THERAVANCE INC
Form 10-K
March 01, 2007

SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

FORM 10-K

(Mark One)

x ANNUAL REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the fiscal year ended December 31, 2006

or

o TRANSITION REPORT PURSUANT TO SECTION 13 OR 15(d) OF THE SECURITIES EXCHANGE ACT OF 1934

For the transition period from to

Commission File No. 0-30319

THERAVANCE, INC.

(Exact name of registrant as specified in its charter)

Delaware	**94-3265960**
(State or other jurisdiction of incorporation or organization)	(I.R.S. Employer Identification No.)
901 Gateway Boulevard, South San Francisco, California	**94080**
(Address of principal executive offices)	(Zip Code)

Registrant s telephone number, including area code: **650-808-6000**

SECURITIES REGISTERED PURSUANT TO SECTION 12(b) OF THE ACT:

Title of Each Class	**Name of Each Exchange On Which Registered**
Common Stock $0.01 Par Value	**Nasdaq Global Market**

SECURITIES REGISTERED PURSUANT TO SECTION 12(g) OF THE ACT: **NONE**

Indicate by check mark whether the registrant is a well-known seasoned issuer, as defined in Rule 405 of the Securities Act. Yes x No o

Indicate by check mark whether the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Act. Yes o No x

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports), and (2) has been subject to such filing requirements for the past 90 days. Yes x No o

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of registrant s knowledge, in definitive proxy or information statements incorporated by reference in Part III of this Form 10-K or any amendment to this Form 10-K. o

Indicate by check mark whether registrant is a large accelerated filer, an accelerated filer or a non accelerated filer. See definition of accelerated filer and large accelerated filer in Rule 12b-2 of the Exchange Act (Check One):

Large Accelerated filer x Accelerated filer o Non-accelerated filer o

Indicate by check mark whether the registrant is a shell company (as defined in Rule 12b-2 of the Exchange Act). Yes o No x

The aggregate market value of the voting and non-voting common equity (consisting of Common Stock, $0.01 par value and Class A Common Stock, $0.01 par value) held by non-affiliates of the registrant based upon the closing price of the Common Stock on the Nasdaq Global Market on June 30, 2006 was $900,065,635. Shares of Common Stock and Class A Common Stock held by each executive officer and director and by each person or group who owns 5% or more of the outstanding Common Stock or Class A Common Stock at June 30, 2006 have been excluded. Exclusion of such shares should not be construed to indicate that any such person possesses the power, direct or indirect, to direct or cause the direction of the management or policies of the registrant or that such person is controlled by or under common control with the registrant.

On February 15, 2007 there were 50,794,120 shares of the registrant s Common Stock and 9,401,498 shares of the Registrant s Class A Common Stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Specified portions of the registrant s definitive Proxy Statement to be issued in conjunction with the registrant s 2007 Annual Meeting of Stockholders, which is expected to be filed not later than 120 days after the registrant s fiscal year ended December 31, 2006, are incorporated by reference into Part III of this Annual Report. Except as expressly incorporated by reference, the registrant s Proxy Statement shall not be deemed to be a part of this Annual Report on Form 10-K.

THERAVANCE, INC.
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Special Note regarding Forward-Looking Statements

This Annual Report on Form 10-K contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. Such forward-looking statements involve substantial risks, uncertainties and assumptions. All statements in this Annual Report on Form 10-K, other than statements of historical facts, including statements regarding our strategy, future operations, future financial position, future revenues, projected costs, prospects, plans, intentions, expectations and objectives could be forward-looking statements. The words anticipates, believes, estimates, expects, intends, may, plans, projects, will, would and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We may not actually achieve the plans, intentions, expectations or objectives disclosed in our forward-looking statements and the assumptions underlying our forward-looking statements may prove incorrect. Therefore, you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions, expectations and objectives disclosed in the forward-looking statements that we make. Factors that we believe could cause actual results or events to differ materially from our forward-looking statements include, but are not limited to, those discussed below in Risk Factors in Item 1A, Management s Discussion and Analysis of Financial Condition and Results of Operations in Item 7 and elsewhere in this Annual Report on Form 10-K and the risks discussed in our other filings with the Securities and Exchange Commission (SEC). Our forward-looking statements in this Annual Report on Form 10-K are based on current expectations and we do not assume any obligation to update any forward-looking statements.

PART I

ITEM 1. BUSINESS

Overview

Theravance is a biopharmaceutical company with a pipeline of internally discovered product candidates. We are focused on the discovery, development and commercialization of small molecule medicines across a number of therapeutic areas including respiratory disease, bacterial infections and gastrointestinal motility dysfunction. Of our five programs in development, two are in late stage our telavancin program focusing on treating serious Gram-positive bacterial infections with Astellas Pharma Inc. (Astellas) and our Beyond Advair collaboration with GlaxoSmithKline plc (GSK). By leveraging our proprietary insight of multivalency to drug discovery focused on validated targets, we are pursuing a next generation drug discovery strategy designed to discover superior medicines in large markets. Our headquarters are located at 901 Gateway Boulevard, South San Francisco, California 94080. Theravance was incorporated in Delaware in November 1996 under the name Advanced Medicine, Inc. and began operations in May 1997. The Company changed its name to Theravance, Inc. in April 2002. None of our products have been approved for marketing and sale to patients and we have not received any product revenue to date.

Our strategy focuses on the discovery, development and commercialization of medicines with superior efficacy, convenience, tolerability and/or safety. By primarily focusing on biological targets that have been clinically validated either by existing medicines or by potential medicines in late-stage clinical studies, we can leverage years of available knowledge regarding a target s activity and the animal models used to test potential medicines against such targets. We move a product candidate into development after it demonstrates superiority to existing medicines or drug candidates in animal models that we believe correlate to human clinical experience. This strategy of developing the next generation of existing medicines or potential medicines is designed to reduce technical risk and increase productivity. We believe that we can enhance the probability of successfully developing and commercializing medicines by identifying at least two structurally different product candidates, whenever practicable in each therapeutic program. In total, our research and development expenses, including stock-based compensation expense

associated with the adoption of the Financial Accounting Standards Board s Statement No. 123 (revised 2004), Share-Based Payment (SFAS 123(R)), incurred for all of our therapeutic programs in 2006, 2005 and 2004 were $166.6 million, $137.9 million and $91.6 million, respectively.

In December 2006, we submitted our first new drug application (NDA) to the U.S. Food and Drug Administration (FDA) for telavancin for the treatment of complicated skin and skin structure infections (cSSSI) caused by Gram-positive bacteria, including methicillin-resistant *Staphylococcus aureus* (MRSA). Telavancin is a rapidly bactericidal, injectable antibiotic with multifunctional mechanisms of action. The NDA submission was based on positive Phase 3 cSSSI results. In addition to the cSSSI indication, telavancin is currently in Phase 3 clinical studies for hospital-acquired pneumonia (HAP) designed to demonstrate non-inferiority of telavancin compared to standard therapy for the treatment of serious Gram-positive infections and superiority over vancomycin in those patients whose infections are due to MRSA. Our goal is for telavancin to become first-line therapy in treating these serious infections.

In November 2005, we entered into a collaboration arrangement with Astellas for the development and commercialization of telavancin. In July 2006, Japan was added to our telavancin collaboration, thereby giving Astellas worldwide rights to this potential medicine. Through December 31, 2006, we have received $101.0 million in upfront and milestone payments from Astellas and we are eligible to receive up to $126.0 million in remaining clinical and regulatory milestone payments. If telavancin is commercialized, we will be entitled to receive royalties on global sales of telavancin ranging, on a percentage basis, from the high teens to the upper twenties depending on sales volume. In addition to the license rights to telavancin, Astellas also received an option to further develop and commercialize TD-1792, our heterodimer antibiotic compound that entered Phase 2 clinical studies in December 2006.

In November 2002, we entered into our Beyond Advair collaboration with GSK to develop and commercialize long-acting beta2 agonist (LABA) product candidates for the treatment of asthma and chronic obstructive pulmonary disease (COPD). These product candidates are intended to be administered via inhalation once daily both as a single new medicine and as part of a new combination medicine with an inhaled corticosteroid (ICS). The collaboration intends to develop a new generation product to replace Advair®, which had approximately $6.1 billion of sales for 2006 as reported by GSK in early 2007. Each company contributed four LABA product candidates to the collaboration and two product candidates are in a Phase 2b program.

In March 2004, we entered into a strategic alliance agreement with GSK. Under this alliance GSK received an option to license product candidates from all of our full drug discovery programs initiated prior to September 1, 2007, on pre-determined terms and on an exclusive, worldwide basis. When GSK exercises its option to license any of our programs, we receive an upfront payment, additional payments upon achievement of future milestones and royalties on any future sales. In addition, GSK funds all of the subsequent development and commercialization costs for product candidates in such programs. Consistent with our strategy, we will be obligated at our sole cost to discover two structurally different product candidates for any programs that are licensed by GSK under the alliance. To date, GSK has licensed our two COPD programs under the terms of the strategic alliance and we have discovered and delivered to GSK two structurally different product candidates for both of these programs. In August 2004, GSK exercised its right to license our long-acting muscarinic antagonist (LAMA) program and informed us of its decision not to license our bacterial infections program, in each case pursuant to the terms of the strategic alliance. In March 2005, GSK exercised its right to license our bifunctional muscarinic antagonist beta2 agonist (MABA) program pursuant to the terms of the strategic alliance, and notified us of its decision not to license our anesthesia program.

GSK currently owns all of our Class A common stock, which represents approximately 15.6% of our outstanding stock as of February 15, 2007. Under the terms of the strategic alliance, GSK s ownership of our stock could increase to approximately 59.4% through the issuance by us to GSK of the number of shares of our common stock that we may be required to redeem from our stockholders. In July 2007,

GSK has the right to require us to redeem, and upon notice of such redemption, each stockholder (including GSK, to the extent GSK holds common stock) will automatically be deemed to have submitted for redemption, 50% of our common stock held by such stockholder at $54.25 per share. This right is referred to as the call. If GSK does not exercise this right, then in August 2007, our stockholders (including GSK, to the extent GSK holds common stock) have the right to require us to redeem up to 50% of their common stock at $19.375 per share. This right is referred to as the put. In either case, GSK is obligated to pay to us the funds necessary for us to redeem the shares of common stock from our stockholders; however, GSK s maximum obligation for the shares subject to the put is capped at $525 million. Alternatively, if our stockholders exercise the put, GSK may elect to purchase such shares directly from our stockholders. We are under no obligation to redeem our shares under the call or the put until we receive such funds from GSK. If GSK s ownership of our stock increases to more than 50% as a result of the call or put, GSK will receive a five-year extension of its exclusive option to our programs, so that the option would cover all of our full drug discovery programs initiated prior to September 1, 2012.

Our Programs

Our drug discovery efforts are based on the principles of multivalency. Multivalency involves the simultaneous attachment of a single molecule to multiple binding sites on one or more biological targets. We have applied our expertise in multivalency to discover product candidates and lead compounds in a wide variety of therapeutic areas. We have conducted extensive research in both relevant laboratory and animal models to demonstrate that by applying the design principles of multivalency, we can achieve significantly stronger and more selective attachment of our compounds to a variety of intended biological targets. We believe that medicines that attach more strongly and selectively to their targets will be superior to many medicines by substantially improving potency, duration of action and/or safety. The table below summarizes the status of our product candidates for internal development or co-development.

In the table above:

- Preclinical refers to formulation development or to safety testing in animal models required prior to initiating human clinical studies.

- Phase 1 indicates initial clinical safety testing in healthy volunteers, or studies directed toward understanding the mechanisms of action of the drug.

- Phase 2 indicates further clinical safety testing and preliminary efficacy testing in a limited patient population.

- Phase 3 indicates evaluation of clinical efficacy and safety within an expanded patient population.

- Based upon our strategy of pursuing new compounds for validated targets, we consider compounds that have successfully completed a Phase 2a study showing efficacy and tolerability as having achieved Proof of Concept.

- Development Status indicates the most advanced stage of development that has been completed or is in process.

Our Relationship with Astellas

2005 License, Development and Commercialization Agreement

In November 2005, we entered into a collaboration arrangement with Astellas for the development and commercialization of telavancin. In July 2006, Japan was added to our telavancin collaboration, thereby giving Astellas worldwide rights to this potential medicine. Through December 31, 2006, we have received $101.0 million in upfront and milestone payments from Astellas and we are eligible to receive up to an additional $126.0 million in clinical and regulatory milestone payments, which includes up to $116.0 million for completion of clinical studies and filing and approval of new drug applications for cSSSI and HAP, and $10 million if the Phase 3 data demonstrates telavancin s superiority over vancomycin for HAP patients infected with MRSA.

If telavancin is commercialized we will be entitled to receive royalties on global sales of telavancin that, on a percentage basis, range from the high teens to the upper twenties depending on sales volume. Under this arrangement, we will be responsible for substantially all costs to develop and obtain U.S. regulatory approval for telavancin for cSSSI and HAP, and Astellas will be responsible for substantially all costs associated with commercialization and further development of telavancin. In addition to the license rights to telavancin, Astellas also received an option to further develop and commercialize TD-1792, our heterodimer antibiotic compound that entered Phase 2 clinical studies in December 2006.

Our Relationship with GlaxoSmithKline

2002 Beyond Advair Collaboration

In November 2002, we entered into our Beyond Advair collaboration with GSK to develop and commercialize long-acting beta2 agonist (LABA) product candidates for the treatment of asthma and COPD. These product candidates are intended to be administered via inhalation once daily both as a single new medicine and as part of a new combination medicine with an ICS. Each company contributed four LABA product candidates to the collaboration, and two product candidates are in Phase 2b clinical programs.

In connection with this collaboration, in 2002 we received from GSK an upfront payment of $10.0 million and sold to an affiliate of GSK shares of our Series E preferred stock for an aggregate purchase price of $40.0 million. In addition, we were eligible to receive up to $495.0 million in development, approval, launch, and sales milestones and royalties on the sales of any product resulting from this collaboration. As of December 31, 2006, we have received a total of $50.0 million in development milestones and have up to $445.0 million in remaining milestones allocated as follows: up to $75.0 million related to the achievement of certain clinical milestones by a Theravance-discovered LABA compound, up to $220.0 million related to approval and launch of a product containing a Theravance-discovered LABA

in multiple regions in the world, and up to $150.0 million related to the achievement of certain sales thresholds, whether the LABA compound was discovered by Theravance or GSK. In the event that a LABA product candidate discovered by GSK is successfully developed and commercially launched in multiple regions in the world, we will be obligated to make payments to GSK of up to $220.0 million. Based on available information, we do not estimate that a significant portion of these potential milestone payments to GSK are likely to be made in the next three years. In addition, we are entitled to receive the same royalties on product sales of medicines from the Beyond Advair collaboration, regardless of whether the product candidate originated with Theravance or with GSK. The royalty structure is downward tiering and would result in an average percentage royalty rate in the low- to mid-teens at annual net sales of up to approximately $4.0 billion and the average royalty rate would decline to single digits at annual net sales of more than $6 billion. Sales of single agent LABA medicines and combination LABA/ICS medicines would be combined for the purposes of this royalty calculation.

2004 Strategic Alliance

In March 2004, we entered into our strategic alliance with GSK. Under this alliance, GSK received an option to license product candidates from all of our full drug discovery programs initiated prior to September 1, 2007, on pre-determined terms and on an exclusive, worldwide basis. We are obligated to use diligent efforts to discover and deliver compounds for the alliance and have committed to initiating at least three new full discovery programs from May 2004 through August 2007. We maintain sole decision-making authority with respect to our discovery programs, including without limitation, decisions relating to initiation and termination of discovery programs, and staffing and resource allocation among discovery programs. Since May 2004 we have initiated three new full discovery programs. In connection with the strategic alliance with GSK, we received from GSK a payment of $20.0 million. In May 2004, GSK purchased through an affiliate 6,387,096 shares of our Class A common stock for an aggregate purchase price of $108.9 million. Through December 31, 2006, we have received $36.0 million in upfront and milestone payments from GSK relating to the strategic alliance agreement.

GSK must exercise its right to license no later than sixty days subsequent to (i) for our inhaled respiratory discovery programs, the development candidate stage (generally defined as the point when the lead candidate is selected for preclinical studies and preparation for entry into a Phase 1 clinical study), or (ii) for programs other than inhaled respiratory programs, the proof-of-concept stage (generally defined as the successful completion of a Phase 2a clinical study showing efficacy and tolerability if the biological target for the drug has been clinically validated by an existing medicine, and successful completion of a Phase 2b clinical study showing efficacy and tolerability if the biological target for the drug has not been clinically validated by an existing medicine). Under the terms of the strategic alliance, GSK has only one opportunity to license each of our programs. Upon its decision to license a program, GSK is responsible for funding all future development, manufacturing and commercialization activities for product candidates in that program. In addition, GSK is obligated to use diligent efforts to develop and commercialize product candidates from any program that it licenses. Consistent with our strategy, we are obligated at our sole cost to discover two structurally different product candidates for any programs that are licensed by GSK under the alliance. If these programs are successfully advanced through development by GSK, we are entitled to receive clinical, regulatory and commercial milestone payments and royalties on any sales of medicines developed from these programs. The royalty structure for a product containing one of our compounds as a single active ingredient would result in an average percentage royalty rate in the low double digits. If a product is successfully commercialized, in addition to any royalty revenue that we receive, the total upfront and milestone payments that we could receive in any given program that GSK licenses range from $130.0 million to $162.0 million for programs with single-agent medicines and up to $252.0 million for programs with both a single-agent and a combination medicine. If GSK chooses not to license a program, we retain all rights to the program and may continue the program alone or with a third party. To date GSK has licensed our two COPD programs: LAMA and MABA. We received a $5.0 million

payment from GSK in connection with its license of each of our LAMA and MABA programs in August 2004 and March 2005, respectively. There can be no assurance that GSK will license any other programs under the terms of the alliance agreement or at all, which could have an adverse effect on our business and financial condition.

As part of the strategic alliance, we amended our certificate of incorporation to provide for the redemption of our common stock under certain circumstances. In July 2007, GSK has a call right to require us to redeem, and upon notice, each stockholder (including GSK, to the extent GSK holds common stock) will automatically be deemed to have submitted for redemption, 50% of our common stock held by such stockholder at $54.25 per share. If GSK does not exercise this call right, then in August 2007, our stockholders (including GSK, to the extent GSK holds common stock) have a put right to cause us to redeem up to 50% of their common stock at $19.375 per share. In either case, GSK is contractually obligated to pay to us the funds necessary for us to redeem the shares of common stock from our stockholders; however, GSK s maximum obligation for the shares subject to the put is capped at $525 million. We are under no obligation to redeem our shares under the call or the put until we receive funds to redeem such shares from GSK. Alternatively, if our stockholders exercise the put, GSK may elect to purchase the shares of common stock that are put directly from our stockholders. GSK s ownership of our stock could increase to approximately 59.4% through the concurrent issuance to GSK of the number of shares of stock that we may be required to redeem from our stockholders. In addition, if GSK s ownership of our stock increases to more than 50% as a result of the call right or put right, GSK will receive an extension of its exclusive option to our full drug discovery programs initiated prior to September 1, 2012; otherwise, this exclusive option does not apply to programs initiated after September 1, 2007.

The effect of the redemption of our common stock pursuant to the call or the put would not cause a decrease to the Company s cash balances, total assets, or total stockholders equity. Accordingly, the Company has classified its common stock within stockholders equity.

In addition, we entered into a governance agreement with GSK which, among other matters, (i) gives GSK the right to nominate directors to our board of directors, (ii) provides GSK with rights regarding certain corporate governance matters, including the right to restrict our ability to take specified significant corporate actions, such as the issuance of debt and equity securities above specified limitations, the sale of significant assets, acquisitions by us and the redemption of our common stock, and (iii) governs future acquisitions or dispositions of our securities by GSK. Pursuant to a partial exercise of its rights under the governance agreement, upon the closing of our initial public offering on October 8, 2004, GSK purchased through an affiliate an additional 433,757 shares of Class A common stock. GSK s ownership position of our outstanding stock was approximately 15.6% as of February 15, 2007.

Our Relationship with AstraZeneca AB

2006 License Agreement with AstraZeneca AB

In May 2006, we entered into a license agreement with AstraZeneca AB (AstraZeneca) pursuant to which we granted an exclusive, worldwide license to AstraZeneca to develop and commercialize our intravenous anesthetic compound TD-4756. Through December 31, 2006, we received a $1.0 million upfront payment from AstraZeneca and are eligible to receive milestone payments and royalties on global sales.

Development Programs

Bacterial Infections

Our bacterial infections program has been dedicated to finding new antibiotics for serious infections due to *Staphylococcus aureus* and other Gram-positive bacteria, including methicillin-resistant *Staphylococcus aureus* (MRSA). Our program resulted in the discovery of telavancin and a unique heterodimer antibiotic, TD-1792.

Telavancin Status

Telavancin is a rapidly bactericidal, injectable antibiotic with multiple mechanisms of action: the inhibition of bacterial cell wall synthesis and the disruption of bacterial cell membrane integrity. We believe the additive mechanisms of action seen with telavancin speed bacterial killing while also reducing the risks of inducing resistance to telavancin or cross-resistance with other antibiotics.

In December 2006, we submitted a NDA for telavancin to the FDA for the treatment of complicated skin and skin structure infections (cSSSI) caused by Gram-positive bacteria, including methicillin-resistant *Staphylococcus aureus* (MRSA). The NDA submission was based on positive Phase 3 cSSSI results, released in August 2006, in which telavancin s rates of clinical cure, microbiological eradication, and overall therapeutic response compared favorably to those for vancomycin. In addition to the cSSSI indication, telavancin is currently in Phase 3 clinical studies for hospital-acquired pneumonia (HAP). The HAP program consists of two studies targeting approximately 750 patients each for a total of approximately 1,500 patients. Our goal in the design and execution of the HAP program is to demonstrate non-inferiority compared to standard therapy in the treatment of Gram-positive infections and to demonstrate superiority over vancomycin in those patients infected by MRSA. Our goals with telavancin are to complete enrollment for the HAP program in the first half of 2007 and, if we receive FDA approval, commercially launch telavancin for the treatment of cSSSI with our partner Astellas in the second half of 2007.

Heterodimer Status

TD-1792 is a unique heterodimer antibiotic that combines the antibacterial activities of a glycopeptide and a beta-lactam in one molecule. The goal of our program with TD-1792 is to develop a next-generation antibiotic that is more efficacious than vancomycin, the current standard of care for the treatment of serious infections caused by MRSA, and which has an improved resistance profile relative to other antibiotics. In December 2006, we initiated Phase 2 clinical studies with TD-1792 for the treatment of cSSSI caused by Gram-positive bacteria, including MRSA. Our goal is to report Phase 2 data in the second half of 2007.

Respiratory

Our respiratory franchise has three development programs directed toward asthma and/or COPD: our Beyond Advair collaboration with GSK, and our LAMA and MABA programs, both of which GSK has licensed pursuant to the terms of our strategic alliance.

Beyond Advair Collaboration

Our Beyond Advair collaboration with GSK is currently developing several long-acting beta2 agonist (LABA) product candidates intended for once-daily administration as a single agent for treatment of COPD or in combination with an ICS for the treatment of asthma and COPD. We believe once-a-day dosing would be a significant convenience and compliance-enhancing advantage leading to improved overall clinical outcomes in patients with asthma or COPD.

The collaboration intends to develop a new generation product to replace GSK s Advair®, an inhaled combination medicine consisting of a long-acting beta2 agonist (salmeterol) and an ICS (fluticasone) taken twice daily, which had sales of approximately $6.1 billion for 2006 as reported by GSK in early 2007.

Beta2 agonists are medicines that work by relaxing the muscles that line the bronchial airways, allowing the capacity of the airways to expand (known as bronchodilation), leading to the relief and/or prevention of many of the symptoms of asthma and COPD. Beta2 agonists, like many other medications to treat asthma and COPD, are administered by inhalation. Patients typically self-administer these

medications by breathing in a measured amount of drug using hand-held devices, such as a metered dose inhaler (MDI), or a dry powder inhaler (DPI).

Beyond Advair Status

The Beyond Advair collaboration has a development pool consisting of eight compounds, five of which are in Phase 2. Two of these compounds, GSK159797 (797) and GSK542444 (444) are in Phase 2b programs designed to evaluate the safety and efficacy of these compounds in multi-day administration to mild-to-moderate asthmatics, and to assess potential commercial dosing. We expect to report data from the ongoing Phase 2b program for 797 and 444 in the first half of 2007.

Bifunctional Muscarinic Antagonist-Beta2 Agonist (MABA)

In our MABA program, we are developing with GSK a long-acting inhaled bronchodilator that is bifunctional, meaning that one small molecule functions both as a muscarinic antagonist and as a beta2 receptor agonist. By combining bifunctional activity and high lung selectivity, we intend to develop a medicine with greater efficacy than single mechanism bronchodilators (such as tiotropium or salmeterol) and with equal or better tolerability. This bifunctional bronchodilator could potentially then serve as a basis for improved triple therapy through co-formulation with another inhaled respiratory compound into a single product that could potentially deliver three complementary therapeutic effects for patients with respiratory disease.

GSK is obligated to fund all development, manufacturing and commercialization activities for product candidates in this program.

MABA Status

The first compound in the MABA program, GSK961081, has successfully completed single- and multiple-dose Phase 1 studies in healthy volunteers. Our goal is to complete the analysis of Phase 1 data and to move into Phase 2 studies.

Long-Acting Muscarinic Antagonist (LAMA)

Inhaled muscarinic antagonists are among the most frequently used bronchodilators for COPD. Inhaled muscarinic antagonists work by inhibiting muscarinic receptors on the bronchial airways, which lead to muscle relaxation, bronchodilation and improved lung function. We are developing with GSK an inhaled LAMA designed to produce a prolonged blockade of the relevant receptor sub-types while also being highly lung-selective, which means that lower concentrations of drug should get into the systemic circulation. We believe this approach will result in improved tolerability over currently available medicines at doses with comparable efficacy.

GSK is obligated to fund all development, manufacturing and commercialization activities for product candidates in this program.

LAMA status

In 2005, the initial results from Phase 1 studies with our first compound TD-5742 suggested that the compound was less potent than we had expected. As a result, the joint steering committee comprised of representatives of GSK and Theravance decided to terminate further development of this compound. Subsequently, we delivered to GSK a second, structurally different, product candidate for this program pursuant to the terms of the strategic alliance. Currently, GSK is evaluating this compound in preclinical studies.

Gastrointestinal (GI) Motility Dysfunction

Our gastrointestinal (GI) motility dysfunction program is dedicated to finding new medicines for GI motility disorders such as chronic constipation, constipation predominant irritable bowel syndrome (C-IBS), functional dyspepsia and delayed gastric emptying.

GI Status

In October 2006, we initiated a Phase 2 clinical study to evaluate the safety and efficacy of a range of doses of TD-5108, an investigational selective 5-HT4 agonist for the treatment of chronic constipation and other disorders related to reduced GI motility. The Phase 2 study is being conducted in the United States with a goal of enrolling approximately 350 patients. We expect to report Phase 2 data in the second half of 2007.

Research Programs

Currently we have three full discovery programs:

- Our peripheral Opioid-Induced Bowel Dysfunction (or PUMA) Program aims to generate a once-daily oral treatment to prevent bowel dysfunction in patients treated with opioid agonists. The PUMA Program is currently in IND-enabling studies.

- Our AT1 Receptor Neprilysin Inhibitor (or ARNI) Program seeks to produce an effective monotherapy for hypertension. The ARNI Program is in discovery stage.

- Our MonoAmine Reuptake Inhibitor (or MARIN) Program is attempting to identify an efficacious oral treatment of chronic pain. The MARIN Program is in discovery stage.

Multivalency

Our proprietary approach combines chemistry and biology to efficiently discover new product candidates for validated targets using our expertise in multivalency. Multivalency refers to the simultaneous attachment of a single molecule to multiple binding sites on one or more biological targets. When compared to monovalency, whereby a molecule attaches to only one binding site, multivalency can significantly increase a compound s potency, duration of action and/or selectivity. Multivalent compounds generally consist of several individual small molecules, at least one of which is biologically active when bound to its target, joined by linking components.

Our approach is based on an integration of the following insights:

- Many targets have multiple binding sites and/or exist in clusters with similar or different targets;

- Biological targets with multiple binding sites and/or those that exist in clusters lend themselves to multivalent drug design;

- Molecules that simultaneously attach to multiple binding sites can exhibit considerably greater potency, duration of action and/or selectivity than molecules that attach to only one binding site; and

- Greater potency, duration of action and/or selectivity provides the basis for superior therapeutic effects, including enhanced convenience, tolerability and/or safety compared to conventional drugs.

Our Strategy

Our objective is to discover, develop and commercialize new medicines with superior efficacy, convenience, tolerability and/or safety. The key elements of our strategy are to:

Apply our expertise in multivalency primarily to validated targets to efficiently discover and develop superior medicines in large markets. We intend to continue to concentrate our efforts on discovering and developing product candidates for validated targets where:

- existing drugs have levels of efficacy, convenience, tolerability and/or safety that are insufficient to meet an important medical need; and

- we believe our expertise in multivalency can be applied to create superior product candidates that are more potent, longer acting and/or more selective than currently available medicines; and

- there are established animal models that can be used to provide us with evidence as to whether our product candidates are likely to provide superior therapeutic benefits relative to current medicines; and

- there is a relatively large commercial opportunity.

Identify two structurally different product candidates in each therapeutic program whenever practicable. We believe that we can increase the likelihood of successfully bringing superior medicines to market by identifying, whenever practicable, two product candidates for development in each program. Our second product candidates are typically in a different structural class from the first product candidate. Applying this strategy can reduce our dependence on any one product candidate and provide us with the potential opportunity to commercialize two compounds in a given area.

Partner with global pharmaceutical companies. Our strategy is to seek collaborations with leading global pharmaceutical companies to accelerate development and commercialization of our product candidates at the strategically appropriate time. Our Beyond Advair collaboration and our strategic alliance with GSK, and our telavancin collaboration with Astellas, are examples of these types of partnerships.

Leverage the extensive experience of our people. We have an experienced senior management team with many years of experience discovering, developing and commercializing new medicines with companies such as Bristol-Myers Squibb Company, Merck & Co., Millennium Pharmaceuticals, Inc., Pfizer Inc, GSK and Gilead Sciences, Inc.

Improve, expand and protect our technical capabilities. We have created a substantial body of know-how and trade secrets in the application of our multivalency approach to drug discovery. We believe this is a significant asset that distinguishes us from our competitors. We expect to continue to make substantial investments in multivalency and other technologies to maintain what we believe are our competitive advantages in drug discovery.

Manufacturing

We currently rely on a number of third-parties, including contract manufacturing organizations and our collaborative partners, to produce our compounds. Manufacturing of compounds in our Beyond Advair, LAMA and MABA programs is handled by GSK. Additionally, GSK will be responsible for the manufacturing of any additional product candidates associated with the programs that it licenses under the strategic alliance agreement. For telavancin, we are responsible for the manufacture of active pharmaceutical ingredient (API) and drug product for the HAP clinical studies as well as for the first six months of commercialization if telavancin is approved for sale by regulatory authorities. Astellas is responsible for manufacturing API and drug product for commercial sale thereafter.

We believe that we have in-house expertise to manage a network of third-party manufacturers. We believe that we will be able to continue to negotiate third party manufacturing arrangements on commercially reasonable terms and that it will not be necessary for us to develop internal manufacturing capacity in order to successfully commercialize our products. However, if we are unable to obtain contract manufacturing, or obtain such manufacturing on commercially reasonable terms, we may not be able to develop or commercialize our products as planned.

Government Regulation

The development and commercialization of our product candidates and our ongoing research will be subject to extensive regulation by governmental authorities in the United States and other countries. Before marketing in the United States, any medicine we develop must undergo rigorous preclinical studies and clinical studies and an extensive regulatory approval process implemented by the United States Food and Drug Administration (FDA) under the Federal Food, Drug, and Cosmetic Act. Outside the United States, our ability to market a product depends upon receiving a marketing authorization from the appropriate regulatory authorities. The requirements governing the conduct of clinical studies, marketing authorization, pricing and reimbursement vary widely from country to country. In any country, however, we will only be permitted to commercialize our medicines if the appropriate regulatory authority is satisfied that we have presented adequate evidence of the safety, quality and efficacy of our medicines.

Before commencing clinical studies in humans in the United States, we must submit to the FDA an Investigational New Drug application that includes, among other things, the results of preclinical studies. If the FDA approves the Investigational New Drug application, clinical studies are usually carried out in three phases and must be conducted under FDA oversight. These phases generally include the following:

Phase 1. The product candidate is introduced into healthy human volunteers and is tested for safety, dose tolerance and pharmacokinetics.

Phase 2. The product candidate is introduced into a limited patient population to assess the efficacy of the drug in specific, targeted indications, assess dosage tolerance and optimal dosage, and identify possible adverse effects and safety risks.

Phase 3. If a compound is found to be potentially effective and to have an acceptable safety profile in Phase 2 evaluations, the clinical study will be expanded to further demonstrate clinical efficacy, optimal dosage and safety within an expanded patient population.

The results of product development, preclinical studies and clinical studies must be submitted to the FDA as part of a new drug application, or NDA. The NDA also must contain extensive manufacturing information. Once the submission has been accepted for filing, the FDA typically takes one year to review the application and respond to the applicant. The review process is often significantly extended by FDA requests for additional information or clarification. Once approved, the FDA may withdraw the product approval if compliance with pre- and post-marketing regulatory standards is not maintained or if problems occur after the product reaches the marketplace. In addition, the FDA may require post-marketing studies, referred to as Phase 4 studies, to monitor the effect of approved products, and may limit further marketing of the product based on the results of these post-marketing studies. The FDA has broad post-market regulatory and enforcement powers, including the ability to suspend or delay issuance of approvals, seize or recall products, withdraw approvals, enjoin violations, and institute criminal prosecution.

If we obtain regulatory approval for a medicine, this clearance will be limited to those diseases and conditions for which the medicine is effective, as demonstrated through clinical studies. Even if this regulatory approval is obtained, a marketed medicine, its manufacturer and its manufacturing facilities are subject to continual review and periodic inspections by the FDA. Discovery of previously unknown

problems with a medicine, manufacturer or facility may result in restrictions on the medicine or manufacturer, including costly recalls or withdrawal of the medicine from the market.

We are also subject to various laws and regulations regarding laboratory practices, the experimental use of animals and the use and disposal of hazardous or potentially hazardous substances in connection with our research. In each of these areas, as above, the FDA and other regulatory authorities have broad regulatory and enforcement powers, including the ability to suspend or delay issuance of approvals, seize or recall products, withdraw approvals, enjoin violations, and institute criminal prosecution, any one or more of which could have a material adverse effect upon our business, financial condition and results of operations.

Outside the United States our ability to market our products will also depend on receiving marketing authorizations from the appropriate regulatory authorities. The regulatory approval process in other countries includes all of the risks associated with FDA approval described above.

Patents and Proprietary Rights

We will be able to protect our technology from unauthorized use by third parties only to the extent that our technology is covered by valid and enforceable patents or is effectively maintained as trade secrets. Our success in the future will depend in part on obtaining patent protection for our product candidates. Accordingly, patents and other proprietary rights are essential elements of our business. Our policy is to seek in the United States and selected foreign countries patent protection for novel technologies and compositions of matter that are commercially important to the development of our business. For proprietary know-how that is not patentable, processes for which patents are difficult to enforce and any other elements of our drug discovery process that involve proprietary know-how and technology that is not covered by patent applications, we rely on trade secret protection and confidentiality agreements to protect our interests. We require all of our employees, consultants and advisors to enter into confidentiality agreements. Where it is necessary to share our proprietary information or data with outside parties, our policy is to make available only that information and data required to accomplish the desired purpose and only pursuant to a duty of confidentiality on the part of those parties.

As of December 31, 2006, we had 86 issued United States patents and have received notices of allowance for 10 other United States patent applications. As of that date, we had 100 pending patent applications in the United States and 316 granted foreign patents. We also have 24 Patent Cooperation Treaty applications that permit us to pursue patents outside of the United States and 656 foreign national patent applications. The claims in these various patents and patent applications are directed to compositions of matter, including claims covering product candidates, lead compounds and key intermediates, pharmaceutical compositions, methods of use, and processes for making our compounds along with methods of design, synthesis, selection and use relevant to multivalency in general and to our research and development programs in particular.

United States issued patents and foreign patents generally expire 20 years after filing. The patent rights relating to telavancin owned by us and licensed to Astellas currently consist of 18 issued United States patents that expire between 2019 and 2023, 2 allowed United States patent applications and 9 pending United States patent applications, and counterpart patents and patent applications in a number of jurisdictions, including Europe. The patent rights relating to GSK 159797 owned by us and licensed to GSK consist of 5 issued United States patents that expire in 2019 and 4 pending United States patent applications, and counterpart patents and patent applications in a number of jurisdictions, including Europe. Nevertheless, issued patents can be challenged, narrowed, invalidated or circumvented, which could limit our ability to stop competitors from marketing similar products and threaten our ability to commercialize our product candidates. Our patent position, similar to other companies in our industry, is generally uncertain and involves complex legal and factual questions. To maintain our proprietary position

we will need to obtain effective claims and enforce these claims once granted. It is possible that, before any of our products can be commercialized, any related patent may expire or remain in force only for a short period following commercialization, thereby reducing any advantage of the patent. Also, we do not know whether any of our patent applications will result in any issued patents or, if issued, whether the scope of the issued claims will be sufficient to protect our proprietary position.

We have entered into a License Agreement with Janssen Pharmaceutical pursuant to which we have licensed rights under certain patents owned by Janssen covering an excipient used in the formulation of telavancin. We believe that the general and financial terms of the agreement with Janssen are ordinary course terms. Pursuant to the terms of this license agreement, we are obligated to pay royalties and milestone payments to Janssen based on any commercial sales of telavancin. Astellas has agreed to assume responsibility for these payments under the terms of our license agreement with them. The license is terminable by us upon prior written notice to Janssen or upon an uncured breach or a liquidation event of one of the parties.

Competition

Our objective is to discover, develop and commercialize new medicines with superior efficacy, convenience, tolerability and/or safety. To the extent that we are able to develop medicines, they are likely to compete with existing drugs that have long histories of effective and safe use and with new therapeutic agents. We expect that any medicines that we commercialize with our collaborative partners or on our own will compete with existing, market-leading medicines.

Many of our potential competitors have substantially greater financial, technical and personnel resources than we have. In addition, many of these competitors have significantly greater commercial infrastructures than we have. Our ability to compete successfully will depend largely on our ability to leverage our experience in drug discovery and development to:

- discover and develop medicines that are superior to other products in the market;
- attract qualified scientific, product development and commercial personnel;
- obtain patent and/or other proprietary protection for our medicines and technologies;
- obtain required regulatory approvals; and
- successfully collaborate with pharmaceutical companies in the discovery, development and commercialization of new medicines.

Telavancin. We anticipate that, if approved, telavancin will compete with vancomycin, a generic drug that is manufactured by a variety of companies, as well as other drugs targeted at Gram-positive bacterial infections. Currently marketed products include but are not limited to daptomycin (marketed by Cubist Pharmaceuticals), linezolid (marketed by Pfizer) and tigecycline (marketed by Wyeth). In addition, several additional compounds are under development, including but not limited to dalbavancin (a Pfizer product which received an approvable letter from the FDA in June 2006) and ceftobiprole (in late-stage clinical development by Basilea Pharmaceutica and Johnson & Johnson) represent potential competition for telavancin.

GSK Beyond Advair Collaboration. We anticipate that, if approved, any product from our Beyond Advair collaboration with GSK w