

This preliminary prospectus supplement and the accompanying prospectus relate to an effective registration statement under the Securities Act of 1933, but the information in this preliminary prospectus supplement is not complete and may be changed. This preliminary prospectus supplement and the accompanying prospectus are not an offer to sell nor do they seek an offer to buy these securities in any jurisdiction where the offer or sale is not permitted.

Filed pursuant to Rule 424(b)(5)
Registration Number 333-171346

SUBJECT TO COMPLETION, DATED MAY 17, 2011

PROSPECTUS SUPPLEMENT
(To prospectus dated January 11, 2011)


\$75,000,000

Common Stock

We are offering \$75,000,000 of our common stock at a price of \$ _____ per share.

Our common stock is listed on the NASDAQ Global Select Market under the symbol "TRGT." The last reported sales price of our common stock on the NASDAQ Global Select Market on May 16, 2011 was \$23.00 per share.

Investing in our common stock involves a high degree of risk. See "[Risk Factors](#)" on page S-6 of this prospectus supplement.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or determined if this prospectus supplement or the accompanying prospectus is truthful or complete. Any representation to the contrary is a criminal offense.

	<u>Per Share</u>	<u>Total</u>
Public offering price	\$	\$
Underwriting discounts and commissions	\$	\$
Proceeds, before expenses, to us	\$	\$

We have granted the underwriters an option for a period of 30 days from the date of this prospectus supplement to purchase up to an additional _____ shares of our common stock on the same terms and conditions set forth above to cover over-allotments of shares, if any.

The underwriters expect to deliver the common stock on or about May _____, 2011.

Deutsche Bank Securities

Sole Book-Running Manager

Lazard Capital Markets

Leerink Swann

Oppenheimer & Co.

The date of this prospectus supplement is May _____, 2011.

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You should rely only on the information contained in or incorporated by reference in this prospectus supplement, the accompanying prospectus and in any free writing prospectus that we have authorized for use in connection with the offering. We have not, and the underwriters have not, authorized anyone to provide you with different information. If anyone provides you with different or inconsistent information, you should not rely on it. We are not, and the underwriters are not, making an offer to sell these securities in any jurisdiction where the offer or sale is not permitted. You should assume that the information appearing in this prospectus supplement, the accompanying prospectus, the documents incorporated by reference in this prospectus supplement and the accompanying prospectus, and in any free writing prospectus that we have authorized for use in connection with this offering, is accurate only as of the date of those respective documents. Our business, financial condition, results of operations and prospects may have changed since those dates. You should read this prospectus supplement and the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering, in their entirety before making an investment decision. You should also read and consider the information in the documents we have referred you to in the sections of this prospectus supplement entitled "Where You Can Find More Information" and "Incorporation of Documents by Reference."

ABOUT THIS PROSPECTUS SUPPLEMENT

This prospectus is a part of a registration statement that we filed with the Securities and Exchange Commission, or the Commission, utilizing a “shelf” registration process. Both this prospectus supplement and the accompanying prospectus include or incorporate by reference important information about us, our common stock and other information you should know before investing. You should read this prospectus supplement, the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering, as well as the additional information described under “Where You Can Find More Information” and “Incorporation of Documents by Reference.”

This prospectus supplement may add to, update or change the information in the accompanying prospectus. If information in this prospectus supplement is inconsistent with information in the accompanying prospectus or in any document incorporated by reference that was filed with the Commission before the date of this prospectus supplement, this prospectus supplement will apply and will supersede that information contained or incorporated by reference in the accompanying prospectus.

Unless the context otherwise requires, “Targacept,” the “Company,” “we,” “us,” “our” and similar names refer to Targacept, Inc.

PROSPECTUS SUPPLEMENT SUMMARY

This summary highlights information contained elsewhere or incorporated by reference in this prospectus supplement and the accompanying prospectus. This summary does not contain all of the information that you should consider before deciding to invest in our common stock. You should read carefully this entire prospectus supplement and the accompanying prospectus and any free writing prospectus that we have authorized for use in connection with this offering, including the "Risk Factors" section contained in this prospectus supplement and our consolidated financial statements and the related notes and the other documents incorporated by reference in this prospectus supplement and the accompanying prospectus.

The Company

We are a biopharmaceutical company engaged in the design, discovery and development of novel NNR Therapeutics™ for the treatment of diseases and disorders of the nervous system. Our NNR Therapeutics selectively target a class of receptors known as neuronal nicotinic receptors, which we refer to as NNRs. NNRs are found on nerve cells throughout the nervous system and serve as key regulators of nervous system activity.

We trace our scientific lineage to a research program initiated by R.J. Reynolds Tobacco Company in 1982 to study the activity and effects of nicotine, a compound that interacts non-selectively with all nicotinic receptors. Based on years of focused research in the NNR area, we believe that compounds that interact selectively with specific NNR subtypes have the potential to achieve positive medical effects by modulating their activity. We have built an extensive patent estate covering the structure or therapeutic use of small molecules designed to regulate nervous system activity by selectively affecting specific NNR subtypes.

We have multiple clinical-stage product candidates and preclinical programs in areas in which we believe there are significant medical need and commercial potential, as well as proprietary drug discovery technologies. We also have two collaboration agreements with AstraZeneca. One is for the global development and potential commercialization of TC-5214 as a treatment for major depressive disorder, or MDD, and we refer to that agreement as our "TC-5214 agreement with AstraZeneca." The other is focused in cognitive disorders, and we refer to that agreement as our "cognitive disorders agreement with AstraZeneca." Our most advanced product candidates are described briefly below.

TC-5214. TC-5214 is a nicotinic channel modulator that is thought to derive antidepressant activity by modulating the activity of various NNR subtypes. We are co-developing TC-5214 with AstraZeneca under our TC-5214 agreement with AstraZeneca as an adjunct, or add-on, therapy for patients with MDD who do not respond adequately to initial antidepressant treatment. Phase 3 clinical trials of TC-5214 are ongoing. We and AstraZeneca are also conducting a Phase 2b clinical trial of TC-5214 as a "switch" monotherapy in patients with MDD who do not respond adequately to initial antidepressant treatment.

TC-5619. TC-5619 is a novel small molecule that modulates the activity of the $\alpha 7$ NNR. We have completed two Phase 2 clinical trials of TC-5619, one in cognitive dysfunction in schizophrenia and one in adults with attention deficit/hyperactivity disorder, or ADHD. In addition, we are conducting clinical and non-clinical studies to support potential future Phase 2 clinical development of TC-5619 in Alzheimer's disease.

AZD3480 (TC-1734). AZD3480 (TC-1734) is a novel small molecule that modulates the activity of the $\alpha 4\beta 2$ NNR and is subject to our cognitive disorders agreement with AstraZeneca. AstraZeneca or we have conducted several clinical studies of AZD3480 in various cognitive disorders and we are in discussions with AstraZeneca regarding potential additional development of the product candidate as a treatment for ADHD. Whether AstraZeneca will decide to conduct any additional development of AZD3480 in ADHD is uncertain in light of reservations about the adequacy of the therapeutic margin to support development across the broad ADHD patient population. We expect AstraZeneca to make its decision in the second half of 2011. In addition, we are progressing plans for a Phase 2 study of AZD3480 in mild to moderate Alzheimer's disease and anticipate initiating the study in the second half of 2011 following planned interactions with applicable European regulatory authorities.

AZD1446 (TC-6683). AZD1446 is a novel small molecule that modulates the activity of the $\alpha 4\beta 2$ NNR and is under consideration for further development as a treatment for Alzheimer's disease under our cognitive disorders agreement with AstraZeneca. We expect AstraZeneca to make an advancement decision in the third quarter of 2011.

TC-6987. TC-6987 is a novel small molecule that modulates the activity of the $\alpha 7$ NNR and is in development as a treatment for inflammatory disorders. We are conducting two Phase 2 clinical studies that are planned to help guide the selection of indications for which TC-6987 is best suited for later-stage development. One of the studies is in asthma and the other is in type 2 diabetes.

TC-6499. TC-6499 is a novel small molecule that modulates the activity of the $\alpha 4\beta 2$ and $\alpha 3\beta 4$ NNRs. The $\alpha 3\beta 4$ NNR is located in the gastrointestinal tract, and we believe TC-6499 may have potential as a treatment for one or more gastrointestinal disorders. We have completed an exploratory four-week study of TC-6499 in 24 subjects with constipation-predominant irritable bowel syndrome and are currently considering potential future development plans.

Pentad™. Our drug discovery activities utilize sophisticated proprietary computer-based molecular design methodologies and extensive biological and chemical data for a library of diverse compounds developed and collected over more than 25 years. We refer to these technologies collectively as Pentad.

Recent Developments

In May 2011, we announced that AstraZeneca would not exercise its option to license TC-5619. AstraZeneca had an option to license TC-5619 and to further develop and potentially commercialize TC-5619 for various conditions characterized by cognitive impairment on terms specified in our cognitive disorders agreement with AstraZeneca, as it was amended in April 2010. As a result, we retain full rights to TC-5619 and plan to use a portion of the net proceeds that we receive from this offering for the further development of this product candidate. See "Use of Proceeds."

Our Business Strategy

Our mission is to provide superior treatment options for complex diseases and disorders to improve the lives of patients by developing innovative new medicines that exploit the unique role of NNRs. To achieve our mission, our goal is to leverage our experience and expertise in the biology of NNRs and the discovery and development of novel drugs that selectively target them to become a leader in the commercialization of NNR Therapeutics for diseases and disorders where there is significant medical need and commercial potential. To achieve this goal, we are pursuing the following strategies:

- *Continue to pursue NNR Therapeutics.* We believe that drugs designed to selectively target specific NNR subtypes can have positive medical effects with limited adverse side effects. We intend to continue to use our scientific expertise and Pentad to discover compounds that selectively target specific NNR subtypes as potential treatments for diseases and disorders of the nervous system.
- *Collaborate selectively.* We have two collaborations with AstraZeneca, one focused on TC-5214 as a treatment for major depressive disorder and one focused in cognitive disorders. We intend to selectively seek additional alliances and collaborations to assist us in furthering the development of some of our product candidates. In particular, we intend to enter into these alliances and collaborations for target indications for which our potential collaborator has particular expertise or that involve large primary care markets that must be served by large sales and marketing organizations. In entering into these alliances and collaborations, our goal will generally be to maintain co-promotion or co-commercialization rights for specialists, particularly in neurology and psychiatry, in the United States and, potentially in some cases, other markets. Under our agreements with AstraZeneca, we have the option to co-promote TC-5214 and AZD3480, as well as AZD1446 and any other licensed compounds that arose out of the preclinical research collaboration, to specified classes of physicians in the United States.
- *Maintain leadership position in NNR space.* We have established ourselves as a leader in NNR research over more than 25 years. Our leadership position in this area is reflected in the numerous NNR-related articles and abstracts published by our scientists in prominent scientific journals, as well as our extensive patent estate. We intend to continue to invest significant resources to remain at the forefront of NNR research, build upon our NNR expertise and expand our intellectual property portfolio. We also plan to augment our own research by collaborating with commercial and academic institutions that seek access to our proprietary knowledge and compounds.
- *Prioritize target indications.* We have identified numerous indications in which NNRs have been implicated and for which we believe that drugs that selectively target specific NNR subtypes can potentially provide a medical benefit. We prioritize our product development opportunities in an effort to apply our product pipeline to indications in which there is a significant medical need and commercial potential.

Corporate Information

We were incorporated under the laws of the State of Delaware in 1997 as a wholly owned subsidiary of R.J. Reynolds Tobacco Company. In August 2000, we became an independent company when we issued and sold stock to venture capital investors. Our principal executive offices are located at 200 East First Street, Suite 300, Winston-Salem, North Carolina 27101 and our telephone number is (336) 480-2100.

Information about us is also available at our website at www.targacept.com, which includes links to reports we have filed with the Commission which are available free of charge. The contents of our website are not incorporated by reference in this prospectus supplement. You may read and copy the materials we have filed with the Commission and other information at the Commission's public reference facilities at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. You can request copies of these documents by writing to the Commission and paying a fee for the copying cost. Please call the Commission at 1-800-SEC-0330 for more information about the operation of the public reference facilities. Commission filings are also available at the Commission's website at <http://www.sec.gov>.

Our trademarks and service marks include, among others, Targacept[®], Pentad[™], NNR Therapeutics[™] and Building Health, Restoring IndependenceSM. Other service marks, trademarks and trade names appearing in this annual report are the properties of their respective owners.

The Offering

Common stock we are offering \$75.0 million of common stock, or shares

Common stock to be outstanding after this offering shares

Use of Proceeds We intend to use the net proceeds from this offering to develop TC-5619 and other clinical-stage product candidates further and otherwise to advance research and development programs, as well as for working capital and other general corporate purposes. Pending the uses described above, we plan to invest the net proceeds from this offering in short- and medium-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government. See "Use of Proceeds."

Risk Factors Investing in our common stock involves a high degree of risk. See "Risk Factors" and other information included and incorporated by reference in this prospectus supplement for a discussion of factors you should carefully consider before deciding to invest in shares of our common stock.

NASDAQ Global Select Market symbol TRGT

The number of shares of our common stock outstanding after this offering is based on 29,061,338 shares of our common stock outstanding as of March 31, 2011. Unless otherwise indicated, the number of shares of common stock presented in this prospectus supplement excludes 3,838,744 shares of common stock issuable upon the exercise of options outstanding as of March 31, 2011, at a weighted average exercise price of \$14.20 per share.

Except as otherwise indicated, all information in this prospectus supplement assumes no exercise by the underwriters of their over-allotment option.

RISK FACTORS

Investing in our common stock involves a high degree of risk. You should carefully consider the risks described below and discussed under the section captioned "Risk Factors" contained in our Annual Report on Form 10-K for the year ended December 31, 2010, which is incorporated by reference in this prospectus supplement and the accompanying prospectus, and all other information contained in this prospectus supplement and the accompanying prospectus and incorporated by reference in this prospectus supplement and the accompanying prospectus before purchasing our common stock. These risks and uncertainties are not the only ones facing us. Additional risks and uncertainties that we are unaware of, or that we currently deem immaterial, also may become important factors that affect us. If any of such risks or the risks described below or in our Annual Report on Form 10-K for the year ended December 31, 2010 occur, our business, financial condition or results of operations could be materially and adversely affected. In that case, the trading price of our common stock could decline, and you may lose some or all of your investment.

Risks Related to this Offering of Our Common Stock

Management will have broad discretion as to the use of proceeds from this offering, and we may use the proceeds in ways that you and other stockholders may not approve.

Our management will have broad discretion to allocate the net proceeds from this offering, and investors will be relying on the judgment of our management regarding the use of these proceeds. Our management could spend the net proceeds in ways that you and other stockholders may not approve or in ways that do not improve our results of operations or enhance the value of our common stock. Our failure to apply these funds effectively could have a material adverse effect on the development of TC-5619 or any of our other product candidates or programs, or otherwise on our business or financial condition, and cause the price of our common stock to decline.

You may experience future dilution as a result of future equity offerings and other issuances of our common stock or other securities.

In order to raise additional capital, we may in the future offer additional shares of our common stock or other securities convertible into or exchangeable for our common stock, including convertible debt. We cannot assure you that we will be able to sell shares or other securities in any other offering at a price per share that is equal to or greater than the price per share paid by investors in this offering, and investors purchasing shares or other securities in the future could have rights that are superior to existing stockholders. The price per share at which we sell additional shares of our common stock or other securities convertible into or exchangeable for our common stock in future transactions may be higher or lower than the price per share in this offering. As of March 31, 2011, 5,171,078 shares of common stock were reserved for future issuance under our 2006 stock incentive plan, which includes outstanding options to purchase 3,838,744 shares of our common stock. You will incur dilution upon the grant of any shares under our 2006 stock incentive plan and upon exercise of any outstanding stock options.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus supplement, the accompanying prospectus, any of the documents we file or have filed with the Securities and Exchange Commission, or SEC, that are incorporated by reference herein and therein and any free writing prospectus that we have authorized for use in connection with this offering include forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, which we refer to as the Securities Act, and Section 21E of the Securities Exchange Act of 1934, as amended, which we refer to as the Exchange Act. For this purpose, any statement contained in this prospectus supplement, the accompanying prospectus, any of the documents we file or have filed with the SEC that are incorporated by reference herein and therein and any free writing prospectus that we have authorized for use in connection with this offering, other than statements of historical fact, regarding, among other things:

- the progress, scope or duration of the development of TC-5214, TC-5619, AZD3480 (TC-1734), AZD1446 (TC-6683), TC-6987, TC-6499 or any of our other product candidates or programs, such as the target indication(s) for development, the size, design, population, conduct, objective or endpoints of any clinical trial, or the timing for initiation or completion of or availability of results from any clinical trial, for submission or approval of any regulatory filing (including a new drug application for TC-5214 with the U.S. Food and Drug Administration), for meeting with regulatory authorities or, where applicable, for an advancement decision by AstraZeneca;
- the benefits that may be derived from any of our product candidates or the commercial opportunity in any target indication;
- any payments that AstraZeneca may make to us;
- our operations, financial position, revenues, costs or expenses; or
- our strategies, prospects, plans, expectations or objectives;

is a forward-looking statement made under the provisions of The Private Securities Litigation Reform Act of 1995. In some cases, words such as “may,” “will,” “could,” “would,” “should,” “expect,” “intend,” “plan,” “anticipate,” “believe,” “estimate,” “predict,” “project,” “potential,” “continue,” “ongoing,” “scheduled” or other comparable words 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 risks and uncertainties relating, among other things, to:

- our dependence on the success of our collaborations with AstraZeneca;
- whether the favorable results of our Phase 2b trial of TC-5214 as an adjunct treatment for major depressive disorder will be replicated in Phase 3 clinical trials;
- whether we and AstraZeneca will receive the regulatory approvals required to market and sell TC-5214;
- whether TC-5214 will be eligible for treatment in the United States as a new chemical entity with a five-year statutory exclusivity period, either because we and AstraZeneca submit a new drug application for TC-5214 prior to October 1, 2012 or because the applicable statutory provision is re-authorized by the U.S. Congress;
- the control or significant influence that AstraZeneca has over the development of TC-5214, AZD3480 and AZD1446, including as to the timing, scope and design of any future clinical trials and as to the conduct at all of further development of AZD3480 in attention deficit/hyperactivity disorder or AZD1446 in Alzheimer’s disease;

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- the conduct and results of clinical trials and non-clinical studies and assessments of any of our product candidates, including the performance of third parties engaged to execute them, delays resulting from any changes to applicable protocols or difficulties or delays in subject enrollment or data analysis;
- whether positive findings from completed clinical trials of TC-5619 will be replicated in any future clinical trials;
- whether applicable regulatory authorities in Europe will approve the planned clinical trial of AZD3480 in Alzheimer's disease;
- whether AstraZeneca will decide to conduct any further development of AZD3480 in ADHD in light of reservations about the adequacy of the therapeutic margin;
- our ability to establish additional strategic alliances, collaborations and licensing or other arrangements on favorable terms;
- our ability to protect our intellectual property; and
- the timing and success of submission, acceptance and approval of regulatory filings.

Risks and uncertainties that we face are described in greater detail under the caption "Risk Factors" in Item 1A of Part I of our Annual Report on Form 10-K for the year ended December 31, 2010 and in other filings that we make with the SEC. As a result of the risks and uncertainties to which our business is subject, the results or events indicated by any forward-looking statement may not occur. We caution you not to place undue reliance on any forward-looking statement.

In addition, any forward-looking statement in this prospectus supplement, the accompanying prospectus, any of the documents we file or have filed with the SEC that are incorporated by reference herein and therein and any free writing prospectus that we have authorized for use in connection with this offering represent our views only as of the respective dates of those documents and should not be relied upon as representing our views as of any later date. We anticipate that subsequent events and developments may cause our views to change. Although we may elect to update these forward-looking statements publicly at some point in the future, we specifically disclaim any obligation to do so, except as required by applicable law. Our forward-looking statements do not reflect the potential impact of any future acquisitions, mergers, dispositions, joint ventures or investments we may make.

USE OF PROCEEDS

We expect to receive net proceeds of approximately \$ million from the sale of shares of our common stock in this offering, or \$ million if the underwriters exercise their over-allotment option in full, after deducting the underwriting discounts and commissions and estimated expenses related to this offering payable by us.

We currently intend to use the net proceeds from this offering to develop TC-5619 and other clinical-stage product candidates further and otherwise to advance research and development programs, as well as for working capital and other general corporate purposes. We may also use a portion of the net proceeds from this offering to acquire or invest in complementary businesses, technologies, product candidates or other intellectual property.

We have not determined the amounts we plan to spend on any of the areas listed above or the timing of these expenditures. The occurrence of unforeseen events or changed business conditions, however, could result in the application of the net proceeds from this offering in a manner other than as described in this prospectus supplement. As a result, our management will have broad discretion to allocate the net proceeds from this offering.

Pending the uses described above, we plan to invest the net proceeds from this offering in short- and medium-term, interest-bearing obligations, investment-grade instruments, certificates of deposit or direct or guaranteed obligations of the U.S. government.

DIVIDEND POLICY

We have never declared or paid cash dividends on any of our shares of capital stock. We currently intend to retain future earnings, if any, to finance the expansion and growth of our business and do not anticipate paying any cash dividends in the foreseeable future. Any future determination to pay dividends will be at the discretion of our board of directors and will depend on our financial condition, results of operations, capital requirements and other factors that our board of directors deems relevant. In addition, the terms of any future debt or credit facility may preclude us from paying dividends.

UNDERWRITING

We have entered into an underwriting agreement with Deutsche Bank Securities Inc., as representative of the underwriters named below, with respect to the common stock subject to this offering. Subject to certain conditions, we have agreed to sell to the underwriters, and the underwriters have severally agreed to purchase from us, at the public offering price less the underwriting discounts and commissions set forth on the cover page of this prospectus supplement, the number of shares of common stock listed next to each underwriter's name below. Our common stock is listed on the NASDAQ Global Select Market under the symbol "TRGT."

<u>Underwriters</u>	<u>Number of Shares</u>
Deutsche Bank Securities Inc.	
Lazard Capital Markets LLC	
Leerink Swann LLC	
Oppenheimer & Co. Inc.	
Total	

The underwriting agreement provides that the obligations of the several underwriters to purchase the shares offered hereby are subject to certain conditions and that the underwriters are obligated to purchase all of the shares offered hereby (other than those covered by the over-allotment option described below) if any of the shares are purchased.

We have been advised by the representative of the underwriters that the underwriters propose to offer the shares of common stock to the public at the offering price set forth on the cover of this prospectus supplement and to dealers at a price that represents a concession not in excess of \$ _____ per share under the offering price. The underwriters may allow, and these dealers may re-allow, a concession of not more than \$ _____ per share to other dealers. After the shares are released for sale to the public, the underwriters may change the offering price and other selling terms at various times.

We have granted the underwriters an over-allotment option. This option, which is exercisable for up to 30 days after the date of this prospectus supplement, permits the underwriters to purchase a maximum of _____ additional shares from us at the public offering price that appears on the cover page of this prospectus supplement, less the underwriting discounts and commissions, to cover over-allotments. If any shares are purchased with this over-allotment option, the underwriters will purchase shares in approximately the same proportion as shown in the table above.

The following table provides information regarding the amount of the discounts and commissions to be paid to the underwriters by us:

Per Share	Without Exercise of Over-Allotment Option	With Full Exercise of Over-Allotment Option
Total	\$	\$

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We estimate that total expenses payable by us with respect to this offering, excluding underwriting discounts and commissions, will be approximately \$275,000.

We and our executive officers and directors have entered into lock-up agreements with the underwriters. Under these lock-up agreements, subject to exceptions, these parties may not, directly or indirectly, offer, pledge, sell, contract to sell, sell any option or contract to purchase, purchase any option or contract to sell, grant any option, right or warrant for the sale of, or otherwise dispose of or transfer, or enter into any swap or any other agreement or any transaction that transfers, in whole or in part, directly or indirectly, the economic consequence of ownership of, any common stock or securities convertible into or exchangeable or exercisable for common stock, without the prior written consent of Deutsche Bank Securities Inc., for a period of 45 days from the date of this prospectus supplement. This consent may be given at any time without public notice.

Pursuant to the underwriting agreement, we have agreed to indemnify the underwriters against certain liabilities, including liabilities under the Securities Act of 1933, as amended, or the Securities Act, or to contribute to payments which the underwriters or such other indemnified parties may be required to make in respect of any such liabilities. The underwriters and their affiliates have either provided, or may in the future provide, various investment banking, commercial banking and other financial services for us for which services they either have received, or may receive in the future, customary fees.

In connection with the offering the underwriters may engage in stabilizing transactions, over-allotment transactions, syndicate covering transactions and penalty bids in accordance with Regulation M under the Securities Exchange Act of 1934, as amended, or the Exchange Act.

Stabilizing transactions permit bids to purchase the underlying security so long as the stabilizing bids do not exceed a specified maximum.

- Over-allotment involves sales by the underwriters of shares in excess of the number of shares the underwriters are obligated to purchase, which creates a syndicate short position. The short position may be either a covered short position or a naked short position. In a covered short position, the number of shares over-allotted by the underwriters is not greater than the number of shares that they may purchase in the over-allotment option. In a naked short position, the number of shares involved is greater than the number of shares in the over-allotment option. The underwriters may close out any covered short position by either exercising their over-allotment option and/or purchasing shares in the open market.
- Syndicate covering transactions involve purchases of the common stock in the open market after the distribution has been completed in order to cover syndicate short positions. In determining the source of shares to close out the short position, the underwriters will consider, among other things, the price of shares available for purchase in the open market as compared to the price at which they may purchase shares through the over-allotment option. A naked short position occurs if the underwriters sell more shares than could be covered by the over-allotment option. This position can only be closed out by buying shares in the open market. A naked short position is more likely to be created if the underwriters are concerned that there could be downward pressure on the price of the shares in the open market after pricing that could adversely affect investors who purchase in the offering.

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- Penalty bids permit the representative to reclaim a selling concession from a syndicate member when the common stock originally sold by the syndicate member is purchased in a stabilizing or syndicate covering transaction to cover syndicate short positions.

These stabilizing transactions, syndicate covering transactions and penalty bids may have the effect of raising or maintaining the market price of our common stock or preventing or retarding a decline in the market price of the common stock. As a result the price of our common stock may be higher than the price that might otherwise exist in the open market. These transactions may be discontinued at any time. Neither we, nor the underwriters, make any representation or prediction as to the direction or magnitude of any effect that the transactions described above may have on the price of the common stock. In addition, neither we, nor the underwriters, make any representation that the underwriters will engage in these stabilizing transactions or that any transaction, once commenced, will not be discontinued without notice.

This prospectus supplement and the accompanying prospectus may be made available in electronic format on the Internet sites or through other online services maintained by the underwriters participating in the offering or by their affiliates. In those cases, prospective investors may view offering terms online and prospective investors may be allowed to place orders online. Other than the prospectus supplement and the accompanying prospectus in electronic format, the information on the underwriters' or our website and any information contained in any other website maintained by the underwriters or by us is not part of the prospectus supplement, the accompanying prospectus or the registration statement of which this prospectus supplement and the accompanying prospectus form a part, has not been approved and/or endorsed by us or the underwriters in their capacity as underwriters and should not be relied upon by investors.

Lazard Frères & Co. LLC referred this transaction to Lazard Capital Markets LLC and will receive a referral fee from Lazard Capital Markets LLC in connection therewith.

European Economic Area

In relation to each Member State of the European Economic Area which has implemented the Prospectus Directive (each, a "Relevant Member State"), each underwriter has represented and agreed that, with effect from and including the date on which the Prospectus Directive is implemented in that Relevant Member State (the "Relevant Implementation Date") it has not made and will not make an offer of shares to the public in that Relevant Member State prior to the publication of a prospectus in relation to the shares which has been approved by the competent authority in that Relevant Member State or, where appropriate, approved in another Relevant Member State and notified to the competent authority in that Relevant Member State, all in accordance with the Prospectus Directive, except that it may, with effect from and including the Relevant Implementation Date, make an offer of shares to the public in that Relevant Member State at any time:

- (a) to legal entities which are authorized or regulated to operate in the financial markets or, if not so authorized or regulated, whose corporate purpose is solely to invest in securities;
- (b) to any legal entity which has two or more of (1) an average of at least 250 employees during the last financial year; (2) a total balance sheet of more than €43,000,000 and (3) an annual net turnover of more than €50,000,000, as shown in its last annual or consolidated accounts;

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- (c) to fewer than 100 natural or legal persons (other than qualified investors as defined in the Prospectus Directive) subject to obtaining the prior consent of the representatives for any such offer; or
- (d) in any other circumstances which do not require the publication by us of a prospectus pursuant to Article 3 of the Prospectus Directive.

For the purposes of this provision, the expression an “offer of shares to the public” in relation to any shares in any Relevant Member State means the communication in any form and by any means of sufficient information on the terms of this offering and the shares to be offered so as to enable an investor to decide to purchase or subscribe for the shares, as the same may be varied in that Relevant Member State by any measure implementing the Prospectus Directive in that Relevant Member State and the expression Prospectus Directive means Directive 2003/71/EC and includes any relevant implementing measure in each Relevant Member State.

United Kingdom

Each underwriter has represented and agreed that:

- (a) it has only communicated or caused to be communicated and will only communicate or cause to be communicated an invitation or inducement to engage in investment activity (within the meaning of Section 21 of the Financial Services and Markets Act (“FSMA”)) received by it in connection with the issue or sale of the shares in circumstances in which Section 21(1) of the FSMA does not apply to the Issuer; and
- (b) it has complied and will comply with all applicable provisions of the FSMA with respect to anything done by it in relation to the shares in, from or otherwise involving the United Kingdom.

Germany

Any offer or solicitation of securities within Germany must be in full compliance with the German Securities Prospectus Act (Wertpapierprospektgesetz—WpPG). The offer and solicitation of securities to the public in Germany requires the publication of a prospectus that has to be filed with and approved by the German Federal Financial Services Supervisory Authority (Bundesanstalt für Finanzdienstleistungsaufsicht—BaFin). This prospectus supplement has not been and will not be submitted for filing and approval to the BaFin and, consequently, will not be published. Therefore, this prospectus supplement does not constitute a public offer under the German Securities Prospectus Act (Wertpapierprospektgesetz). This prospectus supplement and any other document relating to our common stock, as well as any information contained therein, must therefore not be supplied to the public in Germany or used in connection with any offer for subscription of our common stock to the public in Germany, any public marketing of our common stock or any public solicitation for offers to subscribe for or otherwise acquire our common stock. This prospectus supplement and other offering materials relating to the offer of our common stock are strictly confidential and may not be distributed to any person or entity other than the designated recipients hereof.

France

This prospectus supplement has not been prepared in the context of a public offering of financial securities in France within the meaning of Article L.411-1 of the French Code Monétaire et Financier and Title I of Book II of the Règlement Général of the Autorité des marchés financiers (the “AMF”) and therefore has not been and will not be filed with the AMF for prior approval or submitted for clearance to the AMF. Consequently, the shares of our common stock may not be, directly or indirectly, offered or sold to the public in France and offers and sales of the shares of our common stock may only be made in France to qualified investors (investisseurs qualifiés) acting for their own, as defined in and in accordance with Articles L.411-2 and D.411-1 to D.411-4, D.734-1, D.744-1, D.754-1 and D.764-1 of the French Code Monétaire et Financier. Neither this prospectus supplement nor any other offering material may be released, issued or distributed to the public in France or used in connection with any offer for subscription or sale of the shares of our common stock to the public in France. The subsequent direct or indirect retransfer of the shares of our common stock to the public in France may only be made in compliance with Articles L.411-1, L.411-2, L.412-1 and L.621-8 through L.621-8-3 of the French Code Monétaire et Financier.

Sweden

This is not a prospectus under, and has not been prepared in accordance with the prospectus requirements provided for in, the Swedish Financial Instruments Trading Act [lagen (1991:980) om handel med finansiella instrument] nor any other Swedish enactment. Neither the Swedish Financial Supervisory Authority nor any other Swedish public body has examined, approved, or registered this document.

Hong Kong

The shares may not be offered or sold by means of any document other than (i) in circumstances which do not constitute an offer to the public within the meaning of the Companies Ordinance (Cap. 32, Laws of Hong Kong), or (ii) to “professional investors” within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder, or (iii) in other circumstances which do not result in the document being a “prospectus” within the meaning of the Companies Ordinance (Cap. 32, Laws of Hong Kong), and no advertisement, invitation or document relating to the shares may be issued or may be in the possession of any person for the purpose of issue (in each case whether in Hong Kong or elsewhere), which is directed at, or the contents of which are likely to be accessed or read by, the public in Hong Kong (except if permitted to do so under the laws of Hong Kong) other than with respect to shares which are or are intended to be disposed of only to persons outside Hong Kong or only to “professional investors” within the meaning of the Securities and Futures Ordinance (Cap. 571, Laws of Hong Kong) and any rules made thereunder.

Singapore

This prospectus supplement has not been registered as a prospectus with the Monetary Authority of Singapore. Accordingly, this prospectus supplement and any other document or material in connection with the offer or sale, or invitation for subscription or purchase, of the shares may not be circulated or distributed, nor may the shares be offered or sold, or be made the subject of an invitation for subscription or purchase, whether directly or indirectly, to persons in Singapore other than (i) to an institutional investor under Section 274 of the Securities and Futures Act, Chapter 289 of Singapore (the "SFA"), (ii) to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the SFA or (iii) otherwise pursuant to, and in accordance with the conditions of, any other applicable provision of the SFA.

Where the shares are subscribed or purchased under Section 275 by a relevant person which is: (a) a corporation (which is not an accredited investor) the sole business of which is to hold investments and the entire share capital of which is owned by one or more individuals, each of whom is an accredited investor; or (b) a trust (where the trustee is not an accredited investor) whose sole purpose is to hold investments and each beneficiary of which is an accredited investor, shares, debentures and units of shares and debentures of that corporation or the beneficiaries' rights and interest in that trust shall not be transferable for 6 months after that corporation or that trust has acquired the shares under Section 275 except: (1) to an institutional investor under Section 274 of the SFA or to a relevant person, or any person pursuant to Section 275(1A), and in accordance with the conditions, specified in Section 275 of the SFA; (2) where no consideration is given for the transfer; or (3) by operation of law.

Japan

The securities have not been and will not be registered under the Financial Instruments and Exchange Law of Japan (the Financial Instruments and Exchange Law) and each underwriter has agreed that it will not offer or sell any securities, directly or indirectly, in Japan or to, or for the benefit of, any resident of Japan (which term as used herein means any person resident in Japan, including any corporation or other entity organized under the laws of Japan), or to others for re-offering or resale, directly or indirectly, in Japan or to a resident of Japan, except pursuant to an exemption from the registration requirements of, and otherwise in compliance with, the Financial Instruments and Exchange Law and any other applicable laws, regulations and ministerial guidelines of Japan.

LEGAL MATTERS

Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., Boston, Massachusetts, will pass upon the validity of the issuance of the common stock offered by this prospectus. Wilmer Cutler Pickering Hale and Dorr LLP, New York, New York, has acted as counsel to the underwriters in connection with certain legal matters related to this offering.

EXPERTS

The financial statements of Targacept, Inc. appearing in Targacept, Inc.'s Annual Report (Form 10-K) for the year ended December 31, 2010 have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon included therein, and incorporated herein by reference. Such financial statements are, and audited financial statements to be included in subsequently filed documents will be, incorporated herein in reliance upon the report of Ernst & Young LLP pertaining to such financial statements (to the extent covered by consents filed with the Securities and Exchange Commission) given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We are subject to the reporting requirements of the Exchange Act and file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy these reports, proxy statements and other information at the SEC's public reference facilities at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. You can request copies of these documents by writing to the SEC and paying a fee for the copying cost. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference facilities. SEC filings are also available at the SEC's website at <http://www.sec.gov>. Our common stock is listed on The NASDAQ Global Select Market, and you can read and inspect our filings at the offices of the Financial Industry Regulatory Authority located at 1735 K Street, N.W., Washington, D.C. 20006.

This prospectus supplement and the accompanying prospectus are only part of a registration statement on Form S-3 that we have filed with the SEC under the Securities Act and therefore omits certain information contained in the registration statement. We have also filed exhibits with the registration statement that are excluded from this prospectus supplement and the accompanying prospectus, and you should refer to the applicable exhibit for a complete description of any statement referring to any contract or other document. You may inspect a copy of the registration statement, including the exhibits, without charge, at the public reference room or obtain a copy from the SEC upon payment of the fees prescribed by the SEC.

The reports, proxy statements and other information that we file with the SEC are available to you free of charge through the Investor Relations page of our website, www.targacept.com, as soon as reasonably practicable after they have been electronically filed with, or furnished to, the SEC. We have included our website address as a factual reference and do not intend it as an active link to our website. The information contained, or accessible through, our website is not a part of this prospectus supplement or the accompanying prospectus.

INCORPORATION OF DOCUMENTS BY REFERENCE

The SEC allows us to “incorporate by reference” information from other documents that we file, which means that we can disclose important information in this prospectus supplement by referring to those documents. The information incorporated by reference is considered to be part of this prospectus supplement and will automatically add to, update and, if applicable, supersede the information in this prospectus supplement. We incorporate by reference in this prospectus supplement the documents listed below:

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2010, filed on March 11, 2011;
- our Quarterly Report on Form 10-Q for the quarter ended March 31, 2011, filed on May 9, 2011;
- our Current Reports on Form 8-K filed on January 19, 2011, January 21, 2011, March 3, 2011, March 11, 2011, March 24, 2011, April 4, 2011, April 7, 2011 and May 2, 2011;
- our Definitive Proxy Statement on Schedule 14A for the 2011 annual meeting of stockholders filed on April 21, 2011;
- the description of our common stock contained in our Registration Statement on Form 8-A filed on April 6, 2006; and
- all filings that we make pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of the filing of this prospectus supplement and prior to the termination or completion of this offering (except, in each case, for information contained in any such filing that is furnished and not “filed” under the Exchange Act), which filings will be deemed to be incorporated by reference in this prospectus supplement, and to be a part hereof from the respective dates of such filings.

The SEC file number for each of the documents listed above is 000-51173.

We will provide without charge to each person, including any beneficial owner, to whom a copy of this prospectus supplement is delivered, upon the request of any such person, a copy of any or all of the information incorporated herein by reference (exclusive of exhibits to such documents, unless such exhibits are specifically incorporated by reference herein). Requests, whether written or oral, for such copies should be directed to Targacept, Inc., 200 East First Street, Suite 300, Winston-Salem, North Carolina 27101, Attn: Chief Financial Officer, (336) 480-2100.

To the extent that any statements contained in a document incorporated by reference are modified or superseded by any statements contained in this prospectus supplement such statements shall not be deemed incorporated in this prospectus supplement.

PROSPECTUS

\$150,000,000



TARGACEPT, INC.

**COMMON STOCK
PREFERRED STOCK
DEBT SECURITIES
WARRANTS
RIGHTS
PURCHASE CONTRACTS
UNITS**

This prospectus will allow us to issue up to \$150,000,000 of our common stock, preferred stock, debt securities, warrants, rights, purchase contracts and/or units from time to time at prices and on terms to be determined at or prior to the time of the offering. We will provide you with specific terms of any offering in one or more supplements to this prospectus. You should read this document and the applicable prospectus supplement carefully before you invest.

Our common stock is listed on The NASDAQ Global Market under the symbol "TRGT." On December 21, 2010, the last reported sale price of our common stock was \$26.67 per share. Prospective purchasers of securities are urged to obtain current information as to the market prices of our common stock.

Investing in our securities involves a high degree of risk. Before deciding whether to invest in our securities, you should consider carefully the risks that we have described on page 5 of this prospectus under the caption "[Risk Factors](#)." We may also include specific risk factors in supplements to this prospectus under the caption "Risk Factors." This prospectus may not be used to offer or sell our securities unless accompanied by a prospectus supplement.

Our securities may be sold directly by us to investors, through agents designated from time to time or to or through underwriters or dealers. For additional information on the methods of sale, you should refer to the section entitled "Plan of Distribution" in this prospectus. If any underwriters are involved in the sale of our securities with respect to which this prospectus is being delivered, the names of such underwriters and any applicable commissions or discounts and over-allotment options will be set forth in a prospectus supplement. The price to the public of such securities and the net proceeds that we expect to receive from such sale will also be set forth in a prospectus supplement.

Neither the Securities and Exchange Commission nor any state securities commission has approved or disapproved of these securities or passed upon the adequacy or accuracy of this prospectus. Any representation to the contrary is a criminal offense.

The date of this prospectus is January 11, 2011.

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ABOUT THIS PROSPECTUS

This prospectus is part of a registration statement that we filed with the Securities and Exchange Commission, or SEC, utilizing a “shelf” registration process. Under the shelf registration process, we may sell shares of our common stock, shares of our preferred stock, debt securities, warrants, rights, purchase contracts or units, or any combination of these securities, with an aggregate initial offering price of up to \$150,000,000, in one or more offerings. Each time we sell securities subject to the shelf registration, we will provide a prospectus supplement that contains specific information about the terms of that offering.

This prospectus does not contain all of the information included in the registration statement. For a more complete understanding of the offering of securities, you should refer to the registration statement, including its exhibits. Each prospectus supplement may also add to, update or supersede information contained or incorporated by reference in this prospectus. However, no prospectus supplement will fundamentally change the terms that are set forth in this prospectus or offer a security that is not registered and described in this prospectus at the time the registration statement becomes effective. This prospectus, together with the documents incorporated by reference in this prospectus and as supplemented by the prospectus supplement applicable to an offering, includes all material information relating to that offering. You should carefully read this prospectus, the applicable prospectus supplement, the information and documents incorporated by reference in this prospectus and the additional information under the heading “Where You Can Find More Information” before making an investment decision.

You should rely only on the information contained or incorporated by reference in this prospectus, as supplemented by the applicable prospectus supplement. We have not authorized anyone to provide you with information different from that contained or incorporated by reference in this prospectus or a prospectus supplement. No dealer, salesperson or other person is authorized to give any information or to represent anything not contained or incorporated by reference in this prospectus or a prospectus supplement. You must not rely on any unauthorized information or representation. This prospectus is an offer to sell only the securities offered hereby, but only under circumstances and in jurisdictions where it is lawful to do so. You should assume that the information in this prospectus or any prospectus supplement is accurate only as of the date on the front of the document and that any information we have incorporated by reference in this prospectus is accurate only as of the date of the document that is incorporated by reference, regardless of the time of delivery of this prospectus or a prospectus supplement or any sale of a security.

This prospectus may not be used to consummate sales of securities unless it is accompanied by a prospectus supplement. To the extent there are inconsistencies among any prospectus supplement, this prospectus and any documents incorporated by reference in this prospectus, the document with the most recent date will control.

Unless the context otherwise requires, “Targacept,” the “Company,” “we,” “us,” “our” and similar names refer to Targacept, Inc.

TARGACEPT, INC.

We are a biopharmaceutical company engaged in the design, discovery and development of novel NNR Therapeutics for the treatment of diseases and disorders of the nervous system. Our NNR Therapeutics selectively target a class of receptors known as neuronal nicotinic receptors, which we refer to as NNRs. NNRs are found on nerve cells throughout the nervous system and serve as key regulators of nervous system activity.

We have multiple clinical-stage product candidates and preclinical programs in areas where we believe there are significant medical need and commercial potential, as well as proprietary drug discovery technologies. We have two collaboration agreements with AstraZeneca, one that we entered into in December 2009 for the global development and commercialization of TC-5214 as a treatment for major depressive disorder, or MDD, and refer to in this prospectus as our “TC-5214 agreement with AstraZeneca” and the other focused in cognitive disorders that we entered into in December 2005 and refer to in this prospectus as our “cognitive disorders agreement with AstraZeneca.” We also have an alliance agreement with GlaxoSmithKline. Our most advanced product candidates are described below:

- *TC-5214*. TC-5214 is a nicotinic channel blocker that is thought to derive antidepressant activity by modulating the activity of various NNR subtypes. We are co-developing TC-5214 with AstraZeneca under our TC-5214 agreement with AstraZeneca as an adjunct (or add-on) therapy for patients with MDD who do not respond adequately to first-line antidepressant treatment. Phase 3 clinical trials of TC-5214 are ongoing. In addition, we expect a Phase 2 clinical trial of TC-5214 as a second-line “switch” monotherapy to initiate in the first quarter of 2011.
- *TC-5619*. TC-5619 is a novel small molecule that modulates the activity of the $\alpha 7$ NNR. We have two Phase 2 clinical trials of TC-5619 ongoing, one in cognitive dysfunction in schizophrenia, or CDS, and one in adults with attention deficit/hyperactivity disorder, or ADHD. We are also conducting clinical and non-clinical studies to support the potential advancement of TC-5619 into Phase 2 clinical development in Alzheimer’s disease. A decision as to whether to conduct Phase 2 clinical development of TC-5619 as a treatment for Alzheimer’s disease would be made in the future. AstraZeneca has an option for an exclusive license to TC-5619 for various cognitive disorders that is exercisable the first time that TC-5619 achieves Phase 2 clinical proof of concept, whether in CDS, ADHD or Alzheimer’s disease. AstraZeneca also can exercise its license option upon completion of specified clinical and non-clinical studies related to Alzheimer’s disease if TC-5619 does not achieve clinical proof of concept in CDS or ADHD.
- *AZD3480 (TC-1734)*. AZD3480 is a novel small molecule that modulates the activity of the $\alpha 4\beta 2$ NNR and is subject to our cognitive disorders agreement with AstraZeneca. We or AstraZeneca have conducted several clinical studies of AZD3480 in various cognitive disorders and we are in discussions with AstraZeneca regarding potential additional development as a treatment for ADHD. Whether AstraZeneca will decide to conduct any additional development of AZD3480 in ADHD is uncertain in light of reservations about the adequacy of the therapeutic margin to support development across the broad ADHD patient population. We expect AstraZeneca to make its decision in the first quarter of 2011. In addition, we are exploring the practicability of conducting an additional clinical trial of AZD3480 in Alzheimer’s disease.
- *AZD1446 (TC-6683)*. AZD1446 is a novel small molecule that modulates the activity of the $\alpha 4\beta 2$ NNR and is under consideration for further development as a treatment for Alzheimer’s disease under our cognitive disorders agreement with AstraZeneca. We discovered AZD1446 as part of a multi-year preclinical research collaboration conducted under the agreement. AstraZeneca has completed three of four Phase 1/2a clinical studies expected to inform its decision whether to advance AZD1446, and we expect AstraZeneca to make its decision in the first half of 2011.
- *TC-6987*. TC-6987 is a novel small molecule that modulates the activity of the $\alpha 7$ NNR and is in development as a treatment for inflammatory disorders. We have completed a Phase 1 single rising

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dose clinical trial and a Phase 1 multiple rising dose clinical trial of TC-6987. We plan to conduct multiple Phase 2 learning trials to identify the optimal indication for TC-6987, with the first such study to be in asthma and expected to initiate in the first quarter of 2011.

- *TC-6499*. TC-6499 is a product candidate that we previously evaluated and are no longer developing as a pain treatment. Based on the activity of TC-6499 at certain NNR subtypes located in the gastrointestinal tract, we believe it may have potential as a treatment for certain gastrointestinal disorders. We are conducting an ongoing exploratory Phase 2a study of TC-6499 as a treatment for constipation-predominant irritable bowel syndrome.

Under our TC-5214 agreement with AstraZeneca, we and AstraZeneca have jointly designed an initial development program that includes development of TC-5214 as an adjunct therapy and as a second-line “switch” monotherapy, in each case in patients with MDD who do not respond adequately to first-line antidepressant treatment. AstraZeneca is responsible for 80% and we are responsible for 20% of the costs of the initial program, except that AstraZeneca is responsible for 100% of development costs that are required only to obtain or maintain regulatory approval in countries outside the United States and the European Union. We have the right to terminate our obligation to fund our share of the costs of the initial program once we have funded a specified amount. In addition, for each of us and AstraZeneca, costs that were not contemplated at execution to be part of the initial program may in some cases be excluded from the cost-sharing arrangement. If we fund the specified amount and terminate our obligation to fund our share of further costs of the initial program, any future milestones and royalties payable to us under the agreement would be reduced by the amount of our unfunded share plus interest at a specified rate, subject to a maximum reduction that may be applied to any one payment. AstraZeneca is responsible for executing and funding the costs of global commercialization of TC-5214.

Under our cognitive disorders agreement with AstraZeneca:

- we are responsible for conducting and funding the ongoing Phase 2 clinical trials of TC-5619 in CDS and in adults with ADHD, as well as specified clinical and non-clinical studies to support the potential advancement of TC-5619 into Phase 2 clinical development for Alzheimer’s disease; AstraZeneca is responsible for conducting and funding other specified non-clinical studies to support the potential advancement of TC-5619 into Phase 2 clinical development for Alzheimer’s disease;
- except as discussed in the next bullet, AstraZeneca is responsible for substantially all current and future development costs for AZD3480, AZD1446 and each other compound arising from the preclinical research collaboration described below that it elects to advance;
- we are exploring the practicability of conducting an additional clinical trial of AZD3480 in Alzheimer’s disease and have agreed with AstraZeneca on respective roles and responsibilities for such a study; if an Alzheimer’s disease study proceeds, we would be responsible for funding the study but would be entitled to receive approximately \$6.2 million from AstraZeneca (of which we have already received \$500,000 as of the date of this prospectus), in tranches culminating with initial dosing; and
- from January 2006 to January 2010, we and AstraZeneca conducted a preclinical research collaboration under the agreement to discover and develop compounds that act on the a4 β 2 NNR as treatments for conditions characterized by cognitive impairment; AstraZeneca paid us research fees, based on a reimbursement rate specified under the agreement, for research services rendered in the preclinical research collaboration.

In addition to our two collaboration agreements with AstraZeneca, we have an alliance agreement with GlaxoSmithKline that is designed to discover, develop and market product candidates that selectively target specified NNR subtypes in specified therapeutic focus areas. In February 2010, GlaxoSmithKline announced plans to cease discovery research in selected neuroscience areas. Although the overall impact of GlaxoSmithKline’s strategic change on our alliance has not yet been finally determined, we anticipate that at least several therapeutic focus areas in the alliance will be discontinued.

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We trace our scientific lineage to a research program initiated by R.J. Reynolds Tobacco Company in 1982 to study the activity and effects of nicotine in the body. We were incorporated in 1997 as a wholly owned subsidiary of RJR. In August 2000, we became an independent company when we issued and sold stock to venture capital investors. Since our inception, we have had limited revenue from product sales and have funded our operations principally through the sale of equity securities, revenue from collaboration agreements, grants and equipment and building lease incentive financing. We have devoted substantially all of our resources to the discovery and development of our product candidates and technologies, including the design, conduct and management of preclinical and clinical studies and related manufacturing, regulatory and clinical affairs, as well as intellectual property prosecution.

We generated net income for each of the first three quarters of 2010 due primarily to recognition into revenue of a portion of the upfront payment received under our TC-5214 agreement with AstraZeneca. We also generated net income for two other quarterly periods since our inception, in each case due primarily to the achievement in each period of a single milestone event related to AZD3480 under our cognitive disorders agreement with AstraZeneca. Except for these periods, we have not been profitable and we may incur losses in future periods as our clinical-stage and preclinical product candidates advance into later-stage development and as we progress our programs, invest in additional product opportunities and expand our research and development infrastructure. As of September 30, 2010, we had an accumulated deficit of \$216.2 million. Clinical trials and preclinical studies are time-consuming, expensive and may never yield a product that will generate revenue.

Our principal executive offices are located at 200 East First Street, Suite 300, Winston-Salem, North Carolina 27101 and our telephone number is (336) 480-2100. Our internet address is www.targacept.com. The information contained on, or that can be accessed through, our website is not incorporated by reference in this prospectus or any prospectus supplement and does not constitute a part of this prospectus or any prospectus supplement. We have included our website address as a factual reference and do not intend it as an active link to our website.

Our trademarks and service marks include Targacept®, Pentad™, NNR Therapeutics™, TRIDMAC™ and Building Health, Restoring IndependenceSM. Other service marks, trademarks and trade names appearing in this prospectus or any prospectus supplement are the property of their respective owners.

RISK FACTORS

Investing in our securities involves risk. Prior to making a decision about investing in our securities, you should carefully consider all of the information contained or incorporated by reference in this prospectus or the applicable prospectus supplement. In particular, you should carefully consider the risks, uncertainties and assumptions discussed under the heading “Risk Factors” in our most recent annual report on Form 10-K, which is on file with the SEC and incorporated by reference in this prospectus, and in subsequent filings that we make with the SEC, as well as any discussion of risks contained in the applicable prospectus supplement. The risks and uncertainties we have described are not the only ones we face. Additional risks and uncertainties not presently known to us or that we currently deem immaterial may also affect our operations and financial results.

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus, each prospectus supplement and the documents we file or have filed with the SEC that are incorporated by reference in this prospectus include forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, which we refer to as the Securities Act, or Section 21E of the Securities Exchange Act of 1934, as amended, which we refer to as the Exchange Act. For this purpose, any statement contained in this prospectus, any prospectus supplement or any of the documents we file or have filed with the SEC that are incorporated by reference in this prospectus, other than statements of historical fact, regarding, among other things:

- the progress, scope or duration of the development of TC-5214, AZD3480 (TC-1734), AZD1446 (TC-6683), TC-5619, TC-6987, TC-6499 or any of our other product candidates or programs, such as the target indication(s) for development, the size, design, population, conduct, objective or endpoints of any clinical trial, or the timing for initiation or completion of or availability of results from any clinical trial, for submission or approval of any regulatory filing (including a new drug application for TC-5214), for meeting with regulatory authorities or, where applicable, for an advancement decision by AstraZeneca;
- the benefits that may be derived from any of our product candidates;
- any payments that AstraZeneca or GlaxoSmithKline may make to us;
- the impact on our alliance of GlaxoSmithKline's shift in discovery research focus announced in February 2010;
- our operations, financial position, taxable income, revenues, costs or expenses; or
- our strategies, prospects, plans, expectations or objectives

is a forward-looking statement made under the provisions of The Private Securities Litigation Reform Act of 1995. In some cases, words such as "may," "will," "could," "would," "should," "expect," "intend," "plan," "anticipate," "believe," "estimate," "predict," "project," "potential," "continue," "scheduled," "ongoing" or other comparable words identify forward-looking statements. Actual results, performance or experience may differ materially from those expressed or implied by forward-looking statements as a result of various important factors, including our critical accounting policies and risks and uncertainties relating to:

- our dependence on the success of our collaborations with AstraZeneca;
- whether the favorable results of our Phase 2b trial of TC-5214 as an adjunct treatment for MDD will be replicated in Phase 3 clinical trials;
- whether TC-5214 will be eligible for treatment in the United States as a new chemical entity with a five-year statutory exclusivity period, either because we and AstraZeneca submit a new drug application for TC-5214 prior to October 1, 2012 or because the applicable statutory provision is re-authorized by the U.S. Congress;
- the significant control that AstraZeneca has over the development of TC-5214, AZD3480 and AZD1446, including as to the timing, scope and design of clinical trials and as to the conduct at all of further development of AZD3480 in ADHD or AZD1446 in Alzheimer's disease or TC-5619 in Alzheimer's disease;
- whether AstraZeneca exercises its right to license TC-5619 when exercisable;
- the conduct and results of clinical trials and non-clinical studies and assessments of TC-5214, AZD3480, AZD1446, TC-5619, TC-6987, TC-6499 or any of our other product candidates, including the performance of third parties engaged to execute such trials, studies and assessments and difficulties or delays in the completion of subject enrollment or data analysis;

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- our ability to establish additional strategic alliances, collaborations and licensing or other arrangements on favorable terms;
- our ability to protect our intellectual property; and
- the timing and success of submission, acceptance and approval of regulatory filings.

These and other risks and uncertainties are described in more detail under the caption “Risk Factors” in our most recent annual report on Form 10-K and in subsequent filings that we make with the SEC, and may also be described in the applicable prospectus supplement. As a result of the risks and uncertainties, the results or events indicated by the forward-looking statements may not occur. We caution you not to place undue reliance on any forward-looking statement.

Any forward-looking statements in this prospectus, any prospectus supplement or any of the documents we file or have filed with the SEC that are incorporated by reference in this prospectus represent our views only as of the respective dates of those documents and should not be relied upon as representing our views as of any subsequent date. We anticipate that subsequent events and developments may cause our views to change. Although we may elect to update these forward-looking statements publicly at some point in the future, whether as a result of new information, future events or otherwise, we specifically disclaim any obligation to do so, except as required by applicable law. Our forward-looking statements do not reflect the potential impact of any future in-licenses, acquisitions, mergers, dispositions, joint ventures or investments we may make.

RATIO OF EARNINGS TO FIXED CHARGES

The following table sets forth the ratio of our earnings to fixed charges for the nine months ended September 30, 2010. Our earnings were insufficient to cover fixed charges for each of the years ended December 31, 2005, 2006, 2007, 2008 and 2009, and the extent to which earnings were insufficient to cover fixed charges for those periods is also shown in the table. "Earnings" consist of net income (loss) from operations before income taxes plus fixed charges. "Fixed charges" consist of interest expense and the estimated portion of operating lease expense that represents interest.

	Fiscal Year Ended December 31,					Nine Months Ended September 30, 2010
	2005	2006	2007	2008	2009	
Ratio of earnings to fixed charges	—	—	—	—	—	23.54
Deficiency of earnings to fixed charges	\$(29,941)	\$(404)	\$(31,772)	\$(28,144)	\$(40,325)	—

USE OF PROCEEDS

Unless otherwise indicated in the prospectus supplement applicable to an offering, we intend to use any net proceeds from the sale of our securities to fund our operations and for other general corporate purposes, such as working capital, development of our clinical and preclinical product candidates, intellectual property protection and enforcement, capital expenditures, investments, in-licenses and acquisitions. Pending use of the net proceeds as described above, we intend to invest the net proceeds in short-term, interest-bearing, investment grade securities.

DESCRIPTION OF SECURITIES TO BE OFFERED

The descriptions of the securities contained in this prospectus, together with the applicable prospectus supplements, summarize the material terms and provisions of the various types of securities that we may offer. We will describe in the applicable prospectus supplement relating to any securities the particular terms of the securities offered by that prospectus supplement. If we so indicate in the applicable prospectus supplement, the terms of the securities may differ from the terms we have summarized below. We will also include in the prospectus supplement information, where applicable, about material U.S. federal income tax considerations relating to the securities, and the securities exchange, if any, on which the securities will be listed.

We may sell from time to time, in one or more primary offerings, our common stock, preferred stock, debt securities, warrants, rights, purchase contracts or units, or any combination of the foregoing.

In this prospectus, we refer to the common stock, preferred stock, debt securities, warrants, rights, purchase contracts or units, or any combination of the foregoing securities to be sold by us in a primary offering collectively as “securities.” The total dollar amount of all securities that we may issue under this prospectus will not exceed \$150,000,000.

This prospectus may not be used to consummate a sale of securities unless it is accompanied by a prospectus supplement.

DESCRIPTION OF CAPITAL STOCK

The following description of our common stock and preferred stock, together with the additional information we include in any applicable prospectus supplements, summarizes the material terms and provisions of the common stock and preferred stock that we may offer under this prospectus. It may not contain all the information that is important to you. For the complete terms of our common stock and preferred stock, please refer to our Fourth Amended and Restated Certificate of Incorporation and our bylaws, which are incorporated by reference into the registration statement which includes this prospectus. The Delaware General Corporation Law may also affect the terms of these securities. While the terms we have summarized below will apply generally to any future common stock and preferred stock that we may offer, we will describe the particular terms of these securities in more detail in the applicable prospectus supplement. If we so indicate in a prospectus supplement, the terms of any security we offer under that prospectus supplement may differ from the terms we describe below.

Common Stock

Under our Fourth Amended and Restated Certificate of Incorporation, we have authority to issue 100,000,000 shares of our common stock, par value \$0.001 per share. As of December 17, 2010, 28,795,412 shares of our common stock were issued and outstanding. All shares of our common stock will, when issued, be duly authorized, fully paid and nonassessable.

Dividends. Subject to preferential dividend rights of any other class or series of stock, the holders of shares of our common stock are entitled to receive dividends, including dividends of our stock, as and when declared by our board of directors, subject to any limitations applicable by law and to the rights of the holders, if any, of our preferred stock.

Liquidation. In the event we are liquidated, dissolved or our affairs are wound up, after we pay or make adequate provision for all of our known debts and liabilities, each holder of our common stock will be entitled to share ratably in all assets that remain, subject to any rights that are granted to the holders of any class or series of preferred stock.

Voting Rights. For all matters submitted to a vote of stockholders, each holder of our common stock is entitled to one vote for each share registered in his or her name. Except as may be required by law and in connection with some significant actions, such as mergers, consolidations, or amendments to our Fourth Amended and Restated Certificate of Incorporation that affect the rights of stockholders, holders of our common stock vote together as a single class. There is no cumulative voting in the election of our directors, which means that, subject to any rights to elect directors that are granted to the holders of any class or series of preferred stock, a plurality of the votes cast at a meeting of stockholders at which a quorum is present is sufficient to elect a director.

Other Rights and Restrictions. Subject to the preferential rights of any other class or series of stock, all shares of our common stock have equal dividend, distribution, liquidation and other rights, and have no preference, appraisal or exchange rights, except for any appraisal rights provided by Delaware law. Furthermore, holders of our common stock have no conversion, sinking fund or redemption rights, or preemptive rights to subscribe for any of our securities. Our Fourth Amended and Restated Certificate of Incorporation and our bylaws do not restrict the ability of a holder of our common stock to transfer his or her shares of our common stock.

The rights, powers, preferences and privileges of holders of our common stock are subject to, and may be adversely affected by, the rights of holders of shares of any series of preferred stock which we may designate and issue in the future.

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Listing. Our common stock is listed on The NASDAQ Global Market under the symbol “TRGT.”

Transfer Agent and Registrar. The transfer agent for our common stock is American Stock Transfer & Trust Company.

Preferred Stock

Under our Fourth Amended and Restated Certificate of Incorporation, we have authority, subject to any limitations prescribed by law and without further stockholder approval, to issue from time to time up to 5,000,000 shares of preferred stock, par value \$0.001 per share, in one or more series. As of December 21, 2010, no shares of preferred stock were issued and outstanding.

Pursuant to our Fourth Amended and Restated Certificate of Incorporation, we are authorized to issue “blank check” preferred stock, which may be issued from time to time in one or more series upon authorization by our board of directors. Our board of directors, without further approval of the stockholders, is authorized to fix the designation, powers, preferences, relative, participating optional or other special rights, and any qualifications, limitations and restrictions applicable to each series of the preferred stock. The issuance of preferred stock, while providing flexibility in connection with possible acquisitions and other corporate purposes could, among other things, adversely affect the voting power or rights of the holders of our common stock and, under certain circumstances, make it more difficult for a third party to gain control of us, discourage bids for our common stock at a premium or otherwise adversely affect the market price of the common stock.

The preferred stock will have the terms described below unless otherwise provided in the prospectus supplement relating to a particular series of the preferred stock. You should read the prospectus supplement relating to the particular series of the preferred stock being offered for specific terms, including:

- the designation and stated value per share of the preferred stock and the number of shares offered;
- the amount of liquidation preference per share;
- the price at which the preferred stock will be issued;
- the dividend rate, or method of calculation of any dividend, the dates on which dividends will be payable, whether dividends will be cumulative or noncumulative and, if cumulative, the dates from which dividends will accumulate;
- any redemption or sinking fund provisions;
- if other than the currency of the United States, the currency or currencies, including composite currencies, in which the preferred stock is denominated and/or in which payments will or may be payable;
- any conversion provisions; and
- any other rights, preferences, privileges, qualifications, limitations and restrictions on the preferred stock.

The preferred stock will, when issued, be fully paid and nonassessable. Unless otherwise specified in the prospectus supplement, each series of the preferred stock will rank equally as to dividends and liquidation rights in all respects with any other series of preferred stock. The rights of holders of shares of each series of preferred stock will be subordinate to those of our general creditors.

Rank. Unless otherwise specified in the prospectus supplement, the preferred stock will, with respect to dividend rights and rights upon our liquidation, dissolution or winding up of our affairs, rank:

- senior to all classes or series of our common stock and to all equity securities ranking junior to such preferred stock with respect to dividend rights or rights upon our liquidation, dissolution or winding up of our affairs;

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- on a parity with all equity securities issued by us, the terms of which specifically provide that such equity securities rank on a parity with the preferred stock with respect to dividend rights or rights upon our liquidation, dissolution or winding up of our affairs; and
- junior to all equity securities issued by us, the terms of which specifically provide that such equity securities rank senior to the preferred stock with respect to dividend rights or rights upon our liquidation, dissolution or winding up of our affairs.

The term “equity securities” does not include convertible debt securities.

Dividends. Holders of the preferred stock of each series will be entitled to receive, when, as and if declared by our board of directors, cash dividends at such rates and on such dates described in the prospectus supplement. Different series of preferred stock may be entitled to dividends at different rates or based on different methods of calculation. The dividend rate may be fixed or variable or both. Dividends will be payable to the holders of record as they appear on our stock books on record dates fixed by our board of directors, as specified in the applicable prospectus supplement.

Dividends on any series of the preferred stock may be cumulative or noncumulative, as described in the applicable prospectus supplement. If our board of directors does not declare a dividend payable on a dividend payment date on any series of noncumulative preferred stock, then the holders of that noncumulative preferred stock will have no right to receive a dividend for that dividend payment date, and we will have no obligation to pay the dividend accrued for that period, whether or not dividends on that series are declared payable on any future dividend payment dates. Dividends on any series of cumulative preferred stock will accrue from the date we initially issue shares of such series or such other date specified in the applicable prospectus supplement.

Liquidation Preference. Upon any voluntary or involuntary liquidation, dissolution or winding up of our affairs, then, before we make any distribution or payment to the holders of any common stock or any other class or series of our capital stock ranking junior to the preferred stock in the distribution of assets upon any liquidation, dissolution or winding up of our affairs, the holders of each series of preferred stock shall be entitled to receive out of assets legally available for distribution to stockholders, liquidating distributions in the amount of the liquidation preference per share set forth in the applicable prospectus supplement, plus any accrued and unpaid dividends thereon. Such dividends will not include any accumulation in respect of unpaid noncumulative dividends for prior dividend periods. Unless otherwise specified in the prospectus supplement, after payment of the full amount of their liquidating distributions, the holders of preferred stock will have no right or claim to any of our remaining assets. Upon any such voluntary or involuntary liquidation, dissolution or winding up, if our available assets are insufficient to pay the amount of the liquidating distributions on all outstanding preferred stock and the corresponding amounts payable on all other classes or series of our capital stock ranking on parity with the preferred stock and all other such classes or series of shares of capital stock ranking on parity with the preferred stock in the distribution of assets, then the holders of the preferred stock and all other such classes or series of capital stock will share ratably in any such distribution of assets in proportion to the full liquidating distributions to which they would otherwise be entitled.

Redemption. If so provided in the applicable prospectus supplement, the preferred stock will be subject to mandatory redemption or redemption at our option, as a whole or in part, in each case upon the terms, at the times and at the redemption prices set forth in such prospectus supplement.

Voting Rights. Holders of preferred stock will have voting rights as required by law or as indicated in the applicable prospectus supplement.

Conversion Rights. The terms and conditions, if any, upon which any series of preferred stock is convertible into common stock will be set forth in the applicable prospectus supplement relating thereto. Such terms will include the number of shares of common stock into which the shares of preferred stock are convertible, the

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conversion price, rate or manner of calculation thereof, the conversion period, provisions as to whether conversion will be at our option or at the option of the holders of the preferred stock, the events requiring an adjustment of the conversion price and provisions affecting conversion in the event of the redemption.

Transfer Agent and Registrar. Any transfer agent and registrar for the preferred stock will be set forth in the applicable prospectus supplement.

Certain Effects of Authorized but Unissued Stock

We have shares of common stock and preferred stock available for future issuance without stockholder approval. We may issue these additional shares for a variety of corporate purposes, including future public or private offerings to raise additional capital or facilitate corporate acquisitions or for payment as a dividend on our capital stock. The existence of unissued and unreserved preferred stock may enable our board of directors to issue shares of preferred stock with terms that could render more difficult or discourage a third-party attempt to obtain control of us by means of a merger, tender offer, proxy contest or otherwise, thereby protecting the continuity of our management. In addition, if we issue preferred stock, the issuance could adversely affect the voting power of holders of common stock and the likelihood that holders of common stock will receive dividend payments or payments upon liquidation.

DESCRIPTION OF DEBT SECURITIES

Our debt securities, consisting of notes, debentures or other evidences of indebtedness, may be issued from time to time in one or more series pursuant to, in the case of senior debt securities, a senior indenture to be entered into between us and a trustee to be named therein, and in the case of subordinated debt securities, a subordinated indenture to be entered into between us and a trustee to be named therein. The terms of our debt securities will include those set forth in the indentures and those made a part of the indentures by the Trust Indenture Act of 1939, as amended.

Because the following is only a summary of selected provisions of the indentures and the debt securities, it does not contain all information that may be important to you. This summary is not complete and is qualified in its entirety by reference to the base indentures and any supplemental indentures thereto or officer's certificate or resolution of our board of directors related thereto. We urge you to read the indentures because the indentures, not this description, define the rights of the holders of the debt securities. The senior indenture and the subordinated indenture will be substantially in the forms included as exhibits to the registration statement of which this prospectus is a part.

General

The senior debt securities will constitute unsecured and unsubordinated obligations of ours and will rank pari passu with our other unsecured and unsubordinated obligations. The subordinated debt securities will constitute our unsecured and subordinated obligations and will be junior in right of payment to our Senior Indebtedness (including senior debt securities), as described under the heading "Certain Terms of the Subordinated Debt Securities—Subordination."

The debt securities will be our unsecured obligations. Any secured debt or other secured obligations will be effectively senior to the debt securities to the extent of the value of the assets securing such debt or other obligations.

The applicable prospectus supplement will include any additional or different terms of the debt securities being offered, including the following terms:

- the debt securities' designation;
- the aggregate principal amount of the debt securities;
- the percentage of their principal amount (i.e., price) at which the debt securities will be issued;
- the date or dates on which the debt securities will mature and the right, if any, to extend such date or dates;
- the rate or rates, if any, per year, at which the debt securities will bear interest, or the method of determining such rate or rates;
- the date or dates from which such interest will accrue, the interest payment dates on which such interest will be payable or the manner of determination of such interest payment dates and the record dates for the determination of holders to whom interest is payable on any interest payment date;
- the right, if any, to extend the interest payment periods and the duration of that extension;
- the manner of paying principal and interest and the place or places where principal and interest will be payable;
- provisions for a sinking fund purchase or other analogous fund, if any;
- the period or periods, if any, within which, the price or prices at which, and the terms and conditions upon which the debt securities may be redeemed, in whole or in part, at our option or at your option;

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- the form of the debt securities;
- any provisions for payment of additional amounts for taxes and any provision for redemption, if we must pay such additional amounts in respect of any debt security;
- the terms and conditions, if any, upon which we may have to repay the debt securities early at your option;
- the currency, currencies or currency units for which you may purchase the debt securities and the currency, currencies or currency units in which principal and interest, if any, on the debt securities may be payable;
- the terms and conditions upon which conversion or exchange of the debt securities may be effected, if any, including the initial conversion or exchange price or rate and any adjustments thereto and the period or periods when a conversion or exchange may be effected;
- whether and upon what terms the debt securities may be defeased;
- any events of default or covenants in addition to or in lieu of those set forth in the indenture;
- provisions for electronic issuance of debt securities or for debt securities in uncertificated form; and
- any other terms of the debt securities, including any terms which may be required by or advisable under applicable laws or regulations or advisable in connection with the marketing of the debt securities.

We may from time to time, without notice to or the consent of the holders of any series of debt securities, create and issue further debt securities of any such series ranking equally with the debt securities of such series in all respects (or in all respects other than the payment of interest accruing prior to the issue date of such further debt securities or except for the first payment of interest following the issue date of such further debt securities). Such further debt securities may be consolidated and form a single series with the debt securities of such series and have the same terms as to status, redemption or otherwise as the debt securities of such series.

You may present debt securities for exchange and you may present debt securities for transfer in the manner, at the places and subject to the restrictions set forth in the debt securities and the applicable prospectus supplement. We will provide you those services without charge, although you may have to pay any tax or other governmental charge payable in connection with any exchange or transfer, as set forth in the indenture.

Debt securities will bear interest at a fixed rate or a floating rate. Debt securities bearing no interest or interest at a rate that at the time of issuance is below the prevailing market rate (original issue discount securities) may be sold at a discount below their stated principal amount. Special U.S. federal income tax considerations applicable to any such discounted debt securities or to certain debt securities issued at par which are treated as having been issued at a discount for U.S. federal income tax purposes will be described in the applicable prospectus supplement.

We may issue debt securities with the principal amount payable on any principal payment date, or the amount of interest payable on any interest payment date, to be determined by reference to one or more currency exchange rates, securities or baskets of securities, commodity prices or indices. You may receive a payment of principal on any principal payment date, or a payment of interest on any interest payment date, that is greater than or less than the amount of principal or interest otherwise payable on such dates, depending on the value on such dates of the applicable currency, security or basket of securities, commodity or index. Information as to the methods for determining the amount of principal or interest payable on any date, the currencies, securities or baskets of securities, commodities or indices to which the amount payable on such date is linked and certain additional tax considerations will be set forth in the applicable prospectus supplement.

Certain Terms of the Senior Debt Securities

Covenants. Unless otherwise indicated in a prospectus supplement, the senior debt securities will not contain any financial or restrictive covenants, including covenants restricting either us or any of our subsidiaries from incurring, issuing, assuming or guarantying any indebtedness secured by a lien on any of our or our subsidiaries' property or capital stock, or restricting either us or any of our subsidiaries from entering into sale and leaseback transactions.

Consolidation, Merger and Sale of Assets. Unless we indicate otherwise in a prospectus supplement, we may not consolidate with or merge into any other person, in a transaction in which we are not the surviving corporation, or convey, transfer or lease our properties and assets substantially as an entirety to any person, unless:

- the successor entity, if any, is a U.S. corporation, limited liability company, partnership or trust (subject to certain exceptions provided for in the senior indenture);
- the successor entity assumes our obligations on the senior debt securities and under the senior indenture;
- immediately after giving effect to the transaction, no default or event of default shall have occurred and be continuing; and
- certain other conditions are met.

Events of Default. An event of default for any series of senior debt securities is defined under the senior indenture as being:

- our default in the payment of principal or premium on the senior debt securities of such series when due and payable whether at maturity, upon acceleration, redemption or otherwise, if that default continues for a period of five days (or such other period as may be specified for such series);
- our default in the payment of interest on any senior debt securities of such series when due and payable, if that default continues for a period of 60 days (or such other period as may be specified for such series);
- our default in the performance of or breach of any of our other covenants or agreements in the senior indenture applicable to senior debt securities of such series, other than a covenant breach which is specifically dealt with elsewhere in the senior indenture, and that default or breach continues for a period of 90 days after we receive written notice from the trustee or from the holders of 25% or more in aggregate principal amount of the senior debt securities of such series;
- there occurs any other event of default provided for in such series of senior debt securities;
- a court having jurisdiction enters a decree or order for (1) relief in respect of us in an involuntary case under any applicable bankruptcy, insolvency or other similar law now or hereafter in effect; (2) appointment of a receiver, liquidator, assignee, custodian, trustee, sequestrator or similar official of us or for all or substantially all of our property and assets; or (3) the winding up or liquidation of our affairs and such decree or order shall remain unstayed and in effect for a period of 60 consecutive days; or
- we (1) commence a voluntary case under any applicable bankruptcy, insolvency or other similar law now or hereafter in effect, or consent to the entry of an order for relief in an involuntary case under any such law; (2) consent to the appointment of or taking possession by a receiver, liquidator, assignee, custodian, trustee, sequestrator or similar official of ours for all or substantially all of our property and assets; or (3) effect any general assignment for the benefit of creditors.

The default by us under any other debt, including any other series of debt securities, is not a default under the senior indenture.

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If an event of default other than an event of default specified in the last two bullet points above occurs with respect to a series of senior debt securities and is continuing under the senior indenture, then, and in each and every such case, either the trustee or the holders of not less than 25% in aggregate principal amount of such series then outstanding under the senior indenture (each such series voting as a separate class) by written notice to us and to the trustee, if such notice is given by the holders, may, and the trustee at the request of such holders shall, declare the principal amount of and accrued interest, if any, on such senior debt securities to be immediately due and payable.

If an event of default specified in the last two bullet points above occurs with respect to us and is continuing, the entire principal amount of, and accrued interest, if any, on each series of senior debt securities then outstanding shall become immediately due and payable.

Upon a declaration of acceleration, the principal amount of and accrued interest, if any, on such senior debt securities shall be immediately due and payable. Unless otherwise specified in the prospectus supplement relating to a series of senior debt securities originally issued at a discount, the amount due upon acceleration shall include only the original issue price of the senior debt securities, the amount of original issue discount accrued to the date of acceleration and accrued interest, if any.

Upon certain conditions, declarations of acceleration may be rescinded and annulled and past defaults may be waived by the holders of a majority in aggregate principal amount of all the senior debt securities of such series affected by the default, each series voting as a separate class (or, of all the senior debt securities, as the case may be, voting as a single class). Furthermore, subject to various provisions in the senior indenture, the holders of at least a majority in aggregate principal amount of a series of senior debt securities, by notice to the trustee, may waive an existing default or event of default with respect to such senior debt securities and its consequences, except a default in the payment of principal of or interest on such senior debt securities or in respect of a covenant or provision of the senior indenture which cannot be modified or amended without the consent of the holders of each such senior debt security. Upon any such waiver, such default shall cease to exist, and any event of default with respect to such senior debt securities shall be deemed to have been cured, for every purpose of the senior indenture; but no such waiver shall extend to any subsequent or other default or event of default or impair any right consequent thereto. For information as to the waiver of defaults, see “—Modification and Waiver.”

The holders of at least a majority in aggregate principal amount of a series of senior debt securities may direct the time, method and place of conducting any proceeding for any remedy available to the trustee or exercising any trust or power conferred on the trustee with respect to such senior debt securities. However, the trustee may refuse to follow any direction that conflicts with law or the senior indenture, that may involve the trustee in personal liability, or that the trustee determines in good faith may be unduly prejudicial to the rights of holders of such series of senior debt securities not joining in the giving of such direction and may take any other action it deems proper that is not inconsistent with any such direction received from holders of such series of senior debt securities. A holder may not pursue any remedy with respect to the senior indenture or any series of senior debt securities unless:

- the holder gives the trustee written notice of a continuing event of default;
- the holders of at least 25% in aggregate principal amount of such series of senior debt securities make a written request to the trustee to pursue the remedy in respect of such event of default;
- the requesting holder or holders offer the trustee indemnity satisfactory to the trustee against any costs, liability or expense;
- the trustee does not comply with the request within 60 days after receipt of the request and the offer of indemnity; and
- during such 60-day period, the holders of a majority in aggregate principal amount of such series of senior debt securities do not give the trustee a direction that is inconsistent with the request.

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These limitations, however, do not apply to the right of any holder of a senior debt security to receive payment of the principal of or interest, if any, on such senior debt security, or to bring suit for the enforcement of any such payment, on or after the due date for the senior debt securities, which right shall not be impaired or affected without the consent of the holder.

The senior indenture requires certain of our officers to certify, on or before a fixed date in each year in which any senior debt security is outstanding, as to their knowledge of our compliance with all conditions and covenants under the senior indenture.

Discharge and Defeasance. The senior indenture provides that, unless the terms of any series of senior debt securities provides otherwise, we may discharge our obligations with respect to a series of senior debt securities and the senior indenture with respect to such series of senior debt securities if:

- we pay or cause to be paid, as and when due and payable, the principal of and any interest on all senior debt securities of such series outstanding under the senior indenture;
- all senior debt securities of such series previously authenticated and delivered with certain exceptions, have been delivered to the trustee for cancellation and we have paid all sums payable by us under the senior indenture; or
- the senior debt securities of such series mature within one year or all of them are to be called for redemption within one year under arrangements satisfactory to the trustee for giving the notice of redemption, and we irrevocably deposit in trust with the trustee, as trust funds solely for the benefit of the holders of the senior debt securities of such series, for that purpose, the entire amount in cash or, in the case of any series of senior debt securities payments on which may only be made in U.S. dollars, U.S. government obligations (maturing as to principal and interest in such amounts and at such times as will insure the availability of sufficient cash), after payment of all federal, state and local taxes or other charges and assessments in respect thereof payable by the trustee, to pay principal of and interest on the senior debt securities of such series to maturity or redemption, as the case may be, and to pay all other sums payable by us under the senior indenture.

With respect to the first and second bullet points, only our obligations to compensate and indemnify the trustee and our right to recover unclaimed money held by the trustee under the senior indenture shall survive. With respect to the third bullet point, certain rights and obligations under the senior indenture (such as our obligation to maintain an office or agency in respect of such senior debt securities, to have moneys held for payment in trust, to register the transfer or exchange of such senior debt securities, to deliver such senior debt securities for replacement or to be canceled, to compensate and indemnify the trustee and to appoint a successor trustee, and our right to recover unclaimed money held by the trustee) shall survive until such senior debt securities are no longer outstanding. Thereafter, only our obligations to compensate and indemnify the trustee and our right to recover unclaimed money held by the trustee shall survive.

Unless the terms of any series of senior debt securities provide otherwise, on the 121st day after the date of deposit of the trust funds with the trustee, we will be deemed to have paid and will be discharged from any and all obligations in respect of the series of senior debt securities provided for in the funds, and the provisions of the senior indenture will no longer be in effect with respect to such senior debt securities (“legal defeasance”); provided that the following conditions shall have been satisfied:

- we have irrevocably deposited in trust with the trustee as trust funds solely for the benefit of the holders of the senior debt securities of such series, for payment of the principal of and interest on the senior debt securities of such series, cash in an amount or, in the case of any series of senior debt securities payments on which can only be made in U.S. dollars, U.S. government obligations (maturing as to principal and interest at such times and in such amounts as will insure the availability of cash) or a combination thereof sufficient (in the opinion of a nationally recognized firm of independent public accountants expressed in a written certification thereof delivered to the trustee), after payment of all

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federal, state and local taxes or other charges and assessments in respect thereof payable by the trustee, to pay and discharge the principal of and accrued interest on the senior debt securities of such series to maturity or earlier redemption, as the case may be, and any mandatory sinking fund payments on the day on which such payments are due and payable in accordance with the terms of the senior indenture and the senior debt securities of such series;

- such deposit will not result in a breach or violation of, or constitute a default under, the senior indenture or any other material agreement or instrument to which we are a party or by which we are bound;
- no default or event of default with respect to the senior debt securities of such series shall have occurred and be continuing on the date of such deposit;
- we shall have delivered to the trustee either an officer's certificate and an opinion of counsel that the holders of the senior debt securities of such series will not recognize income, gain or loss for federal income tax purposes as a result of our exercising our option under this provision of the senior indenture and will be subject to federal income tax on the same amount and in the same manner and at the same times as would have been the case if such deposit and defeasance had not occurred or a ruling by the Internal Revenue Service to the same effect; and
- we have delivered to the trustee an officer's certificate and an opinion of counsel, in each case stating that all conditions precedent provided for in the senior indenture relating to the contemplated defeasance of the senior debt securities of such series have been complied with.

Subsequent to the legal defeasance above, certain rights and obligations under the senior indenture (such as our obligation to maintain an office or agency in respect of such senior debt securities, to have moneys held for payment in trust, to register the exchange of such senior debt securities, to deliver such senior debt securities for replacement or to be canceled, to compensate and indemnify the trustee and to appoint a successor trustee, and our right to recover unclaimed money held by the trustee) shall survive until such senior debt securities are no longer outstanding. After such senior debt securities are no longer outstanding, only our obligations to compensate and indemnify the trustee and our right to recover unclaimed money held by the trustee shall survive.

Modification and Waiver. We and the trustee may amend or supplement the senior indenture or the senior debt securities without the consent of any holder:

- to convey, mortgage or pledge any assets as security for the senior debt securities of one or more series;
- to evidence the succession of another corporation to us, and the assumption by such successor corporation of our covenants, agreements and obligations under the senior indenture;
- to cure any ambiguity, defect or inconsistency in the senior indenture or in any supplemental indenture or to conform the senior indenture or the senior debt securities to the description of senior debt securities of such series set forth in this prospectus or a prospectus supplement;
- to evidence and provide for the acceptance of appointment hereunder by a successor trustee, or to make such changes as shall be necessary to provide for or facilitate the administration of the trusts in the senior indenture by more than one trustee;
- to provide for or add guarantors with respect to the senior debt securities of any series;
- to establish the form or forms or terms of the senior debt securities as permitted by the senior indenture;
- to add to, delete from or revise the conditions, limitations and restrictions on the authorized amount, terms, purposes of issue, authentication and delivery of any series of senior debt securities;

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- to add to our covenants such new covenants, restrictions, conditions or provisions for the protection of the holders, and to make the occurrence, or the occurrence and continuance, of a default in any such additional covenants, restrictions, conditions or provisions an event of default;
- to make any change to the senior debt securities of any series so long as no senior debt securities of such series are outstanding; or
- to make any change that does not adversely affect the rights of any holder in any material respect.

Other amendments and modifications of the senior indenture or the senior debt securities issued may be made, and our compliance with any provision of the senior indenture with respect to any series of senior debt securities may be waived, with the consent of the holders of not less than a majority of the aggregate principal amount of the outstanding senior debt securities of all series affected by the amendment or modification (voting as one class); provided, however, that each affected holder must consent to any modification, amendment or waiver that:

- extends the stated maturity of the principal of, or any installment of interest on, any senior debt securities of such series;
- reduces the principal amount of, or premium, if any, or interest on, any senior debt securities of such series;
- changes the place or currency of payment of principal of, or premium, if any, or interest on, any senior debt securities of such series;
- changes the provisions for calculating the optional redemption price, including the definitions relating thereto;
- changes the provisions relating to the waiver of past defaults or changes or impairs the right of holders to receive payment or to institute suit for the enforcement of any payment of any senior debt securities of such series on or after the due date therefor;
- reduces the above-stated percentage of outstanding senior debt securities of such series the consent of whose holders is necessary to modify or amend or to waive certain provisions of or defaults under the senior indenture;
- waives a default in the payment of principal of or interest on the senior debt securities;
- adversely affects the rights of such holder under any mandatory redemption or repurchase provision or any right of redemption or repurchase at the option of such holder; or
- modifies any of the provisions of this paragraph, except to increase any required percentage or to provide that certain other provisions cannot be modified or waived without the consent of the holder of each senior debt security of such series affected by the modification.

It shall not be necessary for the consent of the holders under this section of the senior indenture to approve the particular form of any proposed amendment, supplement or waiver, but it shall be sufficient if such consent approves the substance thereof. After an amendment, supplement or waiver under this section of the senior indenture becomes effective, the trustee must give to the holders affected thereby certain notice briefly describing the amendment, supplement or waiver. We will mail supplemental indentures to holders upon request. Any failure by the trustee to give such notice, or any defect therein, shall not, however, in any way impair or affect the validity of any such supplemental indenture or waiver.

No Personal Liability of Incorporators, Stockholders, Officers, Directors. The senior indenture provides that no recourse shall be had under or upon any obligation, covenant or agreement of ours in the senior indenture or any supplemental indenture, or in any of the senior debt securities or because of the creation of any indebtedness represented thereby, against any incorporator, stockholder, officer or director, past, present or future, of ours or

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of any predecessor or successor corporation thereof under any law, statute or constitutional provision or by the enforcement of any assessment or by any legal or equitable proceeding or otherwise. Each holder, by accepting the senior debt securities, waives and releases all such liability.

Concerning the Trustee. The senior indenture provides that, except during the continuance of a default, the trustee will not be liable, except for the performance of such duties as are specifically set forth in the senior indenture. If an event of default has occurred and is continuing, the trustee will exercise such rights and powers vested in it under the senior indenture and will use the same degree of care and skill in its exercise as a prudent person would exercise under the circumstances in the conduct of such person's own affairs.

We may have normal banking relationships with the trustee under the senior indenture in the ordinary course of business.

Unclaimed Funds. All funds deposited with the trustee or any paying agent for the payment of principal, interest, premium or additional amounts in respect of the senior debt securities that remain unclaimed for two years after the maturity date of such senior debt securities will be repaid to us. Thereafter, any right of any noteholder to such funds shall be enforceable only against us, and the trustee and paying agents will have no liability therefor.

Governing Law. The senior indenture and the debt securities will be governed by, and construed in accordance with, the internal laws of the State of New York.

Certain Terms of the Subordinated Debt Securities

Other than the terms of the subordinated indenture and subordinated debt securities relating to subordination, or otherwise as described in the prospectus supplement relating to a particular series of subordinated debt securities, the terms of the subordinated indenture and subordinated debt securities are identical in all material respects to the terms of the senior indenture and senior debt securities. Additional or different subordination terms may be specified in the prospectus supplement applicable to a particular series.

Subordination. The indebtedness evidenced by the subordinated debt securities is subordinate to the prior payment in full of all our Senior Indebtedness, as defined in the subordinated indenture. During the continuance beyond any applicable grace period of any default in the payment of principal, premium, interest or any other payment due on any of our Senior Indebtedness, we may not make any payment of principal of, or premium, if any, or interest on the subordinated debt securities. In addition, upon any payment or distribution of our assets upon any dissolution, winding up, liquidation or reorganization, the payment of the principal of, or premium, if any, and interest on the subordinated debt securities will be subordinated to the extent provided in the subordinated indenture in right of payment to the prior payment in full of all our Senior Indebtedness. Because of this subordination, if we dissolve or otherwise liquidate, holders of our subordinated debt securities may receive less, ratably, than holders of our Senior Indebtedness. The subordination provisions do not prevent the occurrence of an event of default under the subordinated indenture.

The term "Senior Indebtedness" of a person means with respect to such person the principal of, premium, if any, interest on, and any other payment due pursuant to any of the following, whether outstanding on the date of the subordinated indenture or incurred by that person in the future:

- all of the indebtedness of that person for money borrowed;
- all of the indebtedness of that person evidenced by notes, debentures, bonds or other securities sold by that person for money;
- all of the lease obligations which are capitalized on the books of that person in accordance with generally accepted accounting principles;

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- all indebtedness of others of the kinds described in the first two bullet points above and all lease obligations of others of the kind described in the third bullet point above that the person, in any manner, assumes or guarantees or that the person in effect guarantees through an agreement to purchase, whether that agreement is contingent or otherwise; and
- all renewals, extensions or refundings of indebtedness of the kinds described in the first, second or fourth bullet point above and all renewals or extensions of leases of the kinds described in the third or fourth bullet point above;

unless, in the case of any particular indebtedness, lease, renewal, extension or refunding, the instrument or lease creating or evidencing it or the assumption or guarantee relating to it expressly provides that such indebtedness, lease, renewal, extension or refunding is not superior in right of payment to the subordinated debt securities. Our senior debt securities constitute Senior Indebtedness for purposes of the subordinated debt indenture.

DESCRIPTION OF WARRANTS

We may issue warrants to purchase debt securities, preferred stock or common stock. We may offer warrants separately or together with one or more additional warrants, debt securities, preferred stock, common stock or rights, or any combination of those securities in the form of units, as described in the applicable prospectus supplement. If we issue warrants as part of a unit, the accompanying prospectus supplement will specify whether those warrants may be separated from the other securities in the unit prior to the warrants' expiration date. Below is a description of certain general terms and provisions of the warrants that we may offer. Further terms of the warrants will be described in the prospectus supplement.

The applicable prospectus supplement will describe the following terms of any warrants in respect of which this prospectus is being delivered:

- the specific designation and aggregate number of, and the price at which we will issue, the warrants;
- the currency or currency units in which the offering price, if any, and the exercise price are payable;
- the date on which the right to exercise the warrants will begin and the date on which that right will expire or, if you may not continuously exercise the warrants throughout that period, the specific date or dates on which you may exercise the warrants;
- whether the warrants will be issued in fully registered form or bearer form, in definitive or global form or in any combination of these forms;
- any applicable material U.S. federal income tax consequences;
- the identity of the warrant agent for the warrants and of any execution or paying agents, transfer agents, registrars or other agents;
- the proposed listing, if any, of the warrants or any securities purchasable upon exercise of the warrants on any securities exchange;
- the designation and terms of the equity securities purchasable upon exercise of the warrants;
- the designation, aggregate principal amount, currency and terms of the debt securities that may be purchased upon exercise of the warrants;
- if applicable, the designation and terms of the debt securities, preferred stock, common stock, or rights with which the warrants are issued and, the number of warrants issued with each security;
- if applicable, the date from and after which the warrants and the related debt securities, preferred stock, common stock, or rights will be separately transferable;
- the number of shares of preferred stock or common stock purchasable upon exercise of a warrant and the price at which those shares may be purchased;
- if applicable, the minimum or maximum amount of the warrants that may be exercised at any one time;
- information with respect to book-entry procedures, if any;
- the antidilution provisions of the warrants, if any;
- redemption or call provisions of the warrants, if any; and
- any additional terms of the warrants, including terms, procedures and limitations relating to the exchange and exercise of the warrants.

DESCRIPTION OF RIGHTS

We may issue rights to our stockholders to purchase shares of our common stock or preferred stock. We may offer rights separately or together with one or more additional rights, debt securities, preferred stock, common stock or warrants, or any combination of those securities in the form of units, as described in the applicable prospectus supplement. Each series of rights will be issued under a separate rights agreement to be entered into between us and a bank or trust company, as rights agent. The rights agent will act solely as our agent in connection with the certificates relating to the rights of the series of certificates and will not assume any obligation or relationship of agency or trust for or with any holders of rights certificates or beneficial owners of rights. The following description sets forth certain general terms and provisions of the rights to which any prospectus supplement may relate. The particular terms of the rights to which any prospectus supplement may relate and the extent, if any, to which the general provisions may apply to the rights so offered will be described in the applicable prospectus supplement. To the extent that any particular terms of the rights, rights agreement or rights certificates described in a prospectus supplement differ from any of the terms described below, then the terms described below will be deemed to have been superseded by that prospectus supplement. We encourage you to read the applicable rights agreement and rights certificate for additional information before you decide whether to purchase any of our rights.

We will provide in a prospectus supplement the following terms of the rights being issued:

- the date on which stockholders entitled to the rights distribution will be determined;
- the aggregate number of shares of common stock or preferred stock purchasable upon exercise of the rights;
- the exercise price;
- the aggregate number of rights issued;
- the date, if any, on and after which the rights will be separately transferable;
- the date on which the ability to exercise the rights will commence, and the date on which such ability will expire;
- the conditions to the completion of the offering, if any;
- the withdrawal, termination and cancellation rights, if any;
- any applicable material U.S. federal income tax considerations; and
- any other terms of the rights, including terms, procedures and limitations relating to the distribution, exchange and exercise of the rights.

Each right will entitle the holder of rights to purchase, for cash, the number of shares of common stock or preferred stock at the exercise price provided in the applicable prospectus supplement. Rights may be exercised at any time up to the close of business on the expiration date for the rights provided in the applicable prospectus supplement.

Holders may exercise rights as described in the applicable prospectus supplement. Upon receipt of payment and the rights certificate properly completed and duly executed at the corporate trust office of the rights agent or any other office indicated in the prospectus supplement, we will, as soon as practicable, forward the shares of common stock or preferred stock, as applicable, purchasable upon exercise of the rights. If less than all of the rights issued in any rights offering are exercised, we may offer any unsubscribed securities directly to persons other than stockholders, to or through agents, underwriters or dealers or through a combination of such methods, including pursuant to standby arrangements, as described in the applicable prospectus supplement.

DESCRIPTION OF PURCHASE CONTRACTS

We may issue purchase contracts, including contracts obligating holders to purchase from us, and for us to sell to holders, a specific or variable number of our debt securities, shares of common stock, preferred stock, warrants or rights, or securities of an entity unaffiliated with us, or any combination of the above, at a future date or dates. Alternatively, the purchase contracts may obligate us to purchase from holders, and obligate holders to sell to us, a specific or variable number of our debt securities, shares of common stock, preferred stock, warrants, rights or other property, or any combination of the above. The price of the securities or other property subject to the purchase contracts may be fixed at the time the purchase contracts are issued or may be determined by reference to a specific formula described in the purchase contracts. We may issue purchase contracts separately or as a part of units each consisting of a purchase contract and one or more of our other securities described in this prospectus or securities of third parties, including U.S. Treasury securities, securing the holder's obligations under the purchase contract. The purchase contracts may require us to make periodic payments to holders or vice versa and the payments may be unsecured or pre-funded on some basis. The purchase contracts may require holders to secure the holder's obligations in a manner specified in the applicable prospectus supplement.

The applicable prospectus supplement will describe the terms of any purchase contracts in respect of which this prospectus is being delivered, including, to the extent applicable, the following:

- whether the purchase contracts obligate the holder or us to purchase or sell, or both purchase and sell, the securities subject to purchase under the purchase contract, and the nature and amount of each of those securities, or the method of determining those amounts;
- whether the purchase contracts are to be prepaid;
- whether the purchase contracts are to be settled by delivery, or by reference or linkage to the value, performance or level of the securities subject to purchase under the purchase contract;
- any acceleration, cancellation, termination or other provisions relating to the settlement of the purchase contracts;
- any applicable federal income tax considerations; and
- whether the purchase contracts will be issued in fully registered or global form.

The preceding description sets forth certain general terms and provisions of the purchase contracts to which any prospectus supplement may relate. The particular terms of the purchase contracts to which any prospectus supplement may relate and the extent, if any, to which the general provisions may apply to the purchase contracts so offered will be described in the applicable prospectus supplement. To the extent that any particular terms of the purchase contracts described in a prospectus supplement differ from any of the terms described above, then the terms described above will be deemed to have been superseded by that prospectus supplement. We encourage you to read the applicable purchase contract for additional information before you decide whether to purchase any of our purchase contracts.

DESCRIPTION OF UNITS

The following description, together with the additional information that we include in any applicable prospectus supplements summarizes the material terms and provisions of the units that we may offer under this prospectus. While the terms we have summarized below will apply generally to any units that we may offer under this prospectus, we will describe the particular terms of any series of units in more detail in the applicable prospectus supplement. The terms of any units offered under a prospectus supplement may differ from the terms described below.

We will file as exhibits to the registration statement of which this prospectus is a part, or will incorporate by reference from reports that we file with the SEC, the form of unit agreement that describes the terms of the series of units we are offering, and any supplemental agreements, before the issuance of the related series of units. The following summaries of material terms and provisions of the units are subject to, and qualified in their entirety by reference to, all the provisions of the unit agreement and any supplemental agreements applicable to a particular series of units. We urge you to read the applicable prospectus supplements related to the particular series of units that we may offer under this prospectus, as well as any related free writing prospectuses and the complete unit agreement and any supplemental agreements that contain the terms of the units.

General

We may issue units consisting of common stock, preferred stock, one or more debt securities, warrants, rights or purchase contracts for the purchase of common stock, preferred stock and/or debt securities in one or more series, in any combination. Each unit will be issued so that the holder of the unit is also the holder of each security included in the unit. Thus, the holder of a unit will have the rights and obligations of a holder of each included security. The unit agreement under which a unit is issued may provide that the securities included in the unit may not be held or transferred separately, at any time or at any time before a specified date.

We will describe in the applicable prospectus supplement the terms of the series of units being offered, including:

- the designation and terms of the units and of the securities comprising the units, including whether and under what circumstances those securities may be held or transferred separately;
- any provisions of the governing unit agreement that differ from those described below; and
- any provisions for the issuance, payment, settlement, transfer or exchange of the units or of the securities comprising the units.

The provisions described in this section, as well as those described under “Description of Common Stock,” “Description of Preferred Stock,” “Description of Debt Securities,” “Description of Warrants,” “Description of Rights” and “Description of Purchase Contracts” will apply to each unit, as applicable, and to any common stock, preferred stock, debt security, warrant, right or purchase contract included in each unit, as applicable.

Unit Agent

The name and address of the unit agent for any units we offer will be set forth in the applicable prospectus supplement.

Issuance in Series

We may issue units in such amounts and in such numbers of distinct series as we determine.

Enforceability of Rights by Holders of Units

Each unit agent will act solely as our agent under the applicable unit agreement and will not assume any obligation or relationship of agency or trust with any holder of any unit. A single bank or trust company may act as unit agent for more than one series of units. A unit agent will have no duty or responsibility in case of any default by us under the applicable unit agreement or unit, including any duty or responsibility to initiate any proceedings at law or otherwise, or to make any demand upon us. Any holder of a unit may, without the consent of the related unit agent or the holder of any other unit, enforce by appropriate legal action its rights as holder under any security included in the unit.

FORMS OF SECURITIES

Each debt security, warrant or right will be represented either by a certificate issued in definitive form to a particular investor or by one or more global securities representing the entire issuance of securities. Certificated securities in definitive form and global securities will be issued in registered form. Definitive securities name you or your nominee as the owner of the security, and in order to transfer or exchange these securities or to receive payments other than interest or other interim payments, you or your nominee must physically deliver the securities to the trustee, registrar, paying agent or other agent, as applicable. Global securities name a depository or its nominee as the owner of the debt securities or warrants represented by these global securities. The depository maintains a computerized system that will reflect each investor's beneficial ownership of the securities through an account maintained by the investor with its broker/dealer, bank, trust company or other representative, as we explain more fully below.

Global Securities

We may issue the registered debt securities, warrants, or rights in the form of one or more fully registered global securities that will be deposited with a depository or its nominee identified in the applicable prospectus supplement and registered in the name of that depository or nominee. In those cases, one or more registered global securities will be issued in a denomination or aggregate denominations equal to the portion of the aggregate principal or face amount of the securities to be represented by registered global securities. Unless and until it is exchanged in whole for securities in definitive registered form, a registered global security may not be transferred except as a whole by and among the depository for the registered global security, the nominees of the depository or any successors of the depository or those nominees.

If not described below, any specific terms of the depository arrangement with respect to any securities to be represented by a registered global security will be described in the prospectus supplement relating to those securities. We anticipate that the following provisions will apply to all depository arrangements.

Ownership of beneficial interests in a registered global security will be limited to persons, called participants, that have accounts with the depository or persons that may hold interests through participants. Upon the issuance of a registered global security, the depository will credit, on its book-entry registration and transfer system, the participants' accounts with the respective principal or face amounts of the securities beneficially owned by the participants. Any dealers, underwriters or agents participating in the distribution of the securities will designate the accounts to be credited. Ownership of beneficial interests in a registered global security will be shown on, and the transfer of ownership interests will be effected only through, records maintained by the depository, with respect to interests of participants, and on the records of participants, with respect to interests of persons holding through participants. The laws of some states may require that some purchasers of securities take physical delivery of these securities in definitive form. These laws may impair your ability to own, transfer or pledge beneficial interests in registered global securities.

So long as the depository, or its nominee, is the registered owner of a registered global security, that depository or its nominee, as the case may be, will be considered the sole owner or holder of the securities represented by the registered global security for all purposes under the applicable indenture, warrant agreement, rights agreement or rights certificate. Except as described below, owners of beneficial interests in a registered global security will not be entitled to have the securities represented by the registered global security registered in their names, will not receive or be entitled to receive physical delivery of the securities in definitive form and will not be considered the owners or holders of the securities under the applicable indenture, warrant agreement, rights agreement or rights certificate. Accordingly, each person owning a beneficial interest in a registered global security must rely on the procedures of the depository for that registered global security and, if that person is not a participant, on the procedures of the participant through which the person owns its interest, to exercise any rights of a holder under the applicable indenture, warrant agreement, rights agreement or rights certificate. We understand that under existing industry practices, if we request any action of holders or if an owner of a

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beneficial interest in a registered global security desires to give or take any action that a holder is entitled to give or take under the applicable indenture, warrant agreement, rights agreement or rights certificate, the depositary for the registered global security would authorize the participants holding the relevant beneficial interests to give or take that action, and the participants would authorize beneficial owners owning through them to give or take that action or would otherwise act upon the instructions of beneficial owners holding through them.

Principal or premium, if any, and interest payments on debt securities, and any payments to holders with respect to warrants or rights represented by a registered global security registered in the name of a depositary or its nominee will be made to the depositary or its nominee, as the case may be, as the registered owner of the registered global security. None of Targacept, any warrant agent, rights agent or any other agent of Targacept, agent of the trustee or agent of such warrant agent or rights agent will have any responsibility or liability for any aspect of the records relating to payments made on account of beneficial ownership interests in the registered global security or for maintaining, supervising or reviewing any records relating to those beneficial ownership interests.

We expect that the depositary for any of the securities represented by a registered global security, upon receipt of any payment of principal, premium, interest or other distribution of underlying securities or other property to holders of that registered global security, will immediately credit participants' accounts in amounts proportionate to their respective beneficial interests in that registered global security as shown on the records of the depositary. We also expect that payments by participants to owners of beneficial interests in a registered global security held through participants will be governed by standing customer instructions and customary practices, as is now the case with the securities held for the accounts of customers in bearer form or registered in "street name," and will be the responsibility of those participants.

If the depositary for any of these securities represented by a registered global security is at any time unwilling or unable to continue as depositary or ceases to be a clearing agency registered under the Exchange Act, and a successor depositary registered as a clearing agency under the Exchange Act is not appointed by us within 90 days, we will issue securities in definitive form in exchange for the registered global security that had been held by the depositary. Any securities issued in definitive form in exchange for a registered global security will be registered in the name or names that the depositary gives to the relevant warrant agent, rights agent or other relevant agent of ours or theirs. It is expected that the depositary's instructions will be based on directions received by the depositary from participants with respect to ownership of beneficial interests in the registered global security that had been held by the depositary.

PLAN OF DISTRIBUTION

We may offer the securities offered by this prospectus from time to time pursuant to underwritten public offerings, negotiated transactions, block trades or a combination of these methods. We may sell the securities (1) through underwriters or dealers, (2) through agents, (3) in “at the market offerings,” within the meaning of Rule 415(a)(4) of the Securities Act, to or through a market maker or into an existing trading market, on an exchange or otherwise or (4) directly to one or more purchasers, or through a combination of such methods. We may distribute the securities from time to time in one or more transactions at:

- a fixed price or prices, which may be changed;
- market prices prevailing at the time of sale;
- prices related to the prevailing market prices; or
- negotiated prices.

The applicable prospectus supplement will describe the terms of the offering of securities, including:

- the type and number of securities we are offering;
- the name or names of any underwriters;
- any securities exchange or market on which the securities may be listed;
- the purchase price or other consideration to be paid in connection with the sale of our securities being offered and the proceeds we will receive from the sale;
- any over-allotment options pursuant to which the underwriters may purchase additional securities from us;
- any underwriting discounts or agency fees and other items constituting underwriters’ or agents’ compensation; and
- any discounts or concessions allowed or reallocated or paid to dealers.

We may directly solicit offers to purchase the securities. We may also designate agents to solicit offers to purchase the securities from time to time. We will name in a prospectus supplement any agent involved in the offer or sale of the securities.

If we utilize a dealer in the sale of the securities being offered by this prospectus, we will sell the securities to the dealer, as principal. The dealer may then resell the securities to the public at varying prices to be determined by the dealer at the time of resale.

If we utilize an underwriter in the sale of the securities being offered, we will execute an underwriting agreement with the underwriter at the time of sale. In connection with the sale of the securities, we, or the purchasers of the securities for whom the underwriter may act as agent, may compensate the underwriter in the form of underwriting discounts or commissions. The underwriter may sell the securities to or through dealers, and the underwriter may compensate those dealers in the form of discounts, concessions or commissions. Subject to certain conditions, the underwriters will be obligated to purchase all of the securities offered by the prospectus supplement. We may change from time to time the public offering price and any discounts or concessions allowed or reallocated or paid to dealers.

Underwriters, dealers and agents participating in the distribution of the securities may be deemed to be underwriters within the meaning of the Securities Act, and any discounts and commissions received by them and any profit realized by them on resale of the securities may be deemed to be underwriting discounts and commissions. We may enter into agreements to indemnify underwriters, dealers and agents against civil liabilities, including liabilities under the Securities Act, or to contribute to payments they may be required to make in respect thereof.

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If so indicated in the applicable prospectus supplement, we will authorize underwriters or other persons acting as our agents to solicit offers by certain institutions to purchase securities from us pursuant to delayed delivery contracts providing for payment and delivery on the date stated in the prospectus supplement. Each contract will be for an amount not less than, and the aggregate amount of securities sold pursuant to such contracts shall not be less nor more than, the respective amounts stated in the prospectus supplement. Institutions with whom the contracts, when authorized, may be made include commercial and savings banks, insurance companies, pension funds, investment companies, educational and charitable institutions and other institutions, but shall in all cases be subject to our approval. Delayed delivery contracts will not be subject to any conditions except that:

- the purchase by an institution of the securities covered under that contract shall not at the time of delivery be prohibited under the laws of the jurisdiction to which that institution is subject; and
- if the securities are also being sold to underwriters acting as principals for their own account, the underwriters shall have purchased such securities not sold for delayed delivery. The underwriters and other persons acting as our agents will not have any responsibility in respect of the validity or performance of delayed delivery contracts.

Securities sold pursuant to the registration statement of which this prospectus is a part may be authorized for quotation and trading on The NASDAQ Global Market. We can make no assurance as to the liquidity of or the existence of trading markets for any of the securities.

To facilitate an offering of the securities, certain persons participating in the offering may engage in transactions that stabilize, maintain or otherwise affect the price of our securities. This may include over-allotments or short sales of the securities, which involve the sale by persons participating in the offering of more securities than we sell to them. In these circumstances, these persons would cover the over-allotments or short positions by making purchases in the open market or by exercising their over-allotment option. In addition, these persons may stabilize or maintain the price of the securities by bidding for or purchasing the securities in the open market or by imposing penalty bids, whereby selling concessions allowed to underwriters or dealers participating in the offering may be reclaimed if the securities sold by them are repurchased in connection with stabilization transactions. The effect of these transactions may be to stabilize or maintain the market price of our securities at a level above that which might otherwise prevail in the open market. These transactions, if commenced, may be discontinued at any time.

In compliance with guidelines of the Financial Industry Regulatory Authority, or FINRA, the maximum consideration or discount to be received by any FINRA member or independent broker dealer may not exceed 8% of the aggregate amount of the securities offered pursuant to this prospectus and any applicable prospectus supplement.

Underwriters, dealers and agents may engage in other transactions with us, or perform other services for us, in the ordinary course of their business. We will describe such relationships in the applicable prospectus supplement, naming the underwriter and the nature of any such relationship.

LEGAL MATTERS

Mintz, Levin, Cohn, Ferris, Glovsky and Popeo, P.C., Boston, Massachusetts, will pass upon the validity of the issuance of the securities offered by this prospectus.

EXPERTS

The financial statements of Targacept, Inc. appearing in Targacept, Inc.'s Annual Report (Form 10-K) for the year ended December 31, 2009 have been audited by Ernst & Young LLP, independent registered public accounting firm, as set forth in their report thereon included therein, and incorporated herein by reference. Such financial statements are, and audited financial statements to be included in subsequently filed documents will be, incorporated herein in reliance upon the report of Ernst & Young LLP pertaining to such financial statements (to the extent covered by consents filed with the SEC) given on the authority of such firm as experts in accounting and auditing.

WHERE YOU CAN FIND MORE INFORMATION

We are subject to the reporting requirements of the Exchange Act and file annual, quarterly and current reports, proxy statements and other information with the SEC. You may read and copy these reports, proxy statements and other information at the SEC's public reference facilities at 100 F Street, N.E., Room 1580, Washington, D.C. 20549. You can request copies of these documents by writing to the SEC and paying a fee for the copying cost. Please call the SEC at 1-800-SEC-0330 for more information about the operation of the public reference facilities. SEC filings are also available at the SEC's website at <http://www.sec.gov>. Our common stock is listed on The NASDAQ Global Market, and you can read and inspect our filings at the offices of the Financial Industry Regulatory Authority located at 1735 K Street, N.W., Washington, D.C. 20006.

This prospectus is only part of a registration statement on Form S-3 that we have filed with the SEC under the Securities Act and therefore omits certain information contained in the registration statement. We have also filed exhibits with the registration statement that are excluded from this prospectus, and you should refer to the applicable exhibit for a complete description of any statement referring to any contract or other document. You may inspect a copy of the registration statement, including the exhibits, without charge, at the public reference room or obtain a copy from the SEC upon payment of the fees prescribed by the SEC.

The reports, proxy statements and other information that we file with the SEC are available to you free of charge through the Investor Relations page of our website, www.targacept.com, as soon as reasonably practicable after they have been electronically filed with, or furnished to, the SEC. We have included our website address as a factual reference and do not intend it as an active link to our website.

INCORPORATION OF DOCUMENTS BY REFERENCE

The SEC allows us to “incorporate by reference” information from other documents that we file, which means that we can disclose important information in this prospectus by referring to those documents. The information incorporated by reference is considered to be part of this prospectus and will automatically add to, update and, if applicable, supersede the information in this prospectus. We incorporate by reference in this prospectus the documents listed below:

- our Annual Report on Form 10-K for the fiscal year ended December 31, 2009, filed on March 11, 2010;
- our Quarterly Report on Form 10-Q for the quarter ended March 31, 2010, filed on May 10, 2010;
- our Quarterly Report on Form 10-Q for the quarter ended June 30, 2010, filed on August 9, 2010;
- our Quarterly Report on Form 10-Q for the quarter ended September 30, 2010, filed on November 5, 2010;
- our Current Reports on Form 8-K filed on January 25, 2010, May 3, 2010, May 6, 2010, June 15, 2010 and October 7, 2010;
- our Definitive Proxy Statement on Schedule 14A for the 2010 annual meeting of stockholders filed on April 16, 2010;
- the description of our common stock contained in our Registration Statement on Form 8-A filed on April 6, 2006; and
- all filings that we make pursuant to Sections 13(a), 13(c), 14 or 15(d) of the Exchange Act after the date of the filing of the registration statement on Form S-3 of which this prospectus is a part and prior to the termination or completion of any offering of securities under this prospectus and all applicable prospectus supplements (except, in each case, for information contained in any such filing that is furnished and not “filed” under the Exchange Act), which filings will be deemed to be incorporated by reference in this prospectus, as supplemented by the applicable prospectus supplement, and to be a part hereof from the respective dates of such filings.

The SEC file number for each of the documents listed above is 000-51173.

We will provide without charge to each person, including any beneficial owner, to whom a copy of this prospectus is delivered, upon the request of any such person, a copy of any or all of the information incorporated herein by reference (exclusive of exhibits to such documents, unless such exhibits are specifically incorporated by reference herein). Requests, whether written or oral, for such copies should be directed to Targacept, Inc., 200 East First Street, Suite 300, Winston-Salem, North Carolina 27101, Attn: Chief Financial Officer, (336) 480-2100.

To the extent that any statements contained in a document incorporated by reference are modified or superseded by any statements contained in this prospectus, such statements shall not be deemed incorporated in this prospectus.



**\$75,000,000
COMMON STOCK**

Deutsche Bank Securities

**Lazard Capital Markets
Leerink Swann
Oppenheimer & Co.**

Prospectus Supplement

May , 2011