LIGAND PHARMACEUTICALS INC
Form 10-K
March 16, 2009
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UNITED STATES

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, 2008

OR

¨ **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. 001-33093

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 ¨ No x

Indicate by check mark if the registrant is not required to file reports pursuant to Section 13 or Section 15(d) of the Securities Exchange Act of 1934. Yes ¨ 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 ¨

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. x

Indicate by check mark whether the 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 ¨ Accelerated Filer x Non-accelerated Filer ¨

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

The aggregate market value of the Registrant s voting and non-voting stock held by non-affiliates was approximately $216.5 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, 2008. 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 27, 2009, the Registrant had 113,292,801 shares of Common Stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Proxy Statement for the Registrant s 2009 Annual Meeting of Stockholders to be filed with the Commission on or before April 30, 2009 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, as amended. 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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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 AVINZA and PROMACTA royalty revenues, product returns, and product development. Actual events or results may differ materially from Ligand s expectations. For example, there can be no assurance that our revenues or expenses will meet any expectations or follow any trend(s), that we will be able to retain our key employees or that we will be able to enter into any strategic partnerships or other transactions. We cannot assure you that we will receive expected AVINZA and PROMACTA royalties to support our ongoing business or that our internal or partnered pipeline products will progress in their development, gain marketing approval or achieve success in the market. In addition, our ongoing SEC investigation, or future arbitration, litigation or disputes with third parties may have a material adverse effect on us. 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 owned subsidiaries Ligand Pharmaceuticals International, Inc.; Seragen, Inc., or Seragen; Pharmacopeia, LLC; and Nexus Equity VI LLC, or 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 a biotechnology company that focuses on drug discovery and early-stage development of pharmaceuticals that address critical unmet medical needs or that are more effective and/or safer than existing therapies, more convenient to administer and are cost effective. Our goal is to build a profitable company by generating income from research, milestone, and royalty revenues resulting from our collaborations with pharmaceutical partners.

On December 23, 2008, we acquired all of the outstanding common shares of Pharmacopeia, Inc., or Pharmacopeia. As consideration, we issued approximately 18.0 million shares of our common stock to Pharmacopeia stockholders, or approximately 0.60 shares for each outstanding Pharmacopeia share, as well as approximately $9.3 million in cash. Security holders of Pharmacopeia also received contingent value rights, under which they could receive an aggregate cash payment of $15.0 million under certain circumstances. Pharmacopeia was a clinical development stage biopharmaceutical company dedicated to discovering and developing novel small molecule therapeutics to address significant medical needs. Pharmacopeia had a broad portfolio of clinical and preclinical candidates under development internally or by partners.

Our business strategy includes targeted internal drug research and early-stage development capabilities. We believe that we have promising product candidates throughout our internal development programs. We also have research and development collaborations for our product candidates with numerous global pharmaceutical companies. These collaborations include ongoing clinical programs at Bristol-Myers Squibb, or BMS, GlaxoSmithKline, or GSK, Pfizer, Schering-Plough, Wyeth, Cephalon and Celgene. These partnered product candidates are being studied for the treatment of large market indications such as thrombocytopenia, rheumatoid

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arthritis, asthma, osteoporosis, menopausal symptoms and Alzheimer s disease as summarized in the following tables.

Pipeline Overview

Marketed	Under FDA/EU Review	Phase III
Chronic Pain Avinza (King)	Osteoporosis Bazedoxifene (Wyeth)	Menopausal symptoms Bazedoxifene+Premarin (Wyeth)
ITP Eltrombopag/Promacta (GSK)	Osteoporosis Lasofoxifene (Pfizer)	Hepatitis C Eltrombopag (GSK)
	ITP Eltrombopag/Revolade (GSK)	Chronic liver disease Eltrombopag (GSK)
Phase II	**Phase I**	**Preclinical/Research**
DARA	Oncology-related	Alzheimer s BACE inhibitor (Schering)
	Thrombocytopenia-Eltrombopag (GSK)	
ITP-LGD-4665 (GSK)	Leukemia PS095760 (Schering)	Muscle wasting-LGD-4033
Oncology-related thrombocytopenia Eltrombopag (GSK)	Inflammation PS386113 (Schering)	Inflammation-CCR1 antagonist
COPD and Asthma PS291822 (Schering)	Respiratory-PS948115 (Schering)	Hematological-Erythropoietin receptor agonist
RA, psoriasis and atherosclerosis PS540446 (BMS)	Metabolic-PS248288 (Schering)	Inflammation Selective glucocorticoid receptor modulator
	Inflammation-PS873266 (Celgene)	Androgen independent prostate cancer receptor modulators
	Muscle wasting-PS178990	

Marketed Products

We currently receive royalty revenues from King Pharmaceuticals, or King, and GSK. In February 2007, we completed the sale of our AVINZA product line to King. As a result of the sale, we received the right to future royalties on the net sales of AVINZA through 2017. Through October 2008, we received a 15% royalty on AVINZA net sales. Subsequent royalty payments will be based upon calendar year net sales (see Table 2 below).

In December 2008, the U.S. Food and Drug Administration, or FDA, granted accelerated approval of GSK s PROMACTA for the treatment of thrombocytopenia in patients with chronic immune (idiopathic) thrombocytopenic purpura, or ITP, who have had an insufficient response to corticosteroids, immunoglobulins or splenectomy. PROMACTA is the first oral thrombopoietin, or TPO, receptor agonist therapy for the treatment of adult patients with chronic ITP. As a result of the FDA s approval of PROMACTA, we are entitled to receive tiered royalties annual net sales of PROMACTA (Table 2). As part of a settlement agreement and mutual release we entered into on February 12, 2009 with The Rockefeller University, or Rockefeller, we agreed to pay a share of such royalties to Rockefeller. See Item 3. Legal Proceedings.

Near-term potential royalties: Products under FDA/EU review and in Phase III

We also have the potential to receive near-term royalties on product candidates resulting from our research and development collaboration arrangements with third party pharmaceutical companies if and when any such product candidate is ultimately approved by the FDA and successfully marketed. Our near-term product candidates are discussed below.

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In addition to the accelerated approval granted for GSK s PROMACTA for the treatment of thrombocytopenia in patients with chronic ITP, GSK also reported positive Phase II data in patients with thrombocytopenia associated with hepatitis C and initiated two Phase III trials in patients with hepatitis C in the fourth quarter of 2007 and a Phase III trial in patients with chronic liver disease (CLD) in early 2008. A Phase II study in patients with oncology-related thrombocytopenia is ongoing and a Phase I study is ongoing in patients with sarcoma receiving the adriamycin and ifosfamide regimen. In December 2008, GSK submitted a marketing authorization application in EU and international for Revolade (Eltrombopag) for the treatment of thrombocytopenia in patients with chronic immune (idiopathic) thrombocytopenic purpura, or ITP (see pipeline overview Table).

Bazedoxifene (Viviant) is a product candidate that resulted from one of our collaborations with Wyeth. Bazedoxifene is a synthetic drug that was specifically designed to reduce the risk of osteoporotic fractures while at the same time protecting breast and uterine tissue. In June 2006, Wyeth submitted an NDA for bazedoxifene to the FDA for the prevention of postmenopausal osteoporosis. Wyeth also submitted a second NDA for bazedoxifene in the United States in July 2007 for the treatment of osteoporosis and a Marketing Authorization Application, or MAA, to the European Medicines Agency, or EMEA, in September 2007 for the prevention and treatment of osteoporosis. Wyeth has indicated that it will file a complete response in 2009 and expects the FDA to convene an advisory committee to review the pending NDAs for both the treatment and prevention of postmenopausal osteoporosis with VIVIANT. In February 2009, CONBRIZA (EU trade name) received positive Committee for Medicinal Products for Human Use (CHMP) opinion in Europe for the treatment of postmenopausal osteoporosis in women at increased risk of fracture

Wyeth is also developing bazedoxifene in combination with PREMARIN (Aprela) as a progesterone-free treatment for menopausal symptoms. Two Phase III studies with bazedoxifene/conjugated estrogens (Aprela), showed reduced number and severity of hot flashes in symptomatic postmenopausal women by up to 80 percent, when compared with placebo. Wyeth expects to file an initial NDA no earlier than the first half of 2010. We are entitled to receive tiered royalties on these products (see Table 2 below).

Lasofoxifene (FABLYN®) is a product candidate that resulted from our collaboration with Pfizer. Pfizer submitted an NDA and an MAA for FABLYN for osteoporosis treatment in December 2007 and January 2008, respectively. The FDA Advisory Committee in early September 2008 voted 9-3 in favor of approving this drug. In January 2009, Pfizer received a complete response letter from the FDA requesting additional information for FABLYN. Pfizer is reviewing the letter and will work with the FDA to determine the appropriate next steps regarding its application. In December 2008 CHMP granted a positive opinion for the approval of lasofoxifene in the EU for the treatment of osteoporosis in postmenopausal women at increased risk of fracture. Pfizer has also submitted NDA s for osteoporosis prevention and vaginal atrophy, and the FDA issued non-approvable letters for both NDA s. Under the terms of our agreement with Pfizer, we are entitled to receive royalty payments on worldwide net sales of lasofoxifene for any indication. We are entitled to receive royalties on these products (see Table 2 below).

Advanced R&D Programs

PS291822 is a CXCR2 antagonist that resulted from our collaboration with Schering Plough. PS291822 entered Phase II clinical trials in the fourth quarter of 2006 for COPD and asthma. Phase II study in patients with COPD was completed in 4Q 2008. Results from two Phase II studies in asthma are expected later this year.

PS540446 is an orally active p-38 mitogen-activated protein (MAP) kinase inhibitor that resulted from our collaboration with BMS. PS540446 is in Phase II studies for treatment of moderate to severe psoriasis, rheumatoid arthritis (RA) and atherosclerosis. Phase II studies are expected to be complete in 2009. Positive Phase I results in healthy subjects and in patients with stable RA were reported at the 2008 ACR meeting.

DARA (PS433540) is a first-in-class Dual Acting Receptor Agonist (DARA) that targets the angiotensin and endothelin receptors. Given its unique mechanism of action, DARA has the potential to treat diabetic

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nephropathy. In connection with our acquisition of Pharmacopeia, Inc., or the Merger, we assumed an exclusive licensing agreement with BMS, whereby we obtained the rights for worldwide development and commercialization of DARA. In February 2009 we announced preliminary results of a Phase IIb study which compared 200 mg, 400 mg, and 800 mg doses of DARA versus placebo and irbesartan for 12-weeks in hypertensive patients. In this study all doses of DARA reduced blood pressure statistically significantly greater than placebo. The 800 mg DARA dose group showed a statistically significantly higher percentage of patients achieving blood pressure control compared to irbesartan. DARA was generally well tolerated and there were no serious adverse events associated with therapy. Ligand plans to pursue discussions with potential collaborators to partner this program based on data received to date.

In December 2008, we entered into an exclusive, worldwide license agreement with SmithKline Beecham Corporation, doing business as GSK. Pursuant to the terms of the GSK agreement, we granted GSK the exclusive right to develop, manufacture and commercialize our LGD-4665 product candidate, as well as all other TPO-related molecules discovered by us. LGD-4665 is currently in a Phase II trial for treatment of thrombocytopenia, a condition of low-platelet levels commonly associated with a diverse range of clinical disorders. Under the terms of the GSK agreement, GSK paid us $5 million as an upfront license fee and agreed to pay us up to $158.0 million in development and commercial milestones and a fixed royalty on net sales (see Table 2 below). We reported at the December 2008 American Society of Hematology annual meeting that LGD-4665 has the potential for weekly dosing, has differentiated clinical pharmacology from other products on the market and has promising potential efficacy in ITP, based on interim clinical study results.

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 fees 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 set forth below.

Leverage Proprietary Gene Expression and Combinatorial Chemistry Platform Technologies Related to Multiple Novel Drug Discovery Programs. Ligand technology applies the most advanced cell-based assays, and gene-expression tools, ultra-high throughput screening and one of the world s largest chemical libraries to discover new and important medicines:

Intracellular Technology: Ligand pioneered the field of Intracellular receptor (IR) drug discovery using cell-based assays of nuclear receptors, cell signaling enzymes and membrane receptors. Intracellular receptors are families of transcription factors that change cell function by selectively turning on or off specific genes in response to circulating signals that act on cells. Our ability to harness these processes through IR technology has enabled the development of novel, small-molecule drugs that act through intracellular receptors, potentially resulting in more targeted drugs with greater specificity than those currently available.

Chemical Library: In December 2008, Ligand acquired high quality combinatorial libraries and proprietary ultra-high through-put screening technology as a result of the acquisition of Pharmacopeia. Our Encoded Combinatorial Library on Polymeric Support, or ECLiPS , combinatorial library technology provides the power of one of the world s largest chemical collections to identifying drugs for novel receptor and enzyme drug targets. Ligand uses a proprietary combinatorial compound collection wedded to a unique ultra-high throughput screening platform to drive lead generation for itself and its pharma partners. Our collection of drug-like molecules is built by our chemists on polystyrene beads and encoded with molecular tags that can be easily decoded for hit identification. This ECLiPS forms the basis for one of the largest compound collections in the industry. Our proprietary tagging technology obviates the usual deconvolution process and facilitates both accurate and rapid hit identification. This combinatorial chemistry collection is built for chemical diversity and drug-like properties. In this way our hits combine the desired target activity with appropriate physicochemical properties that support continued drug discovery.

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Ultra-High Throughput Screening: Ligand has married this large proprietary compound collection with industry leading ultra-high throughput screening (UHTS) capacity and capability. More than 70% of our screens are in 1536-well plate formats with well volumes of 1 to 9 microliters. We have developed nanovolume liquid dispensing to deliver reagent volumes as low as 50 nL to 1536 plates with exceptional accuracy. Numerous types of screening and detection capabilities are employed, including cell-free and cell-based, functional or binding, fluorescent or radioactive, and many others.

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 source of development payments, license fees, future milestone payments and royalties. They also may provide considerable resources for late-stage product development, regulatory activities, manufacturing and marketing. We believe that focusing on discovery and early-stage drug development while 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. We have numerous collaborations that have 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.

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Collaborative Research and Development Programs

We have entered into multiple research and development collaboration arrangements with third party pharmaceutical companies. The commercial terms of such arrangements typically include some combination of the following types of fees: exclusivity fees, technology access fees, technology development fees and research support payments, as well as milestone payments, license or commercialization fees. We may also receive royalties on product candidates resulting from our research and development collaboration arrangements if and to the extent any such product candidate is ultimately approved by the FDA and successfully marketed (see Table 2 for certain royalties).

Table 2: Royalties*

Product/Program	Partner	Royalty Rate	Royalty Tier
Eltrombopag**	GSK	4.7%	Less than $100M annual sales
(PROMACTA)		6.6%	On portion of sales in range of $100M - $200M
		7.5%	On portion of sales in range of $200M - $400M
		9.4%	On portion of sales greater than $400M
		9.3%	On portion of sales greater than $1.5B
LGD-4665**	GSK	14.5%	All sales (6.5% for first year sales)
Various ongoing GSK	GSK	6%***	Less than $500M annual sales
research collaborations		7%	On portion of sales in range of $500M - $1B
		8%	On portion of sales in range of $1B - $3B
		10%	On portion of sales greater than $3B
Avinza	King	5%	If sales are less than $200M annually
			Higher royalties paid if sales exceed $200M
Bazedoxifene (VIVIANT)	Wyeth	0.5%	Less than $400M annual sales
Basedoxifene (APRELA)		1.5%	On portion of sales in range of $400M - $1.0B annually
		2.5%	On portion of sales greater than $1B annually
Lasofoxifene (FABLYN®)*	Pfizer	3%	All sales
PS873266	Celgene	2%	All sales

* Royalties from other partnered products not listed are either single or double digit royalties as described under collaborative research and development programs. Not all royalties are disclosed due to confidentiality requirements.

** Net of payments due to The Rockefeller University

*** If GSK exercises its Proof of Concept (PoC) Option for a particular Target, Ligand may continue the development until PoC and receive stepped up royalties ranging from 10% to 14% under the categories of annual sales described above.

Our collaborative research and development programs are discussed below.

GlaxoSmithKline Collaboration

PROMACTA and LGD-4665

In December 2008, the FDA granted accelerated approval of GSK s PROMACTA® for the treatment of thrombocytopenia in patients with chronic immune (idiopathic) thrombocytopenic purpura (ITP) who have had an insufficient response to corticosteroids, immunoglobulins or splenectomy. PROMACTA is the first oral TPO receptor agonist therapy for the treatment of adult patients with chronic ITP. As a result of the FDA s approval of

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PROMACTA, we are entitled to receive tiered royalties on annual net sales of PROMACTA (Table 2). As part of a settlement agreement and mutual release we entered into on February 11, 2009 with Rockefeller, we agreed to pay a share of such royalties to Rockefeller. See Item 3. Legal Proceedings.

In December 2008, we entered into an exclusive, worldwide license agreement with SmithKline Beecham Corporation, doing business as GSK. Pursuant to the terms of the license agreement, we granted GSK the exclusive right to develop, manufacture and commercialize our LGD-4665 product candidate, as well as all other TPO-related molecules discovered by us. LGD-4665 is currently in a Phase II trial for treatment of thrombocytopenia, a condition of low-platelet levels commonly associated with a diverse range of clinical disorders. Under the terms of the license agreement, GSK paid us $5 million as an upfront license fee and agreed to pay us up to $158.0 million in development and commercial milestones and a royalty on net sales (Table 2). In the first year of sales, royalties will be one-half of the regular royalty rate. GSK has the exclusive right to develop, manufacture and commercialize LGD-4665, as well as other TPO-related molecules discovered by us. GSK will direct all product development and commercialization and will be responsible for all costs going forward for development, patent maintenance and prosecution, and commercialization. We reported at the December 2008 American Society of Hematology annual meeting that LGD-4665 has the potential for weekly dosing, has differentiated clinical pharmacology from other products on the market and has promising potential efficacy in ITP, based on interim clinical study results.

Agreement with Pharmacopeia

In connection with the Merger, we assumed a product development and commercialization agreement, or the GSK Agreement, with SmithKlineBeecham Corporation and Glaxo Group Limited (together GSK), which was originally entered into in March 2006. Our role in the alliance with GSK is to identify and advance molecules in chosen therapeutic programs to development stage and, subject to certain provisions in the GSK Agreement, further develop the candidates to clinical proof of concept (a demonstration of efficacy in humans). We have agreed not to screen our compound library for other collaborators, or for our own account, against any target we screen under the GSK Agreement for a specified period.

The GSK Agreement provides GSK an exclusive option to license the program which is exercisable at specified points of the development process for each program (up to the point of clinical Proof of Concept). Upon licensing a program, GSK is obligated to conduct preclinical development and/or clinical trials and to commercialize pharmaceutical products resulting from such licensed programs on a worldwide basis. We are entitled to receive success-based milestone payments from GSK, starting in the preclinical research stage, for each drug development program under the alliance. If GSK exercises its Candidate Selection Option for a particular target, GSK is obligated to pay a tiered royalty on the annual net sales of products resulting from a particular target (Table 2). If GSK exercises its Proof of Concept Option for a particular target, Ligand may receive stepped up royalties under the categories of annual sales described in Table 2.

In the event that GSK does not exercise its option to license a program, pursuant to the GSK Agreement we retain all rights to such program and may continue to develop the program and commercialize any products resulting from the program, or we may elect to discontinue the program and/or seek other partners for further development and commercialization. Should we develop or partner such a program and commercialize any products resulting from that program, we are obligated to make success-based milestone payments to GSK and pay royalties to GSK ranging from 3% to 7% of net sales upon the successful commercialization of such products.

We and GSK each have the right to terminate the GSK Agreement in our sole discretion under certain specified circumstances at any time during the term of the GSK Agreement. If we exercise our discretionary termination right at any time during the first five years of the term of the GSK Agreement, under certain circumstances we could be required to refund to GSK a portion of the $15.0 million GSK paid to Pharmacopeia for certain initial discovery activities. Pursuant to the terms of the GSK Agreement, the amount of any such refund will be calculated based upon the date upon which such termination occurs.

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We received $15.0 million in connection with initial discovery activities which we are obligated to perform under the GSK agreement. We recorded deferred revenue of approximately $14.5 million associated with these payments, net of the fair value of the warrants described below. We have also earned non-refundable aggregate milestone payments of $3.0 million from GSK related to the identification of six lead compounds. These milestone payments were also recorded as deferred revenue due to our continuing performance obligations under the GSK agreement. The initial research term of the GSK agreement expires in March 2011.

Wyeth Collaborations

Bazedoxifene Program

Bazedoxifene (VIVIANT) is a product candidate that resulted from a collaboration with Wyeth. Bazedoxifene is a synthetic drug that was specifically designed to reduce the risk of osteoporotic fractures while at the same time protecting breast and uterine tissue. In June 2006, Wyeth submitted an NDA for bazedoxifene to the FDA for the prevention of postmenopausal osteoporosis. The FDA issued an approvable letter for bazedoxifene for this indication in April 2007. Wyeth received a second approvable letter in December 2007 and plans to have further discussions with the FDA to discuss the issues raised for the prevention indication. Wyeth also submitted a second NDA for bazedoxifene in the United States in July 2007 for the treatment of osteoporosis and an MAA to EMEA in September 2007 for the prevention and treatment of osteoporosis. Wyeth received a third approvable letter in the second quarter of 2008 for bazedoxifene for the treatment of osteoporosis. In the letter, the FDA requested information similar to that outlined in its approvable letter for bazedoxifene s NDA for the prevention of postmenopausal osteoporosis issued in December 2007. This included further analyses concerning the incidence of stroke and venous thrombotic events. Wyeth indicated that it will file a complete response in 2009 and expects the FDA will convene an advisory committee to review the pending NDAs for both the treatment and prevention of postmenopausal osteoporosis with VIVIANT. In February 2009, VIVIANT received a positive Committee for Medicinal Products for Human Use (CHMP) opinion in Europe for the treatment of postmenopausal osteoporosis in women at increased risk of fracture.

Wyeth is also developing bazedoxifene in combination with PREMARIN (Aprela) as a progesterone-free treatment for menopausal symptoms. Two Phase III studies with bazedoxifene/conjugated estrogens (Aprela), showed reduced number and severity of hot flashes in symptomatic postmenopausal women by up to 80 percent, when compared with placebo. Wyeth expects to file an initial NDA no earlier than the first half of 2010.

We previously sold to Royalty Pharma AG, or Royalty Pharma, the rights to a total of 3.0% of net sales of bazedoxifene for a period of ten years following the first commercial sale of each product. After giving effect to the royalty sale, we will receive tiered royalties on annual net sales as described in Table 2. Additionally, the royalty owed to Royalty Pharma may be reduced by one third if net product sales exceed certain thresholds across all indications.

JAK3 Program

In connection with the completion of our acquisition of Pharmacopeia, we assumed a research and license agreement with Wyeth, acting through its Wyeth Pharmaceuticals Division, providing for the formation of a new alliance based on our Janus Kinase-3, or JAK3, inhibitor program. The alliance s goal is to identify, develop and commercialize therapeutic products for the treatment of certain immunological conditions in humans. The agreement was originally entered into in December 2006.

Pursuant to the Wyeth Agreement, we and Wyeth each have certain exclusive rights to develop and commercialize products resulting from the JAK3 program and the alliance. We retain the right to develop and commercialize therapeutic products for the employment of topical administration for treatment of dermatological and ocular diseases and Wyeth has the right to develop therapeutic products for all other indications and routes of delivery. Under the terms of the Wyeth Agreement, we have received an up-front non-refundable $5.0 million cash payment, approximately $6.0 million in quarterly research funding, and a non-refundable milestone

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payment of $500 thousand. We may also receive an additional $3.0 million over the remaining portion of the initial three-year research term, which expires in December 2009. In addition, we may receive up to $175.0 million for Wyeth s achievement of development, regulatory and commercialization milestones. Wyeth will pay to Ligand double digit royalties on the net sales of any products commercialized by Wyeth under the collaboration. Each company is responsible for all development, regulatory, manufacturing and commercialization activities for the products it develops and commercializes in its field. The revenue for this research is recognized on a proportional performance basis, which is expected to approximate straight-line recognition of revenue over the initial three year term of the alliance.

Each of the companies has the right to terminate the Wyeth agreement under certain specified circumstances at any time during the term of the Wyeth agreement. In addition, Wyeth has the right, upon providing us six months prior written notice, to terminate the research collaboration and/or the Wyeth agreement in its entirety or in part. Such right to termination would not apply to Wyeth s obligations with respect to any program developed by the collaboration and licensed by Wyeth. No termination will require us to refund to Wyeth any or all of the cash payments described above.

Pfizer Collaboration

Lasofoxifene (FABLYN) is a product candidate that resulted from our collaboration with Pfizer. In April 2007, Pfizer announced completion of the Postmenopausal Evaluation and Risk Reduction with lasofoxifene, or PEARL, Phase III study with favorable efficacy and safety. Pfizer submitted an NDA and an MAA for osteoporosis treatment in December 2007 and January 2008, respectively. The FDA Advisory Committee in early September 2008 voted 9-3 in favor of approval of this drug and in January 2009, Pfizer received a complete response letter from the FDA requesting additional information for FABLYN. Pfizer is reviewing the letter and will work with the FDA to determine the appropriate next steps regarding its application. In December 2008 an EU Drug Panel granted a positive opinion for the approval of lasofoxifene in the EU for the treatment of osteoporosis in postmenopausal women at increased risk of fracture. Pfizer has also submitted NDA s for osteoporosis prevention and vaginal atrophy, and the FDA issued non-approvable letters for both NDA s.

Under the terms of our agreement with Pfizer, we are entitled to receive royalty payments on worldwide net sales of lasofoxifene for any indication. We previously sold to Royalty Pharma the rights to a total of 3% of net sales of lasofoxifene for a period of ten years following the first commercial sale of lasofoxifene. After giving effect to the royalty sale, the amount of net royalties we will receive on annual net sales is described in Table 2.

Schering-Plough Collaboration

1998 Collaboration

In connection with our acquisition of Pharmacopeia, we assumed collaboration and license agreements with Schering-Plough Ltd. and Schering Corporation (collectively Schering-Plough) that were originally entered into in October of 1998. These agreements produced a CXCR2 antagonist that entered Phase II clinical trials in the fourth quarter of 2006 for COPD and asthma, an enzyme inhibitor that entered Phase II clinical trials in November 2008 for oncology, a candidate for inflammatory diseases that entered Phase I clinical trials in March 2007, a candidate for respiratory diseases that entered Phase I clinical trials in September 2007 and a BACE inhibitor for Alzheimer s disease for which a first development milestone was achieved in December 2008. Under the terms of these agreements with Schering-Plough, while our research activities have ceased, the cessation of those research activities did not affect other aspects of those agreements, including the ongoing Phase II and Phase I clinical trials and preclinical programs that Schering-Plough is conducting. We continue to be entitled to payments resulting from the successful achievement by Schering-Plough of clinical and regulatory milestones, as well as royalty payments at different rates depending on the origin of collaboration products from discovery and optimization libraries at Ligand and Schering-Plough, and on net sales of products resulting from compounds being developed by Schering-Plough under those agreements.

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2007 Collaboration

In connection with our acquisition of Pharmacopeia, we also assumed an amended and restated collaboration and license agreement with N.V. Organon, entered into in February 2007. In November 2007, Organon was acquired by, and is now a part of, Schering-Plough. Under the 2007 Schering-Plough agreement, we have agreed to work collaboratively with Schering-Plough to generate lead compounds at targets in mutual therapeutic areas selected by Schering-Plough and agreed upon by a joint research committee. The purpose of the agreement is to produce development-ready compounds, the potential development of which will be handled primarily by Schering-Plough. The 2007 Schering-Plough agreement provides that we will receive up to $4.0 million per year from Schering-Plough in research funding over the remaining portion of the five-year term of the agreement.

Pursuant to the 2007 Schering-Plough agreement, we have the option to purchase the right to co-develop and co-commercialize certain therapeutic candidates of mutual interest discovered through the alliance. For the therapeutic candidates that we do not elect to co-develop and co-commercialize, Schering-Plough will retain exclusive development and commercialization rights, and we will receive milestone payments as a result of Schering-Plough s successful advancement, if any, of each candidate through clinical development. We will also receive up to double-digit royalties on net sales, if any, of pharmaceutical products resulting from the collaboration when the lead optimization was conducted by us, and lower royalties when the lead optimization was conducted by Schering-Plough.

We and Schering-Plough each have the right to terminate the 2007 Schering-Plough agreement at any time during the term of the agreement under certain specified circumstances, and upon other circumstances customary for these types of agreements.

Bristol-Myers Squibb Collaborations

P-38 Kinase Program

In connection with the Merger, we assumed a collaboration and license agreement with BMS which was originally entered into in November 1997. This collaboration has resulted in a compound that entered Phase II clinical trials in September 2007 in psoriasis. BMS has also initiated Phase II clinical trials with this compound targeting rheumatoid arthritis and atherosclerosis. A second compound resulting from that partnership, which is a back-up candidate, entered Phase I clinical trials in Canada in December 2005. The research collaboration portion of the agreement has expired, however we will continue to be entitled to payments resulting from the successful achievement by BMS of certain clinical and regulatory milestones, as well as a royalty on net sales of products resulting from compounds already delivered under the agreement.

Medicinal Chemistry Services

In connection with the Merger, we also assumed a discovery collaboration agreement with BMS, or the Discovery Collaboration Agreement, to provide a portion of our medicinal chemistry resources to a BMS discovery program for a period up to three years beginning in October 2007. The Discovery Collaboration Agreement provides that each such year, we are required to provide a fixed number of full-time workers for the BMS discovery program, divided between employees located in Cranbury, New Jersey and contracted headcount located outside the United States.

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Cephalon Collaboration

In connection with the Merger, we assumed a collaboration and license agreement, or the Cephalon Agreement, with Cephalon, Inc., or Cephalon, originally entered into in May 2006, which provides for the formation of a new drug discovery, development and commercialization alliance. Under the Cephalon agreement, Pharmacopeia received an up-front, non-refundable payment of $15.0 million in June 2006 to support its research efforts.

Pursuant to the terms of the Cephalon Agreement, Cephalon is responsible for identifying hit and lead compounds, after which we and Cephalon agreed to work together to develop related clinical candidates. We are principally responsible for medicinal chemistry research and Cephalon is responsible for providing biology support, including preclinical disease models, as required by the Cephalon Agreement. We have agreed that, for a specified period, we will not screen our compound library for other collaborators, or for our own account, against any target upon which we collaborate under the Cephalon Agreement.

Upon the nomination of any clinical candidates by the alliance, Cephalon will be primarily responsible for their development and commercialization. We retain an option to develop certain candidates from the alliance, subject to Cephalon s agreement. For each clinical candidate advanced under the alliance, the developing company is obligated to make clinical, regulatory and sales milestone payments to the non-developing company. In addition, the company commercializing each resulting product is required to pay the non-commercializing company up to a double-digit royalty based on the sales level achieved

In connection with the acquisition of Pharmacopeia, Ligand and Cephalon executed an amendment in January 2009 to the collaboration agreement dated May 16, 2006. The agreement provided for Ligand to have no obligation to continue research activities with respect to the two active collaboration programs and was released to redeploy FTEs currently assigned to the collaboration. All licenses granted to Pharmacopeia by Cephalon with respect to the two active collaboration programs terminated as of the date of amendment. Ligand will be entitled to milestone and royalty payments associated with only one of the two active programs. In addition, Ligand entered in to an agreement with a third party vendor to provide certain chemistry services to Cephalon for a term of nine months from the date of agreement.

We and Cephalon each have the right to terminate the Cephalon agreement under certain specified circumstances at any time during the term of the agreement. In addition, Cephalon has the right to terminate the agreement, in its sole discretion, upon ninety days written notice to us, during the initial three-year phase of the alliance, which phase may be extended by agreement of the parties. No such termination shall require us to refund to Cephalon any or all of the above research and development funding.

Celgene Collaboration

In connection with the Merger, we assumed a research and license agreement, or the Celgene Agreement, with Celgene Corporation, or Celgene. Under the Celgene Agreement we have no further research requirements. Our relationship with Celgene produced a compound that led to a clinical candidate currently being evaluated for the treatment of fibrotic and inflammatory diseases that entered a Phase I clinical trial in the first quarter of 2008. We are entitled to receive payments resulting from the successful achievement by Celgene of clinical milestones, as well as royalties on net sales of products resulting from the collaboration (Table 2).

Trevena Collaboration

In February 2009 Ligand announced the initiation of a joint research and license alliance to screen targets using Trevena s novel biological platform against Ligand s combinatorial library of compounds, to identify active compounds with potential for development as novel G-protein coupled receptor (GPCR) therapeutics.

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Under the terms of the agreement, Trevena has been granted exclusive worldwide rights to sublicense active compounds resulting from the collaboration. Ligand expects to screen 24 targets over two years and receive payments triggered by a tiered screening paradigm for each target.

Internal Product Development Programs

As summarized in the table below, we are developing several proprietary products for a variety of indications.

Program	Disease/Indication	Development Phase
Dual-Acting angiotensin and endothelin Receptor Antagonist (DARA)	Diabetic Nephropathy*	Phase II
Selective Androgen Receptor Modulators (SARMs) (agonists)	Muscle wasting and frailty	Pre-clinical
Chemokine Receptor (CCR1) antagonist	Inflammatory and autoimmune diseases	Pre-clinical
Small molecule Erythropoiein (EPO) receptor agonists	Chemotherapy-induced anemia, anemia due to kidney failure	Research
Selective Glucocorticoid Receptor Modulators (SGRMs)	Inflammation, cancer	Research
Androgen-independent Prostate Cancer (AiPC)	Prostate cancer	Research

* Phase II clinical trials conducted so far have studied patients with hypertension

Dual-Acting Angiotensin and Endothelin Receptor Antagonist (DARA) Program

In connection with the completion of our previously announced acquisition of Pharmacopeia, Inc. (the Merger), we assumed an exclusive licensing agreement, or the DARA License Agreement, with BMS, originally entered into in March 2006, which provides us with an exclusive license under certain BMS patents with respect to worldwide development and commercialization of DARA (PS433540), as well as certain other compounds discovered by BMS that possess dual angiotensin and endothelin receptor antagonist, or DARA, activity.

DARA has been studied in seven Phase I and two Phase II clinical studies, including a Phase II study in hypertensive patients. Given the drug s unique mechanism targeting the angiotensin and endothelin receptors, we beleive the drug has potential as a treatment for diabetic nephropathy. In May 2008, results were announced for a Phase IIa study of DARA in subjects with Stage I and Stage II hypertension that showed statistically significantly greater blood pressure reductions than placebo. This study met its primary endpoint by showing a statistically significant effect on 24-hour systolic ambulatory blood pressure and also showed statistically significant improvements over placebo in mean 24-hour diastolic ambulatory blood pressure as well as seated blood pressure. There were no serious adverse events in subjects treated with DARA. Three subjects discontinued therapy for adverse events, all of whom were in the placebo group.

In February 2009, we announced preliminary results of a Phase IIb study of DARA which compared 200 mg , 400 mg, and 800 mg doses of PS433540 versus placebo and irbesartan for 12-weeks in hypertensive patients. In this study all doses of DARA reduced blood pressure statistically significantly greater than placebo. The highest dose of DARA (800 mg) showed a statistically significantly higher percentage of patients achieving blood pressure control compared to irbesartan. DARA was generally well tolerated and there were no serious adverse

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events associated with therapy. Ligand plans to pursue discussions with potential collaborators to partner this program based on data received to date.

Under the terms of the DARA License Agreement, we are obligated to pay BMS milestone payments upon the achievement, if any, of further successive clinical and regulatory events in the United States and certain other jurisdictions, and a stepped royalty based on net sales of products, if any, resulting from the DARA program. BMS has a limited right of first negotiation in the event that we desire to license compounds that are the subject of the DARA License Agreement to a third party other than BMS.

In addition, we are required to provide BMS with a set of compound libraries over a period of approximately three years ending in March 2009. In the event we fail to deliver such compound libraries to BMS by the end of March 2010, we could be required to make cash payments to BMS of up to $0.1 million. We expect to complete delivery of these compound libraries by the end of the first quarter of 2009

Selective Androgen Receptor Modulators (SARM) Research and Development Programs

We are developing tissue selective androgen receptor modulators, or 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 frailty, cachexia, osteoporosis, sexual dysfunction and hypogonadism.

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 and seek collaborations with major pharmaceutical companies to exploit broader clinical applications.

LGD-2941, a SARM, was selected as a clinical candidate during our collaboration with TAP. TAP assigned the current SARM agreement to Abbott in the second quarter of 2008 upon the closing of the transaction between Takeda and Abbott to separate portions of the TAP business between the two parties. As part of our joint development and research alliance with TAP Pharmaceutical Products, Inc., or TAP), we exercised an option to select for development one compound and a back-up, LGD-3303 and LGD-3129, respectively, 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.

After the conclusion of our research alliance with TAP, we discovered SARM compounds with androgen effects in bone and skeletal muscle, but with little or no activity in the prostate, oil-secreting glands in the skin, or female genitalia. Preclinical studies conducted on one of these compounds, LGD-4033, suggest that the compound may have favorable activity in the treatment of cachexia, frailty, osteoporosis, hypogonadism as well as other disorders. We filed an Investigational New Drug (IND) in December 2008 for LGD-4033.

In connection with the acquisition of Pharmacopeia, we assumed an exclusive licensing agreement, or the SARM License Agreement, with BMS, originally entered into in October 2007, which provides us exclusive worldwide development and commercialization rights to a third lead non-steroidal SARM, PS178990, for which a Phase I single ascending dose study had been completed. Under the SARM License Agreement, we are required to make milestone payments to BMS upon the submission and approval of a therapeutic product for marketing in the United States and certain other jurisdictions. BMS has a limited right of first negotiation for PS178990 in the event that we attempt to license compounds that are the subject of the SARM License Agreement to a third party other than BMS.

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Chemokine Receptor (CCR1) program

In February 2008, we announced the nomination of PS031291 as a preclinical development compound from our internal chemokine receptor CCR1 program. PS031291 is a potent and highly selective antagonist at the chemokine receptor CCR1, which has been implicated in playing a significant role in multiple inflammatory and autoimmune disease processes. We believe PS031291 may possess significant potential in the treatment of various inflammatory diseases including rheumatoid arthritis. We initiated good laboratory practice (often referred to as GLP) toxicology studies on PS031291 in the second quarter of 2008, and those studies are ongoing.

Erythropoiein (EPO) Research Program

We are developing small molecule agonists for the EPO receptor. EPO stimulates the differentiation of bone marrow stem cells to form red blood cells. Various recombinant human EPO derivatives are marketed for the treatment of anemia due to renal failure or cancer chemotherapy (e.g., Aranesp, Epogen, Eprex, and Procrit). We believe that a small molecule agonist for the EPO receptor would provide additional benefit in the treatment of anemia and the convenience of oral administration compared to recombinant human protein therapeutics. EPO and TPO act on the same bone marrow hematopoietic stem cell to guide the development of blood cells. We expect that our prior experience in developing small molecule TPO mimetic drugs will lead to increased efficiency in discovering small molecule EPO mimetic drugs.

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 studies of these compounds are in the research stage.

Androgen-Independent Prostate Cancer (AiPC) program

AiPC typically occurs within two years of initiation of hormonal therapy and no targeted treatment is currently available. Docetaxel is the current standard of care which could extend survival by approximately six months (from 12 to 18 months). Most prostate-derived tumors are initially androgen dependent and they regress in response to androgen ablation therapy. On average, regression lasts about two years, followed by break-through growth of androgen-independent tumors. There is experimental evidence that these androgen-independent tumors require the androgen receptor, or AR, for continued proliferation (i.e. tumors are receptor dependent). The goal of the AiPC program is to identify compounds that specifically inhibit and degrade the AR. Our studies of these compounds are in the research stage.

Technology

We employ various modern research laboratory methods to discover and conduct preclinical development of new chemical entities. These methods are performed either in our own laboratories or in those of contract research organizations under our direction.

In our efforts to discover new and important medicines, we have concentrated on certain technologies and acquired special expertise related to intracellular receptors and the receptors for hematopoietic growth factors. Intracellular receptors are involved in the actions of non-peptide hormones and drugs such as selective androgen receptor modulators, or SERMs, and SARMs. Hematopoietic growth factor receptors are involved in the differentiation and proliferation of blood cell progenitors, the formation of new blood cells, and the action of drugs such as PROMACTA, Epogen and Neumega. We use and have developed particular expertise in co-transfection assays, which measure gene transcription in response to the activation of a target receptor, and gene expression in cells selected for expression of particular receptors or transfected with cDNA for particular receptors. Some of these methods are covered by patents issued to or licensed by Ligand, are trade secrets, or are

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methods that are in the public domain, but that we may use in novel ways to improve our efficiency in identifying promising leads and developing new chemical entities.

Our drug discovery approach is further supported by our proprietary combinatorial chemistry encoding technology, Encoded Combinatorial Libraries on Polymeric Support, or ECLiPS®, our proprietary collection of chemical compounds, assay technology, production automation, information systems and quality assurance programs. We have employed ECLiPS®, together with other technologies, to assemble what we believe is the largest group of compound libraries held by one company in the pharmaceutical industry. Our small molecule libraries have been engineered to be both drug-like and diverse. Our compound collection and high throughput screening technologies have been proven to be effective against a wide variety of biological targets. Importantly, we have achieved success against some of our collaborators most difficult targets, often after our partners internal drug discovery efforts were unsuccessful.

Our tagging technology used in ECLiPS® has been licensed exclusively from the Trustees of Columbia University, or Columbia, and Cold Spring Harbor Laboratory, or Cold Spring, since 1993. We are obligated to pay a minimum annual license fee of $100,000 to Columbia and Cold Spring. The term of the agreement is the later of (i) July 16, 2013 or (ii) the expiration of the last patent relating to the technology, at which time we will have a fully paid license to the technology. The license granted to us under the agreement can be terminated by Columbia and Cold Spring (i) upon 30 days written notice to us if we materially breach the agreement and we fail to cure such material breach in accordance with the agreement or (ii) if we commit any act of bankruptcy, become insolvent, file a petition under any bankruptcy or insolvency act or have any such petition filed against us that is not dismissed within 60 days. We are also obligated to pay royalties to Columbia and Cold Spring based on net sales of pharmaceutical products we develop, as well as a percentage of all other revenue we recognize from collaborators that is derived from the technology licensed from Columbia and Cold Spring.

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.

Sale of Commercial Businesses

In February 2007, we completed the sale of our AVINZA product line to King Pharmaceuticals, Inc, or King. Pursuant to the AVINZA purchase agreement, King acquired all of our rights in and to AVINZA in the United States, its territories and Canada, including, among other things, all AVINZA inventory, records and related intellectual property, and assumed certain liabilities as set forth in the AVINZA purchase agreement. Pursuant to the AVINZA purchase agreement, we received a total of $295.4 million in net cash proceeds. We also received the right to future royalties on the net sales of AVINZA through 2017.

In October 2006, we completed the sale of our Oncology product line to Eisai Inc., a Delaware corporation, and Eisai Co., Ltd., a Japanese company, which we collectively refer to as Eisai. Pursuant to the Oncology purchase agreement, Eisai acquired all of our worldwide rights in and to our oncology products, including, among other things, all related inventory, equipment, records and intellectual property, and assumed certain liabilities as set forth in the Oncology purchase agreement. The Oncology product line included our four marketed oncology drugs: ONTAK, Targretin capsules, Targretin gel and Panretin gel. Pursuant to the Oncology purchase agreement, we received a total of $205.0 million in net cash proceeds.

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

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Research and Development Expenses

Research and development expenses from continuing operations were $30.8 million, $44.6 million, and $41.5 million in 2008, 2007 and 2006, respectively, of which 100%, 100%, and 95%, respectively, were sponsored by us.

Research and development expenses from discontinued operations were none, $0.1 million, and $13.3 million in 2008, 2007 and 2006 respectively.

Competition

Some of the drugs we are developing may compete with existing therapies or other drugs in development by other companies. 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.

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 an NDA to the FDA and (5) the FDA approval of the NDA prior to any commercial sale or shipment of the drug. 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.

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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.

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.

Royalties we currently receive from King on AVINZA represent a significant portion of our ongoing revenue. The United States patent on AVINZA expires in November 2017; however, an application for a generic form of AVINZA has been submitted to the FDA. The United States patents relating to PROMACTA do not expire until December 2021. 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 February 27, 2009, we had 96 full-time employees, of whom 73 are involved directly in scientific research and development activities. Of these employees, 39 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.

We are substantially dependent on AVINZA and PROMACTA royalties for our revenues.

King is obligated to pay us royalties based on its sales of AVINZA and GSK is obligated to pay us royalties on its sales of PROMACTA. These royalties represent and will for some time represent substantially all of our ongoing revenue. Although we may also receive royalties and milestones from our partners in various past and future collaborations, the amount of revenue from such royalties and milestones is unknown and highly uncertain. As a result, any setback that may occur with respect to AVINZA or PROMACTA could significantly impair our operating results and/or reduce the market price of our stock. 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 products, as well as higher than expected total rebates, returns or discounts.

King and GSK s sales efforts for AVINZA and PROMACTA, respectively, could be affected by a number of factors and decisions regarding their organizations, operations, and activities as well as events both related and unrelated to AVINZA or PROMACTA, including sales force reorganizations and lower than expected sales calls and prescription volumes. AVINZA and PROMACTA could also face stiffer competition from existing or future products. The negative impact on the sales of AVINZA or PROMACTA will negatively affect our royalties, revenues and earnings.

Sales of AVINZA and PROMACTA may also be negatively impacted by higher than expected discounts (especially pharmacy benefit management/group purchasing organization rebates and Medicaid rebates, which can be substantial), returns and chargebacks and/or slower than expected market penetration. Other setbacks that AVINZA could face in the sustained-release opioid market include abuse issues and the inability to obtain sufficient quotas of morphine from the Drug Enforcement Agency to support production requirements.

AVINZA or PROMACTA could also face regulatory action and product safety issues. For example, the FDA previously requested expanded warnings on the AVINZA label to alert doctors and patients to the dangers of using AVINZA with alcohol. Changes were subsequently made to the label. 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.

On September 10, 2007, King reported that Actavis, a manufacturer of generic pharmaceutical products headquartered in Iceland, had filed with the FDA an Abbreviated New Drug Application, or ANDA, with a Paragraph IV Certification pertaining to AVINZA, the rights to which were acquired by King from us in February 2007. According to the report, Actavis s Paragraph IV Certification sets forth allegations that U.S. Patent No. 6,066,339, or the 339 patent, which pertains to AVINZA, and which is listed in the FDA s Approved Drug Products With Therapeutic Equivalence Evaluations, will not be infringed by Actavis s manufacture, use, or sale of the product for which the ANDA was submitted. The expiration date for this patent is November 2017. King, King Pharmaceuticals Research and Development, Inc., Elan Corporation, plc and Elan Pharma International Ltd. jointly filed suit in federal district court in New Jersey on October 18, 2007 against Actavis, Inc. and Actavis Elizabeth LLC for patent infringement under the 339 patent. The lawsuit seeks a judgment that would, among other things, prevent Actavis from commercializing its proposed morphine product until after expiration of the 339 patent.

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AVINZA was licensed from Elan Corporation, or Elan, 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.

Further, pursuant to the agreement with King, beginning in 2009 we will no longer be entitled to receive AVINZA royalties on a quarterly basis, but will collect royalties on an annual basis, which may adversely impact our cash flows.

Our product candidates face significant regulatory hurdles prior to marketing which could delay or prevent sales.

Before we obtain the approvals necessary to sell any of our potential products, we must show through preclinical studies and human testing that each product is safe and effective. We and our partners have a number of products moving toward or currently awaiting regulatory action, including bazedoxifene, lasofoxifene, PS433540 and PS178990. Failure to show any product s safety and effectiveness could delay or prevent regulatory approval of a product and could adversely affect our business. The clinical trials process is complex and uncertain. For example, the results of preclinical studies and initial clinical trials may not necessarily predict the results from later large-scale clinical trials. In addition, clinical trials may not demonstrate a product s safety and effectiveness to the satisfaction of the regulatory authorities. Recently, a number of companies have suffered significant setbacks in advanced clinical trials or in seeking regulatory approvals, despite promising results in earlier trials. The FDA may also require additional clinical trials after regulatory approvals are received. Such additional trials may be expensive and time-consuming, and failure to successfully conduct those trials could jeopardize continued commercialization of a product.

The rate at which we complete our clinical trials depends on many factors, including, but not limited to, our ability to obtain adequate supplies of the products to be tested and patient enrollment. Patient enrollment is a function of many factors, including the size of the patient population, the proximity of patients to clinical sites and the eligibility criteria for the trial. Delays in patient enrollment for our trials may result in increased costs and longer development times. In addition, our collaborative partners have rights to control product development and clinical programs for products developed under the collaborations. As a result, these collaborative partners may conduct these programs more slowly or in a different manner than expected. Moreover, even if clinical trials are completed, we or our collaborative partners still may not apply for FDA approval in a timely manner or the FDA still may not grant approval.

We rely heavily on collaborative relationships, and any disputes or litigation with our collaborative partners or termination or breach of any of the related agreements could reduce the financial resources available to us, including milestone payments and future royalty revenues.

Our strategy for developing and commercializing many of our potential products, including products aimed at larger markets, includes entering into collaborations with corporate partners and others. These collaborations have provided us with funding and research and development resources for potential products for the treatment of a variety of diseases. These agreements also give our collaborative partners significant discretion when deciding whether or not to pursue any development program. Our existing collaborations may not continue or be successful, and we may be unable to enter into future collaborative arrangements to develop and commercialize our product candidates.

In addition, our collaborators may develop drugs, either alone or with others that compete with the types of drugs they are developing with us. This would result in increased competition for our programs. If products are approved for marketing under our collaborative programs, revenues we receive will depend on the manufacturing, marketing and sales efforts of our collaborative partners, who generally retain commercialization rights under the collaborative agreements. Generally, our current collaborative partners also have the right to terminate their collaborations under specified circumstances. If any of our collaborative partners breach or

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terminate their agreements with us or otherwise fail to conduct their collaborative activities successfully, our product development under these agreements will be delayed or terminated. Disputes or litigation may also arise with our collaborators, including disputes or litigation over ownership rights to intellectual property, know-how or technologies developed with our collaborators. Such disputes or litigation could adversely affect our rights to one or more of our product candidates, including our PS433540, PS178990 and LGD-4665 and other small-molecule TPO mimetic compounds. Any such dispute or litigation could delay, interrupt or terminate the collaborative research, development and commercialization of certain potential products, create uncertainty as to ownership rights of intellectual property, or could result in litigation or arbitration. The occurrence of any of these problems could be time-consuming and expensive and could adversely affect our business.

If we consume cash more quickly than expected, and if we are unable to raise additional capital, we may be forced to curtail operations.

Our operations have consumed substantial amounts of cash since inception. Clinical and preclinical development of drug candidates is a long, expensive and uncertain process. Also, we may acquire companies, businesses or products and the consummation of such acquisitions may consume additional cash. For example, as part of the consideration for our recent acquisition of Pharmacopeia we distributed approximately $9.3 million in cash to Pharmacopeia stockholders. Security holders of Pharmacopeia also received contingent value rights under which we could be required to make an aggregate cash payment of $15.0 million to such security holders under certain circumstances.

We believe that our capital resources will be adequate to fund our operations at their current levels at least for the next twelve months. However, changes may occur that would cause us to consume available capital resources before that time. Examples of relevant potential changes that could impact our capital resources include:

- the costs associated with our drug research and development activities, and additional costs we may incur if our development programs are delayed or are more expensive to implement than we currently anticipate;
- changes in existing collaborative relationships, including the funding we receive in connection with those relationships;
- the progress of our milestone and royalty producing activities;
- acquisitions of other businesses or technologies;
- the termination of our lease agreements;
- the purchase of additional capital equipment;
- cash payments or refunds we may be required to make pursuant to certain agreements with third parties;
- competing technological and market developments; and
- the cost of filing, prosecuting, defending and enforcing patent claims and other intellectual property rights, and the outcome of related litigation.

Additional capital may not be available on favorable terms, or at all. If additional capital is not available, we may be required to curtail operations significantly or to obtain funds by entering into arrangements with partners or other third parties that may require us to relinquish rights to certain of our technologies, products or potential markets that we would not otherwise relinquish.

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If, as the result of a merger, or otherwise, our collaborative partners were to change their strategy or the focus of their development and commercialization efforts with respect to our alliance products, the success of our alliance products could be adversely affected.

Our collaborative partners may change the focus of their development and commercialization efforts as the result of a merger. Pharmaceutical and biotechnology companies have historically re-evaluated their priorities from time to time, including following mergers and consolidations which are common in these industries, and two of our collaborative partners have recently entered into merger agreements. In January 2009, Wyeth, a collaborative partner of ours, and Pfizer announced that they have entered into a definitive merger agreement under which Pfizer will acquire Wyeth in a cash and stock transaction. Furthermore, in March 2009, Schering-Plough Corporation, another of our collaborative partners, and Merck & Co., Inc., or Merck, announced that their boards of directors have unanimously approved a definitive merger agreement pursuant to which Merck and Schering-Plough will combine, under the name Merck, in a stock and cash transaction. As a result of the consummation of these mergers our collaborative partners may develop and commercialize, either alone or with others, products and services that are similar to or competitive with our alliance products. Furthermore, the ability of our alliance products to reach their potential could be limited if our collaborative partners reduce or fail to increase spending related to such products as a result of these mergers.

If our collaborative partners terminate their collaborations with us or do not commit sufficient resources to the development, manufacture, marketing or distribution of our alliance products, we could be required to devote additional resources to our alliance products, seek new collaborative partners or abandon such alliance products, all of which could have an adverse effect on our business.

Third party intellectual property may prevent us or our partners from developing our potential products and we may owe a portion of any payments we receive from our collaborative partners to one or more third parties.

Our success will depend on our ability and the ability of our collaborative partners to avoid infringing the proprietary rights of others, both in the United States and in foreign countries. In addition, disputes with licensors under our license agreements may arise which could result in additional financial liability or loss of important technology and potential products and related revenue, if any. Further, the manufacture, use or sale of our potential products or our collaborative partners products or potential products may infringe the patent rights of others. This could impact AVINZA, PROMACTA, bazedoxifene, lasofoxifene, LGD-4665, PS433540, PS178990 and any other products or potential products.

Several drug companies and research and academic institutions have developed technologies, filed patent applications or received patents for technologies that may be related to our business. Others have filed patent applications and received patents that conflict with patents or patent applications we have licensed for our use, either by claiming the same methods or compounds or by claiming methods or compounds that could dominate those licensed to us. In addition, we may not be aware of all patents or patent applications that may impact our ability to make, use or sell any of our potential products. For example, US patent applications may be kept confidential while pending in the United States Patent and Trademark Office and patent applications filed in foreign countries are often first published six months or more after filing.

On March 4, 2008, Rockefeller filed suit in the United States District Court for the Southern District of New York, against us alleging, among other things, a breach by us of our September 30, 1992 license agreement with Rockefeller, as well as other causes of action for unjust enrichment, quantum meruit, specific performance to perform an audit and declaratory relief. In February 2009 we reached a settlement with Rockefeller whereby the parties resolved all disputes that have arisen between them, including Rockefeller s primary claim relating to the development of PROMACTA as well our counterclaims. See Item 3. Legal Proceedings.

Other possible disagreements or litigation with our collaborative partners could delay our ability and the ability of our collaborative partners to achieve milestones or our receipt of other payments. In addition, other

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possible disagreements or litigation could delay, interrupt or terminate the research, development and commercialization of certain potential products being developed by either our collaborative partners or by us. The occurrence of any of the foregoing problems could be time-consuming and expensive and could adversely affect our business.

Third parties have not directly threatened an action or claim against us, although we do periodically receive other communications or have other conversations with the owners of other patents or other intellectual property. If others obtain patents with conflicting claims, we may be required to obtain licenses to those patents or to develop or obtain alternative technology. We may not be able to obtain any such licenses on acceptable terms, or at all. Any failure to obtain such licenses could delay or prevent us from pursuing the development or commercialization of our potential products.

In general, litigation claims can be expensive and time consuming to bring or defend against and could result in settlements or damages that could significantly impact our results of operations and financial condition. We cannot predict or determine the outcome of these matters or reasonably estimate the amount or range of amounts of any fines or penalties that might result from a settlement or an adverse outcome. However, a settlement or an adverse outcome could have a material adverse effect on our financial position, liquidity and results of operations.

We may not be able to hire and/or retain key employees.

If we are unable to hire and/or retain key employees, we may not have sufficient resources to successfully manage our assets or our business, and we may not be able to perform our obligations under various contracts and commitments. Furthermore, there can be no assurance that we will be able to retain all of Pharmacopeia s key management and scientific personnel. If we fail to retain such key employees, we may not realize the anticipated benefits of the merger. Either of these could have substantial negative impacts on our business and our stock price.

Our stock price has been volatile and could experience a sudden decline in value.

Our common stock has experienced significant price and volume fluctuations and may continue to experience volatility in the future. As a result, you may not be able to sell your shares quickly or at the latest market price if trading in our stock is not active or the volume is low. Many factors may have a significant impact on the market price of our common stock, including, but not limited to, the following factors: results of or delays in our preclinical studies and clinical trials; the success of our collaboration agreements; publicity regarding actual or potential medical results relating to products under development by us or others; announcements of technological innovations or new commercial products by us or others; developments in patent or other proprietary rights by us or others; comments or opinions by securities analysts or major stockholders; future sales of our common stock by existing stockholders; regulatory developments or changes in regulatory guidance; litigation or threats of litigation; economic and other external factors or other disaster or crises; the departure of any of our officers, directors or key employees; period-to-period fluctuations in financial results; and limited daily trading volume.

The Financial Industry Regulatory Authority, or FINRA, (formerly the National Association of Securities Dealers, Inc.) and the Securities and Exchange Commission, or SEC, have adopted certain new rules. If we were unable to continue to comply with the new rules, we could be delisted from trading on the NASDAQ Global Market, or Nasdaq, and thereafter trading in our common stock, if any, would be conducted through the over-the-counter market or on the Electronic Bulletin Board of FINRA. As a consequence of such delisting, an investor would likely find it more difficult to dispose of, or to obtain quotations as to the price of, our common stock. Delisting of our common stock could also result in lower prices per share of our common stock than would otherwise prevail.

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We may not be successful in entering into additional out-license agreements on favorable terms, which may adversely affect our liquidity or require us to alter development plans on our products.

We have entered into several out-licensing agreements for the development and commercialization of our products. Although we expend considerable resources on internal research and development for our proprietary programs, we may not be successful in entering into additional out-licensing agreements under favorable terms due to several factors including:

- the difficulty in creating valuable product candidates that target large market opportunities;
- research and spending priorities of potential licensing partners;
- willingness of and the resources available to pharmaceutical and biotechnology companies to in-license product candidates for their clinical pipelines; or
- differences of opinion with potential partners on the valuation of products we are seeking to out-license.

The inability to enter into out-licensing agreements under favorable terms and to earn milestone payments, license fees and/or upfront fees may adversely affect our liquidity and may force us to curtail or delay development of some or all of our proprietary programs, which in turn may harm our business and the value of our stock.

Our product development involves a number of uncertainties, and we may never generate sufficient collaborative payments and royalties from the development of products to become profitable.

We were founded in 1987. We have incurred significant losses since our inception. As of December 31, 2008, our accumulated deficit was $679.6 million.

Most of our products in development will require extensive additional development, including preclinical testing and human studies, as well as regulatory approvals, before they can be marketed. We cannot predict if or when any of the products we are developing or those being developed with our partners will be approved for marketing. There are many reasons why we or our collaborative partners may fail in our efforts to develop our potential products, including the possibility that: preclinical testing or human studies may show that our potential products are ineffective or cause harmful side effects; the products may fail to receive necessary regulatory approvals from the FDA or foreign authorities in a timely manner, or at all; the products, if approved, may not be produced in commercial quantities or at reasonable costs; the products, if approved, may not achieve commercial acceptance; regulatory or governmental authorities may apply restrictions to our products, which could adversely affect their commercial success; or the proprietary rights of other parties may prevent us or our partners from marketing the products.

Any product development failures for these or other reasons, whether with our products or our partners products, may reduce our expected revenues, profits, and stock price.

The past restatement of our consolidated financial statements increased the possibility of legal or administrative proceedings. Any future material weaknesses or deficiencies in our internal control over financial reporting could harm stockholder and business confidence on our financial reporting, our ability to obtain financing and other aspects of our business.

We determined that our consolidated financial statements for the years ended December 31, 2002 and 2003, and for the first three quarters of 2004, as described in more detail in our 2004 Annual Report on Form 10-K, should be restated. As a result of the restatement, we have become subject to a number of additional risks and uncertainties. We expect to continue to incur unanticipated accounting and legal costs as noted below. In addition, the SEC has instituted a formal investigation into our restated consolidated financial statements

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identified above. This investigation will likely continue to divert more of our management s time and attention and cause us to continue to incur substantial costs. Such investigations can also lead to fines or injunctions or orders with respect to future activities, as well as further substantial costs and diversion of management time and attention.

While no material weaknesses were identified as of December 31, 2008, we cannot assure you that material weaknesses will not be identified in future periods. The existence of one or more material weakness or significant deficiency could result in errors in our consolidated financial statements. Substantial costs and resources may be required to rectify any internal control deficiencies. If we fail to achieve and maintain the adequacy of our internal controls in accordance with applicable standards, we may be unable to conclude on an ongoing basis that we have effective internal controls over financial reporting. If we cannot produce reliable financial reports, our business and financial condition could be harmed, investors could lose confidence in our reported financial information, or the market price of our stock could decline significantly. In addition, our ability to obtain additional financing to operate and expand our business, or obtain additional financing on favorable terms, could be materially and adversely affected, which, in turn, could materially and adversely affect our business, our financial condition and the market value of our securities. Moreover, our reputation with customers, lenders, investors, securities analysts and others may be adversely affected.

Challenges to or failure to secure patents and other proprietary rights may significantly hurt our business.

Our success will depend on our ability and the ability of our licensors to obtain and maintain patents and proprietary rights for our potential products both in the United States and in foreign countries. Patents may not be issued from any of these applications currently on file, or, if issued, may not provide sufficient protection. Our patent position, like that of many biotechnology and pharmaceutical companies, is uncertain and involves complex legal and technical questions for which important legal principles are unresolved. We may not develop or obtain rights to products or processes that are patentable. Even if we do obtain patents, such patents may not adequately protect the technology we own or have licensed. In addition, others may challenge, seek to invalidate, infringe or circumvent any patents we own or license and rights we receive under those patents may not provide competitive advantages to us.

Any conflicts resulting from the patent rights of others could significantly reduce the coverage of our patents and limit our ability to obtain meaningful patent protection. We have had and will continue to have discussions with our current and potential collaborative partners regarding the scope and validity of our patents and other proprietary rights. If a collaborative partner or other party successfully establishes that our patent rights are invalid, we may not be able to continue our existing collaborations beyond their expiration. Any determination that our patent rights are invalid also could encourage our collaborative partners to seek early termination of our agreements. Such invalidation could adversely affect our ability to enter into new collaborations.

We may also need to initiate litigation, which could be time-consuming and expensive, to enforce our proprietary rights or to determine the scope and validity of others rights. If litigation occurs, a court may find our patents or those of our licensors invalid or may find that we have infringed on a competitor s rights. In addition, if any of our competitors have filed patent applications in the United States which claim technology we also have invented, the United States Patent and Trademark Office may require us to participate in expensive interference proceedings to determine who has the right to a patent for the technology.

We also rely on unpatented trade secrets and know-how to protect and maintain our competitive position. We require our employees, consultants, collaborative partners and others to sign confidentiality agreements when they begin their relationship with us. These agreements may be breached, and we may not have adequate remedies for any breach. In addition, our competitors may independently discover our trade secrets.

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

In connection with the sale of our AVINZA product line, we have agreed to indemnify King in certain cases for a period of 30 months after the closing of the sale of the AVINZA product line in February 2007, including any breach of certain representations, warranties or covenants contained in the asset purchase agreement. In addition, we have agreed to indemnify Eisai, the purchaser of our Oncology product line, for damages suffered by Eisai arising from any breach of our representations, warranties, covenants or obligations in the asset purchase agreement. Our obligation to indemnify Eisai extends beyond the closing of the sale of our Oncology product line in October 2006 up to, in some cases, 36 months 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 certain circumstances, the asset purchase agreement for the AVINZA product line also allows King to set off indemnification claims against the royalty payments payable to us, including AVINZA royalty payments. Under the asset purchase agreements, our exposure for any indemnification claim brought by King or Eisai is limited to $40.0 million and $30.0 million, respectively. However, in certain matters, our indemnification obligation is not subject to the foregoing limits on liability. For example, we are obligated to indemnify King, without limitation, for all liabilities arising under certain agreements with Catalent Pharma Solutions related to the manufacture of AVINZA. Similarly, we are obligated to indemnify Eisai, without limitation, 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 claims related to our indemnification obligations to King or Eisai could materially and adversely affect our financial condition.

As previously disclosed, in connection with the AVINZA sale transaction, King assumed our obligation to make payments to Organon based on net sales of AVINZA (the fair value of which was $58.5 million as of December 31, 2008). As Organon did not consent to the legal assignment of the co-promote termination obligation from us to King, we remain liable to Organon in the event King defaults on this obligation. Any requirement to pay a material amount to Organon, could adversely affect our business and the price of our securities.

The sale of our commercial product lines also exposes us to product liability risks on products we sold prior to divesting these product lines. For example, such products may need to be recalled to address regulatory issues. A successful product liability claim or series of claims brought against us could result in payment of significant amounts of money and divert management s attention from running our business.

We believe that we carry reasonably adequate insurance for product liability claims. However, we may not be able to maintain our insurance on commercially reasonable terms, or our insurance may not provide adequate protection in the case of a product liability claim. To the extent that product liability insurance, if available, does not cover potential claims, we will be required to self-insure the risks associated with such claims.

If our partners do not reach the market with our alliance products before our competitors offer products for the same or similar uses, or if our partners are not effective in marketing our alliance products, our revenues from product sales, if any, will be reduced.

We face intense competition in our development activities. Our competitors might succeed in obtaining regulatory approval for competitive products more rapidly than our partners can for our products. In addition, competitors might develop technologies and products that are less expensive and perceived to be safer or more effective than those being developed by us or our partners, which could impair our product development and render our technology obsolete.

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We use hazardous materials, which may expose us to significant liability.

In connection with our research and development activities, we handle hazardous materials, chemicals and various radioactive compounds. To properly dispose of these hazardous materials in compliance with environmental regulations, we are required to contract with third parties. We believe that we carry reasonably adequate insurance for toxic tort claims. However, we cannot eliminate the risk or predict the exposure of accidental contamination or injury from the handling and disposing of hazardous materials, whether by us or our third-party contractors. Any accident in the handling and disposing of hazardous materials may expose us to significant liability.

Our shareholder rights plan and charter documents may hinder or prevent change of control transactions.

Our shareholder rights plan and provisions contained in our certificate of incorporation and bylaws may discourage transactions involving an actual or potential change in our ownership. In addition, our Board of Directors may issue shares of preferred stock without any further action by the stockholders. Such restrictions and issuances may have the effect of delaying or preventing a change in our ownership. If changes in our ownership are discouraged, delayed or prevented, it would be more difficult for our current Board of Directors to be removed and replaced, even if you or our other stockholders believe that such actions are in the best interests of us and our stockholders.

We may lose some or all of the value of some of our short term investments.

We engage one or more third parties to manage some of our cash consistent with an investment policy that allows a range of investments and maturities. The investments are intended to maintain safety of principal while providing liquidity adequate to meet projected cash requirements. Risks of principal loss are to be minimized through diversified short and medium term investments of high quality, but the investments are not in every case guaranteed or fully insured. As a result of changes in the credit market, one of our short term investments in commercial paper is in default. We intend to pursue collection efforts, but we might not recoup some or all of our investment in the commercial paper. In addition, from time to time we may suffer other losses on our short term investment portfolio.

We may require additional money to run our business and may be required to raise this money on terms which are not favorable to us or which reduce our stock price.

We may need to complete additional equity or debt financings to fund our operations. Our inability to obtain additional financing could adversely affect our business. Financings may not be available at all or on terms favorable to us. In addition, these financings, if completed, may not meet our capital needs and could result in substantial dilution to our stockholders.

If adequate funds are not available, we may be required to delay, reduce the scope of or eliminate one or more of our research or drug development programs. We may also be required to liquidate our business or file for bankruptcy protection. Alternatively, we may be forced to attempt to continue development by entering into arrangements with collaborative partners or others that require us to relinquish some or all of our rights to technologies or drug candidates that we would not otherwise relinquish.

Our drug development programs will require substantial additional future funding which could hurt our operational and financial condition.

Our drug development programs require substantial additional capital to successfully complete them, arising from costs to: conduct research, preclinical testing and human studies; establish pilot scale and commercial scale manufacturing processes and facilities; and establish and develop quality control, regulatory, marketing, sales and administrative capabilities to support these programs.

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Our future operating and capital needs will depend on many factors, including: the pace of scientific progress in our research and development programs and the magnitude of these programs; the scope and results of preclinical testing and human studies; the time and costs involved in obtaining regulatory approvals; the time and costs involved in preparing, filing, prosecuting, maintaining and enforcing patent claims; competing technological and market developments; our ability to establish additional collaborations; changes in our existing collaborations; the cost of manufacturing scale-up; and the effectiveness of our commercialization activities.

We expect our research and development expenditures over the next three years to continue to be significant. However, we base our outlook regarding the need for funds on many uncertain variables. Such uncertainties include regulatory approvals, the timing of events outside our direct control such as product launches by partners and the success of such product launches, negotiations with potential strategic partners, possible sale of assets or other transactions and other factors. Any of these uncertain events can significantly change our cash requirements.

While we expect to fund our research and development activities from cash generated from AVINZA and PROMACTA royalties and royalties and milestones from our partners in various past and future collaborations to the extent possible, if we are unable to do so, we may need to complete additional equity or debt financings or seek other external means of financing. These financings could depress our stock price. If additional funds are required to support our operations and we are unable to obtain them on terms favorable to us, we may be required to cease or reduce further development or commercialization of our products, to sell some or all of our technology or assets or to merge with another entity.

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. Consequently, 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 negatively impact our financial results. The amount of returns could be affected by a number of factors including, but not limited to, ongoing product demand, product rotation at distributors and wholesalers, and product stability issues.

Our results of operations and liquidity needs could be materially negatively affected by market fluctuations and economic downturn.

Our results of operations could be materially negatively affected by economic conditions generally, both in the U.S. and elsewhere around the world. Continuing concerns over inflation, energy costs, geopolitical issues, the availability and cost of credit, the U.S. mortgage market and a declining residential real estate market in the U.S. have contributed to increased volatility and diminished expectations for the economy and the markets going forward. These factors, combined with volatile oil prices, declining business and consumer confidence and increased unemployment, have precipitated an economic recession and fears of a possible depression. Domestic and international equity markets continue to experience heightened volatility and turmoil. These events and the continuing market upheavals may have an adverse effect on us. In the event of a continuing market downturn, our results of operations could be adversely affected by those factors in many ways, including making it more difficult for us to raise funds if necessary, and our stock price may further decline.

Our investment securities consist primarily of money market funds, corporate debt obligations and U.S. government agency securities. We do not have any auction rate securities. Recently, there has been concern in the credit markets regarding the value of a variety of mortgage-backed securities and the resultant effects on various securities markets. We cannot provide assurance that our investments are not subject to adverse changes in market value. If our investments experience adverse changes in market value, we may have less capital to fund our operations.

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We may be unable to successfully integrate the business of Pharmacopeia and realize the anticipated benefits of the merger.

In December 2008, we completed our merger with Pharmacopeia. The success of the merger will depend, in part, on our ability to realize the anticipated synergies, growth opportunities and cost savings from integrating Pharmacopeia s business with our business. Our success in realizing these benefits and the timing of this realization depend upon the successful integration of the operations of Pharmacopeia. The integration of two independent companies is a complex, costly and time-consuming process. It is possible that the integration process could result in the loss of key employees, diversion of each company s management s attention, the disruption or interruption of, or the loss of momentum in, each company s ongoing business or inconsistencies in standards, controls, procedures and policies, any of which could adversely affect either company s ability to maintain relationships with licensors, collaborators, partners, suppliers and employees or our ability to achieve the anticipated benefits of the merger, or could reduce our earnings or otherwise adversely affect the business and financial results of the combined company and, as a result, adversely affect the market price of our common stock.

We expect to incur significant costs and commit significant management time integrating Pharmacopeia s business operations, technology, development programs, products and personnel with those of ours. If we do not successfully integrate the business of Pharmacopeia, the expenditure of these costs will reduce our cash position.

Impairment charges pertaining to goodwill, identifiable intangible assets or other long-lived assets from the merger with Pharmacopeia could have an adverse impact on our results of operations and the market value of our common stock.

The total purchase price pertaining to our merger with Pharmacopeia has been allocated to Pharmacopeia s net tangible assets, identifiable intangible assets, in process research and development and goodwill. To the extent the value of goodwill or identifiable intangible assets or other long-lived assets become impaired, we will be required to incur material charges relating to the impairment. Any impairment charges could have a material adverse impact on our results of operations and the market value of our common stock.

We may undertake strategic acquisitions in the future and any difficulties from integrating such acquisitions could adversely affect our stock price, operating results and results of operations.

We may acquire companies, businesses and products that complement or augment our existing business. We may not be able to integrate any acquired business successfully or operate any acquired business profitably. Integrating any newly acquired business could be expensive and time-consuming. Integration efforts often take a significant amount of time, place a significant strain on managerial, operational and financial resources and could prove to be more difficult or expensive than we predict. The diversion of our management s attention and any delay or difficulties encountered in connection with any future acquisitions we may consummate could result in the disruption of our on-going business or inconsistencies in standards and controls that could negatively affect our ability to maintain third-party relationships. Moreover, we may need to raise additional funds through public or private debt or equity financing, or issue additional shares, to acquire any businesses or products, which may result in dilution for stockholders or the incurrence of indebtedness.

As part of our efforts to acquire companies, business or product candidates or to enter into other significant transactions, we conduct business, legal and financial due diligence with the goal of identifying and evaluating material risks involved in the transaction. Despite our efforts, we ultimately may be unsuccessful in ascertaining or evaluating all such risks and, as a result, might not realize the intended advantages of the transaction. If we fail to realize the expected benefits from acquisitions we may consummate in the future, whether as a result of unidentified risks, integration difficulties, regulatory setbacks and other events, our business, results of operations and financial condition could be adversely affected. If we acquire product candidates, we will also need to make certain assumptions about, among other things, development costs, the likelihood of receiving regulatory approval and the market for such product candidates. Our assumptions may prove to be incorrect, which could cause us to fail to realize the anticipated benefits of these transactions.

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In addition, we will likely experience significant charges to earnings in connection with our efforts, if any, to consummate acquisitions. For transactions that are ultimately not consummated, these charges may include fees and expenses for investment bankers, attorneys, accountants and other advisors in connection with our efforts. Even if our efforts are successful, we may incur, as part of a transaction, substantial charges for closure costs associated with elimination of duplicate operations and facilities and acquired in-process research and development charges. In either case, the incurrence of these charges could adversely affect our results of operations for particular quarterly or annual periods.

The drug research and development industry is highly competitive and subject to technological change, and we may not have the resources necessary to compete successfully.

Many of our competitors have access to greater financial, technical, research, marketing, sales, distribution, service and other resources than we do. Moreover, the pharmaceutical and biotechnology industries are characterized by continuous technological innovation. We anticipate that we will face increased competition in the future as new companies enter the market and our competitors make advanced technologies available. Technological advances or entirely different approaches that we or one or more of our competitors develop may render our products, services and expertise obsolete or uneconomical. Additionally, the existing approaches of our competitors or new approaches or technologies that our competitors develop may be more effective than those we develop. We may not be able to compete successfully with existing or future competitors.

We have excess space available for sublease at our facilities and we may not be able to find qualified sublease tenants.

We have entered into long-term, non-cancellable real estate arrangements for space which, as a result of reductions in our workforce and our acquisition of Pharmacopeia, are considered to be in excess of our current requirements. We currently have a tenant who is subleasing one of our facilities and we are actively looking for additional sublease tenants to sublease up to approximately 80,000 square feet of vacant space or space that could be made available through changes in the current layout of our operations. We will continue to be responsible for all carrying costs of these facilities until such time as we can sublease these facilities or terminate the applicable leases based on the contractual terms of the lease agreements. However, the commercial real estate market conditions in the United States have resulted in a surplus of business facilities making it difficult to sublease properties. If we are unable to find additional sublease tenants we may not meet our expected estimated levels of sublease income or we may be required to terminate these leases at a substantial cost, and, accordingly, our results of operations could be materially and adversely affected.

Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

We currently occupy an 82,500 square foot office and laboratory facility in San Diego, California leased through November 2021, which is a building we previously owned and sold and leased back on November 9, 2006. We lease approximately 99,000 square feet in three facilities in Cranbury, New Jersey under leases that expire in 2016. We believe these facilities are adequate to meet our space requirements for the foreseeable future.

We also lease a 52,800 square foot facility in San Diego that is leased through July 2015. In January 2008, we began subleasing the 52,800 square foot facility under a sublease through July 2015. We fully vacated this facility in February 2008.

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Item 3. Legal Proceedings

SEC Investigation

The SEC issued a formal order of private investigation dated September 7, 2005, to investigate the circumstances surrounding restatement of our consolidated financial statements for the years ended December 31, 2002 and 2003, and for the first three quarters of 2004. The SEC s investigation is ongoing and we are cooperating with the investigation.

Other Matters

We and Seragen, Inc., our subsidiary, were named parties to *Sergio M. Oliver, et al. v. Boston University, et al.*, a shareholder class action filed on December 17, 1998 in the Court of Chancery in the State of Delaware. We and Seragen were dismissed from the action, but such dismissal is subject to appeal and we and Seragen may have possible indemnification obligations with respect to certain defendants. As of December 31, 2008, we have not accrued an indemnification obligation based on our assessment that our responsibility for any such obligation is not probable or estimable.

On March 4, 2008, Rockefeller filed suit in the United States District Court for the Southern District of New York, against us alleging, among other things, a breach by us of our September 30, 1992 license agreement with Rockefeller, as well as other causes of action for unjust enrichment, quantum meruit, specific performance to perform an audit and declaratory relief. In February 2009, we reached a settlement with Rockefeller whereby the parties resolved all disputes that have arisen between them, including Rockefeller s primary claim relating to the development of PROMACTA as well our counterclaims. As part of the settlement, the parties executed mutual releases and agreed to jointly seek dismissal with prejudice of all claims, demands and causes of action, whether known or unknown, arising out of or based upon the license agreement, the ongoing litigation, PROMACTA, LGD-4665, and any other compound developed by us that was subject to the license agreement. We also agreed to pay Rockefeller, $5.0 million immediately upon settlement, $1.0 million on or before February 10, 2010, $1.0 million on or before February 10, 2011, and 50% of any milestone payment and 5.88% to 7.0% of certain royalties, in each case received by us pursuant to an agreement with SmithKline Beecham Corporation (now known as GlaxoSmithKline) entered into on December 29, 1994. We also agreed to pay Rockefeller 1.5% of world-wide net sales of LGD-4665 as certain payments are received by us pursuant to our agreement with SmithKline Beecham Corporation entered into on December 17, 2008. As of December 31, 2008, we have recorded a liability of $7.0 million related to the settlement.

On October 10, 2008, we received notice that a putative class action complaint was filed in the Superior Court of New Jersey, Mercer County (Equity Division) by Allen Heilman, one of Phamacopeia s stockholders, against Pharmacopeia, the members of its Board of Directors, us and two of our wholly owned subsidiaries. The complaint generally alleges that Pharmacopeia s Board of Directors decision to enter into the proposed transaction with us on the terms contained in the proposed merger agreement constitutes a breach of fiduciary duty and gives rise to other unspecified state law claims. The complaint also alleges that we and two of our wholly owned subsidiaries aided and abetted Pharmacopeia s Board of Directors breach of fiduciary duty. In addition, the complaint alleges that the named plaintiff will seek equitable relief, including among other things, an order preliminarily and permanently enjoining the proposed transaction. While we believe that neither Ligand nor Pharmacopeia engaged in any wrongful acts, in an effort to minimize the cost and expense of any litigation, in December 2008, we entered into a memorandum of understanding, or MOU, with the named plaintiff providing for the settlement of the lawsuit. Subject to court approval and further definitive documentation, the MOU provides a release and settlement by the purported class of all claims against Pharmacopeia, us, and our affiliates and agents in connection with the complaint. Pursuant to the MOU we have agreed not to oppose any fee application by plaintiffs counsel that does not exceed $0.2 million, which has been recorded as a liability at December 31, 2008.

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In addition, from time to time we are subject to various lawsuits and claims with respect to matters arising out of the normal course of our business. Due to the uncertainty of the ultimate outcome of these matters, the impact on future financial results is not subject to reasonable estimates.

Item 4. Submission of Matters to a Vote of Security Holders

There were no matters submitted to a vote of security holders in the fourth quarter ended December 31, 2008.

Executive Officers of the Registrant

The names of the executive officers of the Company and their ages, titles and biographies as of March 1, 2008 are set forth below.

John L. Higgins, 38, joined the Company in January 2007 as President and Chief Executive Officer and he was also appointed to the Board in March 2007. Prior to joining the Company, Mr. Higgins served as Chief Financial Officer at Connetics Corporation, a specialty pharmaceutical company, since 1997, and also served as Executive Vice President, Finance and Administration and Corporate Development at Connetics since January 2002 until its acquisition by Stiefel Laboratories, Inc. in December 2006. Before joining Connetics, he was a member of the executive management team at BioCryst Pharmaceuticals, Inc., a biopharmaceutical company. Currently, he is a Director of BioCryst and serves as Chairperson of its Audit Committee. Before joining BioCryst in 1994, Mr. Higgins was a member of the healthcare banking team of Dillon, Read & Co. Inc., an investment banking firm. Mr. Higgins serves as chairman of CoMentis, Inc, a biopharmaceutical company, and has served as a director of numerous public and private companies. He received his A.B. from Colgate University, graduating Magna Cum Laude.

Martin D. Meglasson, Ph.D., 58, joined the Company in February 2004 as Vice President, Discovery Research. Prior to joining the Company, Dr. Meglasson was Director of Preclinical Pharmacology at Pharmacia, Inc. where he engaged in research and development of drugs for central nervous system and infectious diseases from 1998 to 2003. From 1996 to 1998, Dr. Meglasson served as Director of Endocrine and Metabolic Research, engaged in diabetes and obesity research, and was a member of the Exploratory Development Committee at Pharmacia & Upjohn. From 1988 to 1996, he was a researcher in the fields of diabetes and obesity at The Upjohn Co. Dr. Meglasson has participated in the discovery and development of two marketed drugs, is an inventor of 18 U.S. patents, and author of 70 scientific publications. Dr. Meglasson received his Ph.D. in pharmacology from the University of Houston and post-doctoral training at the University of Pennsylvania School of Medicine.

Zofia E. Dziewanowska, M.D., Ph.D., 67, has served as our Vice President, Clinical Research and Regulatory since February 2008. Dr. Dziewanowska joined the Company in April 2002 and previously served as the Vice President in charge of the Clinical Research Department, responsible for evaluation of all drugs. Her work in the industry began as an Associate Director of International Clinical Pharmacology at Merck Company, N.J. and subsequently at Hoffmann-La Roche Inc., the last few years until 1994 as Vice President and the Head of Clinical Research and Development for the United States. Since 1994, she held successive positions as Senior Vice President of Global Clinical Research and Development at Genta, Inc, Cypros Pharma and MAXIA, Inc. Dr. Dziewanowska also served as Vice Chair of a Medical Section Steering Committee for PhRMA. She has also served as Chair of an International Sub-committee and a Chair of Education Committee for physicians in Pharmaceutical Medicine at AAPP. Dr. Dziewanowska obtained her M.D. from the Medical School University of Warsaw and Ph.D. from the Polish Academy of Science. Academic affiliations include faculty membership at The Medical School of Cornell University, Rockefeller University, and The Medical School of the University of London. Her name is listed in several current Marquis Who is Who .

Syed Kazmi, Ph.D., MBA, 51, has served as our Vice President, Business Development & Strategic Planning since July 2007. Dr. Kazmi has more than 18 years of Pharmaceutical R&D and Business development

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experience. From 1995 until June 2007, he held various positions at Ligand, including Senior Scientist in Molecular Endocrinology, Director of Project Management and leader of multiple drug development teams, and Senior Director of Business Development. Prior to joining Ligand, Dr. Kazmi worked in discovery research at Johnson & Johnson from 1988 to 1995, where his most recent position was Principal Scientist in endocrinology and inflammation drug development programs. From 1985 to 1988, he held his postdoctoral research positions at McMaster University, Hamilton. Dr. Kazmi received a Ph.D. in biochemistry from J.N. University, New Delhi, and an executive MBA from San Diego State University.

John Sharp, CPA, 44, joined the Company in April 2007 as our Vice President, Finance and Chief Financial Officer. From November 2004 to April 2007, Mr. Sharp served as Vice President of Finance of Sequenom, Inc. and served as its Principal Accounting Officer since October 2005. From August 2000 to November 2004, Mr. Sharp served as Director of Accounting at Diversa Corporation, a publicly traded biotech company, where he was responsible for managing the overall accounting function, including financial reporting, internal controls, and corporate governance, during a period of significant company growth. From January 1994 until August 2000, Mr. Sharp was at the public accounting firm PricewaterhouseCoopers, most recently as a Senior Audit Manager. He received a B.S. from San Diego State University, and is a certified public accountant and a member of the Association of BioScience Financial Officers.

Charles S. Berkman, J.D., 40, has served as our Vice President, General Counsel and Secretary since April 2007. Mr. Berkman joined the Company in November 2001 and previously served as Associate General Counsel and Chief Patent Counsel for the Company (and Secretary since March 2007). Prior to joining the Company, Mr. Berkman was an attorney at the international law firm of Baker & McKenzie from November 2000 to November 2001. Before that he served as an attorney at the law firm of Lyon & Lyon from 1993 to November 2000, where he specialized in intellectual property law. Mr. Berkman earned a BS in chemistry from the University of Texas and a JD from the University of Texas School of Law.

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PART II

Item 5. Market for Registrant s Common Equity, Related Stockholder Matters, and Issuer Purchases of Equity Securities

Market Information

Our common stock is traded on the NASDAQ Global Market (formerly NASDAQ National Market) under the symbol LGND .

The following table sets forth the high and low intraday sales prices for our common stock on the NASDAQ Global Market and on the Pink Sheets, as applicable, for the periods indicated:

	Price Range	
	High	Low
Year Ended December 31, 2008:		
1st Quarter	$ 5.00	$ 3.31
2nd Quarter	4.55	2.16
3rd Quarter	3.82	2.58
4th Quarter	2.94	1.10
Year Ended December 31, 2007:		
1st Quarter	$ 13.03	$ 8.86
2nd Quarter	10.30	6.37
3rd Quarter	7.36	5.19
4th Quarter	6.21	3.87

As of February 27, 2009, the closing price of our common stock on the NASDAQ Global Market was $2.71.

Holders

As of February 27, 2009, there were approximately 1,672 holders of record of the common stock.

Dividends

On March 22, 2007, we declared a cash dividend on our common stock of $2.50 per share. As we have an accumulated deficit, the dividend was recorded as a charge against additional paid-in capital. The aggregate amount of $252.7 million was paid on April 19, 2007 to shareholders of record as of April 5, 2007. We had previously never declared or paid any cash dividends on our capital stock. We do not intend to pay any additional cash dividends in the foreseeable future. We currently intend to retain future earnings, if any, to finance future growth.

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Performance Graph

The graph below shows the five-year cumulative total stockholder return assuming the investment of $100 and the reinvestment of dividends (a one-time dividend of $2.50 was declared on the common stock in April 2007) and is based on the returns of the component companies weighted monthly according to their market capitalizations. The graph compares total stockholder returns of the Company s common stock, of all companies traded on the NASDAQ Stock market, as represented by the NASDAQ Composite® Index, and of the NASDAQ Biotechnology Stock Index, as prepared by The NASDAQ Stock Market Inc. The NASDAQ Biotechnology Stock Index tracks approximately 168 domestic biotechnology stocks.

The stockholder return shown on the graph below is not necessarily indicative of future performance and the Company will not make or endorse any predictions as to future stockholder returns.

	12/31/03	12/31/04	12/31/05	12/31/06	12/31/07	12/31/08
Ligand	100%	79%	76%	75%	44%	24%
NASDAQ Composite	100%	109%	110%	121%	132%	79%
NASDAQ Biotechnology Stocks	100%	106%	109%	110%	115%	101%

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Item 6. Selected Consolidated Financial Data

The following selected historical consolidated financial and other data are qualified by reference to, and should be read in conjunction with, our consolidated financial statements and the related notes thereto appearing elsewhere herein and Management s Discussion and Analysis of Financial Condition and Results of Operations. Our selected statement of operations data set forth below for each of the years ended December 31, 2008, 2007, 2006, 2005, and 2004 and the balance sheet data as of December 31, 2008, 2007 2006, 2005, and 2004 are derived from our consolidated financial statements.

	Years Ended December 31,				
	2008	2007	2006 (2)	2005	2004
	(in thousands, except share data)				
Consolidated Statement of Operations Data:					
Royalties	$ 20,305	$ 11,409	$	$	$
Sale of royalty rights, net					31,342
Collaborative research and development and other revenues	7,000	1,485	3,977	10,217	11,300
Research and development expenses	30,770	44,623	41,546	30,710	30,742
General and administrative expenses	23,785	30,410	43,908	23,134	12,580
Write-off of acquired in-process research and development	72,000				
Gain on sale leaseback	1,964	1,964	3,397		
Loss from operations	(97,276)	(60,175)	(78,080)		

While the Company is exposed to significant changes in certain commodity prices and foreign currency exchange rates, the Company actively monitors these exposures and takes various actions to mitigate any negative impacts of these exposures.

Item 4. Controls and Procedures

As of September 27, 2008, the Company carried out an evaluation under the supervision and with the participation of management, including the Chief Executive Officer (CEO) and the Chief Financial Officer (CFO), of the effectiveness of the Company s disclosure controls and procedures (as such term is defined in Rule 13a-15(e) and 15d-15(e) under the Securities Exchange Act of 1934 (the Exchange Act)). Based on this evaluation, the CEO and CFO have concluded that as of September 27, 2008, the Company s disclosure controls and procedures were effective to provide reasonable assurance that information required to be disclosed by the Company in reports that it files or submits under the Exchange Act is recorded,

processed, summarized and reported within the time periods specified under SEC rules and forms and is accumulated and communicated to management, including the CEO and CFO, to allow for timely decisions regarding disclosure. In addition, there was no change in the Company s internal control over financial reporting (as that term is defined in Rules 13a-15(f) and 15d-15(f) under the Exchange Act) that occurred during the quarter ended September 27, 2008 that materially affected, or is reasonably likely to materially affect, the Company s internal control over financial reporting.

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PART II OTHER INFORMATION

Item 1A. Risk Factors

A detailed description of risks that could have a negative impact on the Company s business, revenues and operating results can be found under the caption Risk Factors in the Company s Annual Report on Form 10-K for the year ended December 29, 2007, filed on February 27, 2008.

Item 2. Unregistered Sales of Equity Securities and Use of Proceeds

(c) The table below provides information with respect to purchases by the Company of shares of its common stock during each fiscal month of the third quarter of 2008:

ISSUER PURCHASES OF EQUITY SECURITIES

Period	Total Number of Shares Purchased	Average Price Paid per Share	Total Number of Shares Purchased as Part of Publicly Announced Plans or Programs	Maximum Number of Shares that May Yet Be Purchased Under the Plans or Programs
Jun 29, 2008 to Jul 26, 2008				1,000,000
Jul 27, 2008 to Aug 23, 2008				1,000,000
Aug 24, 2008 to Sep 27, 2008				1,000,000
Total				1,000,000

On April 25, 2008, the Company s Board of Directors authorized the repurchase of up to 1,000,000 shares under a new program for the period May 1, 2008 to April 30, 2009.

Item 6. Exhibits

Exhibit	Description
10.1	Loan Agreement, dated as of September 29, 2008, among Littelfuse, Inc., the lenders named therein and JPMorgan Chase Bank, N.A., as agent
10.2	First Amendment, dated as of September 29, 2008, to that certain Credit Agreement, dated as of July 21, 2006, among Littelfuse, Inc., the lenders named

	therein and Bank of America, N.A., as agent
31.1	Certification of Gordon Hunter, Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
31.2	Certification of Philip G. Franklin, Pursuant to Section 302 of the Sarbanes-Oxley Act of 2002
32.1	Certification Pursuant to Section 906 of the Sarbanes-Oxley Act of 2002

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SIGNATURES

Pursuant to the requirements of the Securities Exchange Act of 1934, the Registrant has duly caused this Quarterly Report on Form 10-Q for the quarter ended September 27, 2008, to be signed on its behalf by the undersigned thereunto duly authorized.

Littelfuse, Inc.

Date: November 3, 2008

By /s/ Philip G. Franklin

Philip G. Franklin
Vice President,
Operations Support
and
Chief Financial
Officer
(As duly authorized
officer and as
the principal
financial and
accounting officer)

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