LIGAND PHARMACEUTICALS INC
Form 10-K
March 14, 2013
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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, 2012

OR

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

For the transition period from to .

Commission File No. 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.)
11119 North Torrey Pines Rd., Suite 200 La Jolla, CA	92037
(Address of Principal Executive Offices)	(Zip Code)

Registrant's telephone number, including area code: (858) 550-7500

Securities registered pursuant to Section 12(b) of the Act:

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

Securities registered pursuant to Section 12(g) of the Act:

None

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

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

Indicate by check mark 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 x No o

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

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

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

The aggregate market value of the Registrant’s voting and non-voting stock held by non-affiliates was approximately $295.9 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, 2012. 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 March 1, 2013, the Registrant had 20,208,248 shares of Common Stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Proxy Statement for the Registrant’s 2013 Annual Meeting of Stockholders to be filed with the Commission on or before April 30, 2013 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

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 royalty revenues, collaborative revenues and milestones, and product development. Actual events or results may differ materially from our 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 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 JVR, Allergan Ligand Retinoid Therapeutics, Seragen, Inc., or Seragen; Pharmacopeia, LLC; Neurogen Corporation, CyDex Pharmaceuticals, Inc., Metabasis Therapeutics, and Nexus Equity VI LLC, or Nexus.

We were incorporated in Delaware in 1987. Our principal executive offices are located at 11119 North Torrey Pines Road, Suite 200, La Jolla, California, 92037. Our telephone number is (858) 550-7500.

Item 1. Business

Overview

We are a biotechnology company that operates with a business model focused on developing or acquiring revenue generating assets and coupling them to a lean corporate cost structure. Our goal is to create a sustainably profitable business and generate meaningful value for our stockholders. Since a portion of our business model is based on the goal of partnering with other pharmaceutical companies to commercialize and market our assets, a significant amount of our revenue is based largely on payments made to us by partners for royalties, milestones and license fees. We recognized the important role of the drug reformulation segment in the pharmaceutical industry and in 2011 added Captisol® to our technology portfolio. Captisol is a powerful formulation technology that has enabled six FDA approved products, including Onyx’s Kyprolis® and Baxter International’s Nexterone® and is currently being developed in a number of clinical-stage partner programs. In comparison to our peers, we believe we have assembled one of the largest and most diversified asset portfolios in the industry with the potential to generate significant revenue in the future. The therapies in our development portfolio address the unmet medical needs of patients for a broad spectrum of diseases including hepatitis, muscle wasting, multiple myeloma, Alzheimer’s disease, dyslipidemia, diabetes, anemia, epilepsy, FSGS and osteoporosis. We have established multiple alliances with the world’s leading pharmaceutical companies including GlaxoSmithKline, Onyx Pharmaceuticals, Merck, Pfizer, Baxter International, Bristol-Myers Squibb, Celgene, Lundbeck Inc., Eli Lilly and Co., Spectrum Pharmaceuticals and The Medicines Company.

Business Strategy

Our business model is designed to create value for stockholders by assembling a diversified portfolio of biotech and pharmaceutical revenue streams and operating that business with an efficient and low corporate cost structure. Our goal is to become a sustainably profitable company that offers investors an opportunity to participate in the promise of the biotech industry in a diversified, lower-risk business than a typical biotech. Our business model is based on the concept of doing what we do best; drug discovery, reformulation and partnering with other pharmaceutical companies to leverage what they do best (late-stage development, regulatory management and commercialization) to ultimately generate our revenue. Our revenue consists mostly of license fees, milestones, royalties from the partners that license our drugs and technologies, and Captisol material sales. In addition to discovering our own proprietary drugs, we use

an aggressive acquisition strategy to bring in new assets, pipelines, and technologies to aid in generating additional potential new revenue streams. The principal elements of our strategy are set forth below.

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We are assembling a large portfolio of fully funded programs through acquisition and licensing to drive future profitability. We have assembled a portfolio of over 70 fully-funded partner programs that are in all stages of development, from preclinical research to awaiting commercialization. These assets represent the next wave of potential marketed drugs that could generate revenue for us. We assemble this portfolio by either licensing out our own proprietary drug development programs or acquiring existing partnered programs from other companies. For our internal programs, we generally plan to advance drug candidates through early-stage drug development and/or clinical proof-of-concept. We believe partnerships are not only a source of research funding, license fees, future milestone payments and royalties, but they also position our assets with companies that have the expertise to obtain regulatory approval and successfully launch and commercialize these assets. 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.

We sell Captisol material to a broad range of customers. We are the sole provider of a proprietary formulation technology known as Captisol. Captisol is a well validated chemically-modified cyclodextrin that improves the solubility, stability, and pharmicokinetics of many drugs. We receive revenue from the selling of Captisol material to our partners that have either licensed our proprietary Captisol-enabled drugs or have taken a license to use Captisol with their own internal programs.

We discover and develop compounds 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. Our goal is to partner our programs early in the development and regulatory life-cycle.

Our Asset Portfolio

We have a portfolio of over 80 current and future potential revenue generating programs, over 70 of which are fully funded by our partners. We expect to receive royalties from seven marketed products in 2013 and have multiple partnered programs at Phase IIb through NDA submission which represent our future upcoming potential revenue generating programs. While many of these programs have been disclosed publicly, a significant number of our partners and their programs remain undisclosed to protect competitive and proprietary information about these programs.

Select Late-Stage Development or Commercial Programs

We have multiple partnered programs in our portfolio that are either in or nearing the regulatory approval process. These programs represent the next series of potential royalty generating assets in our portfolio.

Promacta (GSK)

GSK's Promacta® (Eltrombopag) is the first oral thrombopoietin (TPO) receptor agonist therapy for the treatment of adult patients with chronic immune (idiopathic) thrombocytopenic purpura, or ITP. In late 2008, the U.S. Food and Drug Administration, or FDA, granted accelerated approval of Promacta for the treatment of thrombocytopenia in patients with chronic ITP, who have had an insufficient response to corticosteroids, immunoglobulins or splenectomy.

In 2010, GSK received approval for Revolade® (eltrombopag/Promacta) from the European Medicines Agency's Committee for Medicinal Products for Human Use (CHMP) and from the Japanese Ministry of Health, Labour and Welfare for the oral treatment of thrombocytopenia (reduced platelet count) in adults with the blood disorder chronic ITP.

In February 2011, the FDA granted GSK full approval status for Promacta in the US following the submission of long- term safety data from post-marketing clinical studies, as well as the completion of other commitments that verify the clinical benefit to patients. Additionally, it was reported in November 2011 that the Risk Evaluation and Mitgation Strategies (REMS) program that Promacta had been operating under in the US was being significantly reduced in scope by the FDA due to data that had been submitted by GSK demonstrating the long term safety of Promacta.

In May 2012, GSK submitted a variation to the existing Marketing Authorization Application to the European Medicines Agency for Promacta/Revolade as a treatment for thrombocytopenia in adult patients with chronic hepatitis C infection to enable the initiation of interferon-based therapy and during interferon-based therapy. That application is currently under review by the European Medicines Agency.

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In November 2012, the FDA approved Promacta for the treatment of thrombocytopenia (low blood platelet counts) in patients with chronic hepatitis C to allow them to initiate and maintain interferon-based therapy. Promacta is the first supportive care treatment available to patients who are ineligible or poor candidates for interferon-based therapy due to their low blood platelet counts. Promacta in combination with interferon-based therapy has been shown to improve a patient's chance of achieving a sustained virologic response (SVR) or viral cure.
Promacta is authorized for use in 92 countries. We are entitled to receive tiered royalties on annual net sales of Promacta. GSK has listed a patent in the FDA's Orange Book for Promacta with an expiration date in 2027.

AGGREGATE NET SALES IN EACH CALENDAR YEAR	ROYALTY RATE	
Less than $100M annual sales	4.7	%
On portion of sales in range of $100M - $200M	6.6	%
On portion of sales in range of $200M - $400M	7.5	%
On portion of sales greater than $400M	9.4	%
On portion of sales greater than $1.5B	9.3	%

* Net royalties due Ligand after payment to Rockefeller

Kyprolis (Onyx, Phase III/NDA, Multiple Myeloma)
Ligand (formerly CyDex) and Onyx Pharmaceuticals (formerly Proteolix) entered into a collaboration in 2005 to develop the Captisol-enabled IV formulation of Carfilzomib for refractory multiple myeloma. In July 2012, Onyx received accelerated approval from the FDA for Kyprolis (Carfilzomib) for injection. We earned a milestone payment of $0.6 million upon FDA approval. Kyprolis is formulated with Ligand's Captisol and is used for the treatment of patients with multiple myeloma who have received at least two prior therapies, including bortezomib and an immunomodulatory agent, and have demonstrated disease progression on or within 60 days of completion of the last therapy. The indication for Kyprolis is based on response rate. Under our agreement with Onyx, we are entitled to receive milestones, tiered royalties ranging between 1.5% and 3% as shown in the table below, and revenue from clinical and commercial Captisol material sales.

AGGREGATE NET SALES IN EACH CALENDAR YEAR	ROYALTY RATE	
Up to, and including, $250 million	1.5	%
$251 million to $500 million	2.0	%
$501 million to $750 million	2.5	%
Above $750 million	3.0	%

Avinza (Pfizer)
We currently receive royalty revenues from Pfizer, Inc., or Pfizer, for sales of the pain therapeutic Avinza®. In February 2007, we completed the sale of our Avinza product line to King Pharmaceuticals (or King). As a result of the sale, we receive royalties on the net sales of Avinza through 2017. Royalties are paid at a rate of 5% on sales up to $200 million and a higher rate above $200 million. In October 2010, Pfizer announced the acquisition of King.
Viviant/Conbriza (Pfizer)
In 2010, our partner Pfizer launched Viviant® (bazedoxifene) in Japan for the treatment of postmenopausal osteoporosis. The drug is also marketed in Spain under the brand name Conbriza® through a co-promotion with Almirall, an international pharmaceutical company based in Spain. Viviant was approved in 2009 by the European Commission (under the trade name Conbriza) for the treatment of postmenopausal osteoporosis in women at increased risk of fracture. Viviant, a selective estrogen receptor modulator (SERM), is a result of the successful research collaboration between Wyeth (now a subsidiary of Pfizer) and us that began in 1994. Pfizer is responsible for the registration and worldwide marketing of bazedoxifene, a synthetic drug specifically designed to reduce the risk of osteoporotic fractures while also protecting uterine tissue. We are entitled to receive tiered royalties on net sales of bazedoxifene. Any such royalties may be subject to reduction or offset for past milestone payments and/or may be subject to other terms and conditions set forth in our agreement with Pfizer.

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Nexterone (Baxter International)

In 2006, Ligand outlicensed Nexterone, an injectable formulation combining amiodarone and Captisol, to Baxter International, or Baxter (formerly Prism Pharmaceuticals, Inc.). Under the terms of the agreement, Baxter is responsible, under an exclusive worldwide license, for all development and commercialization of Nexterone at its sole expense. In 2010, Nexterone was approved by the FDA and launched in the United States in 2011. We are supplying Captisol to Baxter for use in accordance with the terms of the license agreement under a separate supply agreement. Baxter has paid milestone payments and is obligated to pay royalties to us on sales of Nexterone through early 2029.

Bazedoxifene/conjugated estrogens (BZA/CE)(Pfizer, Submitted in the US and EU, Post-Menopausal Symptoms)

In 2010, our partner Pfizer launched Viviant (bazedoxifene) in Japan for the treatment of postmenopausal osteoporosis. Pfizer has combined Viviant with Premarin to create a combination therapy for the treatment of post-menopausal symptoms in women. Pfizer has completed Phase III studies of bazedoxifene and filed an approval submission with the FDA and EMA in 2012. For the year ended December 31, 2012, we received $0.3 million for the filing submissions with the FDA and the EMA. We are entitled to receive tiered royalties on all net sales of bazedoxifene, whether alone or in combination with other products. Any such royalties may be subject to reduction or offset against past milestone payments and/or may be subject to other terms and conditions set forth in our agreement with Pfizer.

Promacta (GSK, Oncology)

GSK is conducting Phase II clinical studies of Promacta for oncology-related thrombocytopenia in patients with solid tumors, Myelodysplastic Syndrome (MDS), or Secondary Acute Myeloid Leukemia (AML) after MDS. Promacta is also in Phase II studies for patients with Aplastic Anemia.

Captisol-enabled Melphalan IV (Spectrum Pharmaceuticals, Pivotal, Stem Cell Transplant Conditioning)

In March 2013, we licensed the full world-wide rights to Captisol-enabled melphalan IV to Spectrum Pharmaceuticals, Inc. The Captisol-enabled, PG-free melphalan program uses a new intravenous formulation of melphalan for the multiple myeloma transplant setting, and has been granted Orphan designation by the FDA. The formulation avoids the use of propylene glycol, which has been reported to cause renal and cardiac side-effects that limit the ability to deliver higher quantities of therapeutic compounds. The use of the Captisol® technology to reformulate melphalan is anticipated to allow for longer administration durations and slower infusion rates, potentially enabling clinicians to safely achieve a higher dose intensity of pre-transplant chemotherapy.

Under the terms of the license agreement, we will receive a $3 million license fee and are eligible to receive more than $50 million in potential milestone payments. We are also eligible to receive significant double-digit royalties on future net sales of the Captisol-enabled melphalan product. This program is currently enrolling patients in a pivotal clinical trial.

Merck Captisol Program, Molecule Undisclosed(Merck, Phase III, Undisclosed Indication)

Ligand and Merck entered into a Captisol supply agreement in June 2011 for an undisclosed Merck program. Merck is currently conducting a pivitol study for this program and we expect Merck to potentially file a 505(b)(2) in 2013 for approval to market this Captisol program. Financial terms of the relationship remain undisclosed, but we expect to generate revenue through the supply of Captisol for this program.

Captisol-enabled Clopidogrel (The Medicines Company, Phase III, Anti-coagulant)

In June 2011, we licensed the full world-wide rights to our Captisol-enabled clopidogrel program to The Medicines Company. Clopidogrel is the active ingredient in Plavix®, the world’s leading anti-platelet medication which is currently only available in an oral formulation. The Captisol-enabled clopidogrel formulation is designed to provide an intravenous option in situations where the administration of oral platelet inhibitors is not feasible or desirable. We received an upfront payment of $1.8 million, $0.9 million of which was remitted to the former CyDex shareholders. We are eligible to receive up to $8 million in milestones, net of amounts owed and royalties on annual worldwide net sales. In addition, we will also supply both the clinical and commercial requirements of Captisol for this program, now known as MDCO-157, and if the intravenous formulation is approved for commercialization, we will be the exclusive supplier of Captisol for the product.

The Medicines Company is planning to initiate a pivotal study for the program in 2013 and is developing the product for global markets.

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RE-021 program (Retrophin, Phase II, FSGS)

In early 2012, we licensed the world-wide rights to RE-021 (formerly known as DARA-a Dual Acting Receptor Antagonist of Angiotension and Endothelin receptors) to Retrophin, Inc., or Retrophin. Retrophin intends to develop RE-021 for orphan indications of severe kidney diseases including Focal Segmental Glomerulosclerosis (FSGS) as well as conduct proof-of-concept studies in resistant hypertension and diabetic nephropathy. Certain patient groups with severely compromised renal function exhibit extreme proteinuria resulting in progression to dialysis and a high mortality rate. RE-021, with its unique dual blockade of angiotensin and endothelin receptors, is expected to provide meaningful clinical benefits in mitigating proteinuria in indications where there are no approved therapies. We received an upfront payment of $1 million, net of amounts owed to third parties.

In late 2012, we received a milestone payment of 620,000 shares of common stock in partner Retrophin, Inc. Former license holders are entitled to receive 15% of the proceeds received upon sale of the securities. We may receive over $75 million in milestones as well as 9% in royalties on potential future worldwide sales by Retrophin.

In early 2013 we received a $1.4 million milestone payment from Retrophin, Inc. We will remit $0.2 million to former license holders under the terms of a previous license agreement for RE-021.

Dinaciclib program (Merck, Phase IIb/III, Refractory CLL)

In October 2012, our licensee, Merck, initiated a Phase IIb/III adaptive clinical trial for Dinaciclib for the treatment of patients with refractory chronic lymphocytic leukemia (CLL). As a result, we received a $2 million milestone payment upon initiation of the clinical study. Under our collaboration and license agreement with Merck, we are entitled to receive future milestones and royalties. CLL is a slow-progressing disease, affecting the blood and bone marrow, as well as the lymph nodes or other organs, and is the most common type of leukemia affecting adults. Dinaciclib is derived from a collaboration initiated in 1998 by Pharmacopeia (now a wholly owned subsidiary of Ligand).

Beta-Secretase Inhibitor (Merck, Phase II/III, Alzheimer's Disease)

The development agreement for the beta-secretase inhibitor program (or BACE) was entered into in 2009 between Ligand (formerly Pharmacopeia) and Merck (formerly Schering-Plough), under a 1998 agreement, for the treatment of Alzheimer's disease. This disease is characterized by plaques of the toxic amyloid-beta protein within the brain. Beta secretase is believed to be a key enzyme in the production of amyloid-beta protein. Amyloid-beta is formed when the larger amyloid precursor protein (APP) is cleaved by two enzymes, beta-secretase and gamma-secretase, which releases the amyloid-beta fragment. A beta-secretase inhibitor is expected to reduce amyloid-beta generation in Alzheimer's disease patients.

In December 2012, Merck initiated a Phase II/III clinical trial for its lead BACE inhibitor product candidate, MK-8931, evaluating its safety and efficacy in patients with mild-to-moderate Alzheimer's disease. Ligand is entitled to royalties on potential future sales by Merck.

Captisol-enabled Carbamazepine-IV (Lundbeck, Phase III, Epilepsy)

The development and commercialization agreement for Captisol-enabled carbamazepine-IV began in 2004 between Lundbeck (formerly Ovation Pharmaceuticals) and us for the use of Captisol in the formulation of CE carbamazepine-IV. Lundbeck is developing CE carbamazepine-IV for the management of acute seizure disorder for hospital or emergency settings. CE carbamazepine-IV is currently being evaluated in a Phase III clinical trial.

Captisol-enabled Delafloxacin (Rib-X, Phase III, Infection)

The development and commercialization agreement for Captisol-enabled delafloxacin began in 2008 between Rib-X Pharmaceuticals and us for the use of Captisol in the formation of delafloxacin. Delafloxacin is a novel hospital-focused fluoroquinolone antibiotic candidate with potency against a variety of quinolone-resistant Gram-positive and Gram-negative bacteria, including quinolone-resistant, methicillin-resistant Staphylococcus aureus (MRSA). In the first half of 2013, Rib-X plans to initiate the first of two planned Phase III clinical trials of delafoxacin for the treatment of acute bacterial skin and skin structure infections (ABSSSI), including infections caused by MRSA.

Fructose-1,6-bisphosphatase Inhibitor (Undisclosed, Phase II)
In September 2012, Ligand entered into an option agreement with an undisclosed partner for the clinical development of an undisclosed novel inhibitor of the fructose-1,6-bisphosphatase (FBPase) enzyme for the treatment of type 2 diabetes. The undisclosed partner paid a $50,000 upfront option fee.

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Fablyn (Unpartnered, Estrogen receptor modulator)

In October 2011, we entered into a license agreement with Chiva Pharmaceuticals, Inc., or Chiva. We granted to Chiva an exclusive worldwide license, with sub-license rights, to our intellectual property rights related to Fablyn, a selective estrogen receptor modulator. In October 2012, we entered into a settlement agreement and mutual release with Chiva, pursuant to which we resolved all disputes, including our primary claim in arbitration relating to payments due under the License Agreement. We also agreed to terminate the Fablyn license agreement and all assets related to Fablyn, including all relevant patents, know-how, properties, rights, interests and other tangible and intangible assets owned or controlled by Chiva were returned to us. Under the settlement agreement, Chiva agreed to pay $0.1 million and we agreed to drop our claim for $1.7 million asserted in arbitration.

Under the Fablyn license agreement, we have been paid and will retain $2.5 million in license fees. Having reclaimed the rights to Fablyn per the settlement agreement, we will seek new potential partners or licensees for Fablyn.

Internal Product Development Programs

As summarized in the table below, we are developing several proprietary products for a variety of indications. These programs represent our future licensing opportunities to expand our partnered asset portfolio.

Program	Disease/Indication	Development Phase
Selective Androgen Receptor Modulator	Various	Phase II-ready
Captisol-enabled Topiramate	Epilepsy	Phase I/II
Glucagon Receptor Antagonist	Diabetes	Pre-IND
HepDirect	Liver Diseases	Preclinical
Oral Human Granulocyte Colony Stimulating Factor	Neutropenia	Preclinical
Oral Erythropoietin	Anemia	Preclinical

Selective Androgen Receptor Modulator (SARM)

Our LGD-4033 is a non-steroidal selective androgen receptor modulator (SARM) that is expected to produce the therapeutic benefits of testosterone with improved safety, tolerability and patient acceptance due to a tissue-selective mechanism of action and an oral route of administration. We have discovered several novel orally active, non-steroidal SARM compounds, including LGD-4033, based on tissue-specific gene expression and other functional, cell-based technologies. In animal models, LGD-4033 demonstrated anabolic activity in muscles, anti-resorptive and anabolic activity in bones and a robust selectivity for muscle and bone versus prostate and sebaceous glands. Phase I single and multiple dose escalation studies of LGD-4033 were conducted in a total of 116 healthy male subjects. The safety, tolerability and preliminary efficacy of LGD-4033 was evaluated in the double-blind, placebo-controlled Phase I multiple ascending dose study. Healthy male subjects were randomized to receive 0.1, 0.3 or 1.0 mg LGD-4033 or placebo once daily over 21 days. Key findings of this study included: LGD-4033 was safe and well tolerated at all doses following daily oral administration for three weeks in young healthy males; no clinically significant dose-related adverse events were reported; no clinically significant changes in liver function tests, PSA, hematocrit or ECG were seen; positive dose-dependent trends in lean muscle mass increase were observed with drug-treated subjects; positive dose-dependent trends in functional exercise and strength measures were consistent with anabolic activity. LGD-4033 is positioned to enter into Phase II development, and potential studies include evaluation of LGD-4033 in conditions such as muscle wasting associated with cancer (cachexia), acute rehabilitation (e.g. hip fracture), and acute illness.

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Captisol-enabled Topiramate IV

We are developing a proprietary Captisol-enabled formulation of topiramate for the treatment of acute epileptic seizures. Topiramate is sold under the trade name Topamax® and is currently only available in an oral formulation. The Captisol-enabled topiramate formulation is designed to provide an intravenous or intramuscular option for hospitalized epilepsy patients where oral topiramate is not an option. In completed Phase I studies, Captisol-enabled topiramate has demonstrated a faster onset of action than the orally administered drug.

Glucagon Receptor Antagonist Program

We are currently developing small molecule glucagon receptor antagonists for the treatment of Type II 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 and contributes to hyperglycemia in these patients. Clinical proof of concept studies with glucagon receptor antagonists in Type 2 diabetic patients were reported at the American Diabetes Association Annual Meeting in 2011 and 2012, supporting the potential benefit of this therapeutic target. Our advanced glucagon antagonist compound blocks glucagon action in human hepatocytes in vitro, reduces blood glucose in animal models of Type 1 and Type 2 diabetes, has demonstrated good oral bioavailability in rodents, and has a safety profile in preclinical studies suitable for further clinical development. We are preparing to file an IND for this program.

HepDirect HCV Inhibitor Program

We are developing novel small molecule inhibitors of the Hepatitis C virus using our HepDirect technology platform. Data from current lead molecules suggest that directing these molecules to the liver using the HepDirect technology could produce fewer side effects and has the potential for an overall superior risk-benefit ratio compared to non HepDirect therapies.

Oral Human Granulocyte Colony Stimulating Factor (GCSF) Program

We have discovered a novel series of small molecules that selectively activate human granulocyte colony stimulating factor (GCSF) receptor function in a manner distinct from GCSF, but similar to the mechanism of small-molecule human thrombopoietin receptor (hTPOR) agonists, such as eltrombopag (Promacta®). The goal of our GCSFR agonist program is to develop a non-peptide, small molecule, oral GCSFR agonist that is a convenient, cost-effective alternative as compared to recombinant human GCSF for the treatment of neutropenia and other related indications. The lead compound, LG7455, activates the GCSF-GCSFR signaling pathway and induces the differentiation of human bone marrow cells into granulocytes. Further optimization of the LG7455 structure series could lead to a first-in-class, once-daily, oral medication for the treatment of congenital, chronic or chemotherapy-induced neutropenia.

Oral EPO Program

Erythropoietin (EPO) acts on its receptor to stimulate the differentiation of bone marrow hematopoietic cells to form red blood cells. Various recombinant human EPO derivatives are marketed as erythropoiesis-stimulating agents (ESAs) for the treatment of anemia due to renal failure or cancer chemotherapy. We have discovered a series of orally-available, small molecule partial agonists of the EPO receptor with unique mechanism of action that should provide additional benefit in the treatment of anemia with improved safety, tolerability, and patient acceptance due to the convenience of oral administration and the lack of excessive erythropoietic stimulation. The lead compound, LG5640, has demonstrated high potency and oral bioavailability in the mouse, rat and monkey.

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Other Internal Programs Awaiting Further Development Funding, Either Through Ligand or a Partner

- Aplindore (Phase II, Restless Leg/Parkinson's)
- Captisol-enabled Nasal Budesonide (Phase I, Allergic Rhinitis)
- Thyroid Receptor-beta Agonist (Preclinical, Dyslipidemia)
- Histamine H3 Receptor Antagonist (Preclinical, Cognitive Disorders)
- Glucokinase Activator (Preclinical, Diabetes)
- DGAT Inhibitor (Preclinical, Diabetes)
- CCR1 Inhibitor (Preclinical, Oncology)