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, 2000
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. 0-20720

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

Delaware
(State or other jurisdiciton of incorporation or organization)

77-0160744
(I. R. S. Employer Identification No.)

10275 Science Center Drive San Diego, CA
(Address of Principal Executive Offices)

92121-1117
(Zip Code)

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

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

Securities registered pursuant to Section 12(g) of the Act:
Common Stock, $.001 par value

Preferred Share Purchase Rights
(Title of Class)

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

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

The aggregate market value of the Registrant's voting stock held by non-affiliates as of February 28, 2001 was $578,931,137. For purposes of this calculation, shares of Common Stock held by directors, officers and 5% stockholders known to the Registrant have been deemed to be owned by affiliates which should not be construed to indicate that any such person possesses the power, direct or indirect, to direct or cause the direction of the management or policies of the Registrant or that such person is controlled by or under common control with the Registrant.

As of February 28, 2001 the registrant had 58,791,593 shares of Common Stock outstanding.

DOCUMENTS INCORPORATED BY REFERENCE

Portions of the Registrant's Proxy Statement to be filed not later than 120 days after December 31, 2000, in connection with the Registrant's 2001 Annual Meeting of Stockholders, referred to herein as the "Proxy Statement," are incorporated by reference into Part III of this Form 10-K. Certain exhibits filed with the Registrant's prior registration statements and period reports under the Securities Exchange Act of 1934 are incorporated herein by reference into Part IV of this Report.

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Part I

GLOSSARY

PRODUCTS AND INDICATIONS

ONTAK® (denileukin diftitox)	Approved in February 1999 in the U.S. for the treatment of patients with persistent or recurrent cutaneous T-cell lymphoma whose malignant cells express the CD25 component of the Interleukin-2 receptor.
Targretin® (bexarotene) capsules	Approved in December 1999 for sale in the U.S. for the treatment of cutaneous manifestations of cutaneous T-cell lymphoma in patients who are refractory to at least one prior systemic therapy.
Targretin® (bexarotene) gel 1%	Approved in June 2000 for sale in the U.S. for the topical treatment of cutaneous lesions in patients with cutaneous T-cell lymphoma (Stage 1A and 1B) who have refractory or persistent disease after other therapies or who have not tolerated other therapies.
Panretin® gel (alitretinoin) 0.1%	Approved in February 1999 for sale in the U.S. and in October 2000 for sale in Europe for the topical treatment of cutaneous lesions of patients with AIDS-related Kaposi's sarcoma.

CTCL	Cutaneous T-cell lymphoma
HIV	Human immunodeficiency virus
HRT	Hormone replacement therapy
KS	Kaposi's sarcoma
NHL	Non-Hodgkin's lymphoma
NSCLC	Non-small cell lung cancer

SCIENTIFIC TERMS

AR	Androgen Receptor
ER	Estrogen Receptor
GR	Glucocorticoid Receptor
IR	Intracellular Receptor
JAK	Janus Kinase family of tyrosine protein kinases
MR	Mineralocorticoid Receptor
PPAR	Peroxisome Proliferation Activated Receptor
PR	Progesterone Receptor
RAR	Retinoic Acid Receptor
RR	Retinoid Responsive Intracellular Receptor
RXR	Retinoid X Receptor
SARM	Selective Androgen Receptor Modulator
SERM	Selective Estrogen Receptor Modulator
STAT	Signal Transducer and Activator of Transcription

REGULATORY TERMS

CPMP	Committee for Proprietary Medicinal Products (Europe)
EC	European Commission
EMEA	European Agency for the Evaluation of Medicinal Products
FDA	United States Food and Drug Administration
IND	Investigational New Drug Application (United States)
MA	Marketing Authorization (Europe)
MAA	Marketing Authorization Application (Europe)
NDA	New Drug Application (United States)

PART I

Item 1. Business

The discussion of our business contained in this annual report on form 10-K may contain predictions, estimates and other forward-looking statements that involve a number of risks and uncertainties, including those discussed below at “Risks and Uncertainties.” While this outlook represents management’s current judgment on the future direction of the business, such risks and uncertainties could cause actual results to differ materially from any future performance suggested below. 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.

Our trademarks, trade names and service marks referenced in this annual report include ONTAK®, Panretin® and Targretin®. Each other trademark, trade name or service mark appearing in this annual report belongs to its holder.

References to Ligand Pharmaceuticals Incorporated ("Ligand", the "Company", "we" or "our") include our wholly owned subsidiaries - Glycomed Incorporated; Ligand Pharmaceuticals (Canada) Incorporated; Ligand Pharmaceuticals International, Inc.; and Seragen, Inc. ("Seragen").

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

Overview

Our goal is to build a profitable pharmaceutical company which discovers, develops and markets new drugs that address critical unmet medical needs of patients in the areas of cancer, men’s and women’s health and skin diseases, as well as osteoporosis, metabolic, cardiovascular and inflammatory diseases. We strive to develop drugs that are more effective and/or safer than existing therapies and that are more convenient (taken orally or topically administered) and cost effective. We plan to build a profitable pharmaceutical company by generating income from specialty pharmaceutical products we develop and market and from research, milestone and royalty revenues resulting from collaborations where large pharmaceutical partners develop and market products in large markets beyond our strategic focus or resources.

We currently market four oncology products in the United States, Panretin® gel, ONTAK® and Targretin® capsules, approved by the FDA in 1999 and Targretin® gel, approved by the FDA in 2000. In Europe, the EC granted an MA for Panretin® gel in October 2000 and the CPMP recommended the grant of an MA for Targretin® capsules in November 2000. We also continue efforts to acquire or in-license products, such as ONTAK® (acquired in the 1998 acquisition of Seragen) and Morphelan™ (licensed from Elan Corporation, plc), which have near-term prospects of FDA approval and which can be marketed by our specialty sales force. We are developing additional products through our internal development programs and currently have various products in clinical development, including marketed products for larger market indications such as NSCLC, B-cell NHL, psoriasis and rheumatoid arthritis.

We have research and development collaborations with numerous global pharmaceutical companies, including Abbott Laboratories, Allergan, American Home Products, Bristol-Myers Squibb, Eli Lilly, GlaxoSmithKline, Organon (AKZO-Nobel) and Pfizer. During 2000, our corporate partners had six Ligand compounds in human development, including lasofoxifene being developed by Pfizer for osteoporosis that entered Phase III clinical trials, three compounds on an IND track, and numerous compounds in research and pre-clinical stages. These corporate partner products are being studied for the treatment of large market indications such as osteoporosis, diabetes, contraception and cardiovascular disease.

Internal and collaborative research and development programs utilize our proprietary science technology based on our leadership position in gene transcription technology. Our proprietary technologies involve two natural mechanisms that regulate gene activity: (1) non-peptide hormone activated IRs and (2) cytokine and growth factor activated STATs. Panretin® gel, Targretin® capsules, Targretin® gel and all of our corporate partner products currently on human development track are IR modulators, discovered using our IR technology.

In late 1998, we assembled a specialty oncology and HIV-center sales and marketing team to market in the U.S. products developed, acquired or licensed by us. In late 1999, we expanded our U.S. sales force from approximately 20 to approximately 40 sales representatives to support the launch of Targretin® capsules and Targretin® gel and increase market penetration of ONTAK® and Panretin® gel. In 2001, we expanded our sales force to approximately 50 sales representatives, including approximately 20 full-time contract sales representatives that will focus on the dermatology market. Internationally, through marketing and distribution agreements with Elan, Ferrer International and Alfa Wassermann, we

have established marketing and distribution capabilities in Europe including the major markets in the United Kingdom, Germany, France, Italy, Spain, Greece, Portugal, and Central and South America.

Business Strategy

Our goal is to become a profitable pharmaceutical research, development and marketing company that generates significant cash flow. Building primarily on our proprietary IR and STATs technologies, our strategy is to generate cash flow primarily from (1) the sale in the U.S., Europe and Latin America of specialty pharmaceutical products we develop, acquire or in-license and (2) research, milestone and royalty revenues from the development and sale of products our collaborative partners develop and market.

Building a Specialty Pharmaceutical Franchise in the U.S., Europe and Latin America.

Our strategy with respect to specialty pharmaceutical products is to develop a product pipeline based on our IR and STATs technologies and acquired and in-licensed products and to market these products initially with a specialized sales force in the U.S. and through marketing partners in selected international markets. Focusing initially on niche pharmaceutical and dermatology indications with the possibility of expedited regulatory approval has allowed us to bring products to market quickly. This strategy has allowed us to spread the cost of our sales and marketing infrastructure among multiple products. Our goal is to expand the markets for our products through additional indication approvals and approvals in international markets. To further leverage our sales force, we intend to selectively acquire or license-in complementary technology and/or products in advanced stages of development.

Building a Collaborative-Based Business in Large Product Markets

Our strategy in our collaborative research and development business is to share the risks and benefits of discovering and developing drugs to treat diseases that are beyond our strategic focus or resources. These diseases typically affect large populations often treated by primary care physicians, and drugs to treat these diseases may be more costly to develop and/or to market effectively with a small specialty sales force. Despite these factors, drugs approved for these indications may have large market potential – often in excess of $1 billion in global sales.

We currently have nine collaborations with major pharmaceutical companies focusing on a broad range of disease targets.

Corporate Collaborator	Initiation of Collaboration	Focus
Pfizer Inc.	May 1991	Osteoporosis, breast cancer prevention
Allergan, Inc.	June 1992	Skin disorders
GlaxoSmithKline (Glaxo Wellcome plc)	September 1992	Cardiovascular diseases
Abbott Laboratories	July 1994	Inflammatory diseases
Wyeth-Ayerst, the pharmaceutical division of American Home Products	September 1994	Women's and men's health, oncology
GlaxoSmithKline (SmithKline Beecham)	February 1995	Blood disorders
Eli Lilly	November 1997	Type II diabetes, metabolic and cardiovascular diseases
Organon	February 2000	Women's health
Bristol-Myers Squibb	May 2000	Cardiovascular diseases

Our collaborative programs focus on discovering drugs for cardiovascular, inflammatory, metabolic and other diseases, as well as broad applications for women’s and men’s health. We believe that our collaborators have the resources, including clinical and regulatory experience, manufacturing capabilities and marketing infrastructure, needed to develop and commercialize drugs for these large markets. The arrangements generally provide for collaborative discovery programs funded largely by the corporate partners aimed at discovering new therapies for diseases treated by primary care physicians.

In general, drugs resulting from these collaborations will be developed, manufactured and marketed by the corporate partners. Our collaborative agreements provide for us to receive: (1) research revenue during the drug discovery stage; (2) milestone revenue for compounds successfully moving through clinical development and regulatory submission and approval; and (3) royalty revenue from the sale of approved drugs developed through collaborative efforts.

Ligand Marketed Products

U.S. Specialty Pharmaceutical Franchise. We currently market four pharmaceutical products in the U.S.

Marketed Product	Approved Indication	European Status	Indications in Development
ONTAK®	CTCL	Preparing for submission	B-cell NHL, psoriasis, rheumatoid arthritis
Targretin® capsules	CTCL	CPMP approval recommendation	NSCLC, psoriasis, renal cell cancer
Targretin® gel	CTCL	Preparing for submission	Eczema
Panretin® gel	KS	MA issued	- --

CTCL Market. CTCL is a type of NHL that appears initially in the skin, but over time may involve other organs. CTCL is a cancer of T-lymphocytes, white blood cells that play a central role in the body's immune system. The disease can be extremely disfiguring and debilitating and median survival for late-stage patients is less than three years. The prognosis for CTCL is based in part on the stage of the disease when diagnosed. CTCL is most commonly a slowly progressing cancer, and many patients live with the complications of CTCL for 10 or more years after diagnosis. However, some patients have a much more aggressive form of this disease. CTCL affects an estimated 16,000 people in the U.S. and 12,000 to 14,000 in Europe. With ONTAK®, Targretin® capsules, and Targretin® gel currently approved in the U.S. for the treatment of CTCL, our current strategy is to have multiple products available for treating this disease.

ONTAK®. ONTAK® was approved by the FDA and launched in the U.S. in February 1999 as our first product for the treatment of patients with CTCL and the first treatment to be approved for CTCL in nearly 10 years. ONTAK® is currently in three Phase II clinical trials for the treatment of patients with B-cell NHL. Clinical trials using ONTAK® for the treatment of patients with psoriasis and rheumatoid arthritis have also been conducted with further trials being considered. These indications provide significantly larger market opportunities than CTCL. An MAA filing in Europe for CTCL is targeted for the second half of 2001.

Targretin® capsules. We launched U.S. sales and marketing of Targretin® capsules in January 2000 following receipt of FDA approval in December 1999. Targretin® capsules offer the convenience of a daily oral dose administered by the patient at home. We are developing Targretin® capsules in a variety of larger market opportunities, including NSCLC, moderate to severe plaque psoriasis and renal cell cancer. We are also pursuing approval of Targretin® capsules in Europe for the treatment of patients with CTCL, where the CPMP in November 2000 recommended the grant of an MA.

Targretin® gel. We launched U.S. sales and marketing of Targretin® gel in September 2000 following receipt of FDA approval in June 2000. Targretin® gel offers patients with refractory early stage CTCL a novel, non-invasive, self-administered treatment topically applied only to the affected areas of the skin. Targretin® gel is currently in clinical development for hand eczema. An MAA filing in Europe for CTCL is targeted for the first half of 2001.

Panretin® gel. Panretin gel was approved by the FDA and launched in February 1999 as the first FDA approved patient-applied topical treatment for AIDS-related KS. Panretin gel represents a new non-invasive option to the traditional management of this disease. Most approved therapies require the time and expense of periodic visits to a healthcare facility and administration of the treatment by a doctor or nurse. AIDS-related KS adversely affects the quality of life of thousands of people in the U.S. and Europe. Panretin® gel was approved in Europe for the treatment of patients with KS in October 2000, with an expected launch in the second half of 2001.

Product Development Process

There are three phases in product development — the research phase, the preclinical phase and the clinical trials phase. See "Government Regulation" for a more complete description of the regulatory process involved in development of drugs. Activities during the research phase include research related to specific IR and STATs targets and the identification of lead compounds. Lead compounds are chemicals that have been identified that meet pre-selected criteria in cell culture models for activity and potency against IR or STATs targets. More extensive evaluation is then undertaken to determine if the compound should be selected to enter into preclinical development. Once a lead compound is selected, chemical modification of the compound is then undertaken to create the best drug candidate.

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

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

Ligand Product Development Programs

We are developing several proprietary products for which we have worldwide rights for a variety of cancers and skin diseases, as summarized in the table below, which is not intended to be a comprehensive list of our internal research and development programs. Many of the indications being pursued may present larger market opportunities for our currently marketed products. Our clinical development programs are primarily based on products discovered through our IR technology, with the exception of ONTAK®, which was developed using Seragen's fusion protein technology, and Morphelan™, which was developed by Elan. Five of the products in our proprietary product development programs are retinoids, discovered and developed using our proprietary IR technology. Our research is based on both our IR and STAT technologies. See "Technology" for a discussion of our IR and STAT technologies and retinoids.

Program	Disease/Indication	Development Phase
ONTAK®	CTCL	Marketed in U.S.
	B-cell NHL	Phase II
	Rheumatoid arthritis	Phase II
	Psoriasis (severe)	Phase II
Targretin® capsules	CTCL	Marketed in U.S.
	NSCLC	Phase III
	Advanced breast cancer	Phase II
	Psoriasis (moderate to severe)	Phase II
	Renal cell cancer	Phase II
Targretin® gel	CTCL	Marketed in U.S.
	Atopic dermatitis (eczema)	Planned Phase II
Panretin® gel	KS	Marketed in U.S.
Panretin® capsules	KS	Phase II
	Bronchial metaplasia	Phase II
LGD1550 capsules (RAR agonist)	Acne	Planned Phase I/II
	Psoriasis	Planned Phase I/II
	Advanced cancers	Phase I/II
Morphelan™	Pain management (moderate to severe)	NDA submitted
LGD2226 (Androgen agonist)	Male hypogonadism, HRT, female sexual dysfunction, osteoporosis	IND track
LGD1331 (Androgen antagonist)	Prostate cancer, hirsutism, acne, androgenetic alopecia	Pre-clinical
Glucocorticoid agonist	Inflammation, cancer	Pre-clinical

ONTAK® Development Programs

ONTAK® is the first of a new class of targeted cytotoxic biologic agents called fusion proteins that was acquired in the acquisition of Seragen and is marketed in the U.S. for patients with CTCL. CTCL affects approximately 16,000 people in the U.S. In addition to ongoing CTCL trials, we are or will be conducting clinical trials with ONTAK® in patients with B-cell NHL, rheumatoid arthritis, and psoriasis, indications that represent significantly larger market opportunities than CTCL.

In early 1999, ONTAK® entered Phase II trials for the treatment of patients with NHL. One study is assessing ONTAK® in patients with certain types of low-grade B-cell NHL who have previously been treated with at least one systemic anti-cancer treatment. A second multi-center trial for ONTAK® is being conducted in patients with low-grade B-cell NHL who have been previously treated with at least one chemotherapy regimen and at least one monoclonal antibody therapy. A third trial allows certain patients to enter with low to intermediate grade B-cell NHL. Preliminary results of these trials are expected in the second half of 2001. NHL affects approximately 300,000 people in the U.S. with an estimated target market of approximately 54,000 patients who have failed chemotherapy or monoclonal antibody therapy.

Clinical trials with ONTAK® have demonstrated benefits in patients with long-standing, previously treated severe psoriasis. Based on these positive preliminary results, additional investigations are being considered. Moderate to severe psoriasis affects an estimated 1.1 million people in the U.S. Phase II studies are being planned for the treatment of patients with rheumatoid arthritis. Estimated by the Arthritis Foundation to affect 2.1 million Americans, rheumatoid arthritis is a chronic disease that causes pain, stiffness and swelling in the joints, as well as inflammation in internal organs.

Targretin® capsules Development Programs

Targretin® capsules are marketed in the U.S. for patients with refractory CTCL. Ligand is also investigating the use of Targretin® capsules in several cancer and skin disease markets which represent significantly larger market opportunities in comparison to the CTCL market.

In August 2000, we reported that Phase I/II clinical results demonstrated that Targretin® capsules, in conjunction with chemotherapy, may be an effective treatment for patients with NSCLC and renal cell cancer. The American Cancer Society estimates that 164,100 Americans were diagnosed with lung cancer in 2000; of those approximately 80% were diagnosed with NSCLC. These results add to the phase II/III results and to a growing body of evidence that suggests Targretin® therapy may delay disease progression and extend survival of patients with some forms of solid tumors. This body of evidence is now large enough to begin large-scale Phase III clinical studies to conclusively demonstrate Targretin® capsules' benefit in the treatment of patients with NSCLC. We anticipate launching Phase III trials in both the first and second half of 2001. As this is a large program that is expected to involve well over 1,000 patients, our primary focus for Targretin® capsules during 2001 and 2002 will be NSCLC. We will, however, continue to explore in Phase II trials the potential of Targretin® capsules in combination regimens for the treatment of patients in solid tumor indications as well as psoriasis.

The Phase II trial with Targretin® capsules for the treatment of patients with advanced breast cancer has been fully accrued and nearly all patients have completed treatment. Although a number of patients appeared to benefit from treatment with Targretin® capsules, the overall observed objective anti-tumor response did not meet the protocol-defined target for activity. While we continue to assess whether Phase II combination studies are warranted, it is clear that further laboratory experiments are needed to understand the mechanism of action of Targretin® in breast cancer. A study of changes in various tissue biomarkers that are potentially associated with Targretin® capsules in patients with high risk of developing breast cancer is scheduled to begin soon under the sponsorship of the National Cancer Institute to further evaluate the mechanism.

Preliminary results of the Phase II trial with Targretin® capsules for the treatment of patients with moderate to severe psoriasis showed that Targretin® capsules have activity in psoriasis as a monotherapy at daily doses substantially lower than approved oncology doses. This activity is sufficiently interesting to stimulate further dose-ranging trials in patients with psoriasis and evaluation in the context of a combination drug regiment or as part of multimodality therapy, such as phototherapies.

Targretin® gel Development Program

Targretin® gel is marketed in the U.S. for patients with refractory CTCL. In addition, we are planning a Phase II trial with Targretin® gel for the treatment of patients with eczema. An MAA filing in Europe for Targretin® gel in CTCL is targeted for 2001.

Panretin® capsules Development Programs

Panretin® capsules have demonstrated clinical promise for the systemic treatment of cutaneous AIDS-related KS, other cancers and skin disorders. We have reported favorable results in two Phase II trials with Panretin(R)capsules in patients with KS and are currently evaluating whether to proceed with development for this indication. Phase II trials with Panretin(R)capsules are ongoing in bronchial metaplasia.

LGD1550 capsules Development Programs

LGD1550 is a potent RAR agonist that strongly inhibits growth in vitro of several human cancer cell lines. Phase I/ II clinical trials in advanced cancer have shown that LGD1550 capsules were well tolerated. Investigators observed dose-limiting skin toxicities, diarrhea and abdominal cramps. Other dose-limiting toxicities, such as headache and lipid abnormalities, frequently observed with other retinoids, have not been observed with LGD1550. Unlike all-trans retinoic acid, a retinoid approved for the treatment of acute promyelocytic leukemia, LGD1550 does not appear to induce its own metabolism over the dose range tested since blood levels are maintained with continued therapy. Phase I/II studies with LGD1550 for the treatment of patients with acne and psoriasis are being considered for development.

Morphelan™ Development Program

As part of a broader strategic alliance formed in 1998 with Elan, Elan licensed to Ligand exclusive rights to market Elan's proprietary product Morphelan™ in the U.S. and Canada for pain management in cancer and HIV patients. Morphelan™, a once-daily, oral capsule form of morphine, may provide sustained pain management as compared to current therapies requiring frequent doses. An NDA was submitted in the U.S. by Elan in May 2000. We expect FDA review of the NDA to be completed in the second quarter of 2001. If approved, we will market and sell Morphelan™ in the U.S. and Canada through our existing specialty sales force. Please see note 5 of notes to consolidated financial statements for further details on our strategic alliance with Elan.

SARMs Programs

We are pioneering the development of tissue SARMs, a novel class of non-steroidal, orally active molecules that selectively modulate the activity of the AR in different tissues, providing a wide range of opportunities for the treatment of many diseases and disorders in both men and women. Tissue-selective AR agonists or antagonists may provide utility in male HRT and the treatment of patients with skin disorders, osteoporosis, sexual dysfunction, prostate cancer, benign prostatic hyperplasia and other diseases. The use of androgen antagonists has shown efficacy in the treatment of prostate cancer, with three androgen antagonists currently approved by the FDA for use in the treatment of prostate cancer. However, we believe that there is a substantial medical need for improved androgen modulators for use in the treatment of prostate cancer due to significant side effects seen with currently available drugs that may be eliminated or reduced by SARMs.

Our SARMs programs have been our largest internally funded programs over the past five years. We have assembled an extensive SARM compound library and one of the largest and most experienced AR drug discovery teams in the pharmaceutical industry. We intend to pursue the specialty applications emerging from SARMs internally, but may seek collaborations with major pharmaceutical companies to exploit broader clinical applications.

We have two first generation SARMs in preclinical development: (1) LGD1331, an androgen antagonist for acne, prostate cancer, hirsutism, and androgenetic alopecia, and (2) LGD2226, an androgen agonist for male hypogonadism, female sexual dysfunction, HRT, and osteoporosis. Preclinical studies of LGD1331 indicate that it may have utility for treating acne and hirsutism disorders that affect a significant number of women. In vivo studies of LGD1331 have revealed favorable characteristics, including indirect evidence of diminished effects on the central nervous system, compared with currently marketed drugs of this type for the treatment of these conditions. In March 2000, we announced that LGD2226 had been moved onto the human development track. We believe this candidate represents the first SARM for the treatment of patients with major androgen related diseases and disorders, such as osteoporosis, male hormone replacement, and male and female sexual dysfunction.

STATs Research Programs

In contrast to our IR programs, our STATs programs focus on cytokines and growth factors whose receptors are found on the surface of the cell. STATs play a modulating role in the biology of cytokines and growth factors. Many diseases, such as inflammatory conditions, may result from excessive cytokine activity, and others may result from insufficient cytokine activity. See “Technology — STATs Technology” for a more complete discussion of our STATs technology. In our STATs programs, we seek to develop drug candidates that mimic the activity of thrombopoietin for use in a variety of conditions including cancer and disorders of blood cell formation.

Collaborative Research and Development Programs

We are pursuing several major collaborative drug discovery programs to further develop the research and development of compounds based on our IR and STATs technologies. These collaborations focus on several large market indications as shown in the table below.

Indication	**U.S. Prevalence**
Breast Cancer	2 million
Cardiovascular Disease	58 million
Contraception	35 million
Hormone replacement therapy	46 million
Obesity	48 million
Osteoporosis	12 million
Type II diabetes	15 million

During 2000, six of our collaborative product candidates were in human development - lasofoxifene, TSE424, ERA923, GW544, GW516, AGN4310, and three were on an IND track. Please see note 9 of notes to consolidated financial statements for a description of the financial terms of our key ongoing collaboration agreements. The table below summarizes our collaborative research and development programs, but is not intended to be a comprehensive list of these programs.

Program	Disease/Indication	Development Phase	Marketing Rights
SEX HORMONE MODULATORS			
SERMs			
• Lasofoxifene	Osteoporosis, breast cancer prevention Osteoporosis, HRT	Phase III	Pfizer
• TSE424	Breast cancer	Phase II/III	AHP
• ERA923		Phase II	AHP
PR modulators			
• PR agonists	HRT, contraception, reproductive disorders	Research	Organon
• WAY248 (PR antagonist)	Contraception, reproductive disorders	IND track	AHP
• WAY166989 (PR agonist)	HRT, contraception	Pre-clinical	AHP
MR modulators	Congestive heart failure, hypertension	Research	Bristol-Myers Squibb
METABOLIC/CARDIOVASCULAR DISEASES			
PPAR modulators			
• GW544	Cardiovascular disease, dyslipidemia	Phase I/II	GlaxoSmithKline
• GW516	Cardiovascular disease, dyslipidemia	Phase I	GlaxoSmithKline
• LY510929	Type II diabetes, metabolic diseases, dyslipidemia	IND track	Lilly
• LY519818	Type II diabetes, metabolic diseases	IND track	Lilly
• LYXXX	Dyslipidemia	Pre-clinical	Lilly
RXR modulators	Type II diabetes, metabolic diseases	Pre-clinical	Lilly
HNF-4	Type II diabetes, metabolic diseases	Research	Lilly
INFLAMMATORY DISEASE			
Glucorcorticoid agonists	Inflammation	Pre-clinical	Abbott
STATs/BLOOD DISORDERS			
Hematopoietic growth factors	Thrombocytopenia	Pre-clinical	GlaxoSmithKline
DERMATOLOGY			
AGN4310	Mucocutaneous toxicity	Phase II	Allergan

Sex Hormone Modulators Collaborative Programs

The primary objective of our sex hormone modulators collaborative programs is to develop drugs for hormonally responsive cancers of men and women, hormone replacement therapies, the treatment and prevention of diseases affecting women's health, as well as hormonal disorders prevalent in men. Our programs, both collaborative and internal, in the sex hormone modulators area target development of tissue-selective modulators of the PR, the ER and the AR. Through our collaborations with Pfizer and American Home Products, three SERMs are in development in osteoporosis, breast cancer and HRT. In addition, we seek to enter into collaborations with large global pharmaceutical companies for the development of SARMs in large markets beyond our strategic focus or resources.

Pfizer Collaboration. In 1991, we entered into a research and development collaboration with Pfizer to develop better alternative therapies for osteoporosis. In November 1993, we jointly announced the successful completion of the research phase of our alliance with the identification of a development candidate and backups for the prevention and treatment of osteoporosis. In preclinical studies, the candidates from the program mimic the beneficial effects of estrogen on bone and have an impact on blood serum lipids often associated with cardiac benefits without increasing uterine or breast tissue proliferation.

We have milestone and royalty rights to lasofoxifene which is under development by Pfizer for osteoporosis and breast cancer prevention. Lasofoxifene is a second generation estrogen partial agonist discovered through our collaborative relationship with Pfizer to which Pfizer has retained marketing rights. Lasofoxifene has been shown to reduce bone loss and decrease low-density lipoprotein levels ("LDL", or "bad" cholesterol). In September 2000, Pfizer announced that it initiated Phase III studies of lasofoxifene for the treatment and prevention of osteoporosis in post menopausal women.

American Home Products Collaboration. In 1994, we entered into a research and development collaboration with Wyeth-Ayerst Laboratories, the pharmaceutical division of American Home Products ("AHP"), to discover and develop drugs that interact with ERs or PRs for use in HRT, anti-cancer therapy, gynecological diseases, and central nervous system disorders associated with menopause and fertility control. We granted AHP exclusive worldwide rights to all products discovered in the collaboration that are agonists or antagonists to the PR and ER for application in the fields of women's health and cancer therapy.

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

AHP has ongoing clinical studies with two SERMs from the collaboration. AHP is developing TSE424 for the treatment of post-menopausal osteoporosis, with Phase III trials expected to be initiated in the second or third quarter of 2001. ERA923 is being developed for the treatment of breast cancer. AHP filed an IND for ERA923 for the treatment of women with breast cancer in December 1998 and Phase II trials are ongoing. AHP has also elected to proceed with IND track development of WAY248, a non-steroidal PR antagonist that may be useful in the creation of the first estrogen-free oral contraceptive.

Organon Collaboration. In February 2000, we entered into a research and development collaboration with Organon to focus on small molecule compounds with potential effects for the treatment and prevention of gynecological diseases mediated through the PR. The objective of the collaboration is the discovery of new non-steroidal compounds that are tissue-selective in nature and may have fewer side effects. Such compounds may provide utility in hormone replacement therapy, oral contraception, reproductive diseases, and other hormone-related disorders. The initial research phase concludes in February 2002. Organon may extend the research term for up to two additional years.

Bristol-Myers Squibb Collaboration. In May 2000, we entered into a research and development collaboration with Bristol-Myers Squibb Company to focus on the discovery, design and development of orally active compounds that selectively modulate the MR. This receptor plays a critical role in many illnesses, particularly cardiovascular diseases such as congestive heart failure and hypertension. The initial research term concludes in May 2002. Bristol-Myers Squibb may extend the research term for up to two additional years.

Metabolic and Cardiovascular Disease Collaborative Programs

We are exploring the role of certain IRs, including the peroxisome proliferation activated receptors, in cardiovascular and metabolic diseases. PPARs, a subfamily of orphan IRs, have been implicated in processes that regulate plasma levels of very low density lipoproteins and triglycerides. See "Technology-- Intracellular Receptor Technology" for a discussion of PPARs and orphan IRs. Data implicate PPARs in the mechanism of action of lipid lowering drugs such as Lopid(R). There are three subtypes of the PPAR subfamily with defined novel aspects of their action-- alpha, beta and gamma. The subtype PPAR alpha appears to regulate the metabolism of certain lipids and is useful in treating hyperlipidemia. PPAR gamma plays a role in fat cell differentiation and cellular responses to insulin. Modulators of PPAR gamma activity (e.g., the glitazone class of insulin sensitizers) have utility in the management of type II diabetes. PPARs are believed to function in cells in partnership with RXRs. In addition to compounds that act directly on PPARs and that may have utility in various cardiovascular and metabolic diseases, certain retinoids are able to activate this RXR:PPAR complex (e.g., Targretin(R)capsules) and they may also have utility in these disorders. We have two collaborative partners, GlaxoSmithKline and Lilly, in the areas of cardiovascular and metabolic diseases, with two compounds in clinical development and two on an IND track.

GlaxoSmithKline Collaboration. In 1992, we entered into a research and development collaboration with Glaxo Wellcome plc (now GlaxoSmithKline) to discover and develop drugs for the prevention or treatment of atherosclerosis and other disorders affecting the cardiovascular system. The collaboration focuses on discovering drugs which produce beneficial alterations in lipid and lipoprotein metabolism in three project areas: (1) regulation of cholesterol biosynthesis and expression of a receptor which removes cholesterol from the blood stream, (2) the IRs influencing circulating HDL levels, and (3) PPARs, the subfamily of IRs activated by lipid lowering drugs, such as Lopid® and Atromid-S. The research phase was successfully completed in 1997 with the identification of a novel lead structure that activates selected PPAR subfamily members and the identification of a different lead compound that shows activity in preclinical models for lowering LDL cholesterol by up-regulating LDL receptor gene expression in liver cells. We retained the right to develop and commercialize products arising from the collaboration in markets not exploited by Glaxo or where Glaxo is not developing a product for the same indication.

In 1999, two compounds were advanced to exploratory development: (1) GW544, a PPAR agonist in Phase I/II trials for cardiovascular disease and dyslipidemia; and (2) GW516, a second candidate that is in clinical development for cardiovascular disease and dyslipidemia. Cardiovascular disease affects more than 58 million Americans and is estimated to be responsible for 30% of all deaths worldwide each year.

Eli Lilly Collaboration. In November 1997, we entered into a research and development collaboration with Eli Lilly ("Lilly") for the discovery and development of products based upon our IR technology with broad applications in the fields of metabolic diseases, including diabetes, obesity, dyslipidemia, insulin resistance and cardiovascular diseases associated with insulin resistance and obesity. Under the collaboration, Lilly received: (1) worldwide, exclusive rights to our compounds and technology associated with the RXR receptor in the field; (2) rights to use our technology to develop an RXR compound in combination with a SERM in cancer; (3) worldwide, exclusive rights in certain areas to our PPAR technology, along with rights to use PPAR research technology with the RXR technology; and (4) exclusive rights to our HNF-4 receptor and the obesity gene promoter technology. Lilly has the right to terminate the development of compounds under the agreements. We would receive rights to certain of such compounds in return for a royalty to Lilly, the rate of which is dependent on the stage at which the development is terminated. The initial research term concludes in November 2002. Lilly may extend the term for up to three additional years.

Under the Lilly collaboration, we retained or received: (1) exclusive rights to independently research, develop and commercialize Targretin® and other RXR compounds in the fields of cancer and dermatology; (2) an option to obtain selected rights to one of Lilly's specialty pharmaceutical products; and (3) rights to receive milestones, royalties and options to obtain certain co-development and co-promotion rights for the Lilly-selected RXR compound in combination with a SERM.

Our rights under the initial agreements have changed. In connection with the acquisition of Seragen in 1998, we obtained from Lilly its rights to ONTAK® in satisfaction of our option to obtain selected rights to one of Lilly's specialty pharmaceutical products. In 1999, we agreed to focus our collaborative efforts on the RXR modulator second-generation program, which has compounds with improved therapeutic indices relative to the three first-generation compounds, and on co-agonists of the PPAR receptor program. In early 1999, Lilly opted not to proceed with the development of certain first-generation compounds, including Targretin®, in the RXR program for diabetes. As a result of this decision, all rights to the oral form of Targretin® reverted to us and LGD1268 and LGD1324 returned to the pool of eligible RXR modulators for possible use in oncology in combination with a SERM under the collaboration agreement between Ligand and Lilly.

In September 2000, Lilly declared LY510929, a PPAR agonist, a clinical candidate for development as a novel oral treatment for type II diabetes and cardiovascular disease, and, in December 2000, LY519818, another PPAR agonist, was also declared a clinical candidate for type II diabetes.

Inflammatory Disease Collaborative Program

Abbott Collaboration. In 1994, we entered into a research and development collaboration with Abbott Laboratories ("Abbott") to discover and develop small molecule compounds for the prevention or treatment of inflammatory diseases. The collaborative program includes several molecular approaches to discovering modulators of glucocorticoid receptor activity that have significantly improved therapeutic profiles relative to currently known anti-inflammatory steroids such as prednisone and dexamethasone. The collaboration is focused on the development of novel non-steroidal glucocorticoids that maintain the efficacy of corticosteroids that are currently used to treat inflammatory diseases, but lack some or all of corticosteroids' dose-limiting side effects. The research phase concluded in July 1999. Several compounds discovered during the collaboration have progressed to advanced preclinical testing in an effort to select a clinical candidate.

Abbott received exclusive worldwide rights for all products discovered in the collaboration for use in inflammation. We received exclusive worldwide rights for all anti-cancer products discovered in the collaboration. Abbott will make milestone and royalty payments on products targeted at inflammation resulting from the collaboration, while we will make milestone and royalty payments on products targeted at anti-cancer resulting from the collaboration. Each party will be responsible for the development, registration and commercialization of the products in its respective field.

STATs/Blood Disorders Collaborative Program

Our proprietary STAT technology is distinct from our IR technology platform. STATs are activated through a receptor located on the surface of the cell rather than a receptor located within the cell. STAT technology provides us with a second broadly enabling drug discovery platform that has potential applications in cancer, inflammation, asthma, allergy, infectious

disease, anemia, obesity, diabetes and growth disorders. See "Technology" for a more complete discussion of our STAT technology. We are pursuing product development opportunities based on our STAT technology through a collaboration with GlaxoSmithKline.

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

A number of lead series have been found that mimic the activity of natural growth factors for white cells and platelets. The optimization of compounds that mimic the activity of thrombopoietin, the protein that stimulates production of blood clotting platelets, is nearing completion. A decision on whether to progress a lead compound to an IND track is expected in 2001. The research phase concluded in February 2001.

Under the collaboration, we have the right to select up to three compounds related to hematopoietic targets for development as anti-cancer products other than those compounds selected for development by GlaxoSmithKline. GlaxoSmithKline has the option to co-promote these products with us in North America and to develop and market them outside North America.

Dermatology Program

Allergan. In 1997, in conjunction with the buyback of Allergan Ligand Retinoid Therapeutics, Inc. ("ALRT"), we agreed with Allergan to restructure the terms and conditions relating to research, development, and commercialization and sublicense rights for the ALRT compounds. Under the restructured arrangement, we received exclusive, worldwide development, commercialization and sublicense rights to Panretin® capsules and Panretin® gel, LGD1550, LGD268 and LGD324. Allergan received exclusive, worldwide development, commercialization and sublicense rights to LGD4310, an RAR antagonist. Allergan also received LGD4326 and LGD4204, two advanced preclinical RXR selective compounds. In addition, we participated in a lottery with Allergan for each of the approximately 2,000 retinoid compounds existing in the ALRT compound library as of the closing date, with each party acquiring exclusive, worldwide development, commercialization and sublicense rights to the compounds which they selected. Ligand and Allergan will each pay the other a royalty based on net sales of products developed from the compounds selected by each in the lottery and the other ALRT compounds to which each acquires exclusive rights. We will also pay to Allergan royalties based on our net sales of Targretin® for uses other than oncology and dermatology indications. In the event that we license commercialization rights to Targretin® to a third party, we will pay to Allergan a percentage of royalties payable to us with respect to sales of Targretin® other than in oncology and dermatology indications. Allergan has one compound (AGN4310) in Phase II clinical development for mucocutaneous toxicity.

Technology

In our successful efforts to discover new and important medicines, we and our exclusive academic collaborators and consultants have concentrated on two areas of research: advancing the understanding of the activities of hormones and hormone-related drugs and making scientific discoveries related to IR and STAT technologies. We believe that our expertise in these technologies will enable us to develop novel, small-molecule drugs acting through IRs or STATs with more target-specific properties than currently available drugs, resulting in either improved therapeutic and side effect profiles and new indications for IRs or novel mechanisms of action and oral activity for STATs. Both STATs and IRs are families of transcription factors that change cell function by selectively turning on or off particular genes in response to circulating signals that impinge on cells. In addition to our proprietary IR and STAT technologies, we acquired fusion protein technology, which was utilized by Seragen in the development of ONTAK®.

Intracellular Receptor Technology

Hormones occur naturally within the body and control processes such as reproduction, cell growth, and differentiation. Hormones generally fall into two classes, the non-peptide hormones and the peptide hormones. The non-peptide hormones include the retinoids, sex steroids (estrogens, progestins and androgens), adrenal steroids (glucocorticoids and mineralocorticoids), vitamin D and thyroid hormone. These non-peptide hormones act by binding to their corresponding IRs

to regulate the expression of genes in order to maintain and restore balanced cellular function within the body. Hormonal imbalances can lead to a variety of diseases. The hormones themselves and drugs that mimic or block hormone action may be useful in the treatment of these diseases. Furthermore, hormone mimics (agonists) or blockers (antagonists) can be used in the treatment of diseases in which the underlying cause is not hormonal imbalance. The effectiveness of the IRs as drug targets is clearly demonstrated by currently available drugs acting through IRs for several diseases. However, the use of most of these drugs has been limited by their often significant side effects. Examples of currently marketed hormone-related drugs acting on IRs are glucocorticoids (steroids used to treat inflammation), natural and synthetic estrogens and progesterones (used for hormone replacement therapy and contraception), tamoxifen (an estrogen antagonist used in the treatment of breast cancer), and various retinoids such as Accutane® and Retin-A® (used to treat acne) and Dovonex® (used to treat psoriasis).

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

The understanding of non-peptide hormones and their actions has increased substantially in the last 15 years. Driving this rapid expansion of knowledge has been the discovery of the family of IRs through which all the known small-molecule, non-peptide hormones act. We and our academic collaborators and consultants have made major discoveries pertaining to IRs and small molecule hormones and compounds, which interact with these IRs. These discoveries include: (1) the identification of the IR superfamily, (2) the recognition of IR subtypes, (3) the heterodimer biology of RXR-selective compounds and (4) the discovery of orphan IRs. We believe that each of these broad areas of knowledge provides important opportunities for drug discovery.

IR Superfamily. The receptors for all the non-peptide hormones are closely related members of a superfamily of proteins known as IRs. Human IRs for all of the known non-peptide hormones have now been cloned, in many cases by our scientists or our collaborators. The structure and underlying mechanism of action of the IRs have many common features, such that drug discovery insights about one IR can often be directly applied to other members of the IR superfamily, bringing synergy to our IR-focused drug discovery efforts. First generation drugs were developed and commercialized for their therapeutic benefits prior to the discovery of IRs and often cross-react with the IRs for hormones other than the intended target, which can result in significant side effects. The understanding that IRs are structurally similar has enabled us to determine the basis for the side effects of some first-generation drugs and to discover improved drug candidates.

IR Subtypes. For some of the non-peptide hormones, several closely related but non-identical IRs, known as IR subtypes, have been discovered. These include six subtypes of the IRs for retinoids, two subtypes of the IRs for thyroid hormone, two subtypes for the ER, and three subtypes for the PPARs. Patent applications covering many of these IR subtypes have been exclusively licensed by us. We believe that drugs capable of selective modulation of IR subtypes will allow more specific pharmacological intervention that is better matched to therapeutic need. Targretin®, an RXR selective molecule, was discovered as a result of our understanding of retinoid receptor subtypes.

Retinoid Responsive IRs. Retinoic acid, a derivative of Vitamin A, is one of the body's natural regulatory hormones that has a broad range of biological actions, influencing cell growth, differentiation, programmed cell death and embryonic development. Many chemical analogues of retinoic acid, called retinoids, also have biological activity. Specific retinoids have been approved by the FDA for the treatment of psoriasis and certain severe forms of acne. Evidence also suggests that retinoids can be used to arrest and, to an extent, reverse the effects of skin damage arising from prolonged exposure to the sun. Other evidence suggests that retinoids are useful in the treatment of a variety of cancers, including kidney cancer and certain forms of leukemia. For example, all-trans-Retinoic-acid has been approved by the FDA for the treatment of acute promyelocytic leukemia. Retinoids have also shown an ability to reverse precancerous (premalignant) changes in tissues, reducing the risk of development of cancer, and may have potential as preventive agents for a variety of epithelial malignancies, including skin, head and neck, bladder and prostate cancer. Currently marketed retinoids, which were developed and commercialized prior to the discovery of retinoid-responsive IRs, cause significant side effects. These include severe birth defects if fetal exposure occurs, severe irritation of the skin and mucosal surfaces, elevation of plasma lipids, headache and skeletal abnormalities.

The six RRs that have been identified to date can be grouped in two subfamilies —RARs and RXRs. Patent applications covering members of both families of RRs have been licensed exclusively to us primarily from The Salk Institute. The RR subtypes appear to have different functions, based on their distribution in the various tissues within the body and data arising

from *in vitro* and *in vivo* studies, including studies of transgenic mice. Several of the retinoids currently in commercial use are either non-selective in their pattern of RR subtype activation or are not ideal drugs for other reasons. We are developing chemically synthesized retinoids that, by selectively activating RR subtypes, may preserve desired therapeutic effects while reducing side effects.

We have three retinoid products approved by the FDA (Panretin® gel, Targretin® capsules and Targretin® gel) and four retinoid products in clinical trials (Panretin® capsules, Targretin® capsules, Targretin® gel and LGD1550 capsules). Panretin® gel and Panretin® capsules incorporate 9-*cis* retinoic acid, a retinoid isolated and characterized by us in 1991 in collaboration with scientists at The Salk Institute and Baylor. 9-*cis* retinoic acid is the first non-peptide hormone discovered in over 25 years and appears to be a natural ligand for the RAR and RXR subfamilies of retinoid receptors. Bexarotene, the active substance in Targretin®, is a synthetic retinoid developed by us that shows selective retinoid receptor subtype activity that is different from that of 9-*cis* retinoic acid, the active substance in Panretin®. Targretin® selectively activates a subclass of retinoid receptors called RXRs. RXRs play an important role in the control of a variety of cellular functions. LGD1550 is a potent RAR agonist that strongly inhibits growth of several human cancer cell lines.

RXRs. RXRs can form a dimer with numerous IRs, such as the RAR, thyroid hormone receptor and vitamin D receptor. While RXRs are widely expressed, their IR partners are more selectively expressed in different tissues, such as liver, fat or muscle. As a result, compounds that bind RXRs offer the unique potential to treat a variety of diseases, including cancer and metabolic diseases. In preclinical models of type II diabetes, RXR agonists appear to stimulate the physiological pathways responsive to RXR-PPAR receptor partners expressed in key target tissues that are involved in glucose metabolism. As a result, a discrete set of genes is activated in these tissues, resulting in a decrease in serum glucose levels and insulin.

Orphan Receptors. Over 50 additional members of the IR superfamily, which do not interact with the known non-peptide hormones, have been discovered. These members of the IR superfamily have been designated orphan receptors. We believe that among the orphan IRs may be receptors for uncharacterized small molecule hormones and that the physiological roles of the various orphan IRs are likely to be diverse. We devised strategies to isolate small molecules that interact with orphan IRs. In 1999, we invested in and exclusively licensed specified orphan IR technology to a new private corporation, X-Ceptor Therapeutics, Inc., which is conducting research to identify therapeutic products from orphan nuclear receptors. Please see note 10 of notes to consolidated financial statements for further details regarding our investment in X-Ceptor.

Signal Transducers and Activators of Transcription Technology

STATs are a family of proteins that are a key part of the signal transduction pathway for a variety of biologically important polypeptide hormones (e.g., interferons, interleukins, leptin, and hematopoietic growth factors). STATs play a role in the biology of cytokines and growth factors functionally analogous to that played by IRs in the biology of the non-peptide hormones. When various cytokines or growth factors bind to their receptors on the cell surface, this triggers the activation of specific members of the JAKs, which in turn activate specific STATs. The activated STATs enter the cell nucleus and bind to the control regions of specific target genes and alter their expression, thereby modulating physiologic or pathophysiologic processes.

The discovery of STATs, the elucidation of their roles in interferon signal transduction, and the first cloning of genes encoding STATs were all accomplished by our exclusive collaborator, Dr. James Darnell, and were described initially in 1992. A total of seven members of the STAT family have been identified and a large number of peptide hormones have been shown to utilize STAT signaling pathways. These peptide hormones include the interferons (alpha, beta and gamma), the hematopoietic colony stimulating factors (interleukin-3, EPO, G-CSF, GM-CSF and thrombopoietin), growth hormone, prolactin, leptin and many of the interleukins.

In certain conditions it may prove beneficial to block the actions of specific cytokines. In other pathological states, there is insufficient activity of specific cytokines. For example, in patients with chronic renal failure, diminished erythropoietin (“EPO”) release by the damaged kidneys results in the inadequate production of red blood cells, causing anemia. Recombinant human EPO protein (Epogen®) can be administered to correct this anemia effectively, but must be injected. Other cytokines are useful as injected protein medicines, including interferons (Intron-A®, Roferon®, Betaseron®), interleukins (Proleukin®), G-CSF (Neupogen®). Each of these and many other cytokines appear to exert their actions through JAK/STAT signal transduction pathways.

We have established a collaboration with GlaxoSmithKline to discover and characterize small molecule drugs to modulate specific JAK/STAT pathways to control the formation of red, white and platelet blood cells for treating patients with cancer, anemia, or platelet deficiency disorders. Proof of principle for this approach was achieved with GlaxoSmithKline in the area of G-CSF and thrombopoietin mimics.

Fusion Protein Technology

Our fusion protein technology was developed by Seragen, which we acquired in 1998. Seragen's fusion proteins consist of a fragment of diphtheria toxin genetically fused to a ligand that binds to specific receptors on the surface of target cells. Once bound to the cell, the fusion proteins are designed to enter the cell and destroy the ability of the cell to manufacture proteins, resulting in cell death. Using this platform, Seragen genetically engineered six fusion proteins, each of which consists of a fragment of diphtheria toxin fused to a different targeting ligand, such as a polypeptide hormone or growth factor. ONTAK®, which is approved in the U.S. for the treatment of patients with persistent or recurrent CTCL, is a fusion protein consisting of a fragment of diphtheria toxin genetically fused to a part of interleukin-2. In addition to treatment of CTCL, fusion proteins may have utility in oncology, dermatology, infectious diseases and autoimmune diseases. Seragen has entered into exclusive license agreements with Harvard University and other parties for patents related to fusion protein technology and has been issued four U.S. patents for improvements in the technology licensed from Harvard University.

Academic Collaborations

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

The Salk Institute of Biological Studies. In 1988, we established an exclusive relationship with The Salk Institute, which is one of the research centers in the area of IR technology. Under our agreement, we have an exclusive, worldwide license to certain IR technology developed in the laboratory of Dr. Ronald Evans, a Salk professor and Howard Hughes Medical Institute Investigator. Dr. Evans cloned and characterized the first IR in 1985 and is an inventor of the co-transfection assay used by us to screen for IR modulators. Under the agreement, we are obligated to make certain royalty payments based on sales of certain products developed using the licensed technology, as well as certain minimum annual royalty payments.

We have also entered into an exclusive consulting agreement with Dr. Evans that continues through July 2001. Dr. Evans serves as Chairman of Ligand's Scientific Advisory Board.

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

We work closely with Dr. O'Malley and Baylor in scientific IR research, particularly in the area of sex steroids and orphan IRs. Under the agreement, we are obligated to make payments to Baylor College of Medicine in support of research done in Dr. O'Malley's laboratory through March 2003. We are also obligated to make certain royalty payments based on the sales of products developed using the licensed technology. We have entered into a consulting agreement with Dr. O'Malley that will continue through September 2002. Dr. O'Malley is a member of Ligand's Scientific Advisory Board.

Rockefeller University. In September 1992, we entered into a worldwide, exclusive license agreement with Rockefeller University and exclusive consulting agreements with Dr. James Darnell of Rockefeller University and Dr. David Levy of NYU to develop and commercialize certain technology involving STATs to control gene expression. Dr. Darnell is one of the leading investigators of the control of gene expression by STATs. Rockefeller University will receive a royalty on any commercialized products developed using the technology. Related technology was assigned by NYU to Rockefeller University and is covered by the license agreement with us.

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

Manufacturing

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

Certain raw materials necessary for the commercial manufacturing of our products are custom and must be obtained from a specific sole source. In addition, our finished products are produced by sole source manufacturers. We currently attempt to manage the risk associated with such sole source raw materials and production by actively managing our inventories and

supply and production arrangements. We attempt to remain appraised of the financial condition of our suppliers and their ability to continue to supply our raw materials and finished products in an uninterrupted and timely manner. Unavailability of certain materials or the loss of current sources of production could cause an interruption in production and a reduced supply of finished product pending establishment of new sources, or in some cases, implementation of alternative processes. For a discussion of the risks associated with manufacturing, see "Risks and Uncertainties."

Quality Assurance

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

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

Research and Development Expenses

Research and development expenses were $51.3 million, $59.4 million and $70.3 million in fiscal 2000, 1999 and 1998 respectively, of which approximately 68%, 73% and 75% we sponsored, and the remainder of which was funded pursuant to collaborative research and development arrangements.

Competition

Some of the drugs we are developing will compete with existing therapies. In addition, a number of companies are pursuing the development of novel pharmaceuticals, which target the same diseases that we are targeting. A number of pharmaceutical and biotechnology companies are pursuing IR-related or STAT-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.

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 "Risks and Uncertainties."

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, which apply at the state level. Product development and approval within this regulatory framework takes a number of years and involves the expenditure of substantial resources.

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

by regulatory authorities in such countries under reciprocal agreements with the FDA.

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

For marketing outside the United States before FDA approval to market, we must submit an export permit application to the FDA. We also will be 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. For a discussion of the risks associated with government regulations, see "Risks and Uncertainties."

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.

To date, we have filed or participated as licensee in the filing of approximately 108 currently pending patent applications in the United States relating to our technology, as well as foreign counterparts of certain of these applications in many countries. In addition, we own or are the exclusive licensee to rights covered by approximately 190 patents issued, granted or allowed worldwide, which patents expire between 2013 and 2018. 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 "Risks and Uncertainties."

Human Resources

As of February 28, 2001, we had 356 full-time employees, of whom 207 were involved directly in scientific research and development activities. Of these employees, approximately 64 hold Ph.D. or M.D. degrees.

Risks and Uncertainties

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.

Our product development and commercialization involves a number of uncertainties and we may never generate sufficient revenues from the sale of products to become profitable.

We were founded in 1987. We have incurred significant losses since our inception. At December 31, 2000, our accumulated deficit was $542.7 million. To date, we have received the majority of our revenues from our collaborative arrangements and only began receiving revenues from the sale of pharmaceutical products in 1999. To become profitable, we must successfully develop, clinically test, market and sell our products. Even if we achieve profitability, we cannot predict the level of that profitability or whether we will be able to sustain profitability. We expect that our operating results will fluctuate from period to period as a result of differences in when we incur expenses and receive revenues from product sales, collaborative arrangements and other sources. Some of these fluctuations may be significant.

Most of our products in development will require extensive additional development, including preclinical testing and human studies, as well as regulatory approvals, before we can market them. We do not expect that any products resulting from our product development efforts or the efforts of our collaborative partners, other than those for which marketing approval has already been received, will be available for sale until the second half of the 2001 calendar year at the earliest, if at all. There are many reasons that we or our collaborative partners may fail in our efforts to develop our other potential products, including the possibility that:

- preclinical testing or human studies may show that our potential products are ineffective or cause harmful side effects,
- the products may fail to receive necessary regulatory approvals from the FDA or foreign authorities in a timely manner or at all,
- the products, if approved, may not be produced in commercial quantities or at reasonable costs,
- the products once approved, may not achieve commercial acceptance, or
- the proprietary rights of other parties may prevent us or our partners from marketing the products.

We are building marketing and sales capabilities in the United States and Europe which is an expensive and time-consuming process.

Developing the sales force to market and sell products is a difficult, expensive and time-consuming process. We have developed an approximate 50 person U.S. sales force, some of which are contracted from a third party, and rely on third parties to distribute our products. The distributor is responsible for providing many marketing support services, including customer service, order entry, shipping and billing, and customer reimbursement assistance. In Europe, we will rely initially on other companies to distribute and market our products. We have entered into agreements for the marketing and distribution of our products in territories such as the United Kingdom, Germany, France, Spain, Portugal, Greece, Italy, and Central and South America and have established a subsidiary, Ligand Pharmaceuticals International, Inc., with a branch in London, England, to prepare for our European marketing and operations. We may not be able to continue to expand our sales and marketing capabilities sufficiently to successfully commercialize our products in the territories where they receive marketing approval. To the extent we enter into co-promotion or other licensing arrangements, any revenues we receive will depend on the marketing efforts of others, which may or may not be successful.

Some of our key technologies have not been used to produce marketed products and may not be capable of producing such products.

To date, we have dedicated most of our resources to the research and development of potential drugs based upon our expertise in our IR and STATs technologies. Even though there are marketed drugs that act through IRs, some aspects of our IR technologies have not been used to produce marketed products. In addition, we are not aware of any drugs that have been developed and successfully commercialized that interact directly with STATs. Much remains to be learned about the location and function of IRs and STATs. If we are unable to apply our IR and STAT technologies to the development of our potential products, we will not be successful in developing new products.

Our drug development programs will require substantial additional future capital.

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 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.

For example, we are required under the terms of our agreement with Elan, to spend not less than $7 million through May 2003 to undertake additional clinical activities related to the commercialization of Morphelan. In the event we do not spend this amount, any shortfall would have to be paid to Elan. 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 commercialization of our products, to sell some or all of our technology or assets or to merge with another entity.

Our products must clear significant regulatory hurdles prior to marketing.

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. Our failure to show any product's safety and effectiveness would delay or prevent regulatory approval of the product and could adversely affect our business. The clinical trials process is complex and uncertain. 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. 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, which could be expensive and time-consuming, and failure to successfully conduct those trials could jeopardize continued commercialization.

The rate at which we complete our clinical trials depends on many factors, including 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 may result in increased costs and longer development times. In addition, our collaborative partners have rights to control product development and clinical programs for products developed under the collaborations. As a result, these collaborators may conduct these programs more slowly or in a different manner than we had expected. 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 may not be able to pay amounts due on our outstanding indebtedness when due which would cause defaults under these arrangements.

We and our subsidiaries may not have sufficient funds to make required payments due under existing debt. If we or our subsidiaries do not have adequate funds, we will be forced to refinance the existing debt and may not be successful in doing so. Our subsidiary, Glycomed, is obligated to make payments under convertible subordinated debentures in the total principal amount of $50 million. The debentures incur interest semi-annually at a rate of 7 ½% per annum, are due in 2003 and convertible into our common stock at $26.52 per share. In addition, at December 31, 2000, we had outstanding a $2.5 million convertible note to GlaxoSmithKline due in 2002 with interest at prime and convertible into our common stock at $13.56 per share. We also had outstanding $79.8 million in zero coupon convertible senior notes to Elan, due 2008 with an 8% per annum yield to maturity and convertible into our common stock at approximately $14 per share. Glycomed's failure to make payments when due under its debentures would cause us to default under the outstanding notes to Elan.

We may require additional money to run our business and may be required to raise this money on terms which are not favorable to our existing stockholders.

We have incurred losses since our inception and do not expect to generate positive cash flow to fund our operations for one or more years. As a result, 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 on acceptable terms. In addition, these financings, if completed, still may not meet our capital needs and could result in substantial dilution to our stockholders. For instance, the zero coupon convertible senior notes outstanding to Elan are convertible into common stock at the option of Elan, subject to some limitations, and in January 2001 we issued 2 million shares of our common stock in a private placement. If adequate funds are not available, we may be required to delay, reduce the scope of or eliminate one or more of our drug development programs. 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.

We face substantial competition.

Some of the drugs that we are developing and marketing will compete with existing treatments. In addition, several companies are developing new drugs that target the same diseases that we are targeting and are taking IR-related and STAT-

related approaches to drug development. Many of our existing or potential competitors, particularly large drug companies, have greater financial, technical and human resources than us 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. In addition, academic institutions, governmental agencies and other public and private research organizations are developing products that may compete with the products we are developing. These institutions are becoming more aware of the commercial value of their findings and are seeking patent protection and licensing arrangements to collect payments for the use of their technologies. These institutions also may market competitive products on their own or through joint ventures and will compete with us in recruiting highly qualified scientific personnel.

Our success will depend on third-party reimbursement and may be impacted by health care reform.

Sales of prescription drugs depend significantly on the availability of reimbursement to the consumer from third party payors, such as government and private insurance plans. These third party payors frequently require drug companies to provide predetermined discounts from list prices, and they are increasingly challenging the prices charged for medical products and services. Our current and potential products may not be considered cost-effective and reimbursement to the consumer may not be available or sufficient to allow us to sell our products on a competitive basis.

In addition, the efforts of governments and third-party payors to contain or reduce the cost of health care will continue to affect the business and financial condition of drug companies such as us. A number of legislative and regulatory proposals to change the health care system have been discussed in recent years. In addition, an increasing emphasis on managed care in the United States has and will continue to increase pressure on drug pricing. We cannot predict whether legislative or regulatory proposals will be adopted or what effect those proposals or managed care efforts may have on our business. The announcement and/or adoption of such proposals or efforts could adversely affect our profit margins and business.

We rely heavily on collaborative relationships and termination of any of these programs could reduce the financial resources available to us.

Our strategy for developing and commercializing many of our potential products, including products aimed at larger markets, includes entering into collaborations with corporate partners, licensors, licensees and others. These collaborations provide us with funding and research and development resources for potential products for the treatment or control of metabolic diseases, hematopoiesis, women's health disorders, inflammation, cardiovascular disease, cancer and skin disease, and osteoporosis. These agreements also give our collaborative partners significant discretion when deciding whether or not to pursue any development program. Our collaborations may not continue or be successful.

In addition, our collaborators may develop drugs, either alone or with others, that compete with the types of drugs they currently are developing with us. This would result in less support and increased competition for our programs. If products are approved for marketing under our collaborative programs, any revenues we receive will depend on the manufacturing, marketing and sales efforts of our collaborators, who generally retain commercialization rights under the collaborative agreements. Our current collaborators also generally 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.

We may have disputes in the future with our collaborators, including disputes concerning which of us owns the rights to any technology developed. For instance, we were involved in litigation with Pfizer, which we settled in April 1996, concerning our right to milestones and royalties based on the development and commercialization of droloxifene. These and other possible disagreements between us and our collaborators could delay our ability and the ability of our collaborators to achieve milestones or our receipt of other payments. In addition, any disagreements could delay, interrupt or terminate the collaborative research, development and commercialization of certain potential products, 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.

Our success depends on our ability to obtain and maintain our patents and other proprietary rights.

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 and to avoid infringing the proprietary rights of others, 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. 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.

Our patent position, like that of many 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, they 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. Further, the manufacture, use or sale of our products may infringe the patent rights of others.

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, United States patent applications may be kept confidential while pending in the Patent and Trademark Office, and patent applications filed in foreign countries are often first published six months or more after filing. 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. If other companies 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 license 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.

We have had and will continue to have discussions with our current and potential collaborators regarding the scope and validity of our patent and other proprietary rights. If a collaborator 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 collaborators to terminate their agreements where contractually permitted. Such a determination could also 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 results, a court may find our patents or those of our licensors invalid or may find that we have infringed on a competitor's rights. If any of our competitors have filed patent applications in the United States which claim technology we also have invented, the 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 have learned that Hoffmann-La Roche Inc. has received a United States patent and has made patent filings in foreign countries that relate to our Panretin® capsules and gel products. We filed a patent application with an earlier filing date than Hoffmann-La Roche's patent, which we believe is broader than, but overlaps in part with, Hoffmann-La Roche's patent. We currently are investigating the scope and validity of Hoffmann-La Roche's patent to determine its impact upon our products. The Patent and Trademark Office has informed us that the overlapping claims are patentable to us and has initiated a proceeding to determine whether we or Hoffmann-La Roche are entitled to a patent. We may not receive a favorable outcome in the proceeding. In addition, the proceeding may delay the Patent and Trademark Office's decision regarding our earlier application. If we do not prevail, the Hoffmann-La Roche patent might block our use of Panretin®capsules and gel in specified cancers.

We also rely on unpatented trade secrets and know-how to protect and maintain our competitive position. We require our employees, consultants, collaborators 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.

We rely on third-party manufacturers to supply our products and thus have little control over our manufacturing resources.

We currently have no manufacturing facilities and we rely on others for clinical or commercial production of our marketed and potential products. To be successful, we will need to manufacture our products, either directly or through others, in commercial quantities, in compliance with regulatory requirements and at acceptable cost. Any extended and unplanned manufacturing shutdowns could be expensive and could result in inventory and product shortages. If we are unable to develop our own facilities or contract with others for manufacturing services, our revenues could be adversely affected. In addition, if we are unable to supply products in development, our ability to conduct preclinical testing and human clinical trials will be adversely affected. This in turn could also delay our submission of products for regulatory approval and our initiation of new development programs. In addition, although other companies have manufactured drugs

acting through IRs and STATs on a commercial scale, we may not be able to do so at costs or in quantities to make marketable products.

The manufacturing process also may be susceptible to contamination, which could cause the affected manufacturing facility to close until the contamination is identified and fixed. In addition, problems with equipment failure or operator error also could cause delays in filling our customers' orders.

Our business exposes us to product liability risks or our products may need to be recalled and we may not have sufficient insurance to cover any claims.

Our business exposes us to potential product liability risks. Our products also may need to be recalled to address regulatory issues. A successful product liability claim or series of claims brought against us could result in payment of significant amounts of money and divert management's attention from running the business. Some of the compounds we are investigating may be harmful to humans. For example, retinoids as a class are known to contain compounds which can cause birth defects. We may not be able to maintain our insurance on acceptable terms, or our insurance may not provide adequate protection in the case of a product liability claim. To the extent that product liability insurance, if available, does not cover potential claims, we will be required to self-insure the risks associated with such claims.

We are dependent on our key employees, the loss of whose services could adversely affect us.

We depend on our key scientific and management staff, the loss of whose services could adversely affect our business. Furthermore, we may need to hire new scientific, management and operational personnel. Recruiting and retaining qualified management, operations and scientific personnel is also critical to our success. We may not be able to attract and retain such personnel on acceptable terms given the competition among numerous drug companies, universities and other research institutions for such personnel.

We use hazardous materials which requires us to incur substantial costs to comply with environmental regulations.

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 at substantial cost to us. We cannot completely eliminate the risk of accidental contamination or injury from the handling and disposing of hazardous materials, whether by us or by our third-party contractors. In the event of any accident, we could be held liable for any damages that result, which could be significant.

Our stock price may be adversely affected by volatility in the markets.

The market prices and trading volumes for our securities, and the securities of emerging companies like us, have historically been highly volatile and have experienced significant fluctuations unrelated to operating performance. Future announcements concerning us or our competitors may impact the market price of our common stock. These announcements might include:

- the results of research or development testing of ours or our competitors' products,
- technological innovations related to diseases we are studying,
- new commercial products introduced by our competitors,
- government regulation of our industry,
- receipt of regulatory approvals by competitors,
- our failure to receive regulatory approvals for products under development,
- developments concerning proprietary rights, or
- litigation or public concern about the safety of our products.

Future sales of our common stock may depress our stock price.

Sales of substantial amounts of our common stock in the public market could seriously harm prevailing market prices for our common stock. These sales might make it difficult or impossible for us to sell additional securities when we need to raise capital.

You may not receive a return on your shares other than through the sale of your shares of common stock.

We have not paid any cash dividends on our common stock to date. We intend to retain any earnings to support the expansion of our business and we do not anticipate paying cash dividends in the foreseeable future. Accordingly, other than through a sale of your shares, you will not receive a return on your investment in our common stock.

Our shareholder rights plan and charter documents may prevent transactions that could be beneficial to you.

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, including transactions in which you might otherwise receive a premium for your shares over then-current market prices. These provisions also may limit your ability to approve transactions that you deem to be in your best interests. In addition, our board of directors may issue shares of preferred stock without any further action by you. Such issuances may have the effect of delaying or preventing a change in our ownership.

Item 2. Properties

We currently lease and occupy office and laboratory facilities in San Diego, California. These include a 52,800 square foot facility leased through July 2015, an 82,500 square foot facility leased through February 2014, and a 7,500 square foot facility leased through February 2002. We believe these facilities will be adequate to meet our near-term space requirements.

Item 3. Legal Proceedings

Seragen, Inc., our subsidiary, and Ligand, were named parties to *Sergio M. Oliver, et al. v. Boston University, et* al., a putative shareholder class action filed on December 17, 1998 in the Court of Chancery in the State of Delaware in and for New Castle County, C.A. No. 16570NC, by Sergio M. Oliver and others against Boston University and others, including Seragen, its subsidiary Seragen Technology, Inc. and former officers and directors of Seragen. The complaint, as amended, alleged that Ligand aided and abetted purported breaches of fiduciary duty by the Seragen related defendants in connection with the acquisition of Seragen by Ligand and made certain misrepresentations in related proxy materials and seeks compensatory and punitive damages of an unspecified amount. Defendants thereafter filed motions to dismiss all claims. Rather than oppose the motion, plaintiffs sought and obtained permission to file a second amended complaint asserting essentially the same claims with a shorter class period. On August 23, 1999, defendants again filed motions to dismiss all claims of the second amended complaint. On July 25, 2000, the Delaware Chancery Court granted in part and denied in part defendants' motions. Seragen, Ligand, Seragen Technology, Inc. and our acquisition subsidiary, Knight Acquisition Corporation were dismissed from the action. Claims alleging common law fraud and negligent misrepresentation were also dismissed. Claims of breach of fiduciary duty remain against the remaining defendants, including the former officers and directors of Seragen. On October 10, 2000, plaintiffs filed a motion for class certification, which the remaining defendants have opposed. The hearing on the plaintiffs' motion for class certification took place on February 26, 2001. The court took the matter under submission and has not yet issued a ruling. The litigation is currently in the discovery phase. While Ligand and its subsidiary Seragen have been dismissed from the action, such dismissal is subject to a possible subsequent appeal upon judgment in the action against the remaining parties.

On September 21, 2000, a class action lawsuit was filed in the Superior Court of the State of California against Ligand and a specified former employee of Ligand. The complaint, as amended, alleges claims of invasion of privacy, negligence, fraud and deceit, and negligent infliction of emotional distress based on, among other things, an allegation that Ligand, as successor-in-interest to our Glycomed subsidiary and by reason of its position as employer, negligently and fraudulently allowed a former employee to access and publish private information of the plaintiffs. The complaint seeks damages of an unspecified amount on behalf of a class of plaintiffs consisting of former employees of Glycomed Incorporated. Plaintiffs have not yet filed a motion for class certification. The litigation is currently in the discovery phase.

We believe that each of these lawsuits is without merit and intend to vigorously defend against each of such lawsuits. Due to the uncertainty of the ultimate outcome of these matters, the impact on future financial results is not subject to reasonable estimates.

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

There were no matters submitted to a vote of security holders in the fourth quarter ended December 31, 2000.

PART II

Item 5. Markets for Registrant's Common Stock and Related Stockholder Matters

(a) Market Information

Our common stock trades on the Nasdaq National Market tier of the Nasdaq Stock Market under the symbol "LGND." The following table sets forth the high and low sales prices for our common stock on the Nasdaq National Market for the periods indicated.

	High	Low
Year Ended December 31, 1999:		
1st Quarter	$ 14 3/4	$ 8 3/16
2nd Quarter	11 7/16	8 3/16
3rd Quarter	11 3/16	6 7/16
4th Quarter	13 7/8	7 1/2
Year Ended December 31, 2000:		
1st Quarter	$ 26 1/2	$ 12 1/2
2nd Quarter	18 11/16	9 11/16
3rd Quarter	14	10
4th Quarter	16 5/16	10 1/2

(b) Holders

As of February 28, 2001, there were approximately 2,300 holders of record of the common stock.

(c) Dividends

We have never declared or paid any cash dividends on our capital stock and do not intend to pay any cash dividends in the foreseeable future. We currently intend to retain our earnings, if any, to finance future growth.

Item 6. Selected Consolidated Financial Data

The selected financial data set forth below with respect to our consolidated financial statements has been derived from the audited financial statements. The data set forth below should be read in conjunction with "Management's Discussion and Analysis of Financial Condition and Results of Operations" and the consolidated financial statements and related notes included elsewhere in this filing.

	Year Ended December 31,				
	2000	1999	1998	1997	1996
	(in thousands, except loss per share data)				
CONSOLIDATED STATEMENT OF OPERATIONS DATA:					
Product sales (1)	$ 22,910	$ 11,307	$ 406	$ 418	$ --
Collaborative research and development and other revenues	25,200	26,978	17,267	51,281	36,842
Cost of products sold (1)	8,591	3,563	466	520	--
Research and development expenses	51,287	59,442	70,273	71,906	59,494
Loss from operations (2)	(45,882)	(61,293)	(114,634)	(95,805)	(32,857)
Loss before cumulative effect of a change in accounting principle	(59,277)	(74,719)	(117,886)	(100,150)	(37,313)
Cumulative effect on prior years (to December 31, 1999) of changing method of revenue recognition (3)	(13,099)	--	--	--	--
Net loss	(72,376)	(74,719)	(117,886)	(100,150)	(37,313)
Basic and diluted per share amounts:					
Loss before cumulative effect of a change in accounting principle	$ (1.06)	$ (1.58)	$ (2.92)	$ (3.02)	$ (1.30)
Cumulative effect on prior years (to December 31, 1999) of changing method of revenue recognition (3)	(0.24)	--	--	--	--
Net loss	$ (1.30)	$ (1.58)	$ (2.92)	$ (3.02)	$ (1.30)
Weighted average number of common shares	55,664,921	47,146,312	40,392,421	33,128,372	28,780,914
Pro forma amounts assuming the new revenue recognition method is applied retroactively:					
Net loss	$(59,277)	$(73,131)	$(114,136)	$(118,587)	$(37,313)
Basic and diluted net loss per share	$ (1.06)	$ (1.55)	$ (2.83)	$ (3.58)	$ (1.30)

	Year Ended December 31,				
	2000	1999	1998	1997	1996
	(in thousands)				
CONSOLIDATED BALANCE SHEET DATA:					
Cash, cash equivalents, short term investments and restricted investments (4)	$ 25,097	$ 49,166	$ 72,521	$ 86,287	$ 84,179
Working capital	16,234	35,978	51,098	62,399	71,680
Total assets	113,422	134,645	156,020	107,423	102,140
Long-term debt	134,405	136,634	90,487	51,379	53,914
Accumulated deficit	(542,725)	(470,349)	(395,630)	(277,744)	(177,594)
Total stockholders' equity (deficit)	(55,125)	(25,590)	(11,362)	34,349	34,461

(1) We began selling ONTAK® and Panretin® gel in 1999 and Targretin® capsules and Targretin® gel in 2000.

(2) Includes write-offs of $5 million in 1999, $45 million in 1998 and $65 million in 1997 related to technology acquired from Elan in 1999 and 1998, the acquisition of Seragen in 1998, and the acquisition of ALRT in 1997.

(3) In 2000, we changed our policy for the recognition of revenue related to up-front fees in accordance with a new accounting pronouncement. See note 2 (revenue recognition) of notes to consolidated financial statements.

(4) In January 2001, we received net cash proceeds of $10 million from the issuance of convertible notes to Elan and $22.4 million from a private placement of our common stock. The convertible notes were issued to Elan on December 29, 2000 and the funds received on January 2, 2001.

Item 7. Management's Discussion And Analysis Of Financial Condition And Results Of Operations

This annual report may contain predictions, estimates and other forward-looking statements that involve a number of risks and uncertainties, including those discussed at "Risks and Uncertainties" in "Item 1 - Business" above. This outlook represents our current judgment on the future direction of our business. Such risks and uncertainties 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.

Overview

Our goal is to build a profitable pharmaceutical company which discovers, develops and markets new drugs that address critical unmet medical needs of patients in the areas of cancer, men's and women's health and skin diseases, as well as osteoporosis, metabolic, cardiovascular and inflammatory diseases. Internal and collaborative research and development programs utilize our proprietary science technology based on our leadership position in gene transcription technology. Our proprietary technologies involve two natural mechanisms that regulate gene activity: (1) non-peptide hormone activated IRs and (2) cytokine and growth factor activated STATs.

In 1999, we received marketing approval in the United States for Panretin gel for the treatment of Kaposi's sarcoma in AIDS patients, ONTAK for the treatment of patients with persistent or recurrent cutaneous T-cell lymphoma or CTCL, and Targretin capsules for the treatment of CTCL in patients who are refractory to at least one prior systemic therapy. In June 2000, Targretin gel was granted marketing approval in the United States for the treatment of patients with early stage CTCL. In addition, in May 2000, our strategic partner Elan submitted a new drug application for its product Morphelan for pain management in cancer and HIV patients. We have the exclusive marketing rights to Morphelan in the United States and Canada. In Europe, we were granted a marketing authorization for Panretin gel in October 2000 and have been recommended for a marketing authorization for Targretin capsules. We expect to launch Panretin gel in Europe in the second half of 2001 after pricing has been approved.

During 2000, we were also involved in the research phase of research and development collaborations with Bristol-Myers Squibb Company, Eli Lilly and Company, Organon Company, SmithKline Beecham Corporation (now GlaxoSmithKline), and the Parke-Davis Pharmaceutical research division of Warner-Lambert Company. Collaborations in the development phase are being pursued by Abbott Laboratories, Allergan, Inc., American Home Products, and GlaxoWellcome plc (now GlaxoSmithKline). We receive funding during the research phase of the arrangements and milestone and royalty payments as products are developed and marketed by our corporate partners. Please see note 9 of notes to consolidated financial statements for further details regarding our research and development collaborations.

We have been unprofitable since our inception. We expect to incur substantial additional operating losses until the commercialization of our products generates sufficient revenues to cover our expenses. We expect that our operating results will fluctuate from quarter to quarter as a result of differences in the timing of expenses incurred and revenues earned from product sales and collaborative research and development arrangements. Some of these fluctuations may be significant.

Results of Operations

Year Ended December 31, 2000 ("2000"), as compared with Year Ended December 31, 1999 ("1999")

Total revenues for 2000 were $48.1 million, an increase of $7.2 million as compared to 1999 revenues of $40.9 million. Loss from operations for 2000 was $45.9 million, a decrease of $15.4 million as compared to 1999. Loss before cumulative effect of a change in accounting principle for 2000 was $59.3 million or $(1.06) per share, a decrease of $15.4 million as compared to the 1999 net loss of $74.7 million or $(1.58) per share.

During 2000, we implemented a new accounting pronouncement that changed our method of revenue recognition for non-refundable up-front fees received in multiple element contractual arrangements. The new accounting pronouncement requires the deferral of up-front fees with recognition over the term of the contractual arrangement. The cumulative effect of this change to December 31, 1999 was to increase 2000 net loss by $13.1 million or $(0.24) per share. However, the effect on 2000 was to reduce net loss by $1.3 million or $0.02 per share. For additional details, please see "New Accounting Pronouncements" below and note 2 (revenue recognition) of the notes to consolidated financial statements.

Product sales for 2000 were $22.9 million, as compared to $11.3 million in 1999. The increase of $11.6 million is primarily due to $13.2 million in 2000 revenues from sales of ONTAK, approved for marketing in the United States in February 1999, up from $8.2 million in 1999, $6.7 million in 2000 revenues from sales of Targretin capsules, approved for marketing in the United States in December 1999, and $1.1 million in 2000 revenues from Targretin gel, approved for marketing in the United States in June 2000, offset by a decrease of $900,000 on sales of Panretin gel.

Collaborative research and development and other revenues for 2000 were $25.2 million, a decrease of $1.8 million as compared to 1999. In 2000, collaborative research and development revenues increased $7.2 million as compared to 1999. This increase was primarily due to $4.7 million earned on two new collaborations entered into in 2000 and $3.7 million from the recognition of a portion of an up-front fee received in a prior year that was deferred in accordance with the new

accounting pronouncement. This increase was offset by the absence in 2000 of 1999 revenues of $5.1 million from royalty transactions and a $2.3 million reduction of revenue earned on distribution agreements. The royalty transactions were specific to 1999, while $2.25 million of the 1999 revenue from distribution agreements was up-front payments subject to the new accounting pronouncement. The year to year comparison of collaborative research and development and other revenues is as follows ($,000):

	Year Ended December 31,	
	2000	1999
Collaborative research and development	$ 23,135	$ 15,954
Distribution agreements	922	3,250
Royalties	--	5,102
Other	1,143	2,672
	$ 25,200	$ 26,978

Certain customers accounted for greater than 10% of total revenues in 2000 and 1999. For additional details, please see note 2 (revenue recognition) of the notes to consolidated financial statements.

Contract manufacturing revenues and costs for 1999 were $2.6 million and $6.9 million, respectively, which were generated under contract manufacturing agreements performed at Marathon Biopharmaceuticals. The assets of Marathon were sold on January 7, 2000. For additional details, please see note 6 (sale of contract manufacturing assets) of the notes to consolidated financial statements.

Cost of products sold increased from $3.6 million in 1999 to $8.6 million in 2000. The increase is due primarily to the increased sales of ONTAK in 2000 and the launch of Targretin capsules in January 2000 and Targretin gel in August 2000.

Research and development expenses were $51.3 million in 2000, compared to $59.4 million in 1999. The decrease is primarily due to a general reduction of research and development activities with an increased focus on commercialization of our new products. Specifically, research and development costs were incurred in 1999 related to Targretin capsules, submitted as a new drug application in June 1999 and approved for marketing in the United States in December 1999, and Targretin gel, submitted as a new drug application in December 1999 and approved for marketing in the United States in June 2000.

Selling, general and administrative expenses were $34.1 million in 2000, up from $27.3 million in 1999. The increase was due primarily to increased selling and marketing costs associated with the expansion of our U.S. based sales force from approximately 20 to approximately 40 representatives in late 1999 to support our increased sales efforts, marketing activities related to the launch of Targretin capsules and Targretin gel in 2000, and continued promotion of ONTAK and Panretin gel.

The debt conversion expense relates to incentives provided to Elan for their early conversion of outstanding zero coupon convertible senior notes. For additional details regarding the note conversions, please see note 5 (financing arrangement) of the notes to consolidated financial statements.

We have significant net operating loss carry forwards for federal and state income taxes. For additional details, please see note 11 of the notes to consolidated financial statements.

Year Ended December 31, 1999 ("1999"), as compared with Year Ended December 31, 1998 ("1998")

Total revenues for 1999 were $40.9 million, an increase of $23.2 million as compared to 1998. Loss from operations for 1999 was $61.3 million, a decrease of $53.3 million as compared to 1998. Net loss for 1999 was $74.7 million or $(1.58) per share, a decrease of $43.2 million from the 1998 net loss of $117.9 million or $(2.92) per share.

In 1999, we wrote off $5 million related to a milestone payment made to Elan under the license agreement for its product Morphelan. In 1998 we wrote off $30 million of acquired in-process technology related to the merger with Seragen and $15 million related to the license agreement with Elan. For additional details, please see notes 5 (license agreement) and 6 (merger), respectively, of the notes to consolidated financial statements.

Product sales for 1999 were $11.3 million, as compared to $406,000 in 1998. The increase is due to revenues from sales of ONTAK and Panretin gel, approved by the FDA in February 1999.

Collaborative research and development and other revenues for 1999 were $27 million, an increase of $9.7 million over 1998. The increase in 1999 was due primarily to $5.1 million of revenue earned under royalty arrangements and $3.3 million earned in connection with distribution agreements entered into in 1999. The year-to-year comparison of collaborative research and development and other revenues is as follows ($,000):

	Year Ended December 31,	
	1999	1998
Collaborative research and development	$15,954	$16,914
Royalties	5,102	-- --
Distribution agreements	3,250	-- --
Other	2,672	353
	$26,978	$17,267

Certain customers accounted for greater than 10% of total revenues in 1999 and 1998. For additional details, please see note 2 (revenue recognition) of the notes to consolidated financial statements.

Contract manufacturing revenues and costs for 1999 were $2.6 million and $6.9 million, respectively, which were generated under contract manufacturing agreements performed at the Marathon facility acquired in January 1999.

Cost of products sold increased from $466,000 in 1998 to $3.6 million in 1999. The increase is due to manufacturing costs, amortization of acquired technology, and royalty expenses associated with the sale of ONTAK and Panretin gel.

Research and development expenses were $59.4 million in 1999, compared to $70.3 million in 1998. The decrease was due primarily to the reduction of clinical trial activity related to Panretin gel and Targretin capsules, approved by the FDA in February 1999 and December 1999, respectively, offset in part by increased clinical costs for Targretin gel submitted to the FDA for approval in December 1999. Selling, general and administrative expenses were $27.3 million in 1999, up from $16.6 million in 1998. The increase was due primarily to increased costs associated with the expansion of our sales and marketing activities related to the launch of our new products.

Interest expense in 1999 was $13 million, an increase of $4.7 million over 1998. The increase is due to the accretion related to the $100 million in issue price of zero coupon convertible notes issued to Elan in November 1998 ($40 million), July 1999 ($40 million) and August 1999 ($20 million). The debt conversion expense of $2.2 million relates to the incentive provided to Elan for their conversion of $20 million in notes in December 1999. For additional details, please see note 5 (financing arrangement) of the notes to consolidated financial statements.

Liquidity and Capital Resources

We have financed our operations through private and public offerings of our equity securities, collaborative research and development and other revenues, issuance of convertible notes, capital and operating lease transactions, equipment financing arrangements, product sales and investment income.

Working capital was $16.2 million at December 31, 2000 as compared to $36 million at December 31, 1999. Cash, cash equivalents, short-term investments, restricted investments, and the $10 million of funds receivable from Elan, totaled $35.1 million at December 31, 2000 as compared to $49.2 million at December 31, 1999. However, in January 2001, we raised approximately $22.4 million in a private placement of 2 million shares of our common stock. We primarily invest our cash in United States government and investment grade corporate debt securities.

Significant cash inflows in 2000 included $14.2 million of net cash received from the issuance our common stock upon the exercise of outstanding stock options and warrants, net cash proceeds of $9.7 million resulting from the sale of our contract manufacturing assets, $1.4 million from equipment financing arrangements and $1.1 million from the sale of an investment security. Significant cash out flows included $47.4 million of net cash used to finance operating activities in 2000, as compared to $60.5 million in 1999, $4.2 million in payments under equipment financing arrangements and $1.1 million in purchases of property and equipment.

Our subsidiary, Glycomed, is obligated to make payments under convertible subordinated debentures in the total principal amount of $50 million. The debentures pay interest semi-annually at a rate of 7 ½% per annum, are due in 2003 and are convertible into our common stock at $26.52 per share. In addition, at December 31, 2000, we also had outstanding a $2.5 million convertible note to SmithKline Beecham Corporation, due in 2002 with interest at prime and convertible into our

common stock at $13.56 per share, and $79.8 million in zero coupon convertible senior notes to Elan, due 2008 with an 8% per annum yield to maturity and convertible into our common stock at approximately $14 per share. The final $10 million of such notes was issued on December 29, 2000 with the related cash received on January 2, 2001.

Certain of our property and equipment is pledged as collateral under various equipment financing arrangements. As of December 31, 2000, $8.3 million was outstanding under such arrangements with $3.5 million classified as current. Our equipment financing arrangements have terms of three to seven years with interest ranging from 6.75% to 11.02%. We lease our office and research facilities under operating lease arrangements with varying terms through July 2015.

We may be required to make a milestone payment of $5 million to Elan and are required to spend not less than $7 million through May 2003 for clinical expenditures under the Morphelan license agreement. The milestone payment to Elan may be made through the issuance of shares of our common stock. For additional details, please see note 5 (license agreement) of the notes to consolidated financial statements.

We believe our available cash, cash equivalents, short-term investments and existing sources of funding will be adequate to satisfy our anticipated operating and capital requirements through at least the next 12 months. Our future operating and capital requirements will depend on many factors, including: the effectiveness of our commercialization activities; the pace of scientific progress in our research and development programs; the magnitude of these programs; the scope and results of preclinical testing and clinical trials; the time and costs involved in obtaining regulatory approvals; the costs involved in preparing, filing, prosecuting, maintaining and enforcing patent claims; competing technological and market developments; the ability to establish additional collaborations or changes in existing collaborations; the efforts of our collaborators; and the cost of manufacturing.

Financial Condition

December 31, 2000 ("2000"), as compared with December 31, 1999 ("1999")

Property and equipment decreased $9.6 million due to the sale of our contract manufacturing assets in January 2000, which included tangible assets of $6.7 million, and 2000 depreciation of $3.9 million, offset by 2000 purchases of $1.1 million. Acquired technology increased $2 million due to the capitalization of a $5 million milestone obligation to Lilly related to cumulative sales of ONTAK offset by 2000 amortization of $3 million.

Accrued liabilities increased $4.5 million primarily due to recognition of the $5 million ONTAK obligation to Lilly offset by the payment of $1 million in other liabilities associated with the sale of our contract manufacturing assets. Deferred revenues increased $11.1 million due primarily to implementation of the new accounting pronouncement on revenue recognition that resulted in the deferral of $11.8 million of non-refundable up-front fees received in prior years. Zero coupon convertible senior notes decreased $5.5 million due to Elan's conversion of $20 million in original issue price of such notes plus $1 million in accrued interest offset by 2000 accretion of $5.5 million and the issuance of $10 million of additional notes in December 2000.

Stockholders' deficit increased $29.5 million due primarily to the 2000 net loss of $72.4 million offset by $41.3 million in net equity from the issuance of 3.8 million shares of our common stock and amortization of deferred warrant expense of $1.4 million. In 2000, common stock was issued related to Elan's note conversion, Elan's early conversion incentive, the payment of the Morphelan milestone, and the exercise of outstanding stock options and warrants.

New Accounting Pronouncements

Revenue Recognition - In December 1999, the Securities and Exchange Commission issued Staff Accounting Bulletin ("SAB") No. 101, *Revenue Recognition in Financial Statements*. SAB No. 101 provides guidance in applying accounting principles generally accepted in the United States to revenue recognition in financial statements, including the recognition of non-refundable up-front fees and milestone payments received in conjunction with contractual arrangements that have multiple performance elements and require continuing involvement. SAB No. 101 requires that such fees be recognized as products are delivered or services are performed that represent the culmination of a separate earnings process.

We received non-refundable up-front fees of $18.75 million in 1997, $2.25 million in 1999, and $4.325 million in 2000. We initially recognized those payments as revenue upon receipt, as the fees were non-refundable and we had transferred technology or product rights at contract inception or incurred costs in excess of the up-front fees prior to initiation of each arrangement. However, under the provisions of SAB No. 101, non-refundable up-front fees must be deferred upon receipt and recognized as products are delivered or services are performed during the term of the arrangement. We implemented

SAB No. 101 in the fourth quarter of 2000 as a change in accounting principle by deferring and recognizing these up-front payments over the term designated in the arrangement. The cumulative effect of this change to December 31, 1999, which was recorded in 2000, was $13.1 million or $0.24 per share. However, the effect on 2000 increased revenue and reduced loss before cumulative effect of change in accounting principle by $1.3 million or $0.02 per share. See the consolidated statements of operations and note 13 of the notes to consolidated financial statements for the cumulative and pro forma effects of implementing this new accounting pronouncement.

Stock Based Compensation - In March 2000, the Financial Accounting Standards Board ("FASB") issued FASB Interpretation No. 44 ("FIN 44"), *Accounting for Certain Transactions Involving Stock Compensation*. FIN 44 clarifies certain issues in the application of APB No. 25. Among other issues, FIN 44 clarifies (a) the definition of employee for purposes of applying APB No. 25, (b) the criteria for determining whether a plan qualifies as a non-compensatory plan, (c) the accounting consequence of various modifications to the terms of a previously fixed stock option or award, and (d) the accounting for an exchange of stock compensation awards in a business combination. FIN 44 became effective July 1, 2000, but certain conclusions cover specific events that occur after either December 15, 1998, or January 12, 2000. The adoption of FIN 44 did not have a material impact on us in 2000.

Item 7A. Quantitative and Qualitative Disclosures About Market Risk

At December 31, 2000 and 1999, our investment portfolio included fixed-income securities of $12.4 million and $15.2 million, respectively. These securities are subject to interest rate risk and will decline in value if interest rates increase. However, due to the short duration of our investment portfolio, an immediate 10% change in interest rates would have no material impact on our financial condition, results of operations or cash flows. Declines in interest rates over time will, however, reduce our interest income while increases in interest rates over time will increase our interest expense.

We generally conduct business including sales to foreign customers, in U.S. dollars and as a result we have very limited foreign currency exchange rate risk. The effect of an immediate 10% change in foreign exchange rates would have no material impact on our financial condition, results of operations or cash flows.

Item 8. Consolidated Financial Statements and Supplementary Data

The consolidated financial statements and supplementary data required by this item are set forth at the pages indicated in Item 14(a)(1).

Item 9. Changes in and Disagreements with Accountants on Accounting and Financial Disclosure

Not applicable.

PART III

Item 10. Directors and Executive Officers of the Registrant

The sections labeled “Election of Directors”, “Executive Officers” and “Section 16(a) Beneficial Ownership Reporting Compliance” appearing in the Company’s Proxy Statement to be delivered to stockholders in connection with the 2001 Annual Meeting of Stockholders (the “Proxy Statement”) are incorporated herein by reference.

Item 11. Executive Compensation

The section labeled "Executive Compensation and Other Information" appearing in the Proxy Statement is incorporated herein by reference.

Item 12. Security Ownership of Certain Beneficial Owners and Management

The sections labeled “Principal Stockholders” and “Security Ownership of Directors and Management” appearing in the Proxy Statement are incorporated herein by reference.

Item 13. Certain Relationships and Related Transactions

The sections labeled “Executive Compensation and Other Information” and “Certain Relationships and Related Transactions” appearing in the Proxy Statement are incorporated herein by reference.

PART IV

Item 14. Exhibits, Financial Statement Schedules, and Reports on Form 8-K

(a) (1) Financial Statements

The financial statements required by this item are submitted in a separate section beginning on Page F-1 of this report.

Consolidated Financial Statements of Ligand Pharmaceuticals Incorporated

(b) Reports on Form 8-K.

The following report on Form 8-K was filed by the Company during the fourth quarter of 2000:

Date of Filing	Description
November 6, 2000	Item 4, Changes in Registrant's Certifying Accountant

(c) Exhibits

Exhibit Number	Description
2.1 (1)	Agreement and Plan of Reorganization dated May 11, 1998, by and among the Company, Knight Acquisition Corp. and Seragen, Inc. (Filed as Exhibit 2.1).
2.2 (1)	Option and Asset Purchase Agreement, dated May 11, 1998, by and among the Company, Marathon Biopharmaceuticals, LLC, 520 Commonwealth Avenue Real Estate Corp. and 660 Corporation. (Filed as Exhibit 10.3).
2.3 (19)	Asset Purchase Agreement among CoPharma, Inc., Marathon Biopharmaceuticals, Inc., Seragen, Inc. and the Company dated January 7, 2000. (The schedules referenced in this agreement have not been included because they are either disclosed in such agreement or do not contain information which is material to an investment decision (with certain confidential portions omitted). The Company agrees to furnish a copy of such schedules to the Commission upon request.)
2.4 (3)	Agreement of Merger, dated February 7, 1995 by and among the Company, LG Acquisition Corp. and Glycomed Incorporated (other Exhibits omitted, but will be filed by the Company with the Commission upon request). (Filed as Exhibit 2.1).
2.5 (1)	Form of Certificate of Merger for acquisition of Seragen, Inc. (Filed as Exhibit 2.2).
3.1 (1)	Amended and Restated Certificate of Incorporation of the Company. (Filed as Exhibit 3.2).
3.2 (1)	Bylaws of the Company, as amended. (Filed as Exhibit 3.3).
3.3 (2)	Amended Certificate of Designation of Rights, Preferences and Privileges of Series A Participating Preferred Stock of the Company.
3.5	Certificate of Amendment of the Amended and Restated Certificate of Incorporation of the Company dated June 14, 2000.
4.1 (4)	Specimen stock certificate for shares of Common Stock of the Company.
4.2 (16)	Preferred Shares Rights Agreement, dated as of September 13, 1996, by and between the Company and Wells Fargo Bank, N.A. (Filed as Exhibit 10.1).

Exhibit Number	Description
4.3 (13)	Amendment to Preferred Shares Rights Agreement, dated as of November 9, 1998, between the Company and ChaseMellon Shareholder Services, L.L.C., as Rights Agent. (Filed as Exhibit 99.1).
4.4 (17)	Second Amendment to the Preferred Shares Rights Agreement, dated as of December 23, 1998, between the Company and ChaseMellon Shareholder Services, L.L.C., as Rights Agent (Filed as Exhibit 1).
4.5 (22)	Indenture, dated as of December 23, 1992 by and between Glycomed Incorporated and Chemical Trust Company of California. (Filed as Exhibit 4.3).
4.6 (3)	First Supplement Indenture, dated as of May 18, 1995 by and among the Company, Glycomed Incorporated and Chemical Trust Company of California. (Filed as Exhibit 10.133).
10.1 (3)	The Company's 1992 Stock Option/Stock Issuance Plan, as amended.
10.2 (4)	Form of Stock Option Agreement.
10.3 (4)	Form of Stock Issuance Agreement.
10.12 (4)	1992 Employee Stock Purchase Plan.
10.13 (4)	Form of Stock Purchase Agreement.
10.29 (4)	Consulting Agreement, dated October 20, 1988, between the Company and Dr. Ronald M. Evans, as amended by Amendment to Consulting Agreement, dated August 1, 1991, and Second Amendment to Consulting Agreement, dated March 6, 1992.
10.30 (4)	Form of Proprietary Information and Inventions Agreement.
10.31 (4)	Agreement, dated March 9, 1992, between the Company and Baylor College of Medicine (with certain confidential portions omitted).
10.33 (4)	License Agreement, dated November 14, 1991, between the Company and Rockefeller University (with certain confidential portions omitted).
10.34 (4)	License Agreement and Bailment, dated July 22, 1991, between the Company and the Regents of the University of California (with certain confidential portions omitted).
10.35 (4)	Agreement, dated May 1, 1991, between the Company and Pfizer Inc (with certain confidential portions omitted).
10.36 (4)	License Agreement, dated July 3, 1990, between the Company and the Brigham and Woman's Hospital, Inc. (with certain confidential portions omitted).
10.37 (4)	Compound Evaluation Agreement, dated May 17, 1990, between the Company and SRI International (with certain confidential portions omitted).
10.38 (4)	License Agreement, dated January 5, 1990, between the Company and the University of North Carolina at Chapel Hill (with certain confidential portions omitted).
10.40 (4)	License Agreement, dated January 4, 1990, between the Company and Baylor College of Medicine (with certain confidential portions omitted).
10.41 (4)	License Agreement, dated October 1, 1989, between the Company and Institute Pasteur (with certain confidential portions omitted).
10.42 (4)	Sublicense Agreement, dated September 13, 1989, between the Company and AndroBio Corporation (with certain confidential portions omitted).
10.43 (4)	License Agreement, dated June 23, 1989, between the Company and La Jolla Cancer Research Foundation (with certain confidential portions omitted).
10.44 (4)	License Agreement, dated October 20, 1988, between the Company and the Salk Institute for Biological Studies, as amended by Amendment to License Agreement dated September 15, 1989, Second Amendment to License Agreement, dated December 1, 1989 and Third Amendment to License Agreement dated October 20, 1990 (with certain confidential portions omitted).

Exhibit Number	Description
10.45 (4)	Agreement dated June 12, 1989, between the Company and the Regents of the University of California.
10.46 (4)	Form of Indemnification Agreement between the Company and each of its directors.
10.47 (4)	Form of Indemnification Agreement between the Company and each of its officers.
10.50 (4)	Consulting Agreement, dated October 1, 1991, between the Company and Dr. Bert W. O'Malley.
10.53 (4)	Stock and Warrant Purchase Agreement, dated June 30, 1992 between the Company and Allergan, Inc. and Allergan Pharmaceuticals (Ireland) Ltd., Inc.
10.58 (4)	Stock Purchase Agreement, dated September 9, 1992, between the Company and Glaxo, Inc.
10.59 (4)	Research and Development Agreement, dated September 9, 1992, between the Company and Glaxo, Inc. (with certain confidential portions omitted).
10.60 (4)	Stock Transfer Agreement, dated September 30, 1992, between the Company and the Rockefeller University.
10.61 (4)	Stock Transfer Agreement, dated September 30, 1992, between the Company and New York University.
10.62 (4)	License Agreement, dated September 30, 1992, between the Company and the Rockefeller University (with certain confidential portions omitted).
10.63 (4)	Professional Services Agreement, dated September 30, 1992, between the Company and Dr. James E. Darnell.
10.64 (4)	Letter Agreement, dated August 24, 1992, between the Company and Dr. Howard T. Holden.
10.67 (4)	Letter Agreement, dated September 11, 1992, between the Company and Mr. Paul Maier.
10.69 (5)	Form of Automatic Grant Option Agreement.
10.73 (21)	Supplementary Agreement, dated October 1, 1993, between the Company and Pfizer, Inc. to Agreement, dated May 1, 1991.
10.78 (23)	Research, Development and License Agreement, dated July 6, 1994, between the Company and Abbott Laboratories (with certain confidential portions omitted). (Filed as Exhibit 10.75).
10.79 (23)	Stock and Note Purchase Agreement, dated September 2, 1994, between the Company and American Home Products Corporation (with certain confidential portions omitted).
10.80 (23)	Unsecured Convertible Promissory Note dated September 2, 1994, in the face amount of $10,000,000 executed by the Company in favor of American Home Products Corporation (with certain confidential portions omitted). (Filed as Exhibit 10.78).
10.82 (23)	Research, Development and License Agreement, dated September 2, 1994, between the Company and American Home Products Corporation, as represented by its Wyeth-Ayerst Research Division (with certain confidential portions omitted). (Filed as Exhibit 10.77).
10.83 (23)	Option Agreement, dated September 2, 1994, between the Company and American Home Products Corporation, as represented by its Wyeth-Ayerst Research Division (with certain confidential portions omitted). (Filed as Exhibit 10.80).
10.84 (23)	Distribution and Marketing Agreement, dated September 16, 1994, between the Company and Cetus Oncology Corporation, a wholly owned subsidiary of the Chiron Corporation (with certain confidential portions omitted). (Filed as Exhibit 10.82).
10.93 (6)	Indemnity Agreement, dated June 3, 1995, between the Company, Allergan, Inc. and Allergan Ligand Retinoid Therapeutics, Inc.
10.94 (6)	Tax Allocation Agreement, dated June 3, 1995, between the Company, Allergan, Inc. and Allergan Ligand Retinoid Therapeutics, Inc.
10.95 (6)	Stock Purchase Agreement, dated June 3, 1995, between the Company, Allergan, Inc. and Allergan Pharmaceuticals (Ireland), Ltd.

Exhibit Number	Description
10.97 (6)	Research, Development and License Agreement, dated December 29, 1994, between SmithKline Beecham Corporation and the Company (with certain confidential portions omitted).
10.98 (6)	Stock and Note Purchase Agreement, dated February 2, 1995, between SmithKline Beecham Corporation, S.R. One, Limited and the Company (with certain confidential portions omitted).
10.100 (3)	PHOTOFRIN(R) Distribution Agreement, dated March 8, 1995, between the Company and Quadra Logic Technologies Inc. (with certain confidential portions omitted).
10.119 (28)	Option and Development Agreement, dated August 15, 1990, between Glycomed and Dr. Richard E. Galardy and Dr. Damian Grobelny with exhibit thereto (with certain portions omitted). (Filed as Exhibit 10.20).
10.120 (28)	Option and Development Agreement, dated November 27, 1989, between Glycomed and the President and Fellows of Harvard College with appendices thereto (with certain confidential portions omitted). (Filed as Exhibit 10.21)
10.121 (28)	Option and Development Agreement, dated January 1, 1991, between Glycomed and UAB Research Foundation with exhibits thereto (with certain confidential portions omitted). (Filed as Exhibit 10.22).
10.122 (28)	Joint Venture Agreement, dated December 18, 1990, among Glycomed, Glyko, Inc., Millipore Corporation, Astroscan, Ltd., Astromed, Ltd., Gwynn R. Williams and John Klock, M.D., with exhibits thereto (with certain confidential portions omitted). (Filed as Exhibit 10.23).
10.127 (29)	Research and License Agreement, dated April 29, 1992, between Glycomed and the Alberta Research Council with Appendix thereto (with certain confidential portions omitted). (Filed as Exhibit 10.28).
10.130 (30)	Amendment to Research and License Agreement, dated July 12, 1993, (confidential portions omitted). (Filed as Exhibit 10.32).
10.131 (31)	Amendments to Research and License Agreement, dated October 22, 1993, December 16, 1993 and May 9, 1994 between Glycomed and the Alberta Research Council (with certain confidential portions omitted). (Filed as Exhibit 10.33).
10.132 (31)	License Agreement, dated February 14, 1994 between Glycomed and Sankyo Company, Ltd., for the Far East marketing rights of ophthalmic indications of Galardin(TM) MPI and analogs (with certain confidential portions omitted). (Filed as Exhibit 10.34).
10.133 (31)	Collaborative Technology Research and Development Agreement between Glycomed and Sankyo Company, Ltd., dated June 27, 1994 (with certain confidential portions omitted). (Filed as Exhibit 10.35).
10.136 (32)	Amendment to Research and License Agreement, dated September 22, 1994 between Glycomed and Alberta Research Council (with certain confidential portions omitted). (Filed as Exhibit 10.38).
10.140 (33)	Promissory Notes, General Security Agreements and a Credit Terms and Conditions letter dated March 31, 1995, between the Company and Imperial Bank (Filed as Exhibit 10.101).
10.142 (24)	Stock Purchase Agreement, dated June 27, 1995, between the Company and Sankyo Company, Ltd.
10.144 (24)	Stock Purchase Agreement, dated August 28, 1995, between the Company and Abbott Laboratories.
10.146 (24)	Amendment to Research and Development Agreement, dated January 16, 1996, between the Company and American Home Products Corporation, as amended.
10.147 (24)	Amendment to Stock Purchase Agreement, dated January 16, 1996, between the Company and American Home Products Corporation.
10.148 (24)	Lease, dated July 6, 1994, between the Company and Chevron/Nexus partnership, First Amendment to lease dated July 6, 1994.
10.149 (25)	Successor Employment Agreement, signed May 1, 1996, between the Company and David E. Robinson.

Exhibit Number	Description
10.150 (7)	Master Lease Agreement, signed May 30, 1996, between the Company and USL Capital Corporation.
10.151 (25)	Settlement Agreement and Mutual Release of all Claims, signed April 20, 1996, between the Company and Pfizer, Inc. (with certain confidential portions omitted).
10.152 (25)	Letter Amendment to Abbott Agreement, dated March 14, 1996, between the Company and Abbott Laboratories (with certain confidential portions omitted).
10.153 (26)	Letter Agreement, dated August 8, 1996, between the Company and Dr. Andres Negro-Vilar.
10.155 (7)	Letter Agreement, dated November 4, 1996, between the Company and William Pettit.
10.156 (7)	Letter Agreement, dated February 6, 1997, between the Company and Russell L. Allen.
10.157 (7)	Master Lease Agreement, signed February 13, 1997, between the Company and Lease Management Services.
10.158 (7)	Lease, dated March 7, 1997, between the Company and Nexus Equity VI LLC.
10.161 (34)	Settlement Agreement, License and Mutual General Release between Ligand Pharmaceuticals and SRI/LJCRF, dated August 23, 1995 (with certain confidential portions omitted).
10.162 (35)	Limited Extension of Collaborative Technology Research, Option and Development Agreement between Ligand Pharmaceuticals and Sankyo Company Limited, dated June 24, 1997.
10.163 (35)	Extension of Master Lease Agreement between Lease Management Services and Ligand Pharmaceuticals dated July 29, 1997.
10.164 (27)	Third Amendment to Agreement, dated September 2, 1997, between the Company and American Home Products Corporation.
10.165 (8)	Amended and Restated Technology Cross License Agreement, dated September 24, 1997, among the Company, Allergan, Inc. and Allergan Ligand Retinoid Therapeutics, Inc.
10.166 (8)	Transition Agreement, dated September 24, 1997, among the Company, Allergan, Inc. and Allergan Ligand Retinoid Therapeutics, Inc.
10.167 (8)	Development and License Agreement, dated November 25, 1997, between the Company and Eli Lilly and Company (with certain confidential portions omitted).
10.168 (8)	Collaboration Agreement, dated November 25, 1997, among the Company, Eli Lilly and Company, and Allergan Ligand Retinoid Therapeutics, Inc. (with certain confidential portions omitted).
10.169 (8)	Option and Wholesale Purchase Agreement, dated November 25, 1997, between the Company and Eli Lilly and Company (with certain confidential portions omitted).
10.170 (8)	Stock Purchase Agreement, dated November 25, 1997, between the Company and Eli Lilly and Company.
10.171 (8)	First Amendment to Option and Wholesale Purchase Agreement dated February 23, 1998, between the Company and Eli Lilly and Company (with certain confidential portions omitted).
10.172 (8)	Second Amendment to Option and Wholesale Purchase Agreement, dated March 16, 1998, between the Company and Eli Lilly and Company (with certain confidential portions omitted).
10.174 (9)	Leptin Research, Development and License Agreement, dated March 17, 1998, between the Company and SmithKline Beecham, plc (with certain confidential portions omitted).
10.175 (9)	Stock and Warrant Purchase Agreement, dated March 17, 1998, among the Company, SmithKline Beecham, plc. and SmithKline Beecham Corporation (with certain confidential portions omitted).
10.176 (10)	Secured Promissory Note, dated March 7, 1997, in the face amount of $3,650,000, payable to the Company by Nexus Equity VI LLC. (Filed as Exhibit 10.1).
10.177 (10)	Amended memorandum of Lease effective March 7, 1997, between the Company and Nexus Equity VI LLC. (Filed as Exhibit 10.2).

Exhibit Number	Description
10.178 (10)	First Amendment to Lease, dated March 7, 1997, between the Company and Nexus Equity VI LLC. (Filed as Exhibit 10.3).
10.179 (10)	First Amendment to Secured Promissory Note, date March 7, 1997, payable to the Nexus Equity VI LLC. (Filed as Exhibit 10.4).
10.183 (11)	Extension Option Agreement, dated May 11, 1998, by and among the Company, Seragen, Inc., Marathon Biopharmaceuticals, LLC, 520 Commonwealth Avenue Real Estate Corp. and 660 Corporation. (Filed as Exhibit 99.5).
10.184 (11)	Letter agreement, dated May 11, 1998, by and among the Company, Eli Lilly and Company and Seragen, Inc. (Filed as Exhibit 99.6).
10.185 (1)	Amendment No. 3 to Option and Wholesale Purchase Agreement, dated May 11, 1998, by and between Eli Lilly and Company and the Company. (Filed as Exhibit 10.6).
10.186 (1)	Agreement, dated May 11, 1998, by and among Eli Lilly and Company, the Company and Seragen, Inc. (Filed as Exhibit 10.7).
10.188 (11)	Settlement Agreement, dated May 1, 1998, by and among Seragen, Inc., Seragen Biopharmaceuticals Ltd./Seragen Biopharmaceutique Ltee, Sofinov Societe Financiere D'Innovation Inc., Societe Innovatech Du Grand Montreal, MDS Health Ventures Inc., Canadian Medical Discoveries Fund Inc., Royal Bank Capital Corporation and Health Care and Biotechnology Venture Fund (Filed as Exhibit 99.2).
10.189 (11)	Accord and Satisfaction Agreement, dated May 11, 1998, by and among Seragen, Inc., Seragen Technology, Inc., Trustees of Boston University, Seragen LLC, Marathon Biopharmaceuticals, LLC, United States Surgical Corporation, Leon C. Hirsch, Turi Josefsen, Gerald S.J. and Loretta P. Cassidy, Reed R. Prior, Jean C. Nichols, Elizabeth C. Chen, Robert W. Crane, Shoreline Pacific Institutional Finance, Lehman Brothers Inc., 520 Commonwealth Avenue Real Estate Corp. and 660 Corporation (Filed as Exhibit 99.4).
10.190 (1)	Amendment No. 1 to Service Agreement, dated as of May 11, 1998, by and between Seragen, Inc. and Marathon Biopharmaceuticals, LLC. (Filed as Exhibit 10.11).
10.191 (10)	Letter of Agreement dated September 28, 1998 among the Company, Elan Corporation, plc and Elan International Services, Ltd. (with certain confidential portions omitted), (Filed as Exhibit 10.5).
10.192 (10)	Stock Purchase Agreement dated September 30, 1998 between the Company and Elan International Services, Ltd. (with certain confidential portions omitted), (Filed as Exhibit 10.6).
10.195 (12)	Zero Coupon Convertible Senior Note Due 2008 dated November 9, 1998 between the Company and Elan International Services, Ltd., No. R-1.
10.196 (12)	Zero Coupon Convertible Senior Note Due 2008 dated November 9, 1998 between the Company and Elan International Services, Ltd., No. R-2.
10.197 (14)	Research, Development and License Agreement by and between the Company and Warner-Lambert Company dated September 1, 1999 (with certain confidential portions omitted). (Filed as Exhibit 10.1).
10.198 (14)	Stock Purchase Agreement by and between the Company and Warner-Lambert Company dated September 1, 1999 (with certain confidential portions omitted). (Filed as Exhibit 10.2).
10.200 (14)	Nonexclusive Sublicense Agreement, effective September 8, 1999, by and among Seragen, Inc., Hoffmann-La Roche Inc. and F. Hoffmann-La Roche Ltd. (with certain confidential portions omitted). (Filed as Exhibit 10.4).
10.201 (14)	Amendment to Development, Licence and Supply Agreement between the Company and Elan Corporation, plc dated August 20, 1999 (with certain confidential portions omitted). (Filed as Exhibit 10.5).
10.202 (14)	Ligand Purchase Option (to acquire outstanding capital stock of X-Ceptor Therapeutics, Inc.), contained in Schedule I to the Certificate of Incorporation of X-Ceptor Therapeutics, Inc., as amended. (Filed as Exhibit 10.6).

Exhibit Number	Description
10.203 (14)	License Agreement effective June 30, 1999 by and between the Company and X-Ceptor Therapeutics, Inc. (with certain confidential portions omitted). (Filed as Exhibit 10.7).
10.204 (14)	Zero Coupon Convertible Senior Note Due 2008 dated July 14, 1999 between the Company and Monksland Holdings, B.V., No. R-3. (Filed as Exhibit 10.10).
10.205 (14)	Zero Coupon Convertible Senior Note Due 2008 dated August 31, 1999 between the Company and Monksland Holdings, B.V., No. R-4. (Filed as Exhibit 10.11).
10.206 (14)	Stock Purchase Agreement dated September 30, 1999 by and between the Company and Elan International Services, Ltd. (with certain confidential portions omitted). (Filed as Exhibit 10.13).
10.209 (14)	Series X Warrant dated August 4, 1999 between the Company and Elan International Services, Ltd. (Filed as Exhibit 10.15).
10.210 (15)	Securities Purchase Agreement dated November 6, 1998 among Elan Corporation, plc, Elan International Services, Ltd. and the Company (Filed as Exhibit 1). (Filed as Exhibit 10.8).
10.211 (15)	Development, Licence and Supply Agreement dated November 6, 1998 between Elan Corporation, plc and the Company (Filed as Exhibit 2). (Filed as Exhibit 10.9).
10.212 (15)	Letter Agreement dated August 13, 1999 among the Company, Elan International Services, Ltd. and Elan Corporation, plc (Filed as Exhibit 3). (Filed as Exhibit 10.12).
10.213 (18)	Incentive Agreement dated December 31, 1999 among the Company, Elan International Services, Ltd. and Monksland Holdings, BV. (The schedules referenced in this agreement have not been included because they are either disclosed in such agreement or do not contain information which is material to an investment decision. The Company agrees to furnish a copy of such schedules to the Commission upon request.)
10.216 (18)	Amendment to Ligand Purchase Option (to acquire outstanding capital stock of X-Ceptor Therapeutics, Inc.), contained in Schedule I to the Certificate of Incorporation of X-Ceptor Therapeutics, Inc., as amended October 1, 1999.
10.217 (18)	Amended and Restated Series X Warrant dated November 22, 1999 between the Company and Elan International Services, Ltd.
10.218 (18)	Royalty Stream Purchase Agreement dated as of December 31, 1999 among Seragen, Inc., the Company, Pharmaceutical Partners, L.L.C., Bioventure Investments, Kft, and Pharmaceutical Royalties, LLC. (with certain confidential portions omitted).
10.219 (19)	Supply and Development Agreement among Ligand Pharmaceuticals Incorporated, Seragen, Inc. and CoPharma, Inc. dated January 7, 2000 (with certain confidential portions omitted).
10.220 (19)	Research, Development and License Agreement by and between Organon Company and Ligand Pharmaceuticals Incorporated dated February 11, 2000 (with certain confidential portions omitted).
10.222 (19)	Incentive Agreement dated March 1, 2000 among Ligand Pharmaceuticals Incorporated, Elan International Services, Ltd. and Monksland Holdings, BV. (The schedules referenced in this agreement have not been included because they are either disclosed in such agreement or do not contain information which is material to an investment decision. The Company agrees to furnish a copy of such schedules to the Commission upon request.)
10.223 (19)	Zero Coupon Convertible Senior Note Due 2008 dated July 14, 1999 and amended March 1, 2000 between Ligand Pharmaceuticals Incorporated and Monksland Holdings, BV, No. R-3A.
10.224 (20)	Research, Development and License Agreement by and between Bristol Myers Squibb Company and Ligand Pharmaceuticals Incorporated dated May 19, 2000 (with certain confidential portions omitted).
10.225	Zero Coupon Convertible Senior Note Due 2008 dated December 29, 2000 between Ligand Pharmaceuticals Incorporated and Monksland Holdings, BV, No. R-5.
10.226	Letter Agreement, dated January 5, 1998, between the Company and Steven D. Reich.
10.227	Letter Agreement, dated August 23, 1999, between the Company and Eric S. Groves.

Exhibit Number	Description
10.228	Letter Agreement, dated December 9, 1999, between the Company and Philip A. Duffy.
10.229	Letter Agreement, dated January 17, 2000, between the Company and Thomas H. Silberg.
10.230	Amended and Restated Registration Rights Agreement, dated as of June 29, 2000 among the Company and certain of its investors.
10.231 (2)	Marketing and Distribution Agreement with Ferrer Internacional S.A. to market and distribute Ligand Pharmaceuticals Incorporated products in Spain, Portugal and Greece. (Filed as Exhibit 10.3).
10.232 (2)	Marketing and Distribution Agreement with Ferrer Internacional S.A. to market and distribute Ligand Pharmaceuticals Incorporated products in Central and South America. (Filed as Exhibit 10.4).
21.1	Subsidiaries of Registrant.
23.1	Consent of Deloitte & Touche LLP.
23.2	Consent of Ernst & Young LLP.
24.1	Power of Attorney (See Page 40).

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(1) This exhibit was previously filed as part of, and is hereby incorporated by reference to the numbered exhibit filed with the Company's Registration Statement on Form S-4 (No. 333-58823) filed on July 9, 1998.

(2) This exhibit was previously filed as part of and is hereby incorporated by reference to same numbered exhibit filed with the Company's Quarterly Report on Form 10-Q for the period ended March 31, 1999.

(3) This exhibit was previously filed as part of, and is hereby incorporated by reference to the numbered exhibit filed with the Registration Statement on Form S-4 (No. 33-90160) filed on March 9, 1995, as amended.

(4) This exhibit was previously filed as part of, and is hereby incorporated by reference to the same numbered exhibit filed with the Company's Registration Statement on Form S-1 (No. 33-47257) filed on April 16, 1992 as amended.

(5) This exhibit was previously filed as part of, and is hereby incorporated by reference to Exhibit 99.1 filed with the Company's Form S-8 (No. 33-85366), filed on October 17, 1994.

(6) This exhibit was previously filed as part of, and is hereby incorporated by reference to the same numbered exhibit filed with the Registration Statement on Form S-1/S-3 (No. 33-87598 and 33-87600) filed on December 20, 1994, as amended.

(7) This exhibit was previously filed as part of, and is hereby incorporated by reference to the same numbered exhibit filed with the Company's Annual Report on Form 10-K for the period ended December 31, 1996.

(8) This exhibit was previously filed as part of, and is hereby incorporated by reference to the same numbered exhibit filed with the Company's Annual Report on Form 10-K for the period ended December 31, 1997.

(9) This exhibit was previously filed as part of, and is hereby incorporated by reference to the same numbered exhibit filed with the Company's Quarterly Report on Form 10-Q for the period ended March 31, 1998.

(10) This exhibit was previously filed as part of, and is hereby incorporated by reference to the numbered exhibit filed with the Company's Quarterly Report on Form 10-Q for the period ended September 30, 1998.

(11) This exhibit was previously filed as part of, and is hereby incorporated by reference to the numbered exhibit filed with the Current Report on Form 8-K of Seragen, Inc. filed on May 15, 1998.

(12) This exhibit was previously filed as part of, and is hereby incorporated by reference to the same numbered exhibit filed with the Company's Annual Report on Form 10-K for the period ended December 31, 1998.

(13) This exhibit was previously filed as part of, and is hereby incorporated by reference to the numbered exhibit filed with the Registration Statement on Form 8-A/A Amendment No. 1 (No. 0-20720) filed on November 10, 1998.

(14) This exhibit was previously filed as part of and is hereby incorporated by reference to the numbered exhibit filed with the Company's Quarterly Report on Form 10-Q for the period ended September 30, 1999.

(15) This exhibit was previously filed as part of, and is hereby incorporated by reference to the numbered exhibit filed with the Schedule 13D of Elan Corporation, plc, filed on January 6, 1999, as amended.

(16) This exhibit was previously filed as part of, and is hereby incorporated by reference to the numbered exhibit filed with the Company's Registration Statement on Form S-3 (No. 333-12603) filed on September 25, 1996, as amended.

(17) This exhibit was previously filed as part of, and is hereby incorporated by reference to the numbered exhibit filed with the Registration Statement on Form 8-A/A Amendment No. 2 (No. 0-20720) filed on December 24, 1998.

(18) This exhibit was previously filed as part of, and is hereby incorporated by reference to the same numbered exhibit filed with the Company's Annual Report on Form 10-K for the period ended December 31, 1999.

(19) This exhibit was previously filed as part of, and is hereby incorporated by reference to the same numbered exhibit filed with the Company's Quarterly Report on Form 10-Q for the period ended March 31, 2000.

(20) This exhibit was previously filed as part of, and is hereby incorporated by reference to the same numbered exhibit filed with the Company's Quarterly Report on Form 10-Q for the period ended June 30, 2000.

(21) This exhibit was previously filed as part of, and are hereby incorporated by reference to the same numbered exhibit filed with the Company's Annual Report on Form 10-K for the year ended December 31, 1993.

(22) This exhibit was previously filed as part of, and is hereby incorporated by reference to the numbered exhibit filed with the Registration Statement on Form S-3 of Glycomed Incorporated (Reg. No. 33-55042) filed on November 25, 1992, as amended.

(23) This exhibit was previously filed as part of, and is hereby incorporated by reference to the numbered exhibit filed with the Company's Quarterly Report on Form 10-Q for the period ended September 30, 1994.

(24) This exhibit was previously filed, and is hereby incorporated by reference to the same numbered exhibit filed with the Company's Annual Report on Form 10-K for the year ended December 31, 1995.

(25) This exhibit was previously filed as part of, and is hereby incorporated by reference to the same numbered exhibit filed with the Company's Quarterly report on Form 10-Q for the period ended June 30, 1996.

(26) This exhibit was previously filed as part of, and is hereby incorporated by reference at the same numbered exhibit filed with the Company's Quarterly report on Form 10-Q for the period ended September 30, 1996.

(27) This exhibit was previously filed as part of, and is hereby incorporated by reference to the same numbered exhibit filed with the Company's Quarterly Report on Form 10-Q for the period ended September 30, 1997.

(28) This exhibit was previously filed as part of, and is hereby incorporated by reference to the numbered exhibit filed with Glycomed's Registration Statement on Form S-1 (File No. 33-39961) filed on April 12, 1991, as amended.

(29) This exhibit was previously filed as part of, and is hereby incorporated by reference to the numbered exhibit filed with Glycomed's Annual Report on Form 10-K (File No. 0-19161) filed on September 25, 1992.

(30) This exhibit was previously filed as part of, and is hereby incorporated by reference to the numbered exhibit filed with Glycomed's Annual Report on Form 10-K (File No. 0-19161) filed on September 13, 1993.

(31) This exhibit was previously filed as part of, and is hereby incorporated by reference to the numbered exhibit filed with Glycomed's Annual Report on Form 10-K (File No. 0-19161) filed on September 27, 1994.

(32) This exhibit was previously filed as part of, and is hereby incorporated by reference to the numbered exhibit filed with Glycomed's Quarterly Report on Form 10-Q (File No. 0-19161) filed on February 10, 1995.

(33) This exhibit was previously filed as part of, and are hereby incorporated by reference to the same numbered exhibit filed with the Company's Quarterly report on Form 10-Q for the period ended September 30, 1995.

(34) This exhibit was previously filed as part of, and is hereby incorporated by reference to the same numbered exhibit filed with the Company's Quarterly Report on Form 10-Q for the period ended March 31, 1997.

(35) This exhibit was previously filed as part of, and is hereby incorporated by reference to the same numbered exhibit filed with the Company's Quarterly Report on Form 10-Q for the period ended June 30, 1997.

SIGNATURES

Pursuant to the requirements of Section 13 or 15(d) of the Securities Exchange Act of 1934, the registrant has duly caused this report to be signed on its behalf by the undersigned, thereunto duly authorized.

LIGAND PHARMACEUTICALS INCORPORATED

Date: March 29, 2001

By: /s/ DAVID E. ROBINSON
David E. Robinson
President and Chief Executive Officer

POWER OF ATTORNEY

Know all men by these presents, that each person whose signature appears below constitutes and appoints David E. Robinson or Paul V. Maier, his or her attorney-in-fact, with power of substitution in any and all capacities, to sign any amendments to this Annual Report on Form 10-K, and to file the same with exhibits thereto, and other documents in connection therewith, with the Securities and Exchange Commission, hereby ratifying and confirming all that the attorney-in-fact or his or her substitute or substitutes may do or cause to be done by virtue hereof.

Pursuant to the requirements of the Securities Exchange Act of 1934, this report has been signed below by the following persons on behalf of the registrant and in the capacities and on the dates indicated.

Signature	Title	Date
/s/ DAVID E.ROBINSON David E. Robinson	Chairman of the Board, President, Chief Executive Officer and Director (Principal Executive Officer)	March 22, 2001
/s/ PAUL V. MAIER Paul V. Maier	Senior Vice President, Chief Financial Officer (Principal Financial and Accounting Officer)	March 22, 2001
/s/ HENRY F. BLISSENBACH Henry F. Blissenbach	Director	March 22, 2001
/s/ ALEXANDER D. CROSS Alexander D. Cross	Director	March 22, 2001
/s/ JOHN GROOM John Groom	Director	March 23, 2001
/s/ IRVING S. JOHNSON Irving S. Johnson	Director	March 22, 2001
/s/ CARL C. PECK Carl C. Peck	Director	March 22, 2001
/s/ MICHAEL A. ROCCA Michael A. Rocca	Director	March 23, 2001

INDEX TO FINANCIAL STATEMENTS

REPORTS OF INDEPENDENT AUDITORS

The Board of Directors and Stockholders
Ligand Pharmaceuticals Incorporated

We have audited the accompanying consolidated balance sheet of Ligand Pharmaceuticals Incorporated and subsidiaries as of December 31, 2000, and the related consolidated statements of operations, stockholders' deficit, and cash flows for the year then ended. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audit.

We conducted our audit in accordance with auditing standards generally accepted in the United States of America. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audit provides a reasonable basis for our opinion.

In our opinion, such consolidated financial statements present fairly, in all material respects, the financial position of Ligand Pharmaceuticals Incorporated and subsidiaries as of December 31, 2000, and the consolidated results of their operations and their cash flows for the year then ended in conformity with accounting principles generally accepted in the United States of America.

As discussed in Note 2 to the consolidated financial statements, in 2000 the Company changed its method of revenue recognition to comply with the provisions of Staff Accounting Bulletin No. 101, Revenue Recognition in Financial Statements, issued by the Securities and Exchange Commission.

DELOITTE & TOUCHE LLP
San Diego, California
February 23, 2001

The Board of Directors and Stockholders
Ligand Pharmaceuticals Incorporated

We have audited the accompanying consolidated balance sheet of Ligand Pharmaceuticals Incorporated as of December 31, 1999, and the related consolidated statements of operations, stockholders' deficit, and cash flows for each of the two years in the period ended December 31, 1999. These financial statements are the responsibility of the Company's management. Our responsibility is to express an opinion on these financial statements based on our audits.

We conducted our audits in accordance with auditing standards generally accepted in the United States. Those standards require that we plan and perform the audit to obtain reasonable assurance about whether the financial statements are free of material misstatement. An audit includes examining, on a test basis, evidence supporting the amounts and disclosures in the consolidated financial statements. An audit also includes assessing the accounting principles used and significant estimates made by management, as well as evaluating the overall financial statement presentation. We believe that our audits provide a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated financial position of Ligand Pharmaceuticals Incorporated at December 31, 1999, and the consolidated results of its operations and its cash flows for each of the two years in the period ended December 31, 1999, in conformity with accounting principles generally accepted in the United States.

ERNST & YOUNG LLP
San Diego, California
February 22, 2000

LIGAND PHARMACEUTICALS INCORPORATED

CONSOLIDATED BALANCE SHEETS
(in thousands, except share data)

	December 31,	
	2000	1999
ASSETS		
Current assets:		
Cash and cash equivalents	$ 9,224	$ 29,903
Short-term investments	14,439	17,252
Funds receivable from Elan	10,000	--
Accounts receivable, net	2,824	1,657
Inventories	5,651	5,732
Other current assets	2,511	2,135
Total current assets	44,649	56,679
Restricted investments	1,434	2,011
Property and equipment, net	10,972	20,542
Acquired technology, net	40,924	38,969
Other assets	15,443	16,444
	$ 113,422	$ 134,645
LIABILITIES AND STOCKHOLDERS' DEFICIT		
Current liabilities:		
Accounts payable	$ 3,827	$ 5,395
Accrued liabilities	12,675	8,173
Current portion of deferred revenue	8,435	3,028
Current portion of equipment financing obligations	3,478	4,105
Total current liabilities	28,415	20,701
Long-term portion of deferred revenue	5,727	--
Long-term portion of equipment financing obligations	4,788	6,907
Convertible subordinated debentures	44,651	41,977
Accrued acquisition obligation	2,700	2,900
Convertible note	2,500	2,500
Zero coupon convertible senior notes	79,766	85,250
Total liabilities	168,547	160,235
Commitments and contingencies (Notes 5, 6, 7 and 9)		
Stockholders' deficit:		
Convertible preferred stock, $0.001 par value; 5,000,000 shares authorized; none issued	--	--
Common stock, $0.001 par value; 130,000,000 shares and 80,000,000 shares authorized at December 31, 2000 and 1999, respectively; 56,823,716 shares and 53,018,248 shares issued at December 31, 2000 and 1999, respectively	57	53
Additional paid-in capital	490,484	448,784
Deferred warrant expense	(2,076)	(3,460)
Accumulated other comprehensive income (loss)	46	(607)
Accumulated deficit	(542,725)	(470,349)
	(54,214)	(25,579)
Treasury stock, at cost; 73,842 shares and 1,114 shares at December 31, 2000 and 1999, respectively	(911)	(11)
Total stockholders' deficit	(55,125)	(25,590)
	$ 113,422	$ 134,645

See accompaning notes.

LIGAND PHARMACEUTICALS INCORPORATED

CONSOLIDATED STATEMENTS OF OPERATIONS
(in thousands, except net loss per share data)

	Year ended December 31,		
	2000	1999	1998
Revenues:			
Product sales	$ 22,910	$ 11,307	$ 406
Collaborative research and development and other revenues	25,200	26,978	17,267
Contract manufacturing	--	2,610	--
Total revenues	48,110	40,895	17,673
Operating costs and expenses:			
Cost of products sold	8,591	3,563	466
Contract manufacturing	--	6,926	--
Research and development	51,287	59,442	70,273
Selling, general and administrative	34,114	27,257	16,568
Write-off of acquired technology	--	5,000	45,000
Total operating costs and expenses	93,992	102,188	132,307
Loss from operations	(45,882)	(61,293)	(114,634)
Other income (expense):			
Interest income	2,574	2,470	3,070
Interest expense	(13,119)	(12,979)	(8,322)
Debt conversion expense	(2,025)	(2,200)	--
Other, net	(825)	(717)	2,000
Total other income (expense)	(13,395)	(13,426)	(3,252)
Loss before cumulative effect of a change in accounting principle	(59,277)	(74,719)	(117,886)
Cumulative effect on prior years (to December 31, 1999) of changing method of revenue recognition	(13,099)	--	--
Net loss	$ (72,376)	$ (74,719)	$ (117,886)
Basic and diluted per share amounts:			
Loss before cumulative effect of a change in accounting principle	$ (1.06)	$ (1.58)	$ (2.92)
Cumulative effect on prior years (to December 31, 1999) of changing method of revenue recognition	(0.24)	--	--
Net loss	$ (1.30)	$ (1.58)	$ (2.92)
Weighted average number of common shares	55,664,921	47,146,312	40,392,421
Pro forma amounts assuming the new revenue recognition method is applied retroactively:			
Net loss	$ (59,277)	$ (73,131)	$ (114,136)

Basic and diluted net loss per share.....	$ (1.06)	$ (1.55)	$ (2.83)

See accompaning notes.

LIGAND PHARMACEUTICALS INCORPORATED

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' DEFICIT
(in thousands, except share data)

	Common stock		Additional paid-in capital	Deferred warrant expense
	Shares	Amount		
Balance at January 1, 1998	38,504,459	$ 39	$ 311,681	$ --
Issuance of Common Stock	7,185,608	7	73,034	--
Unrealized losses on available-for-sale securities	--	--	--	--
Net loss	--	--	--	--
Balance at December 31, 1998	45,690,067	46	384,715	--
Issuance of Common Stock	7,328,181	7	59,695	--
Unrealized losses on available-for-sale securities	--	--	--	--
Issuance of warrants	--	--	4,374	(3,990)
Amortization of deferred warrant expense	--	--	--	530
Net loss	--	--	--	--
Balance at December 31, 1999	53,018,248	53	448,784	(3,460)
Issuance of Common Stock	3,805,468	4	41,294	--
Unrealized gains on available-for-sale securities	--	--	--	--
Reclassification adjustment on sale of investment security	--	--	--	--
Foreign currency translation adjustments	--	--	--	--
Stock-based compensation	--	--	406	--
Amortization of deferred warrant expense	--	--	--	1,384
Stock received for milestone payment	--	--	--	--
Net loss	--	--	--	--
Balance at December 31, 2000	56,823,716	$ 57	$ 490,484	$ (2,076)

	Accumulated other comprehensive income (loss)	Accumulated deficit	Treasury stock Shares	Treasury stock Amount
Balance at January 1, 1998	$ 384	$ (277,744)	(1,114)	$ (11)
Issuance of Common Stock	--	--	--	--
Unrealized losses on available-for-sale securities	(866)	--	--	--
Net loss	--	(117,886)	--	--
Balance at December 31, 1998	(482)	(395,630)	(1,114)	(11)

Issuance of Common Stock ..	--	--	--	--
Unrealized losses on available-for-sale securities	(125)	--	--	--
Issuance of warrants	--	--	--	--
Amortization of deferred warrant expense	--	--	--	--
Net loss	--	(74,719)	--	--
Balance at December 31, 1999	(607)	(470,349)	(1,114)	(11)
Issuance of Common Stock ..	--	--	--	--
Unrealized gains on available-for-sale securities	182	--	--	--
Reclassification adjustment on sale of investment security ...	550	--	--	--
Foreign currency translation adjustments ..	(79)	--	--	--
Stock-based compensation ..	--	--	--	--
Amortization of deferred warrant expense	--	--	--	--
Stock received for milestone payment	--	--	(72,728)	(900)
Net loss	--	(72,376)	--	--
Balance at December 31, 2000	$ 46	$(542,725)	(73,842)	$ (911)

	Total stockholders' equity (deficit)	Comprehensive income (loss)
Balance at January 1, 1998.....	$ 34,349	$ (99,688)
Issuance of Common Stock ..	73,041	
Unrealized losses on available-for-sale securities	(866)	$ (866)
Net loss	(117,886)	(117,886)
Balance at December 31, 1998.....	(11,362)	$(118,752)
Issuance of Common Stock ..	59,702	
Unrealized losses on available-for-sale securities	(125)	$ (125)
Issuance of warrants	384	
Amortization of deferred warrant expense	530	
Net loss	(74,719)	(74,719)
Balance at December 31, 1999	(25,590)	$ (74,844)
Issuance of Common Stock ..	41,298	
Unrealized gains on available-for-sale securities	182	$ 182
Reclassification adjustment on sale of investment security ...	550	550

Foreign currency translation adjustments ..	(79)	(79)
Stock-based compensation ..	406	
Amortization of deferred warrant expense	1,384	
Stock received for milestone payment	(900)	
Net loss	(72,376)	(72,376)
Balance at December 31, 2000	$ (55,125)	$ (71,723)

See accompaning notes.

LIGAND PHARMACEUTICALS INCORPORATED

CONSOLIDATED STATEMENTS OF CASH FLOWS
(in thousands)

	Year ended December 31,		
	2000	1999	1998
OPERATING ACTIVITIES			
Net loss	$ (72,376)	$ (74,719)	$(117,886)
Adjustments to reconcile net loss to net cash used in operating activities:			
Accretion of debt discount and interest	8,212	7,942	3,194
Depreciation and amortization of property and equipment	3,928	5,565	4,326
Amortization of acquired technology	3,045	1,343	--
Debt conversion expense	2,025	2,200	--
Write-off of acquired technology	--	5,000	45,000
Other	70	725	257
Changes in operating assets and liabilities net of effects from sale of manufacturing assets:			
Accounts receivable	(1,389)	(1,657)	--
Inventories	81	434	(2,899)
Other current assets	(173)	(275)	(1,031)
Accounts payable and accrued liabilities	(1,912)	(6,011)	891
Deferred revenue	11,134	(1,087)	1,499
Net cash used in operating activities	(47,355)	(60,540)	(66,649)
INVESTING ACTIVITIES			
Purchases of short-term investments	(11,974)	(21,402)	(52,245)
Proceeds from sale of short-term investments	14,908	41,191	35,191
Purchases of property and equipment	(1,085)	(2,385)	(5,365)
Payments on accrued acquisition obligation	(200)	(37,100)	--
Increases in other assets	(1,669)	(7,525)	(4,462)
Decreases in other assets	3,876	2,325	925
Net proceeds from sale of manufacturing assets	9,676	--	--
Proceeds from sale of investment security	1,119	--	--
Net cash paid for Seragen acquisition	--	--	(5,756)
Net cash provided by (used in) investing activities	14,651	(24,896)	(31,712)
FINANCING ACTIVITIES			
Principal payments on equipment financing obligations	(4,188)	(3,381)	(2,983)
Proceeds from equipment financing arrangements	1,442	3,027	3,095
Proceeds from restricted investments	577	543	503
Net proceeds from issuance of zero coupon convertible senior notes	--	60,000	30,000

Net proceeds from issuance of common stock and warrants.....	14,194	22,349	38,295
Net cash provided by financing activities.....	12,025	82,538	68,910
Net decrease in cash and cash equivalents.....	(20,679)	(2,898)	(29,451)
Cash and cash equivalents at beginning of year.....	29,903	32,801	62,252
Cash and cash equivalents at end of year.....	$ 9,224	$ 29,903	$ 32,801

SUPPLEMENTAL DISCLOSURE OF CASH FLOW INFORMATION

Interest paid.....	$ 4,824	$ 4,941	$ 5,736

SUPPLEMENTAL SCHEDULE OF NON-CASH INVESTING AND FINANCING ACTIVITIES

Conversion of zero coupon convertible senior notes to common stock.....	$ 21,022	$ 20,537	$ --
Issuance of common stock and notes for acquired technology	4,000	5,000	15,000
Issuance of common stock for debt conversion incentive	2,025	2,200	--
Accrual of ONTAK obligation for acquired technology	5,000	--	--
Issuance of common stock to satisfy accrued acquisition obligations.....	--	10,000	--
Issuance of warrants to X-Ceptor investors	--	3,990	--
Issuance of common stock to purchase Seragen.....	--	--	25,996
Conversion of convertible note to common stock.....	--	--	3,750

See accompaning notes.

NOTES TO CONSOLIDATED FINANCIAL STATEMENTS

1. The Company and its Business

Ligand Pharmaceuticals Incorporated, a Delaware corporation (the "Company" or "Ligand"), discovers, develops and markets new drugs that address critical unmet medical needs of patients in the areas of cancer, and men's and women's health and skin diseases, as well as osteoporosis, metabolic, cardiovascular and inflammatory diseases. Ligand's drug discovery and development programs are based on gene transcription technology, primarily related to Intracellular Receptors and Signal Transducers and Activators of Transcription. The financial statements include its direct wholly owned subsidiaries, Ligand Pharmaceuticals International, Inc., Glycomed Incorporated ("Glycomed"), Ligand Pharmaceuticals (Canada) Incorporated, and Seragen, Inc. ("Seragen").

In February 1999, the Company was granted U.S. Food and Drug Administration ("FDA") marketing approval for its first two products, Panretin® gel for the treatment of Kaposi's sarcoma in AIDS patients and ONTAK™ for the treatment of patients with persistent or recurrent cutaneous T-cell lymphoma ("CTCL"). In December 1999, the FDA approved Targretin® capsules for the treatment of CTCL in patients who are refractory to at least one prior systemic therapy. In June 2000, the FDA approved Targretin® gel for the treatment of patients with early stage CTCL.

The Company's other potential products are in various stages of development. Potential products that appear to be promising at early stages of development may not reach the market for a number of reasons. Most of the Company's revenues to date have been derived from its research and development agreements with major pharmaceutical collaborators. Prior to generating revenues from these products, the Company or its collaborators must complete the development of the products in the human health care market. No assurance can be given that: (1) product development efforts will be successful, (2) required regulatory approvals for any indication will be obtained, (3) any products, if introduced, will be capable of being produced in commercial quantities at reasonable costs or, (4) patient and physician acceptance of these products will be achieved. There can be no assurance that Ligand will ever achieve or sustain profitability.

The Company faces risks common to companies whose products are in various stages of development. These risks include, among others, the Company's need for additional financing to complete its research and development programs and commercialize its technologies. The Company expects to incur substantial additional research and development expenses, including continued increases in personnel and costs related to preclinical testing, clinical trials, and sales and marketing expenses related to product sales. The Company intends to seek additional funding sources of capital and liquidity through collaborative arrangements, collaborative research or through public or private financing. There is no assurance such funding would be available under favorable terms, if at all.

The Company believes that patents and other proprietary rights are important to its business. The Company's policy is to file patent applications to protect technology, inventions and improvements to its inventions that are considered important to the development of its business. The patent positions of pharmaceutical and biotechnology firms, including the Company, are uncertain and involve complex legal and technical questions for which important legal principles are largely unresolved.

2. Significant Accounting Policies

Principles of Consolidation

The consolidated financial statements include the accounts of the Company and its wholly owned subsidiaries. Intercompany accounts and transactions have been eliminated in consolidation. Certain reclassifications have been made to amounts included in the prior years financial statements to conform to the presentation for the year ended December 31, 2000.

Use of Estimates

The preparation of financial statements in conformity with accounting principles generally accepted in the United States requires management to make estimates and assumptions that affect the amounts reported in the financial statements and disclosures made in the accompanying notes to the consolidated financial statements. Actual results could differ from those estimates.

Cash, Cash Equivalents and Short-term Investments

Cash and cash equivalents consist of cash and highly liquid securities with original maturities at the date of acquisition of three months or less. Investments with an original maturity of more than three months are considered short-term investments and have been classified by management as available-for-sale. Such investments are carried at fair value, with unrealized gains and losses included as a separate component of stockholders' deficit.

Restricted Investments

Restricted investments consist primarily of a certificate of deposit held with a financial institution as collateral under an equipment financing arrangement.

Concentrations of Credit Risk

The Company invests its excess cash principally in United States government debt securities, investment grade corporate debt securities and certificates of deposit. The Company has established guidelines relative to diversification and maturities that maintain safety and liquidity. These guidelines are periodically reviewed and modified to take advantage of trends in yields and interest rates. The Company has not experienced any significant losses on its cash equivalents or short-term investments.

The Company extends credit on an uncollateralized basis primarily to wholesale drug distributors throughout the United States. The Company has not experienced significant credit losses on customer accounts.

Inventories

Inventories are stated at the lower of cost or market value. Cost is determined using the first-in-first-out method. Inventories consist of the following (in thousands):

	December 31,	
	2000	1999
Raw materials	$ 498	$ 705
Work-in-process	4,276	3,645
Finished goods	877	1,382
	$ 5,651	$ 5,732

Property and Equipment

Property and equipment is stated at cost and consists of the following (in thousands):

	December 31,	
	2000	1999
Land	$ 2,649	$ 2,649
Equipment and leasehold improvements	34,612	41,240
Less accumulated depreciation and amortization	(26,289)	(23,347)
	$ 10,972	$ 20,542

Depreciation of equipment is computed using the straight-line method over the estimated useful lives of the assets which range from three to fifteen years. Assets acquired pursuant to capital lease arrangements and leasehold improvements are amortized using the straight-line method over their estimated useful lives or their related lease term, whichever is shorter.

Acquired Technology

Acquired technology represents payments related to the Company's acquisition of its product ONTAK (see Note 6). Acquired technology is being amortized on a straight-line basis over the period estimated to be benefited of 15 years and consists of the following (in thousands):

	December 31,	
	2000	1999
Technology acquired in Seragen merger.....	$ 40,312	$ 40,312
Milestone payment to Eli Lilly	5,000	--
Less accumulated amortization	(4,388)	(1,343)
	$ 40,924	$ 38,969

Impairment of Long-Lived Assets

In accordance with Statement of Financial Accounting Standards ("SFAS") No. 121, Accounting for the Impairment of Long-Lived Assets and for Long-Lived Assets to be Disposed of, if indicators of impairment exist, the Company assesses the recoverability of the affected long-lived assets by determining whether the carrying value of such assets can be recovered through undiscounted future operating cash flows. If impairment is indicated, the Company measures the amount of such impairment by comparing the carrying value of the asset to the present value of the expected future cash flows associated with the use of the asset. While the Company's current and historical operating and cash flow losses are indicators of impairment, the Company believes the future cash flows to be received from the long-lived assets will exceed the assets' carrying value, and accordingly the Company has not recognized any impairment losses through December 31, 2000.

Fair Value of Financial Instruments

The carrying amount of cash, cash equivalents, short-term investments, receivables, restricted investments, accounts payable and accrued liabilities are considered to be representative of their respective fair values because of the short-term nature of those investments. It is not practicable to estimate the fair values of the Company's equipment financing obligations, convertible subordinated debentures, convertible note, and zero coupon convertible senior notes because of the lack of quoted market prices and the inability to estimate fair values without incurring excessive costs. However, management believes that the carrying amounts recorded at December 31, 2000 and 1999 approximates the corresponding fair value.

Revenue Recognition

The Company generates revenue from product sales, collaborative research and development arrangements, and other activities such as distribution agreements, royalties, sales of technology rights, and contract manufacturing services. The Company's collaborative arrangements and distribution agreements may include multiple elements within a single contract. Each element of the contract is separately negotiated. Payments received may include non-refundable fees at the inception of the contract for technology rights under collaborative arrangements or product rights under distribution agreements, fully burdened funding for services performed during the research phase of collaborative arrangements, milestone payments for specific achievements designated in the collaborative or distribution agreements, royalties on sales of products resulting from collaborative arrangements, and payments for the supply of products under distribution agreements.

Revenues from product sales are recognized upon shipment, net of allowances for returns, rebates and chargebacks. The Company is obligated to accept from customers the return of pharmaceuticals which have reached their expiration date. Contract manufacturing and collaborative research and development and other revenues are recognized as services are performed or products are delivered consistent with the performance requirements of the contract. Payments received in advance of performance or delivery are recorded as deferred revenue.

The composition of collaborative research and development and other revenues are as follows (in thousands):

	Year Ended December 31,		
	2000	1999	1998
Collaborative research and development ..	$ 23,135	$ 15,954	$ 16,914
Distribution agreements	922	3,250	--
Royalties	--	5,102	--
Other	1,143	2,672	353
	$ 25,200	$ 26,978	$ 17,267

Significant customers, which accounted for greater than 10% of total revenues, are as follows:

	Year Ended December 31,		
Customer	2000	1999	1998
Eli Lilly and Company	30.9%	24.7%	58.6%
Bergen Brunswig Drug Company	10.2%		
GlaxoSmithKline		21.1%	

In December 1999, the Securities and Exchange Commission issued Staff Accounting Bulletin ("SAB") No. 101, *Revenue Recognition in Financial Statements*. SAB No. 101 provides guidance in applying accounting principles generally accepted in the United States to revenue recognition in financial statements, including the recognition of non-refundable up-front fees and milestone payments received in conjunction with contractual arrangements that have multiple performance elements and require continuing involvement. SAB No. 101 requires that such fees be recognized as products are delivered or services are performed that represent the culmination of a separate earnings process.

The Company received non-refundable up-front fees of $18.75 million in 1997, $2.25 million in 1999, and $4.325 million in 2000. The Company initially recognized those payments as revenue upon receipt, as the fees were non-refundable and the Company had transferred technology or product rights at contract inception or incurred costs in excess of the up-front fees prior to initiation of each arrangement. However, under the provisions of SAB No. 101, non-refundable up-front fees must be deferred upon receipt and recognized as products are delivered or services are performed during the term of the arrangement. The Company implemented SAB No. 101 in the fourth quarter of 2000 as a change in accounting principle by deferring and recognizing these up-front payments over the term designated in the arrangement. The cumulative effect of this change to December 31, 1999, which was recorded in 2000, was $13.1 million or $0.24 per share. However, the effect on 2000 increased revenue and reduced loss before cumulative effect of change in accounting principle by $1.3 million or $0.02 per share. See the consolidated statements of operations and Note 13 for the cumulative and pro forma effects of implementing this new accounting pronouncement.

Costs and Expenses

Cost of products sold includes manufacturing costs, amortization of acquired technology, and royalty expenses associated with the Company's commercial products. Research and development costs are expensed as incurred. Costs and expenses included in research and development expenses related to collaborative research and development arrangements for the years ended December 31, 2000, 1999, and 1998 were $16.2 million, $16 million, and $17.3 million, respectively (see Note 9).

Loss Per Share

Net loss per share is computed using the weighted average number of common shares outstanding. Basic and diluted net loss per share amounts are equivalent for the periods presented as the inclusion of common stock equivalents in the number of shares used for the diluted computation would be anti-dilutive. Common stock equivalents excluded from weighted average common shares outstanding for the years ended December 31, 2000, 1999 and 1998 were 14.7 million, 15.9 million, and 10.9 million, respectively.

Accounting for Stock-Based Compensation

The Company accounts for stock-based compensation in accordance with Accounting Principles Board Opinion No. 25 ("APB No. 25"), *Accounting for Stock Issued to Employees*, and with the disclosure requirements of SFAS No. 123, *Accounting for Stock-Based Compensation* (see Note 8).

In March 2000, the Financial Accounting Standards Board ("FASB") issued FASB Interpretation No. 44 ("FIN 44"), *Accounting for Certain Transactions Involving Stock Compensation*. FIN 44 clarifies certain issues in the application of APB No. 25. Among other issues, FIN 44 clarifies (a) the definition of employee for purposes of applying APB No. 25, (b) the criteria for determining whether a plan qualifies as a non-compensatory plan, (c) the accounting consequence of various modifications to the terms of a previously fixed stock option or award, and (d) the accounting for an exchange of stock compensation awards in a business combination. FIN 44 became effective July 1, 2000, but certain conclusions cover specific events that occur after either December 15, 1998 or January 12, 2000. The adoption of FIN 44 did not have a material impact on the Company in 2000.

Foreign Currency Translation

Gains and losses resulting from foreign currency translation are accumulated as a separate component of stockholders' deficit as accumulated other comprehensive income (loss). Gains and losses resulting from foreign currency transactions are included in the consolidated statements of operations.

Segment Reporting

The Company currently operates in a single operating segment. The Company generates revenue from various sources that result primarily from its underlying research and development activities. In addition, financial results are prepared and reviewed by management as a single operating segment. The Company continually evaluates the benefits of operating in distinct segments and will report accordingly when such distinction is made.

3. Investments

The following table summarizes the various investment categories at (in thousands):

	Cost	Gross Unrealized Gains (Losses)	Estimated Fair Value
DECEMBER 31, 2000			
U.S. government securities	$ 2,290	$ 21	$ 2,311
Corporate obligations	9,955	104	10,059
Certificates of deposit	2,069	--	2,069
	14,314	125	14,439
Certificates of deposit-restricted	1,434	--	1,434
	$ 15,748	$ 125	$ 15,873
DECEMBER 31, 1999			
U.S. government securities	$ 2,610	$ (12)	$ 2,598
Corporate obligations	12,653	(45)	12,608
Certificates of deposit	2,046	--	2,046
	17,309	(57)	17,252
Certificates of deposit-restricted	2,011	--	2,011
Equity securities	693	(550)	143
	$ 20,013	$ (607)	$ 19,406

Equity securities as of December 31, 1999 are included in long-term other assets.

Net realized gains on sales of available-for-sale securities for the years ended December 31, 2000 and 1998 were $426,000 and $2 million, respectively. There were no material realized gains or losses for the year ended December 31, 1999.

The amortized cost and estimated fair value of investments at December 31, 2000 and 1999, by contractual maturity, are shown below (in thousands). Expected maturities will differ from contractual maturities because the issuers of the securities may have the right to prepay obligations without prepayment penalties.

	December 31, 2000		December 31, 1999	
	Cost	Estimated Fair Value	Cost	Estimated Fair Value
Due in one year or less	$ 9,601	$ 9,617	$ 5,606	$ 5,606
Due after one year through three years	5,522	5,620	13,714	13,657
Due after three years	625	636	--	--
	15,748	15,873	19,320	19,263
Equity securities	--	--	693	143
	$ 15,748	$ 15,873	$ 20,013	$ 19,406

4. Other Balance Sheet Details

Accounts receivable comprise the following (in thousands):

	December 31,	
	2000	1999
Trade accounts receivable	$ 3,540	$ 1,989
Less allowances.....	(716)	(332)
	$ 2,824	$ 1,657

Other assets comprise the following (in thousands):

	December 31,	
	2000	1999
Technology license.....	$ 4,000	$ --
Prepaid royalty buyout, net.....	3,672	3,944
Investment in X-Ceptor.....	3,378	5,246
Deferred rent.....	3,373	3,381
Intangible assets acquired.....	--	2,651
Other.....	1,020	1,222
	$ 15,443	$ 16,444

Accrued liabilities comprise the following (in thousands):

	December 31,	
	2000	1999
ONTAK obligation.....	$ 5,000	$ --
Compensation.....	2,412	2,981
Interest.....	1,985	1,972
Royalties.....	1,122	411
Other.....	2,156	2,809
	$ 12,675	$ 8,173

5. Strategic Alliance with Elan Corporation

In September 1998, the Company and Elan Corporation, plc ("Elan") signed a binding letter of agreement, which provided for financing to the Company and a license to Elan's product Morphelan. Significant provisions of these and subsequent arrangements are as follows:

Financing Arrangement

In 1998, Elan purchased approximately $20 million of the Company's Common Stock and $40 million in issue price of zero coupon convertible senior notes, due 2008 with an 8% per annum yield to maturity (the "Notes"), convertible into the Company's Common Stock at $14 per share. In 1999, the Company issued $40 million of Notes to Elan, convertible at $14 per share and $20 million of Notes, convertible at $9.15 per share. In December 1999, Elan converted Notes of $20 million plus accrued interest into 2,244,460 shares of the Company's Common Stock. The Company provided Elan a $2.2 million conversion incentive through the issuance of an additional 188,572 shares of the Company's Common Stock. In March 2000, Elan converted an additional $20 million in Notes plus accrued interest into 1,501,543 shares of the Company's Common Stock. The Company provided Elan a $2 million conversion incentive through the issuance of 98,580 shares of the Company's Common Stock. On December 29, 2000, the Company issued the final $10 million of Notes to Elan provided for under the terms of the agreement, convertible at $14.16 per share. The proceeds were received on January 2, 2001.

The financing arrangement with Elan contains an anti-dilution provision. In accordance with such provision and as a result of other equity issuances by the Company, the Company sold 52,712 shares of Common Stock and 91,406 warrants to Elan in 1999 for $839,000 and 416,667 shares of Common Stock in 2001 for $5 million. Assuming conversion of its outstanding Notes and warrants, Elan would own approximately 18.6% of Ligand's shares on a fully diluted basis.

License Agreement

Elan also agreed to exclusively license to the Company in the United States and Canada its proprietary product Morphelan™, a form of morphine for pain management in oncology and HIV patients. For the rights to Morphelan™ the Company paid Elan certain license fees in 1998, with milestone payments due upon the occurrence of certain events up to and including the approval of the NDA in the United

States. Payments may be in cash, or subject to certain conditions, in the

Company's Common Stock or Notes. In November 1998, the Company paid Elan $5 million through the issuance of 429,185 shares of the Company's Common Stock and $10 million from the issuance of Notes. In December 1999, the Company paid Elan $5 million through the issuance of 498,443 shares of the Company's Common Stock related to Elan completing patient enrollment for Morphelan phase III clinical trials. In June 2000, as a result of Elan's submission of the Morphelan NDA, the Company made a $4 million payment through the issuance of 367,183 shares of the Company's Common Stock. Elan could receive up to $5 million upon approval of Morphelan by the FDA. The Company is also committed to spend not less than $7 million through May 2003 to undertake additional clinical activities related to the commercialization of Morphelan. In the event the Company does not spend this amount, any short fall would be paid to Elan.

Distribution Agreement

In February 2001, the Company and Elan entered into a distribution agreement providing for the distribution of certain of the Company's products in various European and other international territories for a term of ten years. The Company received a payment at contract inception and may receive additional payments as products are submitted and approved in the territories.

6. Seragen

Merger

In August 1998, the Company completed a merger with Seragen (the "Merger"). Under the terms of the merger agreement, Ligand paid merger consideration at closing in the amount of $31.7 million, $5.7 million of which was in cash and $26 million of which was through the issuance of approximately 1,858,515 shares of the Company's Common Stock valued at $13.99 per share, representing the average closing share price for the five trading days prior to signing of the definitive agreement in May 1998. The merger agreement also called for an additional $37 million payment in cash and/or the Company's Common Stock, at the Company's option, to be paid six months after the date of receipt of final FDA approval to market ONTAK. The final FDA approval occurred in February 1999. In August 1999, the Company made a cash payment of $34.1 million. Pending resolution of final contingencies and in accordance with the terms of the merger agreement, the Company has withheld $2.7 million from payments made to certain Seragen stakeholders.

Conditional to the merger with Seragen, the Company had signed a definitive asset purchase agreement to acquire substantially all the assets of Marathon Biopharmaceuticals, LLC ("Marathon"), which provided manufacturing services to Seragen under a service agreement. The Company purchased substantially all of the assets of Marathon for $8 million through the issuance in January 1999 of 402,820 shares of the Company's Common Stock with a fair value of $5 million and a $3 million cash payment in August 1999, six months after the FDA approval of ONTAK.

The Merger was accounted for using the purchase method of accounting. The purchase price, totaling $84.1 million, which included liabilities assumed of $2.4 million, was allocated to the fair value of the assets acquired. The purchase price was composed of and allocated to the fair value of assets acquired as follows (in thousands):

Issuance of Common Stock (including transaction costs)	$ 25,996
Amounts due to Seragen stakeholders, Marathon and Lilly, payable in Common Stock or cash	50,000
Liabilities assumed	2,360
Net cash paid	5,756
	$ 84,112
Inventories	$ 3,230
Property and equipment	7,905
Identifiable intangible assets:	
Write-off of in-process technology	30,000
Acquired technology	40,312
Other intangibles	2,665
	$ 84,112

The following pro forma condensed statement of operations information has been prepared to give effect to the Merger as if such transaction had occurred at the beginning of the period presented. The historical results of operations have been adjusted to reflect (1) adjustment for depreciation resulting from adjusting the basis of certain property and equipment to fair value and amortization over 10 years, (2) amortization of acquired technology over 15 years, (3) elimination of Seragen compensation expense amortization, (4) elimination of interest income for Seragen and reduction of Ligand interest income resulting from use of $6 million for the Merger at an annual interest rate of 5.5%, and (5) elimination of interest expense

related to certain Seragen liabilities. The information presented is not necessarily indicative of the results of future operations of the merged companies. Included in the 1998 net loss is a one-time charge of $30 million related to in-process research and development included in the intangibles acquired.

Pro Forma Results of Operations (Unaudited)
(in thousands, except per share amount)

	Year Ended December 31, 1998
Revenues	$ 20,477
Net loss	$ (124,867)
Weighted average shares outstanding	40,392
Basic and diluted net loss per share	$ (3.09)

Arrangement With Lilly

In conjunction with the merger with Seragen, the Company entered into an agreement with Seragen and Eli Lilly and Company ("Lilly") under which Lilly assigned to the Company Lilly's rights and obligations under its agreements with Seragen, including its sales and marketing rights to ONTAK. The agreement provides for a $5 million milestone payment to Lilly upon approval of ONTAK by the FDA, a $5 million milestone payment to Lilly based on cumulative net sales of ONTAK reaching $20 million, royalties to Lilly on sales of ONTAK, and payments by Lilly to Ligand as reimbursement for certain ONTAK clinical and other costs incurred by the Company. In March 1999, Ligand issued to Lilly 434,546 shares of the Company's Common Stock as payment of the $5 million milestone for approval of ONTAK. In October 2000, cumulative net sales of ONTAK reached $20 million. The Company issued 412,504 shares of its Common Stock to Lilly in March 2001 as payment for this $5 million milestone (see Note 12). Revenues recognized for reimbursement of clinical and other costs for the years ended December 31, 2000, 1999 and 1998 were $1.1 million, $1 million and $353,000, respectively.

Sale of Contract Manufacturing Assets

In January 2000, Ligand sold the assets associated with the contract manufacturing business of Marathon for approximately $10.2 million. In connection with the sale, Seragen entered into a three-year supply and development agreement with the acquirer of the assets for the manufacture of ONTAK and the performance of certain process and production development work for Seragen's next-generation ONTAK product. During 2000, Ligand and Seragen made $2.6 million in purchases under the agreement. The assets sold consisted primarily of property and equipment of $6.7 million and intangibles of $2.7 million.

7. Commitments and Contingencies

Leases and Equipment Notes Payable

The Company has entered into capital lease and equipment note payable agreements which require monthly payments through December 2005 including interest ranging from 6.75% to 11.02%. The carrying value of equipment under these agreements at December 31, 2000 and 1999 was $18.8 million and $20.1 million, respectively. At December 31, 2000 and 1999, accumulated amortization was $8.1 and $7.9 million, respectively. The underlying equipment is used as collateral under the equipment notes payable.

The Company has also entered into operating lease agreements for office and research facilities with varying terms through July 2015. The agreements provide for increases in annual rentals based on changes in the Consumer Price Index or fixed percentage increases varying from 3% to 6%. One of these leases requires an irrevocable standby letter of credit of $1.3 million to secure the performance of the Company's lease obligations. Rent expense for the years ended December 31, 2000, 1999 and 1998 was $3.4 million, $3.2 million and $3.2 million, respectively.

At December 31, 2000, annual minimum payments due under the Company's leases and equipment notes payable are as follows (in thousands):

	Obligations under capital leases and equipment notes payable	Operating leases
2001	$ 4,037	$ 3,213
2002	2,893	2,937
2003	1,669	2,873
2004	659	2,929
2005	153	2,988
Thereafter	--	28,983
Total minimum lease payments	9,411	$ 43,923
Less amounts representing interest	(1,145)	
Present value of minimum lease payments	8,266	
Less current portion	3,478	
	$ 4,788	

Convertible Subordinated Debentures

The convertible subordinated debentures pay interest semi-annually at 7.5% per annum and are due in 2003. The difference between the face value and the fair value at the acquisition date is being accreted up to the face value over the remaining term of the debentures and the accretion is charged to interest expense. The debentures are convertible into the Company’s Common Stock at $26.52 per share.

Convertible Note

The note was issued in connection with the Company’s collaborative arrangement with SmithKline Beecham Corporation (see Note 9). The note is convertible into the Company’s Common Stock at $13.56 per share and is due October 2002. Interest on the note is payable semi-annually at prime (9.5% at December 31, 2000).

Royalty Agreements

The Company has royalty obligations under various technology license agreements. During 2000, royalties were accrued ranging from 1% to 13% of net sales and up to 50% on income generated under license or other royalty arrangements. Royalty expense for the years ended December 31, 2000, 1999 and 1998 was $3.5 million, $967,000 and $75,000, respectively.

In May 1998, the Company elected to make a final one-time $4.1 million royalty payment to The Salk Institute for Biological Studies as an alternative to paying future royalty payments based on total net sales of defined potential products. The one-time payment is being amortized over the life of the related patents of 17 years.

In September 1999, Ligand and Seragen entered into a sublicense agreement with Hoffmann-La Roche Inc. (“Roche”), with respect to Seragen’s rights under a family of patents called the “Strom Patents.” The Strom Patents, licensed by Seragen from Beth Israel Deaconess Medical Center (“Beth Israel”), cover the use of antibodies that target the interleukin-2 receptor to treat transplant rejection and autoimmune diseases. In consideration for the sublicense, Roche paid Seragen a $2.5 million royalty based on sales occurring before the date of the agreement plus Roche will pay royalties on subsequent sales of licensed products. Seragen will also receive milestone payments in the event Roche receives U.S. regulatory approval of licensed products. A non-exclusive license was previously issued by Seragen to Novartis requiring similar royalty payments. Beth Israel receives approximately 35% of the total royalty and milestone payments made related to the Strom Patents.

In December 1999, the Company and Seragen entered into an agreement with Pharmaceutical Partners LLC (“Pharma”) whereby Pharma purchased Seragen’s royalty stream to be received under the Roche and Novartis royalty agreements described above. Pharma paid $3.25 million in December 1999 and will pay an additional $3.25 million should sales exceed a predetermined amount in any of years 2001 through 2004. In addition, Seragen retains the patents and the right to receive the future milestone payments from Roche described above.

Litigation

The Company is subject to various lawsuits and claims with respect to matters arising out of the normal course of business. Due to the uncertainty of the ultimate outcome of these matters, the impact on future financial results is not subject to reasonable estimates.

8. Stockholders' Deficit

Authorized Shares

At its annual meeting of stockholders held on May 25, 2000, the Company's stockholders approved an increase in the authorized number of shares of Common Stock from 80,000,000 to 130,000,000.

Warrants

At December 31, 2000, the Company had outstanding warrants to purchase 1,240,119 shares of the Company's Common Stock. The warrants have exercise prices ranging from $10 to $20 per share and expire at various dates through October 6, 2006.

Treasury Stock

In 2000, under the terms of a previously established agreement with a collaborative research and development partner, the Company received 72,748 shares of its Common Stock as payment by the partner of a $900,000 development milestone. The stock had previously been sold to the partner at the inception of the collaborative arrangement. The stock was placed in treasury, which totaled 73,842 shares at December 31, 2000.

Stock Plans

The Company's 1992 Stock Option Stock Issuance Plan provides for the issuance of options to purchase up to 9,573,457 shares of the Company's Common Stock. The options granted generally have 10 year terms and vest over four years of continued employment. The Company's employee stock purchase plan also provides for the sale of up to 405,000 shares of the Company's Common Stock.

Following is a summary of the Company's stock option plan activity and related information:

	Shares	Weighted Average Exercise Price
Balance at January 1, 1998	4,068,506	$ 10.26
Granted	1,584,604	11.10
Exercised	(211,524)	7.52
Cancelled	(396,567)	11.30
Balance at December 31, 1998	5,045,019	10.56
Granted	894,792	10.67
Exercised	(228,991)	8.29
Cancelled	(405,361)	11.82
Balance at December 31, 1999	5,305,459	10.58
Granted	1,156,481	12.90
Exercised	(511,872)	9.25
Cancelled	(285,519)	11.63
Balance at December 31, 2000	5,664,549	$ 11.11
Options exercisable at December 31, 2000	3,736,967	$ 10.73
Options exercisable at December 31, 1999	3,344,575	$ 10.33
Options exercisable at December 31, 1998	2,814,876	$ 9.79

Following is a further breakdown of the options outstanding as of December 31, 2000:

Options Outstanding				Options Exercisable	
Range of exercise prices	Options outstanding	Weighted average remaining life in years	Weighted average exercise price	Number Exercisable	Weighted average exercise price
$4.62-$ 8.65	837,656	4.44	$ 7.35	748,617	$ 7.32
9.00- 9.60	959,381	5.58	9.39	742,466	9.34
9.77- 11.25	1,127,866	7.18	10.63	669,018	10.62
11.26- 13.00	1,680,241	7.46	12.11	987,990	12.25
13.25- 16.38	1,059,405	7.67	14.62	588,876	14.39
	5,664,549	6.68	$11.11	3,736,967	$10.73

At December 31, 2000, 391,870 shares were available under the plans for future grants of stock options or sale of stock.

Pro forma information regarding net loss and loss per share is required by SFAS No. 123, and has been determined as if the Company had accounted for its employee stock options under the fair value method of that Statement. The estimated weighted average fair value at grant date for the options granted during 2000, 1999 and 1998 was $8.32, $6.73, and $6.65 per option, respectively. The fair value for these options was estimated at the dates of grant using the Black-Scholes option valuation model with the following weighted-average assumptions for 2000, 1999 and 1998:

	2000	1999	1998
Risk free interest rates	4.75%	6.3%	4.8%
Dividend yields	--	--	--
Volatility	75%	70%	62%
Weighted average expected life	5 years	5 years	5 years

The Black-Scholes option valuation model was developed for use in estimating the fair value of traded options which have no vesting restrictions and are fully transferable. In addition, option valuation models require the input of highly subjective assumptions including the expected stock price volatility. Because the Company's employee stock options have characteristics significantly different from those of traded options, and because changes in the subjective input assumptions can materially affect the fair value estimate, in management's opinion, the existing models do not necessarily provide a reliable single measure of the fair value of its employee stock options.

For purposes of pro forma disclosures, the estimated fair value of the options is amortized to expense over the options' vesting period. The Company's pro forma information is as follows (in thousands, except for net loss per share information):

	Year Ended December 31,		
	2000	1999	1998
Net loss as reported	$ (72,376)	$ (74,719)	$ (117,886)
Net loss pro forma	(78,714)	(80,549)	(121,916)
Net loss per share as reported	(1.30)	(1.58)	(2.92)
Net loss per share pro forma	(1.41)	(1.71)	(3.01)

The pro forma effect on net loss for 2000, 1999 and 1998 is not representative of the pro forma effect on net loss in future years because it does not take into consideration pro forma compensation expense related to grants made prior to 1995.

Shareholder Rights Plan

In September 1996, the Company's Board of Directors adopted a preferred shareholder rights plan (the "Shareholder Rights Plan"), as amended, which provides for a dividend distribution of one preferred share purchase right (a "Right") on each outstanding share of the Company's Common Stock. Each Right entitles stockholders to buy 1/1000th of a share of Ligand Series A Participating Preferred Stock at an exercise price of $100, subject to adjustment. The Rights will become exercisable following the tenth day after a person or group announces an acquisition of 20% or more of the Common Stock, or announces commencement of a tender offer, the consummation of which would result in ownership by the person or group of 20% or more of the Common Stock. The Company will be entitled to redeem the Rights at $0.01 per Right at any time on or before the earlier of the tenth day following acquisition by a person or group of 20% or more of the Common Stock and September 13, 2006.

In November 1998, the Shareholder Rights Plan was amended to exclude Elan or any of its affiliates as an acquiring person to the extent of their ownership on or before November 9, 2005 of up to 25% of the Company's Common Stock on a fully diluted basis or thereafter to the extent their ownership exceeds 20% on November 9, 2005. However, shares acquired pursuant to the arrangements with Elan described in Note 5 are not counted in such determination unless additional shares of the Company's Common Stock have been acquired by Elan outside of such arrangements.

9. Collaborative Research and Development Agreements

The Company is party to various research and development collaborations with large pharmaceutical companies including Bristol-Myers Squibb Company, Organon Company, Eli Lilly and Company, SmithKline Beecham Corporation (now GlaxoSmithKline), American Home Products, Pfizer, Inc., Abbott Laboratories, Allergan, Inc., and Glaxo Wellcome plc (now GlaxoSmithKline). These arrangements generally provide for the license of certain technologies and a collaborative research period ranging from one to five years. Drugs resulting from these collaborations are then developed, manufactured and marketed by the corporate partners. The arrangements may provide for the Company to receive revenue from the transfer of technology rights at contract inception, collaborative research revenue during the research phase, milestone revenue for compounds moving through clinical development, and royalty revenue from the sale of drugs developed through the collaborative efforts.

The following are details regarding the collaborative arrangements that were in the research phase during the years ended December 31, 2000, 1999 and 1998.

Bristol-Myers Squibb

In May 2000, the Company entered into a research and development collaboration with Bristol-Myers Squibb to focus on the discovery, design and development of orally active compounds that selectively modulate the mineralocorticoid receptor. This receptor plays a critical role in many illnesses, particularly cardiovascular diseases such as congestive heart failure and hypertension. The initial research term concludes in May 2002. Bristol-Myers Squibb may extend the research term for up to two additional years. Collaborative research revenues recognized under the agreement for the year ended December 31, 2000 were $2 million.

Organon

In February 2000, the Company entered into a research and development collaboration with Organon to focus on small molecule compounds with potential effects for the treatment and prevention of gynecological diseases mediated through the progesterone receptor. The objective of the collaboration is the discovery of new non-steroidal compounds that are tissue-selective in nature and may have fewer side effects. Such compounds may provide utility in hormone replacement therapy, oral contraception, reproductive diseases, and other hormone-related disorders. The initial research phase concludes in February 2002. Organon may extend the research term for up to two additional years. Collaborative research revenues recognized under the agreement for the year ended December 31, 2000 were $2.7 million.

Parke-Davis

In September 1999, Ligand entered into a research and development collaboration with the Parke-Davis Pharmaceutical Research Division of Warner-Lambert Company (now part of Pfizer, Inc.) to discover, characterize, design and develop small molecule compounds with beneficial effects for the treatment and prevention of diseases mediated through the estrogen receptor. Some of the diseases affected by drugs that act upon the estrogen receptor are osteoporosis, cardiovascular disease, breast cancer, and mood and cognitive disorders. In 2000, Pfizer informed the Company that it would not extend the collaboration. Collaborative research revenues recognized under the agreement for the year ended December 31, 2000 were $2.5 million.

Eli Lilly

In November 1997, the Company entered into a research and development collaboration with Lilly for the discovery and development of products based on Ligand's Intracellular Receptor technology. Collaborative research revenues recognized under the agreement for the years ended December 31, 2000, 1999 and 1998 were $13.7 million, $9.1 million and $10 million, respectively. The initial research term concludes in November 2002. Lilly may extend the term for up to three additional years. The Company also had the option to obtain selected rights to one Lilly specialty pharmaceutical product. In connection with the August 1998 acquisition of Seragen, Ligand obtained from Lilly its rights to ONTAK and entered into an agreement where Lilly is to fund certain clinical and other regulatory costs incurred by Ligand as mandated by the FDA in

the approval of ONTAK (see Note 6).

GlaxoSmithKline

In February 1995, the Company entered into a research and development collaboration with SmithKline Beecham Corporation (now GlaxoSmithKline) to discover and characterize small molecule drugs to control hematopoiesis for the treatment of a variety of blood cell deficiencies. The research phase was completed in February 2001. Collaborative research revenues recognized under the agreement for the years ended December 31, 2000, 1999 and 1998 were $820,000, $2.7 million and $3 million, respectively. In April 1998, SmithKline Beecham and the Company initiated a new collaboration to develop small molecule drugs for the treatment or prevention of obesity. The research phase was completed in May 2000. Collaborative research revenues recognized under the agreement for the years ended December 31, 2000, 1999 and 1998 were $240,000, $1 million and $700,000, respectively.

American Home Products

In September 1994, the Company entered into a research and development collaboration with Wyeth-Ayerst Laboratories, the pharmaceutical division of American Home Products, to discover and develop drugs which interact with the estrogen or progesterone receptors. The research phase was completed in September 1998. Collaborative research revenues recognized under the agreement for the year ended December 31, 1998 were $1.3 million.

Abbott Laboratories

In July 1994 the Company entered into a research and development collaboration with Abbott Laboratories to discover and develop drugs for the prevention or treatment of inflammatory diseases. The research phase was completed in July 1999. Collaborative research revenues recognized under the agreement for the years ended December 31, 1999 and 1998 were $600,000 and $1.2 million, respectively.

10. X-Ceptor Therapeutics, Inc.

In June 1999, Ligand became a minority equity investor in a new private corporation, X-Ceptor Therapeutics, Inc. (“X-Ceptor”), whose mission is to conduct research in and identify therapeutic products from the field of orphan nuclear receptors. Ligand invested $6 million in X-Ceptor through the acquisition of convertible preferred stock and owns approximately 17% of X-Ceptor’s outstanding capital stock.

Ligand has the right but not the obligation to acquire all, but not less than all, of the outstanding X-Ceptor stock at June 30, 2002 or upon the cash balance of X-Ceptor falling below a pre-determined amount. Upon certain conditions, Ligand may extend the option by 12 months by providing additional funding of $5 million. The option price, payable pro-rata based on total cumulative non-Ligand funding, is up to $59.3 million at June 30, 2002 (or earlier, in certain circumstances) or up to $77.1 million upon extension. The option price may be paid in cash or shares of Ligand Common Stock, or any combination of the two, at Ligand’s sole discretion.

Ligand granted to X-Ceptor an exclusive license to use the Ligand orphan nuclear receptors technology that is not currently committed to other partnership programs and a nonexclusive license to use Ligand’s enabling proprietary process technology as it relates to drug discovery using orphan nuclear receptors. In 1999, X-Ceptor made a payment of $2 million to Ligand as reimbursement of a portion of Ligand’s prior research and development expenses incurred in the establishment of its orphan receptor program. Ligand recognized $1.7 million as revenue in 1999 representing the third-party ownership of X-Ceptor. Ligand has not performed any research and development activities on behalf of X-Ceptor.

Ligand also issued warrants to X-Ceptor investors, founders and certain employees to purchase 950,000 shares of Ligand Common Stock with an exercise price of $10 per share and expiration date of October 6, 2006. The warrants were recorded at their fair value of $4.20 per warrant or $3.9 million as deferred warrant expense within stockholders’ deficit and are being amortized to operating expense through June 2002. Amortization for the years ended December 31, 2000 and 1999 was $1.4 million and $530,000, respectively.

Ligand is accounting for its investment in X-Ceptor using the equity method of accounting. Ligand’s interest in X-Ceptor losses for the years ended December 31, 2000 and 1999 were $1.7 million and $754,000, respectively, which are included in other income (expense) in the consolidated statements of operations. Included in the losses recognized is the amortization of the $1.7 million excess of the Company’s investment in X-Ceptor over Ligand’s equity in the net assets acquired, which is being amortized through June 2002.

11. Income Taxes

At December 31, 2000, the Company had consolidated federal and combined California income tax net operating loss carryforwards of approximately $455 million and $88 million, respectively. The difference between the federal and California tax loss carryforwards is primarily attributable to the capitalization of research and development expenses for California income tax purposes and the 55% limitation on California loss carryforwards. Any unutilized federal tax loss carryforward will begin to expire in 2002. The California tax loss carryforwards began expiring in 1998. The Company also had foreign net operating loss carryforwards of approximately $5 million, which will begin to expire in 2001 unless previously utilized. The Company also had consolidated federal and combined California research tax credit carryforwards of approximately $20 million and $7 million, respectively, which will begin to expire in 2002 unless previously utilized.

Pursuant to Internal Revenue Code Sections 382 and 383, use of a portion of net operating loss and credit carryforwards will be limited because of cumulative changes in ownership of more than 50% which occurred within three periods during 1989, 1992 and 1996. However, the Company does not believe the limitations will have a material impact upon the future utilization of these carryforwards. In addition, use of Glycomed's and Seragen's preacquisition tax net operating and credit carryforwards will also be limited because the acquisitions by the Company represent changes in ownership of more than 50%. Such tax net operating loss and credit carryforwards have been reduced, including the related deferred tax assets.

The Company did not provide any current or deferred federal, state or foreign income tax provision or benefit for any period presented because it has experienced operating losses since inception. Significant components of the Company's deferred tax assets and liabilities as of December 31, 2000 and 1999 are shown below. A valuation allowance has been recognized to fully offset the net deferred tax assets as of December 31, 2000 and 1999 as realization of such assets is uncertain.

	December 31,	
	2000	1999
	(in thousands)	
Deferred tax liabilities:		
Acquired subordinated debt	$ 2,345	$ 3,270
Original issue discount	4,747	--
Purchased intangible assets	11,375	16,964
Total deferred tax liabilities	18,467	20,234
Deferred tax assets:		
Net operating loss carryforwards	166,156	144,440
Research and development credits	24,729	21,065
Capitalized research and development	11,859	9,366
Accrued expenses	1,328	910
Fixed assets and intangibles	8,226	5,898
Deferred revenue	5,743	--
Other, net	4,171	4,330
Total deferred tax assets	222,212	186,009
Net deferred tax assets	203,745	165,775
Valuation allowance for deferred tax assets.	(203,745)	(165,775)
	$ --	$ --

As of December 31, 2000, approximately $3.9 million of the valuation allowance for deferred tax assets related to benefits of stock option deductions which, when recognized, will be allocated directly to paid-in capital.

12. Subsequent Events

Private Placement

In January 2001, the Company raised net proceeds of approximately $22.4 million in a private placement of 2 million shares of its Common Stock.

Distribution Agreement

In February 2001, the Company entered into a distribution agreement with Elan (see Note 5).

Payment of ONTAK Obligation

In March 2001, the Company issued 412,504 shares of its Common Stock to Lilly in satisfaction of its $5 million milestone payable as a result of cumulative net sales of ONTAK reaching $20 million (see Note 6).

13. Summary of Unaudited Quarterly Financial Information

The following is a summary of the unaudited quarterly results of operations for the years ended December 31, 2000 and 1999 (in thousands, except per share amounts). The results for 2000 reflect the Company's adoption of SAB No. 101 in the fourth quarter of 2000 (see Note 2). The effect of the change on results previously reported for the first three quarters of 2000 are detailed below. The effect of the change on the fourth quarter of 2000 was to increase revenues and decrease net loss by $1.5 million or $0.03 per share. The pro forma effect assuming retroactive treatment of SAB No. 101 on each quarter of 1999 is also presented.

	Quarter Ended			
	March 31	June 30	September 30	December 31
2000 (RESTATED FOR SAB NO. 101)				
Total revenues	$ 10,816	$ 9,870	$ 13,591	$ 13,833
Cost of products sold	2,080	2,010	2,238	2,263
Research and development costs	12,498	12,766	13,229	12,794
Total operating costs and expenses	22,370	24,348	24,027	23,247
Net loss	(28,907)	(17,360)	(13,405)	(12,704)
Basic and diluted net loss per share	$ (0.54)	$ (0.31)	$ (0.24)	$ (0.22)
Weighted average number of common shares	53,804	55,600	56,605	56,642
Net loss originally reported	$(14,955)	$(16,459)	$(14,926)	
Cumulative effect to December 31, 1999	(13,099)	--	--	
Effect of change	(853)	(901)	1,521	
Net loss as restated	$(28,907)	$(17,360)	$(13,405)	
Basic and diluted per share amounts:				
Net loss originally reported	$ (0.28)	$ (0.30)	$ (0.26)	
Cumulative effect to December 31, 1999	(0.24)	--	--	
Effect of change	(0.02)	(0.01)	0.02	
Net loss as restated	$ (0.54)	$ (0.31)	$ (0.24)	
1999				
Total revenues	$ 10,281	$ 8,421	$ 9,765	$ 12,428
Cost of products and services sold	2,583	2,432	3,163	2,311
Research and development costs	14,469	14,612	15,717	14,644
Total operating costs and expenses	22,927	25,211	24,895	29,155
Net loss	(14,559)	(18,993)	(18,306)	(22,861)
Basic and diluted net loss per share	$ (0.32)	$ (0.40)	$ (0.39)	$ (0.48)
Weighted average number of common shares	45,794	47,033	47,476	47,938
Pro forma to reflect SAB No. 101:				
Net loss	$(15,122)	$(18,026)	$(17,339)	$(22,644)
Basic and diluted net loss per share	$ (0.33)	$ (0.38)	$ (0.37)	$ (0.47)

EXHIBIT 3.5

STATE OF DELAWARE

OFFICE OF THE SECRETARY OF STATE

PAGE 1

I, EDWARD J. FREEL, SECRETARY OF STATE OF THE STATE OF DELAWARE, DO HEREBY CERTIFY THE ATTACHED IS A TRUE AND CORRECT COPY OF THE CERTIFICATE OF AMENDMENT OF "LIGAND PHARMACEUTICALS INCORPORATED", FILED IN THIS OFFICE ON THE THIRTEENTH DAY OF JUNE, A.D. 2000, AT 9 O'CLOCK A.M.

A FILED COPY OF THIS CERTIFICATE HAS BEEN FORWARDED TO THE KENT COUNTY RECORDER OF DEEDS.

/s/EDWARD J. FREEL
[SEAL] ----------
Edward J. Freel, Secretary of State
AUTHENTICATION: 0494994
DATE: 06-14-00

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STATE OF DELAWARE
SECRETARY OF STATE
DIVISION OF CORPORATIONS
FILED 09:O0 AM 06/13/2000
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CERTIFICATE OF AMENDMENT
OF THE AMENDED AND RESTATED
CERTIFICATE OF INCORPORATION
OF

LIGAND PHARMACEUTICALS INCORPORATED
A DELAWARE CORPORATION

Ligand Pharmaceuticals Incorporated, a corporation organized and existing under and by virtue of the General Corporation Law of the State of Delaware (the "Corporation"), does hereby certify:

FIRST: That resolutions were duly adopted by the Board of Directors of the Corporation setting forth a proposed amendment to the Amended and Restated Certificate of Incorporation of the Corporation, and declaring said amendment to be advisable and recommended for approval by the stockholders of the Corporation. The resolutions setting forth the proposed amendment are as follows:

RESOLVED, that paragraph (A) of ARTICLE IV of the Amended and Restated Certificate of Incorporation of this Corporation is hereby amended to read in its entirety as follows:

(A) CLASSES OF STOCK. This corporation is authorized to issue two classes of stock to be designated, respectively, "Common Stock" and "Preferred Stock." The total number of shares of all classes of capital stock which this corporation shall have authority to issue is one hundred thirty-five million (135,000,000) of which one

hundred thirty million (130,000,000) shares of the par value of one-tenth of one cent ($.001) each shall be Common Stock and five million (5,000,000) shares of the par value of one-tenth of one cent ($.001) each shall be Preferred Stock. The number of authorized shares of Common Stock may be increased or decreased (but not below the number of shares thereof then outstanding) by affirmative vote of the holders of the majority of the shares of stock of this corporation entitled to vote in the election of directors.

SECOND: That, thereafter, the stockholders of said Corporation approved the amendment by vote of the outstanding shares in accordance with Sections 211 and 222 of the Delaware General Corporation Law.

THIRD: That said amendment was duly adopted in accordance with the provisions of Section 242 of the Delaware General Corporation Law.

FOURTH: That the capital of said Corporation shall not be reduced under or by reason of said amendment.

IN WITNESS WHEREOF, this Certificate of Amendment of Amended and Restated Certificate of Incorporation has been executed as of this 13th day of June, 2000.

LIGAND PHARMACEUTICALS INCORPORATED

By: /s/PAUL V. MAIER

Paul V. Maier, Senior Vice President and Chief Financial Officer

[SIGNATURE PAGE TO CERTIFICATE OF AMENDMENT]

THE SECURITY EVIDENCED HEREBY HAS NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "ACT"), MAY NOT BE SOLD, TRANSFERRED OR OTHERWISE DISPOSED OF IN THE ABSENCE OF AN EFFECTIVE REGISTRATION STATEMENT UNDER THE ACT OR PURSUANT TO A VALID EXEMPTION THEREFROM AND HAS BEEN SOLD IN RELIANCE ON THE EXEMPTION FROM REGISTRATION PROVIDED BY REGULATION S UNDER THE ACT ("REGULATION S"). THE SECURITY EVIDENCED HEREBY MAY NOT BE SOLD, TRANSFERRED OR OTHERWISE DISPOSED OF EXCEPT IN ACCORDANCE WITH THE PROVISIONS OF REGULATION S (SS.230.901 THROUGH SS.230.905, AND PRELIMINARY NOTES).

THE TRANSFER OF THE SECURITY EVIDENCED HEREBY IS SUBJECT TO THE CONDITIONS SPECIFIED IN THE SECURITIES PURCHASE AGREEMENT, DATED AS OF NOVEMBER 6, 1998, BY AND AMONG THE COMPANY, ELAN INTERNATIONAL SERVICES, LTD. AND ELAN CORPORATION, PLC, AND THE COMPANY RESERVES THE RIGHT TO REFUSE THE TRANSFER OF SUCH SECURITY UNTIL SUCH CONDITIONS HAVE BEEN FULFILLED WITH RESPECT TO SUCH TRANSFER. A COPY OF SUCH CONDITIONS WILL BE FURNISHED BY THE COMPANY TO THE HOLDER HEREOF WITHOUT CHARGE.

LIGAND PHARMACEUTICALS INCORPORATED

ZERO COUPON CONVERTIBLE SENIOR NOTE DUE 2008

No. R-5

Issue Date: December 29, 2000

Issue Price: $10,000,000
($539.56 for each $1,000 Principal Amount)

Original Issue Discount: $8,533,710
($460.44 for each $1,000 Principal Amount)

Ligand Pharmaceuticals Incorporated, a Delaware corporation, promises to pay to Monksland Holdings, B.V. or registered assigns, on November 9, 2008, the Principal Amount of Eighteen Million, Five Hundred and Thirty-three Thousand, Seven Hundred and Ten Dollars ($18,533,710) or such Principal Amount as may result from an Accrual Increase as specified on the other side of this Security.

This Security shall not bear interest except as specified on the other side of this Security. Original Issue Discount will accrue as specified on the other side of this Security. This Security is convertible into Common Stock as specified on the other side of this Security.

Additional provisions of this Security are set forth on the other side of this Security.

This Security is a Zero Coupon Convertible Note due 2008 issued pursuant to the Securities Purchase Agreement, dated as of November 6, 1998, by and among Ligand Pharmaceuticals Incorporated, Elan International Services, Ltd. and Elan Corporation, plc (the "Purchase Agreement").

IN WITNESS WHEREOF, Ligand Pharmaceuticals Incorporated has caused this instrument to be duly executed.

LIGAND PHARMACEUTICALS INCORPORATED

By: /s/DAVID E. ROBINSON

Name: David E. Robinson
Title: President and
Chief Executive Officer

Attest

By: /s/PAUL V. MAIER

Name: Paul V. Maier
Title: Senior Vice President,
Chief Financial Officer

Dated: December 29, 2000

LIGAND PHARMACEUTICALS INCORPORATED

ZERO COUPON CONVERTIBLE SENIOR NOTE DUE 2008

1. INTEREST

(a) This Security shall not bear interest, except as specified in this paragraph or in paragraph 12 hereof. If the Principal Amount hereof or any portion of such Principal Amount is not paid when due (whether upon acceleration pursuant to paragraph 9 hereof, upon the date set for payment of the Redemption Price pursuant to paragraph 3 hereof, upon the date set for payment of a Purchase Price or a Company Change of Control Purchase Price pursuant to paragraph 4 hereof, upon the date set for payment of the Elan Change of Control Purchase Price pursuant to paragraph 5 hereof or upon the Stated Maturity of this Security) or if shares of Common Stock (and cash in lieu of fractional shares) in respect of a conversion of this Security in accordance with paragraph 6 hereof are not delivered when due, then, in each such case, the overdue amount shall bear interest at the rate of 10.0% per annum, compounded semiannually (to the extent that the payment of such interest shall be legally enforceable), which interest shall accrue from the date such overdue amount was due to the date payment of such amount, including interest thereon, has been made. All such interest shall be payable on demand. The accrual of such interest on overdue amounts shall be in lieu of, and not in addition to, the continued accrual of Original Issue Discount.

(b) Original Issue Discount (the difference between the Issue Price and the Principal Amount of a Security) in the period during which a Security remains outstanding shall accrue at 8.0% per annum, on a semiannual bond equivalent basis using a 360-day year consisting of twelve 30-day months, commencing on the Issue Date of this Security, and shall cease to accrue on the earlier of (i) the date on which the Principal Amount hereof or any portion of such Principal Amount becomes due and payable and (ii) any Redemption Date, Purchase Date, Company Change of Control Payment Date, Elan Change of Control Payment Date or Conversion Date.

(c) In the event that the Company defaults in the performance or observance of any agreement, covenant, term or condition contained in the Registration Rights Agreement or the New Registration Rights Agreement, as the case may be, and such default continues for a period of 30 days after receipt by the Company of notice thereof (provided that, if such default is

not cured on or prior to the last day of such 30 day period and such breach is then capable of being cured and the Company is then working in good faith to cure such default, such 30 day period shall be extended by an additional 20 days from the last day of such 30 day period) (a "Registration Rights Default"), the Company acknowledges that the Holders of the Securities will suffer damages and

that it would not be feasible to ascertain the extent of such damages with precision. Accordingly, the Company agrees that, as liquidated damages, the rate at which Original Issue Discount or interest pursuant to paragraph 1(a) or 12 hereof, if any, accrues shall be increased over and above the rate stated in paragraph 1(b), 1(a) and 12(a), respectively (an "Accrual Increase"), by an additional 50 basis points for each 90-day period in which a Registration Rights Default continues; PROVIDED that the aggregate of such Accrual Increase shall not exceed 200 basis points over and above the rate set forth in paragraph 1(b), 1(a) and 12(a) hereof, as the case may be; PROVIDED, FURTHER, that any Accrual Increase shall immediately cease upon the cure of any such Registration Rights Default. Whenever, in this Security, there is mentioned, in any context, Principal Amount, Original Issue Discount or interest, or any other amount payable under or with respect to this Security, including the Redemption Price, the Purchase Price, the Company Change of Control Purchase Price and the Elan Change of Control Purchase Price, such mention shall be deemed to include mention of an Accrual Increase to the extent that, in such context, such Accrual Increase is, was or would be in effect.

2. METHOD OF PAYMENT

Holders must surrender Securities to the Company to collect payments in respect of the Securities. The Company will pay cash amounts in money of the United States that at the time of payment is legal tender for payment of public and private debts (and all references in the Securities to "$" or "dollars" shall refer to such currency) by wire transfer in immediately available funds, to an account or accounts designated in writing by each Holder not less than 5 Business Days prior to the date of the applicable payment.

3. REDEMPTION AT THE OPTION OF THE COMPANY

(a) No sinking fund is provided for the Securities. The Securities are redeemable as a whole at any time, or in part from time to time, at the option of the Company, at the redemption prices (each, a "Redemption Price") set forth in

paragraph 3(b) hereof; PROVIDED that the Securities are not redeemable prior to November 9, 2001.

(b) The table below shows the Redemption Prices of a Security per $1,000 Principal Amount on the dates shown below and at Stated Maturity, which prices reflect accrued Original Issue Discount calculated to each such date. The Redemption Price of a Security redeemed between such dates would include an additional amount reflecting the additional Original Issue Discount accrued since the next preceding date in the table to the actual Redemption Date.

<TABLE>
<CAPTION>

REDEMPTION DATE	(1) Security Issue Price	(2) Accrued Original Issue Discount	(3) Redemption Price At 8.0%	(1) + (2)
<S>	<C>	<C>	<C>	
November 9, 2001.....	$539.56	$37.92	$577.48	
November 9, 2002.....	539.56	85.04	624.60	
November 9, 2003.....	539.56	136.01	675.56	
November 9, 2004.....	539.56	191.13	730.69	
November 9, 2005.....	539.56	250.76	790.31	
November 9, 2006.....	539.56	315.25	854.80	
November 9, 2007.....	539.56	385.00	924.56	
At maturity.....	539.56	460.44	1,000.00	

</TABLE>

If converted to a semiannual coupon note following the occurrence of a Tax Event, the Securities will be redeemable at the Restated Principal Amount PLUS interest accrued and unpaid from, and including, the date of such

conversion to, but excluding, the Redemption Date.

(c) If less than all of the Securities are to be redeemed, the Company shall select the Securities to be redeemed pro rata. If any Security selected for redemption is thereafter surrendered for conversion in part, the converted portion of such Security shall be deemed (so far as may be), solely for purposes of determining the aggregate Principal Amount of Securities to be redeemed by the Company, the portion selected for redemption. Nothing in this paragraph 3 shall affect the right of any Holder to convert any Security pursuant to paragraph 6 hereof.

(d) Provisions of this Security that apply to the redemption of all of a Security also apply to the redemption of any portion of such Security.

(e) At least 30 days but not more than 60 days before a Redemption Date, the Company shall cause notice of redemption to be mailed, by first-class mail, postage prepaid, to each Holder of Securities at such Holder's address appearing on the register maintained by the Company. Such notice shall identify the Securities to be redeemed and shall state:

(i) the Redemption Date;

(ii) the Redemption Price;

(iii) the Conversion Price in effect on the date of such notice;

(iv) that Securities called for redemption may be converted at any time prior to the close of business on the Redemption Date;

(v) that Securities called for redemption must be surrendered to the Company to collect the Redemption Price and the procedures to be followed to so surrender such Securities;

(vi) if fewer than all the outstanding Securities are to be redeemed, the identification and Principal Amounts of the particular Securities to be redeemed;

(vii) that, unless the Company defaults in payment of the Redemption Price, Original Issue Discount on the Securities called for redemption and interest, if any, will cease to accrue on and after the Redemption Date;

(viii) that Holders whose Securities are being redeemed only in part will, without charge, be issued a new Security equal in Principal Amount to the unredeemed portion of the Securities; and

(ix) that the Redemption Price for any Security called for redemption will be paid one Business Day following the later of (x) the Redemption Date and (y) the date such Security is surrendered to the Company.

(f) Once notice of redemption is given, Securities called for redemption shall become due and payable on the Redemption Date and at the Redemption Price stated in such notice, except for Securities that are converted. The Redemption Price for the Securities called for redemption shall be paid one Business Day following the later of (x) the Redemption Date

and (y) the date such Securities are surrendered to the Company.

(g) Receipt by the Company of the Securities called for redemption prior to, on or after the Redemption Date shall be a condition to the receipt by the Holder of the Redemption Price therefor.

(h) Upon surrender of a Security that is redeemed in part, the Company shall, without charge, execute and deliver to the Holder a new Security equal in Principal Amount to the unredeemed portion of such Security.

4. PURCHASE BY THE COMPANY AT THE OPTION OF THE HOLDER

(a) PURCHASE AT THE OPTION OF THE HOLDER. The Company shall be obligated to purchase, at the option of the Holder, the Securities held by such Holder on the following purchase dates (each, a "Purchase Date") and at the following purchase prices per $1,000 Principal Amount (each, a "Purchase Price"), which Purchase Prices reflect accrued Original Issue Discount to each such date. Such Purchase Prices may be paid, at the option of the Company, in cash or by the issuance and delivery of shares of Common Stock, subject to the conditions set forth in paragraph 4(a)(iv) hereof.

<TABLE>
<CAPTION>

PURCHASE DATE	(1) Security Issue Price	(2) Accrued Original Issue Discount At 8.0%	(3) Purchase Price (1) + (2)
<S>	<C>	<C>	<C>
November 9, 2002.....	$539.56	$85.04	$624.60
November 9, 2005.....	539.56	250.76	790.31

</TABLE>

If, prior to the Purchase Date, the Securities have been converted to a semiannual coupon note following the occurrence of a Tax Event, the Purchase Price will be equal to the Restated Principal Amount PLUS interest accrued and unpaid from, and including, the date of such conversion to, but excluding, the Purchase Date.

(i) In order to have Securities purchased pursuant to this paragraph 4(a), the Holder shall (x) deliver to the Company (for each Security or portion thereof to be purchased) a written notice of purchase in the form attached to this Security as Annex A (a "Purchase Notice") at any time on or prior to the close of business on such

Purchase Date and (y) surrender such Securities to the Company prior to, on or after the Purchase Date, such surrender being a condition to receipt by the Holder of the Purchase Price therefor.

Provisions of this Security that apply to the purchase of all of a Security also apply to the purchase of any portion of such Security.

Subject to the right of a Holder to convert Securities as to which a Purchase Notice has been delivered into Common Stock at any time prior to the close of business on the Purchase Date, such Holder may not withdraw such Purchase Notice.

Any purchase of Securities contemplated pursuant to this paragraph 4(a) shall be consummated by the delivery of the Purchase Price to be received by the Holder (in cash or Common Stock, as the case may be) one Business Day following the later of (x) the Purchase Date and (y) the date such Securities are surrendered to the Company.

(ii) The Securities to be purchased pursuant to this paragraph 4(a) may be paid for, at the option of the Company, in cash or Common Stock, subject to the conditions set forth in paragraph 4(a)(iv) hereof. The Company shall designate, in the Company Notice (as defined below) delivered pursuant to paragraph 4(a)(v) hereof, whether the Company will purchase the Securities for cash or Common Stock; PROVIDED that the Company will pay cash for fractional shares of Common Stock pursuant to paragraph 4(a)(iv)(A) hereof. The Company may not change its election with respect to the consideration to be paid once the Company has given the Company Notice, except pursuant to paragraph 4(a)(iv)(B) hereof.

(iii) On each Purchase Date, if the Company Notice shall state that the Company will purchase Securities for cash, the Securities in respect of which a Purchase Notice has been given shall be purchased by the Company with cash in an amount equal to the aggregate Purchase Price of such Securities.

(iv) On each Purchase Date, if the Company Notice shall state that the Company will purchase Securities for Common Stock, the Securities in respect of which a Purchase Notice has been given shall be purchased by the Company by the issuance of a number of whole shares of Common

Stock equal to the quotient obtained by dividing (x) the amount of cash to which the Holder would have been entitled had the Company elected to pay the Purchase Price of such Securities in cash by (y) the average of the Closing Prices of the Common Stock for the 20 consecutive trading days ending on and including the second trading day immediately preceding the Purchase Date, subject to paragraph 4(a)(iv)(A) hereof.

(A) The Company will not issue a fractional share of Common Stock in payment of the Purchase Price. Instead, the Company will pay cash in an amount equal to the current market value of the fractional share. The current market value of a fraction of a share of Common Stock shall be determined by multiplying the average of the Closing Prices of the Common Stock for the 20 consecutive trading days ending on and including the second trading day immediately preceding the Purchase Date by such fraction and rounding to the nearest whole cent, with one-half cent being rounded upward. It is understood that if a Holder elects to have more than one Security purchased, the number of whole shares of Common Stock shall be based on the aggregate amount of Securities to be purchased.

(B) The Company's right to elect to purchase the Securities of any Holder through the issuance of shares of Common Stock shall be conditioned upon the following: (x) assuming compliance with all applicable state securities or "Blue Sky" laws, and assuming the accuracy of the statements of such Holder set forth in the Purchase Notice, the issuance of such shares of Common Stock shall be exempt from the registration requirements of Section 5 of the Securities Act, (y) no consent, approval, authorization or order of any court or governmental agency or body or third party shall be required for the issuance by the Company of such shares of Common Stock and (z) such Holder shall have received an Opinion of Counsel (which shall be included with the Company Notice) stating that the terms of the issuance of such Common Stock are in conformity with this paragraph 4(a), that such Common Stock has been duly authorized and, upon issuance, will be validly issued, nonassessable and fully paid, will not be issued in violation of any preemptive or similar rights and will be free of any liens, encumbrances or restrictions on transfer

imposed by the Company other than those imposed by the Securities Act and applicable state securities or "Blue Sky" laws (provided that such Opinion of Counsel may state that, insofar as it relates to the absence of preemptive or similar rights, it is given upon the best knowledge of such counsel) and that clause (x) of this paragraph 4(a)(iv)(B) has been satisfied.

(C) If the conditions set forth in paragraph 4(a)(iv)(B) hereof are not satisfied as of the Purchase Date, and the Company shall have elected to purchase the Securities through the issuance of shares of Common Stock, the Company shall, without further notice, pay the Purchase Price in cash.

(v) The Company shall cause a notice of its election to pay the Purchase Price with cash or Common Stock (the "Company Notice") to be sent by first-class mail, postage prepaid, to the Holders at their addresses appearing in the register maintained by the Company. The Company Notice shall be sent to Holders on a date not less than 20 Business Days prior to the Purchase Date (such date being herein referred to as the "Company Notice Date"); PROVIDED that, in the event that the Company shall not have delivered the Company Notice on or prior to the Company Notice Date, the Company shall be deemed to have irrevocably elected to pay the Purchase Price in cash. The Company Notice shall state the manner of payment elected and shall contain the following information:

In the event that the Company has elected to pay the Purchase Price with Common Stock, the Company Notice shall state that each Holder will receive Common Stock (except for any cash amount to be paid in lieu of fractional shares) in accordance with this paragraph 4(a) and shall be accompanied by the Opinion of Counsel described in paragraph 4(a)(iv)(B) hereof.

In any case, each Company Notice will include the Purchase Notice to be completed by the Holder and shall state:

(A) the Purchase Price on such Purchase Date and the Conversion Price in effect on the date of the Company Notice;

(B) that Securities must be surrendered to the Company to collect payment and any procedures to be followed in so surrendering the Securities;

(C) that Securities as to which a Purchase Notice has been given may be converted at any time prior to the close of business on the applicable Purchase Date;

(D) that, unless the Company defaults in the payment of the Purchase Price, Original Issue Discount on all Securities in respect of which a Purchase Notice has been delivered or interest, if any, will cease to accrue on and after the Purchase Date;

(E) that Holders whose Securities are being purchased only in part will, without charge, be issued a new Security equal in Principal Amount to the unpurchased portion of the Securities; and

(F) that the Purchase Price for any Security as to which a Purchase Notice has been given will be paid one Business Day following the later of (x) the Purchase Date and (y) the date such Security is surrendered to the Company.

(vi) All shares of Common Stock delivered upon purchase of the Securities shall be newly issued shares or treasury shares, shall be duly and validly issued, fully paid and nonassessable, shall not be issued in violation of any preemptive or similar rights and shall be free of any liens, encumbrances or restrictions on transfer other than those imposed by the Securities Act and applicable state securities or "Blue Sky" laws.

(vii) Receipt of such Security by the Company prior to, on or after the Purchase Date shall be a condition to the receipt by the Holder of the Purchase Price therefor.

(viii) On the Business Date immediately following the later of (x) the Purchase Date and (y) the date on which such Securities are surrendered to the Company, the Company shall deliver to each Holder entitled to receive Common Stock a certificate for the number of full shares of Common Stock issuable in payment of the Purchase Price and cash in lieu of any fractional shares.

(ix) If a Holder is paid in Common Stock, the Company shall pay any documentary, stamp or similar issue or transfer tax due on such issuance of Common Stock.

(x) Upon surrender of a Security that is to be purchased only in part, the Company shall, without charge, execute and deliver to the Holder a new Security equal in Principal Amount to the unpurchased portion of such Security.

(b) PURCHASE AT THE OPTION OF THE HOLDER UPON COMPANY CHANGE OF CONTROL. Upon a Change of Control of the Company, the Company shall be obligated to make an offer to purchase all outstanding Securities (the "Company Change of Control Offer") at a purchase price per $1,000 Principal Amount (the "Company

Change of Control Purchase Price") equal to the sum of (x) the Issue Price PLUS (y) accrued Original Issue Discount to the Company Change of Control Payment Date. If, prior to the Company Change of Control Payment Date, the Securities have been converted to a semiannual coupon note following the occurrence of a Tax Event, the Company Change of Control Purchase Price will be equal to the Restated Principal Amount PLUS interest accrued and unpaid from, and including, the date of such conversion to, but excluding, the Company Change of Control Payment Date.

(i) Within 10 days after the occurrence of a Change of Control of the Company, the Company shall cause a notice of the Company Change of Control Offer (the "Company Change of Control Offer Notice") to be sent by first-class mail, postage prepaid, to the Holders at their addresses appearing in the register maintained by the Company, stating:

(A) the event or events causing such Change of Control of the Company and the date such Change of Control occurred;

(B) that the Company Change of Control Offer is being made pursuant to this paragraph 4(b);

(C) the Company Change of Control Purchase Price and the purchase date (which shall be a Business Day no earlier than 10 days nor later than 30 days from the date such notice is mailed (the "Company Change of Control Payment Date"));

(D) that a Company Change of Control Purchase Notice (as defined below) must be delivered to the Company on or prior to the close of business on the Company Change of Control Payment Date and that Securities must be surrendered to the Company prior to, on or after the Company Change of Control Payment Date to collect payment, including any procedures to be followed in so surrendering the Securities;

(E) that any Security as to which a Company Change of Control Purchase Notice has not been delivered will continue to accrue Original Issue Discount or interest, if any;

(F) the Conversion Price in effect on the date of the Company Change of Control Offer Notice and any adjustments thereto resulting from such Change of Control;

(G) that the Securities as to which a Company Change of Control Purchase Notice has been given may be converted into Common Stock at any time prior to the close of business on the Company Change of Control Payment Date;

(H) that, unless the Company defaults in the payment of the Company Change of Control Payment, Original Issue Discount on all Securities as to which a Company Change of Control Purchase Notice has been delivered or interest, if any, will cease to accrue on and after the Company Change of Control Payment Date;

(I) that Holders whose Securities are being purchased only in part will, without charge, be issued a new Security equal in Principal Amount to the unpurchased portion of the Securities; and

(J) that the Company Change of Control Purchase Price for any Security as to which a Company Change of Control Purchase Notice has been given will be paid one Business Day following the later of (x) the Company Change of Control Payment Date and (y) the date such Security is surrendered to the Company.

(ii) A Holder may elect to have its Securities purchased pursuant to a Company Change of Control Offer upon delivery of a written notice of purchase (the "Company

Change of Control Purchase Notice") to the Company at any time prior to the close of business on the Company Change of Control Payment Date, stating:

(A) the certificate number of each Security which the Holder will deliver to be purchased; and

(B) the portion of the Principal Amount of such Security which the Holder has elected to have purchased.

(iii) Receipt of such Security by the Company prior to, on or after the Company Change of Control Payment Date shall be a condition to the receipt by the Holder of the Company Change of Control Purchase Price therefor.

(iv) Provisions of this Security that apply to the purchase of all of a Security also apply to the purchase of any portion of such Security.

(v) Any purchase of Securities contemplated pursuant to this paragraph 4(b) shall be consummated by the delivery of the Company Change of Control Purchase Price to be received by the Holder one Business Day following the later of (x) the Company Change of Control Payment Date and (y) the date such Securities are surrendered to the Company.

(vi) If any Security is to be purchased only in part, the Company shall, without charge, issue to the Holder a new Security equal in Principal Amount to the unpurchased portion of such Security.

(vii) The Company will comply with the requirements of Section 14(e) under the Exchange Act and any other securities laws and regulations thereunder to the extent such laws and regulations are applicable in connection with the repurchase of the Securities pursuant to a Company Change of Control Offer. To the extent that the provisions of any securities laws or regulations conflict with the provisions of this paragraph 4(b), the Company shall comply with the applicable securities laws and regulations and shall not be deemed to have breached its obligations under this paragraph 4(b) by virtue thereof.

5. PURCHASE AT THE OPTION OF THE COMPANY UPON ELAN CHANGE OF CONTROL

(a) Upon a Change of Control of Elan occurring prior to November 9, 2001, the Company may, at its option, repurchase (the "Elan Change of Control Purchase") the Securities held by Elan or any of its Affiliates on the date of such Change of Control, in whole but not in part, at a cash purchase price per $1,000 Principal Amount (the "Elan Change of Control Purchase Price") equal to the greater of (i) the sum of (A) the Issue Price PLUS (B) accrued Original Issue Discount to the Elan Change of Control Payment Date (provided that if, prior to the Elan Change of Control Payment Date, the Securities have been converted to a semiannual coupon note following the occurrence of a Tax Event, the sum set forth in this clause (i) shall be the Restated Principal Amount PLUS interest accrued and unpaid from, and including, the date of such conversion to, but excluding, the Elan Change of Control Payment Date) and (ii) the product of (a) the number of shares of Common Stock into which the Securities to be redeemed may be converted pursuant to paragraph 6 hereof on the day immediately preceding the Elan Change of Control Payment Date and (b) the average of the Closing Prices of the Common Stock for the 20 consecutive trading days ending on and including the second trading day immediately prior to the Elan Change of Control Payment Date (as defined below); PROVIDED that, as a condition to any such repurchase, the Company shall repurchase all, but not less than all, of the Initial Shares, the Shares, the Conversion Shares and the License Shares, in each case, held by Elan and its Affiliates on the date of such Change of Control, pursuant to and in accordance with the terms of the Purchase Agreement.

(b) If an Elan Change of Control Purchase is to be made by the Company, the Company shall, on or prior to the 10th day following receipt of an Elan Change of Control Notice, cause an irrevocable notice of the Elan Change of Control Purchase (the "Elan Change of Control Purchase Notice") to be sent by first-class mail, postage prepaid, to Elan stating:

(i) that the Elan Change of Control Purchase is being made pursuant to this paragraph 5;

(ii) the Elan Change of Control Purchase Price and the purchase date (which shall be a Business Day no earlier than 10 days nor later than 20 days from the date of the Elan Change of Control Purchase Notice (the "Elan Change of Control Payment Date"));

(iii) that the Elan Change of Control Purchase Price for any Security as to which the Elan Change of Control Purchase Notice relates will be paid on the Business Day following the later of (x) the Elan Change of Control Payment Date and (y) the date such Security is surrendered to the Company;

(iv) that Elan shall, and shall cause its Affiliates to, surrender to the Company on or prior to the Elan Change of Control Payment Date all Securities owned by any of them on the date of the Change of Control of Elan and the procedures to be followed in so surrendering such Securities; and

(v) that, unless the Company defaults in the payment of the Elan Change of Control Purchase Price, Original Issue Discount on all such Securities or interest, if any, will cease to accrue on and after the Elan Change of Control Payment Date and, effective upon the date of the Change of Control of Elan, such Securities shall cease to be convertible.

(c) In the event that the Company fails to deliver the Elan Change of Control Purchase Notice on or prior to the 10th day following receipt of an Elan Change of Control Notice pursuant to paragraph 5(b) hereof, such failure shall be deemed to be a waiver by the Company of its right to repurchase the Securities pursuant to this paragraph 5.

(d) Upon the giving of the Elan Change of Control Purchase Notice pursuant to this paragraph 5, such notice may not be revoked by the Company and all Securities as to which such Elan Change of Control Purchase Notice relates shall become due and payable in accordance with this paragraph 5 at the Elan Change of Control Purchase Price.

(e) Receipt of such Securities by the Company prior to, on or after the Elan Change of Control Payment Date shall be a condition to the receipt by the Holder of the Elan Change of Control Purchase Price therefor.

6. CONVERSION

(a) A Holder of a Security may, on or prior to November 9, 2008, convert in whole at any time or in part from time to time such Security into Common Stock; PROVIDED, HOWEVER, that if a Security is called for redemption, the Holder may convert it at any time before the Redemption Date. A Secu-

rity in respect of which the Holder has delivered a Purchase Notice or a Company Change of Control Purchase Notice exercising the option of such Holder to require the Company to purchase such Security may, notwithstanding such notice, convert the Security in accordance with this paragraph 6 until the close of business on the Payment Date or the Company Change of Control Payment Date, as the case may be. Upon the occurrence of a Change of Control of Elan, the Securities then held by Elan and its Affiliates may not be converted on or prior to the 10th day following the giving of an Elan Change of Control Notice; PROVIDED that, if an Elan Change of Control Purchase Notice is given by the Company pursuant to paragraph 5(b) hereof, the Securities may not be converted unless the Company defaults in the payment of the Elan Change of Control Purchase Price for all Securities as to which such Elan Change of Control Purchase Notice relates. Notwithstanding the foregoing, neither Elan nor any of its Affiliates may convert any Security held by it if, at the time of such conversion, Elan is in violation of Section 14(c) of the Purchase Agreement.

(b) This Security shall be convertible into a number shares of Common Stock equal to (x) the Issue Price PLUS all accrued Original Issue Discount to the applicable Conversion Date (as defined below) (provided that if, prior to

the applicable Conversion Date, the Securities have been converted to a semiannual coupon note following the occurrence of a Tax Event, this clause (x) shall be the Restated Principal Amount PLUS interest accrued and unpaid from, and including, the date of such conversion to, but excluding, such Conversion Date) DIVIDED BY (y) $14.16, as adjusted to the Conversion Date (the "Conversion Price"). Provisions of this Security that apply to conversion of all of a Security also apply to conversion of a portion of such Security.

(c) The shares of Common Stock issuable upon conversion of this Security shall, to the extent required, bear the following legends:

> THE SHARES REPRESENTED BY THIS CERTIFICATE HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "ACT"), AND MAY NOT BE SOLD, TRANSFERRED OR OTHERWISE DISPOSED OF IN THE ABSENCE OF AN EFFECTIVE REGISTRATION STATEMENT UNDER THE ACT OR PURSUANT TO A VALID EXEMPTION THEREFROM. THE SHARES REPRESENTED BY THIS CERTIFICATE MAY NOT BE SOLD, TRANSFERRED OR OTHERWISE DISPOSED OF EXCEPT IN

> ACCORDANCE WITH THE PROVISIONS OF REGULATION S (SS.230.901 THROUGH SS.230.905, AND PRELIMINARY NOTES). HEDGING TRANSACTIONS INVOLVING THE SHARES REPRESENTED BY THIS CERTIFICATE MAY NOT BE CONDUCTED UNLESS IN COMPLIANCE WITH THE ACT.
>
> THE TRANSFER OF THE SHARES REPRESENTED BY THIS CERTIFICATE IS SUBJECT TO THE CONDITIONS SPECIFIED IN A SECURITIES PURCHASE AGREEMENT, DATED AS OF NOVEMBER 6, 1998, BY AND AMONG THE COMPANY, ELAN INTERNATIONAL SERVICES, LTD. AND ELAN CORPORATION, PLC, AND THE COMPANY RESERVES THE RIGHT TO REFUSE THE TRANSFER OF SUCH SHARES UNTIL SUCH CONDITIONS HAVE BEEN FULFILLED WITH RESPECT TO SUCH TRANSFER. A COPY OF SUCH CONDITIONS WILL BE FURNISHED BY THE COMPANY TO THE HOLDER HEREOF WITHOUT CHARGE.

(d) To convert this Security a Holder must (i) complete and duly sign a conversion notice in the form attached hereto as Annex B (the "Conversion Notice") and deliver such notice to the Company and (ii) surrender this Security to the Company. The date on which a Holder of Securities satisfies all the foregoing requirements is the conversion date (the "Conversion Date"). Not more than three Business Days after the Conversion Date, the Company shall deliver to the Holder a certificate for the number of full shares of Common Stock issuable upon such conversion and cash in lieu of any fractional share. The Person in whose name the certificate is registered shall be treated as a stockholder of record on and after the Conversion Date; PROVIDED, HOWEVER, that no surrender of a Security on any date when the stock transfer books of the Company shall be closed shall be effective to constitute the Person or Persons entitled to receive the shares of Common Stock upon such conversion as the record holder or holders of such shares of Common Stock on such date, but such surrender shall be effective to constitute the Person or Persons entitled to receive such shares of Common Stock as the record holder or holders thereof for all purposes at the close of business on the next succeeding day on which such stock transfer books are open; such conversion shall be at the Conversion Price in effect on the date that such Security shall have been surrendered for conversion, as if the stock transfer books of the Company had not been closed. Upon conversion of a Security, such Person shall no

longer be a Holder of such Security. Any Security for which a Conversion Notice is delivered on any Business Day shall be deemed to be converted simultaneously with all other Securities for which a Conversion Notice is delivered on such Business Day, subject to the surrender of such Securities to the Company pursuant to this paragraph 6.

(e) If a Holder converts more than one Security at the same time, the number of shares of Common Stock issuable upon such conversion shall be based on the sum of (x) the aggregate Issue Price PLUS (y) the aggregate accrued Original Issue Discount, in each case, of the Securities converted; PROVIDED that if, prior to the applicable Conversion Date, the Securities have been converted to a semiannual coupon note following the occurrence of a Tax Event, such conversion shall be based on the sum of (x) the aggregate Restated Principal Amount PLUS (y) the aggregate interest accrued and unpaid from, and including, the date of such conversion to, but excluding, such Conversion Date. Upon surrender of a Security that is converted in part, the Company shall execute and deliver to the Holder a new Security in a denomination equal in Principal Amount to the unconverted portion of the Security surrendered. If the last day on which a Security may be converted is not a Business Day, such Security may be surrendered to the Company on the next succeeding Business Day.

(f) The Company shall not issue a fractional share of Common Stock upon conversion of a Security. Instead, the Company shall deliver cash in an amount equal to the current market value of the fractional share. The current market value of a fraction of a share shall be determined to the nearest 1/10,000th of a share by multiplying the average of the Closing Prices of the Common Stock for the 20 consecutive trading days immediately prior to the applicable Conversion Date by such fraction and rounding to the nearest whole cent, with one-half cent being rounded upward.

(g) If a Holder converts a Security, the Company shall pay any documentary, stamp or similar issue or transfer tax due on the issue of shares of Common Stock upon such conversion.

(h) The Company shall reserve out of its authorized but unissued Common Stock a sufficient number of shares of Common Stock to permit the conversion of the Securities. All shares of Common Stock delivered upon conversion of the Securities shall be newly issued shares or treasury shares, shall be validly issued, nonassessable and fully paid, shall not be is-

sued in violation of any preemptive or similar rights and shall be free of any liens, encumbrances or restrictions on transfer imposed by the Company other than those imposed by the Securities Act and applicable state securities or "Blue Sky" laws. The Company shall cause all such reserved shares of Common Stock to be listed on the Nasdaq National Market or any other United States securities exchange or market where the Common Stock is principally traded.

(i) The Conversion Price shall be adjusted from time to time by the Company as follows:

(i) In case the Company shall, at any time or from time to time on or after the Issue Date, (A) pay a dividend or make a distribution on its Common Stock in shares of Common Stock, (B) subdivide its outstanding Common Stock into a greater number of shares, (B) combine its outstanding Common Stock into a smaller number of shares or (D) issue by reclassification of its Common Stock any other shares of its Capital Stock, then, in each such case, the Conversion Price in effect immediately prior to such action shall be adjusted so that the Holder of any Security thereafter surrendered for conversion shall be entitled to receive the number of shares of Common Stock or other Capital Stock of the Company which such Holder would have owned or have been entitled to receive after the happening of any of the events described above had such Security been converted immediately prior to the happening of such event. If any dividend or distribution of the type described in clause (A) above is not so paid or made, the Conversion Price shall again be adjusted to the Conversion Price which would then be in effect if such dividend or distribution had not been declared. An adjustment made pursuant to this paragraph 6(i)(i) shall become effective immediately after the record date in the case of a dividend or distribution and shall become effective immediately after the effective date in the case of subdivision, combination or reclassification. If, after an adjustment made pursuant to this paragraph 6(i)(i), the Holder of any Security thereafter converted shall become entitled to receive shares of two or more classes of Capital Stock of the Company, the board of directors of the Company shall determine the allocation of the adjusted Conversion Price between or among such classes of Capital Stock, which determination shall be final and binding on all Holders. After such

allocation, the Conversion Price of each class of Capital Stock of the Company shall there-

after be subject to adjustment on terms comparable to those applicable to Common Stock in this paragraph 6(i).

(ii) If, at any time or from time to time on or after the Issue Date, the Company issues or sells any Common Stock for consideration in an amount per share less than the average of the Closing Prices of the Common Stock for the 20 consecutive trading days ending on and including the second trading day immediately prior to such issuance or sale, the Conversion Price shall be adjusted in accordance with the following formula:

$$E' = E \times \frac{O + M}{O + \frac{P}{A}}$$

where:

E' = the adjusted Conversion Price.

E = the then current Conversion Price.

O = the number of shares of Common stock outstanding immediately prior to the issuance or sale of such additional shares of Common Stock.

P = the aggregate consideration received for the issuance or sale of such additional shares of Common Stock.

M = the average Closing Prices of the Common Stock for the 20 consecutive trading days ending on and including the second trading day immediately prior to the date of the issuance or sale of such additional shares of Common Stock.

A = the number of shares of Common Stock outstanding immediately after the issuance or sale of such additional shares of Common Stock.

The adjustments shall be made successively whenever any such issuance or sale is made, and shall become effective immediately after such issuance or sale.

This paragraph 6(i)(ii) does not apply to:

(A) the issuance of the License Shares pursuant to and in accordance with the License Agreement and the Purchase Agreement;

(B) the conversion of the Securities or the conversion, exercise or exchange of any other securities convertible into, or exercisable or exchangeable for, Common Stock;

(C) the issuance of Common Stock pursuant to a valid and binding written agreement with any Person, the terms of which provide that such Common Stock is to be issued on a date after the execution of such agreement and upon the occurrence of specified events (other than solely the passage of time);

(D) the issuance Common Stock to the shareholders of any Person which mergers into the Company or any Subsidiary of the Company in proportion to such shareholders' ownership of the securities of such Person, upon such merger; or

(E) Common Stock issued in a bona fide public offering pursuant to a firm commitment or "best efforts" underwriting.

(iii) If, at any time or from time to time on or after the Issue Date, the Company shall issue rights, options or warrants to all holders of its Common Stock entitling them (for a period expiring within 60 days after the record date mentioned below) to subscribe for or purchase shares of Common Stock at a price per share less than the greater of (x) the average of the Closing Prices of the Common Stock for the 20 consecutive trading days ending on and including the second trading day immediately prior to the record date and (y) the then current Conversion Price, the Conversion Price shall be adjusted in accordance with the following formula:

$$E' = E \times \frac{O + \frac{N \times P}{M}}{O + N}$$

where:

E' = the adjusted Conversion Price.

E = the then current Conversion Price.

O = the number of shares of Common Stock outstanding on the record date fixed for determination of stockholders entitled to participate in such issuance.

N = the number of additional shares of Common Stock offered pursuant to such issuance.

P = the offering price per share of such additional shares of Common Stock.

M = the greater of (x) the average of the Closing Prices of the Common Stock for the 20 consecutive trading days ending on and including the second trading day immediately prior to the record date and (y) the then current Conversion Price.

The adjustment shall be made successively whenever any such issuance is made and shall become effective immediately after the record date fixed for the determination of stockholders entitled to participate in such issuance.

To the extent that shares of Common Stock are not delivered after the expiration of such rights, options or warrants, the Conversion Price shall be readjusted to the Conversion Price which would then be in effect had the adjustments made upon the issuance of such rights, options or warrants been made on the basis of delivery of only the number of shares of Common Stock actually delivered. If such rights, options or warrants are not so issued, the Conversion Price shall again be adjusted to be the Conversion Price which would then be in effect if the record date for the determination of stockholders entitled to participate in such distribution had not been fixed. In determining whether any rights, options or warrants entitle the Holders to subscribe for or purchase shares of Common Stock at a price per share less than the average of the Closing Prices of the Common Stock for the 20 consecutive trading days ending on and including the second trading day immediately preceding the record date, and in determining the aggregate offering price of such shares of Common Stock, there shall be taken into account any consideration received by the Company for such rights, options or warrants, the value of such consideration, if other than cash, to be determined in good faith by the board of directors of the Company (irrespective of the accounting treatment thereof), which determination shall be final and binding on all Holders. Such determination

shall be described in a board resolution. Notwithstanding the foregoing provisions of this paragraph 6(i)(iii), an event which would otherwise give rise to an adjustment under this paragraph 6(i)(iii) shall

not give rise to such an adjustment if the Company includes the Holders in such distribution on a pro rata basis as if each such Holder held the number of shares of Common Stock into which such Holder's Securities are convertible on the record date fixed for determination of the stockholders entitled to participate in such distribution and with the same notice as is provided to such stockholders.

This paragraph 6(i)(iii) does not apply to transactions described in paragraph 6(i)(iv).

(iv) If, at any time or from time to time on or after the Issue Date, the Company shall, by dividend or otherwise, distribute to all holders of its Common Stock any class of Capital Stock of the Company (other than Common Stock) or evidences of its indebtedness or assets (excluding cash dividends or other cash distributions from current or retained earnings other than any Extraordinary Cash Dividend) or rights, options or warrants to subscribe for or purchase any of the foregoing, the Conversion Price shall be adjusted in accordance with the following formula:

$$E' = \frac{E \times M - F}{M}$$

where

E' = the adjusted Conversion Price.

E = the then current Conversion Price.

M = the greater of (x) the average of the Closing Prices of the Common Stock for the 20 consecutive trading days ending on and including the second trading day immediately prior to the record date mentioned below and (y) the then current Conversion Price.

F = the fair market value on the record date fixed for determination of the stockholders entitled to participate in such distribution of the assets, securities, rights, options or warrants applicable to one share of Common stock. The

board of directors shall determine such fair market value in good faith (irrespective of the accounting treatment thereof), which determination shall be final and binding on the Holders. Such determination shall be described in a board resolution.

The adjustment shall be made successively whenever any such distribution is made and shall become effective immediately after the record date fixed for the determination of stockholders entitled to receive such distribution. To the extent that shares of Common Stock are not so delivered after the expiration of such rights, options, or warrants, the Conversion Price shall be readjusted to the Conversion Price which would then be in effect had the adjustment made upon the issuance of such rights, options or warrants been made on the basis of the delivery of only the number of shares of Common Stock actually delivered. Notwithstanding the foregoing provisions of this paragraph 6(i)(iv), an event which would otherwise give rise to an adjustment under this paragraph 6(i)(iv) shall not give rise to such an adjustment if the Company includes the Holders in such distribution on a pro rata basis as if each such Holder held the number of shares of Common Stock into which such Holder's Securities are convertible on the record date fixed for determination of the stockholders entitled to participate in such distribution and with the same notice as is provided to such stockholders.

This paragraph 6(i)(iv) does not apply to any transaction described in paragraph 6(i)(iii) hereof.

(v) If, at any time or from time to time on or after the Issue Date, the Company shall (x) enter into any valid and binding written agreement with any Person to issue or sell Common Stock on a date after the execution

of such agreement and upon the occurrence of specified events (other than solely the passage of time) or (y) issue or sell any securities convertible into, or exercisable or exchangeable for, Common Stock, in each case, for consideration per share of Common Stock less than the average of the Closing Prices of the Common Stock for the 20 consecutive trading days ending on and including the second trading day immediately prior to, in the case of clause (x), the date of execution of such agreement, and, in the case of clause (y), the date of such issuance or sale, the Conversion Price shall be adjusted in accordance with the following formula:

$$E' = E \times \frac{O + M}{O + D - P}$$

where:

E' = the adjusted Conversion Price.

E = the then current Conversion Price.

O = the number of shares of Common Stock outstanding immediately prior to, in the case of clause (x) above, the date of execution of such agreement, and, in the case of clause (y) above, the issuance or sale of such securities.

P = (a) in the case of clause (x) above, the minimum aggregate amount of consideration payable to the Company upon the issuance or sale of such Common Stock (including the minimum aggregate amount of cash payments to be made by the Company to the other Person or Persons party to such agreement in lieu of which such Common Stock may be issued) and (b) in the case of clause (y) above, the aggregate consideration received for the issuance or sale of such securities PLUS the minimum aggregate amount of additional consideration, other than the surrender of such securities, payable to the Company upon conversion, exercise or exchange of such securities.

M = the Closing Prices of the Common stock for the 20 consecutive trading days ending on and including the second trading day immediately prior to, in the case of clause (x) above, the date of execution of such agreement, and, in the case of clause (y) above, the date of such issuance or sale.

D = the maximum stated number of shares deliverable pursuant to such agreement or upon conversion, exercise or exchange of such securities, as the case may be.

The adjustment shall be made successively whenever any such agreement is executed or such issuance or sale is made, and shall become effective immediately after the execution of such agreement or such issuance or sale.

If all of the Common Stock deliverable pursuant to any such agreement or upon conversion, exercise or exchange of such securities have not been issued upon the expiration or termination of such agreement or when such securities are no longer outstanding, as the case may be, then the Conversion Price shall be readjusted to the Conversion Price which would then be in effect had the adjustment made upon the execution of such agreement or the issuance or sale of such securities been made on the basis of the actual number of shares of Common Stock issued pursuant to such agreement or upon conversion, exercise or exchange of such securities.

This paragraph 6(i)(v) does not apply to:

(A) any stock options issued to employees and consultants (other than officers or directors) of the Company pursuant to any employee stock option or purchase plan or program approved by the board of directors of the Company;

(B) the issuance of the Securities; or

(C) any transaction described in paragraph 6(i)(iii) or (iv).

In the event of any change in the number of shares of Common Stock deliverable, or in the consideration payable to the Company, pursuant to any such agreement or upon the conversion, exercise or exchange of such securities, including, but not limited to, a change resulting from any anti-dilution provisions thereof, the Conversion Price shall, on the date of such change, be recomputed to reflect such change.

(vi) For purposes of any computation respecting consideration received pursuant to paragraph 6(i)(ii) and (v) hereof, the following shall apply:

(A) in the case of the issuance or sale of shares of Common Stock for cash, the consideration shall be the amount of such cash; PROVIDED that in no event shall any deduction be made for any commissions, discounts or other expenses incurred by the Company in connection therewith;

(B) in the case of the issuance or sale of shares of Common Stock for a consideration in whole or in part other than cash, the consideration other than cash shall be deemed to be the fair market value thereof as determined in good faith by the board of directors of the Company (irrespective of the accounting treatment thereof), which determination shall be final and binding on the Holders. Such determination shall be described in a board resolution; and

(C) in the case of any agreement referred to in clause (x) of paragraph 6(i)(v) hereof or the issuance or sale of securities referred to in clause (y) of paragraph 6(i)(v) hereof, the consideration, if any, to be received by the Company for the issuance or sale of Common Stock pursuant to such agreement or upon the conversion, exercise or exchange of such securities shall determined in the same manner as provided in clauses (A) and (B) of this paragraph 6(i)(vi).

(vii) No adjustment in the Conversion Price need be made unless the adjustment would require a decrease of at least 1% in the Conversion Price then in effect; PROVIDED that any adjustment that would otherwise be required to be made shall be carried forward and taken into account in any subsequent adjustment. All calculations under this paragraph 6(i) shall be made to the nearest cent or to the nearest 1/10,000th of a share, as the case may be.

(viii) No adjustment need be made for rights to purchase Common Stock pursuant to a Company plan for reinvestment of dividends or interest. No adjustment need be made for a change in the par value or no par value of the Common Stock. To the extent that the Securities become convertible into cash, no adjustment need by made thereafter as to the amount of cash into which such Securities are convertible. Neither Original Issue Discount nor interest will accrue on cash.

(ix) Whenever the Conversion Price is adjusted, the Company shall promptly mail to each Holder, by first-class mail, postage prepaid, at its address appearing on the register maintained by the Company, a notice of the adjustment.

(x) In case:

(A) the Company shall take any action that would require an

adjustment in the Conversion Price pursuant to paragraph 6(i)(i), (ii), (iii), (iv) or (v) hereof;

(B) of any event described in paragraph 6(i)(xi) hereof; or

(C) of the voluntary or involuntary dissolution, liquidation or winding-up of the Company;

the Company shall cause to be mailed to each Holder, by first-class mail, postage prepaid, at its address appearing on the register maintained by the Company, as promptly as possible but in any event at least 15 days prior to the applicable date hereinafter specified, a notice stating (x) the date on which a record is to be taken for the purpose of any dividend or distribution or (y) the date on which any reclassification, consolidation, merger, sale, transfer, dissolution, liquidation or winding-up is expected to become effective or occur. Failure to give such notice, or any defect therein, shall not affect the legality or validity of such dividend, distribution, reclassification, consolidation, merger, sale, transfer, dissolution, liquidation or winding-up.

(xi) In the event of: (a) any reclassification or change of outstanding shares of Common Stock (other than a change in par value, or from par value to no par value, or from no par value to par value, or as a result of a subdivision or combination), (b) any consolidation or amalgamation with, or merger with or into, another Person as a result of which holders of Common Stock shall be entitled to receive cash, securities or other property with respect to or in exchange for such Common Stock or (c) any sale, transfer, assignment, lease, conveyance or other disposition of all or substantially all of the assets of the Company (in one transaction or series of related transactions) to any other Person as a result of which holders of Common Stock shall be entitled to receive cash, securities or other property with respect to or in exchange for such Common Stock, then the Company or the Person (if other than the Company) formed by such consolidation or amalgamation or into which the Company is merged or to which the properties and assets are sold, assigned, transferred, leased, conveyed or otherwise disposed of, as the case may be, shall expressly agree in writing, in form and substance satisfactory to a majority of Holders of Securities

then outstanding (excluding Securities then held by the Company or any of its Affiliates), that each Security shall be convertible into the kind and amount of securities, cash or other assets which the Holder of such Security would have owned immediately after such reclassification, change, consolidation, amalgamation, merger, sale, transfer, assignment, lease, conveyance or other disposition if such Holder had exercised such Security immediately before the record date or effective date, as the case may be, of the transaction. Such written agreement shall provide for adjustments which shall be as nearly equivalent as may be practicable to the adjustments provided for in this paragraph 6(i).

The Company shall cause notice of the execution of such written agreement to be mailed to each Holder, by first-class mail, postage prepaid, at its address appearing on the register maintained by the Company, within 20 days after execution thereof. Failure to deliver such notice shall not affect the legality or validity of such agreement.

The above provisions of this paragraph 7(i)(xi) shall similarly apply to successive reclassifications, changes, consolidations, amalgamations, mergers, sales, transfers, assignments, leases, conveyances or other dispositions.

If this paragraph 6(i)(ix) applies to any event or occurrence, paragraph 6(i)(i), (ii), (iii), (iv) and (v) hereof shall not apply.

(xii) Rights or warrants distributed by the Company to all holders of Common Stock entitling the holders thereof to subscribe for or purchase shares of the Company's Capital Stock (either initially or under certain circumstances), which rights or warrants, until the occurrence of a specified event or events (each, a "Trigger Event"): (i) are deemed to be transferred with such shares of Common Stock, (ii) are not exercisable and

(iii) are also issued in respect of future issuances of Common Stock, shall be deemed not to have been distributed for purposes of this paragraph 6(i) (and no adjustment to the Conversion Price under this paragraph 6(i) will be required) until the occurrence of the earliest Trigger Event, whereupon such rights and warrants shall be deemed to have been distributed and an appropriate adjustment (if any is required) to the Conversion Price shall be made under this paragraph 6(i). If any such right or warrant, including

any such existing rights or warrants distributed prior to the Issue Date, are subject to events, upon the occurrence of which such rights or warrants become exercisable to purchase different securities, evidences of indebtedness or other assets, then the date of the occurrence of any and each such event shall be deemed to be the date of distribution with respect to new rights or warrants with such rights (and a termination or expiration of the existing rights or warrants without exercise by any of the holders thereof). In addition, in the event of any distribution (or deemed distribution) of rights or warrants, or any Trigger Event or other event (of the type described in the preceding sentence) with respect thereto that was counted for purposes of calculating a distribution amount for which an adjustment to the Conversion Price under this paragraph 6(i) was made, (A) in the case of any such rights or warrants which shall have been redeemed or repurchased without exercise by any holders thereof, the Conversion Price shall be readjusted upon such final redemption or repurchase to give effect to such distribution or Trigger Event, as the case may be, as though it were a cash distribution, equal to the per share redemption or repurchase price received by a holder or holders of Common Stock with respect to such rights or warrants (assuming such holder had retained such rights or warrants), made to all holders of Common Stock as of the date of such redemption or repurchase and (B) in the case of such rights or warrants which shall have expired or been terminated without exercise by any holders thereof, the Conversion Price shall be readjusted as if such rights and warrants had not been issued. Notwithstanding the foregoing, no Holder shall be entitled to any adjustment in the Conversion Price of the Notes held by such Holder pursuant to this paragraph 6(i) if the applicable Trigger Event shall have been caused by the acquisition of securities of the Company by such Holder or any of its Affiliates.

(j) After an adjustment to the Conversion Price under paragraph 6(i), (ii), (iii), (iv) or (v) hereof, any subsequent event requiring an adjustment shall cause an adjustment to the Conversion Price as so adjusted.

(k) No adjustment shall be made pursuant to paragraph 6(i)(i), (ii), (iii), (iv) or (v) hereof if, as a result thereof, the Conversion Price would be increased.

7. COVENANTS

(a) PAYMENT OF SECURITIES. The Company shall promptly make all payments in respect of the Securities on the dates and in the manner provided herein.

The Company shall, to the extent permitted by law, pay interest on overdue amounts at the rate set forth in paragraph 1 of the Securities, which interest on overdue amounts (to the extent that the payment of such interest shall be legally enforceable) shall accrue from the date such amounts became overdue.

(b) SEC REPORTS. The Company shall deliver to each Holder, by first-class mail, postage prepaid, at its address appearing on the register maintained by the Company, at the time the Company distributes them to the holders of its Common Stock, copies of its annual reports to shareholders and its proxy statements. In addition, the Company shall deliver to Elan, by first-class mail, postage prepaid, at its address appearing on the register maintained by the Company, within 30 days after the Company files them with the SEC, copies of all other information, documents and reports (or copies of such portions of any of the foregoing as the SEC may by rules and regulations prescribe) which the Company is required to file with the SEC pursuant to

Section 13 or 15(d) of the Exchange Act (or any successor provision thereof). In the event that the Company is at any time no longer subject to the reporting requirements of the Exchange Act (or any such successor provision), it shall deliver to each Holder, by first-class mail, postage prepaid, at its address appearing on the register maintained by the Company, reports containing substantially the same information as would have been required to be filed with the SEC had the Company continued to have been subject to such reporting requirements, including, with respect to annual information only, a report thereon by the Company's certified independent public accountants as such would be required in such reports to the SEC and, in each case, together with a management's discussion and analysis of financial condition and results of operations as such would be so required. In such event, such reports shall be so delivered at the time the Company would have been required to provide such reports had it continued to have been subject to such reporting requirements.

(c) COMPLIANCE CERTIFICATES; NOTICE OF DEFAULTS.

(i) The Company shall deliver to each Holder, within 90 days after the end of each fiscal year, an Officers'

Certificate stating that a review of the activities of the Company and its Subsidiaries during such fiscal year has been made under the supervision of the signing Officers with a view to determining whether the Company has kept, observed, performed and fulfilled its obligations under the Securities, and further stating, as to each such Officer signing such certificate, that to the best of his or her knowledge, the Company has kept, observed, performed and fulfilled each and every covenant contained in the Securities and is not in default in the performance or observance of any of the terms, provisions and conditions contained in the Securities (or, if a Default or Event of Default shall have occurred, describing all such Defaults or Events of Default of which he or she may have knowledge and what action the Company is taking or proposes to take with respect thereto).

(ii) The Company shall, so long as any of the Securities are outstanding, deliver to each Holder, forthwith upon any Officer becoming aware of any Default or Event of Default, an Officers' Certificate specifying such Default or Event of Default and what action the Company is taking or proposes to take with respect thereto.

(d) FURTHER INSTRUMENTS AND ACTS. Upon request of the Holders of at least a majority in the aggregate Principal Amount of the outstanding Securities (excluding Securities at the time owed by the Company and its Affiliates), the Company will execute and deliver such further instruments and do such further acts as may be reasonably necessary or proper to carry out more effectively the provisions of the Securities.

(e) TAXES. The Company shall, and shall cause each of its Subsidiaries to, pay prior to delinquency all material taxes, assessments and governmental levies, except as contested in good faith and by appropriate proceedings.

(f) LEGAL EXISTENCE. Subject to paragraph 8 hereof, the Company shall do or cause to be done all things necessary to preserve and keep in full force and effect its legal existence, and the corporate, partnership or other existence of each of its Subsidiaries, in accordance with their respective organizational documents (as the same may be amended from time to time) and the rights (charter and statutory), licenses and franchises of the Company and its Subsidiaries; PROVIDED that the Company shall not be required to preserve any such right, license or franchise, or the corporate, partnership or other existence of any of its Subsidiaries if the board of directors

of the Company shall determine that the preservation thereof is no longer desirable in the conduct of the business of the Company and its Subsidiaries, taken as a whole.

(g) WITHHOLDING TAXES. All transfers of Securities by the Holders

thereof and all payments made by the Company under or with respect to the Securities (including the issuance of securities upon the conversion of the Securities) shall be made free and clear of and without withholding or deduction for or on account of any present or future Taxes, unless the Company is required to withhold or deduct Taxes by law or by the interpretation or administration thereof. If the Company is required by law or by the interpretation or administration thereof to withhold or deduct any amount of Taxes in connection with the Securities, such amount shall be withheld and deducted by the Company without alteration of or increase in its obligations under the Securities; PROVIDED, HOWEVER, that, if the Holder thereof has delivered to the Company a complete, manually-signed copy of Internal Revenue Service Form 1001 (or any successor form) or Internal Revenue Service Form 4224 (or any successor form) properly certifying to such Holder's entitlement to a complete exemption from U.S. withholding Tax with respect to such payment under applicable United States Treasury Regulations, such payment shall be made free and clear of and without withholding or deduction for or on account of any Taxes. In connection with any payment made by the Company under any Security which is made in whole or in part through the delivery of shares of Common Stock of the Company (including upon the conversion of the Securities), the amount required to be withheld or deducted shall first be withheld or deducted from the amount of cash (up to the total amount thereof) which would otherwise be paid at such time. Any additional amount required to be withheld or deducted, unless otherwise agreed by the Company and the Holder of a Security, shall be withheld and deducted by reducing the number of shares of Common Stock to be delivered by that number of shares of Common Stock equal to the remaining amount required to be withheld or deducted divided by the Conversion Price in effect on the date of such payment.

(h) LINE OF BUSINESS. The Company and its Subsidiaries will not engage in any businesses other than the business of researching, developing, marketing, selling, manufacturing, distributing or licensing pharmaceutical, medical, biologic, genetic or related products and services and financing activities related solely thereto, including the businesses in which the Company and its Subsidiaries are engaged on the Issue Date.

(i) USE OF PROCEEDS. The Company will use the gross proceeds from the issuance of any Additional Notes in accordance with Section 1(b) of the Purchase Agreement and otherwise in accordance with the Purchase Request related thereto.

(j) MAINTENANCE OF PROPERTIES; INSURANCE; BOOKS AND RECORDS; COMPLIANCE WITH LAW.

(i) The Company shall, and shall cause each of its Subsidiaries to, at all times cause all material properties used or useful in the conduct of its business to be maintained and kept in good condition, repair and working order (reasonable wear and tear excepted) and supplied with all necessary equipment, and shall cause to be made all necessary repairs, renewals, replacements, betterments and improvements thereto; PROVIDED that, subject to the other provisions of the Securities, nothing in this paragraph 7(j)(i) shall prevent the Company or any of its Subsidiaries from selling, abandoning or otherwise disposing of any property (including any lease of property) if in the judgment of the Company the same is no longer useful in the business of the Company or such Subsidiary, as the case may be.

(ii) The Company shall maintain, and shall cause to be maintained for each of its Subsidiaries, insurance covering such risks as are usually and customarily insured against by corporations similarly situated, in such amounts as shall be customary for corporations similarly situated and with such deductibles and by such methods as shall be customary and reasonably consistent with past practice.

(iii) The Company shall, and shall cause each of its Subsidiaries to, keep proper books of record and account, in which full and correct entries shall be made of all financial transactions and the assets and business of the Company and each Subsidiary of the Company, in accordance with U.S. generally accepted accounting principles consistently applied to the Company and its Subsidiaries, taken as a whole.

(iv) The Company shall, and shall cause each of its Subsidiaries to,

comply with all statutes, laws, ordinances or government rules and regulations to which they are subject, non-compliance with which would materially adversely affect the business, prospects, earnings, prop-

erties, assets or financial condition of the Company and its Subsidiaries, taken as a whole.

8. SUCCESSOR CORPORATION

(a) The Company shall not consolidate with, amalgamate with, merge with or into, or sell, assign, transfer, lease, convey or otherwise dispose of all or substantially all of its assets (as an entirety or substantially as an entirety in one transaction or a series of related transactions), to any Person unless:

(i) (x) the Company shall be the continuing Person, or (y) the Person (if other than the Company) formed by such consolidation or amalgamation or into which the Company is merged or to which the properties and assets of the Company are sold, assigned, transferred, leased, conveyed or otherwise disposed of (in any case, the "Successor Company") shall be a corporation organized and existing under the laws of the United States or any State thereof or the District of Columbia and the Successor Company shall expressly affirm, in writing, the due and punctual performance of all of the terms, covenants, agreements and conditions of the Securities to be performed or observed by the Company, and such obligations shall remain in full force and effect; and

(ii) immediately before and immediately after giving effect to such transaction, no Default or Event of Default shall have occurred and be continuing.

(b) In connection with any consolidation, amalgamation, merger or sale, assignment, transfer, lease, conveyance or other disposition of assets contemplated by this paragraph 8, prior to the consummation of such transaction or transactions the Company shall deliver, or cause to be delivered, to each Holder, by first-class mail, postage prepaid, at its address appearing in the register maintained by the Company, an Opinion of Counsel stating that (i) such consolidation, amalgamation, merger or sale, assignment, transfer, lease, conveyance or other disposition of assets complies with this paragraph 8, (ii) all conditions precedent herein provided for relating to such transaction or transactions have been complied with and (iii) the affirmation provided for in this paragraph 8 has been duly authorized, executed and delivered by the Successor Company and the Securities are valid and legally binding obligations of the Successor Company enforceable against it in accordance with their terms (subject to bankruptcy, insolvency, re-

organization and similar laws affecting the rights and remedies of creditors generally and general equitable principles).

(c) For purposes of paragraph 8(a) and (b) hereof, the transfer (by sale, assignment, lease, conveyance or other disposition, in a single transaction or series of related transactions) of all or substantially all of the properties or assets of one or more Subsidiaries of the Company, the Capital Stock of which constitutes all or substantially all of the properties and assets of the Company, shall be deemed to be the transfer of all or substantially all of the properties and assets of the Company.

(d) Upon any consolidation, amalgamation or merger, or any sale, assignment, transfer, lease, conveyance or other disposition of all or substantially all of the assets of the Company in accordance with this paragraph 8, the Successor Company shall succeed to, and be substituted for, and may exercise every right and power of, the Company under the Securities with the same effect as if such Successor Company had been named as the Company in the Securities, and thereafter the predecessor corporation shall be relieved of all obligations and covenants under the Securities.

9. DEFAULTS AND REMEDIES

(a) An "Event of Default" occurs if:

(i) after exercise of its option pursuant to paragraph 12 hereof following a Tax Event, the Company defaults in the payment of interest upon any Security or delivery of any Tax Event Option related thereto, when such interest becomes due and payable, and such default continues for a period of 30 days;

(ii) the Company defaults in the payment of the Principal Amount, Issue Price, accrued Original Issue Discount, Redemption Price, Purchase Price, Company Change of Control Purchase Price or Elan Change of Control Purchase Price on any Security when the same becomes due and payable at its Stated Maturity, upon redemption, upon declaration, when due for purchase by the Company or otherwise;

(iii) the Company defaults in the observance or performance of any agreement, covenant, term or condition contained in any Security (other than those referred to in clause (i) and (ii) above) and such failure continues for 30 days after receipt by the Company of notice thereof

(except in the case of a failure or default with respect to paragraph 8 hereof, which shall constitute an Event of Default with such notice requirement but without such passage of time requirement);

(iv) the Company defaults in any payment of principal of or interest on any other obligation for money borrowed or the Company fails to perform or observe any other agreement, covenant, term or condition contained in any agreement under which any such obligation is created and the effect of such default or failure is to cause, or the holder or holders of such obligation (or a trustee on behalf of such holder or holders), as a consequence of such default or failure shall take action to cause, such obligation to become due prior to any stated maturity thereof; PROVIDED that the aggregate amount of all obligations as to which such acceleration shall occur is equal to or greater than $4.0 million;

(v) any final judgment or judgments which can no longer be appealed for the payment of money in excess of $4.0 million (in excess of amounts covered by insurance and as to which the insurer has acknowledged coverage) shall be rendered against the Company or any Subsidiary thereof, and shall not be discharged for any period of 60 consecutive days during which a stay of enforcement shall not be in effect;

(vi) the Company or any Subsidiary thereof pursuant to or within the meaning of any Bankruptcy Law:

(A) commences a voluntary case,

(B) consents to the entry of an order for relief against it in an involuntary case,

(C) consents to the appointment of a Custodian of it or for all or substantially all of its property,

(D) makes a general assignment for the benefit of its creditors, or

(E) generally is not paying its debts as they become due;

(vii) a court of competent jurisdiction enters an order or decree under any Bankruptcy Law that:

(A) is for relief against either of the Company or any Subsidiary thereof in an involuntary case,

(B) appoints a Custodian of either of the Company or any Subsidiary thereof or for all or substantially all of the property of

either of the Company or any Subsidiary thereof, or

(C) orders the liquidation of either of the Company or any Subsidiary thereof,

and the order or decree remains unstayed and in effect for 60 days; or

(viii) the Company fails to deliver shares of Common Stock (or cash in lieu of fractional shares) when such Common Stock (or cash in lieu of fractional shares) is required to be delivered, upon conversion of a Security and such failure is not remedied for a period of 10 days.

(b) If an Event of Default (other than an Event of Default specified in paragraph 9(a)(vi) or (vii) hereof occurs and is continuing, the Holders of at least 25% in aggregate Principal Amount of the Securities at the time outstanding (excluding Securities at the time owned by the Company and its Affiliates) by notice to the Company, may declare the Issue Price and accrued Original Issue Discount (or, if the Securities have been converted to a semiannual coupon note following a Tax Event, the Restated Principal Amount and accrued and unpaid interest) through the date of declaration on all the Securities to be immediately due and payable. Upon such a declaration, such Issue Price and accrued Original Issue Discount (or, if the Securities have been converted to a semiannual coupon note following a Tax Event, the Restated Principal Amount and accrued and unpaid interest) shall become and be due and payable immediately. If an Event of Default specified in paragraph 9(a)(vi) or (vii) hereof occurs and is continuing, the Issue Price and accrued Original Issue Discount (or, if the Securities have been converted to a semiannual coupon note following a Tax Event, the Restated Principal Amount and accrued and unpaid interest) on all the Securities shall become and be immediately due and payable without any declaration or other act on the part of any Holders. The Holders of a majority in aggregate Principal Amount of the Securities at the time outstanding (excluding Securities at the time owned by the Company and its Affiliates), by notice to the Company (and without notice to any other Holder), may rescind an acceleration and its consequences if the rescission would not conflict with any judgment

or decree and if all existing Events of Default have been cured or waived except nonpayment of the Issue Price and accrued Original Issue Discount (or accrued and unpaid interest) that have become due solely as a result of acceleration. No such rescission shall affect any subsequent or other Default or Event of Default or impair any consequent right.

(c) If an Event of Default occurs and is continuing, any Holder may pursue any available remedy to collect the payment of the Issue Price and accrued Original Issue Discount (or, if the Securities have been converted to a semiannual coupon note following a Tax Event, the Restated Principal Amount and accrued and unpaid interest) on the Securities or to enforce the performance of any provision of the Securities.

A delay or omission by any Holder in exercising any right or remedy accruing upon an Event of Default shall not impair the right or remedy or constitute a waiver of, or acquiescence in, the Event of Default. No remedy is exclusive of any other remedy. All available remedies are cumulative.

(d) The Holders of a majority in aggregate Principal Amount of the Securities at the time outstanding (excluding Securities at the time owned by the Company and its Affiliates), by notice to the Company (and without notice to any other Holder), may waive an existing Default or Event of Default and its consequences except (i) an Event of Default described in paragraph 9(a)(i), (ii) or (viii) hereof or (ii) a Default in respect of a provision that under paragraph 11 hereof cannot be amended without the consent of each Holder affected. When a Default or Event of Default is waived, it is deemed cured, but no such waiver shall extend to any subsequent or other Default or Event of Default or impair any consequent right.

(e) Notwithstanding any other provision of the Securities, the right of any Holder to receive payment of the Principal Amount, Issue Price, accrued Original Issue Discount, Redemption Price, Purchase Price, Company Change of Control Purchase Price, Elan Change of Control Purchase Price or interest, if any, in respect of the Securities held by such Holder, on or after the

respective due dates expressed in the Securities and to convert the Securities in accordance with paragraph 6 hereof, or to bring suit for the enforcement of any such payment on or after such respective dates or the right to convert the Securities, shall not be impaired or affected adversely without the consent of each such Holder.

(f) The Company covenants (to the extent it may lawfully do so) that it will not at any time insist upon, or plead, or in any manner whatsoever claim or take the benefit or advantage of, any stay or extension law or any usury or other law wherever enacted, now or at any time hereafter in force, which would prohibit or forgive the Company from paying all or any portion of the Principal Amount, Issue Price plus accrued Original Issue Discount, Redemption Price, Purchase Price, Company Change of Control Purchase Price or Elan Change of Control Purchase Price, in each case, in respect of Securities, or any interest on such amounts, as contemplated herein, or which may affect the covenants or the performance of the Securities; and the Company (to the extent it may lawfully do so) hereby expressly waives all benefit or advantage of any such law, and covenants that it will not hinder, delay or impede the execution of any power herein granted to the Holders, but will suffer and permit the execution of every power as though no such law had been enacted.

10. REGISTRATION, REGISTRATION OF TRANSFER AND EXCHANGE

(a) The Company shall cause to be kept at its offices a register in which the Company shall provide for the registration of Securities and of transfers of Securities. Upon surrender for registration of transfer of any Security, the Company shall execute, in the name of the designated transferee or transferees, one or more Securities of a like aggregate Principal Amount and bearing such restrictive legends as may be required by the terms of the Securities.

At the option of the Holder, and subject to the other provisions of the Securities, Securities may be exchanged for other Securities of a like aggregate Principal Amount, upon surrender of the Securities to be exchanged to the Company. Whenever any Securities are so surrendered for exchange, and subject to the other provisions of the Securities, the Company shall execute and deliver the Securities which the Holder making the exchange is entitled to receive. Every Security presented for registration of transfer or exchange shall be accompanied by the written instrument of transfer in the form attached hereto as Annex C, duly executed by the Holder thereof.

All Securities issued upon any registration of transfer or exchange of Securities shall be the valid obligations of the Company, evidencing the same debt, and subject to the same provisions as the Securities surrendered upon such registration of transfer or exchange.

Subject to paragraph 7(g) hereof and notwithstanding any other provision of this Section 10(a), no transfer of any Security shall be permitted, and no registration of transfer shall be effected unless, prior to the time of such transfer or registration of transfer, the Holder has made arrangements reasonably satisfactory to the Company for payment or reimbursement of any and all Taxes which would, in the absence of payment by the transferor, be required to be paid by the Company as a result of such transfer. No service charge shall be made for any registration of transfer or exchange. The Company acknowledges that Treasury Regulation Section 1.441-2(b)(3) (effective January 1, 1999) is not applicable to any Security issued prior to January 1, 1999.

In the event of a redemption of the Securities, the Company will not be required (i) to register the transfer of or exchange Securities for a period of 5 days immediately preceding the date notice of any redemption is given pursuant to paragraph 3(e) hereof or (ii) to register the transfer of or exchange any Security, or portion thereof, called for redemption.

(b) Except as permitted by this paragraph (b), each Security (and all Securities issued in exchange therefor or substitution thereof) shall, so long as appropriate, bear a legend (the "Legend") to substantially the following effect (each, a "Transferred Restricted Security"):

THE SECURITY EVIDENCED HEREBY HAS NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "ACT"), MAY NOT BE SOLD, TRANSFERRED OR OTHERWISE DISPOSED OF IN THE ABSENCE OF AN EFFECTIVE REGISTRATION STATEMENT UNDER THE ACT OR PURSUANT TO A VALID EXEMPTION THEREFROM.

THE TRANSFER OF THE SECURITY EVIDENCED HEREBY IS SUBJECT TO THE CONDITIONS SPECIFIED IN A SECURITIES PURCHASE AGREEMENT, DATED AS OF NOVEMBER 6, 1998, BY AND AMONG THE COMPANY, ELAN INTERNATIONAL SERVICES, LTD. AND ELAN CORPORATION, PLC, AND THE COMPANY RESERVES THE RIGHT TO REFUSE THE TRANSFER OF SUCH SECURITY UNTIL SUCH CONDITIONS HAVE BEEN FULFILLED WITH RESPECT TO SUCH TRANSFER. A COPY OF SUCH CONDITIONS WILL BE

FURNISHED BY THE COMPANY TO THE HOLDER HEREOF WITHOUT CHARGE.

At such time as any Transfer Restricted Security may be freely transferred without registration under the Securities Act and without being subject to transfer restrictions pursuant to the Securities Act, the Company shall permit the Holder of such Transfer Restricted Security to exchange such Transfer Restricted Security for a new Security which does not bear the applicable portion of the Legend upon receipt of certification from such Holder substantially in the form attached hereto as Annex D and, at the request of the Company, upon receipt of an opinion of counsel addressed to the Company that the transfer restrictions contained in the Legend are no longer applicable. In addition, at such time as such Security is no longer subject to the transfer conditions set forth in the Purchase Agreement, the Company shall permit the Holder of such Security to exchange such Security for a new Security which does not bear the portion of the Legend referring to such transfer conditions.

In addition to the Legend, until the expiration of the "one-year distribution compliance period" within the meaning of Rule 903 of Regulation S under the Securities Act, each Security (and all Securities issued in exchange therefor or substitution thereof) shall bear a legend (the "Reg. S Legend") to substantially the following effect:

THE SHARES REPRESENTED BY THIS CERTIFICATE MAY NOT BE SOLD, TRANSFERRED OR OTHERWISE DISPOSED OF EXCEPT IN ACCORDANCE WITH THE PROVISIONS OF REGULATION S (SS.230.901 THROUGH SS.230.905, AND PRELIMINARY NOTES). HEDGING TRANSACTIONS INVOLVING THE SHARES REPRESENTED BY THIS CERTIFICATE MAY NOT BE CONDUCTED UNLESS IN COMPLIANCE WITH THE ACT.

At the expiration of such "one-year distribution compliance period," the Company shall permit the Holder of such Security to exchange such Security for a new Security which does not bear the Reg. S Legend.

(c) If any mutilated Security is surrendered to the Company, the Company shall execute and deliver a new Security of like aggregate Principal Amount.

If there is delivered to the Company:

(i) evidence to its reasonable satisfaction of the destruction, loss or theft of any Security; and

(ii) such security or indemnity as may be reasonably satisfactory to the Company to save it harmless,

then, in the absence of actual notice to the Company that such Security has been acquired by a bona fide purchaser, the Company shall execute and deliver, in

lieu of any such destroyed, lost or stolen Security, a new Security of like aggregate Principal Amount.

In case any such mutilated, destroyed, lost or stolen Security has become or is about to become due and payable, the Company, in its discretion, but subject to conversion rights, may, instead of issuing a new Security, pay such Security, upon satisfaction of the conditions set forth in the preceding paragraph.

11. AMENDMENTS AND WAIVERS

(a) Any term, covenant, agreement or condition of the Securities may, with the consent of the Company, be amended, or compliance therewith may be waived (either generally or in a particular instance and either retroactively or prospectively), by one or more substantially concurrent written instruments signed by the Holders of at least a majority in aggregate Principal Amount of the Securities at the time outstanding (excluding Securities at the time owned by the Company and its Affiliates); PROVIDED that, without the consent of each Holder affected, no such amendment or waiver, including a waiver pursuant to paragraph 9(d) hereof, shall:

(i) make any change in the Principal Amount of Securities whose Holders must consent to an amendment or waiver;

(ii) make any change to the manner or rate of accrual in connection with Original Issue Discount, reduce the interest rate referred to in paragraph 1 of the Securities, reduce the rate of interest referred to in paragraph 12 of the Securities upon the occurrence of a Tax Event or extend the time for payment of accrued Original Issue Discount or interest, if any, on any Security;

(iii) reduce the Principal Amount or the Issue Price of or extend the Stated Maturity of any Security;

(iv) reduce the Redemption Price, Purchase Price, Company Change of Control Purchase Price or Elan Change of Control Purchase Price or extend the date on which the Redemption Price, Purchase Price, Company Change of Control Purchase Price or Elan Change of Control Purchase Price of any Security is payable;

(v) make any Security payable in money or securities other than that stated in the Securities;

(vi) make any change in paragraph 9(d) hereof or this paragraph 11(a), except to increase any percentage referred to, or make any change in paragraph 9(e) hereof;

(vii) make any change that adversely affects the right to convert any Security (including the right to receive cash in lieu of fractional shares);

(viii) make any change that adversely affects the right to require the Company to purchase Securities in accordance with their terms; or

(ix) impair the right to institute suit for the enforcement of any payment with respect to, or conversion of, the Securities.

(b) No waiver shall extend to or affect any obligation not expressly waived or impair any right consequent thereto.

(c) The Company will not solicit, request or negotiate for or with respect to any proposed amendment or waiver of any provisions of any Security unless each Holder of Securities (irrespective of the amount of Securities then owned by it) shall be informed thereof by the Company and shall be afforded the opportunity of considering the same and shall be supplied by the Company with sufficient information to enable it to make an informed decision with respect thereto; PROVIDED, HOWEVER, that preliminary discussions with one or more Holders regarding any such proposed amendment shall not constitute any such solicitation, request or negotiation. Executed or true copies of any amendment or waiver effected pursuant to this paragraph 11 shall be delivered by the

Company to each Holder of Securities, by first class mail, postage prepaid, at its address appearing on the register maintained by the Company, forthwith following

the date on which the same shall have been executed and delivered by the Holder or Holders of the requisite amount of outstanding Securities. The Company will not, directly or indirectly, pay or cause to be paid, remuneration, whether by way of fees or otherwise, to any Holder of Securities as consideration for or as an inducement to the entering into by such Holder of any amendment or waiver unless such remuneration is concurrently paid, on the same terms, ratably to the Holders of all Securities then outstanding.

(d) Any amendment or waiver pursuant to this paragraph 11 shall (except as provided in paragraph 11(a)(i) through (ix) above) apply equally to all Holders and shall be binding upon them, upon each future Holder and upon the Company.

(e) In determining whether the Holders of the requisite amount of outstanding Securities have given any authorization, consent or waiver under this paragraph 11, Securities owned by the Company or any of its Affiliates shall be disregarded and deemed not to be outstanding.

12. TAX EVENT CONVERSION

(a) From and after the date (the "Tax Event Date") of the occurrence of a Tax Event, at the option of the Company, interest in lieu of future Original Issue Discount shall accrue at 8.0% per annum on a principal amount per Security (the "Restated Principal Amount") equal to the Issue Price plus accrued Original Issue Discount to the date immediately prior to the Tax Event Date or the date on which the Company exercises the option described in this paragraph 12(a), whichever is later (such date, the "Option Exercise Date"). Such interest shall accrue from the Option Exercise Date and shall be payable on November 9 and May 9 of each year (the "Interest Payment Date") to the Holders of record at the close of business on October 25 and April 24 (each, a "Regular Record Date") immediately preceding such Interest Payment Date. Interest will be computed on the basis of a 360-day year consisting of twelve 30-day months and will accrue from the most recent date on which interest has been paid or, if no interest has been paid, from the Option Exercise Date. Within 15 days of the occurrence of a Tax Event, the Company shall mail a written notice of such Tax Event to each Holder, by first-class mail, postage prepaid, at its address appearing on the register maintained by the Company.

(b) On each Interest Payment Date, concurrently with the payment of the interest due and payable on such date, the Company shall issue and deliver to each Holder of a Security to whom such interest is paid, an option (which option shall be in the form of a written instrument duly executed by the Company (a "Tax Event Option") to purchase a number of shares of Common Stock equal to the quotient obtained by dividing (x) the aggregate amount of such interest due and payable to such Holder on such Interest Payment Date in respect of such Security by (y) the Conversion Price of such Security in effect on the Business Day immediately prior to such Interest Payment Date. Such Tax Event Option shall be exercisable, in whole at any time or in part from time to time, on or prior to November 9, 2008. Each Tax Event Option shall include provisions substantially similar to those set forth in paragraph 6(c), (d), (e), (f), (g), (h) and (i) hereof. Each Tax Event Option shall be transferable by the holder thereof only together with the Security in respect of which such Tax Event Option was issued, subject to compliance with all applicable transfer restrictions of federal and state securities laws.

(c) Interest on any Security that is payable, and is punctually paid or duly provided for, on any Interest Payment Date shall be paid to the person in whose name that Security is registered at the close of business on the Regular Record Date for such interest. Each installment of interest on any Security shall be paid by wire transfer in immediately - available funds to an account designated in writing by the payee at least 2 Business Days prior to the Interest Payment Date applicable thereto.

(d) Subject to the foregoing provisions of this paragraph 12, each Security upon registration of transfer, or in exchange for or in lieu of any other Security, shall carry the rights to interest accrued and unpaid, and to accrue, which were carried by such other Security.

13. MISCELLANEOUS

(a) Any notices or other communications required or permitted hereunder shall be sufficiently given if delivered personally, sent by nationally recognized overnight delivery service or facsimile (receipt confirmed) or mailed by first-class mail, postage prepaid, addressed as follows:

(i) if to the Company, to:

Ligand Pharmaceuticals Incorporated
10275 Science Center Drive
San Diego, California 92121
Attn: General Counsel
Fax No.: (619) 550-1825

with a copy to:

Brobeck, Phleger & Harrison LLP
550 West C Street, Suite 1300
San Diego, California 92101-3532
Attn: Faye H. Russell, Esq.
Fax No.: (619) 234-3848

(ii) if to any Holder, at its address appearing in the register maintained by the Company pursuant to paragraph 10(a) hereof

(iii) (x) on the date delivered, if delivered by facsimile or personally, (y) on the day after the notice is delivered into the possession and control of a nationally recognized overnight delivery service, duly marked for delivery to the receiving party or (z) three Business Days after being mailed by first-class mail, postage prepaid. The Company, by written notice to each of the Holders, may designate a different address for subsequent notices or communications.

(b) All agreements of the Company in this Security shall bind its successor.

(c) Each provision of this Security shall be considered separable and if for any reason any provision which is not essential to the effectuation of the basic purpose of this Security shall be invalid, illegal or unenforceable, the validity, legality and enforceability of the remaining provisions shall not in any way be affected or impaired thereby.

(d) THIS SECURITY SHALL BE GOVERNED BY AND CONSTRUED IN ACCORDANCE WITH THE LAWS OF THE STATE OF NEW YORK, AS APPLIED TO CONTRACTS MADE AND PERFORMED WITHIN THE STATE OF NEW YORK, WITHOUT GIVING EFFECT TO THE PRINCIPLES OF CONFLICTS OF LAW TO THE EXTENT THAT THE APPLICATION OF LAWS OF ANOTHER JURISDICTION WOULD BE REQUIRED THEREBY.

(e) Upon conversion of this Security in accordance with the terms hereof, the Holder will be entitled to the benefits of the Registration Rights Agreement or the New Registra-

tion Rights Agreement, as the case may be, with respect to the shares of Common Stock issuable to such Holder upon such conversion.

14. DEFINITIONS

"Accrual Increase" has the meaning specified in paragraph 1(c) hereof.

"Additional Amounts" has the meaning specified in paragraph 7(g) hereof.

"Affiliate" of any specified Person means any other Person directly or indirectly controlling or controlled by or under direct or indirect common control with such specified Person. For the purposes of this definition, "control," when used with respect to any specified Person means the power to direct or cause the direction of the management and policies of such Person, directly or indirectly, whether through the ownership of Voting Stock, by contract or otherwise; and the terms "controlling" and "controlled" have meanings correlative to the foregoing.

"Bankruptcy Law" means Title 11, U.S. Code or any similar federal or state law for the relief of debtors.

"Business Day" means each day of the year on which banking institutions are not required or authorized to close in The City of New York.

"Capital Stock" means, with respect to any Person, any and all shares, interests, participations or other equivalents (however designated and whether or not voting) of corporate stock, partnership interests or any other participation, right or other interest in the nature of an equity interest in such Person including, without limitation, common stock and preferred stock of such Person, or any option, warrant or other security convertible into any of the foregoing.

A "Change of Control" of any Person shall be deemed to have occurred at such time as (i) any other Person or group of related Persons for purposes of Section 13(d) of the Exchange Act ("Group") becomes the beneficial owner (as defined under Rule 13d-3 under the Exchange Act), directly or indirectly, of 50.0% or more of the total Voting Stock of such specified Person, (ii) there shall be consummated any consolidation or merger of such specified Person in which such specified Person is not the continuing or surviving corporation or

pursuant to which the Voting Stock of such specified Person would be converted into cash, securities or other property, other than a merger or consolidation of such specified Person in which the holders of the Voting Stock of such specified Person outstanding immediately prior to the consolidation or merger hold, directly or indirectly, at least a majority of all Voting Stock of the continuing or surviving corporation immediately after such consolidation or merger or (iii) during any period of two consecutive years, individuals who at the beginning of such period constituted the board of directors of such specified Person (together with any new directors whose election by such board of directors or whose nomination for election by the shareholders of such specified Person has been approved by a majority of the directors then still in office who either were directors at the beginning of such period or whose election or recommendation for election was previously so approved) cease to constitute a majority of the board of directors of such specified Person.

"close of business" means, with respect to any date, 5:00 PM, San Diego time, on such date, or such other city in which the Company's principal place of business may then be located.

"Closing Price" means, with respect to the Common Stock on any trading day, the last reported per share sales price of the Common Stock on such trading day, as reported by the Nasdaq National Market or, if the Common Stock is listed on a United States securities exchange, the closing per share sales price, regular way, on such trading day on the principal United States securities exchange on which the Common Stock is traded or, if no such sale takes place on such trading day, the average of the closing bid and asked prices on such day.

"Common Stock" means the common stock, par value $0.001 per share, of the Company, as such class exists on the date of this Security as originally executed or any other shares of Capital Stock into which such common stock shall be reclassified or changed.

"Company" means Ligand Pharmaceuticals Incorporated, a Delaware corporation.

"Company Change of Control Offer" has the meaning specified in paragraph 4(b) hereof.

"Company Change of Control Offer Notice" has the meaning specified in paragraph 4(b)(i) hereof.

"Company Change of Control Payment Date" has the meaning specified in paragraph 4(b)(i)(C) hereof.

"Company Change of Control Purchase Price" has the meaning specified in paragraph 4(b) hereof.

"Company Notice" has the meaning specified in paragraph 4(a)(v) hereof.

"Company Notice Date" has the meaning referred to in paragraph 4(a)(v) hereof.

"Conversion Date" has the meaning specified in paragraph 6(d) hereof.

"Conversion Notice" has the meaning specified in paragraph 6(d) hereof.

"Conversion Price" has the meaning specified in paragraph 6(b) hereof.

"Conversion Shares" has the meaning specified in the Purchase Agreement.

"Custodian" means any receiver, trustee, assignee, liquidator or similar official under any Bankruptcy Law.

"Default" means any event which is, or after notice or passage of time or both would be, an Event of Default.

"Distributed Securities" has the meaning specified in paragraph 6(i)(iv) hereof.

"Elan" means Elan Corporation, plc, a public limited company organized and existing under the laws of Ireland.

"Elan Change of Control Notice" has the meaning specified in the Purchase Agreement.

"Elan Change of Control Payment Date" has the meaning specified in paragraph 5(b)(ii) hereof.

"Elan Change of Control Purchase" has the meaning specified in paragraph 5(a) hereof.

"Elan Change of Control Purchase Notice" has the meaning specified in paragraph 5(b) hereof.

"Elan Change of Control Purchase Price" has the meaning specified in paragraph 5(a) hereof.

"Event of Default" has the meaning specified in paragraph 10(a).

"Exchange Act" means the Securities Exchange Act of 1934, as amended, and the rules and regulations of the SEC promulgated thereunder.

"Extraordinary Cash Dividend" means cash dividends with respect to the Common Stock the aggregate amount of which in any fiscal year exceeds the greater of (i) 10% of the consolidated net income of the Company for the fiscal year immediately preceding the payment of such dividend and (ii) $200,000.

"Holder" means a Person in whose name this Security is registered on the books of the Company.

"Initial Shares" has the meaning specified in the Purchase Agreement.

"Interest Payment Date" has the meaning specified in paragraph 12(a) hereof.

"Issue Date" of this Security means the date on which this Security was originally issued or deemed issued as set forth on the face of this Security.

"Issue Price" of this Security means, in connection with the original issuance of this Security, the initial issue price at which this Security is issued as set forth on the face of this Security. "Legend" has the meaning specified in paragraph 10(b) hereof.

"License Agreement" has the meaning specified in the Purchase Agreement.

"License Shares" has the meaning specified in the Purchase Agreement.

"Nasdaq National Market" means the electronic interdealer quotation system operated by Nasdaq Stock Market, Inc., a subsidiary of the National Association of Securities Dealers, Inc.

"New Registration Rights Agreement" has the meaning specified in the Purchase Agreement.

"Officer" means the Chief Executive Officer, the President, any Vice President, the Treasurer or the Secretary of the Company.

"Officers' Certificate" means a written certificate, signed in the name of the Company by (i) its Chief Executive Officer, its President or any Vice President and (ii) its Treasurer or its Secretary.

"Opinion of Counsel" means a written opinion from legal counsel. The counsel may be an employee of, or counsel to, the Company or any Successor Company.

"Option Exercise Date" has the meaning specified in paragraph 12(a) hereof.

"Original Issue Discount" of this Security means the difference between the Issue Price and the Principal Amount of this Security as set forth on the face of this Security. For purposes of this Security, accrual of Original Issue Discount shall be calculated on a semi-annual bond equivalent basis using a 360 day year consisting of twelve 30-day months.

"Person" means any individual, corporation, partnership, limited liability company, joint venture, association, joint-stock company, trust, unincorporated organization or government, or any agency or political subdivision thereof.

"Principal" or "Principal Amount" of this Security means the Principal Amount as set forth on the face of this Security.

"Purchase Agreement" has the meaning specified on the face of this Security.

"Purchase Date" has the meaning specified in paragraph 4(a) hereof.

"Purchase Notice" has the meaning specified in paragraph 4(a)(i) hereof.

"Purchase Price" has the meaning specified in paragraph 4(a) hereof.

"Purchase Request" has the meaning specified in the Purchase Agreement.

"Redemption Date" means a date specified for redemption of this Security in accordance with the terms hereof.

"Redemption Price" has the meaning specified in paragraph 3(a) hereof.

"Registration Rights Agreement" has the meaning specified in the Purchase Agreement.

"Registration Rights Default" has the meaning specified in paragraph 1(c) hereof.

"Regular Record Date" has the meaning specified in paragraph 12(a) hereof.

"Restated Principal Amount" has the meaning specified in paragraph 12(a) hereof.

"SEC" means the Securities and Exchange Commission.

"Securities" means any of the Company's Zero Coupon Convertible Senior Notes due 2008, as amended and supplemented from time to time in accordance with the terms hereof, issued pursuant to the Purchase Agreement.

"Securities Act" means the Securities Act of 1933, as amended, and the rules and regulations of the SEC promulgated thereunder.

"Shares" has the meaning specified in the Purchase Agreement.

"Stated Maturity" means November 9, 2008.

"Subsidiary" of any specified Person means any corporation, partnership, joint venture, limited liability company, association or other business entity, whether now existing or hereafter organized or acquired, (i) in the case of a corporation, of which more than 50% of the total voting power of the Capital Stock entitled (without regard to the occurrence of any contingency) to vote in the election of directors, officers or trustees thereof is held by such specified Person or any of its Subsidiaries or (ii) in the case of a partnership, joint venture, limited liability company, association or other business entity, with respect to which such specified Person or any of

its Subsidiaries has the power to direct or cause the direction of the management and policies of such entity by contract or otherwise.

"Successor Company" has the meaning specified in paragraph 8(a)(1) hereof.

"Tax Event" means that the Company shall have received an opinion from independent tax counsel experienced in such matters to the effect that, on or after the date of this Security, as a result of (a) any amendment to, or change (including any announced prospective change) in, the laws (or any regulations thereunder) of the United Sates or any political subdivision or taxing authority thereof or therein or (b) any amendment to, or change in, an interpretation or application of such laws or regulations by any legislative body, court, governmental agency or regulatory authority, in each case, which amendment or change is enacted, promulgated, issued or announced or which interpretation is issued or announced or which action is taken, on or after the date of this Security, there is more than an insubstantial risk that interest (including Original Issue Discount) payable on the Securities either (i) would not be deductible on a current accrual basis or (ii) would not be deductible under any other method, in either case, in whole or in part, by the Company, by reason of deferral, disallowance or otherwise) for United States federal income tax purposes.

"Tax Event Date" has the meaning specified in paragraph 12(a) hereof.

"Tax Event Option" has the meaning specified in paragraph 12(b) hereof.

"Taxes" means any present or future tax, duty, levy, impost, assessment or other government charge (including penalties, interest and any other liabilities related thereto) imposed or levied by or on behalf of a any government or any political subdivision or territory or possession of any

government or any authority or agency therein or thereof having power to tax.

"Transfer Restricted Security" has the meaning specified in paragraph 10(b) hereof.

"Voting Stock" means stock of any class or classes, however designated, having general voting power under ordinary circumstances to elect a majority of the board of directors,

managers or trustees of a Person, other than stock having such power only by reason of the occurrence of a contingency.

ANNEX A

FORM OF PURCHASE NOTICE
OF
ZERO COUPON CONVERTIBLE SENIOR NOTE DUE 2008

Ligand Pharmaceuticals Incorporated
10275 Science Center Drive
San Diego, California 92121

Attention: General Counsel

1. Pursuant to the terms of the Zero Coupon Convertible Senior Note due 2008 (certificate no. [ ] in the Principal Amount of $[ ] (the "Security"), the undersigned hereby elects to cause Ligand Pharmaceuticals Incorporated (the "Company") to purchase $[_____] Principal Amount of the Security at the Purchase Price set forth in the Security on [November 9, 2002] [November 9, 2005], subject to the right of the undersigned to convert the Security at any time prior to the close of business on the Purchase Date. Capitalized terms used herein and not otherwise defined have the meanings specified in the Security.

2. In the event that the Security is purchased in part, please execute and deliver to the undersigned a new Security in a denomination equal in Principal Amount to the unpurchased portion of the Security.

3. In the event that the Company has elected to pay the Purchase Price with Common Stock (the "Shares") pursuant to paragraph 4(a)(iv) of the Security, the undersigned confirms that:

(a) We understand that the Shares have not been registered under the Securities Act and may not be offered or sold except as permitted in the following sentence. We agree that if we should sell or otherwise transfer the Shares, we will do so only (i) to the Company or its Subsidiaries, (ii) inside the United States to an institutional "accredited investor" (as defined below), (iii) outside the United States in accordance with Regulation S under the Securities Act, (iv) pursuant to the exemption from registration provided by Rule 144 under the Securities Act (if available) or (v) pursuant to an effective registration statement under the Securities Act.

(b) We understand that the certificates representing the Shares will, so long as appropriate, bear the following legends:

> THE SHARES REPRESENTED BY THIS CERTIFICATE HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "ACT"), MAY NOT BE SOLD, TRANSFERRED OR OTHERWISE DISPOSED OF IN THE ABSENCE OF AN EFFECTIVE REGISTRATION STATEMENT UNDER THE ACT OR PURSUANT TO A VALID EXEMPTION THEREFROM. THE SHARES REPRESENTED BY THIS

CERTIFICATE MAY NOT BE SOLD, TRANSFERRED OR OTHERWISE DISPOSED OF EXCEPT IN ACCORDANCE WITH THE PROVISIONS OF REGULATION S (SS.230.901 THROUGH SS.230.905, AND PRELIMINARY NOTES). HEDGING TRANSACTIONS INVOLVING THE SHARES REPRESENTED BY THIS CERTIFICATE MAY NOT BE CONDUCTED UNLESS IN COMPLIANCE WITH THE ACT.

THE TRANSFER OF THE SECURITY EVIDENCED HEREBY IS SUBJECT TO THE CONDITIONS SPECIFIED IN A SECURITIES PURCHASE AGREEMENT, DATED AS OF NOVEMBER 6, 1998, BY AND AMONG THE COMPANY, ELAN INTERNATIONAL SERVICES, LTD. AND ELAN CORPORATION, PLC, AND THE COMPANY RESERVES THE RIGHT TO REFUSE THE TRANSFER OF SUCH SECURITY UNTIL SUCH CONDITIONS HAVE BEEN FULFILLED WITH RESPECT TO SUCH TRANSFER. A COPY OF SUCH CONDITIONS WILL BE FURNISHED BY THE COMPANY TO THE HOLDER HEREOF WITHOUT CHARGE.

(c) We are acquiring the Shares for our own account and are either (i) an institutional "accredited investor" (as defined in Rule 501(a)(1), (2), (3) or (7) of Regulation D under the Securities Act) or (ii) a foreign purchaser that is outside the United States (as such terms are used under Regulations S under the Securities Act). We have such knowledge and experience in financial and business matters to be capable of evaluating the merits and risks of our investment in the Shares and we are able to bear the economic risk of our investment for an indefinite period of time.

This certificate and the statements contained herein are made for the benefit of the Company.

_____
Signature of Holder

Date: _____

ANNEX B

CONVERSION NOTICE
OF
ZERO COUPON CONVERTIBLE SENIOR NOTE DUE 2008

Ligand Pharmaceuticals Incorporated
10275 Science Center Drive
San Diego, California 92121

Attention: General Counsel

1. Pursuant to the terms of the Zero Coupon Convertible Senior Note due 2008 (certificate no. [ ] in the Principal Amount of $[ ] attached hereto (the "Security"), the undersigned hereby elects to cause Ligand Pharmaceuticals Incorporated (the "Company") to convert $[_____] Principal Amount of the Security pursuant to paragraph 6 of the Security at the Conversion Price. Capitalized terms used herein and not otherwise defined have the meanings specified in the Security.

2. In the event that the undersigned has elected to convert the

Security in part, please execute and deliver to the undersigned a new Security in a denomination equal in Principal Amount to the unconverted portion of the Security.

3. In connection with the conversion of the Security, the undersigned confirms that:

(a) We understand that the securities to be issued upon such conversion have not been registered under the Securities Act and may not be offered or sold except as permitted in the following sentence. We agree that if we should sell or otherwise transfer such securities, we will do so only (i) to the Company or its Subsidiaries, (ii) inside the United States to an institutional "accredited investor" (as defined below), (iii) outside the United States in accordance with Regulation S under the Securities Act, (iv) pursuant to the exemption from registration provided by Rule 144 under the Securities Act (if available) or (v) pursuant to an effective registration statement under the Securities Act.

(b) We understand that the certificates representing such securities will, so long as appropriate, bear the following legends:

THE SHARES REPRESENTED BY THIS CERTIFICATE HAVE NOT BEEN REGISTERED UNDER THE SECURITIES ACT OF 1933, AS AMENDED (THE "ACT"), MAY NOT BE SOLD, TRANSFERRED OR OTHERWISE DISPOSED OF IN THE ABSENCE OF AN EFFECTIVE REGISTRATION STATEMENT UNDER THE ACT OR PURSUANT TO A VALID EXEMPTION THEREFROM. THE SHARES REPRESENTED BY THIS CERTIFICATE MAY NOT BE SOLD, TRANSFERRED OR OTHERWISE DISPOSED OF EXCEPT IN ACCORDANCE WITH THE PROVISIONS OF REGULATION S (SS.230.901 THROUGH SS.230.905, AND PRELIMINARY NOTES). HEDGING TRANSACTIONS INVOLVING THE SHARES REPRESENTED BY THIS CERTIFICATE MAY NOT BE CONDUCTED UNLESS IN COMPLIANCE WITH THE ACT.

THE TRANSFER OF THE SECURITY EVIDENCED HEREBY IS SUBJECT TO THE CONDITIONS SPECIFIED IN A SECURITIES PURCHASE AGREEMENT, DATED AS OF NOVEMBER 6, 1998, BY AND AMONG THE COMPANY, ELAN INTERNATIONAL SERVICES, LTD. AND ELAN CORPORATION, PLC, AND THE COMPANY RESERVES THE RIGHT TO REFUSE THE TRANSFER OF SUCH SECURITY UNTIL SUCH CONDITIONS HAVE BEEN FULFILLED WITH RESPECT TO SUCH TRANSFER. A COPY OF SUCH CONDITIONS WILL BE FURNISHED BY THE COMPANY TO THE HOLDER HEREOF WITHOUT CHARGE.

(c) We are acquiring the securities to be issued upon conversion of the Security for our own account and are either (i) an institutional "accredited investor" (as defined in Rule 501(a)(1), (2), (3) or (7) of Regulation D under the Securities Act) or (ii) a foreign purchaser that is outside the United States. We have such knowledge and experience in financial and business matters to be capable of evaluating the merits and risks of our investment in the securities and we are able to bear the economic risk of our investment for an indefinite period of time.

This certificate and the statements contained herein are made for the benefit of the Company.

_____
Signature of Holder

Date: _____

ANNEX C

FORM OF CERTIFICATE FOR
REGISTRATION OF TRANSFER OR EXCHANGE
OF
ZERO COUPON CONVERTIBLE SENIOR NOTE DUE 2008

Ligand Pharmaceuticals Incorporated
10275 Science Center Drive
San Diego, California 92121

Attention: General Counsel

1. Reference is hereby made to the Zero Coupon Convertible Senior Note due 2008 (certificate no. [ ] in the Principal Amount of $[ ] attached hereto (the "Security"). Capitalized terms used herein and not otherwise defined have the meanings specified in the Security.

2. In connection with the registration of transfer or exchange of such Security, the undersigned hereby certifies that:

CHECK ONE

_____ The Security is being acquired for the undersigned's own account, without transfer; or

_____ The Security is being transferred to the Company; or

_____ The Security is being transferred in a transaction permitted by Rule 144 under the Securities Act; or

_____ The Security is being transferred pursuant to an effective registration statement; or

_____ The Security is being transferred in a transaction permitted by Rule 904 under the Securities Act; or

_____ the Security is being transferred pursuant to an exemption from the registration requirements of the Securities Act other than Rule 144 or Rule 904, and the undersigned hereby further certifies that the Security is being transferred in compliance with the exemption claimed, which certification is supported by an opinion of

counsel, if required by the Company, provided by the undersigned or the transferee (a copy of which the undersigned has attached to this certification) in form reasonably satisfactory to the Company, to the effect that such transfer is in compliance with the Securities Act;

and the Security is being transferred in compliance with any applicable state securities or "Blue Sky" laws of any state of the United States.

3. This certificate and the statements contained herein are made for the benefit of the Company.

_____
Signature of Holder

Date: _____

ANNEX D

FORM OF UNRESTRICTED SECURITIES CERTIFICATE
OF
ZERO COUPON CONVERTIBLE SENIOR NOTE DUE 2008

Ligand Pharmaceuticals Incorporated
10275 Science Center Drive
San Diego, California 92121

Attention: General Counsel

1. Reference is hereby made to the Zero Coupon Convertible Senior Note due 2008 (certificate no. [ ] in the Principal Amount of $[ ] attached hereto (the "Security"). Capitalized terms used herein and not otherwise defined have the meanings specified in the Security.

2. The undersigned, the registered owner of the Security, has requested that the Security be exchanged for a new Security bearing no portion of the Legend (excluding that portion of the Legend relating to transfer conditions set forth in the Purchase Agreement). In connection with such exchange, the undersigned hereby certifies that the exchange is occurring after a period of at least two years has elapsed since the date the Security was acquired from the Company or any affiliate (as such term is defined under Rule 144 under the Securities Act) of the Company, whichever is later, and the undersigned is not, and during the preceding three months has not been, an affiliate of the Company. The undersigned also acknowledges that future transfers of the Security must comply with all applicable state securities or "Blue Sky" laws.

3. This certificate and the statements contained herein are made for the benefit of the Company.

_____
Signature of Holder

Date: _____

January 5, 1998

Steven D. Reich, M.D.
Senior Vice President, Clinical Research
LIGAND PHARMACEUTICALS INCORPORATED
9393 Towne Centre Drive
San Diego, CA 92121

Dear Steve:

The purpose of this letter agreement is to document the terms of the severance package to which you will be entitled should your employment with Ligand Pharmaceuticals Incorporated (the "Company") terminate under certain specified circumstances.

Part One of this letter agreement sets forth certain definitional provisions to be in effect for purposes of determining your benefit entitlements. Part Two specifies the terms and conditions upon which you may become entitled to receive severance benefits in the event your employment with the Company were to be terminated involuntarily whether in connection with certain changes in control of the Company or otherwise. Part Three concludes this agreement with a series of general terms and conditions applicable to your severance benefits.

PART ONE -- DEFINITIONS

DEFINITIONS. For purposes of this letter agreement, including in particular the application of the special benefit limitations of Part Three, the following definitions will be in effect:

AVERAGE COMPENSATION means your average W-2 wages from the Company for the five (5) calendar years completed immediately prior to the calendar year in which the Change in Control is effected. Any W-2 wages for a partial year of employment will be annualized, in accordance with the frequency with which such wages are paid during such partial year, before inclusion within your Average Compensation.

BOARD means the Company's Board of Directors.

CHANGE IN CONTROL means any of the following events:

(i) a merger or consolidation in which the Company is not the surviving entity, except for a transaction the principal purpose of which is to change the state in which the Company is incorporated,

(ii) the sale, transfer or other disposition of all or substantially all of the assets of the Company other than in the ordinary course,

(iii) any reverse merger in which the Company ceases to exist as an independent corporation and becomes the subsidiary of another corporation,

(iv) any Hostile Take-Over,

(v) the acquisition by any person (or related group of persons), whether by tender or exchange offer made directly to the Company's stockholders, private purchases from one or more of the Company's stockholders, open market purchases or any other transaction, of beneficial ownership of securities possessing more than thirty percent (30%) of the total combined voting power of the Company's outstanding securities,

(vi) the acquisition by any person (or related group of persons), whether by tender or exchange offer made directly to the Company's stockholders, private purchases from one or more of the Company's stockholders, open market purchases or any other transaction, of additional

securities of the Company which increase the total holdings of such person (or group) to a level of securities possessing more than fifty percent (50%) of the total combined voting power of the Company's outstanding securities, or

(vii) the acquisition by any person (or related group of persons), whether by tender or exchange offer made directly to the Company's stockholders, private purchases from one or more of the Company's stockholders, open market purchases or any other transaction, of securities of the Company possessing sufficient voting power in the aggregate to elect an absolute majority of the members of the Board (rounded up to the nearest whole number).

CODE means the Internal Revenue Code of 1986, as amended.

COMMON STOCK means the Company's common stock, par value $0.001 per share.

EQUITY INCENTIVE PLANS mean any of the following equity incentive plans of the Company: 1992 Stock Option/Stock Issuance Plan, as amended; Restricted Stock Purchase Plan, as amended; and 1988 Stock Option Plan, as amended.

HEALTH CARE COVERAGE means the continued health care coverage to which you and your eligible dependents may become entitled under this agreement upon the Involuntary Termination of your employment other than Termination for Cause.

HOSTILE TAKE-OVER means either of the following events:

(i) the acquisition by any person (or related group of persons) whether by tender or exchange offer made directly to the Company's stockholders, private purchases from one or more of the Company's stockholders, open market purchases or any other transaction, of beneficial ownership of securities possessing more than thirty percent (30%) of the total combined voting power of the Company's outstanding securities pursuant to a tender offer made directly to the Company's stockholders which the Board does not recommend such stockholders to accept, or

(ii) a change in the composition of the Board over a period of thirty-six (36) consecutive months or less such that a majority of the Board members (rounded up to the next whole number) ceases, by reason of one or more contested elections for Board membership, to be comprised of individuals who either (a) have been Board members continuously since the beginning of such period or (b) have been elected or nominated for election as Board members during such period by at least a majority of the Board members described in clause (a) who were still in office at the time such election or nomination was approved by the Board.

INVOLUNTARY TERMINATION means the termination of your employment with the Company:

(i) involuntarily upon your discharge or dismissal, or

(ii) voluntarily upon your resignation in connection with any of the following changes to the terms and conditions of your employment: (A) a change in your position with the Company which materially reduces your level of responsibility, (B) a greater than ten percent (10%) reduction in your level of compensation (including base salary, fringe benefits and participation in non-discretionary bonus programs under which awards are payable pursuant to objective financial or performance standards) or (C) a

relocation of your principal place of employment by more than fifty (50) miles.

The following guidelines shall determine whether one or more reductions in compensation should be taken into account for purposes of clause (ii)(B):

- Any reduction in compensation which occurs in connection with an across-the-board reduction in the level of compensation payable to the Company's executive officers or senior management shall not constitute grounds for a clause (ii)(B) resignation, unless implemented within eighteen (18) months after a Change in Control.

- In the event of a Hostile Take-Over, the greater than ten percent (10%) standard of clause (ii)(B) shall be reduced to zero percent (0%) so that any reduction in the level of your compensation shall constitute grounds for a clause (ii)(B) resignation.

In no event shall an Involuntary Termination be deemed to occur should your employment terminate by reason of death or permanent disability.

OPTION means any option granted to you under any of the Equity Incentive Plans which is outstanding at the time of your Involuntary Termination or any earlier Change in Control. Your outstanding options are to be divided into two separate categories as follows:

- ACQUISITION-ACCELERATED OPTIONS: any outstanding Option (or installment thereof) which accelerates upon a Change in Control in

accordance with the automatic acceleration provisions of the Equity Incentive Plans.

- SEVERANCE-ACCELERATED OPTIONS: any outstanding Option (or installment thereof) which is not an Acquisition-Accelerated Option but which accelerates upon your Involuntary Termination, whether or not in connection with a Change in Control, as part of your severance benefits under this agreement.

EQUITY PARACHUTE PAYMENT means, with respect to any Option (whether Acquisition-Accelerated or Severance-Accelerated) or unvested Stock Issuance, the portion deemed to be a parachute payment under Code Section 280G and the Treasury Regulations issued thereunder. Such Equity Parachute Payment shall be calculated in accordance with the valuation provisions established under Code Section 280G and the applicable Treasury Regulations and will include an appropriate dollar adjustment to reflect the lapse of your obligation to remain in the Company's employ as a condition to your vesting in the accelerated portion of such Option or Stock Issuance.

OTHER PARACHUTE PAYMENTS mean any payments in the nature of compensation to which you may become entitled under this letter agreement (other than the Equity Parachute Payment) or any other arrangement with the Company, to the extent such payments qualify as parachute payments within the meaning of Code Section 280G(b)(2) and the Treasury Regulations issued thereunder or would so qualify if the aggregate present value of such payments exceeded the amount specified in Code Section 280G(b)(2)(ii).

STOCK ISSUANCE means the issuance of unvested shares of Common Stock under the Company's Restricted Stock Plan or any other Equity Incentive Plan.

TERMINATION FOR CAUSE means an Involuntary Termination of your employment with the Company by reason of your conviction of any felony or other criminal act, your commission of any act of fraud or embezzlement, your unauthorized use or disclosure of confidential information or trade secrets of the Company or its subsidiaries, or any other intentional misconduct on your part which adversely affects the business or affairs of the Company in a material manner.

PART TWO -- INVOLUNTARY TERMINATION BENEFITS

You will be entitled to receive the severance benefits specified below should there occur an Involuntary Termination of your employment during the term of this letter agreement effected in connection with a Change in Control, other than an Involuntary Termination which constitutes a Termination for Cause. However, in the absence of a Hostile Take-Over, these benefits will continue to be paid you only for so long as you remain available for any consulting services required of you under Part Two, Paragraph 4 and abide by the restrictive covenants set forth in Part Two, Paragraph 5.

1. SEVERANCE PAYMENTS. You will receive severance payments from the Company for a period of twelve (12) months following your Involuntary Termination in an aggregate amount equal to the sum of (A) one (1) times the annual rate of base salary in effect for you at the time of your Involuntary Termination plus (B) one (1) times the average of the bonuses paid to you for services rendered in the two (2) fiscal years immediately preceding the fiscal year of your Involuntary Termination. If a bonus is paid to you for only one of those years, then the bonus amount under Clause (B) will be equal to one (1) times such bonus amount. The aggregate severance payments shall be paid to you in equal installments over the twelve-month period in accordance with the Company's normal payroll practices and subject to all applicable withholding taxes. The severance payments will immediately terminate in the event you should cease to remain available for the consulting services required of you under Paragraph 4 or in the event you fail to abide by the restrictive covenants set forth in Paragraph 5. However, in the event your Involuntary Termination occurs in connection with a Hostile Take-Over, your severance payments will be paid to you in the form of a single lump sum amount within thirty (30) days after such Involuntary Termination, and the provisions of Paragraphs 4 and 5 will not apply.

2. HEALTH CARE COVERAGE. The Company will, at its expense, provide you and your eligible dependents with continued health care coverage under the Company's medical/dental plan until the EARLIER of ------- (i) twelve (12) months after the effective date of your Involuntary Termination or (ii) the first date that you are covered under another employer's health benefit program which provides substantially the same level of benefits without exclusion for pre-existing medical conditions. Such coverage will be in lieu of any other continued health care

coverage to which you or your dependents would otherwise be entitled pursuant to the requirements of Code Section 4980B by reason of your termination of employment.

3. OPTION ACCELERATION AND LAPSE OF RESTRICTIONS. Each of your outstanding Options under the Equity Incentive Plans will (to the extent not then otherwise exercisable) automatically accelerate so that each such Option will become immediately exercisable for the total number of shares of Common Stock at the time subject to that Option. Each such accelerated Option, together with all of your other vested Options, will remain exercisable for a period of twelve (12) months following your Involuntary Termination until the end of the specified ten (10)-year option term and may be exercised for any or all of the option shares in accordance with the exercise provisions of the option agreement evidencing the grant. In addition, all restrictions applicable to the Stock Issuances you hold (to the extent those restrictions have not previously lapsed in accordance with the terms of the issuance agreements) will automatically lapse upon your Involuntary Termination.

4. CONSULTING SERVICES. Unless your Involuntary Termination occurs in connection with a Hostile Take-Over, you will make yourself available to perform consulting services reasonably requested of you during the twelve (12)-month period following your Involuntary Termination. You will be compensated at an hourly rate to be agreed upon by you and the Company at the time such consulting services are to be rendered, and you will be reimbursed for all reasonable out-of-pocket expenses incurred in rendering such services upon your submission of appropriate documentation for those expenses.

5. RESTRICTIVE COVENANTS. For the one hundred twenty (120)-day period following your Involuntary Termination:

(i) You will not directly or indirectly, whether for your own account or as an employee, director, consultant or advisor, provide services to any business enterprise which is at the time in competition with any of the Company's then existing or formally planned product lines

and which is located geographically in an area where the Company maintains substantial business activities, unless you obtain the prior written consent of the Board of Directors.

(ii)You will not directly or indirectly encourage or solicit any individual to leave the Company's employ for any reason or interfere in any other manner with the employment relationships at the time existing between the Company and its current or prospective employees.

(iii)You will not induce or attempt to induce any customer, supplier, distributor, licensee or other business relation of the Company to cease doing business with the Company or in any way interfere with the existing business relationship between any such customer, supplier, distributor, licensee or other business relation and the Company.

You acknowledge that monetary damages may not be sufficient to compensate the Company for any economic loss which may be incurred by reason of your breach of the foregoing restrictive covenants. Accordingly, in the event of any such breach, the Company shall, in addition to the cessation of the severance benefits provided you under this agreement and any remedies available to the Company at law, be entitled to obtain equitable relief in the form of an injunction precluding you from continuing to engage in such breach.

None of the foregoing restrictive covenants shall be applicable in the event your Involuntary Termination occurs in connection with a Hostile Take-Over.

6. BENEFIT REDUCTION. In the event of a Change in Control, the following limitations shall become applicable:

a. BENEFIT REDUCTION. If the Change in Control does not constitute a Hostile Take-Over, first the dollar amount of your severance payment under Paragraph 1 will be reduced to the extent necessary to assure that the present value of those benefits will not, when added to the present value of your Equity Parachute Payment and your Other Parachute Payments, exceed 2.99 times your Average Compensation. In the event of a Hostile Take-Over, no reduction will be made to your severance payment (or any other benefit to which you become entitled hereunder), unless necessary to provide you with the maximum after-tax benefit available, after taking into account any parachute excise tax which might otherwise be payable by you under Code Section 4999 and any analogous State income tax provision.

b. RESOLUTION OF DISPUTES. In the event there is any disagreement between you and the Company as to whether one or more benefits to which you become entitled (whether under this letter agreement or otherwise) in connection with

a Change in Control constitute Equity Parachute Payments or Other Parachute Payments, such dispute is to be resolved as follows:

- In the event temporary, proposed or final Treasury Regulations in effect at the time under Code Section 280G specifically address the status of such benefits or the method for their valuation, the characterization afforded to such benefits by the Regulations, together with the methods prescribed for their valuation, shall be controlling.

- In the event such Regulations do not address the status of the benefits in dispute, the matter shall be submitted for resolution to independent counsel mutually acceptable to you and the Company ("Independent Counsel"). The resolution reached by Independent Counsel shall be final and controlling. However, should the Independent Counsel determine that the status of the benefits in dispute can be resolved through the obtainment of a private letter ruling from the Internal Revenue Service, a formal and proper request for such ruling shall be prepared and submitted by Independent Counsel, and the determination made by the Internal Revenue Service in the issued ruling shall be controlling. All expenses incurred in connection with the retention of Independent Counsel and (if applicable) the preparation and submission of the ruling request shall be paid by the Company.

- The present value of each Equity Parachute Payment and each of the Other Parachute Payments (including your severance payment and Health Care Coverage) shall be determined in accordance with the provisions of Code Section 280G(d)(4) and the Treasury Regulations issued thereunder.

The full amount of your severance benefit under Paragraph 1 shall not be paid to you until any amounts in dispute under this Paragraph 6.b. have been resolved in accordance herewith. However, any portion of such severance payment which would not otherwise exceed the benefit limitation of Paragraph 6.a. even if all amounts in dispute under this Paragraph 6.b. were to be resolved against you will be paid to you in accordance with the applicable provisions of this letter agreement.

c. OVERRIDING LIMITATION. You will in all events be entitled to receive the full amount of your severance payment under Paragraph 1, to the extent those benefits, when added to the present value of your Equity Parachute Payment and your Other Parachute Payments (excluding such severance payment), will nevertheless qualify as reasonable compensation within the standards established under Code Section 280G(b)(4).

d. INTERPRETATION. The provisions of this Paragraph 6 shall in all events be interpreted in such manner as will avoid the imposition of excise taxes under Code

Section 4999, and the disallowance of deductions under Code Section 280G(a), with respect to your severance benefits under this letter agreement.

PART THREE -- MISCELLANEOUS PROVISIONS

1. TERMINATION FOR CAUSE. Should your Involuntary Termination constitute a Termination for Cause, then the Company shall only be required to pay you (i) any unpaid compensation earned for services previously rendered through the date of such termination and (ii) any accrued but unpaid vacation benefits or sick days, and no benefits will be payable to you under Part Two or Part Three of this letter agreement.

2. TERM OF AGREEMENT. The provisions of this letter agreement will continue in effect for a period of five (5) years from the date hereof.

3. GENERAL CREDITOR STATUS. The benefits to which you may become entitled under this letter agreement (except those attributable to your Options

or Stock Issuances) will be paid, when due, from the general assets of the Company. Your right (or the right of the executors or administrators of your estate) to receive any such payments will at all times be that of a general creditor of the Company and will have no priority over the claims of other general creditors of the Company.

4. DEATH. Should you die before receipt of all benefits to which you become entitled under this letter agreement, then the payment of such benefits will be made, on the due date or dates hereunder had you survived, to the executors or administrators of your estate. Should you die before you exercise your Severance-Accelerated Options (if any) or any other of your outstanding vested Options, then each such Option may be exercised, during the applicable exercise period in effect hereunder for those options at the time of your death, by the executors or administrators of your estate or by person to whom the Option is transferred pursuant to your will or in accordance with the laws of inheritance.

5. MISCELLANEOUS. The provisions of this letter agreement will be construed and interpreted under the laws of the State of California. This agreement incorporates the entire agreement between you and the Company relating to the subject of severance benefits and supersedes all prior agreements and understandings with respect to such subject matter. This agreement may only be amended by written instrument signed by you and another duly-authorized officer of the Company. If any provision of this letter agreement as applied to any party or to any circumstance should be adjudged by a court of competent jurisdiction to be void or unenforceable for any reason, the invalidity of that provision shall in no way affect (to the maximum extent permissible by law) the application of such provision under circumstances different from those adjudicated by the court, the application of any other provision of this letter agreement, or the enforceability or invalidity of this letter agreement as a whole. Should any provision of this letter agreement become or be deemed invalid, illegal or unenforceable in any jurisdiction by reason of the scope, extent or duration of its coverage, then such provision shall be deemed amended to the extent necessary to conform to applicable law so as to be valid and enforceable or, if such provision cannot be so amended without materially altering the intention of the parties, then such provision shall be stricken and the remainder of this letter agreement shall continue in full force and effect.

6 REMEDIES. All rights and remedies provided pursuant to this letter agreement or by law will be cumulative, and no such right or remedy will be exclusive of any other. A party may pursue any one or more rights or remedies hereunder or may seek damages or specific performance in the event of another party's breach hereunder or may pursue any other remedy by law or equity, whether or not stated in this letter agreement.

7. ARBITRATION. Any controversy which may arise between you and the Company with respect to the construction, interpretation or application of any of the terms, provisions or conditions of this agreement or any monetary claim arising from or relating to this agreement will be submitted to final and binding arbitration in San Diego, California in accordance with the rules of the American Arbitration Association then in effect.

8. NO EMPLOYMENT OR SERVICE CONTRACT. Nothing in this agreement shall confer upon you any right to continue in the employment of the Company for any period of specific duration or interfere with or otherwise restrict in any way the rights of the Company or you, which rights are hereby expressly reserved by each, to terminate your employment at any time for any reason whatsoever, with or without cause.

9. PROPRIETARY INFORMATION. You hereby acknowledge that the Company may, from time to time during your employment with the Company, disclose to you confidential information pertaining to the Company's business and affairs. All

information and data, whether or not in writing, of a private or confidential nature concerning the business or financial affairs of the Company (collectively, "Proprietary Information") is and will remain the sole and exclusive property of the Company. In connection with such Proprietary Information, you agree as follows:

(i) You will not, during your employment with the Company or at any time thereafter, disclose to any third party or directly or indirectly make use of any such Proprietary Information other than in connection with, and in furtherance of, the Company's business and affairs.

(ii) You agree that you will use all files, letters, memoranda, reports, records, data or other written, reproduced or other tangible manifestations of the Proprietary Information, whether created by you or others, to which you have access during your employment with the Company, only in the performance of your duties with the Company. You will return all such materials (whether written, printed or otherwise reproduced or recorded) to the Company immediately upon the termination of your employment with the Company or upon any earlier request by the Company, without retaining any copies, notes or excerpts thereof.

(iii) Your obligations under this Paragraph 9 will continue in effect after the termination of your employment with the Company, whatever the reason or reasons for such termination, and the Company will have the right to communicate with any future or prospective employer concerning your continuing obligations under this Paragraph 9.

Please indicate your acceptance of the foregoing provisions of this severance agreement by signing the enclosed copy of this letter agreement and returning it to the Company.

Very truly yours,

LIGAND PHARMACEUTICALS INCORPORATED

/s/DAVID E. ROBINSON

David E. Robinson
Chairman, President and CEO

DER:bjo
agree\severance.pri

ACCEPTED BY AND AGREED TO

Signature:/s/STEVEN D. REICH

Dated: February 2, 1998

August 23, 1999

Eric S. Groves, M.D., Ph.D.
Vice President, Project Management
LIGAND PHARMACEUTICALS INCORPORATED
10275 Science Center Drive
San Diego, CA 92121

Dear Eric:

The purpose of this letter agreement is to document the terms of the severance package to which you will be entitled should your employment with Ligand Pharmaceuticals Incorporated (the "Company") terminate under certain specified circumstances.

Part One of this letter agreement sets forth certain definitional provisions to be in effect for purposes of determining your benefit entitlements. Part Two specifies the terms and conditions upon which you may become entitled to receive severance benefits in the event your employment with the Company were to be terminated involuntarily whether in connection with certain changes in control of the Company or otherwise. Part Three concludes this agreement with a series of general terms and conditions applicable to your severance benefits.

PART ONE -- DEFINITIONS

DEFINITIONS. For purposes of this letter agreement, including in particular the application of the special benefit limitations of Part Three, the following definitions will be in effect:

AVERAGE COMPENSATION means your average W-2 wages from the Company for the five (5) calendar years completed immediately prior to the calendar year in which the Change in Control is effected. Any W-2 wages for a partial year of employment will be annualized, in accordance with the frequency with which such wages are paid during such partial year, before inclusion within your Average Compensation.

BOARD means the Company's Board of Directors.

CHANGE IN CONTROL means any of the following events:

(i) a merger or consolidation in which the Company is not the surviving entity, except for a transaction the principal purpose of which is to change the state in which the Company is incorporated,

(ii) the sale, transfer or other disposition of all or substantially all of the assets of the Company other than in the ordinary course,

(iii) any reverse merger in which the Company ceases to exist as an independent corporation and becomes the subsidiary of another corporation,

(iv) any Hostile Take-Over,

(v) the acquisition by any person (or related group of persons), whether by tender or exchange offer made directly to the Company's stockholders, private purchases from one or more of the Company's stockholders, open market purchases or any other transaction, of beneficial ownership of securities possessing more than thirty percent (30%) of the total combined voting power of the Company's outstanding securities,

(vi) the acquisition by any person (or related group of persons), whether by tender or exchange offer made directly to the Company's stockholders, private purchases from one or more of the Company's stockholders, open market purchases or any other transaction, of additional securities of the Company which increase the total holdings of such person

(or group) to a level of securities possessing more than fifty percent (50%) of the total combined voting power of the Company's outstanding securities, or

(vii) the acquisition by any person (or related group of persons), whether by tender or exchange offer made directly to the Company's stockholders, private purchases from one or more of the Company's stockholders, open market purchases or any other transaction, of securities of the Company possessing sufficient voting power in the aggregate to elect an absolute majority of the members of the Board (rounded up to the nearest whole number).

CODE means the Internal Revenue Code of 1986, as amended.

COMMON STOCK means the Company's common stock, par value $0.001 per share.

EQUITY INCENTIVE PLANS mean any of the following equity incentive plans of the Company: 1992 Stock Option/Stock Issuance Plan, as amended; Restricted Stock Purchase Plan, as amended; and 1988 Stock Option Plan, as amended.

HEALTH CARE COVERAGE means the continued health care coverage to which you and your eligible dependents may become entitled under this agreement upon the Involuntary Termination of your employment other than Termination for Cause.

HOSTILE TAKE-OVER means either of the following events:

(i) the acquisition by any person (or related group of persons) whether by tender or exchange offer made directly to the Company's stockholders, private purchases from one or more of the Company's stockholders, open market purchases or any other transaction, of beneficial ownership of securities possessing more than thirty percent (30%) of the total combined voting power of the Company's outstanding securities pursuant to a tender offer made directly to the Company's stockholders which the Board does not recommend such stockholders to accept, or

(ii) a change in the composition of the Board over a period of thirty-six (36) consecutive months or less such that a majority of the Board members (rounded up to the next whole number) ceases, by reason of one or more contested elections for Board membership, to be comprised of individuals who either (a) have been Board members continuously since the beginning of such period or (b) have been elected or nominated for election as Board members during such period by at least a majority of the Board members described in clause (a) who were still in office at the time such election or nomination was approved by the Board.

INVOLUNTARY TERMINATION means the termination of your employment with the Company:

(i) involuntarily upon your discharge or dismissal, or

(ii) voluntarily upon your resignation in connection with any of the following changes to the terms and conditions of your employment: (A) a change in your position with the Company which materially reduces your level of responsibility, (B) a greater than ten percent (10%) reduction in your level of compensation (including base salary, fringe benefits and participation in non-discretionary bonus programs under which awards are payable pursuant to objective financial or performance standards) or (C) a relocation of your principal place of employment by more than fifty (50) miles.

The following guidelines shall determine whether one or more reductions in compensation should be taken into account for purposes of clause (ii)(B):

- Any reduction in compensation which occurs in connection with an across-the-board reduction in the level of compensation payable to the Company's executive officers or senior management shall not constitute grounds for a clause (ii)(B) resignation, unless implemented within eighteen (18) months after a Change in Control.

- In the event of a Hostile Take-Over, the greater than ten percent (10%) standard of clause (ii)(B) shall be reduced to zero percent (0%) so that any reduction in the level of your compensation shall constitute grounds for a clause (ii)(B) resignation.

In no event shall an Involuntary Termination be deemed to occur should your employment terminate by reason of death or permanent disability.

OPTION means any option granted to you under any of the Equity Incentive Plans which is outstanding at the time of your Involuntary Termination or any earlier Change in Control. Your outstanding options are to be divided into two separate categories as follows:

- ACQUISITION-ACCELERATED OPTIONS: any outstanding Option (or installment thereof) which accelerates upon a Change in Control in

accordance with the automatic acceleration provisions of the Equity Incentive Plans.

- SEVERANCE-ACCELERATED OPTIONS: any outstanding Option (or installment thereof) which is not an Acquisition-Accelerated Option but which accelerates upon your Involuntary Termination, whether or not in connection with a Change in Control, as part of your severance benefits under this agreement.

EQUITY PARACHUTE PAYMENT means, with respect to any Option (whether Acquisition-Accelerated or Severance-Accelerated) or unvested Stock Issuance, the portion deemed to be a parachute payment under Code Section 280G and the Treasury Regulations issued thereunder. Such Equity Parachute Payment shall be calculated in accordance with the valuation provisions established under Code Section 280G and the applicable Treasury Regulations and will include an appropriate dollar adjustment to reflect the lapse of your obligation to remain in the Company's employ as a condition to your vesting in the accelerated portion of such Option or Stock Issuance.

OTHER PARACHUTE PAYMENTS mean any payments in the nature of compensation to which you may become entitled under this letter agreement (other than the Equity Parachute Payment) or any other arrangement with the Company, to the extent such payments qualify as parachute payments within the meaning of Code Section 280G(b)(2) and the Treasury Regulations issued thereunder or would so qualify if the aggregate present value of such payments exceeded the amount specified in Code Section 280G(b)(2)(ii).

STOCK ISSUANCE means the issuance of unvested shares of Common Stock under the Company's Restricted Stock Plan or any other Equity Incentive Plan.

TERMINATION FOR CAUSE means an Involuntary Termination of your employment with the Company by reason of your conviction of any felony or other criminal act, your commission of any act of fraud or embezzlement, your unauthorized use or disclosure of confidential information or trade secrets of the Company or its subsidiaries, or any other intentional misconduct on your part which adversely affects the business or affairs of the Company in a material manner.

PART TWO -- INVOLUNTARY TERMINATION BENEFITS

You will be entitled to receive the severance benefits specified below should there occur an Involuntary Termination of your employment during the term of this letter agreement effected in connection with a Change in Control, other than an Involuntary Termination which constitutes a Termination for Cause. However, in the absence of a Hostile Take-Over, these benefits will continue to be paid you only for so long as you remain available for any consulting services required of you under Part Two, Paragraph 4 and abide by the restrictive covenants set forth in Part Two, Paragraph 5.

1. SEVERANCE PAYMENTS. You will receive severance payments from the Company for a period of twelve (12) months following your Involuntary Termination in an aggregate amount equal to the sum of (A) one (1) times the annual rate of base salary in effect for you at the time of your Involuntary Termination plus (B) one (1) times the average of the bonuses paid to you for services rendered in the two (2) fiscal years immediately preceding the fiscal year of your Involuntary Termination. If a bonus is paid to you for only one of those years, then the bonus amount under Clause (B) will be equal to one (1) times such bonus amount. The aggregate severance payments shall be paid to you in equal installments over the twelve-month period in accordance with the Company's normal payroll practices and subject to all applicable withholding taxes. The severance payments will immediately terminate in the event you should cease to remain available for the consulting services required of you under Paragraph 4 or in the event you fail to abide by the restrictive covenants set forth in Paragraph 5. However, in the event your Involuntary Termination occurs in connection with a Hostile Take-Over, your severance payments will be paid to you in the form of a single lump sum amount within thirty (30) days after such Involuntary Termination, and the provisions of Paragraphs 4 and 5 will not apply.

2. HEALTH CARE COVERAGE. The Company will, at its expense, provide you and your eligible dependents with continued health care coverage under the Company's medical/dental plan until the EARLIER of (i) twelve (12) months after the effective date of your Involuntary Termination or (ii) the first date that you are covered under another employer's health benefit program which provides substantially the same level of benefits without exclusion for pre-existing medical conditions. Such coverage will be in lieu of any other continued health care

coverage to which you or your dependents would otherwise be entitled pursuant to the requirements of Code Section 4980B by reason of your termination of employment.

3. OPTION ACCELERATION AND LAPSE OF RESTRICTIONS. Each of your outstanding Options under the Equity Incentive Plans will (to the extent not then otherwise exercisable) automatically accelerate so that each such Option will become immediately exercisable for the total number of shares of Common Stock at the time subject to that Option. Each such accelerated Option, together with all of your other vested Options, will remain exercisable for a period of twelve (12) months following your Involuntary Termination until the end of the specified ten (10)-year option term and may be exercised for any or all of the option shares in accordance with the exercise provisions of the option agreement evidencing the grant. In addition, all restrictions applicable to the Stock Issuances you hold (to the extent those restrictions have not previously lapsed in accordance with the terms of the issuance agreements) will automatically lapse upon your Involuntary Termination.

4. CONSULTING SERVICES. Unless your Involuntary Termination occurs in connection with a Hostile Take-Over, you will make yourself available to perform consulting services reasonably requested of you during the twelve (12)-month period following your Involuntary Termination. You will be compensated at an hourly rate to be agreed upon by you and the Company at the time such consulting services are to be rendered, and you will be reimbursed for all reasonable

out-of-pocket expenses incurred in rendering such services upon your submission of appropriate documentation for those expenses.

5. RESTRICTIVE COVENANTS. For the one hundred twenty (120)-day period following your Involuntary Termination:

(i) You will not directly or indirectly, whether for your own account or as an employee, director, consultant or advisor, provide services to any business enterprise which is at the time in competition with any of the Company's then existing or formally planned product lines

and which is located geographically in an area where the Company maintains substantial business activities, unless you obtain the prior written consent of the Board of Directors.

(ii)You will not directly or indirectly encourage or solicit any individual to leave the Company's employ for any reason or interfere in any other manner with the employment relationships at the time existing between the Company and its current or prospective employees.

(iii)You will not induce or attempt to induce any customer, supplier, distributor, licensee or other business relation of the Company to cease doing business with the Company or in any way interfere with the existing business relationship between any such customer, supplier, distributor, licensee or other business relation and the Company.

You acknowledge that monetary damages may not be sufficient to compensate the Company for any economic loss which may be incurred by reason of your breach of the foregoing restrictive covenants. Accordingly, in the event of any such breach, the Company shall, in addition to the cessation of the severance benefits provided you under this agreement and any remedies available to the Company at law, be entitled to obtain equitable relief in the form of an injunction precluding you from continuing to engage in such breach.

None of the foregoing restrictive covenants shall be applicable in the event your Involuntary Termination occurs in connection with a Hostile Take-Over.

6. BENEFIT REDUCTION. In the event of a Change in Control, the following limitations shall become applicable:

a. BENEFIT REDUCTION. If the Change in Control does not constitute a Hostile Take-Over, first the dollar amount of your severance payment under Paragraph 1 will be reduced to the extent necessary to assure that the present value of those benefits will not, when added to the present value of your Equity Parachute Payment and your Other Parachute Payments, exceed 2.99 times your Average Compensation. In the event of a Hostile Take-Over, no reduction will be made to your severance payment (or any other benefit to which you become entitled hereunder), unless necessary to provide you with the maximum after-tax benefit available, after taking into account any parachute excise tax which might otherwise be payable by you under Code Section 4999 and any analogous State income tax provision.

b. RESOLUTION OF DISPUTES. In the event there is any disagreement between you and the Company as to whether one or more benefits to which you become entitled (whether under this letter agreement or otherwise) in connection with a Change in Control constitute Equity Parachute Payments or Other Parachute Payments, such dispute is to be resolved as follows:

- In the event temporary, proposed or final Treasury Regulations in effect at the time under Code Section 280G specifically address the status of such benefits or the method for their valuation, the characterization afforded to such benefits by the Regulations, together with the methods prescribed for

their valuation, shall be controlling.

- In the event such Regulations do not address the status of the benefits in dispute, the matter shall be submitted for resolution to independent counsel mutually acceptable to you and the Company ("Independent Counsel"). The resolution reached by Independent Counsel shall be final and controlling. However, should the Independent Counsel determine that the status of the benefits in dispute can be resolved through the obtainment of a private letter ruling from the Internal Revenue Service, a formal and proper request for such ruling shall be prepared and submitted by Independent Counsel, and the determination made by the Internal Revenue Service in the issued ruling shall be controlling. All expenses incurred in connection with the retention of Independent Counsel and (if applicable) the preparation and submission of the ruling request shall be paid by the Company.

- The present value of each Equity Parachute Payment and each of the Other Parachute Payments (including your severance payment and Health Care Coverage) shall be determined in accordance with the provisions of Code Section 280G(d)(4) and the Treasury Regulations issued thereunder.

The full amount of your severance benefit under Paragraph 1 shall not be paid to you until any amounts in dispute under this Paragraph 6.b. have been resolved in accordance herewith. However, any portion of such severance payment which would not otherwise exceed the benefit limitation of Paragraph 6.a. even if all amounts in dispute under this Paragraph 6.b. were to be resolved against you will be paid to you in accordance with the applicable provisions of this letter agreement.

c. OVERRIDING LIMITATION. You will in all events be entitled to receive the full amount of your severance payment under Paragraph 1, to the extent those benefits, when added to the present value of your Equity Parachute Payment and your Other Parachute Payments (excluding such severance payment), will nevertheless qualify as reasonable compensation within the standards established under Code Section 280G(b)(4).

d. INTERPRETATION. The provisions of this Paragraph 6 shall in all events be interpreted in such manner as will avoid the imposition of excise taxes under Code Section 4999, and the disallowance of deductions under Code Section 280G(a), with respect to your severance benefits under this letter agreement.

PART THREE -- MISCELLANEOUS PROVISIONS

1. TERMINATION FOR CAUSE. Should your Involuntary Termination constitute a Termination for Cause, then the Company shall only be required to pay you (i) any unpaid compensation earned for services previously rendered through the date of such termination and (ii) any accrued but unpaid vacation benefits or sick days, and no benefits will be payable to you under Part Two or Part Three of this letter agreement.

2. TERM OF AGREEMENT. The provisions of this letter agreement will continue in effect for a period of five (5) years from the date hereof.

3. GENERAL CREDITOR STATUS. The benefits to which you may become entitled under this letter agreement (except those attributable to your Options or Stock Issuances) will be paid, when due, from the general assets of the Company. Your right (or the right of the executors or administrators of your estate) to receive any such payments will at all times be that of a general creditor of the Company and will have no priority over the claims of other general creditors of the Company.

4. DEATH. Should you die before receipt of all benefits to which you become entitled under this letter agreement, then the payment of such benefits will be made, on the due date or dates hereunder had you survived, to the executors or administrators of your estate. Should you die before you exercise your Severance-Accelerated Options (if any) or any other of your outstanding

vested Options, then each such Option may be exercised, during the applicable exercise period in effect hereunder for those options at the time of your death, by the executors or administrators of your estate or by person to whom the Option is transferred pursuant to your will or in accordance with the laws of inheritance.

5. MISCELLANEOUS. The provisions of this letter agreement will be construed and interpreted under the laws of the State of California. This agreement incorporates the entire agreement between you and the Company relating to the subject of severance benefits and supersedes all prior agreements and understandings with respect to such subject matter. This agreement may only be amended by written instrument signed by you and another duly-authorized officer of the Company. If any provision of this letter agreement as applied to any party or to any circumstance should be adjudged by a court of competent jurisdiction to be void or unenforceable for any reason, the invalidity of that provision shall in no way affect (to the maximum extent permissible by law) the application of such provision under circumstances different from those adjudicated by the court, the application of any other provision of this letter agreement, or the enforceability or invalidity of this letter agreement as a whole. Should any provision of this letter agreement become or be deemed invalid, illegal or unenforceable in any jurisdiction by reason of the scope, extent or duration of its coverage, then such provision shall be deemed amended to the extent necessary to conform to applicable law so as to be valid and enforceable or, if such provision cannot be so amended without materially altering the intention of the parties, then such provision shall be stricken and the remainder of this letter agreement shall continue in full force and effect.

6 REMEDIES. All rights and remedies provided pursuant to this letter agreement or by law will be cumulative, and no such right or remedy will be exclusive of any other. A party may pursue any one or more rights or remedies hereunder or may seek damages or specific performance in the event of another party's breach hereunder or may pursue any other remedy by law or equity, whether or not stated in this letter agreement.

7. ARBITRATION. Any controversy which may arise between you and the Company with respect to the construction, interpretation or application of any of the terms, provisions or conditions of this agreement or any monetary claim arising from or relating to this agreement will be submitted to final and binding arbitration in San Diego, California in accordance with the rules of the American Arbitration Association then in effect.

8. NO EMPLOYMENT OR SERVICE CONTRACT. Nothing in this agreement shall confer upon you any right to continue in the employment of the Company for any period of specific duration or interfere with or otherwise restrict in any way the rights of the Company or you, which rights are hereby expressly reserved by each, to terminate your employment at any time for any reason whatsoever, with or without cause.

9. PROPRIETARY INFORMATION. You hereby acknowledge that the Company may, from time to time during your employment with the Company, disclose to you confidential information pertaining to the Company's business and affairs. All information and data, whether or not in writing, of a private or confidential nature concerning the business or financial affairs of the Company (collectively, "Proprietary Information") is and will remain the sole and exclusive property of the Company. In connection with such Proprietary Information, you agree as follows:

(i) You will not, during your employment with the Company or at any time thereafter, disclose to any third party or directly or indirectly make use of any such Proprietary Information other than in connection with, and in furtherance of, the Company's business and affairs.

(ii) You agree that you will use all files, letters, memoranda,

reports, records, data or other written, reproduced or other tangible manifestations of the Proprietary Information, whether created by you or others, to which you have access during your employment with the Company, only in the performance of your duties with the Company. You will return all such materials (whether written, printed or otherwise reproduced or recorded) to the Company immediately upon the termination of your employment with the Company or upon any earlier request by the Company, without retaining any copies, notes or excerpts thereof.

(iii) Your obligations under this Paragraph 9 will continue in effect after the termination of your employment with the Company, whatever the reason or reasons for such termination, and the Company will have the right to communicate with any future or prospective employer concerning your continuing obligations under this Paragraph 9.

Please indicate your acceptance of the foregoing provisions of this severance agreement by signing the enclosed copy of this letter agreement and returning it to the Company.

Very truly yours,

LIGAND PHARMACEUTICALS INCORPORATED

/s/DAVID E. ROBINSON

David E. Robinson
Chairman, President and CEO

DER:bjo

agree\severance.esg

ACCEPTED BY AND AGREED TO

Signature:/s/ERIC S. GROVES

Dated: November 5, 1999

December 9, 1999

Mr. Philip A. Duffy
Vice President, Technical Operations
LIGAND PHARMACEUTICALS INCORPORATED
10275 Science Center Drive
San Diego, CA 92121

Dear Phil:

The purpose of this letter agreement is to document the terms of the severance package to which you will be entitled should your employment with Ligand Pharmaceuticals Incorporated (the "Company") terminate under certain specified circumstances.

Part One of this letter agreement sets forth certain definitional provisions to be in effect for purposes of determining your benefit entitlements. Part Two specifies the terms and conditions upon which you may become entitled to receive severance benefits in the event your employment with the Company were to be terminated involuntarily whether in connection with certain changes in control of the Company or otherwise. Part Three concludes this agreement with a series of general terms and conditions applicable to your severance benefits.

PART ONE -- DEFINITIONS

DEFINITIONS. For purposes of this letter agreement, including in particular the application of the special benefit limitations of Part Three, the following definitions will be in effect:

AVERAGE COMPENSATION means your average W-2 wages from the Company for the five (5) calendar years completed immediately prior to the calendar year in which the Change in Control is effected. Any W-2 wages for a partial year of employment will be annualized, in accordance with the frequency with which such wages are paid during such partial year, before inclusion within your Average Compensation.

BOARD means the Company's Board of Directors.

CHANGE IN CONTROL means any of the following events:

(i) a merger or consolidation in which the Company is not the surviving entity, except for a transaction the principal purpose of which is to change the state in which the Company is incorporated,

(ii) the sale, transfer or other disposition of all or substantially all of the assets of the Company other than in the ordinary course,

(iii) any reverse merger in which the Company ceases to exist as an independent corporation and becomes the subsidiary of another corporation,

(iv) any Hostile Take-Over,

(v) the acquisition by any person (or related group of persons), whether by tender or exchange offer made directly to the Company's stockholders, private purchases from one or more of the Company's stockholders, open market purchases or any other transaction, of beneficial ownership of securities possessing more than thirty percent (30%) of the total combined voting power of the Company's outstanding securities,

(vi) the acquisition by any person (or related group of persons), whether by tender or exchange offer made directly to the Company's stockholders, private purchases from one or more of the Company's stockholders, open market purchases or any other transaction, of additional securities of the Company which increase the total holdings of such person

(or group) to a level of securities possessing more than fifty percent (50%) of the total combined voting power of the Company's outstanding securities, or

(vii) the acquisition by any person (or related group of persons), whether by tender or exchange offer made directly to the Company's stockholders, private purchases from one or more of the Company's stockholders, open market purchases or any other transaction, of securities of the Company possessing sufficient voting power in the aggregate to elect an absolute majority of the members of the Board (rounded up to the nearest whole number).

CODE means the Internal Revenue Code of 1986, as amended.

COMMON STOCK means the Company's common stock, par value $0.001 per share.

EQUITY INCENTIVE PLANS mean any of the following equity incentive plans of the Company: 1992 Stock Option/Stock Issuance Plan, as amended; Restricted Stock Purchase Plan, as amended; and 1988 Stock Option Plan, as amended.

HEALTH CARE COVERAGE means the continued health care coverage to which you and your eligible dependents may become entitled under this agreement upon the Involuntary Termination of your employment other than Termination for Cause.

HOSTILE TAKE-OVER means either of the following events:

(i) the acquisition by any person (or related group of persons) whether by tender or exchange offer made directly to the Company's stockholders, private purchases from one or more of the Company's stockholders, open market purchases or any other transaction, of beneficial ownership of securities possessing more than thirty percent (30%) of the total combined voting power of the Company's outstanding securities pursuant to a tender offer made directly to the Company's stockholders which the Board does not recommend such stockholders to accept, or

(ii) a change in the composition of the Board over a period of thirty-six (36) consecutive months or less such that a majority of the Board members (rounded up to the next whole number) ceases, by reason of one or more contested elections for Board membership, to be comprised of individuals who either (a) have been Board members continuously since the beginning of such period or (b) have been elected or nominated for election as Board members during such period by at least a majority of the Board members described in clause (a) who were still in office at the time such election or nomination was approved by the Board.

INVOLUNTARY TERMINATION means the termination of your employment with the Company:

(i) involuntarily upon your discharge or dismissal, or

(ii) voluntarily upon your resignation in connection with any of the following changes to the terms and conditions of your employment: (A) a change in your position with the Company which materially reduces your level of responsibility, (B) a greater than ten percent (10%) reduction in your level of compensation (including base salary, fringe benefits and participation in non-discretionary bonus programs under which awards are payable pursuant to objective financial or performance standards) or (C) a relocation of your principal place of employment by more than fifty (50) miles.

The following guidelines shall determine whether one or more reductions in compensation should be taken into account for purposes of clause (ii)(B):

- Any reduction in compensation which occurs in connection with an across-the-board reduction in the level of compensation payable to the Company's executive officers or senior management shall not constitute grounds for a clause (ii)(B) resignation, unless implemented within eighteen (18) months after a Change in Control.

- In the event of a Hostile Take-Over, the greater than ten percent (10%) standard of clause (ii)(B) shall be reduced to zero percent (0%) so that any reduction in the level of your compensation shall constitute grounds for a clause (ii)(B) resignation.

In no event shall an Involuntary Termination be deemed to occur should your employment terminate by reason of death or permanent disability.

OPTION means any option granted to you under any of the Equity Incentive Plans which is outstanding at the time of your Involuntary Termination or any earlier Change in Control. Your outstanding options are to be divided into two separate categories as follows:

- ACQUISITION-ACCELERATED OPTIONS: any outstanding Option (or installment thereof) which accelerates upon a Change in Control in

accordance with the automatic acceleration provisions of the Equity Incentive Plans.

- SEVERANCE-ACCELERATED OPTIONS: any outstanding Option (or installment thereof) which is not an Acquisition-Accelerated Option but which accelerates upon your Involuntary Termination, whether or not in connection with a Change in Control, as part of your severance benefits under this agreement.

EQUITY PARACHUTE PAYMENT means, with respect to any Option (whether Acquisition-Accelerated or Severance-Accelerated) or unvested Stock Issuance, the portion deemed to be a parachute payment under Code Section 280G and the Treasury Regulations issued thereunder. Such Equity Parachute Payment shall be calculated in accordance with the valuation provisions established under Code Section 280G and the applicable Treasury Regulations and will include an appropriate dollar adjustment to reflect the lapse of your obligation to remain in the Company's employ as a condition to your vesting in the accelerated portion of such Option or Stock Issuance.

OTHER PARACHUTE PAYMENTS mean any payments in the nature of compensation to which you may become entitled under this letter agreement (other than the Equity Parachute Payment) or any other arrangement with the Company, to the extent such payments qualify as parachute payments within the meaning of Code Section 280G(b)(2) and the Treasury Regulations issued thereunder or would so qualify if the aggregate present value of such payments exceeded the amount specified in Code Section 280G(b)(2)(ii).

STOCK ISSUANCE means the issuance of unvested shares of Common Stock under the Company's Restricted Stock Plan or any other Equity Incentive Plan.

TERMINATION FOR CAUSE means an Involuntary Termination of your employment with the Company by reason of your conviction of any felony or other criminal act, your commission of any act of fraud or embezzlement, your unauthorized use or disclosure of confidential information or trade secrets of the Company or its subsidiaries, or any other intentional misconduct on your part which adversely affects the business or affairs of the Company in a material manner.

PART TWO -- INVOLUNTARY TERMINATION BENEFITS

You will be entitled to receive the severance benefits specified below should there occur an Involuntary Termination of your employment during the term of this letter agreement effected in connection with a Change in Control, other than an Involuntary Termination which constitutes a Termination for Cause. However, in the absence of a Hostile Take-Over, these benefits will continue to be paid you only for so long as you remain available for any consulting services required of you under Part Two, Paragraph 4 and abide by the restrictive covenants set forth in Part Two, Paragraph 5.

1. SEVERANCE PAYMENTS. You will receive severance payments from the Company for a period of twelve (12) months following your Involuntary Termination in an aggregate amount equal to the sum of (A) one (1) times the annual rate of base salary in effect for you at the time of your Involuntary Termination plus (B) one (1) times the average of the bonuses paid to you for services rendered in the two (2) fiscal years immediately preceding the fiscal year of your Involuntary Termination. If a bonus is paid to you for only one of those years, then the bonus amount under Clause (B) will be equal to one (1) times such bonus amount. The aggregate severance payments shall be paid to you in equal installments over the twelve-month period in accordance with the Company's normal payroll practices and subject to all applicable withholding taxes. The severance payments will immediately terminate in the event you should cease to remain available for the consulting services required of you under Paragraph 4 or in the event you fail to abide by the restrictive covenants set forth in Paragraph 5. However, in the event your Involuntary Termination occurs in connection with a Hostile Take-Over, your severance payments will be paid to you in the form of a single lump sum amount within thirty (30) days after such Involuntary Termination, and the provisions of Paragraphs 4 and 5 will not apply.

2. HEALTH CARE COVERAGE. The Company will, at its expense, provide you and your eligible dependents with continued health care coverage under the Company's medical/dental plan until the EARLIER of (i) ------- twelve (12) months after the effective date of your Involuntary Termination or (ii) the first date that you are covered under another employer's health benefit program which provides substantially the same level of benefits without exclusion for pre-existing medical conditions. Such coverage will be in lieu of any other continued health care

coverage to which you or your dependents would otherwise be entitled pursuant to the requirements of Code Section 4980B by reason of your termination of employment.

3. OPTION ACCELERATION AND LAPSE OF RESTRICTIONS. Each of your outstanding Options under the Equity Incentive Plans will (to the extent not then otherwise exercisable) automatically accelerate so that each such Option will become immediately exercisable for the total number of shares of Common Stock at the time subject to that Option. Each such accelerated Option, together with all of your other vested Options, will remain exercisable for a period of twelve (12) months following your Involuntary Termination until the end of the specified ten (10)-year option term and may be exercised for any or all of the option shares in accordance with the exercise provisions of the option agreement evidencing the grant. In addition, all restrictions applicable to the Stock Issuances you hold (to the extent those restrictions have not previously lapsed in accordance with the terms of the issuance agreements) will automatically lapse upon your Involuntary Termination.

4. CONSULTING SERVICES. Unless your Involuntary Termination occurs in connection with a Hostile Take-Over, you will make yourself available to perform consulting services reasonably requested of you during the twelve (12)-month period following your Involuntary Termination. You will be compensated at an hourly rate to be agreed upon by you and the Company at the time such consulting services are to be rendered, and you will be reimbursed for all reasonable out-of-pocket expenses incurred in rendering such services upon your submission

of appropriate documentation for those expenses.

5. RESTRICTIVE COVENANTS. For the one hundred twenty (120)-day period following your Involuntary Termination:

(i) You will not directly or indirectly, whether for your own account or as an employee, director, consultant or advisor, provide services to any business enterprise which is at the time in competition with any of the Company's then existing or formally planned product lines

and which is located geographically in an area where the Company maintains substantial business activities, unless you obtain the prior written consent of the Board of Directors.

(ii)You will not directly or indirectly encourage or solicit any individual to leave the Company's employ for any reason or interfere in any other manner with the employment relationships at the time existing between the Company and its current or prospective employees.

(iii)You will not induce or attempt to induce any customer, supplier, distributor, licensee or other business relation of the Company to cease doing business with the Company or in any way interfere with the existing business relationship between any such customer, supplier, distributor, licensee or other business relation and the Company.

You acknowledge that monetary damages may not be sufficient to compensate the Company for any economic loss which may be incurred by reason of your breach of the foregoing restrictive covenants. Accordingly, in the event of any such breach, the Company shall, in addition to the cessation of the severance benefits provided you under this agreement and any remedies available to the Company at law, be entitled to obtain equitable relief in the form of an injunction precluding you from continuing to engage in such breach.

None of the foregoing restrictive covenants shall be applicable in the event your Involuntary Termination occurs in connection with a Hostile Take-Over.

6. BENEFIT REDUCTION. In the event of a Change in Control, the following limitations shall become applicable:

a. BENEFIT REDUCTION. If the Change in Control does not constitute a Hostile Take-Over, first the dollar amount of your severance payment under Paragraph 1 will be reduced to the extent necessary to assure that the present value of those benefits will not, when added to the present value of your Equity Parachute Payment and your Other Parachute Payments, exceed 2.99 times your Average Compensation. In the event of a Hostile Take-Over, no reduction will be made to your severance payment (or any other benefit to which you become entitled hereunder), unless necessary to provide you with the maximum after-tax

benefit available, after taking into account any parachute excise tax which might otherwise be payable by you under Code Section 4999 and any analogous State income tax provision.

b. RESOLUTION OF DISPUTES. In the event there is any disagreement between you and the Company as to whether one or more benefits to which you become entitled (whether under this letter agreement or otherwise) in connection with a Change in Control constitute Equity Parachute Payments or Other Parachute Payments, such dispute is to be resolved as follows:

- In the event temporary, proposed or final Treasury Regulations in effect at the time under Code Section 280G specifically address the status of such benefits or the method for their valuation, the characterization afforded to such benefits by the Regulations, together with the methods prescribed for

their valuation, shall be controlling.

- In the event such Regulations do not address the status of the benefits in dispute, the matter shall be submitted for resolution to independent counsel mutually acceptable to you and the Company ("Independent Counsel"). The resolution reached by Independent Counsel shall be final and controlling. However, should the Independent Counsel determine that the status of the benefits in dispute can be resolved through the obtainment of a private letter ruling from the Internal Revenue Service, a formal and proper request for such ruling shall be prepared and submitted by Independent Counsel, and the determination made by the Internal Revenue Service in the issued ruling shall be controlling. All expenses incurred in connection with the retention of Independent Counsel and (if applicable) the preparation and submission of the ruling request shall be paid by the Company.

- The present value of each Equity Parachute Payment and each of the Other Parachute Payments (including your severance payment and Health Care Coverage) shall be determined in accordance with the provisions of Code Section 280G(d)(4) and the Treasury Regulations issued thereunder.

The full amount of your severance benefit under Paragraph 1 shall not be paid to you until any amounts in dispute under this Paragraph 6.b. have been resolved in accordance herewith. However, any portion of such severance payment which would not otherwise exceed the benefit limitation of Paragraph 6.a. even if all amounts in dispute under this Paragraph 6.b. were to be resolved

against you will be paid to you in accordance with the applicable provisions of this letter agreement.

c. OVERRIDING LIMITATION. You will in all events be entitled to receive the full amount of your severance payment under Paragraph 1, to the extent those benefits, when added to the present value of your Equity Parachute Payment and your Other Parachute Payments (excluding such severance payment), will nevertheless qualify as reasonable compensation within the standards established under Code Section 280G(b)(4).

d. INTERPRETATION. The provisions of this Paragraph 6 shall in all events be interpreted in such manner as will avoid the imposition of excise taxes under Code Section 4999, and the disallowance of deductions under Code Section 280G(a), with respect to your severance benefits under this letter agreement.

PART THREE -- MISCELLANEOUS PROVISIONS

1. TERMINATION FOR CAUSE. Should your Involuntary Termination constitute a Termination for Cause, then the Company shall only be required to pay you (i) any unpaid compensation earned for services previously rendered through the date of such termination and (ii) any accrued but unpaid vacation benefits or sick days, and no benefits will be payable to you under Part Two or Part Three of this letter agreement.

2. TERM OF AGREEMENT. The provisions of this letter agreement will continue in effect for a period of five (5) years from the date hereof.

3. GENERAL CREDITOR STATUS. The benefits to which you may become entitled under this letter agreement (except those attributable to your Options or Stock Issuances) will be paid, when due, from the general assets of the Company. Your right (or the right of the executors or administrators of your estate) to receive any such payments will at all times be that of a general creditor of the Company and will have no priority over the claims of other general creditors of the Company.

4. DEATH. Should you die before receipt of all benefits to which you become entitled under this letter agreement, then the payment of such benefits will be made, on the due date or dates hereunder had you survived, to the

executors or administrators of your estate. Should you die before you exercise your Severance-Accelerated Options (if any) or any other of your outstanding vested Options, then each such Option may be exercised, during the applicable exercise period in effect hereunder for those options at the time of your death, by the executors or administrators of your estate or by person to whom the Option is transferred pursuant to your will or in accordance with the laws of inheritance.

5. MISCELLANEOUS. The provisions of this letter agreement will be construed and interpreted under the laws of the State of California. This agreement incorporates the entire agreement between you and the Company relating to the subject of severance benefits and supersedes all prior agreements and understandings with respect to such subject matter. This agreement may only be amended by written instrument signed by you and another duly-authorized officer of the Company. If any provision of this letter agreement as applied to any party or to any circumstance should be adjudged by a court of competent jurisdiction to be void or unenforceable for any reason, the invalidity of that provision shall in no way affect (to the maximum extent permissible by law) the application of such provision under circumstances different from those adjudicated by the court, the application of any other provision of this letter agreement, or the enforceability or invalidity of this letter agreement as a whole. Should any provision of this letter agreement become or be deemed invalid, illegal or unenforceable in any jurisdiction by reason of the scope, extent or duration of its coverage, then such provision shall be deemed amended to the extent necessary to conform to applicable law so as to be valid and enforceable or, if such provision cannot be so amended without materially altering the intention of the parties, then such provision shall be stricken and the remainder of this letter agreement shall continue in full force and effect.

6 REMEDIES. All rights and remedies provided pursuant to this letter agreement or by law will be cumulative, and no such right or remedy will be exclusive of any other. A party may pursue any one or more rights or remedies hereunder or may seek damages or specific performance in the event of another party's breach hereunder or may pursue any other remedy by law or equity, whether or not stated in this letter agreement.

7. ARBITRATION. Any controversy which may arise between you and the Company with respect to the construction, interpretation or application of any of the terms, provisions or conditions of this agreement or any monetary

claim arising from or relating to this agreement will be submitted to final and binding arbitration in San Diego, California in accordance with the rules of the American Arbitration Association then in effect.

8. NO EMPLOYMENT OR SERVICE CONTRACT. Nothing in this agreement shall confer upon you any right to continue in the employment of the Company for any period of specific duration or interfere with or otherwise restrict in any way the rights of the Company or you, which rights are hereby expressly reserved by each, to terminate your employment at any time for any reason whatsoever, with or without cause.

9. PROPRIETARY INFORMATION. You hereby acknowledge that the Company may, from time to time during your employment with the Company, disclose to you confidential information pertaining to the Company's business and affairs. All information and data, whether or not in writing, of a private or confidential nature concerning the business or financial affairs of the Company (collectively, "Proprietary Information") is and will remain the sole and exclusive property of the Company. In connection with such Proprietary Information, you agree as follows:

(i) You will not, during your employment with the Company or at any time thereafter, disclose to any third party or directly or indirectly make use of any such Proprietary Information other than in connection with, and in furtherance of, the Company's business and affairs.

(ii) You agree that you will use all files, letters, memoranda, reports, records, data or other written, reproduced or other tangible manifestations of the Proprietary Information, whether created by you or others, to which you have access during your employment with the Company, only in the performance of your duties with the Company. You will return all such materials (whether written, printed or otherwise reproduced or recorded) to the Company immediately upon the termination of your employment with the Company or upon any earlier request by the Company, without retaining any copies, notes or excerpts thereof.

(iii) Your obligations under this Paragraph 9 will continue in effect after the termination of your employment with the Company, whatever the reason or reasons for such termination, and the Company will

have the right to communicate with any future or prospective employer concerning your continuing obligations under this Paragraph 9.

Please indicate your acceptance of the foregoing provisions of this severance agreement by signing the enclosed copy of this letter agreement and returning it to the Company.

Very truly yours,

LIGAND PHARMACEUTICALS INCORPORATED

/s/DAVID E. ROBINSON

David E. Robinson
Chairman, President and CEO

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agree\severance.pad

ACCEPTED BY AND AGREED TO

Signature:/s/PHILIP A. DUFFY

Philip A. Duffy

Dated: February 27, 2000

January 17, 2000

Mr. Thomas H. Silberg
Senior Vice President, Commercial Operations
LIGAND PHARMACEUTICALS INCORPORATED
10275 Science Center Drive
San Diego, CA 92121

Dear Tom:

The purpose of this letter agreement is to document the terms of the severance package to which you will be entitled should your employment with Ligand Pharmaceuticals Incorporated (the "Company") terminate under certain specified circumstances.

Part One of this letter agreement sets forth certain definitional provisions to be in effect for purposes of determining your benefit entitlements. Part Two specifies the terms and conditions upon which you may become entitled to receive severance benefits in the event your employment with the Company were to be terminated involuntarily whether in connection with certain changes in control of the Company or otherwise. Part Three concludes this agreement with a series of general terms and conditions applicable to your severance benefits.

PART ONE -- DEFINITIONS

DEFINITIONS. For purposes of this letter agreement, including in particular the application of the special benefit limitations of Part Three, the following definitions will be in effect:

AVERAGE COMPENSATION means your average W-2 wages from the Company for the five (5) calendar years completed immediately prior to the calendar year in which the Change in Control is effected. Any W-2 wages for a partial year of employment will be annualized, in accordance with the frequency with which such wages are paid during such partial year, before inclusion within your Average Compensation.

BOARD means the Company's Board of Directors.

CHANGE IN CONTROL means any of the following events:

(i) a merger or consolidation in which the Company is not the surviving entity, except for a transaction the principal purpose of which is to change the state in which the Company is incorporated,

(ii) the sale, transfer or other disposition of all or substantially all of the assets of the Company other than in the ordinary course,

(iii) any reverse merger in which the Company ceases to exist as an independent corporation and becomes the subsidiary of another corporation,

(iv) any Hostile Take-Over,

(v) the acquisition by any person (or related group of persons), whether by tender or exchange offer made directly to the Company's stockholders, private purchases from one or more of the Company's stockholders, open market purchases or any other transaction, of beneficial ownership of securities possessing more than thirty percent (30%) of the total combined voting power of the Company's outstanding securities,

(vi) the acquisition by any person (or related group of persons), whether by tender or exchange offer made directly to the Company's stockholders, private purchases from one or more of the Company's stockholders, open market purchases or any other transaction, of additional

securities of the Company which increase the total holdings of such person (or group) to a level of securities possessing more than fifty percent (50%) of the total combined voting power of the Company's outstanding securities, or

(vii) the acquisition by any person (or related group of persons), whether by tender or exchange offer made directly to the Company's stockholders, private purchases from one or more of the Company's stockholders, open market purchases or any other transaction, of securities of the Company possessing sufficient voting power in the aggregate to elect an absolute majority of the members of the Board (rounded up to the nearest whole number).

CODE means the Internal Revenue Code of 1986, as amended.

COMMON STOCK means the Company's common stock, par value $0.001 per share.

EQUITY INCENTIVE PLANS mean any of the following equity incentive plans of the Company: 1992 Stock Option/Stock Issuance Plan, as amended; Restricted Stock Purchase Plan, as amended; and 1988 Stock Option Plan, as amended.

HEALTH CARE COVERAGE means the continued health care coverage to which you and your eligible dependents may become entitled under this agreement upon the Involuntary Termination of your employment other than Termination for Cause.

HOSTILE TAKE-OVER means either of the following events:

(i) the acquisition by any person (or related group of persons) whether by tender or exchange offer made directly to the Company's stockholders, private purchases from one or more of the Company's stockholders, open market purchases or any other transaction, of beneficial ownership of securities possessing more than thirty percent (30%) of the total combined voting power of the Company's outstanding securities pursuant to a tender offer made directly to the Company's stockholders which the Board does not recommend such stockholders to accept, or

(ii) a change in the composition of the Board over a period of thirty-six (36) consecutive months or less such that a majority of the Board members (rounded up to the next whole number) ceases, by reason of one or more contested elections for Board membership, to be comprised of individuals who either (a) have been Board members continuously since the beginning of such period or (b) have been elected or nominated for election as Board members during such period by at least a majority of the Board members described in clause (a) who were still in office at the time such election or nomination was approved by the Board.

INVOLUNTARY TERMINATION means the termination of your employment with the Company:

(i) involuntarily upon your discharge or dismissal, or

(ii) voluntarily upon your resignation in connection with any of the following changes to the terms and conditions of your employment: (A) a change in your position with the Company which materially reduces your level of responsibility, (B) a greater than ten percent (10%) reduction in your level of compensation (including base salary, fringe benefits and participation in non-discretionary bonus programs under which awards are payable pursuant to objective financial or performance standards) or (C) a relocation of your principal place of employment by more than fifty (50) miles.

The following guidelines shall determine whether one or more reductions in compensation should be taken into account for purposes of clause (ii)(B):

- Any reduction in compensation which occurs in connection with an across-the-board reduction in the level of compensation payable to the Company's executive officers or senior management shall not constitute grounds for a clause (ii)(B) resignation, unless implemented within eighteen (18) months after a Change in Control.

- In the event of a Hostile Take-Over, the greater than ten percent (10%) standard of clause (ii)(B) shall be reduced to zero percent (0%) so that any reduction in the level of your compensation shall constitute grounds for a clause (ii)(B) resignation.

In no event shall an Involuntary Termination be deemed to occur should your employment terminate by reason of death or permanent disability.

OPTION means any option granted to you under any of the Equity Incentive Plans which is outstanding at the time of your Involuntary Termination or any earlier Change in Control. Your outstanding options are to be divided into two separate categories as follows:

- ACQUISITION-ACCELERATED OPTIONS: any outstanding Option (or installment thereof) which accelerates upon a Change in Control in

accordance with the automatic acceleration provisions of the Equity Incentive Plans.

- SEVERANCE-ACCELERATED OPTIONS: any outstanding Option (or installment thereof) which is not an Acquisition-Accelerated Option but which accelerates upon your Involuntary Termination, whether or not in connection with a Change in Control, as part of your severance benefits under this agreement.

EQUITY PARACHUTE PAYMENT means, with respect to any Option (whether Acquisition-Accelerated or Severance-Accelerated) or unvested Stock Issuance, the portion deemed to be a parachute payment under Code Section 280G and the Treasury Regulations issued thereunder. Such Equity Parachute Payment shall be calculated in accordance with the valuation provisions established under Code Section 280G and the applicable Treasury Regulations and will include an appropriate dollar adjustment to reflect the lapse of your obligation to remain in the Company's employ as a condition to your vesting in the accelerated portion of such Option or Stock Issuance.

OTHER PARACHUTE PAYMENTS mean any payments in the nature of compensation to which you may become entitled under this letter agreement (other than the Equity Parachute Payment) or any other arrangement with the Company, to the extent such payments qualify as parachute payments within the meaning of Code Section 280G(b)(2) and the Treasury Regulations issued thereunder or would so qualify if the aggregate present value of such payments exceeded the amount specified in Code Section 280G(b)(2)(ii).

STOCK ISSUANCE means the issuance of unvested shares of Common Stock under the Company's Restricted Stock Plan or any other Equity Incentive Plan.

TERMINATION FOR CAUSE means an Involuntary Termination of your employment with the Company by reason of your conviction of any felony or other criminal act, your commission of any act of fraud or embezzlement, your unauthorized use or disclosure of confidential information or trade secrets of the Company or its subsidiaries, or any other intentional misconduct on your part which adversely affects the business or affairs of the Company in a material manner.

PART TWO -- INVOLUNTARY TERMINATION BENEFITS

You will be entitled to receive the severance benefits specified below should there occur an Involuntary Termination of your employment during the term of this letter agreement effected in connection with a Change in Control, other than an Involuntary Termination which constitutes a Termination for Cause. However, in the absence of a Hostile Take-Over, these benefits will continue to be paid you only for so long as you remain available for any consulting services required of you under Part Two, Paragraph 4 and abide by the restrictive covenants set forth in Part Two, Paragraph 5.

1. SEVERANCE PAYMENTS. You will receive severance payments from the Company for a period of twelve (12) months following your Involuntary Termination in an aggregate amount equal to the sum of (A) one (1) times the annual rate of base salary in effect for you at the time of your Involuntary Termination plus (B) one (1) times the average of the bonuses paid to you for services rendered in the two (2) fiscal years immediately preceding the fiscal year of your Involuntary Termination. If a bonus is paid to you for only one of those years, then the bonus amount under Clause (B) will be equal to one (1) times such bonus amount. The aggregate severance payments shall be paid to you in equal installments over the twelve-month period in accordance with the Company's normal payroll practices and subject to all applicable withholding taxes. The severance payments will immediately terminate in the event you should cease to remain available for the consulting services required of you under Paragraph 4 or in the event you fail to abide by the restrictive covenants set forth in Paragraph 5. However, in the event your Involuntary Termination occurs in connection with a Hostile Take-Over, your severance payments will be paid to you in the form of a single lump sum amount within thirty (30) days after such Involuntary Termination, and the provisions of Paragraphs 4 and 5 will not apply.

2. HEALTH CARE COVERAGE. The Company will, at its expense, provide you and your eligible dependents with continued health care coverage under the Company's medical/dental plan until the EARLIER of (i) ------- twelve (12) months after the effective date of your Involuntary Termination or (ii) the first date that you are covered under another employer's health benefit program which provides substantially the same level of benefits without exclusion for pre-existing medical conditions. Such coverage will be in lieu of any other continued health care

coverage to which you or your dependents would otherwise be entitled pursuant to the requirements of Code Section 4980B by reason of your termination of employment.

3. OPTION ACCELERATION AND LAPSE OF RESTRICTIONS. Each of your outstanding Options under the Equity Incentive Plans will (to the extent not then otherwise exercisable) automatically accelerate so that each such Option will become immediately exercisable for the total number of shares of Common Stock at the time subject to that Option. Each such accelerated Option, together with all of your other vested Options, will remain exercisable for a period of twelve (12) months following your Involuntary Termination until the end of the specified ten (10)-year option term and may be exercised for any or all of the option shares in accordance with the exercise provisions of the option agreement evidencing the grant. In addition, all restrictions applicable to the Stock Issuances you hold (to the extent those restrictions have not previously lapsed in accordance with the terms of the issuance agreements) will automatically lapse upon your Involuntary Termination.

4. CONSULTING SERVICES. Unless your Involuntary Termination occurs in connection with a Hostile Take-Over, you will make yourself available to perform consulting services reasonably requested of you during the twelve (12)-month period following your Involuntary Termination. You will be compensated at an hourly rate to be agreed upon by you and the Company at the time such consulting services are to be rendered, and you will be reimbursed for all reasonable out-of-pocket expenses incurred in rendering such services upon your submission of appropriate documentation for those expenses.

5. RESTRICTIVE COVENANTS. For the one hundred twenty (120)-day period following your Involuntary Termination:

(i) You will not directly or indirectly, whether for your own account or as an employee, director, consultant or advisor, provide services to any business enterprise which is at the time in competition with any of the Company's then existing or formally planned product lines

and which is located geographically in an area where the Company maintains substantial business activities, unless you obtain the prior written consent of the Board of Directors.

(ii)You will not directly or indirectly encourage or solicit any individual to leave the Company's employ for any reason or interfere in any other manner with the employment relationships at the time existing between the Company and its current or prospective employees.

(iii)You will not induce or attempt to induce any customer, supplier, distributor, licensee or other business relation of the Company to cease doing business with the Company or in any way interfere with the existing business relationship between any such customer, supplier, distributor, licensee or other business relation and the Company.

You acknowledge that monetary damages may not be sufficient to compensate the Company for any economic loss which may be incurred by reason of your breach of the foregoing restrictive covenants. Accordingly, in the event of any such breach, the Company shall, in addition to the cessation of the severance benefits provided you under this agreement and any remedies available to the Company at law, be entitled to obtain equitable relief in the form of an injunction precluding you from continuing to engage in such breach.

None of the foregoing restrictive covenants shall be applicable in the event your Involuntary Termination occurs in connection with a Hostile Take-Over.

6. BENEFIT REDUCTION. In the event of a Change in Control, the following limitations shall become applicable:

a. BENEFIT REDUCTION. If the Change in Control does not constitute a Hostile Take-Over, first the dollar amount of your severance payment under Paragraph 1 will be reduced to the extent necessary to assure that the present value of those benefits will not, when added to the present value of your Equity Parachute Payment and your Other Parachute Payments, exceed 2.99 times your Average Compensation. In the event of a Hostile Take-Over, no reduction will be made to your severance payment (or any other benefit to which you become entitled hereunder), unless necessary to provide you with the maximum after-tax

benefit available, after taking into account any parachute excise tax which might otherwise be payable by you under Code Section 4999 and any analogous State income tax provision.

b. RESOLUTION OF DISPUTES. In the event there is any disagreement between you and the Company as to whether one or more benefits to which you become entitled (whether under this letter agreement or otherwise) in connection with a Change in Control constitute Equity Parachute Payments or Other Parachute Payments, such dispute is to be resolved as follows:

- In the event temporary, proposed or final Treasury Regulations in effect at the time under Code Section 280G specifically address the status of such benefits or the method for their valuation, the characterization afforded to such benefits by the Regulations, together with the methods prescribed for their valuation, shall be controlling.

- In the event such Regulations do not address the status of the benefits in dispute, the matter shall be submitted for resolution to independent counsel mutually acceptable to you and the Company ("Independent Counsel"). The resolution reached by Independent Counsel shall be final and controlling. However, should the Independent Counsel determine that the status of the benefits in dispute can be resolved through the obtainment of a private letter ruling from the Internal Revenue Service, a formal and proper request for such ruling shall be prepared and submitted by Independent Counsel, and the determination made by the Internal Revenue Service in the issued ruling shall be controlling. All expenses incurred in connection with the retention of Independent Counsel and (if applicable) the preparation and submission of the ruling request shall be paid by the Company.

- The present value of each Equity Parachute Payment and each of the Other Parachute Payments (including your severance payment and Health Care Coverage) shall be determined in accordance with the provisions of Code Section 280G(d)(4) and the Treasury Regulations issued thereunder.

The full amount of your severance benefit under Paragraph 1 shall not be paid to you until any amounts in dispute under this Paragraph 6.b. have been resolved in accordance herewith. However, any portion of such severance payment which would not otherwise exceed the benefit limitation of Paragraph 6.a. even if all amounts in dispute under this Paragraph 6.b. were to be resolved

against you will be paid to you in accordance with the applicable provisions of this letter agreement.

c. OVERRIDING LIMITATION. You will in all events be entitled to receive the full amount of your severance payment under Paragraph 1, to the extent those benefits, when added to the present value of your Equity Parachute Payment and your Other Parachute Payments (excluding such severance payment), will nevertheless qualify as reasonable compensation within the standards established under Code Section 280G(b)(4).

d. INTERPRETATION. The provisions of this Paragraph 6 shall in all events be interpreted in such manner as will avoid the imposition of excise taxes under Code Section 4999, and the disallowance of deductions under Code Section 280G(a), with respect to your severance benefits under this letter agreement.

PART THREE -- MISCELLANEOUS PROVISIONS

1. TERMINATION FOR CAUSE. Should your Involuntary Termination constitute a Termination for Cause, then the Company shall only be required to pay you (i) any unpaid compensation earned for services previously rendered through the date of such termination and (ii) any accrued but unpaid vacation benefits or sick days, and no benefits will be payable to you under Part Two or Part Three of this letter agreement.

2. TERM OF AGREEMENT. The provisions of this letter agreement will continue in effect for a period of five (5) years from the date hereof.

3. GENERAL CREDITOR STATUS. The benefits to which you may become entitled under this letter agreement (except those attributable to your Options or Stock Issuances) will be paid, when due, from the general assets of the Company. Your right (or the right of the executors or administrators of your estate) to receive any such payments will at all times be that of a general creditor of the Company and will have no priority over the claims of other general creditors of the Company.

4. DEATH. Should you die before receipt of all benefits to which you become entitled under this letter agreement, then the payment of such benefits will be made, on the due date or dates hereunder had you survived, to the

executors or administrators of your estate. Should you die before you exercise your Severance-Accelerated Options (if any) or any other of your outstanding vested Options, then each such Option may be exercised, during the applicable exercise period in effect hereunder for those options at the time of your death, by the executors or administrators of your estate or by person to whom the Option is transferred pursuant to your will or in accordance with the laws of inheritance.

5. MISCELLANEOUS. The provisions of this letter agreement will be construed and interpreted under the laws of the State of California. This agreement incorporates the entire agreement between you and the Company relating to the subject of severance benefits and supersedes all prior agreements and understandings with respect to such subject matter. This agreement may only be amended by written instrument signed by you and another duly-authorized officer of the Company. If any provision of this letter agreement as applied to any party or to any circumstance should be adjudged by a court of competent jurisdiction to be void or unenforceable for any reason, the invalidity of that provision shall in no way affect (to the maximum extent permissible by law) the application of such provision under circumstances different from those adjudicated by the court, the application of any other provision of this letter agreement, or the enforceability or invalidity of this letter agreement as a whole. Should any provision of this letter agreement become or be deemed invalid, illegal or unenforceable in any jurisdiction by reason of the scope, extent or duration of its coverage, then such provision shall be deemed amended to the extent necessary to conform to applicable law so as to be valid and enforceable or, if such provision cannot be so amended without materially altering the intention of the parties, then such provision shall be stricken and the remainder of this letter agreement shall continue in full force and effect.

6 REMEDIES. All rights and remedies provided pursuant to this letter agreement or by law will be cumulative, and no such right or remedy will be exclusive of any other. A party may pursue any one or more rights or remedies hereunder or may seek damages or specific performance in the event of another party's breach hereunder or may pursue any other remedy by law or equity, whether or not stated in this letter agreement.

7. ARBITRATION. Any controversy which may arise between you and the Company with respect to the construction, interpretation or application of any of the terms, provisions or conditions of this agreement or any monetary

claim arising from or relating to this agreement will be submitted to final and binding arbitration in San Diego, California in accordance with the rules of the American Arbitration Association then in effect.

8. NO EMPLOYMENT OR SERVICE CONTRACT. Nothing in this agreement shall confer upon you any right to continue in the employment of the Company for any period of specific duration or interfere with or otherwise restrict in any way the rights of the Company or you, which rights are hereby expressly reserved by each, to terminate your employment at any time for any reason whatsoever, with or without cause.

9. PROPRIETARY INFORMATION. You hereby acknowledge that the Company may, from time to time during your employment with the Company, disclose to you confidential information pertaining to the Company's business and affairs. All information and data, whether or not in writing, of a private or confidential nature concerning the business or financial affairs of the Company (collectively, "Proprietary Information") is and will remain the sole and exclusive property of the Company. In connection with such Proprietary Information, you agree as follows:

(i) You will not, during your employment with the Company or at any time thereafter, disclose to any third party or directly or indirectly make use of any such Proprietary Information other than in connection with, and in furtherance of, the Company's business and affairs.

(ii) You agree that you will use all files, letters, memoranda, reports, records, data or other written, reproduced or other tangible manifestations of the Proprietary Information, whether created by you or others, to which you have access during your employment with the Company, only in the performance of your duties with the Company. You will return all such materials (whether written, printed or otherwise reproduced or recorded) to the Company immediately upon the termination of your employment with the Company or upon any earlier request by the Company, without retaining any copies, notes or excerpts thereof.

(iii) Your obligations under this Paragraph 9 will continue in effect after the termination of your employment with the Company, whatever the reason or reasons for such termination, and the Company will

have the right to communicate with any future or prospective employer concerning your continuing obligations under this Paragraph 9.

Please indicate your acceptance of the foregoing provisions of this severance agreement by signing the enclosed copy of this letter agreement and returning it to the Company.

Very truly yours,

LIGAND PHARMACEUTICALS INCORPORATED

/s/DAVID E. ROBINSON

David E. Robinson
Chairman, President and CEO

DER:bjo
agree\severance.ths

ACCEPTED BY AND AGREED TO

Signature:/s/THOMAS H. SILBERG

Thomas H. Silberg

Dated: March 1, 2000

AMENDED AND RESTATED REGISTRATION RIGHTS AGREEMENT

THIS AMENDED AND RESTATED REGISTRATION RIGHTS AGREEMENT ("Agreement") is made as of the 29th day of June, 2000, by and among Ligand Pharmaceuticals Incorporated, a Delaware corporation (the "Company"), and those entities and individuals (the "Investor(s)") set forth on attached SCHEDULE A (the "Schedule of Investors").

RECITALS

WHEREAS, the Investors are parties to that certain Amended Registration Rights Agreement dated as of June 24, 1994, as further amended prior to the date hereof (the "Prior Agreement");

WHEREAS, pursuant to Section 1.17 of the Prior Agreement, the rights granted by the Prior Agreement terminated with respect to certain of the parties to the Prior Agreement, other than the Investors, as of December 31, 1999;

WHEREAS, the Company and the Investors desire to amend and restate the Prior Agreement to, among other things, (a) amend the definition of "Registrable Securities" to include only those securities with respect to which the Company's obligations did not expire as of December 31, 1999 and (b) pursuant to an agreement among the Company, Elan Corporation, plc ("Elan") and Elan International Services, Ltd. ("EIS") entered into prior to December 31, 1999, extend the period within which the rights granted under the Prior Agreement may be exercised by Elan and EIS; and

WHEREAS, Section 2.6(b) of the Prior Agreement provides that any term of the Prior Agreement may be amended with the written consent of the Company and the holders of a majority of the Registrable Securities then outstanding (as defined in the Prior Agreement).

NOW, THEREFORE, in consideration of the mutual promises and covenants set forth herein, the Investors hereby agree that the Prior Agreement shall be terminated and superseded and replaced in its entirety by this Agreement, and the parties further agree as follows:

1. REGISTRATION RIGHTS. The Company covenants and agrees as follows:

1.1 DEFINITIONS. For purposes of this Section 1:

(a) The term "Act" means the Securities Act of 1933, as amended.

(b) The term "Form S-3" means such form under the Act as in effect on the date hereof or any registration form under the Act subsequently adopted by the SEC in substitution for such form which permits inclusion or incorporation of substantial information by reference to other documents filed by the Company with the SEC.

(c) The term "Holder" means any person owning or having the right to acquire Registrable Securities or any assignee thereof in accordance with Section 1.13 hereof.

(d) The term "1934 Act" shall mean the Securities Exchange Act of 1934, as amended.

(e) The term "register", "registered" and "registration" refer to a registration effected by preparing and filing a registration statement or similar document in compliance with the Act, and the declaration or ordering of effectiveness of such registration statement or document.

(f) The term "Registrable Securities" means (i) the shares of Common Stock (or the shares of such other class of stock into which the Common Stock is converted) issuable upon conversion of those certain Unsecured Convertible Promissory Notes dated October 30, 1997 issued to S.R. One Limited (the "S.R. One Notes") pursuant to the Stock and Note Purchase Agreement dated February 3,

1995 (and upon such conversion of the S.R. One Notes, SCHEDULE A shall be updated to include such shares), (ii) the shares of Common Stock (or the shares of such other class of stock into which the Common Stock is converted) issuable upon conversion of that certain Warrant (the "Warrant") issued to SmithKline Beecham plc pursuant to the Stock Purchase Agreement dated April 24, 1998 (and upon such conversion of the Warrant, SCHEDULE A shall be updated to include such shares), (iii) the 1,278,970 shares of Common Stock (or that number of shares of such other class of stock into which the Common Stock is converted) issued to EIS pursuant to the Stock Purchase Agreement dated September 30, 1998, (iv) the 437,768 shares of Common Stock (or that number of shares of such other class of stock into which the Common Stock is converted) issued to EIS pursuant to the Securities Purchase Agreement, dated November 6, 1998 (the "Elan Securities Purchase Agreement"), (v) the shares of Common Stock (or the shares of such other class of stock into which the Common Stock is converted) issued or issuable upon conversion of the Zero Coupon Convertible Senior Notes due 2008 (the "Elan Notes") issued pursuant to the Elan Securities Purchase Agreement (and upon such conversion of the Elan Notes, SCHEDULE A shall be updated to include such shares), (vi) the 429,185 shares of Common Stock (or the shares of such other class of stock into which the Common Stock is converted) issued to Elan pursuant to the Development, Licence and Supply Agreement dated November 9, 1998, and as amended (the "Elan License Agreement"), (vii) the shares of Common Stock that may be issued to Elan pursuant to the Elan License Agreement (and upon each such issuance, SCHEDULE A shall be updated to include such shares), (viii) the shares of Common Stock (or the shares of such other class of stock into which the Common Stock is converted) issuable to EIS upon exercise of that certain Warrant (the "EIS Warrant") dated August 4, 1999 (and upon such exercise of the EIS Warrant, SCHEDULE A shall be updated to include such shares), (ix) the 52,742 shares of Common Stock (or the shares of such other class of stock into which the Common Stock is converted) issued to EIS pursuant to the Stock Purchase Agreement dated September 30, 1999, (x) the shares of Common Stock (or the shares of such other class of stock into which the Common Stock is converted) issuable upon exercise of those certain Series X Warrants dated October 6, 1999 (the "X-Ceptor Warrants") (and upon any such exercise of the X-Ceptor Warrants, SCHEDULE A shall be updated to include such shares), (xi) the 188,572 shares of Common Stock (or that number of shares of such other class of stock into which the Common Stock is converted) issued to EIS pursuant to the Incentive Agreement dated December 31, 1999, (xii) the 98,580 shares of Common Stock (or that number of shares of such other class of stock into which the Common Stock is converted) issued to EIS pursuant to the Incentive Agreement dated March 1, 2000, and (xiii) any Common Stock of the Company issued as (or issuable upon the conversion or exercise of any warrant, right or other

security which is issued as) a dividend or other distribution with respect to, or in exchange for or in replacement of the shares referenced in (i), (ii), (iii), (iv), (v), (vi), (vii), (viii), (ix), (x), (xi) and (xii) above, excluding in all cases, however, any Registrable Securities sold by a person in a transaction in which rights under this Agreement are not assigned.

(g) The number of shares of "Registrable Securities then outstanding" shall be determined by the number of shares of Common Stock (or such other class of stock into which the Common Stock is converted) outstanding which are, and the number of shares of Common Stock (or such other class of stock into which the Common Stock is converted) issuable pursuant to then exercisable or convertible securities which are, Registrable Securities, but shall exclude any Registrable Securities which have been previously sold to the public pursuant to Rule 144 or pursuant to a registered public offering.

(h) The term "SEC" shall mean the Securities and Exchange Commission.

1.2 FORM S-3 REGISTRATION. Each Holder may make a written request that the Company effect a registration on Form S-3 and any related qualification or compliance with respect to all or a part of the Registrable Securities owned by such Holder, subject to the limitations set forth in subsection 1.2(b) below. In such event, the Company shall:

(a) promptly give written notice of the proposed registration, and any related qualification or compliance, to all other Holders, and

(b) as soon as practicable, effect such registration and all such qualifications and compliances as may be so requested and as would permit or

facilitate the sale and distribution of all or such portion of such Holder's Registrable Securities as are specified in such request, together with all or such portion of the Registrable Securities of any other Holder or Holders joining in such request as are specified in a written request given within 15 days after receipt of such written notice from the Company; PROVIDED, HOWEVER, that the Company shall not be obligated to effect any such registration, qualification or compliance, pursuant to this Section 1.2: (i) if Form S-3 is not available for such offering by the Holders; (ii) if the Holder proposes to sell Registrable Securities at an aggregate price to the public (net of any underwriters' discounts or commissions) of less than $500,000; (iii) if the Company shall furnish to the Holder a certificate signed by the president of the Company stating that in the good faith judgment of the Board of Directors of the Company, it would be materially detrimental to the Company and its stockholders for such Form S-3 Registration to be effected at such time, (without taking into account the costs to the Company), in which event the Company shall have the right to defer the filing of the Form S-3 registration statement for a period of not more than 60 days after receipt of the request of the Holder under this Section 1.2; PROVIDED, HOWEVER, that the Company shall not utilize this right more than once in any twelve (12) month period; (iv) if the Company has, within the twelve (12) month period preceding the date of such request, already effected two registrations on Form S-3 for the Holders pursuant to this Section 1.2; or (v) in any particular jurisdiction in which the Company would be required to qualify to do business or to execute a general consent to service of process in effecting such registration, qualification or compliance.

(c) Subject to the foregoing, the Company shall file a registration statement covering the Registrable Securities so requested to be registered as soon as practicable after

receipt of the request or requests of the Holders. All expenses incurred in connection with a registration requested pursuant to Section 1.2, including (without limitation) all registration, filing, qualification, printer's and accounting fees and the reasonable fees and disbursements of counsel shall be paid by the Company with respect to the first Form S-3 Registration requested by a Holder pursuant to Section 1.2 (excepting only the fees and disbursements of counsel for the selling Holder or Holders and any underwriters' discounts or commissions associated with Registrable Securities, which shall be borne pro rata by the Holder or Holders participating in the Form S-3 Registration). All expenses incurred in connection with a second and all subsequent registrations requested by a Holder pursuant to Section 1.2 shall be borne pro rata by the Holder or Holders participating in the Form S-3 Registration. Registrations effected pursuant to this Section 1.2 shall not be counted as demands for registration or registrations effected pursuant to Section 1.3.

1.3 REQUEST FOR REGISTRATION.

(a) If Form S-3 is not available to register the resale of any Holder's Registrable Securities and if the Company shall receive, during such time of unavailability of Form S-3, a written request from a Holder that the Company file a registration statement under the Act covering the registration of at least that number of Registrable Securities such that the anticipated aggregate offering price, net of underwriting discounts and commissions, would exceed $1,500,000, then the Company shall, within ten (10) days of the receipt thereof, give written notice of such request to all Holders and shall, subject to the limitations of subsection 1.3(b), effect as soon as practicable, and in any event shall use its best efforts to effect within 60 days of the receipt of such request, the filing of a registration statement under the Act of all Registrable Securities which the Holders request to be registered within twenty (20) days of the mailing of such notice by the Company in accordance with Section 2.4.

(b) If the Holder initiating the registration request hereunder ("Initiating Holder") intends to distribute the Registrable Securities covered by its request by means of an underwriting, it shall so advise the Company as a part of its request made pursuant to this Section 1.3 and the Company shall include such information in the written notice referred to in subsection 1.3(a). The underwriter shall be selected by the Company and shall be reasonably acceptable to the Initiating Holder. In such event, the right of any Holder to include its Registrable Securities in such registration shall be conditioned upon such Holder's participation in such underwriting and the inclusion of such

Holder's Registrable Securities in the underwriting (unless otherwise mutually agreed by the Initiating Holder and such Holder) to the extent provided herein. All Holders proposing to distribute their securities through such underwriting shall (together with the Company as provided in subsection 1.5(e)) enter into an underwriting agreement in customary form with the underwriter or underwriters selected for such underwriting by the Initiating Holder. Notwithstanding any other provision of this Section 1.3, if the underwriter advises the Initiating Holder or the Company in writing that marketing factors require a limitation of the number of shares to be underwritten, then the Initiating Holder or the Company shall so advise all Holders of Registrable Securities which would otherwise be underwritten pursuant hereto, and the number of shares of Registrable Securities that may be included in the underwriting shall be allocated among all Holders thereof, including the Initiating Holder, in proportion (as nearly as practicable) to the amount of Registrable Securities of the Company owned by each Holder; PROVIDED, HOWEVER, that the number of shares of Registrable

Securities to be included in such underwriting shall not be reduced unless all other securities which the Company proposes to sell are first entirely excluded from the underwriting.

(c) The Company is obligated to effect only one (1) such registration for each Holder holding more than $1,500,000 of Registrable Securities pursuant to this Section 1.3; PROVIDED, HOWEVER, that if the Initiating Holder's Registrable Securities included in the offering pursuant to this Section 1.3 are reduced by the underwriter or underwriters selected for such underwriting by more than twenty-five percent (25%) of that number of shares of Registrable Securities set forth in its initiating request, the registration initiated by such Initiating Holder shall not be counted as a registration pursuant to this Section 1.3(c).

(d) The Company is obligated to effect only one (1) such registration statement for all Holders pursuant to this Section 1.3 every six (6) months.

(e) Notwithstanding the foregoing:

(i) If the Company shall furnish to the Initiating Holder, a certificate signed by the President of the Company stating that in the good faith judgment of the Board of Directors of the Company, it would be materially detrimental to the Company and its stockholders for such registration statement to be effected at such time (without taking into account the costs to the Company), the Company shall have the right to defer taking action with respect to beginning the preparation of such filing for a period of not more than 60 days after receipt of the request of the Initiating Holder; PROVIDED, HOWEVER, that the Company may not utilize this right more than once in any twelve (12)-month period; and

(ii) If the Company proposes to register (including for this purpose a registration effected by the Company for stockholders other than the Holders) any of its stock or other securities under the Act in connection with the public offering of such securities solely for cash (other than a registration relating solely to the sale of securities to participants in a Company stock plan, or a registration on any form which does not include substantially the same information as would be required to be included in a registration statement covering the sale of the Registrable Securities), the Company may include such stock or other securities in a registration pursuant to this Section 1.3, subject to reduction pursuant to Section 1.3(b); PROVIDED, HOWEVER, that in the event the Company does so include any of its stock or other securities in such registration, the registration initiated by the Initiating Holder shall not be counted as a registration pursuant to this Section 1.3.

1.4 COMPANY REGISTRATION. If (but without any obligation to do so) the Company proposes to register (including for this purpose a registration effected by the Company for stockholders other than the Holders) any of its stock or other securities under the Act in connection with the public offering of such securities solely for cash (other than a registration relating solely to the sale of securities to participants in a Company stock plan, or a registration on any form which does not include substantially the same information as would be required to be included in a registration statement covering the sale of the Registrable Securities), the Company shall, at such time, promptly give each

Holder written notice of such registration. Upon the written request of a Holder given within twenty (20) days after mailing of such notice by the Company in accordance with Section 2.4, the Company shall, subject to the provisions of

Section 1.9, cause to be registered under the Act all of the Registrable Securities that such Holder has requested to be registered.

1.5 OBLIGATIONS OF THE COMPANY. Whenever required under this Section 1 to effect the registration of any Registrable Securities, the Company shall, as expeditiously as reasonably possible:

(a) Prepare and file with the SEC a registration statement with respect to such Registrable Securities and use its best efforts to cause such registration statement to become effective, and, upon the request of the Holders of a majority of the Registrable Securities registered thereunder, keep such registration statement effective for up to one hundred twenty (120) days for a filing under Section 1.3 or 1.4, and up to one hundred eighty (180) days for a filing under Section 1.2.

(b) Prepare and file with the SEC such amendments and supplements to such registration statement and the prospectus used in connection with such registration statement as may be necessary to comply with the provisions of the Act with respect to the disposition of all securities covered by such registration statement.

(c) Furnish to the Holders such numbers of copies of a prospectus, including a preliminary prospectus, as then amended or supplemented in conformity with the requirements of the Act, and such other documents as they may reasonably request in order to facilitate the disposition of Registrable Securities owned by them.

(d) Use its best efforts to register and qualify the securities covered by such registration statement under such other securities or Blue Sky laws of such jurisdictions as shall be reasonably requested by the Holders, provided that the Company shall not be required in connection therewith or as a condition thereto to qualify to do business or to file a general consent to service of process in any such states or jurisdictions.

(e) In the event of any underwritten public offering, enter into and perform its obligations under an underwriting agreement, in usual and customary form, with the managing underwriter of such offering. Each Holder participating in such underwriting shall also enter into and perform its obligations under such an agreement.

(f) Notify each Holder of Registrable Securities covered by such registration statement at any time when a prospectus relating thereto is required to be delivered under the Act or on the happening of any event as a result of which the prospectus included in such registration statement, as then in effect, includes an untrue statement of a material fact or omits to state a material fact required to be stated therein or necessary to make the statements therein not misleading in the light of the circumstances then existing, and at the request of a Holder, as promptly as practicable prepare and furnish the Holder a reasonable number of copies of a prospectus included in an effective post-effective amendment or the supplemented prospectus correcting such misstatement or omission.

(g) Furnish, at the request of any Holder requesting registration of Registrable Securities pursuant to this Section 1, on the closing date that such Registrable Securities are delivered to the underwriters for sale in connection with a registration pursuant to this Section 1,

if such securities are being sold through underwriters, or, if such securities are not being sold through underwriters, on the date that the registration statement with respect to such securities becomes effective, (i) an opinion, dated such date, of the counsel representing the Company for the purposes of such registration, in form and substance as is customarily given to underwriters in an underwritten public offering, addressed to the underwriters, if any, and to the Holders requesting registration of Registrable Securities and (ii) a

letter dated such date, from the independent certified public accountants of the Company, in form and substance as is customarily given by independent certified public accountants to underwriters in an underwritten public offering, addressed to the underwriters, if any, and to the Holders requesting registration of Registrable Securities.

1.6 FURNISH INFORMATION.

(a) It shall be a condition precedent to the obligations of the Company to take any action pursuant to this Section 1 with respect to the Registrable Securities of any selling Holder that such Holder shall furnish to the Company such information regarding itself, the Registrable Securities held by it, and the intended method of disposition of such Registrable Securities as shall be required to effect the registration of such Holder's Registrable Securities.

(b) The Company shall have no obligation with respect to any registration requested pursuant to Section 1.2 or Section 1.3 if, due to the operation of subsection 1.6(a), the number of shares or the anticipated aggregate offering price of the Registrable Securities to be included in the registration does not equal or exceed the number of shares or the anticipated aggregate offering price required to originally trigger the Company's obligation to initiate such registration as specified in subsection 1.2(b)(ii) or subsection 1.3(a), whichever is applicable.

1.7 EXPENSES OF DEMAND REGISTRATION. All expenses other than underwriting discounts and commissions incurred in connection with registrations, filings or qualifications pursuant to Section 1.3 (which right may be assigned as provided in Section 1.13), including (without limitation) all registration, filing and qualification fees, printers' and accounting fees, fees and disbursements of counsel for the Company, and the reasonable fees and disbursements of one counsel for the selling Holders selected by them shall be borne by the Company; PROVIDED, HOWEVER, that the Company shall not be required to pay for any expenses of any registration proceeding begun pursuant to Section 1.3 if the registration request is subsequently withdrawn solely due to and at the request of the Holders owning at least 51% of the securities being registered (in which case all participating Holders shall bear such expenses), unless the Initiating Holder agrees to forfeit its right to one demand registration pursuant to Section 1.3; PROVIDED FURTHER, HOWEVER, that if at the time of such withdrawal, (a) the Initiating Holder has learned of a material adverse change in the assets, business, condition, properties or prospects, financially or otherwise, of the Company from that known to the Initiating Holder at the time of its request and has withdrawn its request with reasonable promptness following Initiating Holder's learning of such material adverse change, or (b) the Company has filed a registration statement covering securities other than Registrable Securities for its own account or for the account of any other person after receipt of the Initiating Holder's request and the Initiating Holder notifies the Company of its decision not to proceed with its requested registration due to the effects of such separate registration on the market for the Company's securities, then the Initiating Holder (and all other Holders whose Registrable Securities are included therein) shall

not be required to pay any of such expenses and the Initiating Holder shall retain its rights pursuant to Section 1.3.

1.8 EXPENSES OF COMPANY REGISTRATION. The Company shall bear and pay all expenses incurred in connection with any registration, filing or qualification of Registrable Securities with respect to the registrations pursuant to Section 1.4 for each Holder (which right may be assigned as provided in Section 1.13), including (without limitation) all registration, filing and qualification fees, printers and accounting fees, fees and disbursements of counsel for the Company and the fees and disbursements of one counsel for the selling Holders selected by them, but excluding underwriting discounts and commissions relating to Registrable Securities.

1.9 UNDERWRITING REQUIREMENTS. In connection with any offering involving an underwriting of shares of the Company's capital stock, the Company shall not be required under Section 1.3(e)(ii) to include any of the Holders' securities in such underwriting unless they accept the terms of the underwriting as agreed upon between the Company and the underwriters selected by it (or by other

persons entitled to select the underwriters), and then only in such quantity as will not, in the opinion of the underwriters, jeopardize the success of the offering by the Company. If the Company has initiated the registration and the total amount of securities, including Registrable Securities, requested by stockholders to be included in such offering exceeds the amount of securities to be sold by selling stockholders that the underwriters reasonably believe compatible with the success of the offering, then the Company shall be required to include in the offering only that number of such securities, including Registrable Securities, which the underwriters believe will not jeopardize the success of the offering (the securities so included to be apportioned pro rata among the selling stockholders according to the total amount of securities entitled to be included therein owned by each selling stockholder or in such other proportions as shall mutually be agreed to by such selling stockholders) but in no event shall the amount of securities of the selling Holders included in the offering be reduced below thirty percent (30%) of the total amount of securities included in such offering. For purposes of the preceding parenthetical concerning apportionment, for any selling stockholder which is a holder of Registrable Securities and which is a partnership or corporation, the partners, retired partners and stockholders of such holder, or the estates and family members of any such partners and retired partners and any trusts for the benefit of any of the foregoing persons shall be deemed to be a single "selling Holder," and any pro-rata reduction with respect to such "selling Holder" shall be based upon the aggregate amount of shares carrying registration rights owned by all entities and individuals included in such "selling Holder," as defined in this sentence.

1.10 DELAY OF REGISTRATION. No Holder shall have any right to obtain or seek an injunction restraining or otherwise delaying any such registration as the result of any controversy that might arise with respect to the interpretation or implementation of this Section 1.

1.11 INDEMNIFICATION. In the event any Registrable Securities are included in a registration statement under this Section 1:

(a) To the extent permitted by law, the Company will indemnify and hold harmless each Holder, any underwriter (as defined in the Act) for such Holder and each person, if any, who controls such Holder or underwriter within the meaning of the Act or the 1934 Act,

and their respective officers and directors, against any losses, claims, damages, or liabilities (joint or several) to which they may become subject under the Act, the 1934 Act or other federal or state law, insofar as such losses, claims, damages, or liabilities (or actions in respect thereof) arise out of or are based upon any of the following statements, omissions or violations (collectively, a "Violation"): (i) any untrue statement or alleged untrue statement of a material fact contained in such registration statement, including any preliminary prospectus, final prospectus, summary prospectus, notification or offering circular contained therein or otherwise used or approved for use by the Company in the offering pursuant thereto, or any amendments or supplements thereto, (ii) the omission or alleged omission to state therein a material fact required to be stated therein, or necessary to make the statements therein not misleading, or (iii) any violation or alleged violation by the Company of the Act, the 1934 Act, any state securities law or any rule or regulation promulgated under the Act, and the Company will pay to each such Holder, underwriter, controlling person, officer or director any legal or other expenses reasonably incurred by them in connection with investigating or defending any such loss, claim, damage, liability, or action or successfully enforcing the provisions hereof; PROVIDED, HOWEVER, that the indemnity agreement contained in this subsection 1.11(a) shall not apply to amounts paid in settlement of any such loss, claim, damage, liability, or action if such settlement is effected without the consent of the Company (which consent shall not be unreasonably withheld), nor shall the Company be liable in any such case for any such loss, claim, damage, liability, or action to the extent that it arises out of or is based upon a Violation which occurs in reliance upon and in conformity with written information furnished expressly for use in connection with such registration by any such Holder, underwriter or controlling person.

(b) To the extent permitted by law, each selling Holder will indemnify and hold harmless the Company, each of its directors, each of its officers who has signed the registration statement, each person, if any, who controls the

Company within the meaning of the Act, any underwriter, any other Holder selling securities in such registration statement and any controlling person of any such underwriter or other Holder, against any losses, claims, damages, or liabilities (joint or several) to which any of the foregoing persons may become subject, under the Act, the 1934 Act or other federal or state law, insofar as such losses, claims, damages, or liabilities (or actions in respect thereto) arise out of or are based upon any Violation, in each case to the extent (and only to the extent) that such Violation occurs in reliance upon and in conformity with written information furnished by such Holder expressly for use in connection with such registration; and each such Holder will pay any legal or other expenses reasonably incurred by any person intended to be indemnified pursuant to this subsection 1.11(b), in connection with investigating or defending any such loss, claim, damage, liability, or action or successfully enforcing the provisions hereof; PROVIDED, HOWEVER, that the indemnity agreement contained in this subsection 1.11(b) shall not apply to amounts paid in settlement of any such loss, claim, damage, liability or action if such settlement is effected without the consent of the Holder, which consent shall not be unreasonably withheld; PROVIDED, that, in no event shall any indemnity under this subsection 1.11(b) exceed the proceeds from the offering received by such Holder.

(c) Promptly after receipt by an indemnified party under this Section 1.11 of notice of the commencement of any action (including any governmental action), such indemnified party will, if a claim in respect thereof is to be made against any indemnifying party under this Section 1.11, deliver to the indemnifying party a written notice of the commencement thereof and the indemnifying party shall have the right to participate in, and, to the extent the

indemnifying party so desires, jointly with any other indemnifying party similarly noticed, to assume the defense thereof with counsel mutually satisfactory to the parties; PROVIDED, HOWEVER, that an indemnified party (together with all other indemnified parties which may be represented without conflict by one counsel) shall have the right to maintain its own defense and to retain separate counsel, with the fees and expenses to be paid by the indemnifying party, if in the indemnified party's reasonable judgment, actual or potential differing interests may exist between such indemnified party and any other party in such proceeding. The failure to deliver written notice to the indemnifying party within a reasonable time of the commencement of any such action, shall relieve such indemnifying party of any liability to the indemnified party under this Section 1.11 to the extent that the indemnifying party is actually prejudiced by such failure to give notice, but the omission so to deliver written notice to the indemnifying party will not relieve the indemnifying party of any liability that it may have to any indemnified party otherwise than under this Section 1.11.

(d) The obligations of the Company and the Holders under this Section 1.11 shall survive the completion of any offering of Registrable Securities in a registration statement under this Section 1, and otherwise.

1.12 REPORTS UNDER SECURITIES EXCHANGE ACT OF 1934. With a view to making available to the Holders the benefits of Rule 144 promulgated under the Act and any other rule or regulation of the SEC that may at any time permit a Holder to sell securities of the Company to the public without registration or pursuant to a registration on Form S-3, the Company agrees to:

(a) make and keep public information available, as those terms are understood and defined in Rule 144 promulgated under the Act, at all times;

(b) take such action, including the voluntary registration of such other class of stock into which the Common Stock are converted under section 12 of the 1934 Act, as is necessary to enable the Holders to utilize Form S-3 for the sale of their Registrable Securities, such action to be taken as soon as practicable after the end of the fiscal year in which the Common Stock is converted;

(c) file with the SEC in a timely manner all reports and other documents required of the Company under the Act and the 1934 Act; and

(d) furnish to any Holder, so long as the Holder owns any Registrable Securities, forthwith upon request (i) a written statement by the Company that

it has complied with the reporting requirements of Rule 144, the Act and the 1934 Act, or that it qualifies as a registrant whose securities may be resold pursuant to Form S-3 (at any time that it continues to so qualify), (ii) a copy of the most recent annual or quarterly report of the Company and such other reports and documents so filed by the Company, and (iii) such other information as may be reasonably requested in availing any Holder of any rule or regulation of the SEC which permits the selling of any such Registrable Securities without registration or pursuant to Form S-3.

1.13 ASSIGNMENT OF REGISTRATION RIGHTS. The right to cause the Company to register Registrable Securities pursuant to this Section 1 may be assigned (but only with all related obligations) by a Holder to a transferee or assignee of such securities who, after such assignment

or transfer, holds at least 50,000 shares of Registrable Securities (subject to appropriate adjustment for stock splits, stock dividends, combinations and other recapitalizations); PROVIDED, in each case, the Company is, within a reasonable time after such transfer, furnished with written notice of the name and address of such transferee or assignee and the securities with respect to such registration rights are being assigned; and PROVIDED, FURTHER, that such assignment shall be effective only if immediately following such transfer the further disposition of such securities by the transferee or assignee is restricted under the Act.

1.14 LIMITATIONS ON SUBSEQUENT REGISTRATION RIGHTS. From and after the date of this Agreement, the Company may, without the consent of any Holder, enter into an agreement with any holder or prospective holder of any securities of the Company which would allow such holder to have registration rights with respect to securities of the Company so long as such registration rights are not superior during the period ending December 31, 2003 to those granted hereunder. The (a) grant of piggyback registration rights or (b) the grant of rights to request registration on Form S-3, shall be deemed to not be superior to those rights granted hereunder. The prior written consent of the Holders of a majority of the outstanding Registrable Securities shall be required only for the grant of registration rights from and after the date of this Agreement if such registration rights are superior to those granted hereunder.

1.15 "MARKET STAND-OFF" AGREEMENT. Each of the Holders hereby agrees that during the period of duration not to exceed 120 days specified by the Company and an underwriter of Common Stock or other securities of the Company, following the effective date of a registration statement of the Company filed under the Act, it shall not, to the extent requested by the Company and such underwriter (and provided the same restriction is agreed to by the officers and directors of the Company), directly or indirectly sell, offer to sell, contract to sell (including, without limitation, any short sale but excluding private placements in reliance on the so-called "4(1-1/2)" exemption under the Securities Act), grant any option to purchase or otherwise transfer or dispose of (other than to donees who agree to be similarly bound) any securities of the Company held by it at any time during such period except Common Stock included in such registration. In order to enforce the foregoing covenant, the Company may impose stop-transfer instructions with respect to the Registrable Securities of the Holders (and the shares or securities of every other person subject to the foregoing restriction) until the end of such period.

The Company agrees, if and to the extent so required by the underwriter, not to effect any public sale or distribution of its equity securities or securities convertible into or exchangeable or exercisable for any of such securities, during the period of up to 120 days specified by the underwriter following the effective date of any underwritten registration pursuant to Section 1.3 hereof, (180 days for an underwritten registration under Section 1.2), except as part of such underwritten registration and except pursuant to a registration of securities to be offered and sold (i) pursuant to a stock option plan, stock purchase plan or similar plan, (ii) pursuant to an acquisition of a business, merger or exchange of stock for stock on Form S-4 (or any successor form), or (iii) in an offering of securities other than for the account of the Company pursuant to a registration effective at the time of such underwritten registration.

1.16 INTENTIONALLY OMITTED.

1.17 TERMINATION OF REGISTRATION RIGHTS. No Holder shall be entitled to exercise any

right provided for in this Agreement after the earlier of (a) the later of December 31, 1999 or, with respect to only those shares of Registrable Securites which are issued upon exercise of warrants or other convertible securities issued on or subsequent to June 1, 1994, the second anniversary of the exercise of such warrants or convertible securities into Registrable Securities, or (b) the date after which all shares of Registrable Securities then held by such Holder may immediately be sold under Rule 144(k); provided, however, that as to only those shares of Registrable Securities which were originally issued to Elan or EIS, the date in (a) above shall be the later of December 31, 2003 or the date on which no Securities (as defined in Section 13(a) of the Elan Securities Purchase Agreement) are outstanding.

2. MISCELLANEOUS.

2.1 GOVERNING LAW. This Agreement shall be governed by and construed under the laws of the State of California as applied to agreements among California residents entered into and to be performed entirely within California.

2.2 COUNTERPARTS. This Agreement may be executed in two or more counterparts, each of which shall be deemed an original, but all of which together shall constitute one and the same instrument.

2.3 TITLES AND SUBTITLES. The titles and subtitles used in this Agreement are used for convenience only and are not to be considered in construing or interpreting this Agreement.

2.4 NOTICES. Unless otherwise provided, any written communication or notice required or permitted under this Agreement shall be addressed and sent to the party at the address set forth below:

If to the Company:
Ligand Pharmaceuticals Incorporated
10275 Science Center Drive
San Diego, California 92121
Attn: General Counsel
Tel: (858) 550-7500
Fax: (858) 550-1825

If to Investor:

At the address set forth below such Investors name on the signature page attached hereto

or to such party at any address notified to the other party under this Section by (a) air mail or (b) facsimile transmission with prompt confirmation by air mail.

2.5 EXPENSES. If any action at law or in equity is necessary to enforce or interpret the terms of this Agreement, the prevailing party shall be entitled to reasonable attorneys' fees, costs and necessary disbursements in addition to any other relief to which such party may be entitled.

2.6 AMENDMENTS AND WAIVERS.

(a) The addition of Investors as parties to this Agreement, and the amendment of SCHEDULE A in connection therewith, after the original date of execution of this Agreement shall not be considered an amendment of this Agreement requiring the consent of the Investors. Such new Investors shall execute counterpart signature pages to this Agreement and Schedule A will be amended as appropriate to reflect such additional Investors. The definition of "Registrable Securities" shall be automatically amended to include the shares of Common Stock issued or issuable to such new Investors without the need to obtain the consent or signature of the holders of Registrable Securities. The Company shall provide to each party a copy of such amended SCHEDULE A and definition of

"Registrable Securities" to reflect the addition of such new Investors.

(b) Any term of this Agreement which applies to all Holders may be amended and the observance of any term of this Agreement which applies to all Holders may be waived (either generally or in a particular instance and either retroactively or prospectively), only with the written consent of the Company and the holders of a majority of the Registrable Securities then outstanding. Any amendment or waiver effected in accordance with this paragraph shall be binding upon each holder of any Registrable Securities, each future holder of all Registrable Securities and the Company.

2.7 SEVERABILITY. If one or more provisions of this Agreement are held to be unenforceable under applicable law, such provision shall be excluded from this Agreement and the balance of the Agreement shall be interpreted as if such provision were so excluded and shall be enforceable in accordance with its terms.

2.8 AGGREGATION OF STOCK. All shares of Registrable Securities held or acquired by affiliated entities or persons shall be aggregated together for the purpose of determining the availability of any rights under this Agreement.

2.9 ENTIRE AGREEMENT. This Agreement (including the Schedules and Exhibits hereto, if any) constitutes the full and entire understanding and agreement between the parties with regard to the subjects hereof and thereof.

2.10 CONSENT TO AMENDMENT. Execution of this Agreement by Investors who are holders of greater than 50% of the "Registrable Securities" then outstanding of the Company (as defined in the Prior Agreement) shall signify the consent of the Investors to accept the rights created hereunder in lieu of the rights granted to them under the Prior Agreement.

2.11 PUBLICITY. No party to this Agreement shall make any public statement regarding the execution and subject matter of this Agreement, unless required by law in the opinion of the disclosing party's counsel.

[Remainder of This Page Intentionally Left Blank]

IN WITNESS WHEREOF, the parties have executed this Agreement as of the date first above written.

LIGAND PHARMACEUTICALS INCORPORATED

By: /s/DAVID E. ROBINSON

David E. Robinson, President
10275 Science Center Drive
San Diego, California 92121

INVESTORS:

S.R. One Limited

By:

Its:

Address: 565 E. Swsedesford Road, Suite 315
Wayne, Pennsylvania 19087

SmithKline Beecham, plc

By:

Its:

Address: One Franklin Plaza (FP2225)
P.O. Box 7929
Philadelphia, Pennsylvania 19102

Elan Corporation, plc

By: /s/THOMAS LYNCH

Its: Executive Vice President,
Chief Financial Officer

Address: Lincoln House
Lincoln Place
Dublin 2
Ireland

[COUNTERPART SIGNATURE PAGE TO
AMENDED REGISTRATION RIGHTS AGREEMENT]

Elan International Services, Ltd.

By: /s/KEVIN INSLEY

Its: President

Address: 102 St. James Court
Flatts, Smith Parish
Bermuda, FL 04

[COUNTERPART SIGNATURE PAGE TO
AMENDED REGISTRATION RIGHTS AGREEMENT]

SCHEDULE A
SCHEDULE OF INVESTORS

<TABLE>
<CAPTION>

NAME	SHARES ISSUED
<S>	<C>
Elan Corporation, plc	429,185
Elan International Services, Ltd.	6,668,261
TOTAL:	7,097,446

</TABLE>

EXHIBIT 21.1

SUBSIDIARIES OF THE REGISTRANT
LIGAND PHARMACEUTICALS, INCORPORATED
LIST OF SUBSIDIARIES

<TABLE>
<CAPTION>

Name	Jurisdiction of Incorporation
<S>	<C>
Glycomed Incorporated	California
Ligand Pharmaceuticals (Canada) Incorporated	Saskatchewan, Canada
Allergan Ligand Retinoid Therapeutics, Inc.	Delaware
Ligand Pharmaceuticals International, Inc.	Delaware
Ligand JVR, Inc.	Delaware
Seragen Incorporated	Delaware
Seragen Technology, Inc.	Delaware
Seragen Biopharmaceuticals Ltd.	Vancouver, Canada
Ligand Pharmaceuticals UK Limited	United Kingdom

</TABLE>

EXHIBIT 23.1

INDEPENDENT AUDITORS' CONSENT

We consent to the incorporation by reference in Registration Statement No. 333-53992 on Form S-3 and Registration Statement Nos. 333-43252, 333-79447, 333-69919, 333-32297, 333-12913, 033-92436, 033-92470, 033-85366, 033-66186 and 033-54674 on Form S-8 of Ligand Pharmaceuticals Incorporated, of our report dated February 23, 2001, appearing in this Annual Report on Form 10-K of Ligand Pharmaceuticals Incorporated for the year ended December 31, 2000.

DELOITTE & TOUCHE LLP

San Diego, California
March 26, 2001

EXHIBIT 23.2

CONSENT OF ERNST & YOUNG LLP, INDEPENDENT AUDITORS

We consent to the incorporation by reference in the Registration Statements (on Form S-3 No. 333-53992 and Forms S-8 Nos. 333-43252, 333-79447, 333-69919, 333-32297, 333-12913, 033-92436, 033-92470, 033-85366, 033-66186 and 033-54674) of our report dated February 22, 2000, with respect to the consolidated financial statements of Ligand Pharmaceuticals Incorporated included in its Annual Report (Form 10-K) for the year ended December 31, 2000.

Ernst & Young LLP
San Diego, California
March 26, 2001