LIGAND PHARMACEUTICALS INC
Form 10-K
March 03, 2010
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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, 2009

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.)
11085 North Torrey Pines Rd., Suite 300 San Diego, CA (Address of Principal Executive Offices)	**92121** (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 whether the registrant has submitted electronically and posted on its corporate Web site, if any, every Interactive Data File required to be submitted and posted pursuant to Rule 405 of Regulation S-T (§ 232.405 of this chapter) during the preceding 12 months (or for such shorter period that the registrant was required to submit and post such files). Yes ¨ 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. ¨

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

Large Accelerated Filer ¨	Accelerated Filer x	Non-accelerated Filer ¨ (Do not check if a smaller reporting company)	Smaller reporting company ¨

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 $288.6 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, 2009. 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 11, 2010, the Registrant had 117,335,286 shares of Common Stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Proxy Statement for the Registrant s 2010 Annual Meeting of Stockholders to be filed with the Commission on or before April 29, 2010 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, collaborative revenues and milestones 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 or other revenues 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, 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; Neurogen Corporation and Nexus Equity VI LLC, or Nexus.

We were incorporated in Delaware in 1987. Our principal executive offices are located at 11085 North Torrey Pines Road, Suite 300, 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.

Our business strategy includes targeted internal drug research and early-stage development capabilities. We believe 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, Merck & Co., or Merck, Roche, Cephalon and Celgene. These partnered product candidates are being studied for the treatment of large market indications such as thrombocytopenia, rheumatoid arthritis, chronic obstructive pulmonary disease, or COPD, asthma, osteoporosis, menopausal symptoms and Alzheimer s disease as summarized in the following tables.

Table 1: Pipeline Overview

Marketed	Under FDA/EU Review	Phase III
ITP Eltrombopag/PROMACTA (GSK)	Osteoporosis Bazedoxifene (Pfizer)	Hepatitis C Eltrombopag (GSK)
Chronic Pain Avinza (King)	Osteoporosis Lasofoxifene (Pfizer)	Menopausal symptoms Bazedoxifene+Premarin (Pfizer)
		Acadesine Coronary Artery Bypass Graft (CABG) (Pericor and Merck)

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Phase II	Phase I	Preclinical/Research
Leukemia (AML & ALL) Dinaciclib (Merck)	Advanced Myelodysplastic Syndrome (MDS) or Secondary Acute Myeloid Leukemia After MDS Eltrombopag (GSK)	HepDirect nucleoside for hepatitis C (Roche)
Mantle Cell Lymphoma or B-Cell Chronic Lymphocytic Leukemia Dinaciclib (Merck)	Sarcoma Eltrombopag (GSK)	Hematological-Erythropoietin receptor small molecule agonist
Advanced Breast and Lung Cancers Dinaciclib (Merck)	Alzheimer s Beta secretase (BACE) inhibitor (Merck)	Diabetes Glucagon receptor antagonist
COPD and Asthma PS291822 (Merck)	Muscle wasting LGD-4033 (unpartnered)	Hyperlipidemia Thyroid receptor beta agonist
RA, psoriasis and atherosclerosis PS540446 (BMS)	Inflammation PS873266 (Celgene)	VR1antagonist for pain and cough (Merck)
ITP-LGD-4665 (GSK)	Atherosclerosis XL-652 (Exelixis)	Inflammation JAK-3 inhibitor (Pfizer)
		Eight collaboration programs with undisclosed targets

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. Our technology applies the most advanced cell-based assays, gene-expression tools, ultra-high throughput screening and one of the world s largest chemical libraries to discover new and important medicines:

Intracellular Technology: We 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, we acquired high quality combinatorial libraries and proprietary ultra-high throughput screening technology as a result of our acquisition of Pharmacopeia. Our Encoded Combinatorial Library on Polymeric Support, or ECLiPS technology, 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. We use a proprietary combinatorial compound collection wedded to a unique ultra-high throughput screening platform to drive lead generation for us and our 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

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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.

Ultra-High Throughput Screening: We have 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 that 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 us. We believe the revenue generated from these and future potential collaborations will fund our business and potentially provide profits to our shareholders.

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 (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 also approved under the trade name Revolade(R) in Venezuela, Kuwait, Chile and Russia. GSK also filed a regulatory application for PROMACTA in Japan in September 2009. PROMACTA is the first oral thrombopoietin, or TPO, receptor agonist therapy for the treatment of adult patients with chronic ITP. In December 2009, GSK received a positive opinion for Revolade (eltrombopag/PROMACTA) from the European Medicines Agency s Committee for Medicinal Products for Human Use (CHMP) for the oral treatment of thrombocytopenia (reduced platelet count) in adults with the blood disorder chronic ITP. As a result of the regulatory approvals of 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 The Rockefeller University, or Rockefeller, we agreed to pay a share of such royalties to Rockefeller. See Item 3. Legal Proceedings.

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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.

In addition to the accelerated approval granted for GSK s PROMACTA for the treatment of thrombocytopenia in patients with chronic ITP, GSK also reported new phase III results for PROMACTA in chronic ITP at the 2009 14th Congress of European Hematology meeting and completed enrollment of two Phase III trials in patients with hepatitis C in the fourth quarter of 2009. A Phase I/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.

Bazedoxifene (Viviant) is a product candidate that resulted from one of our collaborations with Wyeth (now Pfizer). 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. Regarding Viviant, the FDA has advised that it expects to convene an advisory committee to review the pending NDAs for both the treatment and prevention indications. Approvable letters were received for each of these NDAs in which, among other things, the FDA requested further analyses and discussion concerning the incidence of stroke and venous thrombotic events, identified certain issues concerning data collection and reporting, and requested additional source documents. An FDA-requested advisory committee meeting is expected to be scheduled following submission of the complete response to the approvable letters. In April 2009, Pfizer received approval in the EU for CONBRIZA (the EU trade name for Viviant) for the treatment of postmenopausal osteoporosis in women at increased risk of fracture. We expect CONBRIZA to be launched in the EU in 2010.

Wyeth (now Pfizer) is also developing bazedoxifene in combination with PREMARIN (Aprela) which is a tissue selective estrogen complex under development for menopausal symptoms and osteoporosis. Two Phase III studies with bazedoxifene/conjugated estrogens (Aprela) showed a reduced number and severity of hot flashes in symptomatic postmenopausal women by up to 80 percent, when compared with placebo. Pfizer 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 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. In February 2009, FABLYN received approval in the EU for the treatment of osteoporosis. Pfizer reported that following a strategic review, it decided to explore strategic options for FABLYN, including out-licensing or sale. Under the terms of our agreement with Pfizer, we are entitled to receive royalty payments on worldwide net sales of lasofoxifene for any indication (see Table 2 below). few expect ABLYN to be launched in the EU in 2010.

Advanced R&D Programs

PS291822 is a CXCR2 antagonist that resulted from our collaboration with Schering-Plough (now Merck). PS291822 entered Phase II clinical trials in the fourth quarter of 2006 for COPD and asthma. A Phase II study in patients with COPD was completed in October 2008. Phase II studies in asthma were completed in February 2009. Merck has recently initiated two Phase IIb studies in COPD and asthma with 500 patients each.

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

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Recent Acquisitions

Neurogen

On December 23, 2009, we acquired all of the outstanding common shares of Neurogen Corporation, or Neurogen. As consideration, we issued approximately 4.2 million shares of our common stock to Neurogen stockholders, or approximately 0.061 of a share of our common stock for each outstanding Neurogen share, as well as approximately $0.6 million in cash. Security holders of Neurogen also received contingent value rights, under which they could receive cash payments under certain circumstances. Neurogen was a drug development company historically focusing on small-molecule drugs to improve the lives of patients suffering from psychiatric and neurological disorders with significant unmet medical needs. Neurogen has conducted its drug development independently and, when advantageous, collaborated with world-class pharmaceutical companies to access additional resources and expertise.

Primary Acquired Assets

- Fully Funded Partnership with Merck for Vanilloid Receptor Subtype 1 (VR1) Antagonists in development for pain and cough.
- H3 Antagonist Program for the potential treatment of sleep disorders (e.g. narcolepsy), attention deficit hyperactivity disorder (ADHD), and cognitive deficits (e.g. schizophrenia and Alzheimer s) in preclinical development.
- Oral Erythropoietin (EPO) Research Program we have been conducting internal research on orally active erythropoietin agonists. Neurogen conducted its own drug discovery efforts in the area and provided novel chemical scaffolds and additional know-how that could further enhance our oral EPO program.
- Cash and net operating loss carryforwards we gained approximately $7.4 million in cash from this transaction. Neurogen has more than $180 million in net operating loss carryforwards. While there will be significant limitation to the utilization of the net operating losses over time, the net operating losses may be usable to some extent by us, should the combined companies become profitable.

Metabasis

On January 27, 2010, we completed the acquisition of Metabasis Therapeutics, Inc., or Metabasis, following approval of the transaction by Metabasis stockholders. As a result, we gained a fully funded partnership with Hoffman-La Roche Inc., or Roche, additional pipeline assets and drug discovery technologies and resources. We paid $1.6 million in cash or about $0.046 per Metabasis share to Metabasis stockholders. In addition, Metabasis stockholders received four tradable Contingent Value Rights (CVRs), one CVR from each of four respective series of CVRs, for each Metabasis share. The CVRs will entitle Metabasis stockholders to cash payments as frequently as every six months as cash is received by us from proceeds from Metabasis partnership with Roche or the sale or partnering of any of the Metabasis drug development programs, among other triggering events.

Primary Acquired Assets

- Fully funded partnership with Roche to develop new treatments for hepatitis C viral infection utilizing the proprietary HepDirect® liver-targeting technology.
- Glucagon Receptor Antagonist Program for diabetes in pre-clinical development.
- Thyroid Receptor Beta Agonist Program for hyperlipidemia in Phase I and preclinical development.

PeriCor Therapeutics a common stock ownership position in privately-held PeriCor Therapeutics, Inc. PeriCor licensed acadesine to Schering-Plough Corporation (now Merck & Co.) and the compound is in a Phase III clinical trial for the prevention of adverse cardiovascular and cerebrovascular outcomes in patients undergoing coronary artery bypass graft surgery.

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HepDirect Technology HepDirect technology supplements our core drug discovery technology platform of ligand-dependent gene expression and ultra-high throughput combinatorial chemistry screening. HepDirect is a prodrug technology that targets delivery of certain drugs to the liver by using a proprietary chemical modification that renders a drug biologically inactive until cleaved by a liver-specific enzyme.

Other Product Candidates and R&D Programs other product candidates, including MB07803 for diabetes and pradefovir for hepatitis B, which have been evaluated in clinical trials and early stage R&D programs including glucokinase activators for diabetes and DGAT-1 inhibitors for obesity.

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 (now Pfizer)	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
JAK-3 inhibitor	Pfizer	Tiered double digit royalties	
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, we may continue the development until PoC and receive stepped up royalties ranging from 10% to 14% under the categories of annual sales described above.

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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 a splenectomy. In December 2009, GSK received a positive opinion for Revolade(R) (eltrombopag/PROMACTA) from the European Medicines Agency s Committee for Medicinal Products for Human Use (CHMP) for the oral treatment of thrombocytopenia (reduced platelet count) in adults with the blood disorder chronic ITP. Revolade is expected to be launched in the EU in the first half of 2010. 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 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 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. Under the terms of the GSK agreement, GSK paid us $5.0 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. In the first year of sales, royalties will be one-half of the regular royalty rate. 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. The term of the license agreement expires ten years from the date of the first commercial sale of the first licensed product in any country worldwide or until the expiration of the last licensed patent with a valid claim, whichever term is longer, although some obligations servive termination. Prior to the expiration of the license agreement, GSK has the right to terminate the agreement upon a specified number of days notice and we may not terminate the agreement unless GSK provides its prior written consent. Any such termination will not relieve the terminating party from obligations that have accrued prior to such termination or that expressly survive such termination. No termination will require us to refund to GSK any or all payments made to us by GSK under the agreement. In the event a party is in breach of any of its material obligations under the license agreement, the other party will have the right to seek damages and such other remedies as may be available to it.

Agreement with Pharmacopeia

In connection with our merger with Pharmacopeia, 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

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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, we 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, 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. The initial research term of the GSK agreement expires in March 2011.

Pfizer Collaborations

Bazedoxifene Program

Bazedoxifene (Viviant) is a product candidate that resulted from one of our collaborations with Wyeth (now Pfizer). 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. Regarding Viviant, the FDA has advised that it expects to convene an advisory committee to review the pending NDAs for both the treatment and prevention indications. Approvable letters were received for each of these NDAs in which, among other things, the FDA requested further analyses and discussion concerning the incidence of stroke and venous thrombotic events, identified certain issues concerning data collection and reporting, and requested additional source documents. An FDA-requested advisory committee meeting is expected to be scheduled following submission of the complete response to the approvable letters. In April 2009, Pfizer received approval in the EU for CONBRIZA (the EU trade name for Viviant) for the treatment of postmenopausal osteoporosis in women at increased risk of fracture. We expect CONBRIZA to be launched in the EU in 2010.

Pfizer is also developing bazedoxifene in combination with PREMARIN (Aprela) which is a tissue selective estrogen complex under development for menopausal symptoms and osteoporosis, 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. Pfizer 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).

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.

Lasofoxifene Program

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.

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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 February 2009, FABLYN received approval in the EU for the treatment of osteoporosis.

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. The amount of net royalties we will receive on annual net sales after giving effect to the royalty sale is described in Table 2.

JAK3 Program

In connection with the completion of our acquisition of Pharmacopeia, we assumed a research and license agreement with Wyeth (now Pfizer), 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 Agreement, we and Pfizer each have certain exclusive rights to develop and commercialize products resulting from the JAK3 program and the alliance. In November 2009, Pfizer extended its research collaboration with us for JAK3 by one year. The Research and License Agreement entered into in December 2006 with Wyeth provided for an initial three year research term. Under this extension, we will receive $3.1 million in research payments to continue conducting drug discovery and lead candidate optimization. Under the original agreement, we are entitled to receive up to $175 million in milestone payments for the successful development and commercialization of multiple products. In addition, we will receive royalties on product sales.

Schering-Plough Collaboration (now Merck)

1998 Collaboration

In connection with our acquisition of Pharmacopeia, we assumed collaboration and license agreements with Schering-Plough Ltd. (now Merck) 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 that entered Phase I clinical trials in early 2009.

PS 291822 (SCH-527123), the lead in a series of CXCR2 antagonists, is being developed for the potential oral treatment of chronic obstructive pulmonary disorder (COPD) and asthma. Merck has completed phase II trials in COPD, neutrophilic asthma, mild allergen-induced asthma and psoriasis. In January 2010, Merck initiated two large Phase II dose-ranging studies with 500 patients each in COPD and severe asthma.

Dinaciclib (SCH-727965, PS-095760), a pro-apoptotic inhibitor of cyclin-dependent kinases is under clinical development for the potential treatment of cancer. Three Phase II trials are ongoing;

- A phase II trial in patients with advanced breast cancer and non-small cell lung cancer (NSCLC)
- A phase II trial in acute myelogenous leukemia (AML) and acute lymphoblastic leukemia (ALL)
- A phase II trial in mantle cell lymphoma (MCL) and B-cell chronic lymphocytic leukemia (B-CLL)

A Beta-Secretase inhibitor is in clinical development for Alzheimer s disease. We received a milestone payment of $1.0 million from Merck for lead selection and Phase I initiation. Merck reported the completion of Phase I single dose trial study with a 58% reduction in A-Beta peptide in cerebral/spinal fluid. Phase I multi-dose trial is ongoing, and a Phase II trial initiation is projected to start in 2010.

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Under the terms of these agreements with Merck, 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 Merck is conducting. We continue to be entitled to payments resulting from the successful achievement by Merck of clinical and regulatory milestones, as well as royalty payments at various rates depending on the origin of collaboration products from discovery and optimization libraries at Ligand and Merck, and on net sales of products resulting from compounds being developed by Merck under those agreements.

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 (now Merck). We mutually terminated the collaboration and license agreement with Merck in July 2009. As part of the termination, Merck continued to fund research through a wind-down period ending December 31, 2009. In addition, we are entitled to receive future royalties and milestones as a result of Merck s successful advancement through clinical development of therapeutic candidates discovered as a result of the collaboration which result in commercial sales. Merck is solely responsible for the further development and commercialization of all collaboration products after programs are handed over by us, and for all development and commercialization costs.

We received a total of $4.0 million in milestone payments at termination of the collaboration agreement and are entitled to receive further milestones and royalties on programs with identified leads.

Bristol-Myers Squibb Collaborations

Discovery Collaboration Agreement Dated October 11, 2007

On December 9, 2009, we entered into an amendment to the discovery collaboration agreement dated October 11, 2007 between Pharmacopeia and BMS. Pursuant to the terms of the amendment, the research term under the collaboration agreement terminated on December 31, 2009 and the research program under the collaboration agreement was transferred to BMS. We are no longer obligated to provide research support to BMS after December 31, 2009, other than providing certain data and compound transfer services to BMS through June 30, 2010. In connection with the amendment, we paid $1.0 million to BMS, and BMS is no longer required to make milestone payments to us under the collaboration agreement.

SARM

On November 6, 2009, we provided notice to BMS, that pursuant to the terms of the license agreement dated October 11, 2007 between BMS and us, we are exercising our right to terminate the license agreement without cause, effective three months following the date of delivery of written notice of such termination (or February 9, 2010). Under the terms of the license agreement, BMS provided us exclusive worldwide development and commercialization rights to a selective androgen receptor modulator, or SARM, program. There is no financial penalty for us associated with the termination of the license agreement.

P-38 Kinase Program

In connection with the merger with Pharmacopeia, 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 for psoriasis. BMS has also completed a Phase II study in rheumatoid arthritis and a Phase II trial in atherosclerosis is ongoing. 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.

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Roche

Collaboration for Hepatitis C

In connection with our merger with Metabasis in January 2010, we acquired a fully funded partnership with Roche to develop new treatments for hepatitis C viral infection utilizing the proprietary HepDirect(R) liver-targeting technology. The lead HepDirect nucleoside, MB11362, was declared a clinical candidate in the second quarter of 2009. Roche will fund 100% of program costs and will make milestone and royalty payments upon the achievement of certain development events and commercialization of MB11362 and/or other applicable HepDirect compounds.

Merck

Collaboration for VR1

In connection with our merger with Neurogen, we acquired a fully funded partnership with Merck for Vanilloid Receptor Subtype 1 (VR1) Antagonists. Merck will fund 100% of program costs and make milestone and royalty payments upon the achievement of certain development events and commercialization of any applicable VR1 compounds.

Cephalon Collaboration

In connection with the merger with Pharmacopeia, 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.

We and Cephalon executed an amendment in January 2009 to the collaboration agreement dated May 16, 2006. The agreement provided that we would have no obligation to continue research activities with respect to the two active collaboration programs and were free 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. We will be entitled to milestone and royalty payments associated with only one of the two active programs. In addition, we agreed to provide certain chemistry services to Cephalon through a third party vendor for a term of nine months from the date of agreement, which ended in September 2009.

Celgene Collaboration

In connection with the merger with Pharmacopeia, 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).

Exelixis Collaboration

We exclusively licensed certain technology to X-Ceptor Therapeutics in 1999. X-Ceptor was subsequently acquired by Exelixis Inc. in October 2004. Exelixis has three partnered programs based on X-Ceptor technologies, including (a) XL-652, a LXR agonist, is in Phase I development with BMS for the potential treatment of atherosclerosis and other coronary artery diseases, (b) FXR-450, a Farnesoid X receptor modulator, is in preclinical development with Pfizer for the potential treatment of hyperlipidemia including hypertriglyceridemia, and (c) Xl-550, a mineralocorticoid receptor modulator, is in preclinical development with Daiichi-Sankyo for the potential treatment of metabolic disorders and cardiovascular diseases. Ligand is entitled to receive royalties on net sales of products.

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PeriCorTherapeutics

We assumed a common stock ownership position in privately-held PeriCor Therapeutics, Inc. through our acquisition of Metabasis. PeriCor sublicensed rights from Metabasis to acadesine and three additional Adenosine Regulating Agents in 2005. PeriCor licensed acadesine to Schering-Plough Corporation (now Merck & Co.) and the compound is in a Phase III clinical trial for the prevention of adverse cardiovascular and cerebrovascular outcomes in patients undergoing coronary artery bypass graft surgery.

Trevena Collaboration

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

Under the terms of the agreement, Trevena has been granted exclusive worldwide rights to sublicense active compounds resulting from the collaboration. We expect to screen targets 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
Selective Androgen Receptor Modulators (SARMs) (agonists)	Muscle wasting and frailty	Phase I
Thyroid receptor beta agonists	Hyperlipidemia	Phase I and Preclinical
Small molecule Erythropoietin (EPO) receptor agonists	Chemotherapy-induced anemia, anemia due to kidney failure	Preclinical
Glucagon receptor antagonists	Diabetes	Preclinical
Histamine 3 (H3) receptor antagonists	Cognitive disorders	Research

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. LGD-4033, our current lead, is a next-generation SARM designed to provide the benefits of androgen receptor stimulation on skeletal muscle and bone without the side effects of currently marketed androgens.

Preclinical studies conducted with LGD-4033 suggest that the compound may have favorable activity in the treatment of cachexia, frailty, osteoporosis, hypogonadism as well as other disorders. LGD-4033 has anabolic activity in muscle and bone and in animal models of osteoporosis and muscle wasting restores these tissues to normal levels. By comparison, the compound has weak, partial agonist activity on the prostate and has little effect on this tissue at expected therapeutic doses. The tissue selective properties of LGD-4033 are independent of local drug concentration indicating that tissue selectivity is inherent in the compound. We filed an Investigational New Drug (IND) in December 2008 for LGD-4033. Phase I clinical trials began in June 2009. We

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completed Phase I single ascending dose trial in the fourth quarter of 2009. LGD-4033 was found to be well absorbed with good pharmacokinetics consistent with a once-a-day dosing and there were no serious or dose dependent adverse events. A Phase I Multiple Ascending Dose clinical trial has been initiated with results expected in the third quarter of 2010.

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

Erythropoietin (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. Compounds have been discovered that potently and selectively stimulate differentiation by human bone marrow stem cells to form erythrocytes in vitro. Advanced compounds are orally absorbed by animals and demonstrate pharmacokinetic properties consistent with once daily, oral administration to humans.

Glucagon Receptor Antagonist Research Program

We are developing small molecule glucagon receptor antagonists for the treatment of Type 2 diabetes mellitus. Compounds that block the action of glucagon may reduce the hyperglycemia that is characteristic of this disease. Glucagon stimulates the production of glucose by the liver and its release into the blood stream. In diabetic patients, glucagon secretion is abnormally elevated which contributes to hyperglycemia in these patients. Compounds have been discovered that block the action of glucagon on human hepatocytes *in vitro*. Our advanced glucagon antagonist compounds demonstrate oral bioavailability in rodents.

Thyroid Hormone Receptor Beta Agonist Research Program

Thyroid hormone acts throught two distinct receptors, referred to as TR-alpha and TR-beta. TR-beta receptor agonists have been shown to reduce plasma concentration of cholesterol and lipoprotein a, or Lp(a). These actions may be of benefit to patients with dyslipidemia at increased increased risk of cardiovascular disease. Our compounds are designed for preferential drug delivery to the liver where they upregulate LDL uptake and excretion. Tissue-selective drug distribution may improve the safety of these compounds compared to thyroid hormone. Advanced compounds bind TR-beta receptors with high affinity, demonstrate oral absorption, and reduce the plasma cholesterol concentration in animal models of dyslipidemia.

Histamine H3 Receptor Inverse Agonist Research Program

Histamine acts through four distinct receptors, H1-H4. Highly successful drugs have been developed that target the H1 receptor (e.g., CLARITIN™, and ZYRTEC™) and H2 receptors (e.g., ZANTAC™ and PEPCID™). No H3 receptor blockers are currently approved. An H3-selective inverse agonist will block the action of histamine at the H3 receptor when its endogenous levels are elevated. H3 receptors are widely distributed in the brain where they regulate the secretion of neurotransmitters such as histamine, norepinephrine, dopamine, and serotonin. Our H3 inverse agonists regulate sleep/wakefulness cycles in rodents indicating they may be useful for daytime sleepiness-associated disorders. Published results from a variety of sources suggest that H3 antagonists/inverse agonists may also be useful to improve cognitive dysfunction in schizophrenia, Alzeheimer s disease, and attention deficit disorder.

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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 estrogen 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 us, are trade secrets, or are 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, or a percentage of all other revenue we recognize from collaborators that is derived from the technology licensed from Columbia and Cold Spring.

In connection with our merger with Metabasis, we acquired certain HepDirect Technology. HepDirect technology supplements our core drug discovery technology platform of ligand-dependent gene expression and ultra-high throughput combinatorial chemistry screening. HepDirect is a prodrug technology that targets delivery of certain drugs to the liver by using a proprietary chemical modification that renders a drug biologically inactive until cleaved by a liver-specific enzyme.

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.

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 $39.9 million, $30.8 million, and $44.6 million in 2009, 2008 and 2007, respectively, of which 47%, 100%, and 100%, respectively, were sponsored by us.

There were no research and development expenses from discontinued operations in 2009 and 2008. Research and development expenses from discontinued operations were $0.1 million in 2007.

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, applications for generic forms of AVINZA have 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 1, 2010, we had 72 full-time employees, of whom 53 are involved directly in scientific research and development activities. Of these employees, 29 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.

Royalties based on sales of AVINZA and PROMACTA represent a substantial portion of our revenues.

King Pharmaceuticals, or King, is obligated to pay us royalties based on its sales of AVINZA and GlaxoSmithKline, or GSK, is obligated to pay us royalties on its sales of PROMACTA. These royalties represented 21% and 74% of total revenues for the years ended December 31, 2009 and 2008, respectively, and will continue to be a substantial portion of our ongoing revenues for some time. We also receive milestones and collaborative revenue from our partners in various collaborations, but the amount of such revenue 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, as could any reduction in our expected milestone and collaborative revenue. Setbacks for AVINZA and PROMACTA 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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On July 21, 2009, 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 against Sandoz Inc., or Sandoz, for patent infringement under the 339 patent. According to the complaint, Sandoz filed an ANDA for morphine sulfate extended release capsules and, in connection with the ANDA filing, Sandoz provided written certification to the FDA alleging that the claims of the 339 patent are invalid, unenforceable and/or will not be infringed by the manufacture, use or sale of Sandoz s proposed morphine product. Similar to the lawsuit against Actavis, this lawsuit seeks a judgment that would, among other things, prevent Sandoz from commercializing its proposed morphine product until after expiration of the 339 patent.

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, we may no longer 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 development and regulatory hurdles prior to marketing which could delay or prevent sales and/or milestone revenue.

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 and lasofoxifene. 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 are 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. For example, the trial entitled Eltrombopag To Reduce The Need For Platelet Transfusion In Subjects With Chronic Liver Disease And Thrombocytopenia Undergoing Elective Invasive Procedures (ELEVATE) was suspended in October 2009 in accordance with an IDMC Recommendation. GSK terminated the ELEVATE study and the program is under review. 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

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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 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. 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. Security holders of Neurogen and Metabasis also received contingent value rights under which we could be required to make unspecified payments under certain circumstances.

In December 2009, the Internal Revenue Service, or IRS, issued to us a Notice of Proposed Adjustment, or NOPA, seeking an increase to our taxable income for the 2007 fiscal year of $71.5 million and a $4.1 million penalty for substantial underpayment of tax in fiscal 2007. We responded to the NOPA in February 2010, disagreeing with the conclusions reached by the IRS in the NOPA. We recorded a FIN 48 liability of $25.1 million related to the income tax effect of the NOPA and $3.0 million related to estimated interest due on the proposed underpayment of tax. We also recorded deferred income tax assets of $25.1 million associated with the ability to carry back losses from 2008 and 2009 to offset the NOPA. In addition, we recorded an income tax receivable of $4.5 million associated with changes in income tax law in relation to prior AMT taxes paid on carry back periods. We have not recorded the penalties proposed by the IRS in our financial statements as we believe that we met the appropriate standard for the tax position on our 2007 tax return. If we are unsuccessful in our negotiations with the IRS, we may be required to pay the $4.1 million penalty and utilize a significant amount of our net operating loss carryforwards.

We believe that our capital resources, including our currently available cash, cash equivalents, and short-term investments as well as our current and future royalty revenues, 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;

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changes in existing collaborative relationships, including the funding we receive in connection with those relationships;

the progress of our milestone and royalty producing activities;

our ability to reach a favorable resolution with the IRS with respect to their audit of our fiscal 2007 federal tax return, or to other potential tax assessments;

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.

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 October 2009, Wyeth, a collaborative partner of ours, and Pfizer announced that Pfizer had completed its acquisition of Wyeth in a cash and stock transaction. Furthermore, in November 2009, Schering-Plough Corporation, another of our collaborative partners, and Merck & Co., Inc., or Merck, announced that Merck and Schering-Plough had combined, 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.

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;

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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.

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, 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.

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 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.

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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.

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.

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, 2009, our accumulated deficit was $681.6 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

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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.

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 our key management and scientific personnel. If we fail to retain such key employees, we may not realize the anticipated benefits of our mergers. Either of these could have substantial negative impacts on our business and our stock price.

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.

We agreed to indemnify Eisai and King under certain circumstances pursuant to the asset purchase agreements we entered into with Eisai and King in connection with the sale of our commercial product lines. Some of our indemnification obligations still remain and our potential liability in certain circumstances is not limited to specific dollar amounts. 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.

In addition, King assumed our obligation to make payments to Organon based on net sales of AVINZA (the fair value of which was $40.8 million as of December 31, 2009). 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 does not relieve us of exposure to product liability risks on products we sold prior to divesting these product lines. A successful product liability claim or series of claims brought against us may not be insured and could result in payment of significant amounts of money and divert management s attention from running our business.

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.

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

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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.

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

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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 businesses of Neurogen, Metabasis and/or Pharmacopeia and realize the anticipated benefits of the mergers.

In December 2008, we completed our merger with Pharmacopeia. In 2009, we completed our merger with Neurogen and in January 2010, we completed our merger with Metabasis. The success of these mergers will depend, in part, on our ability to realize the anticipated synergies, growth opportunities and cost savings from integrating Pharmacopeia s, Neurogen s and/or Metabasis 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, Neurogen and/or Metabasis. The integration of independent companies is a complex, costly and time-consuming process. It is possible that the integration processes 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, Neurogen s and Metabasis business operations, technology, development programs, products and personnel with those of ours. If we do not successfully integrate the business of Pharmacopeia, Neurogen and Metabasis, the expenditure of these costs will reduce our cash position.

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.

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.

While no material weaknesses were identified as of December 31, 2009, 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

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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.

Impairment charges pertaining to goodwill, identifiable intangible assets or other long-lived assets from our mergers 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 mergers with Pharmacopeia and Neurogen have been allocated to 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.

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.

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Item 1B. Unresolved Staff Comments

None.

Item 2. Properties

We currently occupy approximately 30,000 square feet of office and laboratory facility in San Diego, California leased through December 2011. 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.

Neurogen Corporation conducted its operations in laboratory and administrative facilities on a single site located in Branford, Connecticut. The total facilities, which were owned by Neurogen comprised approximately 142,000 square feet, of which approximately 21,000 square feet was leased by another company month to month. On February 2, 2010, we sold the facilities, which included approximately 120,000 square feet of laboratory and office space, approximately 40,000 square feet of warehouse space, and the surrounding land for approximately $3.5 million in cash, less expenses.

Item 3. Legal Proceedings

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. On December 21, 2009, the remaining parties entered into a Stipulation and Agreement of Compromise, Settlement and Release, or the Stipulation. The Stipulation is subject to Court approval and a hearing to consider approval of the stipulation has been scheduled for March 15, 2010. As of December 31, 2009, we have not accrued an indemnification obligation based on our assessment that our responsibility for any such obligation is not probable or estimable.

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, Ligand and two of Ligand s wholly owned subsidiaries. The complaint generally alleged that Pharmacopeia s Board of Directors decision to enter into the proposed transaction with Ligand on the terms contained in the merger agreement constitutes a breach of fiduciary duty and gives rise to other unspecified state law claims. The complaint also alleged that Ligand and two of Ligand s wholly owned subsidiaries aided and abetted Pharmacopeia s Board of Directors breach of fiduciary duty. In addition, the complaint alleged that the named plaintiff sought equitable relief, including among other things, an order preliminarily and permanently enjoining the proposed transaction. While management believes that neither Ligand nor Pharmacopeia engaged in any wrongful acts, in an effort to minimize the cost and expense of any litigation, the parties entered into a stipulation of settlement, pursuant to which Pharmacopeia agreed to make certain additional disclosures in its SEC Form 14d-9 and not oppose a fee award to plaintiffs attorneys of up to $180,000, which is included in current portion of accrued litigation settlement costs at September 30, 2009. On October 20, 2009, the court granted final approval of the stipulation of settlement and dismissed the class action with prejudice.

On September 9, 2009, we received notice that a class action complaint was filed in the Connecticut Superior Court for the Judicial District of New Haven by Gabriel Guzman, one of Neurogen s stockholders, against Neurogen, the members of its Board of Directors, Ligand and one of Ligand s wholly owned subsidiaries.

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The amended complaint generally alleged that Neurogen s Board of Directors decision to enter into the transaction with Ligand on the terms contained in the merger agreement constituted a breach of fiduciary duty. The amended complaint also alleges that Ligand and one of Ligand s wholly owned subsidiaries aided and abetted Neurogen s Board of Directors breach of fiduciary duty. Management believes that neither Ligand nor Neurogen engaged in any wrongful acts and on October 22, 2009, we filed a motion to strike the complaint. The plaintiff filed a Withdrawal of Action to voluntarily dismiss the case in December 2009.

In December 2009, the Internal Revenue Service, or IRS, issued to us a Notice of Proposed Adjustment, or NOPA, seeking an increase to our taxable income for the 2007 fiscal year of $71.5 million and a $4.1 million penalty for substantial underpayment of tax in fiscal 2007. We responded to the NOPA in February 2010, disagreeing with the conclusions reached by the IRS in the NOPA. We recorded a FIN 48 liability of $25.1 million related to the income tax effect of the NOPA and $3.0 million related to estimated interest due on the proposed underpayment of tax. We also recorded deferred income tax assets of $25.1 million associated with the ability to carry back losses from 2008 and 2009 to offset the NOPA. In addition, we recorded an income tax receivable of $4.5 million associated with changes in income tax law in relation to prior AMT taxes paid on carry back periods. We have not recorded the penalties proposed by the IRS in our financial statements as we believe that we met the appropriate standard for the tax position on our 2007 tax return. If we are unsuccessful in our negotiations with the IRS, we may be required to pay the $4.1 million penalty and utilize a significant amount of our net operating loss carryforwards.

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. Reserved

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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 for the periods indicated:

	Price Range	
	High	Low
Year Ended December 31, 2009:		
1st Quarter	$ 3.20	$ 1.86
2nd Quarter	3.18	2.51
3rd Quarter	3.21	2.21
4th Quarter	2.43	1.63
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

As of February 11, 2010, the closing price of our common stock on the NASDAQ Global Market was $1.66.

Holders

As of February 11, 2010, there were approximately 1,648 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 our 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 we will not make or endorse any predictions as to future stockholder returns.

	12/31/04	12/31/05	12/31/06	12/31/07	12/31/08	12/31/09
Ligand	100%	96%	94%	55%	31%	25%
NASDAQ Market (U.S. Companies) Index	100%	102%	112%	122%	59%	84%
NASDAQ Biotechnology Stocks	100%	103%	104%	109%	95%	110%

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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, 2009, 2008, 2007, 2006, and 2005 and the balance sheet data as of December 31, 2009, 2008 2007, 2006, and 2005 are derived from our consolidated financial statements.

	Year Ended December 31,				
	2009	2008	2007	2006(2)	2005
	(in thousands, except share data)				
Consolidated Statement of Operations Data:					
Royalties	$ 8,334	$ 20,305	$ 11,409	$	$
Collaborative research and development and other revenues	30,606	7,000	1,485	3,977	10,217
Research and development expenses	39,870	30,770	44,623	41,546	30,710
General and administrative expenses	15,211	23,785	30,410	43,908	23,134
Lease termination costs					