LIGAND PHARMACEUTICALS INC
Form 10-K
March 16, 2007

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SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

FORM 10-K

Mark One

þ **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. 0-20720

LIGAND PHARMACEUTICALS INCORPORATED
(Exact name of registrant as specified in its charter)

Delaware	**77-0160744**
(State or other jurisdiction of incorporation or organization)	**(IRS Employer Identification No.)**
10275 Science Center Drive San Diego, CA	**92121-1117**
(Address of Principal Executive Offices)	**(Zip Code)**

Registrant s telephone number, including area code: (858) 550-7500
Securities registered pursuant to Section 12(b) of the Act:

Title of Each Class	**Name of Each Exchange on Which Registered**
Common Stock, par value $.001 per share	The NASDAQ Global Market of The NASDAQ Stock Market LLC
Preferred Share Purchase Rights	The NASDAQ Global Market of The NASDAQ Stock Market LLC

Securities registered pursuant to Section 12(g) of the Act:
None

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

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 of Section 15(d) of the Securities Exchange Act of 1934. Yes o No þ

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 þ 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. þ

Indicate by check mark whether the registrant is a large accelerated filer, an accelerated filer, or a non-accelerated filer.

Large Accelerated Filer o Accelerated Filer þ Non-accelerated Filer o

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

The aggregate market value of the Registrant s voting and non-voting stock held by non-affiliates was approximately $597.4 million based on the last sales price of the Registrant s Common Stock on the NASDAQ Global Market of the NASDAQ Stock Market LLC on June 30, 2006. For purposes of this calculation, shares of Common Stock held by directors, officers and 10% stockholders known to the Registrant have been deemed to be owned by affiliates which 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.

As of February 28, 2007, the Registrant had 101,008,348 shares of Common Stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Proxy Statement for the Registrant s 2007 Annual Meeting of Stockholders to be filed with the Commission on or before April 30, 2007 are incorporated by reference in Part III of this Annual Report on Form 10-K. With the exception of those portions that are specifically incorporated by reference in this Annual Report on Form 10-K, such Proxy Statement shall not be deemed filed as part of this Report or incorporated by reference herein.

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AVAILABLE INFORMATION:

We file electronically with the Securities and Exchange Commission (or SEC) our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K and, as necessary, amendments to these reports, pursuant to Section 13(a) or 15(d) of the Securities Exchange Act of 1934. The public may read or copy any materials we file with the SEC at the SEC s Public Reference Room at 100 F Street, NE, Washington, DC 20549. The public

may obtain information on the operation of the Public Reference Room by calling the SEC at 1-800-SEC-0330. The SEC maintains an Internet site that contains reports, proxy and information statements, and other information regarding issuers that file electronically with the SEC. The address of that site is <http://www.sec.gov>.

You may obtain a free copy of our annual reports on Form 10-K, quarterly reports on Form 10-Q and current reports on Form 8-K and amendments to those reports which are posted as soon as reasonably practicable after filing on our website at <http://www.ligand.com>, by contacting the Investor Relations Department at our corporate offices by calling (858) 550-7500 or by sending an e-mail message to investors@ligand.com. You may also request information via the Investor Relations page of our website.

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Glossary
PRODUCTS AND INDICATIONS

AVINZA®	Approved in March 2002 for sale in the U.S. for the once-daily treatment of moderate-to-severe pain in patients who require continuous, around-the-clock opioid therapy for an extended period of time.**
ONTAK® (denileukin diftitox) ONZAR	Approved in February 1999 for sale in the U.S. for the treatment of patients with persistent or recurrent cutaneous T-cell lymphoma whose malignant cells express the CD25 component of the Interleukin-2 receptor.*
Targretin® (bexarotene) capsules	Approved in December 1999 for sale in the U.S. and in March 2001 for sale in Europe for the treatment of cutaneous manifestations of cutaneous T-cell lymphoma in patients who are refractory to at least one prior systemic therapy.*
Targretin® (bexarotene) gel 1%	Approved in June 2000 for sale in the U.S. for the topical treatment of cutaneous lesions in patients with cutaneous T-cell lymphoma (Stage 1A and 1B) who have refractory or persistent disease after other therapies or who have not tolerated other therapies.*
Panretin® gel (alitretinoin) 0.1%	Approved in February 1999 for sale in the U.S. and in October 2000 for sale in Europe for the topical treatment of cutaneous lesions of patients with AIDS-related Kaposi s sarcoma.*
CTCL	Cutaneous T-Cell Lymphoma
HIV	Human Immunodeficiency Virus
HT	Hormone Therapy
NSCLC	Non-Small Cell Lung Cancer

SCIENTIFIC TERMS

AR	Androgen Receptor
ER	Estrogen Receptor
IR	Intracellular Receptor
PPAR	Peroxisome Proliferation Activated Receptor
PR	Progesterone Receptor
RAR	Retinoic Acid Receptor
RR	Retinoid Responsive Intracellular Receptor
RXR	Retinoid X Receptor
SARM	Selective Androgen Receptor Modulator
SERM	Selective Estrogen Receptor Modulator
SGRM	Selective Glucocorticoid Receptor Modulator
TPO	Thrombopoietin

REGULATORY TERMS

EMEA	European Agency for the Evaluation of Medicinal Products
FDA	United States Food and Drug Administration

IND	Investigational New Drug Application (United States)
MAA	Marketing Authorization Application (Europe)
NDA	New Drug Application (United States)

* ONTAK, Targretin, and Panretin were acquired by Eisai, Inc. in October 2006 in the sale of the Company s oncology product line.

** AVINZA was acquired by King Pharmaceuticals, Inc. in February 2007 in the sale of the Company s pain product line.

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PART I

Item 1. Business

Caution: This discussion and analysis may contain predictions, estimates and other forward-looking statements that involve a number of risks and uncertainties, including those discussed in Item 1A. Risk Factors. This outlook represents our current judgment on the future direction of our business. These statements include those related to our restructuring process, AVINZA royalty revenues, product returns, product development, our 2005 restatement, and material weaknesses or deficiencies in internal control over financial reporting. Actual events or results may differ materially from Ligand s expectations. For example, there can be no assurance that our recognized revenues or expenses will meet any expectations or follow any trend(s), that our internal control over financial reporting will be effective or produce reliable financial information on a timely basis, or that our restructuring process will be successful or yield preferred results. We cannot assure you that the Company will be able to successfully or timely complete its restructuring, that we will receive expected AVINZA royalties to support our ongoing business, or that our internal or partnered pipeline products will progress in their development, gain marketing approval or success in the market. In addition, the Company s ongoing SEC investigation may have an adverse effect on the Company. Such risks and uncertainties, and others, could cause actual results to differ materially from any future performance suggested. We undertake no obligation to release publicly the results of any revisions to these forward-looking statements to reflect events or circumstances arising after the date of this annual report. This caution is made under the safe harbor provisions of Section 21E of the Securities Exchange Act of 1934 as amended.

References to Ligand Pharmaceuticals Incorporated (Ligand , the Company , we or our) include our wholly owne subsidiaries Ligand Pharmaceuticals (Canada) Incorporated; Ligand Pharmaceuticals International, Inc.; Seragen, Inc. (Seragen); and Nexus Equity VI LLC (Nexus).

We were incorporated in Delaware in 1987. Our principal executive offices are located at 10275 Science Center Drive, San Diego, California, 92121. Our telephone number is (858) 550-7500.

Overview

We are an early-stage biotech company that focuses on discovering and developing new drugs that address critical unmet medical needs in the areas of thrombocytopenia, cancer, hepatitis C, hormone-related diseases, osteoporosis and inflammatory diseases. We strive to develop drugs that are more effective and/or safer than existing therapies, that are more convenient to administer and that are cost effective. We plan to build a profitable company by generating income from research, milestone, royalty and co-promotion revenues resulting from our collaborations with pharmaceutical partners.

In October 2006, we completed the sale of our oncology product line to Eisai Co., LTD (Tokyo) and Eisai Inc. (New Jersey) for approximately $205.0 million. Of this amount, $185.0 million was received in cash and $20.0 million was funded into an escrow account to support any indemnification claims made by Eisai following the closing of the sale. Such cash proceeds are exclusive of transaction fees and costs. The sale included our four marketed oncology drugs: ONTAK, Targretin capsules, Targretin gel and Panretin gel. In addition, certain of our employees were offered employment by Eisai.

In February 2007, we completed the sale of our AVINZA product line to King Pharmaceuticals, Inc (King). We received $280.4 million in net cash proceeds at the closing from King which is net of $15.0 million that was funded into an escrow account to support any indemnification claims made by King following the closing of the sale. The net cash amount represents a purchase price of $246.3 million which includes certain inventory-related adjustments, plus approximately $49.1 million in reimbursement of payments to Organon and others. Such net cash proceeds are exclusive of transaction fees and costs. We have now completed the sale of our commercial businesses, thus allowing us to focus our business strategy on a targeted internal research and development effort. We have what we believe are promising products through our internal development programs, including the potential of LGD-4665, which is currently in clinical development.

We have formed research and development collaborations for our products with numerous global pharmaceutical companies with ongoing clinical programs at GlaxoSmithKline, Wyeth, Pfizer Inc. and TAP Pharmaceutical

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Products, Inc. (TAP). These partnered products are being studied for the treatment of large market indications such as thrombocytopenia, osteoporosis, menopausal symptoms and frailty.

Eltrombopag (Promacta), a small-molecule TPO mimetic, is being developed by GlaxoSmithKline for thrombocytopenia. Eltrombopag (Promacta) advanced to Phase III in February 2006, in patients with Immune Thrombocytopenic Purpura. Additional Phase I and II studies are ongoing in patients with hepatitis C and chemotherapy-induced thrombocytopenia.

Wyeth is developing bazedoxifene (Viviant) as a monotherapy for osteoporosis and Aprela which is bazedoxifene in combination with Wyeth s PREMARIN for osteoporosis prevention, and vasomotor symptoms of menopause. Wyeth filed an NDA for bazedoxifene (Viviant) in June 2006. Another partnered product, lasofoxifene (Oporia), is being developed by Pfizer for osteoporosis and vaginal atrophy. Pfizer filed an NDA with the FDA in August 2004 for the use of lasofoxifene (Oporia) in the prevention of osteoporosis and then filed a supplemental NDA in December 2004 for the use of lasofoxifene (Oporia) in the treatment of vaginal atrophy. In September 2005 and February 2006, respectively, Pfizer announced the receipt of non-approvable letters from the FDA for both indications. However, lasofoxifene (Oporia) continues in Phase III clinical trials by Pfizer for the treatment of osteoporosis.

In June 2005, GlaxoSmithKline commenced Phase I studies of SB-559448, a second product for thrombocytopenia and in April 2005, TAP commenced Phase I studies for LGD-2941 for the treatment of osteoporosis and frailty.

Internal and collaborative research and development programs are built around our proprietary science technology, which is based on our leadership position in gene transcription technology. LGD-4665 as well as our partnered products currently in human development, are modulators of gene transcription, working through key cellular or intracellular receptor targets discovered using our IR technology.

Business Strategy

We aim to create value for shareholders by advancing our internally developed programs through early clinical development and then entering licensing agreements with larger pharmaceutical and biotechnology companies with substantially greater development and commercialization infrastructure. In addition to advancing our R&D programs, we expect to collect licensing and royalties from existing and future license agreements. We aim to build a profitable company by generating income from our corporate licenses. The principal elements of our strategy are:

Leverage Proprietary Intracellular Receptor Gene Expression Technology. We have accumulated substantial expertise in IR gene expression technology applicable to drug discovery and development. Building on our scientific findings about the molecular basis of hormone action, we have created proprietary new tools to explore and manipulate hormone and growth factor action for potential therapeutic benefit. We employ a proprietary cell-culture based assay system for small molecules that can modulate IRs, referred to as the co-transfection assay. The co-transfection assay system simulates the actual cellular processes controlled by IRs and is able to detect whether a compound interacts with a particular human IR and whether this interaction mimics or blocks the effects of the natural regulatory molecules on target gene expression.

Discover and Develop Targeted Modulators that are Promising Drug Candidates. We discover, synthesize and test numerous compounds to identify those that are most promising for clinical development. We perform extensive target profiling and base our selection of promising development candidates on product characteristics such as initial indications of safety and efficacy. We believe that this focused strategy allows us to eliminate unpromising candidates from consideration sooner without incurring substantial clinical costs.

License Drug Candidates to Other Parties. We generally plan to advance drug candidates through initial and/or early-stage drug development. For larger disease indications requiring complex clinical trials, our strategy is to license drug candidates to pharmaceutical or biotechnology partners for final development and global marketing. We believe partnerships are a good source of development payments, license fees, future event payments and royalties. They also provide considerable benefit regarding late-stage product development, regulatory approval, manufacturing and marketing. We believe that focusing on discovery and early-stage drug development while

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benefiting from our partners proven development and commercialization expertise will reduce our internal expenses and allow us to have a larger number of drug candidates progress to later stages of drug development. However, after establishing a lead product candidate, we are willing to license that candidate during any stage of the development process we determine to be beneficial to the company and to the ultimate development and commercialization of that drug candidate.

Generate Revenue through Partnerships to Fund Our Business and Drive Future Profitability. We have multiple sources of potential license and royalty revenue from existing corporate agreements and we may enter additional partnerships that will provide additional revenue opportunities. In particular, in February 2007, we divested our AVINZA product line to King in exchange for cash and ongoing royalties from product revenues. With the close of that transaction, we expect immediately to begin generating royalty revenue based on King s sales with the product. We have numerous collaborations, including our agreement with GlaxoSmithKline for eltrombopag (Promacta) that has the potential to generate future royalties for Ligand. The revenue generated from these and future potential collaborations will fund our business and potentially provide profits to our shareholders.

General Product Development Process

There are three general phases in product development the research phase, the preclinical phase and the clinical trials phase. See Government Regulation for a more complete description of the regulatory process involved in developing drugs. At Ligand, activities during the research phase include research related to specific IR targets and the identification of lead compounds. Lead compounds are chemicals that have been identified to meet preselected criteria in cell culture models for activity and potency against IR targets. More extensive evaluation is then undertaken to determine if the compound should enter preclinical development. Once a lead compound is selected, chemical modification of the compound is undertaken to create an optimal drug candidate.

The preclinical phase includes pharmacology and toxicology testing in preclinical models (*in vitro* and *in vivo*), formulation work and manufacturing scale-up to gather necessary data to comply with applicable regulations prior to commencing human clinical trials. Development candidates are lead compounds that have successfully undergone *in vitro* and *in vivo* evaluation to demonstrate that they have an acceptable profile that justifies taking them through preclinical development with the intention of filing an IND and initiating human clinical testing.

Clinical trials are typically conducted in three sequential phases that may overlap. In Phase I, the initial introduction of the pharmaceutical into humans, the emphasis is on testing for adverse effects, dosage tolerance, absorption, metabolism, distribution, excretion and clinical pharmacology. Phase II involves studies in a representative patient population to determine the efficacy of the pharmaceutical for specific targeted indications, to determine dosage tolerance and optimal dosage, and to identify related adverse side effects and safety risks. Once a compound is found to be effective and to have an acceptable safety profile in Phase II studies, Phase III trials are undertaken to evaluate clinical efficacy further and to test further for safety. Sometimes Phase I and II trials or Phase II and III trials are combined. In the U.S., the FDA reviews both clinical plans and results of trials, and may discontinue trials at any time if there are significant safety concerns. Once a product has been approved, Phase IV post-market clinical studies may be performed to support the marketing of the product.

Ligand Product Development Programs

We are developing several proprietary products for which we have worldwide rights for a variety of cancers, thrombocytopenia and inflammation and hormonal disorders, as summarized in the table below. Our development programs are primarily based on products discovered through our IR technology. See Technology for a discussion of our IR technology.

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Program	Disease/Indication	Development Phase
LGD-4665 (Thrombopoietin oral mimetic)	Idiopathic Thrombocytopenia Purpura; other thrombocytopenias	Phase I
Selective androgen receptor modulators (agonists)	Hypogonadism, osteoporosis, sexual dysfunction, frailty, cachexia	Pre-clinical
Selective glucocorticoid receptor modulators	Inflammation, cancer	Research
Selective androgen receptor modulators (antagonists)	Prostate cancer Research	Research

Thrombopoietin (TPO) Research Programs

In our TPO program, we seek to develop our own drug candidates that mimic the activity of thrombopoietin for use in the treatment or prophylaxis of thrombocytopenia with indications in a variety of conditions including Idiopathic Thrombocytopenic Purpura (ITP), cancer, hepatitis C and other disorders of blood cell formation. These are large markets with unmet medical needs. For example, the US prevalence of a few target diseases with thrombocytopenia is 200,000 patients with ITP, 1.3 million cancer patients receiving chemotherapy and 2.7 million patients with hepatitis C.

Thrombocytopenia can be caused by insufficient platelet production, splenic sequestration of platelets or increased destruction of platelets predominantly by a patient s own immune system. Thrombocytopenia in cancer patients can be treatment-related (chemotherapy) or cancer-related. Platelet transfusion is the standard of care for thrombocytopenia. However, repeated transfusions can result in the development of platelet alloantibodies that could significantly reduce the effectiveness of transfusions. In addition, patients are at increased risk of infections and allergic reactions. Currently, there is only one approved drug (Neumega) for the prevention of severe thrombocytopenia and the reduction of the need for platelet transfusions in patients with nonmyeloid malignancies. However, we believe that there is a substantial medical need for improved platelet enhancing agents for use in the treatment of thrombocytopenia due to the significant side effects seen with current therapies. Thus, a small molecule TPO mimetic with no apparent immunogenic potential and oral activity that may facilitate dosing may provide an attractive therapeutic profile for a major unmet medical need.

In 1997, we formed a joint research and development alliance with SmithKline Beecham (now GlaxoSmithKline) to focus on the discovery and development of small molecule TPO mimetics. Our partner has two TPO mimetics that were part of our collaboration with them in clinical trials: eltrombopag (Promacta) in Phase II and Phase III trials for multiple indications and SB-559448 in Phase I. For a discussion of these clinical trials, see Collaborative Research and Development Programs Thrombopoietin (TPO) Mimetics Collaborative Program GlaxoSmithKline Collaboration.

After a wash-out period following the termination of the research collaboration with GlaxoSmithKline, each party retained rights to perform research and development of new drugs to control hematopoiesis. This wash-out period ended in February 2003 at which time we began to research and later selected a TPO mimetic, LGD-4665, as a clinical candidate and completed preclinical studies in 2006. We initiated Phase I clinical studies in November 2006. We may pursue the specialty applications emerging from our TPO mimetics internally, but may seek collaborations with major pharmaceutical companies to exploit broader clinical applications.

Selective Androgen Receptor Modulators (SARM) Research and Development Programs

We are pioneering the development of tissue selective SARMs, a novel class of non-steroidal, orally active molecules that selectively modulate the activity of the androgen receptor in different tissues, providing a wide range of opportunities for the treatment of many diseases and disorders in both men and women. Tissue-selective androgen receptor agonists may provide utility in the treatment of patients with hypogonadism, osteoporosis, sexual dysfunction and frailty. Tissue-selective androgen receptor antagonists may provide utility in the treatment of patients with

prostate cancer, acne, androgenetic alopecia and other diseases. The use of androgen antagonists has shown efficacy in the treatment of prostate cancer, with three androgen antagonists currently approved by the FDA

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for use in the treatment of the disease. However, we believe there is a substantial medical need for improved androgen modulators for use in the treatment of prostate cancer due to the significant side effects seen with currently available drugs.

We have assembled an extensive SARM compound library and, we believe, one of the most experienced androgen receptor drug discovery teams in the pharmaceutical industry. We may pursue the specialty applications emerging from SARMs internally, but may seek collaborations with major pharmaceutical companies to exploit broader clinical applications.

Consistent with this strategy, we formed in 2001 a joint research and development alliance with TAP Pharmaceutical Products to focus on the discovery and development of SARMs. The research component of this collaboration ended in June 2006. TAP continues to develop the lead SARM compound in Phase I. Please see the Selective Androgen Receptor Modulators (SARM) Collaborative Programs section below for more details on this alliance.

As part of our alliance with TAP, we exercised an option to select for development one compound and a back-up, LGD-3303 and LGD-3129, out of a pool of compounds available for development. Preclinical studies we have conducted with LGD-3303 indicate that the compound may have utility for osteoporosis, sexual dysfunction, frailty and hypogonadism. *In vivo* studies in rodents indicate a favorable profile with anabolic effects on bone, but an absence of the prostatic hypertrophy that occurs with the currently marketed androgens.

Selective Glucocorticoid Receptor Modulators (SGRM) Research and Development Program

We are developing SGRMs for inflammation, cancer indications and other therapeutic applications. We have a library of compounds that we are optimizing with the goal to identify one or more compounds to enter human trials. Our most advanced compound LGD-5552 was on track to enter clinical trials in 2007; however Good Laboratory Practice studies failed to demonstrate the desired preclinical safety characteristics for a drug to treat rheumatoid arthritis. We decided in the first quarter of 2007 not to proceed with the development of LGD-5552.

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Collaborative Research and Development Programs

We have several major collaborative programs to further develop the research and development of compounds based on our IR technologies. These collaborations focus on numerous large market indications. As of December 31, 2006, several of our collaborative product candidates were in varying stages of human development. Please see Note 15 of the consolidated financial statements for a description of the financial terms of our key collaboration agreements. The table below summarizes our collaborative research and development programs, but is not intended to be a comprehensive summary of these programs.

LEADING PARTNERED DEVELOPMENT PROGRAMS

Program	Disease/Indication	Development Phase	Marketing Rights
THROMBOPOIETIN (TPO) MIMETICS			
Eltrombopag (Promacta) (TPO agonist)	Thrombocytopenia (Idiopathic Thrombocytopenic Purpura, ITP)	Phase III	GlaxoSmithKline
	Thrombocytopenia (hepatitis C)	Phase II	GlaxoSmithKline
	Thrombocytopenia (Chemotherapy-Induced, CIT)	Phase II	GlaxoSmithKline
	Thrombocytopenia (hepatic, renal, CITs)	Phase I	GlaxoSmithKline
SB-559448 (TPO agonist)	Thrombocytopenia	Phase I	GlaxoSmithKline
SELECTIVE ESTROGEN RECEPTOR MODULATORS (SERMs)			
Bazedoxifene (Viviant)	Osteoporosis	NDA filed	Wyeth
Bazedoxifene CE (Aprela)	Osteoporosis prevention Vasomotor symptoms	Phase III	Wyeth
Lasofoxifene (Oporia)(1)	Osteoporosis prevention, vaginal atrophy	NDA and SNDA filed (1)	Pfizer
	Osteoporosis treatment	Phase III	Pfizer
SELECTIVE ANDROGEN RECEPTOR MODULATORS (SARMs)			
LGD-2941 (androgen agonist)	Osteoporosis, frailty and sexual dysfunction	Phase I	TAP

(1) In September 2005 and February 2006, respectively, Pfizer announced receipt of non-approvable

letters from the FDA for the prevention of osteoporosis and vaginal atrophy. Pfizer also indicated that the NDAs may be resubmitted with additional clinical data.

Thrombopoetin (TPO) Mimetics Collaborative Program

GlaxoSmithKline Collaboration. In 1995, we entered into a research and development collaboration with SmithKline Beecham (now GlaxoSmithKline) to use our proprietary expertise to discover and characterize small molecule, orally bioavailable drugs to control hematopoiesis (the formation and development of blood cells) for the treatment of a variety of blood cell deficiencies. In 1998, we announced the discovery of the first non-peptide small molecule that mimics in mice the activity of Granulocyte-Colony Stimulating Factor (G-CSF), a natural protein that stimulates production of infection-fighting neutrophils (a type of white blood cell). While this lead compound has only been shown to be active in mice, its discovery is a major scientific milestone and suggests that orally active, small-molecule mimetics can be developed not only for G-CSF, but for other cytokines as well.

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A number of lead molecules have been found that mimic the activity of natural growth factors for white cells and platelets. In 2002, we earned a $2.0 million milestone payment from GlaxoSmithKline, in connection with the commencement of human trials of eltrombopag (Promacta), an oral, small molecule drug that mimics the activity of thrombopoietin, a protein factor that promotes growth and production of blood platelets. In 2005, we announced that we had earned a $1.0 million milestone payment from GlaxoSmithKline with that company s commencement of Phase II trials of eltrombopag (Promacta). In 2005, we earned a $2.0 million milestone payment as SB-559448, a second TPO agonist, began Phase I development. Additionally, in February 2006, we earned a $2.0 million milestone in connection with the commencement of Phase III trials of eltrombopag (Promacta). There are no approved oral TPO mimetic agents for the treatment or prevention of thrombocytopenias (decreased platelet count). Investigational use of injectable forms of recombinant human TPO has been effective in raising platelet levels in cancer patients undergoing chemotherapy, and has led to accelerated hematopoietic recovery when given to stem cell donors. Some of these investigational treatments have not moved forward to registration due to the development of neutralizing antibodies. Thus, a small molecule TPO mimetic with no apparent immunogenic potential and oral activity that may facilitate dosing may provide an attractive therapeutic profile for a major unmet medical need.

The research phase of the GlaxoSmithKline collaboration concluded in February 2001. After a wash-out period following the termination of the research collaboration, each party has rights to perform research and development of new drugs to control hematopoiesis. This wash-out period ended in February 2003 at which time we began to research and later selected a TPO mimetic, LGD-4665, as a clinical candidate and completed preclinical studies in 2006. We initiated Phase I clinical studies in November 2006. In addition, under the collaboration we have the right to select, but have not selected up to three compounds related to hematopoietic targets for development as anti-cancer products other than those compounds selected for development by GlaxoSmithKline. GlaxoSmithKline has the option to co-promote any selected products with us in North America and to develop and market such products outside North America. We may pursue the specialty applications emerging from our TPO mimetics internally, but may seek collaborations with major pharmaceutical companies to exploit broader clinical applications (see Ligand Product Development Programs).

Selective Estrogen Receptor Modulators (SERM) Collaborative Programs

The primary objective of our estrogen receptor modulators collaborative programs is to develop drugs for hormonally responsive cancers, hormone therapies, the treatment and prevention of diseases affecting women s health, and hormonal disorders prevalent in men. Our programs, both collaborative and internal, target development of tissue-selective modulators of the progesterone receptor the estrogen receptor and the androgen receptor. Through our collaborations with Wyeth and Pfizer, three SERM compounds are in development for osteoporosis, vaginal atrophy and vasomotor symptoms of menopause.

Wyeth Collaboration. In 1994, we entered into a research and development collaboration with Wyeth-Ayerst Laboratories (now Wyeth) to discover and develop drugs that interact with estrogen and progesterone receptors for use in hormone therapy, anti-cancer therapy, gynecological diseases and central nervous system disorders associated with menopause and fertility control. We granted Wyeth exclusive worldwide rights to all products discovered in the collaboration that are agonists or antagonists to the progesterone and estrogen receptors for application in the fields of women s health and cancer therapy.

As part of this collaboration, we tested Wyeth s extensive chemical library for activity against a selected set of targets. In 1996, Wyeth exercised its option to include compounds we discovered that modulate progesterone receptors, and to expand the collaboration to encompass the treatment or prevention of osteoporosis through the estrogen receptors. Wyeth also added four advanced chemical compound series from its internal estrogen receptor osteoporosis program to the collaboration. The research phase of the collaboration ended in August 1998.

In December 2005, the Company entered into an Amended and Restated Agreement with Wyeth to better define, simplify and clarify: the universe of research compounds resulting from the research and development efforts of the parties; combine and clarify categories of those compounds as well as related milestones, royalties and resolve a number of milestone payment issues.

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Wyeth has ongoing clinical studies with two SERMs from the collaboration. Wyeth is developing bazedoxifene (Viviant) and bazedoxifene in combination with PREMARIN (Aprela) for the treatment of post-menopausal osteoporosis. We have milestone and royalty rights for Viviant and Aprela. Portions of these royalty rights have been sold to Royalty Pharma AG. See Royalty Pharma Agreement.

In June 2006, Wyeth announced that an NDA for bazedoxifene (Viviant) had been submitted to the FDA. Wyeth is developing bazedoxifene CE (Aprela) as a progesterone-free treatment for menopausal symptoms. Bazedoxifene (Viviant) is a synthetic drug that was specifically designed to increase bone density and reduce cholesterol levels while at the same time protecting breast and uterine tissue.

Pfizer Collaboration. We have a research and development collaboration with Pfizer to develop therapies for osteoporosis. The collaboration produced a drug candidate, lasofoxifene (Oporia), that Pfizer has advanced through late-stage clinical development.

Lasofoxifene (Oporia) is an estrogen partial agonist being developed for osteoporosis prevention and other diseases. Pfizer has retained marketing rights to the drug. We have milestone and royalty rights to lasofoxifene (Oporia). Portions of these royalty rights have been sold to Royalty Pharma AG. See Royalty Pharma Agreement.

In 2004, Pfizer submitted an NDA to the FDA for lasofoxifene (Oporia) for the prevention of osteoporosis in postmenopausal women. We earned a development milestone of approximately $2.0 million from Pfizer in connection with the filing. In September 2005, Pfizer announced the receipt of a non-approvable letter from the FDA for the prevention of osteoporosis. However, lasofoxifene (Oporia) continues in Phase III clinical trials by Pfizer for the treatment of osteoporosis.

In 2004, Pfizer filed a supplemental NDA for the use of lasofoxifene (Oporia) for the treatment of vaginal atrophy for which no additional milestone was due. In February 2006, Pfizer announced the receipt of a non-approval letter from the FDA for this indication.

Selective Androgen Receptor Modulators (SARM) Collaborative Programs

TAP Collaboration. In June 2001, we entered into a joint research and development alliance with TAP Pharmaceutical Products to focus on the discovery and development of SARMs. SARMs may contribute to the prevention and treatment of diseases including sexual dysfunction, osteoporosis and frailty. The three-year collaboration carried an option to extend by up to two additional one-year terms. In December 2004, we announced the second extension of this collaboration for an additional year, which was successfully concluded in June 2006.

Under the terms of the agreement, TAP received exclusive worldwide rights to manufacture and sell any products resulting from the collaboration in its field, which would include treatment and prevention of male hypogonadism, male sexual dysfunction, female osteoporosis and other indications not retained by Ligand. Ligand retained certain rights in the androgen receptor field, including the prevention or treatment of prostate cancer, benign prostatic hyperplasia, acne and hirsutism. Following expiration of the research collaboration, Ligand has the right to perform research and development of new SARM drugs independently of TAP. We may also receive milestones and up to double-digit royalties as compounds are developed and commercialized. LGD-2941, an androgen agonist targeting osteoporosis and frailty, commenced Phase I development in April 2005.

In addition, we had an option at the expiration of the original three-year term to develop one compound not developed by TAP in its field, with TAP retaining an option to negotiate to co-develop and co-promote such compounds with Ligand. We exercised our option to select one compound and a back-up for development, LGD-3303 and LGD-3129, out of a pool of compounds available for development in the TAP field. TAP retains certain royalty rights and an option to negotiate to co-develop and co-promote such compounds with us up to the end of Phase II development (see Ligand Product Development Programs).

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Metabolic and Cardiovascular Disease Collaborative Programs

We have collaborative partnerships with GlaxoSmithKline and Eli Lilly and Company (Lilly) in the areas of cardiovascular and metabolic diseases. Multiple PPAR modulators have entered clinical development under these partnerships. However, further studies with these compounds are either on hold or have been discontinued.

GlaxoSmithKline Collaboration. In 1992, we entered into a research and development collaboration with Glaxo Wellcome plc (now GlaxoSmithKline) to discover and develop drugs for the prevention or treatment of atherosclerosis and other disorders affecting the cardiovascular system. The research phase was successfully completed in 1997 with the identification of a novel lead structure that activates selected PPAR subfamily members and the identification of a different lead compound that shows activity in preclinical models for lowering LDL cholesterol by up-regulating LDL receptor gene expression in liver cells. We retain the right to develop and commercialize products arising from the collaboration in markets not exploited by GlaxoSmithKline, or where GlaxoSmithKline is not developing a product for the same indication.

In 1999, several PPAR leads were advanced to exploratory development. GW501516 was selected for clinical development and Phase II trials were initiated for cardiovascular disease and dyslipidemia. GW501516 is currently on hold pending the review of preclinical studies.

Eli Lilly Collaboration. In 1997, we entered into a research and development collaboration with Lilly for the discovery and development of products for metabolic disorders. The research phase of the collaboration ended in November 2004.

Lilly selected three PPAR modulators, naveglitazar, LY929 and LY674, for clinical development. Ligand earned milestone payments for IND filings and initiation of Phase II studies. Naveglitazar entered Phase II studies early in 2003, resulting in a $1.5 million milestone payment. In 2004, Lilly announced its decision to move naveglitazar into Phase III registration studies. However, in May 2006, after review of all preclinical and clinical data including two year animal safety studies, Lilly informed us that it had decided not to pursue further development of naveglitazar at this time. This decision was specific with regard to naveglitazar.

In 2002, Lilly filed with the FDA an IND for LY929, a PPAR modulator for the treatment of Type II diabetes, metabolic diseases and dyslipidemias. A third IND was filed with the FDA in November 2002 for LY674, a PPAR modulator for the treatment of atherosclerosis. In July 2005, LY674 entered Phase II studies. In September 2006, Lilly informed us that it had suspended an ongoing mid-stage human trial of LY674 in order to assess unexpected findings noted during animal safety studies of the same compound and evaluate collective clinical efficacy and safety from the human data already gathered.

Royalty Pharma Agreement

In March 2002, we announced an agreement with Royalty Pharma AG, which purchased rights to a share of future royalty payments from our collaborative partners sales of three SERMs then in Phase III development. The SERM products included in the transaction are Oporia, which is being developed for osteoporosis and other indications at Pfizer, bazedoxifene (Viviant) and bazedoxifene CE, PREMARIN combo (Aprela) which are in development at Wyeth for osteoporosis and for vasomotor symptoms of menopause (see the detailed discussions of these products under the Pfizer and Wyeth collaborations above). Since March 2002, and following certain amendments to the original agreement, Royalty Pharma has acquired cumulative rights to 3.0125% of the potential future net sales of the three SERM products for an aggregate of $63.3 million.

Under the terms of the agreements, payments from the royalty rights purchase are non-refundable, regardless of whether the products are ever successfully registered or marketed. Milestone payments owed by our partners as the products complete development and registration are not included in the Royalty Pharma agreement and will be paid to us as earned.

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Technology

In our efforts to discover new and important medicines, we and our academic collaborators and consultants have concentrated on two areas of research: advancing the understanding of the activities of hormones and hormone-related drugs, and making scientific discoveries related to IR technology. We believe that our expertise in this technology will enable us to develop novel, small-molecule drugs acting through IRs with more target-specific properties than currently available drugs. Our efforts may result in improved therapeutic and side effect profiles and new indications for IRs. IRs are families of transcription factors that change cell function by selectively turning on or off particular genes in response to circulating signals that impinge on cells.

Intracellular Receptor Technology

Hormones occur naturally within the body and control processes such as reproduction, cell growth and differentiation. Hormones generally fall into two classes, non-peptide hormones and peptide hormones. Non-peptide hormones include retinoids, sex steroids (estrogens, progestins and androgens), adrenal steroids (glucocorticoids and mineralocorticoids), vitamin D and thyroid hormone. These non-peptide hormones act by binding to their corresponding IRs to regulate the expression of genes in order to maintain and restore balanced cellular function within the body. Hormonal imbalances can lead to a variety of diseases. The hormones themselves and drugs that mimic or block hormone action may be useful in the treatment of these diseases. Furthermore, hormone mimetics (agonists) or blockers (antagonists) can be used to treat diseases in which the underlying cause is not hormonal imbalance. The effectiveness of IRs as drug targets is clearly demonstrated by currently available drugs acting through IRs for several diseases. However, the use of most of these drugs has been limited by their often significant side effects.

We have accumulated substantial expertise in IRs applicable to drug discovery and development. Building on our scientific findings about the molecular basis of hormone action, we have created proprietary new tools to explore and manipulate non-peptide hormone action for potential therapeutic benefit. We employ a proprietary cell-culture based assay system for small molecules that can modulate IRs, referred to as the co-transfection assay. The co-transfection assay system simulates the actual cellular processes controlled by IRs and is able to detect whether a compound interacts with a particular human IR and whether this interaction mimics or blocks the effects of the natural regulatory molecules on target gene expression.

In 1999, we invested in and exclusively licensed particular IR technology to a new corporation, X-Ceptor Therapeutics, Inc. (X-Ceptor). X-Ceptor was subsequently acquired by Exelixis Inc. in October 2004. Under the 1999 license agreement, we will receive a royalty on net sales of any products that are discovered using the licensed technologies.

Fusion Protein Technology

Our fusion protein technology was developed by Seragen, which we acquired in 1998. Seragen s fusion proteins consist of a fragment of diphtheria toxin genetically fused to a ligand that binds to specific receptors on the surface of target cells. Once bound to the cell, the fusion proteins are designed to enter the cell and destroy the ability of the cell to manufacture proteins, resulting in cell death. Using this platform, Seragen genetically engineered six fusion proteins, each of which consists of a fragment of diphtheria toxin fused to a different targeting ligand, such as a polypeptide hormone or growth factor. Fusion proteins may have utility in oncology, dermatology, infectious diseases and autoimmune diseases.

Academic Collaborations

To date, we have licensed technology from The Salk Institute, Baylor College of Medicine and other academic institutions and developed relationships with key scientists to further the development of our core IR technology.

The Salk Institute of Biological Studies. In 1988, we established an exclusive relationship with The Salk Institute, which is one of the research centers in the area of IR technology. We amended and restated this agreement in April 2002. Under our agreement, we have an exclusive, worldwide license to certain IR technology developed in the laboratory of Dr. Ronald Evans, a Salk professor and Howard Hughes Medical Institute Investigator. Dr. Evans

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cloned and characterized the first IR in 1985 and is an inventor of the co-transfection assay we use to screen for IR modulators. Under the agreement, we are obligated to make royalty payments based on sales of certain products developed using the licensed technology, as well as certain minimum annual royalty payments and a percentage of milestones and certain other payments received. The agreement also provides that we have the option of buying out future royalty payments as well as milestone and other payment-sharing obligations on a product-by-product basis by paying the Salk a lump sum calculated using a formula in the agreement. In March 2004, we paid The Salk Institute $1.1 million to exercise this buyout option with respect to lasofoxifene (Oporia), a product under development by Pfizer for the prevention of osteoporosis in postmenopausal women. In December 2004 Pfizer filed a supplemental NDA for the use of lasofoxifene (Oporia) for the treatment of vaginal atrophy. As a result of the supplemental lasofoxifene (Oporia) NDA filing, we exercised an option in January 2005 to pay The Salk Institute $1.1 million to buy out royalty payments due on future sales of the product in this additional indication. See the discussion above regarding Collaborative Research and Development Programs.

We have also entered into a consulting agreement with Dr. Evans that continues through February 2008. Dr. Evans serves as Chairman of Ligand s Scientific Advisory Board.

Baylor College of Medicine. In 1990, we established an exclusive relationship with Baylor, which is a center of IR technology. We entered into a series of agreements with Baylor under which we have an exclusive, worldwide license to IR technology developed at Baylor and to future improvements made in the laboratory of Dr. Bert W. O Malley through the life of the related patents. Dr. O Malley is a professor and the Chairman of the Department of Molecular and Cellular Biology at the Baylor College of Medicine.

We continue to work with Dr. O Malley and Baylor in scientific IR research, particularly in the area of sex steroids and orphan IRs. Under our agreement, we are obligated to make certain royalty payments based on the sales of products developed using the licensed technology. Dr. O Malley is a member of Ligand s Scientific Advisory Board.

In addition to the collaborations discussed above, we also have a number of other consulting, licensing, development and academic agreements by which we strive to advance our technology.

Manufacturing

We currently have no manufacturing facilities and, accordingly, rely on third parties, including our collaborative partners, for clinical production of any products or compounds.

Quality Assurance

Our success depends in great measure upon customer confidence in the quality of our products and in the integrity of the data that support their safety and effectiveness. The quality of our products arises from our commitment to quality in all aspects of our business, including research and development, purchasing, manufacturing and distribution. Quality assurance procedures have been developed relating to the quality and integrity of our scientific information and production processes.

Control of production processes involves rigid specifications for ingredients, equipment, facilities, manufacturing methods, packaging materials and labeling. Control tests are made at various stages of production processes and on the final product to assure that the product meets all regulatory requirements and our standards. These tests may involve chemical and physical testing, microbiological testing, preclinical testing, human clinical trials or a combination thereof.

Commercial

Through September 2006, we promoted AVINZA, our pain product, with approximately 102 sales representatives and our oncology products with approximately 32 sales representatives . On September 7, 2006, we announced the sale of our ONTAK, Targretin capsules, Targretin gel and Panretin products to Eisai, Inc. (Eisai). The Eisai sales transaction subsequently closed on October 25, 2006.

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AVINZA was also co-promoted by Organon Pharmaceuticals USA Inc. (Organon). On January 17, 2006, we signed an agreement with Organon that terminated the AVINZA co-promotion agreement between the two companies and returned AVINZA rights to Ligand. The effective date of the termination agreement is January 1, 2006; however, the parties agreed to continue to cooperate during a transition period that ended September 30, 2006 to promote the product. The transition period co-operation included a minimum number of product sales calls per quarter (100,000 for Organon and 30,000 for Ligand with an aggregate of 375,000 and 90,000, respectively, for the transition period) as well as the transition of ongoing promotions, managed care contracts, clinical trials and key opinion leader relationships to Ligand. During the transition period, we paid Organon an amount equal to 23% of AVINZA net sales as reported by us. We also paid and were responsible for the design and execution of all clinical, advertising and promotion expenses and activities. Additionally, in consideration of the early termination and return of rights under the terms of the agreement, we unconditionally paid Organon $37.8 million in October 2006. We further paid Organon $10.0 million on January 16, 2007. In addition, after the termination, we agreed to make quarterly royalty payments to Organon equal to 6.5% of AVINZA net sales through December 31, 2012 and thereafter 6% through patent expiration, currently anticipated to be November of 2017.

On September 7, 2006 we announced the sale of AVINZA and related assets to King Pharmaceuticals, Inc. (King) and we closed that sale on February 26, 2007. Under the asset purchase agreement with King (the AVINZA Purchase Agreement), King acquired all of our rights in and to AVINZA, assumed certain liabilities, and reimbursed us the $47.8 million paid to Organon. King also assumed our co-promote termination obligation to make payments to Organon based on net sales of AVINZA (approximately $93.3 million as of December 31, 2006). Under the agreement with Organon, we remain liable to Organon in the event of King s default of this royalty obligation.

On September 6, 2006, we entered into a contract sales agreement with King whereby King agreed to perform certain minimum monthly product details (i.e. sales calls) which commenced effective October 1, 2006 and continued until the closing of the AVINZA sales transaction. In connection with the sales call agreement, on January 3, 2007, we executed an amendment to the AVINZA Purchase Agreement with King whereby the parties agreed that King could make offers to the Ligand sales representatives and its regional business managers, such offers to be contingent on the closing. The parties agreed on certain related termination, bonus and severance terms with respect to those employees who did not receive employment offers from King. Accordingly, 23 Ligand sales representatives and regional business managers were informed of their termination and related benefits on December 6, 2006. The termination was effective January 2, 2007. This contract sales agreement terminated with the closing of the AVINZA asset sale to King.

Substantially all of our revenues were attributable to customers in the United States; likewise, substantially all of our long-lived assets are located in the United States. For the year ended December 31, 2006, shipments to three wholesale distributors each accounted for more than 10% of total shipments and in the aggregate represented 79% of total shipments. These wholesale distributors were AmerisourceBergen Corporation, Cardinal Health, Inc. and McKesson Corporation.

For further discussion of these items, see below under Item 7. Management s Discussion and Analysis of Financial Condition and Results of Operations.

Research and Development Expenses

Research and development expenses from continuing operations were $41.9 million, $33.1 million and $32.7 million in 2006, 2005 and 2004, respectively, of which approximately 95%, 89% and 76%, respectively, we sponsored, and the remainder of which was funded pursuant to collaborative research and development arrangements.

Research and development expenses from discontinued operations were $12.9 million, $23.0 million and $32.5 million in 2006, 2005 and 2004 respectively.

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Competition

Some of the drugs we are developing will compete with existing therapies. In addition, a number of companies are pursuing the development of novel pharmaceuticals that target the same diseases we are targeting. A number of pharmaceutical and biotechnology companies are pursuing IR-related approaches to drug discovery and development. Furthermore, academic institutions, government agencies and other public and private organizations conducting research may seek patent protection with respect to potentially competing products or technologies and may establish collaborative arrangements with our competitors.

Many of our existing or potential competitors, particularly large pharmaceutical companies, have greater financial, technical and human resources than we do and may be better equipped to develop, manufacture and market products. Many of these companies also have extensive experience in preclinical testing and human clinical trials, obtaining FDA and other regulatory approvals and manufacturing and marketing pharmaceutical products. For example, GlaxoSmithKline is developing eltrombopag (Promacta), a TPO mimetic that could compete with our LGD-4665 if both were to be approved for marketing.

Our competitive position also depends upon our ability to attract and retain qualified personnel, obtain patent protection or otherwise develop proprietary products or processes, and secure sufficient capital resources for the often substantial period between technological conception and commercial sales. For a discussion of the risks associated with competition, see below under Item 1A. Risk Factors.

Government Regulation

The manufacturing and marketing of our products, our ongoing research and development activities and products being developed by our collaborative partners are subject to regulation for safety and efficacy by numerous governmental authorities in the United States and other countries. In the United States, pharmaceuticals are subject to rigorous regulation by federal and various state authorities, including the FDA. The Federal Food, Drug and Cosmetic Act and the Public Health Service Act govern the testing, manufacture, safety, efficacy, labeling, storage, record keeping, approval, advertising and promotion of our products. There are often comparable regulations that apply at the state level. Product development and approval within this regulatory framework takes a number of years and involves the expenditure of substantial resources.

The steps required before a pharmaceutical agent may be marketed in the United States include (1) preclinical laboratory tests, (2) the submission to the FDA of an IND, which must become effective before human clinical trials may commence, (3) adequate and well-controlled human clinical trials to establish the safety and efficacy of the drug, (4) the submission of a NDA to the FDA and (5) the FDA approval of the NDA prior to any commercial sale or shipment of the drug. A company must pay a one-time user fee for NDA submissions, and annually pay user fees for each approved product and manufacturing establishment. In addition to obtaining FDA approval for each product, each domestic drug-manufacturing establishment must be registered with the FDA and, in California, with the Food and Drug Branch of California. Domestic manufacturing establishments are subject to pre-approval inspections by the FDA prior to marketing approval, then to biennial inspections, and must comply with current Good Manufacturing Practices (cGMP). To supply products for use in the United States, foreign manufacturing establishments must comply with cGMP and are subject to periodic inspection by the FDA or by regulatory authorities in such countries under reciprocal agreements with the FDA.

For both currently marketed and future products, failure to comply with applicable regulatory requirements after obtaining regulatory approval can, among other things, result in the suspension of regulatory approval, as well as possible civil and criminal sanctions. In addition, changes in existing regulations could have a material adverse effect to us.

For marketing outside the United States before FDA approval to market, we must submit an export permit application to the FDA. We also are subject to foreign regulatory requirements governing human clinical trials and marketing approval for drugs. The requirements relating to the conduct of clinical trials, product licensing, pricing and reimbursement vary widely from country to country and there can be no assurance that we or any of our partners will meet and sustain any such requirements.

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We are also increasingly subject to regulation by the states. A number of states now regulate, for example, pharmaceutical marketing practices and the reporting of marketing activities, controlled substances, clinical trials and general commercial practices. We have developed and are developing a number of policies and procedures to ensure our compliance with these state laws, in addition to the federal regulations described above. Significant resources are now required on an ongoing basis to ensure such compliance. For a discussion of the risks associated with government regulations, see below under Item 1A. Risk Factors.

Patents and Proprietary Rights

We believe that patents and other proprietary rights are important to our business. Our policy is to file patent applications to protect technology, inventions and improvements to our inventions that are considered important to the development of our business. We also rely upon trade secrets, know-how, continuing technological innovations and licensing opportunities to develop and maintain our competitive position.

As of December 31, 2006, we have filed or participated as licensee in the filing of approximately 37 currently pending patent applications in the United States relating to our technology, as well as foreign counterparts of certain of these applications in multiple countries. In addition, we own or have licensed rights covered by approximately 260 patents issued or applications, granted or allowed worldwide, including United States patents and foreign counterparts to United States patents. Except for a few patents and applications that are not material to our commercial success, these patents and applications will expire between 2008 and 2023. Starting in 2007, we receive royalties from King Pharmaceuticals Inc. on AVINZA representing substantially all of our ongoing revenue. AVINZA is expected to have patent protection in the United States until November 2017. Subject to compliance with the terms of the respective agreements, our rights under our licenses with our exclusive licensors extend for the life of the patents covering such developments. For a discussion of the risks associated with patent and proprietary rights, see below under Item 1A. Risk Factors.

Human Resources

As of March 12, 2007, we had 122 full-time employees including 37 employees who will be supporting the Company providing transitional services for various time periods throughout 2007, following the restructuring announced in January 2007. Following the termination of the transitional employees, we expect to have approximately 85 full time employees of whom 55 will be involved directly in scientific research and development activities. Of these employees, 32 hold Ph.D. or M.D. degrees.

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ITEM 1A. RISK FACTORS

The following is a summary description of some of the many risks we face in our business. You should carefully review these risks in evaluating our business, including the businesses of our subsidiaries. You should also consider the other information described in this report.

Risks Related To Us and Our Business.

Failure to timely or successfully restructure our business could have adverse consequences for the Company.

We completed the sale of our commercial businesses in February 2007. In connection with these sales we are also restructuring our remaining businesses, principally our research and development. We will also be consolidating our staff and facilities. If we are unable to successfully and timely complete this restructuring, our remaining assets could lose value, we may not be able to retain key employees, we may not have sufficient resources to successfully manage those assets or our business, and we may not be able to perform our obligations under various contracts and commitments. Any of these could have substantial negative impacts on our business and our stock price.

We are substantially dependent on AVINZA royalties for our revenues.

We recently completed the sale of our two commercial product lines, oncology and pain, which in recent years provided substantially all of our continuing revenue. In each sale we received a one-time upfront cash payment. The consideration for the sale of the pain (AVINZA) franchise also included royalties that we will receive in the future from sales of AVINZA by King Pharmaceuticals, Inc., who acquired the AVINZA rights from us. These consist of a 15% royalty on AVINZA sales for the first 20 months, and then royalty payments ranging from 5-15% of AVINZA sales, depending on the level of total annual sales. These royalties represent and will represent substantially all of our ongoing revenue for the foreseeable future. Although we may also receive royalties and milestones from our partners in various past and future collaborations, the amount of revenue from these royalties and milestones is unknown and highly uncertain.

Thus, any setback that may occur with respect to AVINZA could significantly impair our operating results and/or reduce the market price for our securities. Setbacks could include problems with shipping, distribution, manufacturing, product safety, marketing, government licenses and approvals, intellectual property rights, competition with existing or new products and physician or patient acceptance of the product, as well as higher than expected total rebates, returns or discounts.

AVINZA was licensed from Elan Corporation which is its sole manufacturer. Any problems with Elan s manufacturing operations or capacity could reduce sales of AVINZA, as could any licensing or other contract disputes with Elan, raw materials suppliers, or others.

Similarly, King s AVINZA sales efforts could be affected by a number of factors and decisions regarding its organization, operations, and activities as well as events both related and unrelated to AVINZA. Historically, AVINZA sales efforts, including our own and our prior co-promotion partners, have encountered a number of difficulties, uncertainties and challenges, including sales force reorganizations and lower than expected sales call and prescription volumes, which have hurt and could continue to hurt AVINZA sales growth. AVINZA could also face stiffer competition from existing or future pain products. The negative impact on the product s sales growth in turn may cause our royalties, revenues and earnings to be disappointing.

AVINZA sales also may be susceptible to higher than expected discounts (especially PBM/GPO rebates and Medicaid rebates, which can be substantial), returns and chargebacks and/or slower than expected market penetration that could reduce sales. Other setbacks that AVINZA could face in the sustained-release opioid market include product safety and abuse issues, regulatory action, intellectual property disputes and the inability to obtain sufficient quotas of morphine from the Drug Enforcement Agency (DEA) to support production requirements.

In particular, with respect to regulatory action and product safety issues, the FDA previously requested expanded warnings on the AVINZA label to alert doctors and patients to the dangers of using AVINZA with alcohol.

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Changes were made to the label, however, the FDA also requested clinical studies to investigate the risks associated with taking AVINZA with alcohol. Any additional warnings, studies and any further regulatory action could have significant adverse effects on AVINZA sales.

Significant returns of products we sold prior to selling our commercial businesses could harm our operating results.

Under our agreements to sell our commercial businesses, we remain financially responsible for returns of our products sold before those businesses were transferred to their respective buyers. Thus if returns of those products are higher than expected, we could incur substantial expenses for processing and issuing refunds for those returns which, in turn, could hurt our operating results. The amount of returns could be affected by a number of factors including ongoing product demand, product rotation at distributors and wholesalers, and product stability issues.

Return from any dividend is speculative; you may not receive a return on your securities.

We have not paid any cash dividends on our common stock to date. In general, we intend to retain any earnings to support the expansion of our business. We have announced that our Board of Directors is considering a special dividend of a substantial portion of the net proceeds from our product line asset sales. However, other than this special dividend, we do not anticipate paying cash dividends on any of our securities in the foreseeable future. The Board has not determined the amount of any such special dividend, and the amount available for such a dividend depends on a number of factors including our capital surplus, cash on hand and estimated cash needs for our continuing business. In addition, such a special dividend would reduce our assets and could reduce our stock price by a proportional amount. Because the amount of any special dividend and the amount of any associated stock price reduction are both unknown, the investment return from such a dividend is speculative. Thus, any returns you receive from our stock will be highly dependent on increases in the market price for our securities, if any. The price for our common stock has been highly volatile and may decrease.

We will have continuing obligations to indemnify the buyers of our commercial businesses, and may be subject to other liabilities as a result of the sale of our commercial product lines.

In connection with the sale of our AVINZA product line, we have agreed to indemnify King for a period of 16 months after the closing for a number of specified matters including the breach of our representations, warranties and covenants contained in the asset purchase agreement, and in some cases for a period of 30 months following the closing of the asset sale. In addition, we have agreed to indemnify Eisai, the purchaser of our oncology product line, after the closing of the asset sale, for damages suffered by Eisai arising for any breach of any of the representations, warranties, covenants or obligations we have made in the asset purchase agreement. Our obligation to indemnify Eisai survives the closing in some cases up to 18 or 36 months following the closing, and in other cases, until the expiration of the applicable statute of limitations. In a few instances, our obligation to indemnify Eisai survives in perpetuity. Under our agreement with King, $15 million of the total upfront cash payment was deposited into an escrow account to secure our indemnification obligations to King following the closing. Similarly, our agreement with Eisai required that $20 million of the total upfront cash payment be deposited into an escrow account to secure our indemnification obligations to Eisai after the closing.

Our indemnification obligations under the asset purchase agreements could cause us to be liable to King or Eisai under certain circumstances, in excess of the amounts set forth in the escrow accounts. The AVINZA asset purchase agreement also allows King, under certain circumstances, to set off indemnification claims against the royalty payments payable to us. Under the asset purchase agreements, our liability for any indemnification claim brought by King and Eisai is generally limited to $40 million and $30 million, respectively. However, our obligation to provide indemnification on certain matters is not subject to these indemnification limits. For example, we agreed to retain, and provide indemnification without limitation to King for, all liabilities arising under certain agreements with Cardinal Health PTS, LLC related to the manufacture of AVINZA. Similarly, we agreed to retain, and provide indemnification without limitation to Eisai for, all liabilities related to certain claims regarding promotional materials for the ONTAK and Targretin drug products. We cannot predict the liabilities that may arise as a result of these matters. Any liability claims related to these matters or any indemnification claims made by King or Eisai could materially and adversely affect our financial condition.

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We may also be subject to other liabilities related to the products we recently sold. For example, we received a letter in March 2007 from counsel to the Salk Institute for Biological Studies alleging that we owe The Salk Institute royalties on prior sales of Targretin as well as a percentage of the amounts received from Eisai. Salk alleges that they are owed at least 25% of the consideration paid by Eisai for that portion of