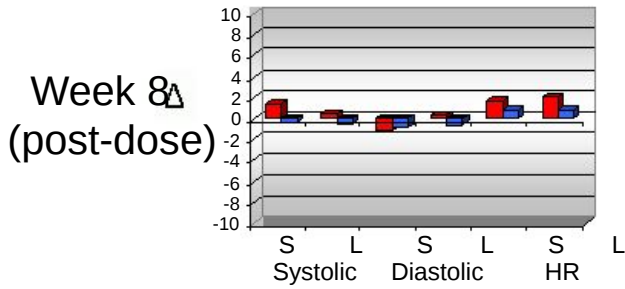


Adverse Event	Placebo + citalopram (N 135) N (%)	TC-5214 + citalopram (N = 135) N (%)	Total (N = 270) N (%)
Subjects w/ AE	43 (32%)	54 (40%)	97 (35%)
Headache	4 (3%)	12 (9%)	16 (5%)
Constipation	1 (1%)	11 (8%)	12 (4%)
Dizziness	4 (3%)	8 (6%)	12 (4%)
Pyrexia	4 (3%)	3 (2%)	7 (3%)
Asthenia	0 (0%)	6 (4%)	6 (2%)
Gastritis	4 (3%)	1 (1%)	5 (2%)
Insomnia	2 (1%)	3 (2%)	5 (2%)
Nasopharyngitis	3 (2%)	2 (1%)	5 (2%)
Somnolence	3 (2%)	1 (1%)	4 (1%)
Myalgia	1 (1%)	1 (1%)	2 (1%)

# Vital Signs: No Clinically Meaningful Changes from Baseline



■ Placebo + citalopram  
■ TC-5214 + citalopram



# ECG, Biochemistry, Hematology and Urine Analysis: No Clinically Meaningful Changes



- No clinically meaningful changes on ECG (especially QTc)
- No clinically meaningful changes in biochemistry
  - Absolute values
  - Change values
  - Shift tables
- No clinically meaningful changes in hematology
  - Absolute values
  - Change values
  - Shift tables
- No change in urine analysis



Baseline Variable	Placebo + citalopram	TC-5214 + citalopram
	N = 132 Mean (sd)	N = 133 Mean (sd)
HAMD-17 Total Score	<b>23.7</b> (4.68)	<b>23.5</b> (5.19)
CGI-SI Score	<b>4.1</b> (0.35)	<b>4.3</b> (0.47)
MADRS Total Score	<b>29.8</b> (5.59)	<b>30.0</b> (5.25)
QIDS-SR Total Score	<b>14.2</b> (4.31)	<b>14.4</b> (4.26)

# TC-5214: Highly Statistically Significant Results Across All Efficacy Endpoints



Parameter	Placebo + citalopram Adj. Mean (SE) (N = 132)	TC-5214 + citalopram Adj. Mean (SE) (N = 133)	Difference (95% Confidence Interval)	P-value
HAMD-17	-7.75 (0.62)	-13.75 (0.62)	<b>-6.0</b> (-7.72, -4.27)	<b>&lt;0.0001</b>
MADRS	-9.72 (0.88)	-17.26 (0.88)	<b>-7.54</b> (-9.98, -5.10)	<b>&lt;0.0001</b>
QIDS-SR	-4.28 (0.42)	-8.07 (0.41)	<b>-3.79</b> (-4.94, -2.63)	<b>&lt;0.0001</b>
Anxiety/ Somatization (from HAMD-17)	-2.65 (0.23)	-4.58 (0.23)	<b>-1.93</b> (-2.57, -1.29)	<b>&lt;0.0001</b>
CGI-SI	-0.91 (0.10)	-1.79 (0.10)	<b>-0.87</b> (-1.14, -0.61)	<b>&lt;0.0001</b>
CGI-GI	2.70 (0.09)	1.91 (0.09)	<b>-0.79</b> (-1.04, -0.54)	<b>&lt;0.0001</b>

**HAMD-17 Effect Size = 0.78**

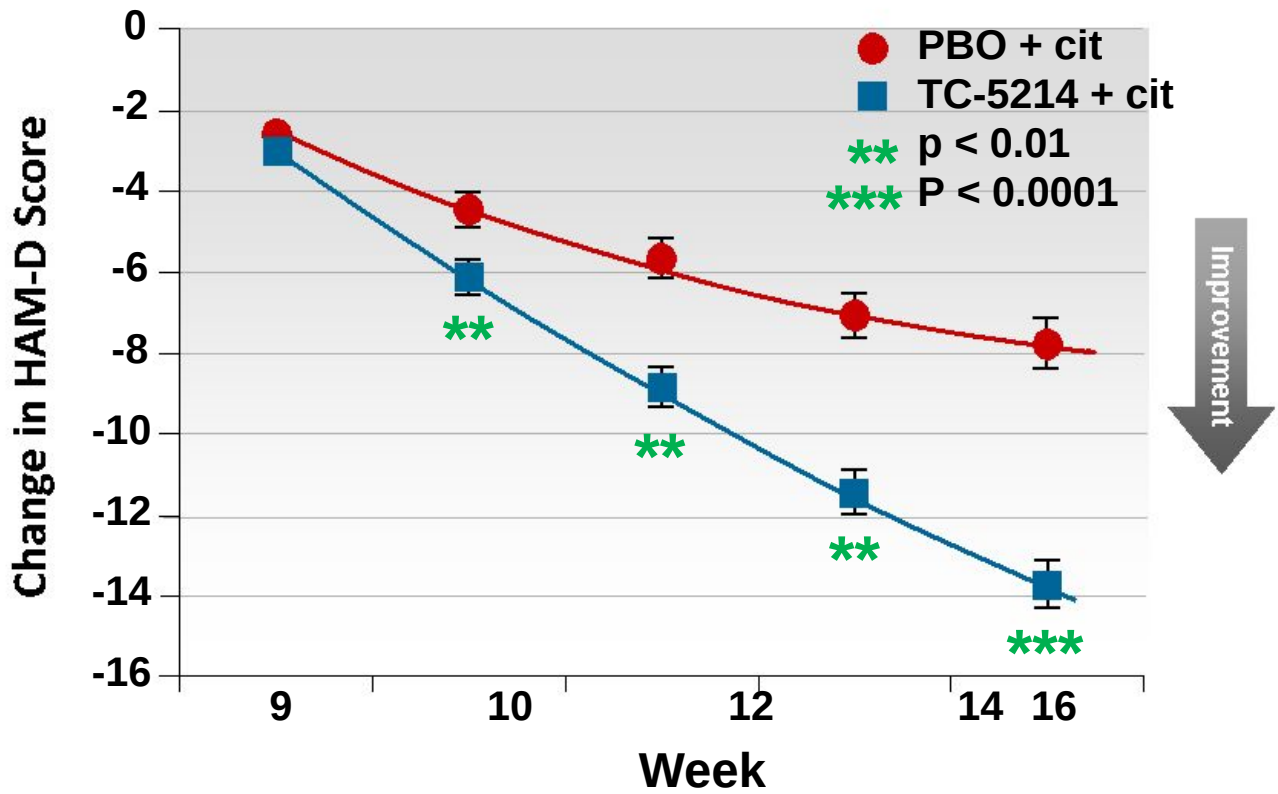
# TC-5214: Highly Statistically Significant Results Across All Efficacy Endpoints



Parameter	Placebo + citalopram Adj. Mean (SE) (N = 132)	TC-5214 + citalopram Adj. Mean (SE) (N = 133)	Difference (95% Confidence Interval)	P-value
Sheehan Disability Scale (SDS)	-4.58 (0.53)	-9.18 (0.53)	<b>-4.60</b> (-6.08, -3.13)	<b>&lt;0.0001</b>
Sheehan Irritability Scale (SIS)	-9.45 (1.12)	-18.21 (1.11)	<b>-8.76</b> (-11.85, -5.67)	<b>&lt;0.0001</b>
SIG-Cognition	8.66 (0.27)	6.52 (0.27)	<b>-2.15</b> (-2.89, -1.41)	<b>&lt;0.0001</b>
SIG-Attention	2.85 (0.09)	2.13 (0.09)	<b>-0.72</b> (-0.96, -0.47)	<b>&lt;0.0001</b>
SIG-Memory	2.90 (0.09)	2.23 (0.09)	<b>-0.67</b> (-0.93, -0.42)	<b>&lt;0.0001</b>
SIG-Speed	2.92 (0.09)	2.16 (0.09)	<b>-0.76</b> (-1.02, -0.50)	<b>&lt;0.0001</b>



# TC-5214: Early Onset of Effect by Two Weeks and Increasing Improvement over Duration of Trial

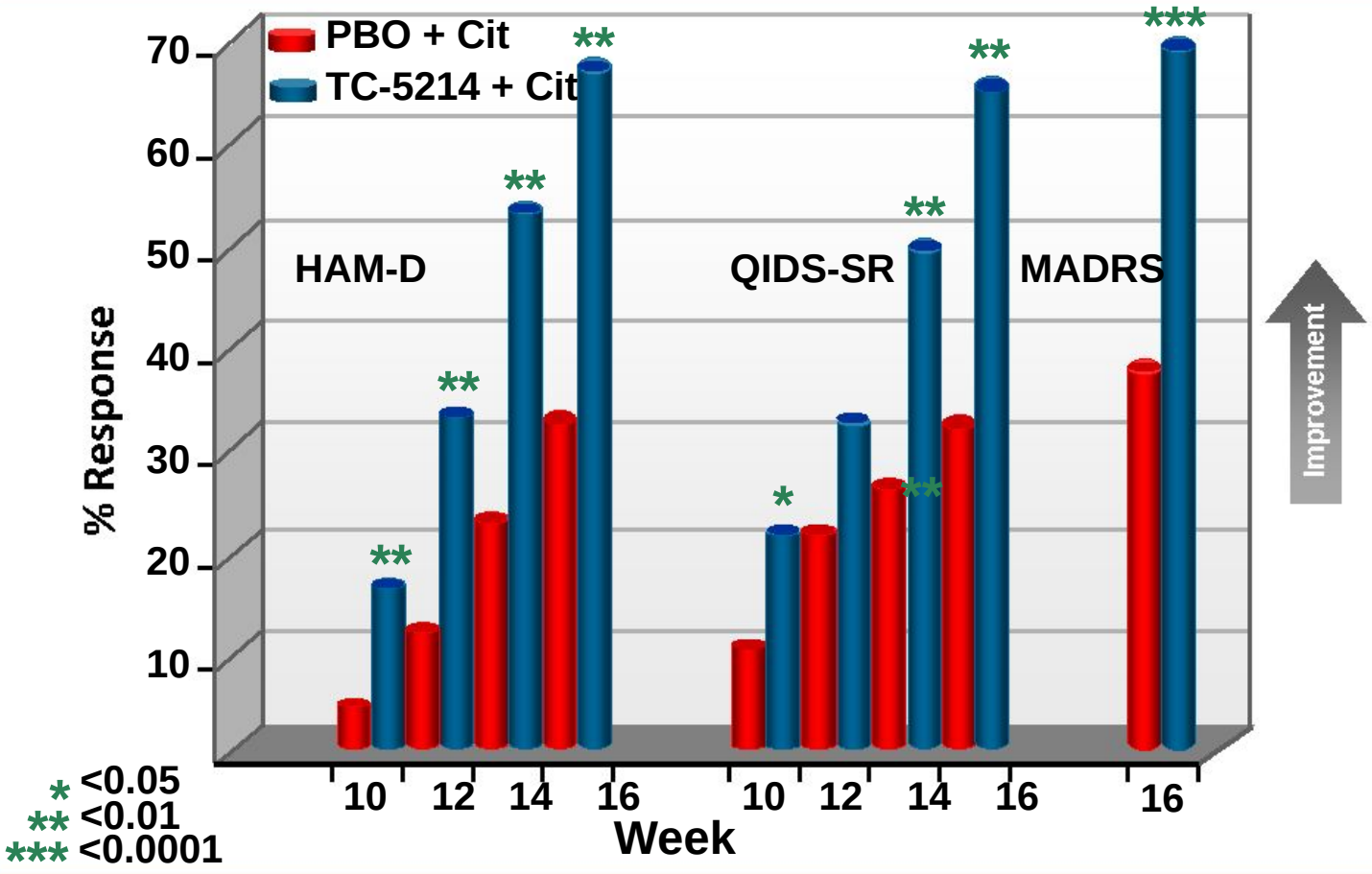


# HAMD-17 Results by End Dose (PP N=225)

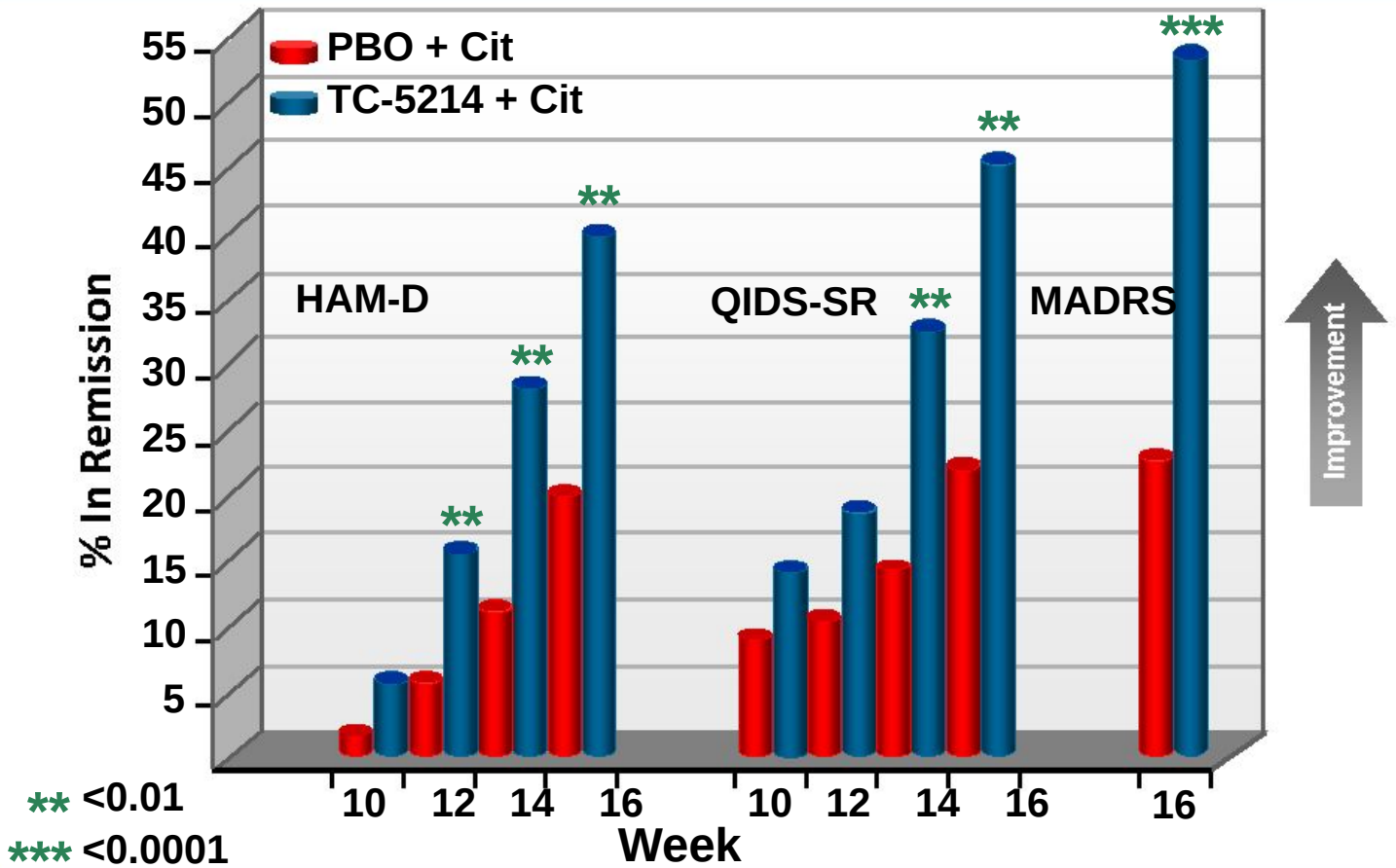


End Dose	Placebo + citalopram Adj. Mean (SE) [n]	TC-5214 + citalopram Adj. Mean (SE) [n]	Difference (95% confidence interval)	P-value
2mg	-7.75 (0.62) [132]	-15.00 (1.11) [41]	<b>-7.25</b> (-9.75, 4.74)	<b>&lt;0.0001</b>
4mg	-7.75 (0.62) [132]	-11.78 (1.16) [38]	<b>-4.02</b> (-6.60, -1.45)	<b>0.002</b>
8mg	-7.75 (0.62) [132]	-14.19 (0.97) [54]	<b>-6.44</b> (-8.70, 4.18)	<b>&lt;0.0001</b>

# Response Rates (ITT N=265): Improvement > 50% (HAM-D; QIDS-SR; MADRS)



# Remission Rates (ITT N=265): HAM-D $\leq 7$ / QIDS-SR $\leq 5$ / MADRS $\leq 10$



# Efficacy Results in Context: Aripiprazole Augmentation Data



	Aripiprazole *	
	Placebo (n=172)	Drug (n=177)
<b>MADRS Score</b>	-6.4	-10.1
Change from Placebo		<b>-3.7</b>
		P<0.001
<b>Remission</b>	18.9%	36.8%
Change from Placebo		<b>-17.9%</b>
		P<0.001
<b>Response</b>	26.6%	46.6%
Change from Placebo		<b>-20.0%</b>
		P<0.001

	TC-5214	
	Placebo + Citalopram (n=132)	TC-5214 + Citalopram (n=133)
<b>MADRS Score</b>	-9.82	-17.26
Change from Placebo		<b>-7.5</b>
		P<0.0001
<b>Remission</b>	21%	52%
Change from Placebo		<b>-31%</b>
		P<0.0001
<b>Response</b>	36%	67%
Change from Placebo		<b>-31%</b>
		P<0.0001

\* From Bernaert et al., *CNS Spectr* 14: 197-206(2009)

# Efficacy Results in Context: Quetiapine Augmentation Data



	Quetiapine Phase 3 *		
	Placebo	150 mg	300 mg
<b>Study 1</b>	(n=143)	(n=143)	(n=146)
MADRS Score	-11.7	-13.6	-14.7
Change from Placebo		<b>-1.9</b>	<b>-2.99</b>
		p=0.067	P=0.004
<b>Study 2</b>	(n=160)	(n=166)	(n=161)
MADRS Score	-12.2	-15.3	-14.9
Change from Placebo		<b>-3.05</b>	<b>-2.73</b>
		P=0.002	P=0.005

TC-5214	
Placebo + Citalopram	TC-5214 + Citalopram
(n=132)	(n=133)
-9.82	-17.26
	<b>-7.5</b>
	P<0.0001

\* FDA SBA: Study 1 (U.S.); Study 2 (Europe, S. Africa, N. America, Australia)



- Present study provides strong support for a favorable safety and tolerability profile of TC-5214 in depressed subjects
- Incidence and severity of adverse events reduced compared with earlier mecamylamine trial
  - Constipation (8% vs. 27%) and dizziness (6% vs. 15%) were much reduced
- Minimal effect of cardiovascular variables including ECG
- No meaningful changes on biochemistry, hematology or urinary variables

# Summary of Efficacy Results



- Present study provides compelling evidence for TC-5214 as a beneficial augmentation treatment for subjects who are inadequate responders to first line SSRI therapy
  - Exceptional agreement between physician and subject assessments
  - Strong effect on symptoms of irritability, anxiety and impaired cognition may have particular therapeutic benefits
- This study is the second Targacept trial to show antidepressant effects of a nicotinic channel blocker, further supporting this new mechanism of action as a promising approach for treating depression



- These clinical results with TC-5214 suggest an efficacy profile as good or better than aripiprazole or quetiapine, with a superior tolerability profile
- Remission rate as measured by the QIDS of 43% compares favorably with the 35% seen in STAR\*D trial
- These factors combined indicate TC-5214 has the potential to become the augmentation treatment of choice in depression



***Positive effects of the nicotinic channel blocker bTCC-5214  
as augmentation treatment in patients  
with major depressive disorder  
who are inadequate responders to a first-line SSR***

Geoffrey C. Dunbar, M.D.  
*Targacept*

**Targacept Presents Data from Highly Successful Phase 2b Trial of TC-5214  
as Augmentation Treatment for Major Depressive Disorder**

**Six Point Advantage over Placebo ( $p < 0.0001$ ) on Primary Outcome Measure (HAM-D)**

**Highly Statistically Significant Results ( $p < 0.0001$ ) on All Primary and Secondary Outcome Measures**

Winston-Salem, North Carolina, October 15, 2009 - Targacept, Inc. (NASDAQ: [TRGT](#)), a clinical-stage biopharmaceutical company developing a new class of drugs known as NNR Therapeutics™, today announced the presentation of data from its recently completed Phase 2b clinical trial of TC-5214 as an augmentation (add-on) treatment in subjects with major depressive disorder, or MDD, who did not respond adequately to first-line treatment with the representative SSRI citalopram hydrobromide. In the trial, the add-on TC-5214 arm (TC-5214 + citalopram) outperformed the add-on placebo arm (placebo + citalopram) on the primary outcome measure, the Hamilton Rating Scale for Depression-17, or HAM-D, and all of the secondary outcome measures, with high statistical significance.

Selective serotonin reuptake inhibitors, or SSRIs, are the most commonly prescribed class of drugs for depression, but many patients do not respond well to SSRIs. The National Institute of Mental Health, or NIMH, has estimated that 14.8 million American adults suffer from MDD. In the NIMH's large-scale Sequenced Treatment Alternatives to Relieve Depression, or STAR\*D, study, approximately 63% of participants did not achieve remission following initial treatment with citalopram alone.

In the TC-5214 trial, the magnitude of clinical response (change from double blind baseline after eight weeks) on HAM-D was 6.0 points greater for the add-on TC-5214 arm (13.75 point improvement) than for the add-on placebo arm (7.75 point improvement). This result was highly statistically significant ( $p < 0.0001$ ) on an intent to treat basis. Highly statistically significant results ( $p < 0.0001$ ) were also achieved on an intent to treat basis on all of the trial's secondary outcome measures, including the Montgomery-Asberg Depression Rating Scale, or MADRS, the Quick Inventory of Depressive Symptomatology – Self Reporting scale and assessments of irritability, disability, cognition, severity of illness and global improvement. As previously reported, TC-5214 exhibited a favorable tolerability profile in the trial.

The data from the TC-5214 trial was presented today by Geoffrey C. Dunbar, M.D., Targacept's Vice President, Clinical Development and Regulatory Affairs, at the Nicotinic Acetylcholine Receptors as Therapeutic Targets Symposium (*nAChR2009*), a satellite meeting of the 39<sup>th</sup> annual meeting of the Society for Neuroscience.

"This clinical trial provides compelling evidence for TC-5214 as a beneficial augmentation treatment with promise for providing relief for millions of patients who do not respond well to first-line SSRI therapy and restoring their quality of life," commented Stuart A. Montgomery, M.D., Emeritus Professor of Psychiatry at the Imperial College School of Science and Medicine, University of London. "The impressive outcomes across the efficacy measures and favorable tolerability profile demonstrated in the trial indicate the potential of TC-5214 to become the augmentation treatment of choice in depression."

"We are excited about the potential of TC-5214 to provide a new mechanistic approach for the treatment of depression. The STAR\*D study indicates that nearly two-thirds of subjects do not achieve full relief from depressive symptoms on their initial SSRI medication, and we believe that a well tolerated add-on treatment with strong antidepressant effects would represent a major breakthrough," said J. Donald deBethizy, Ph.D., Targacept's President and Chief Executive Officer. "We have multiple clinical opportunities in addition to TC-5214 that we believe hold great promise, including AZD3480 (TC-1734) in development for ADHD. The tremendous diversity of the NNR class and the broad potential therapeutic applications for our NNR Therapeutics were evident at *nAChR2009*, reinforcing our mission to develop new medicines to build health and restore independence."

## 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 MADRS 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 add-on TC-5214 (TC-5214 + citalopram) and add-on 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

Recent scientific evidence suggests that depressive symptoms are associated with an overstimulation of NNRs and other receptors in the brain that are activated by the neurotransmitter acetylcholine. This overstimulation is referred to as increased cholinergic tone. TC-5214 has unique properties in modulating forms of the alpha4beta2 NNR subtype thought to be involved in the increased cholinergic tone associated with depression [1]. In particular, TC-5214 blocks certain NNR channels, which is believed to help normalize cholinergic tone resulting in antidepressant effects.

## About Major Depressive Disorder

According to the World Health Organization, depression is a common mental disorder that presents with depressed mood, loss of interest or pleasure, feelings of guilt or low self-worth, disturbed sleep or appetite, low energy, and poor concentration. These problems can become chronic or recurrent and lead to substantial impairments in an individual's ability to take care of his or her everyday responsibilities. At its worst, depression can lead to suicide, a tragic fatality associated with the loss of about 850,000 lives every year. Depression is common, affecting about 121 million people worldwide.

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%. [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 clinical-stage product candidates in development for major depressive disorder, attention deficit/hyperactivity disorder, Alzheimer's disease and cognitive dysfunction in schizophrenia, as well as multiple preclinical programs. Targacept 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](http://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 or future commercial position of TC-5214, AZD3480 or any of Targacept's other product candidates, 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 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.

NNR Therapeutics™ is a trademark of Targacept, Inc. Any other service marks, trademarks and trade names appearing in this press release are the properties of their respective owners.

- [1] Fedorov NB, Benson LC, *et al.* Differential Pharmacologies of Mecamylamine Enantiomers: Positive Allosteric Modulation and Non-competitive Inhibition. *J Pharmacol Exp Ther* 328 (2) 525-532, 2009.
- [2] Greenberg, Kessler, Birnbaum, *et al.* The Economic Burden of Depression in the United States: How Did it Change Between 1990 and 2000? *Journal of Clinical Psychiatry*. December 2003; 64(12): 1465-1475.

## Contacts:

Alan Musso, VP and CFO

**Targacept, Inc.**

Tel: (336) 480-2186

Email: [alan.musso@targacept.com](mailto:alan.musso@targacept.com)

Michelle Linn

**Linnden Communications**

Tel: (508) 362-3087

Email: [linnmich@comcast.com](mailto:linnmich@comcast.com)