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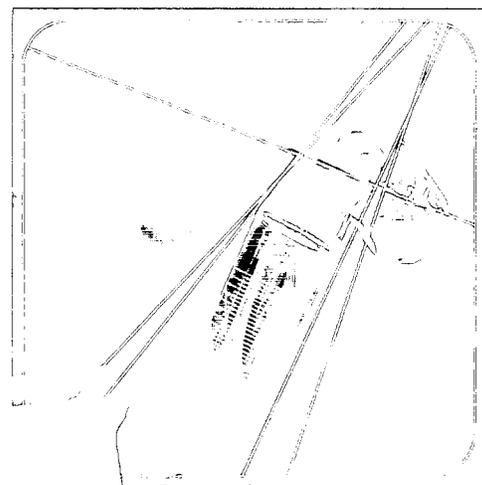
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ANNUAL REPORT 2001

# PATHWAYS AND RHYTHMS



The theme of this annual report, "Pathways and Rhythms," is one way to interpret Ligand's progress in 2001. The strategic pathway we forged years ago - to build two diversified product pipelines on the foundation of our core nuclear receptor technology - has brought us to the verge of operating profitability with a rich and diverse product portfolio. Against this backdrop, the rhythms of our business have accelerated substantially as our commercial operations mature and gain traction, as Phase III trials advance for diseases such as lung cancer and osteoporosis, and as a new wave of products emerges from our research labs. Ligand moved ahead steadfastly and briskly in 2001, and we anticipate more of the same in 2002.

#### 01 HIGHLIGHTS

- Posted annual revenue of \$76.3 million and product sales of \$45.6 million. Product sales doubled compared to 2000, and operating losses declined by roughly half.
- U.S. FDA issued Elan an approvable letter for Morphelan™ (now Avinza™), which would become Ligand's fifth marketed product.
- Phase II studies showed Targretin® capsules extend survival of patients with non-small cell lung cancer; Phase III registration trials began.
- Pfizer conducted Phase III trials of lasofoxifene for osteoporosis, began Phase III risk-reduction study for fractures, breast cancer, cardiovascular disease.
- Wyeth (formerly American Home Products) began Phase III studies of bazedoxifene (formerly TSE-424) and bazedoxifene/PREMARIN® for osteoporosis and hormone replacement therapy.

#### 02 GOALS

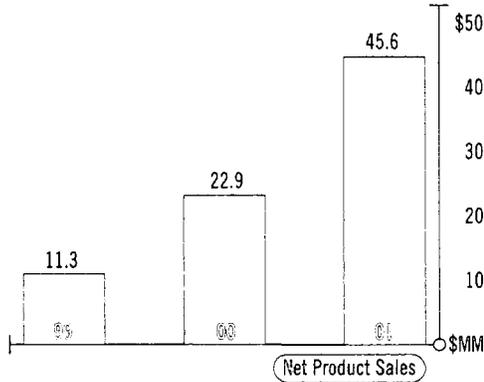
- Achieve positive operating profit for full year.
- Launch Avinza and maximize sales in chronic, moderate-to-severe pain.
- Continue to improve capital structure by further reducing debt and non-operating expenses.
- Publish data from Phase II/IV clinical studies for Targretin in non-small cell lung cancer, psoriasis; for ONTAK® in T-cell non-Hodgkin's lymphoma, chronic lymphocytic leukemia, graft-versus-host disease.
- Wyeth to begin Phase III studies of ERA-923 in breast cancer.
- Wyeth, GlaxoSmithKline, Lilly and TAP move various partner products into Phase I or II clinical studies.

#### Caution Regarding Forward-Looking Statements

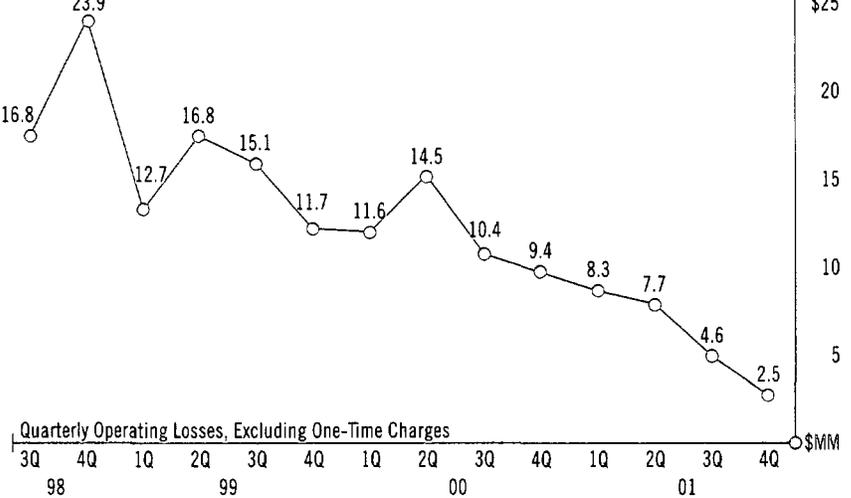
This annual report contains goals, estimates and other forward-looking statements. You can usually identify these statements by forward-looking words such as "may," "will," "expect," "anticipate," "believe," "should," "plan," "hope," "achieve," "look," "project," "future," and "continue" or similar words. Forward-looking statements are only predictions and are subject to a number of risks and uncertainties, including those listed in our filings with the Securities and Exchange Commission ([www.sec.gov](http://www.sec.gov)) and in our press releases. These risks and uncertainties could cause actual results to differ materially from our current judgment. This caution is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995.

LIGAND 2001 FINANCIAL HIGHLIGHTS

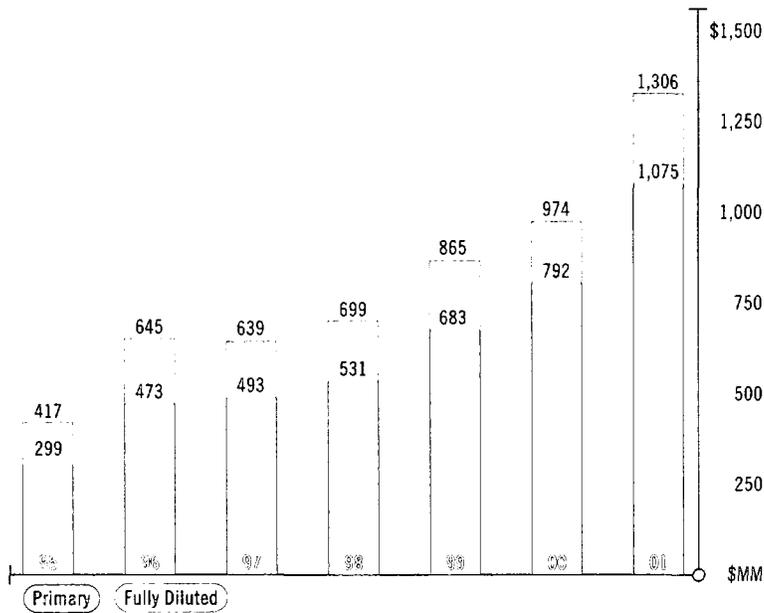
*Product Sales Doubling Annually*



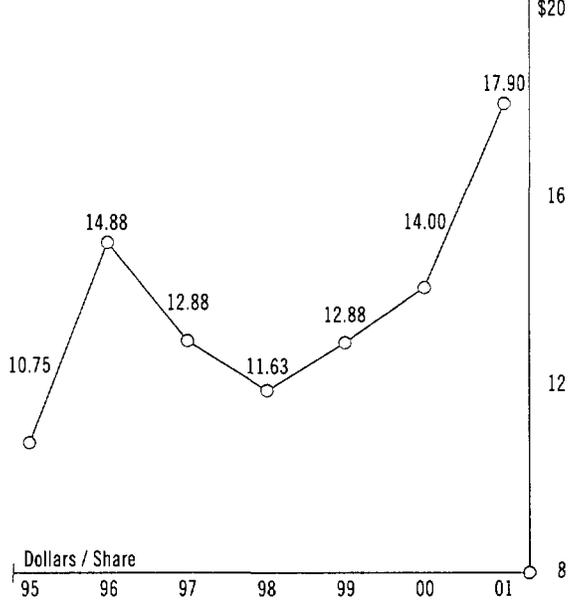
*Operating Breakeven Draws Near*



*Year-End Market Cap Exceeds \$1 Billion*



*Year-End Stock Price Up 28%*



## Dear Fellow Shareholders:



"Ligand's strategy has long been to build a profitable, high-growth pharmaceutical company based on two diversified product pipelines. . . . I am happy to report that our progress accelerated substantially in 2001." David E. Robinson, Chairman, President and CEO

**2001 WAS AN EXCELLENT YEAR FOR LIGAND, AND OUR FUTURE PROSPECTS CONTINUE TO STRENGTHEN** It was a year in which we progressed rapidly and aggressively down the strategic pathway we established more than a decade ago. And it was a year in which the rhythm of our business accelerated across several fronts – commercial, scientific and financial. For example:

- Product sales once again doubled, this time to \$45.6 million, and we expect robust growth to continue in 2002 upon the expected approval of our fifth product, Avinza™ (formerly Morphelan™), which we licensed from Elan.
- The U.S. FDA issued an approvable letter to Elan for Avinza, a pain medicine we plan to launch into our largest initial market to date.
- We began Phase III clinical trials of our marketed product Targretin® in non-small cell lung cancer (NSCLC), the leading cause of cancer death.
- Three corporate partner products progressed through Phase III studies for osteoporosis and as hormone replacement therapy (HRT), two multibillion-dollar markets.
- We cut annual operating losses in half, to \$23.1 million, and expect to show a profit on an operating basis in 2002.

- We increased shareholders' equity, reduced outstanding debt by \$61.8 million, or 45%, and cut non-operating expenses by \$5.0 million for 2002 and beyond through debt conversion by Elan that was finalized in early 2002.
- Our stock price appreciated in 2001 from \$14 to \$17.90, an increase of 28% in a year that saw the NASDAQ composite drop 21% and the AMEX biotech index fall 8%.

Ligand's strategy has long been to build a profitable, high-growth pharmaceutical company based on two diversified product pipelines. In Ligand Specialty Pharmaceutical Products (LSPP), our goal is to generate traditional pharmaceutical revenue and operating profit. In Ligand Corporate Partner Products (LCPP), we strive to build milestone and royalty revenue from leading pharmaceutical companies that are leveraging the value of our research platform into major markets. I am happy to report that our progress accelerated substantially in 2001.

**SALES OF OUR FOUR LSPP PRODUCTS DOUBLED AGAIN TO \$45.6 MILLION** ONTAK® was our best-selling product in 2001, with sales increasing 84% to \$24.3 million. ONTAK sales grew strongly in the product's approved indication, cutaneous T-cell lymphoma (CTCL). In addition, we have great confidence in ONTAK's future

growth, because by year-end roughly a third of its sales were being generated from other diseases, including B-cell non-Hodgkin's lymphoma (NHL), other T-cell lymphomas, chronic lymphocytic leukemia (CLL) and severe psoriasis. We received encouraging preliminary results from studies in CLL and psoriasis during 2001. In 2002, we hope to see interim data on the use of ONTAK in B-cell NHL, other T-cell lymphomas and graft-versus-host disease. We believe the indications we are pursuing for ONTAK represent, in total, a multibillion-dollar market. While we do not aspire to be a front-line player in all these indications, we recognize that establishing a foothold in a few for refractory patient populations will contribute substantially to ONTAK's future growth.

Sales of Targretin® capsules increased 118% in 2001 to \$14.6 million, primarily as a result of rapid uptake to treat early- and mid-stage CTCL. Based on trends we have observed with ONTAK and other oncology drugs, we expect off-label use of Targretin to increase in 2002, the product's third year on the market. We are particularly excited about Targretin's potential in NSCLC, an unfortunately common and aggressive form of cancer. Published Phase II data indicate that Targretin, in combination with chemotherapy, may extend survival in patients with late-stage

NSCLC. Based on these very encouraging results, we began Phase III registration trials for Targretin in NSCLC during 2001. Other smaller, physician-driven lung cancer studies also are underway. Interim results from these studies may be published or presented in 2002, further contributing to doctors' expanded use of Targretin.

The next major value driver in our LSPP portfolio will be the sustained-release (SR) opioid Avinza,™ which we licensed from Elan and plan to launch, pending approval, for chronic, moderate-to-severe pain in 2002. Sales of sustained-release opioids were \$2.3 billion in 2001, so Avinza clearly represents our largest initial market opportunity. To realize Avinza's upside potential, we decided in 2001 to increase the size of our existing oncology sales force, to create a new sales force to target general pain centers, and to begin negotiations with Elan to co-promote the product in market segments that are beyond the reach of our sales forces.

**OUR CORPORATE PARTNERS ADVANCED THREE PRODUCTS IN PHASE III IN 2001, ALL FOR MULTIBILLION-DOLLAR MARKETS** An important testament to our research productivity are the 16 potential products moving through our LCPP pipeline, all of

which are being developed by leading pharmaceutical firms. Our most advanced corporate partner product is lasofoxifene, a second-generation selective estrogen receptor modulator, or SERM, for which Pfizer is conducting two Phase III registration studies in osteoporosis. Pfizer announced that these studies were fully enrolled in 2001. As further evidence of lasofoxifene's potential, Pfizer also has begun a third Phase III study to evaluate whether it reduces the risk of vertebral fractures, breast cancer and cardiovascular disorders.

Wyeth, formerly American Home Products, the leading pharmaceutical player in women's health, announced in 2001 that they have taken bazedoxifene (formerly TSE-424), another second-generation SERM licensed from Ligand, into Phase III studies as monotherapy and in combination with PREMARIN® for osteoporosis and as hormone replacement therapy. Results from Phase II studies indicate that the combination of bazedoxifene and PREMARIN® may have substantial benefits for postmenopausal women, with a much-improved side effect profile.

**LIGAND'S NEXT WAVE OF PRODUCTS IS EMERGING FROM OUR RESEARCH LABS AND MOVING INTO EARLY HUMAN DEVELOPMENT**  
As these products advance, they are playing an integral role in the rhythm and momentum of our company. For example, on the

LSPD side of our business we have moved into late preclinical development several glucocorticoid receptor (GR) modulators for oncology and inflammatory diseases, and expect to select a clinical candidate in 2002. In LCPP, a family of selective, second-generation peroxisome proliferation activated receptor (PPAR) modulators are in late preclinical and early Phase I development at Lilly and GlaxoSmithKline. We earned an undisclosed milestone payment in 2001 when Lilly filed an Investigational New Drug (IND) application for the most advanced PPAR, LY519818, and we are excited about the potential of PPARs in diabetes and dyslipidemias. Likewise, we are pleased to report that through our partnership with TAP Pharmaceutical Products, LGD2226 advanced to IND track in 2001, triggering a \$1 million milestone for our most advanced selective androgen receptor modulator, or SARM. Preclinical studies have shown that SARMs have promise in male and female osteoporosis, sexual dysfunction and hypogonadism.

**OUR RECORD 2001 FINANCIAL RESULTS REFLECT PROGRESS ACROSS THE BUSINESS** For the year, total revenues were \$76.3 million, up 59% over 2000. Importantly, product sales were 60% of total revenues in 2001, compared to 48% in 2000, and we expect this percentage to increase further in coming years. We continued to maintain tight control over cost of goods and

"As we look ahead, we see ourselves taking bigger, faster strides down our strategic path of becoming a profitable, high-growth specialty pharmaceutical company." David E. Robinson, Chairman, President and CEO

operating expenses in 2001. As a result, our operating loss declined to \$23.1 million for the year, a 50% improvement over 2000, and we expect to show a profit on an operating basis in 2002. Our fourth-quarter operating loss of \$2.5 million was our smallest quarterly loss since we began commercial operations in 1999. Our net loss for 2001 declined to \$43.0 million, a 41% improvement over 2000, even including one-time charges of \$7.5 million.

We booked one charge for a debt conversion that improved our capital structure and reduced non-operating expenses. Specifically, we worked with Elan on an early conversion of zero-coupon notes with an original issue price of \$50 million into Ligand stock. Starting in 2002, the transaction strengthens our balance sheet by reducing debt and increasing shareholders' equity, and eliminates \$5 million of annual interest expense. Most importantly, the reduction in interest expense enhances our ability to translate future operating profits into earnings per share (EPS).

As we look ahead, we see ourselves taking bigger, faster strides down our strategic path of becoming a profitable, high-growth specialty pharmaceutical company. Looking beyond our breakthrough to operating profits, we will pursue several strategic

priorities in coming years to drive revenue and positive EPS.

These priorities are to:

- Maximize Avinza™ sales following its expected approval.
- Accelerate development programs for expanded indications of Targretin® capsules and ONTAK®.
- Ramp up our next wave of R&D for early-stage products, moving at least three into the clinic.
- Expand our portfolio of marketed specialty products through in-licensing or acquisition of at least one product.
- Continue improving our capital structure by further reducing outstanding debt and non-operating expense.

By achieving these strategic priorities, we hope to deliver excellent long-term returns to our shareholders. We believe Ligand is poised for continued success, which we will achieve through the continued support of our shareholders and through the hard work and dedication of our talented employees.



DAVID E. ROBINSON  
*Chairman, President and Chief Executive Officer*

LIGAND SPECIALTY PHARMACEUTICAL PRODUCTS

LSPP Pipeline

PRODUCT	INDICATION	STATUS/PHASE
ONTAK®	Cutaneous T-cell Lymphoma <sup>1</sup> B-cell Non-Hodgkin's Lymphoma Rheumatoid Arthritis Psoriasis (Severe)	Marketed in U.S., Filed in Europe Phase II Phase II Phase II
Targretin® capsules	Cutaneous T-cell Lymphoma <sup>2,3</sup> Non-Small Cell Lung Cancer Advanced Breast Cancer Psoriasis (Moderate-to-Severe) Renal Cell Cancer Prostate/Colon Cancer	Marketed in U.S., Europe Phase III Phase II Phase II Planned Phase II
Targretin® gel	Cutaneous T-cell Lymphoma <sup>4</sup> Hand Dermatitis (Eczema) Psoriasis	Marketed in U.S., Filed in Europe Phase II Phase II
Avinza™ (Formerly Morphelan™)	Chronic, Moderate-to-Severe Pain <sup>5</sup>	MDA Submitted, Approvable Letter Received
Panretin® gel	Kaposi's Sarcoma <sup>6,7</sup>	Marketed in U.S., Europe
Panretin® capsules	Kaposi's Sarcoma Bronchial Metaplasia	Phase II Phase II
RAR AGONIST		
LGD1550	Advanced Cancers Acne Psoriasis	Phase I/II Complete Planned Phase I/II Planned Phase I/II
SARMS		
LGD1331	Prostate Cancer, Hirsutism, Acne, Androgenetic Alopecia Androgen Antagonist	Preclinical
INFLAMMATORY DISEASES, ONCOLOGY, ANEMIA		
Glucocorticoid Agonists	Inflammation, Cancer	Preclinical
DIABETES, METABOLIC DISEASES, CARDIOVASCULAR DISEASE		
Mineralocorticoid Receptor Modulators	Congestive Heart Failure, Hypertension	Research

1 In February 1999, the FDA granted accelerated approval for ONTAK (denileukin diftitox, DAB<sub>339</sub>IL-2) for the treatment of patients with persistent or recurrent CTCL whose malignant cells express the CD25 component of the interleukin-2 receptor.  
 2 In December 1999, the FDA granted marketing approval for Targretin (bexarotene) capsules with once-daily oral administration for the treatment of cutaneous manifestations of CTCL in patients who are refractory to at least one prior systemic therapy.  
 3 In March 2001, the European Commission granted marketing authorization for Targretin (bexarotene) capsules for the treatment of patients with skin manifestations of advanced-stage CTCL who are refractory to at least one systemic therapy.  
 4 In June 2000, the FDA granted marketing clearance for Targretin (bexarotene) gel 1% for the topical treatment of cutaneous lesions in patients with early-stage (TNM Stage IA and IB) CTCL who have refractory or persistent disease after other therapies or who have not tolerated other therapies.  
 5 Licensed from Elan for chronic, moderate-to-severe pain.  
 6 In February 1999, the FDA granted marketing clearance for Panretin gel (alitretinoin) 0.1% for the topical treatment of cutaneous lesions of patients with AIDS-related KS.  
 7 In October 2000, the European Commission granted marketing authorization for Panretin gel (alitretinoin) 0.1% for the topical treatment of cutaneous lesions in patients with AIDS-related KS.

Note: This list is not intended to be a complete list of all Ligand products, partnered products and their indications.

LIGAND CORPORATE PARTNER PRODUCTS

## LCPP Pipeline

PRODUCT	INDICATION	STATUS/PHASE	PARTNER
<b>WOMEN'S HEALTH</b>			
<b>SERMs</b>			
Lasofloxifene	Osteoporosis, Breast Cancer Prevention	Phase III	Pfizer
Bazedoxifene (Formerly TSE-424)	Osteoporosis	Phase III	Wyeth <sup>1</sup>
Bazedoxifene/PREMARIN®	Hormone Replacement Therapy	Phase III	Wyeth
ERA-923	Breast Cancer	Phase II	Wyeth
Progesterone Agonist NSP-989 <sup>2</sup>	Hormone Replacement Therapy, Contraception	IND Track	Wyeth
Progesterone Antagonist	Contraception, Reproductive Disorders	Preclinical	Wyeth
Progesterone Agonists	Hormone Replacement Therapy, Contraception, Reproductive Disorders	Preclinical	Organon
<b>DIABETES, METABOLIC DISEASES, CARDIOVASCULAR DISEASE</b>			
<b>PPAR Modulators</b>			
GW516	Cardiovascular Disease, Dyslipidemia	Phase I	GlaxoSmithKline
LY818 <sup>3</sup>	Type II Diabetes, Metabolic Diseases	Phase I	Lilly
LY929 <sup>4</sup> /LYZZZ <sup>5</sup>	Type II Diabetes, Metabolic Diseases, Dyslipidemia	IND Track	Lilly
LYXXX <sup>5</sup>	Dyslipidemia	IND Track	Lilly
HNF-4 Modulators	Type II Diabetes, Metabolic Diseases	Research	Lilly
<b>INFLAMMATORY DISEASES, ONCOLOGY, ANEMIA</b>			
Glucocorticoid Agonists	Inflammation	Preclinical	Abbott
Hematopoietic Growth Factors	Thrombocytopenia	IND Track	GlaxoSmithKline
<b>SARMs</b>			
LGD2226 Androgen Agonist	Male Hypogonadism, Hormone Replacement Therapy, Female Sexual Dysfunction, Osteoporosis	IND Track	TAP

<sup>1</sup> Formerly American Home Products

<sup>2</sup> Formerly WAY166989

<sup>3</sup> LY518818

<sup>4</sup> LY518929

<sup>5</sup> Compound number not disclosed.

Note: This list is not intended to be a complete list of all Ligand products, partnered products and their indications.

## LSPP: Four Products with Accelerating Revenue, Fifth Pending Approval

Ligand's Specialty Pharmaceutical Products business has an excellent track record of drug discovery, development and commercialization in oncology and dermatology, with four marketed products and a fifth pending approval from the U.S. Food and Drug Administration.

Ligand's strategy to focus first on niche markets in oncology and dermatology allowed us to bring our four products to market quickly. We are now working to accelerate revenue growth by developing our products in large-market diseases such as non-small cell lung cancer, B-cell non-Hodgkin's lymphoma, chronic lymphocytic leukemia, psoriasis and rheumatoid arthritis.

We expect our fifth marketed product, Avinza™, to be a natural complement to our growing oncology and dermatology franchise. If approved to treat chronic, moderate-to-severe pain, Avinza will be marketed by our specialty oncology and dermatology/HIV sales forces and by a new Ligand sales force targeting general pain centers. In addition, Elan is expected to co-promote the product, providing us an excellent opportunity to capture more of the largest initial market we have entered to date.

### LSPP HIGHLIGHTS 2001

#### 1Q

Ligand completes European marketing and distribution network by signing agreement with Elan to sell Ligand's near-term oncology products in Western and Eastern Europe.

#### 2Q

Phase I/II clinical studies show that adding Targretin® to chemotherapy treatment may prolong the survival of patients with non-small cell lung cancer. Results are presented at the American Society of Clinical Oncology annual meeting. Phase III registration program underway.

#### 2Q

European Commission grants marketing approval for Targretin capsules; Ligand submits European regulatory application to market Targretin gel. For achieving these milestones, Ligand receives \$3.5 million from marketing partner Elan.

#### 3Q

Ligand announces that the U.S. Food and Drug Administration has issued Elan an approvable letter for Morphelan™ (now Avinza), a sustained-release opioid for chronic, moderate-to-severe pain. Ligand licensed from Elan the rights to market Avinza in the United States and Canada.

#### 4Q

New published data demonstrate that Targretin may increase response of CTCL patients to ONTAK®, and that ONTAK has anti-cancer activity in CLL patients. In a separate publication, new, low-dose ONTAK regimen demonstrates comparable activity, better tolerability than those used in previous ONTAK trials for severe psoriasis.

#### 4Q

Ligand posts record year-end financial results. Total revenues increase to \$76.3 million, up 59% over 2000, and net loss declines to \$43.0 million, down 41%. Product sales nearly double to \$45.6 million, and operating losses decline 50% to \$23.1 million.

Ligand submits European regulatory application to market ONZAR™ (ONTAK), triggering a \$1 million milestone from Elan.



2002 GOALS

- A Continue to accelerate product sales growth by further penetrating the CTCL market, and by increasing expanded use in other cancers and dermatologic diseases.
- B Launch Avinza™ for chronic, moderate-to-severe pain following its expected approval. Maximize sales through existing oncology and dermatology/HIV sales forces, new sales force focused on general pain centers, and co-promotion with Elan.
- C Publish data from Phase II/IV clinical studies for Targretin® in non-small cell lung cancer, psoriasis; for ONTAK® in T-cell non-Hodgkin's lymphoma, chronic lymphocytic leukemia, graft-versus-host disease; and for Targretin gel in hand dermatitis.



## Expanded Use of ONTAK® Increasing

ONTAK WAS LIGAND'S LARGEST-SELLING PRODUCT IN 2001. Sales grew strongly to \$24.3 million, up 84% compared to 2000. In CTCL, where we market ONTAK primarily for late-stage disease, sales growth was driven by increases in the number of patients treated, the number of treatment cycles per patient, and the average starting dose. In addition, doctors continued to learn how to optimize treatment with ONTAK. A Phase I/II study presented at the American Society of Hematology (ASH) annual meeting showed that pre-treating CTCL patients with Targretin® boosted the activity of ONTAK and increased patient response rates.

ONTAK sales also are increasing rapidly outside of CTCL. By year-end, approximately 35% of sales came from treating diseases including chronic lymphocytic leukemia (CLL),

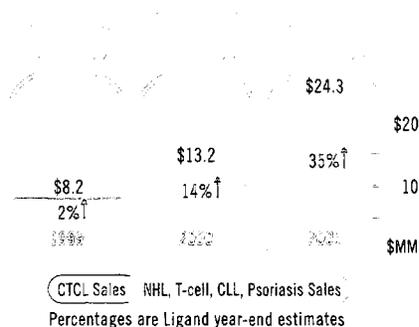
B- and T-cell non-Hodgkin's lymphoma, and severe psoriasis. These "expanded use" sales were due in part to new clinical studies published during 2001. A Phase II study published at the ASH meeting demonstrated, for the first time, that ONTAK had anti-cancer activity in patients with CLL. Another study, published in the *Journal of the American Academy of Dermatology*, showed that even low doses of ONTAK generated meaningful responses in patients with severe psoriasis, but with fewer side effects compared to previous ONTAK studies.

Also in 2001, we submitted a regulatory application to market ONTAK in Europe, where it will be called ONZAR™ if approved.

"Participating in a clinical trial for the drug that became ONTAK gave me the unique opportunity to see the complicated process involved in bringing a drug to market. ONTAK worked when I wasn't responding to other CTCL treatments, and it has given other patients with this rare disease hope for the future. Ligand's dedication to patients is as strong as its dedication to the marketplace."

Judy Jones, Founder, The Mycosis Fungoides Foundation

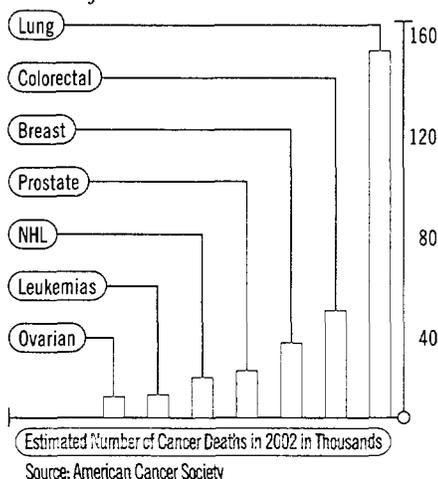
ONTAK Grows in CTCL, Other Cancers





## Pivotal Lung Cancer Studies Begin for Targretin® Capsules

### Lung Cancer is Leading Cause of Cancer Death

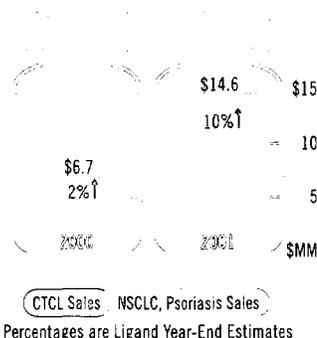


TARGETIN CAPSULES CONTINUED TO PENETRATE THE CTCL MARKET RAPIDLY IN 2001. Sales were \$14.6 million, up 118% compared to 2000. Sales growth was driven by strong product acceptance among dermatologists and oncologists, and by increasing use in patients with earlier stage CTCL. In addition, we launched the product in Europe through our network of marketing and distribution partners.

We achieved a major milestone in 2001 by beginning Phase III registration trials for Targretin capsules in non-small cell lung cancer. NSCLC is Ligand's most important clinical development program, with two 600-patient registration studies underway worldwide. We hope to accrue 40% of the patients in 2002, and expect off-label use to accelerate as physicians gain experience with Targretin in lung cancer.

Phase II studies showed that among late-stage lung cancer patients who took Targretin with standard combination chemotherapy, median survival was about 14 months, compared to 7-9 months in several other chemotherapy trials. The Targretin studies were presented in 2001 at the American Society of Clinical Oncology annual meeting and published in the *Journal of Clinical Oncology*.

### Sales of Targretin Capsules Increase in CTCL, Expanded Use





## Gel Products Continue Solid Growth

TOPICAL FORMULATIONS PROVIDE IMPORTANT OPTION FOR CTCL, KS Combined sales of Targretin® gel and Panretin® gel were \$6.6 million in 2001, up 156% compared to 2000. Targretin gel is used to treat patients with early-stage CTCL, while Panretin gel is used to treat patients with AIDS-related Kaposi's sarcoma.

The strong growth of the gel products was due in part to Ligand's decision to form a specialty sales force to focus on the unique needs of dermatologists.

In 2001, Ligand launched Panretin gel through our partner network in Europe and filed a European Marketing Authorization Application for Targretin gel.

Additional opportunities for Targretin gel include hand dermatitis, for which we expect to see interim Phase I/II data in 2002, and mild-to-moderate psoriasis.



"Ligand has been a wonderful corporate partner with whom the Lymphoma Research Foundation has been privileged to work over the years. Their willingness to bring to market three new therapies so vital to improving the lives of individuals with cutaneous T-cell lymphoma has brought hope to a patient population that often endures pain and lifestyle limitations. We are extremely grateful to Ligand for both its support of and belief in our mission: the eradication of lymphoma and the support of those touched by this disease."

Suzanne Bliss, Executive Director, Lymphoma Research Foundation



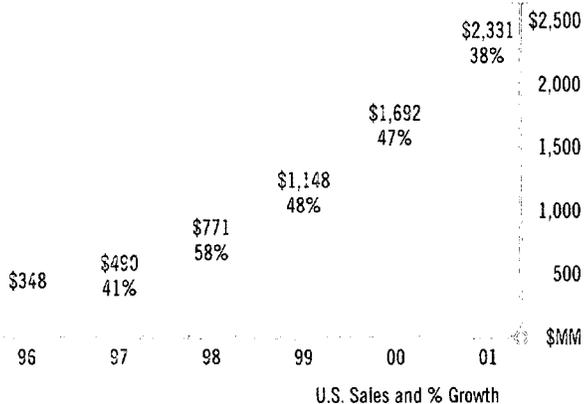
## Avinza<sup>™</sup> Represents Our Largest Initial Market Opportunity

**SUSTAINED-RELEASE OPIOID AWAITING U.S. MARKETING APPROVAL.** Ligand licensed the U.S. rights to Avinza (formerly Morphelan<sup>™</sup>) from Elan, which received an approvable letter from the Food and Drug Administration in 2001. If approved for chronic, moderate-to-severe pain, Avinza would represent our fifth product and largest initial market opportunity.

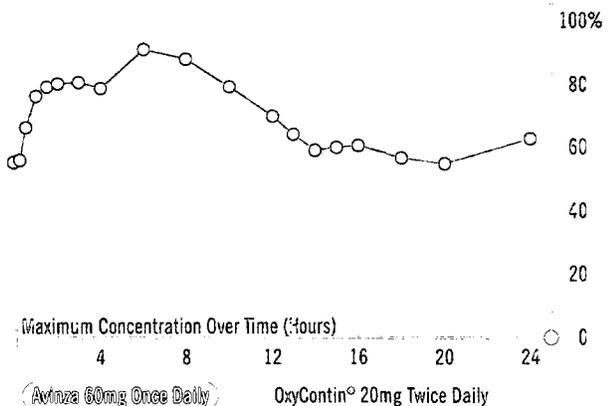
Ligand plans to launch Avinza into the sustained-release opioid market, which totaled an estimated \$2.3 billion in 2001 and is expected to continue growing rapidly. Ligand's existing sales forces will target healthcare practitioners who treat patients with pain from cancer and HIV. In addition, we made a strategic decision in 2001 to form a new sales force to target general pain centers not served by our existing representatives. Finally, we are negotiating for Elan to co-promote Avinza in markets beyond the reach of our sales forces.

We believe that Avinza may offer significant advantages to patients and physicians based on its true once-daily dosing, its smooth pharmacokinetic profile compared to twice-daily products, and its unique formulation that combines immediate- and sustained-release components.

*Sustained-Release Opioids Represent Multibillion-Dollar, Rapidly Growing Market*



*Avinza Provides Similar Rapid Opioid Release, More Stable Blood Levels than OxyContin<sup>®</sup>\**



Source: IMS RP&PP

Source: Journal of Oncology Pharmacy Practice (Vol. 7, 2001)  
\*Blood levels do not necessarily translate to clinical efficacy.

## LCPP: Collaborations Generate Increasing Milestones; Future Royalties Draw Near

Ligand's partnerships with leading global pharmaceutical companies have produced a pipeline of 16 products, all targeting major markets. Three of these products are in Phase III, raising the potential of increasing milestone payments and royalties in the 2002-2004 time frame. In addition, Ligand's partners are developing another potential product in Phase II, two in Phase I, six on human development track and four in preclinical. Our partnered products address indications in multi-billion-dollar markets such as type II diabetes, dyslipidemias, HRT, osteoporosis, cardiovascular disease, breast cancer and contraception.

### LCPP HIGHLIGHTS 2001

#### 2Q

Wyeth begins pivotal Phase III studies of bazedoxifene (formerly TSE-424), a second-generation selective estrogen receptor modulator (SERM), and bazedoxifene/PREMARIN® for the prevention and treatment of osteoporosis and as hormone replacement therapy, resulting in an undisclosed milestone payment to Ligand.

#### 2Q

Ligand initiates a joint research and development alliance with TAP Pharmaceutical Products to focus on the discovery and development of selective androgen receptor modulators (SARMs). TAP subsequently declares Ligand's lead SARM, LGD2226, a clinical candidate, triggering a \$1.0 million milestone payment to Ligand.

#### 3Q

Lilly files an IND for LY519818, a novel peroxisome proliferation activated receptor (PPAR) agonist for the treatment of type II diabetes and metabolic diseases. An undisclosed milestone payment is made to Ligand under the terms of the Ligand/Lilly alliance.

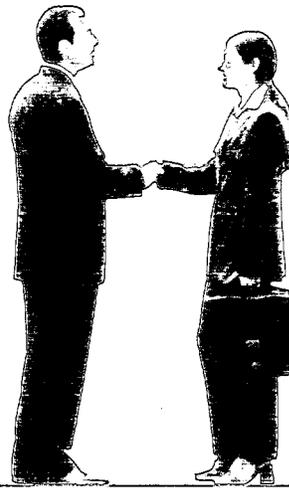
#### 4Q

Pfizer presents at its annual analysts meeting final one-year Phase II data on lasofoxifene, another second-generation SERM licensed from Ligand. The data show an improvement over raloxifene, the leading first-generation SERM, in spinal bone mass density and lipid-lowering effects. Pfizer announces that Phase III studies of lasofoxifene in osteoporosis are fully enrolled, and that an additional Phase III risk-reduction study has begun.



2002 GOALS

- A Wyeth moves NSP-888 to Phase I, makes TRN-928 Phase II decision
- B Lilly moves compounds to Phase I
- C NIP moves L3D2228 to Phase I



## Lasofoxifene Phase III Osteoporosis Trials Underway at Pfizer; Phase III Risk-Reduction Trial Initiated

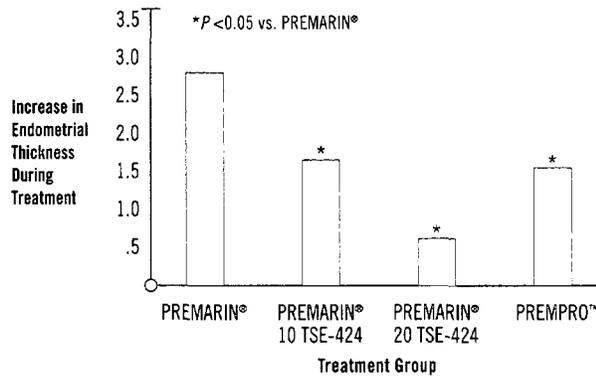
**IN PHASE II STUDIES, LASOFOXIFENE IMPROVES BONE DENSITY, CHOLESTEROL LEVELS MORE THAN RALOXIFENE**  
Lasofoxifene is a SERM in Phase III clinical trials for the prevention and treatment of osteoporosis in postmenopausal women. In Phase II studies compared to raloxifene (a first-generation SERM marketed by Lilly as Evista®), lasofoxifene produced a greater increase in bone mineral density in the lumbar spine, and a greater decrease in LDL (bad) cholesterol. Lasofoxifene also exhibited a strong safety profile.

Pfizer has two phase III trials underway in osteoporosis prevention that have completed enrollment with more than 1,800 patients. In addition, Pfizer has begun a third worldwide Phase III trial to evaluate whether lasofoxifene reduces the risk of vertebral fractures, breast cancer and cardiovascular disease.

Overall, lasofoxifene may be useful in multibillion-dollar markets, so approval could represent a significant royalty revenue stream for Ligand.

**PREMARIN®/TSE-424: Reduces Estrogen Induced Endometrial Stimulation**

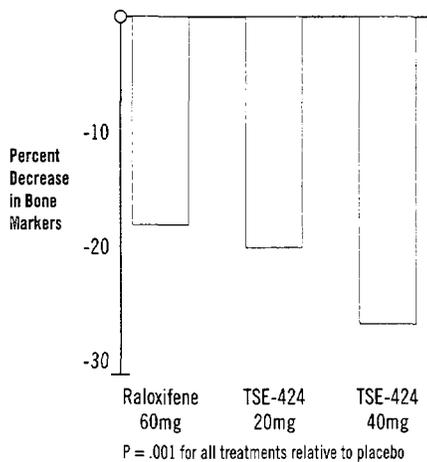
Results of Phase II Study



**Wyeth Advances Bazedoxifene and Bazedoxifene/PREMARIN® into Phase III for Osteoporosis and HRT**

**TSE-424 vs. Raloxifene Activity on Bone Markers**

Results of Phase II Study



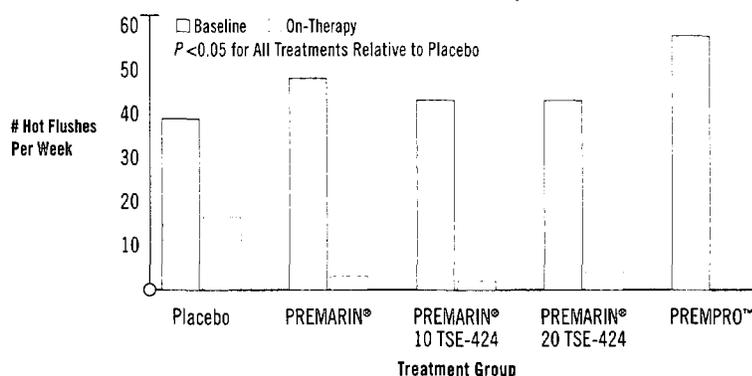
PRODUCT MAY PROVIDE BENEFITS OF HRT WITH FEWER SIDE EFFECTS Bazedoxifene (formerly TSE-424) is a selective estrogen receptor modulator (SERM) developed by Ligand and Wyeth for the prevention and treatment of osteoporosis. In 2001, Wyeth initiated two Phase III trials to evaluate bazedoxifene for osteoporosis. Wyeth also decided in 2001 to begin a Phase III trial with bazedoxifene/PREMARIN® for the treatment of menopause. PREMARIN® is Wyeth's product for the treatment of menopausal symptoms.

Specifically designed to prevent osteoporosis while having little or no adverse effect on breast or endometrial tissue, bazedoxifene boasts an excellent safety profile. Phase II studies indicated that bazedoxifene/PREMARIN® significantly reduced vasomotor symptoms of menopause and estrogen-induced endometrial stimulation, and had a beneficial effect on bone markers. Thus, bazedoxifene/PREMARIN® may provide a novel, first-line treatment of menopause.

Wyeth is also studying ERA-923, another SERM, in Phase II trials for breast cancer. ERA-923 has shown potent anti-tumor activity in human breast cancer and tamoxifen-resistant breast cancer models.

**PREMARIN®/TSE-424: Reduces Vasomotor Symptoms of Menopause**

Results of Phase II Study



## Family of PPARs Offers Broad Potential in Diabetes and Cardiovascular Disease

LILLY, GSK HAVE COMPOUNDS IN EARLY CLINICAL AND LATE PRECLINICAL STUDIES Ligand's partner pipeline in diabetes and cardiovascular diseases, which is built around novel peroxisome proliferation activated receptor (PPAR) modulators, is among the most prolific in the industry.

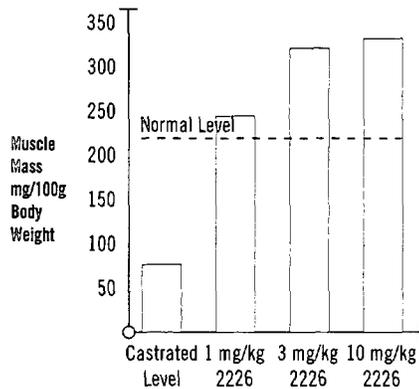
In 2001, Ligand received an undisclosed milestone payment from Lilly as a result of Lilly's filing with the FDA an Investigational New Drug (IND) application for LY519818, a novel PPAR agonist for the treatment of type II diabetes and metabolic diseases. PPARs are critical to the processes that regulate insulin sensitivity as well as the metabolic processes that affect lipid metabolism. LY519818 is one of several PPAR modulators being pursued under Ligand's collaboration with Lilly.

An estimated 15 million Americans suffer from diabetes, and more than 40 million from dyslipidemias. In these indications, Ligand's partners have five compounds in Phase I trials or on an IND track. U.S. market potential is approximately \$18 billion.

In cardiovascular disease, GW516, a product of Ligand's collaboration with GlaxoSmithKline, is in Phase I studies. In preclinical studies, GW516 has been shown to improve triglyceride and HDL levels significantly.

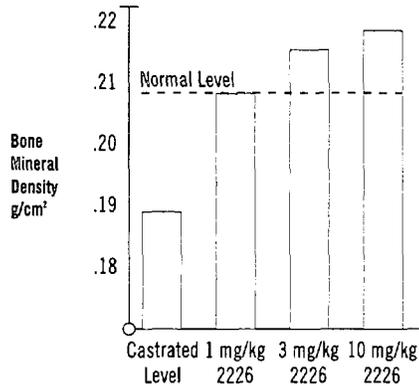
**LGD2226 in Testosterone Deficient Adult Male Rats**

*LGD2226 Improves Muscle Mass...*



**Ligand, TAP Advance LGD2226 to IND Track**

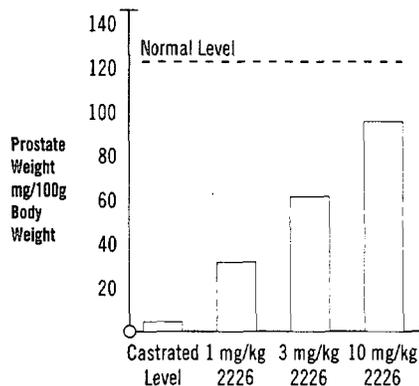
*...and Bone Density...*



**SARM MAY HOLD PROMISE IN DISEASES OF TESTOSTERONE DEFICIENCY** Ligand entered into an R&D collaboration with TAP Pharmaceutical Products in 2001, and the collaboration declared as a clinical candidate LGD2226. Ligand earned from TAP a \$1.0 million milestone payment as a result of the advancement of LGD2226.

LGD2226 is a non-steroidal, selective androgen receptor modulator (SARM) for the treatment of major diseases and disorders caused by testosterone deficiency, such as hypogonadism, osteoporosis, and male and female sexual dysfunction. In preclinical studies, LGD2226 prevented the substantial loss of bone density observed in adult rats with low testosterone levels. LGD2226 also increased muscle mass without overstimulating prostate growth, a common undesirable side effect seen with current androgen therapies. An increasing elderly population creates a large and growing potential market for SARMs.

*...Without Overstimulating Prostate Growth*





## Ligand's R&D Productivity Has Been Pacesetting

Ligand's research and development activities have been among the most productive in all the biotechnology industry. Since 1989, we have invested a cumulative \$358 million on research, which has yielded 25 New Chemical Entities, 11 of which have advanced to clinical development. Similarly, the \$293 million we have spent on development has produced five approved or approvable drugs and a total of 15 product candidates. In addition, our R&D productivity extends to our regulatory operations – all seven regulatory applications we have submitted in the United States, Canada and Europe have been approved.

Ligand's R&D productivity continued in 2001. For example, we moved several selective glucocorticoid receptor modulators, or SGRMs, into late preclinical development, and hope to select a clinical candidate in 2002. These non-steroidal molecules have anti-inflammatory activity that may be useful against diseases such as asthma and rheumatoid arthritis, as well as anti-proliferative effects that could be benefi-

cial in treating certain leukemias and myelomas. Our goal is to develop novel products that maintain the efficacy of corticosteroids but lack the side effects of current therapies, which can include osteoporosis, hyperglycemia and hypertension.

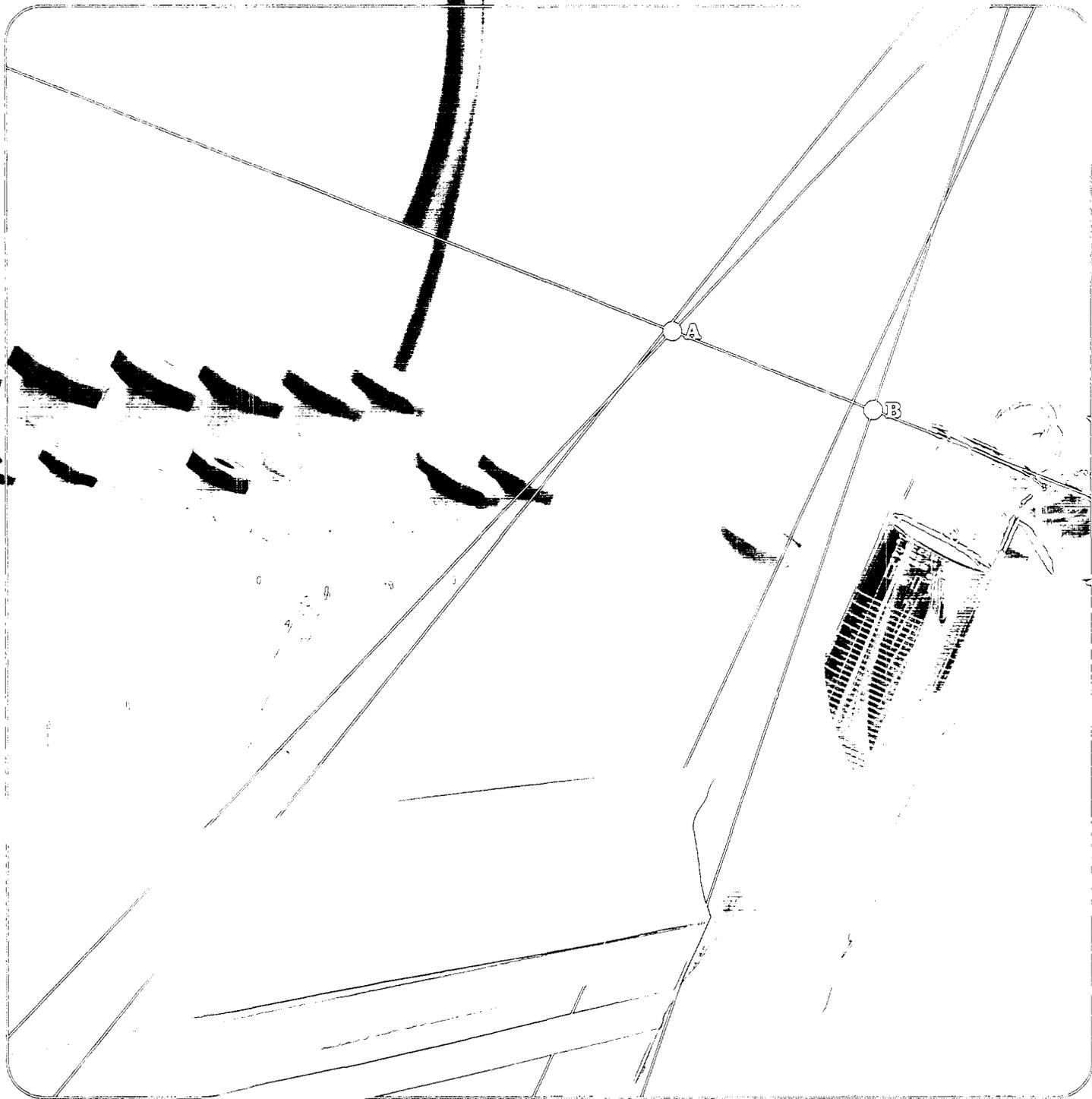
The R&D programs that fuel our LSPP and LCPP pipelines are built on a foundation that integrates our leadership position in gene transcription technology, our expertise in hormones and hormone-related drugs, and our scientific discoveries related to natural intracellular receptor-mediated mechanisms that regulate cellular activity.

To complement our core technology platform, Ligand owns a minority stake in X-Cepto Therapeutics, a private company formed in 1999 to identify drugs that target orphan nuclear receptors. Ligand has the rights to acquire X-Cepto in the future, an arrangement that allows us to explore the huge potential of early-stage orphan receptor technology.



"I have been suffering from cutaneous T-cell lymphoma for over 10 years. All treatments had ceased to have an effect when I started taking Targretin. Within two weeks, I improved to Stage 1 of the lymphoma. Targretin has given me my life back, allowed me to watch my grandchildren grow up and plan for old age with my wife."

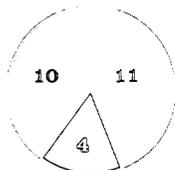
Larry Kincaid, Attorney



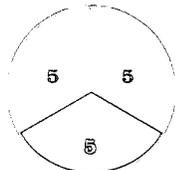
*Ligand's Pacesetting R&D Productivity*

Research: \$358MM / 25 NCEs

Development: \$293MM / 15 Products



NCEs Advanced to Preclinical Development Stage  
 NCEs Advanced to Clinical Stage  
 NCEs Advanced to IND Track or Equivalent



Compounds in Preclinical or on IND Track  
 NDAs and BLAs Approved or Submitted  
 Phase II and III Products

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Productivity based on R&D costs from start to market excluding commercialization costs.

Complete return on investment for R&D is achieved for each product.

Form 10-K

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F-1	Financial Statements

# SECURITIES AND EXCHANGE COMMISSION

Washington, D.C. 20549

## FORM 10-K

Mark One

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

For the Fiscal Year Ended December 31, 2001

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 jurisdiction of  
incorporation or organization)

77-0160744  
(IRS 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  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, 2002 was \$684,050,490. 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, 2002 the registrant had 64,545,145 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, 2001, 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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## GLOSSARY

### PRODUCTS AND INDICATIONS

ONTAK® (denileukin diftitox)	Approved in February 1999 for sale in the U.S. for the treatment of patients with persistent or recurrent cutaneous T-cell lymphoma whose malignant cells express the CD25 component of the Interleukin-2 receptor.
Targretin® (bexarotene) capsules	Approved in December 1999 for sale in the U.S. and in March 2001 for sale in Europe for the treatment of cutaneous manifestations of cutaneous T-cell lymphoma in patients who are refractory to at least one prior systemic therapy.
Targretin® (bexarotene) gel 1%	Approved in June 2000 for sale in the U.S. for the topical treatment of cutaneous lesions in patients with cutaneous T-cell lymphoma (Stage 1A and 1B) who have refractory or persistent disease after other therapies or who have not tolerated other therapies.
Panretin® gel (alitretinoin) 0.1%	Approved in February 1999 for sale in the U.S. and in October 2000 for sale in Europe for the topical treatment of cutaneous lesions of patients with AIDS-related Kaposi's sarcoma.

CTCL	Cutaneous T-cell lymphoma
HIV	Human immunodeficiency virus
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
EMA	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

*Caution:* The discussion and analysis 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 at "Risks and Uncertainties" in "Item 1 - Business". 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. This caution is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995.

Our trademarks, trade names and service marks referenced in this annual report include Ligand<sup>®</sup>, ONTAK<sup>®</sup>, Panretin<sup>®</sup>, Targretin<sup>®</sup>, and Avinza<sup>™</sup>. Each other trademark, trade name or service mark appearing in this annual report belongs to its owner.

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

We currently market four oncology products in the United States: Panretin<sup>®</sup> gel, ONTAK<sup>®</sup> and Targretin<sup>®</sup> capsules, each of which were approved by the FDA in 1999; and Targretin<sup>®</sup> gel, which was approved by the FDA in 2000. In Europe, the EC granted a Marketing Authorization (MA) for Panretin<sup>®</sup> gel in October 2000 and an MA for Targretin<sup>®</sup> capsules in March 2001. We submitted Marketing Authorization Applications (MAAs) to the European Agency for the Evaluation of Medicinal Products (EMEA) for Targretin<sup>®</sup> gel in March 2001 and for ONZAR<sup>™</sup> (the brand name of ONTAK<sup>®</sup> in Europe) in December 2001. We also continue efforts to acquire or in-license products, such as ONTAK<sup>®</sup> (acquired in the 1998 acquisition of Seragen) and Avinza<sup>™</sup> (licensed from Elan Corporation, plc and formerly called Morphelan<sup>™</sup>), which have near-term prospects of FDA approval and which can be marketed by our specialty sales forces. We are developing additional products through our internal development programs and currently have various products in clinical development, including marketed products that we are testing for larger market indications such as non-small cell lung cancer (NSCLC), B-cell non-Hodgkin's Lymphoma (NHL), psoriasis and rheumatoid arthritis.

We have research and development collaborations with numerous global pharmaceutical companies, including Abbott Laboratories, Allergan, Bristol-Myers Squibb, Eli Lilly & Co., GlaxoSmithKline, Organon (AKZO-Nobel), Pfizer, Takeda-Abbott Pharmaceuticals (TAP) and Wyeth (formerly American Home Products). At the end of 2001, our corporate partners had six Ligand products in human development, six products 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. Three of these partner products are in pivotal Phase III clinical trials: lasofoxicifene, which is being developed by Pfizer for

osteoporosis; and bazedoxifene (formerly TSE-424), which is being developed by Wyeth as monotherapy for osteoporosis and in combination with Wyeth's PREMARIN® as hormone replacement therapy (HRT).

Internal and collaborative research and development programs are built around our proprietary science technology, which is based on our leadership position in gene transcription technology. Our proprietary technologies involve two natural mechanisms that regulate gene activity: non-peptide hormone-activated IRs, and 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 who focus on the dermatology market. In anticipation of the launch of Avinza™ in 2002, pending regulatory approval, we also announced in 2001 a strategic decision to form another sales force of approximately 20 representatives to target general pain centers not served by our existing representatives. Internationally, through marketing and distribution agreements with Elan, Ferrer International and Alfa Wassermann, we have established marketing and distribution capabilities in Europe, as well as 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 STAT technologies, our strategy is to generate cash flow primarily from the sale in the U.S., Europe and Latin America of specialty pharmaceutical products we develop, acquire or in-license, and from 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 STAT 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. Ligand's international partners are Elan (principally in Western and Eastern Europe), Ferrer (in Spain, Portugal, Greece, Central and South America) and Alfa Wassermann (in Italy).

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 also has allowed us to spread the cost of our sales and marketing infrastructure across multiple products. Our goal is to expand the markets for our products through approvals in additional indications and in international markets. To further leverage our sales forces, we intend to acquire selectively 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. Drugs to treat these diseases may be more costly to develop and/or market effectively with a small specialty sales force. On the other hand, drugs approved for these indications may have large market potential – often in excess of \$1 billion in global sales.

We currently have 10 collaborations with global pharmaceutical companies focusing on a broad range of disease targets.

<u>Corporate Collaborator</u>	<u>Initiation of Collaboration</u>	<u>Focus</u>
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 (formerly American Home Products)	September 1994	Women's and men's health, oncology
GlaxoSmithKline (SmithKline Beecham)	February 1995	Blood disorders
Eli Lilly & Company	November 1997	Type II diabetes, metabolic and cardiovascular diseases
Organon	February 2000	Women's health
Bristol-Myers Squibb	May 2000	Cardiovascular diseases
TAP Pharmaceutical Products, Inc.	June 2001	Men's and women's health

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: research revenue during the drug discovery stage; milestone revenue for compounds successfully moving through clinical development and regulatory submission and approval; and 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.

<u>Marketed Product</u>	<u>Approved Indication</u>	<u>European Status</u>	<u>Indications in Development</u>
ONTAK <sup>®</sup>	CTCL	MAA submitted	B-cell NHL, rheumatoid arthritis, psoriasis
Targretin <sup>®</sup> capsules	CTCL	MA issued	NSCLC, psoriasis, renal cell cancer, prostate/colon cancer
Targretin <sup>®</sup> gel	CTCL	MAA submitted	Hand dermatitis, psoriasis
Panretin <sup>®</sup> gel	KS	MA issued	None

**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. 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<sup>®</sup>, Targretin<sup>®</sup> capsules, and Targretin<sup>®</sup> gel currently approved in the U.S. for the treatment of CTCL, our strategy is to have multiple products available for treating this disease.

*ONTAK<sup>®</sup>.* ONTAK<sup>®</sup> 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. ONTAK<sup>®</sup> was the first treatment to be approved for CTCL in nearly 10 years. ONTAK<sup>®</sup> is currently in three Phase II clinical trials for the treatment of patients with B-cell NHL, and we expect to see interim results from these studies in 2002. Clinical trials using ONTAK<sup>®</sup> for the treatment of patients with psoriasis, rheumatoid arthritis and CLL also have been conducted, and further trials are being considered. These indications provide significantly larger market opportunities than CTCL. A European MAA for CTCL was filed in December 2001. In Europe, ONTAK<sup>®</sup> will be marketed as ONZAR<sup>™</sup> if approved.

*Targretin<sup>®</sup> capsules.* We launched U.S. sales and marketing of Targretin<sup>®</sup> capsules in January 2000 following receipt of FDA approval in December 1999. Targretin<sup>®</sup> capsules offer the convenience of a daily oral dose administered by the patient at home. We are developing Targretin<sup>®</sup> capsules in a variety of larger market opportunities, including NSCLC, moderate to severe plaque psoriasis and renal cell cancer. In March 2001, the European Commission granted marketing authorization for Targretin<sup>®</sup> capsules in Europe for the treatment of patients with CTCL, and our network of distributors began marketing the drug in the fourth quarter of 2001 in Europe.

*Targretin<sup>®</sup> gel.* We launched U.S. sales and marketing of Targretin<sup>®</sup> gel in September 2000 following receipt of FDA approval in June 2000. Targretin<sup>®</sup> 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. Preliminary data presented at the American Academy of Dermatology meeting in March 2001 showed that Targretin<sup>®</sup> gel produced an overall response rate of 75% in patients with untreated, early-stage CTCL. Targretin<sup>®</sup> gel is currently in clinical development for hand dermatitis, and we expect to see interim Phase I/II data in 2002. We filed an MAA in Europe for CTCL in March of 2001.

*Panretin<sup>®</sup> gel.* Panretin<sup>®</sup> 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<sup>®</sup> gel represents a 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, where treatment is administered 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<sup>®</sup> gel was approved in Europe for the treatment of patients with KS in October 2000, and was launched through our distributor network in the fourth quarter of 2001 in Europe.

#### 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 developing drugs. At Ligand, 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 to 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 enter preclinical development. Once a lead compound is selected, chemical modification of the compound is 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 commencing human clinical trials. Development candidates are lead compounds that have successfully undergone *in vitro* and *in vivo* evaluation to demonstrate that they have an acceptable profile that justifies taking them through preclinical development with the intention of filing an IND and initiating human clinical testing.

Clinical trials are typically conducted in three sequential phases that may overlap. In Phase I, the initial introduction of the pharmaceutical into humans, the emphasis is on testing for adverse effects, dosage tolerance, absorption, metabolism, distribution, excretion and clinical pharmacology. Phase II involves studies in a representative patient population to determine the efficacy of the pharmaceutical for specific targeted indications, to

determine dosage tolerance and optimal dosage, and to identify related adverse side effects and safety risks. Once a compound is found to be effective and to have an acceptable safety profile in Phase II studies, Phase III trials are undertaken to evaluate clinical efficacy further and to test further for safety. Sometimes Phase I and II trials or Phase II and III trials are combined. In the U.S., the FDA reviews both clinical plans and results of trials, and may discontinue trials at any time if there are significant safety 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. This table 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 Avinza™, 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.

<u>Program</u>	<u>Disease/Indication</u>	<u>Development Phase</u>
ONTAK®	CTCL B-cell NHL Rheumatoid arthritis Psoriasis (severe)	Marketed in U.S. Phase II Phase II Phase II
Targretin® capsules	CTCL NSCLC Advanced breast cancer Psoriasis (moderate to severe) Renal cell cancer Prostate/colon cancer	Marketed in U.S. Phase III Phase II Phase II Phase II Planned Phase II
Targretin® gel	CTCL Hand dermatitis (eczema) Psoriasis	Marketed in U.S. Phase II Phase II
Panretin® gel	KS	Marketed in U.S.
Panretin® capsules	KS Bronchial metaplasia	Phase II Phase II
LGD1550 (RAR agonist)	Acne Psoriasis Advanced cancers	Planned Phase I/II Planned Phase I/II Phase I/II complete
Avinza™ (formerly Morphelan™)	Chronic, moderate to severe pain	NDA submitted; FDA approvable letter received
LGD1331 (Androgen antagonist)	Prostate cancer, hirsutism, acne, androgenetic alopecia	Pre-clinical
Glucocorticoid agonists	Inflammation, cancer	Pre-clinical
Mineralocorticoid receptor modulators	Congestive heart failure, hypertension	Research

### *ONTAK® Development Programs*

ONTAK® is the first of a new class of targeted cytotoxic biologic agents called fusion proteins. ONTAK® was acquired in the acquisition of Seragen in 1998 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 may 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 first half of 2002. NHL affects approximately 300,000 people in the U.S.

ONTAK® also has been evaluated to treat chronic lymphocytic leukemia (CLL), which affects 10,000 to 12,000 people in the U.S. At the American Society of Hematology (ASH) annual meeting in 2001, researchers from Wake Forest University reported results from a preliminary Phase II study that showed for the first time that ONTAK® demonstrated anti-cancer activity in patients with fludarabine-refractory CLL.

Clinical trials with ONTAK® have demonstrated benefits in patients with long-standing, previously treated severe psoriasis. For example, a study published in the Journal of the American Academy of Dermatology in 2001 showed that almost half of patients with severe psoriasis who were treated with a low-dose regimen of ONTAK® had a clinically meaningful response and fewer, less severe side effects than patients in previous ONTAK® studies. Based on these positive preliminary results, additional investigations are being considered. The National Psoriasis Foundation estimates that more than 1.4 million people in the U.S. have moderate to severe psoriasis. Phase II studies also 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.

Finally, researchers continued to learn how to optimize treatment with ONTAK® in 2001. At the ASH meeting, Tufts researchers presented data from a pilot Phase I study that showed treating CTCL patients with Targretin® capsules boosted the activity of ONTAK® and increased patient response rates. In addition, data published in the Journal of Clinical Oncology in 2001 showed that ONTAK® produced meaningful responses (30% response overall) in advanced-stage, heavily pre-treated CTCL patients.

### *Targretin® Capsules Development Programs*

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

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. These results were published in the May 2001 issue of the Journal of Clinical Oncology. These results add 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 led us to begin two large-scale Phase III clinical studies in 2001 to demonstrate conclusively Targretin® capsules' benefit in the treatment of patients with NSCLC. One of these multi-center studies will evaluate Targretin® in combination with the chemotherapy drugs cisplatin and vinorelbine, and will be conducted primarily in Europe. The other multi-center study will examine Targretin® in combination with carboplatin and paclitaxel, and will be conducted mainly in the U.S. Both studies are randomized with approximately 600 patients each, and have survival as the primary endpoint. Our goal is to enroll more than 40% of the required patients in 2002, and to complete the studies in the 2003-4 timeframe. The studies are designed to support a supplemental indication for Targretin® capsules for first-line treatment of patients with advanced NSCLC. The American Cancer Society estimates that 169,000 Americans were diagnosed with lung cancer in 2000; of those

approximately 80% were diagnosed with NSCLC.

Our primary focus for Targretin<sup>®</sup> capsules during 2002 and 2003 will be NSCLC. We will, however, continue to explore in Phase II trials the potential of Targretin<sup>®</sup> capsules in combination regimens for the treatment of patients in solid tumor indications as well as psoriasis. For example, researchers from the University of Wisconsin presented in 2001 results of a multi-center, Phase I/II study that showed combination therapy with Targretin<sup>®</sup> capsules and INTRON<sup>®</sup> A (Interferon Alfa-2B) may improve survival and delay tumor growth in some advanced-stage renal cell patients. In addition, a study is underway under the sponsorship of the National Cancer Institute to evaluate the mechanism of action of Targretin<sup>®</sup> capsules in patients at high risk of developing breast cancer.

Preliminary results of a Phase II trial with Targretin<sup>®</sup> capsules for the treatment of patients with moderate to severe psoriasis showed that Targretin<sup>®</sup> capsules have activity in psoriasis as monotherapy at daily doses substantially lower than approved oncology doses. This activity was 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. These studies are underway, and we anticipate seeing preliminary results in the second half of 2002.

#### ***Targretin<sup>®</sup> Gel Development Program***

Targretin<sup>®</sup> gel is marketed in the U.S. for patients with refractory CTCL. In addition, a Phase II trial with Targretin<sup>®</sup> gel for the treatment of patients with hand dermatitis is underway, and we expect to see interim data in 2002. In Europe, we filed an MAA for Targretin<sup>®</sup> gel in CTCL in March 2001.

#### ***Panretin<sup>®</sup> Capsules Development Programs***

Panretin<sup>®</sup> 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<sup>®</sup> capsules in patients with KS. Phase II trials with Panretin<sup>®</sup> 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. In Phase I/II clinical trials in advanced cancer, LGD1550 capsules were well tolerated. Investigators observed dose-limiting skin toxicities, diarrhea and abdominal cramps. Other potentially 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.

#### ***Glucocorticoid Receptor Research and Development Program***

As part of the research and development collaboration we entered into with Abbott in 1994, Ligand received exclusive worldwide rights for all anti-cancer products discovered in the collaboration. In 2001, we moved several selective glucocorticoid receptor modulators, or SGRMs, into late preclinical development, and hope to select a clinical candidate in 2002. These non-steroidal molecules have anti-inflammatory activity that may be useful against diseases such as asthma and rheumatoid arthritis, as well as anti-proliferative effects that could be beneficial in treating certain leukemias and myelomas. Our goal is to develop novel products that maintain the efficacy of corticosteroids but lack the side effects of current therapies, which can include osteoporosis, hyperglycemia and hypertension.

#### ***Avinza<sup>™</sup> 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 Avinza<sup>™</sup> (formerly called Morphelan<sup>™</sup>) in the U.S. and Canada for chronic,

moderate-to-severe pain. Avinza™, 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, and we expect launch of the product in 2002, pending regulatory approval. If approved, we will market and sell Avinza™ in the U.S. and Canada through our existing specialty sales forces. In anticipation of the launch of Avinza™, we announced in 2001 a strategic decision to form another sales force of approximately 20 representatives to target general pain centers not served by our existing representatives. In addition, Elan has announced its desire to co-promote the product with us in areas outside of oncology and HIV. In 2001, the U.S. market for sustained-release opioids was \$2.3 billion, so if approved Avinza™ will be launched into our largest initial market to date. Please see note 5 of notes to consolidated financial statements for further details on our strategic alliance with Elan.

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

Our SARM programs have been our largest internally funded programs over the past six 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.

Consistent with this strategy, we formed in June 2001 a joint research and development alliance with TAP Pharmaceutical Products to focus on the discovery and development of SARMs, including LGD2226, the current lead product candidate. Please see the "Collaborative Research and Development Programs" section below for more details on this alliance.

Apart from the TAP alliance, Ligand is conducting preclinical development for LGD1331, an androgen antagonist for acne, prostate cancer, hirsutism and androgenetic alopecia. 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.

#### *STAT Research Programs*

In contrast to our IR programs, our STAT 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 — STAT Technology" for a more complete discussion of our STATs technology. In our STAT 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 STAT technologies. These collaborations focus on several large market indications as estimated in the table below.

<u>Indication</u>	<u>U.S. Prevalence</u>
Breast cancer	2 million
Cardiovascular disease	61 million
Contraception	35 million
Hormone replacement therapy	46 million
Obesity	48 million
Osteoporosis	44 million
Type II diabetes	16 million

At the end of 2001, six of our collaborative product candidates were in human development - lasofoxifene, bazedoxifene (TSE-424), bazedoxifene+PREMARIN®, ERA-923, GW516 and LY818; and six 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.

<u>Program</u>	<u>Disease/Indication</u>	<u>Development Phase</u>	<u>Marketing Rights</u>
<b>SEX HORMONE MODULATORS</b>			
<u>SERMs</u>			
• Lasofoxifene	Osteoporosis, breast cancer prevention	Phase III	Pfizer
• Bazedoxifene (TSE-424)	Osteoporosis	Phase III	Wyeth (formerly American Home Products)
• Bazedoxifene+PREMARIN®	HRT	Phase III	Wyeth
• ERA-923	Breast cancer	Phase II	Wyeth
<u>PR modulators</u>			
• PR agonists	HRT, contraception, reproductive disorders	Pre-clinical	Organon
• PR antagonist	Contraception, reproductive disorders	Pre-clinical	Wyeth
• NSP-989 (formerly WAY-989) (PR agonist)	HRT, contraception	IND track	Wyeth
<u>SARMs</u>			
• LGD2226 (androgen agonist)	Male hypogonadism, HRT; female sexual dysfunction, osteoporosis	IND track	TAP
<b>METABOLIC/CARDIOVASCULAR DISEASES</b>			
<u>PPAR modulators</u>			
• GW516	Cardiovascular disease, dyslipidemia	Phase I	GlaxoSmithKline
• LY929/LYZZZ*	Type II diabetes, metabolic diseases, dyslipidemia	IND track	Lilly
• LY818	Type II diabetes, metabolic diseases	Phase I	Lilly
• LYXXX*	Dyslipidemia	IND track	Lilly
HNF-4 modulators	Type II diabetes, metabolic diseases	Research	Lilly
<b>INFLAMMATORY DISEASES, ONCOLOGY, ANEMIA</b>			
Glucocorticoid agonists	Inflammation	Pre-clinical	Abbott
Hematopoietic growth factors	Thrombocytopenia	IND track	GlaxoSmithKline

\* Compound number not disclosed

### *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, and hormonal disorders prevalent in men. Our programs, both collaborative and internal, target development of tissue-selective modulators of the PR, the ER and the AR. Through our collaborations with Pfizer and Wyeth, three SERM compounds are in development for osteoporosis, breast cancer and HRT. In addition, we entered into a joint research and development program in 2001 with TAP Pharmaceutical Products to focus on the discovery and development of SARMs. The collaboration's first product is now on an IND track.

*Pfizer Collaboration.* In 1991, we entered into a research and development collaboration with Pfizer to develop better 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 being developed by Pfizer for osteoporosis prevention and other diseases. Lasofoxifene is a second-generation estrogen partial agonist discovered through our collaboration with Pfizer. Pfizer has retained marketing rights to the drug. Lasofoxifene has been shown in Phase II clinical studies to reduce bone loss and decrease low-density lipoprotein ("LDL", or "bad" cholesterol) levels. In September 2000, Pfizer announced that it initiated Phase III studies of lasofoxifene for the treatment and prevention of osteoporosis in post menopausal women. In December 2001, Pfizer announced that two Phase III studies were fully enrolled with more than 1800 patients, and that an additional Phase III risk reduction trial was underway to evaluate lasofoxifene's effects on bone mineral density, lipid-lowering and breast cancer prevention.

*Wyeth 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. AHP has since changed its name to Wyeth. We granted Wyeth 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 Wyeth's extensive chemical library for activity against a selected set of targets. In 1996, Wyeth exercised its option to include compounds we discovered that modulate PRs, and to expand the collaboration to encompass the treatment or prevention of osteoporosis through the ER. Wyeth 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.

Wyeth has ongoing clinical studies with two SERMs from the collaboration. Wyeth is developing bazedoxifene (TSE-424) and bazedoxifene+PREMARIN<sup>®</sup> for the treatment of post-menopausal osteoporosis and as HRT. Phase III trials were initiated in June 2001. ERA-923 is being developed for the treatment of breast cancer, and Phase II trials are ongoing. AHP also has elected to proceed with IND track development of NSP-989 (formerly WAY-989), a progesterone agonist that may be useful in HRT and contraception. During 2001, Wyeth elected not to proceed with development of WAY-248, a non-steroidal PR antagonist for contraception, although Wyeth continues to do pre-clinical work in this area.

*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 that 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 concluded in February 2002, and a preclinical candidate has been identified.

*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. Bristol-Myers Squibb terminated this collaboration in June 2001.

**TAP Collaboration.** In June 2001, we entered into a joint research and development alliance with TAP Pharmaceutical Products to focus on the discovery and development of SARMs. SARMs may contribute to the prevention and treatment of diseases including hypogonadism (low testosterone), male and female sexual dysfunction, male and female osteoporosis, frailty, and male HRT. The three-year collaboration carries an option to extend by up to two additional one-year terms. Ligand received \$1 million when TAP declared LGD2226 a clinical candidate in 2001. An IND for LGD2226 could be filed in 2002.

Under the terms of the agreement, TAP received exclusive worldwide rights to manufacture and sell any products resulting from the collaboration in its field, which would include treatment and prevention of hypogonadism, male sexual dysfunction, female osteoporosis, male HRT and other indications not retained by Ligand. Ligand retains certain rights in the androgen receptor field, including the prevention or treatment of prostate cancer, benign prostatic hyperplasia, acne and hirsutism. In addition, Ligand has an option at the expiration of the original three-year term to develop one compound not being developed by TAP in its field, with TAP retaining an option to negotiate to co-develop and co-promote such compounds with Ligand.

#### ***Metabolic and Cardiovascular Disease Collaborative Programs***

We are exploring the role of certain IRs, including the PPARs, 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<sup>®</sup>. 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 managing 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 (e.g., Targretin<sup>®</sup> capsules) are able to activate this RXR:PPAR complex and 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 three 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 that produce beneficial alterations in lipid and lipoprotein metabolism in three project areas: (1) regulation of cholesterol biosynthesis and expression of a receptor that 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<sup>®</sup> 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 retain the right to develop and commercialize products arising from the collaboration in markets not exploited by GlaxoSmithKline, or where GlaxoSmithKline is not developing a product for the same indication.

In 1999, two compounds were advanced to exploratory development: (1) GW544, a PPAR agonist for cardiovascular disease and dyslipidemia; and (2) GW516, a second candidate that is in clinical development for cardiovascular disease and dyslipidemia. In 2001, GlaxoSmithKline elected not to proceed with development of GW544. GW516 remains in Phase I studies. The American Heart Association estimates that 62 million Americans have some form of cardiovascular disease, and that cardiovascular disease accounts for more than 40% of deaths in the U.S. annually.

*Eli Lilly Collaboration.* In November 1997, we entered into a research and development collaboration with Eli Lilly & Co. (Lilly) for the discovery and development of products based upon our RXR 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 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<sup>®</sup> 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<sup>®</sup> 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<sup>®</sup>, in the RXR program for diabetes. As a result of this decision, all rights to the oral form of Targretin<sup>®</sup> 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. In December 2000, LY519818, another PPAR agonist, was also declared a clinical candidate for type II diabetes. In September 2001, Ligand announced that it had earned an undisclosed milestone from Lilly as a result of Lilly's filing with the FDA an IND for LY519818. Ligand will receive additional milestones if LY519818 continues through the development process, and royalties on product sales if the product receives marketing approval. LY510929 remains on an IND track. During 2001, Lilly also moved to IND track two other PPAR products, the compound numbers for which have not been disclosed. Lilly also has an active preclinical development program.

#### *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, 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. Our goal is to select a clinical candidate during 2002.

### *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 use 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 molecules 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. In 2001, GlaxoSmithKline moved a lead compound to an IND track for thrombocytopenia. 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<sup>®</sup> capsules and Panretin<sup>®</sup> 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 that 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<sup>®</sup> for uses other than oncology and dermatology indications. In the event that we license commercialization rights to Targretin<sup>®</sup> to a third party, we will pay to Allergan a percentage of royalties payable to us with respect to sales of Targretin<sup>®</sup> other than in oncology and dermatology indications. During 2001, Allergan elected not to proceed with development of AGN4310 for mucocutaneous toxicity.

### **Technology**

In our successful efforts to discover new and important medicines, we and our academic collaborators and consultants have concentrated on two areas of research: advancing the understanding of the activities of hormones and hormone-related drugs, and making scientific discoveries related to IR 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. Our efforts may result either in improved therapeutic and side effect profiles and new indications for IRs, or in novel mechanisms of action and oral

activity for STATs. Both IRs and STATs 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 have acquired fusion protein technology, which was used by Seragen in the development of ONTAK<sup>®</sup>.

### *Intracellular Receptor Technology*

Hormones occur naturally within the body and control processes such as reproduction, cell growth and differentiation. Hormones generally fall into two classes, non-peptide hormones and peptide hormones. Non-peptide hormones include retinoids, sex steroids (estrogens, progestins and androgens), adrenal steroids (glucocorticoids and mineralocorticoids), vitamin D and thyroid hormone. These non-peptide hormones act by binding to their corresponding IRs to regulate the expression of genes in order to maintain and restore balanced cellular function within the body. Hormonal imbalances can lead to a variety of diseases. The hormones themselves and drugs that mimic or block hormone action may be useful in the treatment of these diseases. Furthermore, hormone mimics (agonists) or blockers (antagonists) can be used to treat diseases in which the underlying cause is not hormonal imbalance. The effectiveness of IRs as drug targets is clearly demonstrated by currently available drugs acting through IRs for several diseases. However, the use of most of these drugs has been limited by their often significant side effects. Examples of currently marketed hormone-related drugs acting on IRs are glucocorticoids (steroids used to treat inflammation), natural and synthetic estrogens and progestones (used for hormone replacement therapy and contraception), tamoxifen (an estrogen antagonist used in the treatment of breast cancer), and various retinoids such as Accutane<sup>®</sup> and Retin-A<sup>®</sup> (used to treat acne) and Dovonex<sup>®</sup> (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 known small-molecule, non-peptide hormones act. We and our academic collaborators and consultants have made major discoveries pertaining to IRs and to small molecule hormones and compounds that 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 non-peptide hormones are closely related members of a superfamily of proteins known as IRs. Human IRs for all the known non-peptide hormones now have been cloned, in many cases by our scientists or our collaborators. The structure and underlying mechanism of action of IRs have many common features, such that drug discovery insights about one IR often can 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. As a result, they 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<sup>®</sup>, 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 to treat acute promyelocytic leukemia. Retinoids also have shown an ability to reverse precancerous (pre-malignant) 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 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<sup>®</sup> gel, Targretin<sup>®</sup> capsules and Targretin<sup>®</sup> gel) and four retinoid products in clinical trials (Panretin<sup>®</sup> capsules, Targretin<sup>®</sup> capsules, Targretin<sup>®</sup> gel and LGD1550 capsules). Panretin<sup>®</sup> gel and Panretin<sup>®</sup> 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 more than 25 years and appears to be a natural ligand for the RAR and RXR subfamilies of retinoid receptors. Bexarotene, the active substance in Targretin<sup>®</sup>, 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<sup>®</sup>. Targretin<sup>®</sup> 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.** More than 50 additional members of the IR superfamily that 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 have 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<sup>®</sup>) can be administered to correct this anemia effectively, but must be injected. Other cytokines are useful as injected protein medicines, including interferons (Intron-A<sup>®</sup>, Roferon<sup>®</sup>, Betaseron<sup>®</sup>) and interleukins (Proleukin<sup>®</sup>) and G-CSF (Neupogen<sup>®</sup>). 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<sup>®</sup>, 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 February 2004. 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. He leads IR research at Baylor.

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 also are 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 apprised 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, 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 \$51.1 million, \$51.3 million and \$59.4 million in fiscal 2001, 2000 and 1999 respectively, of which approximately 70%, 68% and 73% 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 that target the same diseases 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 that apply at the state level. Product development and approval within this regulatory framework takes a number of years and involves the expenditure of substantial resources.

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

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

For marketing outside the United States before FDA approval to market, we must submit an export permit application to the FDA. We also are subject to foreign regulatory requirements governing human clinical trials and marketing approval for drugs. The requirements relating to the conduct of clinical trials, product licensing, pricing and reimbursement vary widely from country to country and there can be no assurance that we or any of our partners will meet and sustain any such requirements. 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 115 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 have licensed rights covered by approximately 243 patents issued, granted or allowed worldwide, including United States patents and foreign counterparts to United States patents. With a few immaterial exceptions, these patents will expire between 2002 and 2022. 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, 2002, we had 351 full-time employees, of whom 217 were involved directly in scientific research and development activities. Of these employees, approximately 68 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, 2001, our accumulated deficit was approximately \$586 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 cannot predict if or when any of the products we are developing or those being co-developed with our partners will be approved for marketing. 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 and may increase our operating losses.*

Developing the sales force to market and sell products is a difficult, expensive and time-consuming process. We have developed a U.S. sales force of about 55 people, some of whom are contracted from a third party, and we 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 coordinate 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.

*Our small number of products means our results are vulnerable to setbacks with respect to any one product.*

We currently have only 4 products approved for marketing, one additional product (Avinza™), for which the licensor (Eian) has received an "approvable letter" by the FDA, but has not been approved, and a handful of other products/indications that have made significant progress through development and the regulatory approval process. Because these numbers are small, especially the number of marketed products, any significant setback with respect to any one of them could significantly impair our operating results and/or reduce the market price for shares of our stock. Setbacks could include problems with shipping, manufacturing, product safety, marketing, government licenses and approvals, intellectual property rights and physician or patient acceptance of the product.

*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 STAT 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 funding which could hurt our income.*

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 Avinza™, formerly 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 face significant regulatory hurdles prior to marketing which could delay or prevent sales.*

Before we obtain the approvals necessary to sell any of our potential products, we must show through preclinical studies and human testing that each product is safe and effective. 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, 2001, 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 \$86.1 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 or which reduce our stock price.*

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 at all or on favorable 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. These transactions have resulted in the issuance of significant numbers of new shares. 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 which may limit our revenues.*

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.

*Third-party reimbursement and health care reform policies may reduce our future sales.*

Sales of prescription drugs depend significantly on the availability of reimbursement to the consumer from third party payers, such as government and private insurance plans. These third party payers 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 payers 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.

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

Our success will depend on our ability and the ability of our licensors to obtain and maintain patents and proprietary rights for our potential products 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<sup>®</sup> 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 believe we were the first to invent the relevant technology and therefore are entitled to a patent on the application we filed. The Patent and Trademark Office 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<sup>®</sup> capsules and gel in specified cancers.

We have also learned that Novartis AG has filed an opposition to our European patent that covers the principal active ingredient of our ONTAK<sup>®</sup> drug. We are currently investigating the scope and merits of this opposition. If the opposition is successful, we could lose our ONTAK<sup>®</sup> patent protection in Europe which could substantially reduce our ONTAK<sup>®</sup> sales in that region. We could also incur substantial costs in asserting our rights in this opposition proceeding, as well as in other interference proceedings in the United States.

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.

*Reliance on third-party manufacturers to supply our products risks supply interruption or contamination and difficulty controlling costs.*

We currently have no manufacturing facilities and we rely on others for clinical or commercial production of our marketed and potential products. In addition, certain raw materials necessary for the commercial manufacturing of our products are custom and must be obtained from a specific sole source. To be successful, we will need to ensure continuity of the manufacture of 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 and an 82,500 square foot facility leased through February 2014. 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. On July 25, 2000, the Delaware Chancery Court granted in part and denied in part defendants' motions to dismiss. Seragen, Ligand, Seragen Technology, Inc. and our acquisition subsidiary, Knight Acquisition Corporation were dismissed from the action. Claims of breach of fiduciary duty remain against the remaining defendants, including the former officers and directors of Seragen. The hearing on the plaintiffs' motion for class certification took place on February 26, 2001. The court certified a class consisting of shareholders as of the date of the acquisition and on the date of an earlier business unit sale by Seragen. 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 December 11, 2001, a lawsuit was filed in the United States District Court for the District of Massachusetts against the Company by the Trustees of Boston University and other former stakeholders of Seragen. The complaint alleges breach of contract, breach of the implied covenants of good faith and fair dealing and unfair and deceptive trade practices abased on, among other things, allegations that the Company wrongfully withheld approximately \$2.1 million in consideration due the plaintiffs under the Seragen acquisition agreement. The complaint seeks payment of the withheld consideration and treble damages. The complaint has not been served and the Company has not responded to the complaint.

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.

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 parties have signed a settlement pursuant to which plaintiffs will dismiss this litigation with prejudice.

#### 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, 2001.

## 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.

	<u>Price Range</u>	
	<u>High</u>	<u>Low</u>
<b>Year Ended December 31, 2000:</b>		
1st Quarter .....	\$ 26.500	\$ 12.500
2nd Quarter .....	18.688	9.688
3rd Quarter .....	14.000	10.000
4th Quarter .....	16.313	10.500
<b>Year Ended December 31, 2001:</b>		
1st Quarter .....	14.750	7.813
2nd Quarter .....	14.040	8.063
3rd Quarter .....	11.750	7.300
4th Quarter .....	19.100	8.730

#### (b) Holders

As of February 28, 2002, there were approximately 2,164 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,				
	2001	2000	1999	1998	1997
	(in thousands, except loss per share data)				
<b>Consolidated Statement of Operations Data:</b>					
Product sales (1).....	\$ 45,623	\$ 22,910	\$ 11,307	\$ 406	\$ 418
Collaborative research and development and other revenues .....	30,718	25,200	29,588	17,267	51,281
Cost of products sold (1).....	13,947	8,591	3,563	466	520
Research and development expenses .....	51,104	51,287	59,442	70,273	71,906
Loss from operations (2) .....	(23,137)	(45,882)	(61,293)	(114,634)	(95,805)
Loss before cumulative effect of a change in accounting principle .....	(42,995)	(59,277)	(74,719)	(117,886)	(100,150)
Cumulative effect on prior years (to December 31, 1999) of changing method of revenue recognition (3) .....	—	(13,099)	—	—	—
Net loss .....	(42,995)	(72,376)	(74,719)	(117,886)	(100,150)
<b>Basic and diluted per share amounts:</b>					
Loss before cumulative effect of a change in accounting principle .....	\$ (0.72)	\$ (1.06)	\$ (1.58)	\$ (2.92)	\$ (3.02)
Cumulative effect on prior years (to December 31, 1999) of changing method of revenue recognition (3) .....	—	(0.24)	—	—	—
Net loss .....	<u>\$ (0.72)</u>	<u>\$ (1.30)</u>	<u>\$ (1.58)</u>	<u>\$ (2.92)</u>	<u>\$ (3.02)</u>
Weighted average number of common shares .....	<u>59,413,270</u>	<u>55,664,921</u>	<u>47,146,312</u>	<u>40,392,421</u>	<u>33,128,372</u>
<b>Pro forma amounts assuming the changed revenue recognition method is applied retroactively:</b>					
Net loss .....		<u>\$ (59,277)</u>	<u>\$ (73,131)</u>	<u>\$ (114,136)</u>	<u>\$ (118,587)</u>
Basic and diluted net loss per share .....		<u>\$ (1.06)</u>	<u>\$ (1.55)</u>	<u>\$ (2.83)</u>	<u>\$ (3.58)</u>

	December 31,				
	2001	2000	1999	1998	1997
	(in thousands)				
<b>Consolidated Balance Sheet Data:</b>					
Cash, cash equivalents, short-term investments and restricted investments (4).....	\$ 40,058	\$ 25,097	\$ 49,166	\$ 72,521	\$ 86,287
Working capital .....	21,848	16,234	35,978	51,098	62,399
Total assets.....	117,473	113,422	134,645	156,020	107,423
Long-term debt .....	139,458	134,405	136,634	90,487	51,379
Accumulated deficit .....	(585,720)	(542,725)	(470,349)	(395,630)	(277,744)
Total stockholders' equity (deficit) .....	(57,875)	(55,125)	(25,590)	(11,362)	34,349

- (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

*Caution:* This discussion and analysis may contain predictions, estimates and other forward-looking statements that involve a number of risks and uncertainties, including those discussed 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. This caution is made under the safe harbor provisions of the Private Securities Litigation Reform Act of 1995.

Our trademarks, trade names and service marks referenced herein include ONTAK<sup>®</sup>, Panretin<sup>®</sup>, Targretin<sup>®</sup>, and Avinza<sup>™</sup>. Each other trademark, trade name or service mark appearing in this annual report belongs to its owner.

### Overview

We discover, develop and market drugs that address patients' critical unmet medical needs in the areas of cancer, men's and women's health, skin diseases, osteoporosis, and metabolic, cardiovascular and inflammatory diseases. Our drug discovery and development programs are based on our proprietary gene transcription technology, primarily related to Intracellular Receptors, also known as IRs, and Signal Transducers and Activators of Transcription, also known as STATs.

We currently market four products in the United States: ONTAK, for the treatment of patients with persistent or recurrent cutaneous T-cell lymphoma ("CTCL"); Targretin capsules and Targretin gel, for the treatment of CTCL in patients who are refractory to at least one prior systemic therapy; and Panretin gel, for the treatment of Kaposi's sarcoma in AIDS patients. In May 2000, our strategic partner Elan submitted a new drug application ("NDA") for its product Morphelan (now called "Avinza") for the relief of chronic, moderate to severe pain. The FDA has issued an approvable letter for the Avinza NDA and Elan has submitted a response to the FDA's questions in the letter. We have exclusive marketing rights to Avinza in the United States and Canada. In Europe, we were granted a marketing authorization for Panretin gel in October 2000 and for Targretin capsules in March 2001 and have a marketing authorization application under review for Targretin gel. In December 2001, we submitted a marketing authorization application for ONZAR (ONTAK in the U.S.) Targretin capsules and Panretin gel were launched in Europe in the fourth quarter of 2001.

During 2001 we were involved in the research phase of research and development collaborations with Eli Lilly and Company, Organon Company and TAP Pharmaceutical Products Inc. ("TAP"). Collaborations in the development phase are being pursued by Abbott Laboratories, Allergan, Inc., GlaxoSmithkline, Pfizer and Wyeth. 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. In addition, in connection with some of these collaborations, we received non-refundable up-front payments. Please refer to 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 additional operating losses until sales of our products generate sufficient revenues to cover our expenses. We expect that our operating results will fluctuate from period to period 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

Total revenues for 2001 increased to \$76.3 million, compared to \$48.1 million in 2000 and \$40.9 million in 1999. Net loss for 2001 decreased to \$43.0 million or \$0.72 per share, compared to \$72.4 million or \$1.30 per share in 2000 and \$74.7 million or \$1.58 per share in 1999. As more fully described in Note 2 of the notes to consolidated financial statements, results for 2000 reflect the implementation of SAB No. 101 effective January 1, 2000. The cumulative effect of this change to December 31, 1999, which was recorded in 2000, was \$13.1 million or \$0.24 per share. The effect on 2000 increased revenue and reduced loss before cumulative effect of a change in accounting principle by \$1.3 million or \$0.02 per share.

### Product Sales

Product sales for 2001 were \$45.6 million compared to \$22.9 million in 2000 and \$11.3 million in 1999. The 2001 increase was driven by an increase in sales of ONTAK to \$24.3 million in 2001 from \$13.2 million in 2000 and \$8.2 in 1999, and an increase in sales of Targretin capsules to \$14.6 million in 2001 compared to \$6.7 million in 2000. Targretin capsules were approved for marketing in the United States in December 1999. Sales of Targretin gel and Panretin gel increased to \$6.6 million for 2001 compared to \$2.6 million in 2000 and \$2.4 million in 1999. Targretin gel was approved for marketing in the U.S. in June 2000.

Product sales in 2001 benefited from increased penetration of private oncology practices, price increases and increased "off-label" use for indications where our products may be effective but for which clinical trials have not been completed and for which FDA approval has not yet been granted. We estimate that at the end of the fourth quarter, approximately 35% and 10% of sales of ONTAK and Targretin capsules, respectively, were from off-label use and expect that off-label sales as a percentage of total product sales will continue to increase in 2002. Results from clinical trials that indicate a product is not effective in treating certain indications would have a detrimental effect on off-label use of that product and the sales generated therefrom. The increase in sales of ONTAK and Targretin capsules in the fourth quarter of 2001 further reflect the impact of purchases made in advance of announced price increases effective in 2002 and for ONTAK, the initiation of wholesaler distribution stocking.

For 2001, there were five wholesale distributors that individually represented 10% or more of the Company's product sales and in the aggregate represented 72% of product sales. As of December 31, 2001, gross amounts due from these distributors totaled \$10.3 million of which 88% was collected in January 2002.

### Collaborative Research and Development and Other Revenues

Collaborative research and development and other revenues for 2001 were \$30.7 million, compared to \$25.2 million for 2000 and \$29.6 million for 1999. The comparison of collaborative research and development and other revenues is as follows (in thousands):

	Year Ended December 31,		
	2001	2000	1999
Collaborative research and development	\$ 25,725	\$ 23,135	\$ 15,954
Distribution agreements	4,787	922	3,250
Royalties	—	—	5,102
Contract manufacturing	—	—	2,610
Other	206	1,143	2,672
	<u>\$ 30,718</u>	<u>\$ 25,200</u>	<u>\$ 29,588</u>

Collaborative research and development revenue includes reimbursement for ongoing research activities, earned development milestones and SAB No. 101 recognition of prior years' up-front fees.

The increase in 2001 collaborative research and development revenue compared to 2000 is due to a new collaboration agreement entered into with TAP in June 2001 which generated 2001 revenues of \$4.3 million. The increase in 2000 compared to 1999 is primarily due to \$4.7 million earned under collaboration arrangements entered into in 2000 with Bristol-Myers Squibb and Organon, and the \$3.7 million recognition in 2000 of a portion of an up-front fee received in a prior year.

The increase in revenue from distributor agreements in 2001 reflects milestones earned under a 2001 distribution agreement with Elan for the European submission of Marketing Authorization Approval ("MAA") for Targretin gel and ONTAK and the European grant of an MAA for Targretin capsules. The decrease in revenue from distribution agreements in 2000 compared to 1999 reflects fees and milestones earned under other European distribution agreements entered into in 1999.

The increase in 2001 and 2000 collaborative research and development revenue compared to 1999 is offset by decreases to royalty revenue specific to 1999 transactions and the loss of contract manufacturing revenues earned

under agreements performed at Marathon Biopharmaceuticals. The assets of Marathon were sold in January 2000.

Certain customers accounted for greater than 10% of total revenues in 2001, 2000 and 1999. For additional details, please see note 2 (revenue recognition) of the notes to consolidated financial statements.

#### *Gross Margin*

Gross margin on product sales was 69.4% in 2001, compared to 62.5% in 2000 and 68.5% in 1999. The increase in the 2001 margin compared to 2000 is due to higher product sales over which we spread fixed costs (amortization of acquired technology), and a more favorable product mix due to higher proportionate sales of higher margin products. The decrease in margins from 1999 to 2000 is due to a contractual increase in the royalty rate for ONTAK.

#### *Operating Expenses*

Research and development expenses were \$51.1 million in 2001 compared to \$51.3 million in 2000 and \$59.4 million in 1999. The 2001 expense relative to 2000 reflects increased spending on studies of our products for potential new indications offset by reduced registration activities. The decrease from 1999 is primarily due to a reduction of registration activities with an increased focus on commercialization of our 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. We expect development expenses in 2002 to increase due to the funding of significant clinical trials including phase III trials for Targretin capsules in non-small cell lung cancer.

Selling, general and administrative expenses were \$34.4 million for 2001 compared to \$34.1 million in 2000 and \$27.3 million in 1999. The 2001 expense reflects increased costs associated with the implementation of fully dedicated oncology and dermatology sales forces including the addition of 10 sales representatives, post marketing clinical trials for our existing products and clinical studies related to the commercialization of Avinza. These increases were largely offset by higher promotion and advertising expenses incurred in 2000 in connection with the launches of Targretin capsules and gel. If the FDA approves Avinza, we expect 2002 selling expenses to further increase due to costs associated with the launch of Avinza and the formation of a new sales force to target general pain centers not served by our existing representatives.

The results for 1999 include a technology write-off of \$5 million related to a milestone payment made to Elan under the license agreement for Avinza. Refer to note 5 (license agreement) of the notes to consolidated financial statements for additional details.

#### *Other Expenses*

Other expense, net increased to \$19.9 million from \$13.4 million in each of 2000 and 1999. The 2001 expense includes debt conversion expenses of \$5 million related to an incentive provided to Elan in connection with the early conversion of \$50 million in issue price of zero coupon convertible senior notes. This compares with incentives provided to Elan in 2000 and 1999 of \$2.0 million and \$2.2 million, respectively, in connection with debt conversions transacted in each of those years. In addition, 2001 expenses include a \$2.5 million charge related to an estimated payment to be made to one of our licensors in connection with discussions concerning the clarification and amendment of an existing license agreement.

Other expenses include interest expense of \$13.6 million in 2001 compared to \$13.1 million in 2000 and \$13.0 million in 1999. As a result of the Elan debt conversion discussed above, we expect to eliminate approximately \$5 million of annual interest charges starting in 2002.

#### *Net Operating Losses*

At December 31, 2001, we had consolidated federal and combined California income tax net operating loss carryforwards of approximately \$483 million and \$76 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. The federal tax loss carryforward will begin to expire in 2002, unless previously utilized. The California tax loss carryforwards began expiring in 1998. At December 31, 2001, we also had consolidated federal and combined California research tax credit carryforwards of approximately \$22 million and \$9 million, respectively, which will begin to expire in 2002 unless utilized.

### 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 \$21.8 million at December 31, 2001 compared to \$16.2 million at December 31, 2000. Cash, cash equivalents, short-term investments, and restricted investments totaled \$40.1 million at December 31, 2001 compared to \$35.1 million, including \$10 million of funds receivable from Elan, at December 31, 2000. We primarily invest our cash in United States government and investment grade corporate debt securities.

Operating activities used cash of \$19.9 million in 2001 compared to \$45.2 million in 2000 and \$59.7 million in 1999. The improvement in operating cash flow in 2001 is primarily due to increased product sales. Changes in operating assets and liabilities had a neutral impact on 2001 operating cash flows with an increase in accounts receivable due to higher product sales offset by a decrease in inventory levels and higher accounts payable and accrued liabilities. Operating asset and liability changes in 2000 reflect an increase in deferred revenue resulting from the implementation of SAB101 partially offset by an increase in accounts receivable and a decrease in accounts payable and accrued liabilities.

We expect cash flows from operating activities in 2002 to continue to improve as a result of increasing product sales, offset in part by higher development expenses to fund clinical trials of our existing products in new indications including two Phase III registration trials for Targretin capsules in non-small cell lung cancer. If the FDA approves Avinza, we also expect an increase in marketing and selling expenses in connection with the launch of Avinza and the formation of a new sales force to target general pain centers not served by our existing representatives.

Investing activities used cash of \$4.2 million in 2001 and \$25.8 in 1999 and provided cash of \$12.5 million in 2000. The use of cash in 2001 reflects the net purchase of short-term investments of \$2.5 million and capital expenditures of \$2.0 million primarily for lab and computer equipment. Investing activities for 2000 reflect \$9.7 million received from the sale of the assets of Marathon Biopharmaceuticals and \$2.9 million net proceeds from the sale of short-term investments. Cash used for investing activities in 1999 includes payments made in connection with our acquisition of Seragen, Inc. and a \$6 million equity investment in X-Ceptor Therapeutics, Inc., partially offset by net proceeds from sales of short-term investments of \$19.8 million. We have the right to acquire all, but not less than all, of the outstanding X-Ceptor stock at June 30, 2002 for any combination of cash and stock. We can also extend the purchase option by 12 months by providing X-Ceptor additional cash funding of \$5 million. In the event we do not exercise our option to acquire the remaining shares of X-Ceptor at June 30, 2002 or extend the option, X-Ceptor can require us to purchase up to 2.5 million shares of X-Ceptor preferred stock at a price per share of \$1.00.

Financing activities provided cash of \$35.6 million in 2001 compared to \$12.0 million in 2000 and \$82.5 million in 1999. Cash received in 2001 includes \$22.4 million from a private placement of our common stock, \$10 million in connection with the issuance of zero coupon convertible senior notes to Elan, and \$6.2 million upon the exercise of employee stock options, partially offset by net repayments of \$2.0 million on equipment financing arrangements.

Cash provided from financing activities in 2000 include \$14.2 million of cash received from the issuance of our common stock upon the exercise of outstanding stock options and warrants partially offset by net payments on equipment financing obligations of \$2.7 million. Financing activities in 1999 provided cash of \$60 million through the issuance of zero coupon convertible senior notes to Elan and \$22.0 million from the issuance of common stock.

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, 2001, we had outstanding a \$2.5 million convertible note to SmithKline Beecham Corporation, due in October 2002 with interest at prime and convertible into our common stock at \$13.56 per share, and \$86.1 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. In December 2001, we reached agreement with Elan to convert \$61.8 million, including accrued interest, of the zero coupon convertible senior notes owed at December 31, 2001. These notes converted into shares of our common stock in February 2002 subsequent to regulatory approval. The conversion will reduce our annual interest expense by approximately \$5 million starting in 2002.

Certain of our property and equipment is pledged as collateral under various equipment financing arrangements. As of December 31, 2001, \$6.2 million was outstanding under such arrangements with \$2.9 million classified as current. Our equipment financing arrangements have terms of three to five years with interest ranging from 4.85% to 10.66%.

We lease our office and research facilities under operating lease arrangements with varying terms through July 2015. Our corporate headquarters is leased from a limited liability company (the "LLC") in which we hold a 1% ownership interest. The lease terminates in 2014 and can be extended for a period of five years. We also have the right, but not the obligation, to purchase either the LLC or the leased premises from the LLC at a purchase price equal to the outstanding debt on the property plus a calculated return on the investment made by the LLC's other shareholder.

In accordance with existing accounting standards, the lease is treated as an operating lease for financial reporting purposes. The FASB, however, is considering modifications to existing accounting principles that under certain conditions could result in consolidation of such entities or treatment of such lease arrangements as capital leases. If Ligand were required to treat such lease arrangement as a financing obligation, the Company's consolidated balance sheet as of December 31, 2001 would reflect additional property and equipment of \$14.1 million and additional debt of \$13.0 million. The impact of such treatment on the Company's 2001, 2000 and 1999 operating results would not be significant.

As of December 31, 2001, future minimum payments due under our contractual lease obligations are as follows (in thousands):

	Payments Due by Period				
	Total	Less than 1 year	1-3 years	4-5 years	After 5 years
Capital lease obligations	\$ 6,997	\$ 3,324	\$ 3,276	\$ 397	—
Operating leases	<u>41,465</u>	<u>3,029</u>	<u>6,083</u>	<u>6,300</u>	<u>\$ 26,053</u>
Total contractual lease obligations	<u>\$ 48,462</u>	<u>\$ 6,353</u>	<u>\$ 9,359</u>	<u>\$ 6,697</u>	<u>\$ 26,053</u>

If Avinza is approved by the FDA, we will be required to make a \$5 million milestone payment to Elan. This payment can be made in either cash or shares of common stock. We are also required to spend not less than \$7 million through May 2003 for clinical expenditures under the Avinza license agreement with Elan. As of December 31, 2001, we have incurred more than 50% against this commitment.

We are currently discussing the clarification and amendment of an existing license agreement with one of our licensors. While the exact payments by and to the licensor are still being determined, we expect to pay \$2.5 million to the licensor as a result of these discussions which was recorded as a charge to non-operating expenses in the fourth quarter of 2001.

We believe our available cash, cash equivalents, short-term investments and existing sources of funding will be sufficient 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 commercial 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 production.

### *Critical Accounting Policies*

Our significant accounting policies are disclosed in Note 2 to our consolidated financial statements. Certain of our policies require the application of management judgement in making estimates and assumptions that affect the amounts reported in the consolidated financial statements and disclosures made in the accompanying notes. Those estimates and assumptions are based on historical experience and various other factors deemed to be applicable and reasonable under the circumstances. The use of judgement in determining such estimates and assumptions is by nature, subject to a degree of uncertainty. Accordingly, actual results could differ from the estimates made. Our significant accounting policies include:

#### *Revenue Recognition and Accounts Receivable*

We recognize revenue upon product shipment, net of allowances for returns, rebates, discounts and chargebacks. Our policy for returns allows customers, primarily wholesale distributors, to return the product three months prior to and six months after expiration. The level of actual returns can be influenced by a number of factors including the dating of product when shipped to the customer, the amount of product subsequently shipped by the wholesale distributor to their retail customers, pricing adjustments, and competing products. In recording adjustments to sales for estimated returns, we consider each of these factors as well as historical return patterns of our products, independent reports of the level of our product in the distribution channel, and industry trends. Actual product returns may differ from our estimates.

We record allowances for doubtful accounts for estimated losses resulting from our customers' inability to pay amounts owed. If the financial condition of one or more of our customers were to deteriorate, we may be required to record additional allowances or write-off all or a portion of the amount due us.

We recognize collaborative research and development and other revenues as services are performed consistent with the performance requirements of the contract. Non-refundable contract fees for which no further performance obligation exists and where we have no continuing involvement are recognized upon the earlier of when payment is received or collection is assured. Revenue from non-refundable contract fees where we have continuing involvement through research and development collaborations or other contractual obligations is recognized ratably over the development period or the period for which we continue to have a performance obligation. Revenue from performance milestones is recognized upon the achievement of the milestones as specified in the respective agreement provided payment is proportionate to the effort expended. Payments received in advance of performance or delivery are recorded as deferred revenue.

#### *Inventories*

Our inventories are stated at the lower of cost or market value. Cost is determined using the first-in, first-out method. We record reserves for estimated obsolescence to account for unsaleable products including products that are nearing or have reached expiration, and slow-moving inventory.

#### *Impairment of Long-Lived Assets*

We review long-lived assets, including acquired technology and property and equipment, whenever events or circumstances indicate that the carrying amount of the assets may not be fully recoverable. We believe that the future cash flows to be received from our long-lived assets will exceed the assets' carrying value, and accordingly have not recorded any impairment losses through December 31, 2001.

## **New Accounting Pronouncements**

In July 2001, the Financial Accounting Standards Board ("FASB") issued Statement of Financial Accounting Standards ("SFAS") No. 141, "Business Combinations" which requires the use of the purchase method of accounting for all business combinations initiated after June 30, 2001 and eliminates the pooling-of-interests method. The adoption of SFAS No. 141 did not have a material impact on our operations or financial position.

In July 2001, the FASB issued SFAS No. 142, "Goodwill and Other Intangible Assets" which requires that goodwill and other intangible assets with indefinite lives no longer be amortized, but instead tested for impairment at least annually. In addition, the standard includes provisions for the reclassification of certain existing intangibles as goodwill and reassessment of the useful lives of existing recognized intangibles. SFAS No. 142 is effective for fiscal years beginning after December 31, 2001.

In October 2001, the FASB issued SFAS No. 144, "Accounting for the Impairment or Disposal of Long-Lived Assets" which establishes one accounting model to be used for long-lived assets to be disposed of by sale and broadens the presentation of discontinued operations to include more disposal transactions. SFAS No. 144 supercedes SFAS No. 121, "Accounting for the Impairment of Long-Lived Assets and for Long-Lived Assets to Be Disposed Of" and the accounting and reporting provisions of APB Opinion No. 30. SFAS No. 144 is effective for fiscal years beginning after December 15, 2001.

The adoption of SFAS No. 142 and SFAS No. 144 effective January 1, 2002 did not have a material effect on our operations or financial position.

### **Item 7A. Quantitative and Qualitative Disclosures About Market Risk**

At December 31, 2001 and 2000, our investment portfolio included fixed-income securities of \$15.5 million and \$12.4 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 do not have a significant level of transactions denominated in currencies other than 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 2002 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 section labeled "Stock Ownership" appearing in the Proxy Statement is 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**

Reports of Independent Auditors .....	F-2
Consolidated Balance Sheets at December 31, 2001 and 2000 .....	F-3
Consolidated Statements of Operations for each of the three years in the period ended December 31, 2001 .....	F-4
Consolidated Statements of Stockholders' Deficit for each of the three years in the period ended December 31, 2001 ....	F-5
Consolidated Statements of Cash Flows for each of the three years in the period ended December 31, 2001 .....	F-6
Notes to Consolidated Financial Statements.....	F-7

**(b) Reports on Form 8-K.**

No reports on Form 8-K were filed during the quarter ended December 31, 2001.

**(c) Exhibits**

<b><u>Exhibit Number</u></b>	<b><u>Description</u></b>
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 (31)	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).

<u>Exhibit Number</u>	<u>Description</u>
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).
10.38 (4)	License Agreement, dated January 5, 1990, between the Company and the University of North Carolina at Chapel Hill (with certain confidential portions omitted).
10.41 (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).
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.

<u>Exhibit Number</u>	<u>Description</u>
10.50 (4)	Consulting Agreement, dated October 1, 1991, between the Company and Dr. Bert W. O'Malley.
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).
10.82 (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.
10.97 (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).
10.140 (28)	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).
10.146 (24)	Amendment to Research and Development Agreement, dated January 16, 1996, between the Company and American Home Products Corporation, as amended.
10.148 (24)	Lease, dated July 6, 1994, between the Company and Chevron/Nexus partnership, First Amendment to lease dated July 6, 1994.

<u>Exhibit Number</u>	<u>Description</u>
10.149 (25)	Successor Employment Agreement, signed May 1, 1996, between the Company and David E. Robinson.
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.
10.157 (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 (29)	Settlement Agreement, License and Mutual General Release between Ligand Pharmaceuticals and SRILJCRF, dated August 23, 1995 (with certain confidential portions omitted).
10.163 (30)	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.
10.167 (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).

<u>Exhibit Number</u>	<u>Description</u>
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).
10.184 (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).
10.191 (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).
10.196 (12)	Zero Coupon Convertible Senior Note Due 2008 dated November 9, 1998 between the Company and Elan International Services, Ltd., No. R-2.
10.198 (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-Cepto Therapeutics, Inc.), contained in Schedule I to the Certificate of Incorporation of X-Cepto Therapeutics, Inc., as amended. (Filed as Exhibit 10.6).
10.203 (14)	License Agreement effective June 30, 1999 by and between the Company and X-Cepto Therapeutics, Inc. (with certain confidential portions omitted). (Filed as Exhibit 10.7).
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).

<u>Exhibit Number</u>	<u>Description</u>
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.)
10.224 (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 (31)	Zero Coupon Convertible Senior Note Due 2008 dated December 29, 2000 between Ligand Pharmaceuticals Incorporated and Monksland Holdings, BV, No. R-5.
10.227 (31)	Letter Agreement, dated August 23, 1999, between the Company and Eric S. Groves.
10.228 (31)	Letter Agreement, dated December 9, 1999, between the Company and Philip A. Duffy.
10.229 (31)	Letter Agreement, dated January 17, 2000, between the Company and Thomas H. Silberg.
10.230 (31)	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).
10.233 (32)	Second Amendment to the Research, Development and License Agreement, dated as of September 2, 1994, between the Company and American Home Products Corporation (with certain confidential portions omitted).

<u>Exhibit Number</u>	<u>Description</u>
10.234 (32)	Fourth Amendment to the Research, Development and License Agreement, dated as of September 2, 1994, between the Company and American Home Products Corporation (with certain confidential portions omitted).
10.235 (32)	Distributorship Agreement, dated February 29, 2001, between the Company and Elan Pharma International Limited (with certain confidential portions omitted).
10.236 (32)	Second Amendment to the Development, Licence and Supply Agreement dated November 9, 1998, between the Company and Elan Corporation, plc.
10.237 (33)	Form of Stock Purchase Agreement dated as of January 5, 2001, between the investors listed on Exhibit A and the Company.
10.238 (33)	Letter Agreement, dated May 17, 2001, between the Company and Gian Aliprandi.
10.239 (33)	Research, Development and License Agreement by and between the Company and TAP Pharmaceutical Products Inc. dated June 22, 2001 (with certain confidential portions omitted).
10.240	Letter Agreement, dated December 13, 2001, between the Company and Warner R. Broaddus, Esq.
10.241	Incentive Agreement dated December 20, 2001 among the Company, Elan International Services, Ltd. and Monksland Holdings, BV.
10.242	First Addendum to Amended and Restated Registration Rights Agreement dated June 29, 2000, effective as of December 20, 2001.
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 46).

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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 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.
- (29) 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.

- (30) 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.
- (31) 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, 2000.
- (32) 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, 2001.
- (33) 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, 2001.

## 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

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

Date: March 19, 2002

## 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.

<u>Signature</u>	<u>Title</u>	<u>Date</u>
<u>/s/ DAVID E. ROBINSON</u> David E. Robinson	Chairman of the Board, President, Chief Executive Officer and Director (Principal Executive Officer)	March 18, 2002
<u>/s/ PAUL V. MAIER</u> Paul V. Maier	Senior Vice President, Chief Financial Officer (Principal Financial and Accounting Officer)	March 18, 2002
<u>/s/ HENRY F. BLISSENBACH</u> Henry F. Blissenbach	Director	March 17, 2002
<u>/s/ ALEXANDER D. CROSS</u> Alexander D. Cross	Director	March 16, 2002
<u>/s/ JOHN GROOM</u> John Groom	Director	March 17, 2002
<u>/s/ IRVING S. JOHNSON</u> Irving S. Johnson	Director	March 16, 2002
<u>/s/ CARL C. PECK</u> Carl C. Peck	Director	March 15, 2002
<u>/s/ MICHAEL A. ROCCA</u> Michael A. Rocca	Director	March 19, 2002

## INDEX TO FINANCIAL STATEMENTS

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## REPORTS OF INDEPENDENT AUDITORS

The Board of Directors and Stockholders  
Ligand Pharmaceuticals Incorporated

We have audited the accompanying consolidated balance sheets of Ligand Pharmaceuticals Incorporated and subsidiaries as of December 31, 2001 and 2000, and the related consolidated statements of operations, stockholders' deficit, and cash flows for the years 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 audits.

We conducted our audits 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 audits provide 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, 2001 and 2000, and the consolidated results of their operations and their cash flows for the years 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 22, 2002

The Board of Directors and Stockholders  
Ligand Pharmaceuticals Incorporated

We have audited the accompanying consolidated statements of operations, stockholders' deficit, and cash flows of Ligand Pharmaceuticals Incorporated for the year 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 audit.

We conducted our audit 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 audit provides a reasonable basis for our opinion.

In our opinion, the financial statements referred to above present fairly, in all material respects, the consolidated results of operations and cash flows of Ligand Pharmaceuticals Incorporated for the year 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)

**ASSETS**

	December 31,	
	2001	2000
Current assets:		
Cash and cash equivalents.....	\$ 20,741	\$ 9,224
Short-term investments.....	16,947	14,439
Funds receivable from Elan.....	—	10,000
Accounts receivable, net.....	9,798	2,824
Inventories.....	3,756	5,651
Other current assets.....	<u>2,332</u>	<u>2,511</u>
Total current assets.....	53,574	44,649
Restricted investments.....	2,370	1,434
Property and equipment, net.....	9,690	10,972
Acquired technology, net.....	37,879	40,924
Other assets.....	<u>13,960</u>	<u>15,443</u>
	<u>\$ 117,473</u>	<u>\$ 113,422</u>

**LIABILITIES AND STOCKHOLDERS' DEFICIT**

Current liabilities:		
Accounts payable.....	\$ 5,385	\$ 3,827
Accrued liabilities.....	12,245	12,675
Current portion of deferred revenue.....	8,729	8,435
Current portion of equipment financing obligations.....	2,867	3,478
Convertible note.....	<u>2,500</u>	<u>—</u>
Total current liabilities.....	31,726	28,415
Long-term portion of deferred revenue.....	4,164	5,727
Long-term portion of equipment financing obligations.....	3,354	4,788
Convertible subordinated debentures.....	47,326	44,651
Accrued acquisition obligation.....	2,700	2,700
Convertible note.....	—	2,500
Zero coupon convertible senior notes.....	<u>86,078</u>	<u>79,766</u>
Total liabilities.....	<u>175,348</u>	<u>168,547</u>
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 authorized; 60,164,840 shares and 56,823,716 shares issued at December 31, 2001 and 2000, respectively.....	60	57
Additional paid-in capital.....	529,374	490,484
Deferred warrant expense.....	(692)	(2,076)
Accumulated other comprehensive income.....	14	46
Accumulated deficit.....	<u>(585,720)</u>	<u>(542,725)</u>
	(56,964)	(54,214)
Treasury stock, at cost; 73,842 shares.....	<u>(911)</u>	<u>(911)</u>
Total stockholders' deficit.....	<u>(57,875)</u>	<u>(55,125)</u>
	<u>\$ 117,473</u>	<u>\$ 113,422</u>

See accompanying notes.

LIGAND PHARMACEUTICALS INCORPORATED

CONSOLIDATED STATEMENTS OF OPERATIONS

(in thousands, except net loss per share data)

	Year ended December 31.		
	2001	2000	1999
Revenues:			
Product sales.....	\$ 45,623	\$ 22,910	\$ 11,307
Collaborative research and development and other revenues .....	30,718	25,200	29,588
Total revenues .....	76,341	48,110	40,895
Operating costs and expenses:			
Cost of products sold .....	13,947	8,591	3,563
Contract manufacturing .....	—	—	6,926
Research and development .....	51,104	51,287	59,442
Selling, general and administrative.....	34,427	34,114	27,257
Write-off of acquired technology.....	—	—	5,000
Total operating costs and expenses.....	99,478	93,992	102,188
Loss from operations .....	(23,137)	(45,882)	(61,293)
Other income (expense):			
Interest income .....	2,106	2,574	2,470
Interest expense .....	(13,601)	(13,119)	(12,979)
Debt conversion expense .....	(5,043)	(2,025)	(2,200)
Other, net.....	(3,320)	(825)	(717)
Total other expense, net .....	(19,858)	(13,395)	(13,426)
Loss before cumulative effect of a change in accounting principle .....	(42,995)	(59,277)	(74,719)
Cumulative effect on prior years (to December 31, 1999) of changing method of revenue recognition .....	—	(13,099)	—
Net loss.....	\$ (42,995)	\$ (72,376)	\$ (74,719)
Basic and diluted per share amounts:			
Loss before cumulative effect of a change in accounting principle .....	\$ (0.72)	\$ (1.06)	\$ (1.58)
Cumulative effect on prior years (to December 31, 1999) of changing method of revenue recognition .....	—	(0.24)	—
Net loss.....	\$ (0.72)	\$ (1.30)	\$ (1.58)
Weighted average number of common shares .....	59,413,270	55,664,921	47,146,312
Pro forma amounts assuming the changed method of recognizing revenue is applied retroactively (Note 2):			
Net loss.....		\$ (59,277)	\$ (73,131)
Basic and diluted net loss per share .....		\$ (1.06)	\$ (1.55)

See accompanying notes.

LIGAND PHARMACEUTICALS INCORPORATED

CONSOLIDATED STATEMENTS OF STOCKHOLDERS' DEFICIT

(in thousands, except share data)

	Common stock		Additional paid-in capital	Deferred warrant expense	Accumulated other comprehensive income (loss)	Treasury stock	Total stockholders' equity (deficit)	Comprehensive income (loss)
	Shares	Amount						
Balance at January 1, 1999	45,690,067	\$ 46	\$ 384,715	\$ —	\$ (482)	\$ (11)	\$ (11,362)	\$ (118,752)
Issuance of common stock	7,328,181	7	59,695	—	—	—	59,702	—
Unrealized losses on available-for-sale securities	—	—	—	—	(125)	—	(125)	\$ (125)
Issuance of warrants	—	—	4,374	(3,990)	—	—	384	—
Amortization of deferred warrant expense	—	—	—	530	—	—	530	—
Net loss	—	—	—	—	(74,719)	—	(74,719)	(74,719)
Balance at December 31, 1999	53,018,248	53	448,784	(3,460)	(607)	(11)	(25,590)	\$ (74,844)
Issuance of common stock	3,805,468	4	41,294	—	—	—	41,298	—
Unrealized gains on available-for-sale securities	—	—	—	—	182	—	182	\$ 182
Reclassification adjustment on sale of investment security	—	—	—	—	550	—	550	550
Foreign currency translation adjustments	—	—	—	—	(79)	—	(79)	(79)
Stock-based compensation	—	—	406	—	—	—	406	—
Amortization of deferred warrant expense	—	—	—	1,384	—	—	1,384	—
Stock received for milestone payment	—	—	—	—	—	(900)	(900)	—
Net loss	—	—	—	—	(72,376)	—	(72,376)	(72,376)
Balance at December 31, 2000	56,823,716	57	490,484	(2,076)	46	(911)	(55,125)	\$ (71,723)
Issuance of common stock	3,341,124	3	38,677	—	—	—	38,680	—
Unrealized gains on available-for-sale securities	—	—	—	—	29	—	29	\$ 29
Foreign currency translation adjustments	—	—	—	—	(61)	—	(61)	(61)
Stock-based compensation	—	—	213	—	—	—	213	—
Amortization of deferred warrant expense	—	—	—	1,384	—	—	1,384	—
Net loss	—	—	—	—	(42,995)	—	(42,995)	(42,995)
Balance at December 31, 2001	60,164,840	60	529,374	(692)	14	(911)	(57,875)	\$ (43,027)

See accompanying notes.

**LIGAND PHARMACEUTICALS INCORPORATED**  
**CONSOLIDATED STATEMENTS OF CASH FLOWS**  
(in thousands)

	Year ended December 31.		
	2001	2000	1999
Operating activities			
Net loss .....	\$ (42,995)	\$ (72,376)	\$ (74,719)
Adjustments to reconcile net loss to net cash used in operating activities:			
Accretion of debt discount and interest .....	8,988	8,212	7,942
Depreciation and amortization of property and equipment .....	3,256	3,928	5,565
Equity in loss of affiliate .....	930	1,868	754
Amortization of acquired technology .....	3,317	3,317	1,479
Debt conversion expense.....	5,043	2,025	2,200
Write-off of acquired technology .....	—	—	5,000
Other .....	1,597	70	725
Changes in operating assets and liabilities net of effects from sale of manufacturing assets in 2000:			
Accounts receivable .....	(6,974)	(1,389)	(1,657)
Inventories.....	1,895	81	434
Other current assets .....	178	(173)	(275)
Accounts payable and accrued liabilities.....	6,128	(1,912)	(6,011)
Deferred revenue .....	(1,269)	11,134	(1,087)
Net cash used in operating activities .....	<u>(19,906)</u>	<u>(45,215)</u>	<u>(59,650)</u>
Investing activities			
Purchases of short-term investments .....	(18,263)	(11,974)	(21,402)
Proceeds from sale of short-term investments .....	15,784	14,908	41,191
Purchases of property and equipment.....	(1,974)	(1,085)	(2,385)
Payments on accrued acquisition obligation .....	—	(200)	(37,100)
Decrease (increase) in other assets .....	281	67	(6,090)
Net proceeds from sale of manufacturing assets .....	—	9,676	—
Proceeds from sale of investment security .....	—	1,119	—
Net cash (used in) provided by investing activities .....	<u>(4,172)</u>	<u>12,511</u>	<u>(25,786)</u>
Financing activities			
Principal payments on equipment financing obligations .....	(3,597)	(4,188)	(3,381)
Proceeds from equipment financing arrangements .....	1,552	1,442	3,027
(increase) decrease in restricted investments .....	(936)	577	543
Net proceeds from issuance of zero coupon convertible senior notes.....	10,000	—	60,000
Net proceeds from issuance of common stock and warrants .....	<u>28,576</u>	<u>14,194</u>	<u>22,349</u>
Net cash provided by financing activities .....	<u>35,595</u>	<u>12,025</u>	<u>82,538</u>
Net increase (decrease) in cash and cash equivalents .....	11,517	(20,679)	(2,898)
Cash and cash equivalents at beginning of year .....	<u>9,224</u>	<u>29,903</u>	<u>32,801</u>
Cash and cash equivalents at end of year .....	<u>\$ 20,741</u>	<u>\$ 9,224</u>	<u>\$ 29,903</u>
Supplemental disclosure of cash flow information			
Interest paid .....	\$ 4,595	\$ 4,824	\$ 4,941
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 .....	5,000	4,000	5,000
Issuance of common stock for debt conversion incentive .....	5,043	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

See accompanying notes.

## LIGAND PHARMACEUTICALS INCORPORATED

### 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, men's and women's health, skin diseases, osteoporosis, and 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, ONTAK<sup>®</sup> for the treatment of patients with persistent or recurrent cutaneous T-cell lymphoma ("CTCL") and Panretin<sup>®</sup> gel for the treatment of Kaposi's sarcoma in AIDS patients. In December 1999, the FDA approved Targretin<sup>®</sup> 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<sup>®</sup> 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. A significant portion of the Company's revenues to date have been derived from 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 and clinical trials, and sales and marketing expenses related to product sales.

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.

##### *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 consolidated financial statements and disclosures made in the accompanying notes. 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 of certificates of deposit held with a financial institution as collateral under equipment financing and third-party service provider arrangements.

### *Concentrations of Credit Risk*

Financial instruments that potentially subject the Company to significant concentrations of credit risk consist primarily of investments and trade accounts receivable.

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, short-term investments or restricted investments.

Trade accounts receivable represent the Company's most significant credit risk. The Company extends credit on an uncollateralized basis primarily to wholesale drug distributors throughout the United States. Prior to entering sales agreements with new customers, the Company performs detailed credit evaluations. These evaluations are updated on a periodic basis when deemed appropriate. To date, the Company has not experienced significant losses on customer accounts.

For 2001, there were five wholesale distributors that individually represented 10% or more of the Company's product sales and in the aggregate represented 72% of product sales. As of December 31, 2001, gross amounts due from these distributors totaled \$10.3 million of which 88% was collected in January 2002.

### *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):

	<u>December 31,</u>	
	<u>2001</u>	<u>2000</u>
Raw materials.....	\$ 143	\$ 498
Work-in-process.....	2,729	4,276
Finished goods .....	884	877
	<u>\$ 3,756</u>	<u>\$ 5,651</u>

### *Property and Equipment*

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

	<u>December 31,</u>	
	<u>2001</u>	<u>2000</u>
Land .....	\$ 2,649	\$ 2,649
Equipment and leasehold improvements .....	36,582	34,612
Less accumulated depreciation and amortization ....	<u>(29,541)</u>	<u>(26,289)</u>
	<u>\$ 9,690</u>	<u>\$ 10,972</u>

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 amortized on a straight-line basis over 15 years, the period estimated to be benefited, and consists of the following (in thousands):

	<u>December 31,</u>	
	<u>2001</u>	<u>2000</u>
Technology acquired in Seragen merger .....	\$ 40,312	\$ 40,312
Milestone payment to Eli Lilly .....	5,000	5,000
Less accumulated amortization .....	<u>(7,433)</u>	<u>(4,388)</u>
	<u>\$ 37,879</u>	<u>\$ 40,924</u>

#### *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. The Company believes the future cash flows to be received from its long-lived assets will exceed the assets' carrying value, and accordingly has not recognized any impairment losses through December 31, 2001.

Effective January 1, 2002, the Company adopted SFAS No. 144, *Accounting for the Impairment or Disposal of Long-Lived Assets*, which supercedes SFAS No. 121. The adoption of SFAS No. 144 did not have an impact on the Company's financial statements or the assessment of recoverability of long-lived assets performed under SFAS No. 121 as of December 31, 2001.

#### *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 instruments. It is not practicable to estimate the fair values of the Company's 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, 2001 and 2000 approximate 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, discounts and chargebacks. The Company is obligated to accept from customers the return of pharmaceuticals that have reached their expiration date. Collaborative research and development and other revenues are recognized as services are

performed consistent with the performance requirements of the contract. Non-refundable contract fees for which no further performance obligation exists and where the Company has no continuing involvement are recognized upon the earlier of when payment is received or collection is assured. Revenue from non-refundable contract fees where Ligand has continuing involvement through research and development collaborations or other contractual obligations is recognized ratably over the development period or the period for which Ligand continues to have a performance obligation. Revenue from performance milestones is recognized upon the achievement of the milestones as specified in the respective agreement provided payment is proportionate to the effort expended. Payments received in advance of performance or delivery are recorded as deferred revenue.

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

	Year ended December 31.		
	2001	2000	1999
Collaborative research and development .....	\$ 25,725	\$ 23,135	\$ 15,954
Distribution agreements .....	4,787	922	3,250
Royalties .....	—	—	5,102
Contract manufacturing .....	—	—	2,610
Other .....	206	1,143	2,672
	<u>\$ 30,718</u>	<u>\$ 25,200</u>	<u>\$ 29,588</u>

Significant customers, that individually accounted for 10% or more of total revenues are as follows:

	Year ended December 31.		
	2001	2000	1999
Eli Lilly and Company.....	18.2%	30.9%	24.7%
Cardinal Health .....	10.6%	9.9%	—
Bergen Brunswig Drug Company.....	10.0%	10.2%	—

#### *Cumulative Effect of Accounting Change*

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 \$4.3 million in 2000, \$2.3 million in 1999, and \$18.8 million in 1997. The Company initially recognized these 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. The effect on 2000 increased revenue and reduced loss before cumulative effect of a 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 SAB No. 101.

#### *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. Research and development expenses were \$51.1 million, \$51.3 million and \$59.4 million in 2001, 2000 and 1999 respectively, of which approximately 70%, 68% and 73% were sponsored by Ligand, and the remainder of which was funded pursuant to collaborative research and development arrangements.

### *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, 2001, 2000 and 1999 were 14.8 million, 14.7 million, and 15.9 million, respectively.

### *Accounting for Stock-Based Compensation*

The Company accounts for stock-based compensation in accordance with Accounting Principles Board Opinion ("APB") No. 25, *Accounting for Stock Issued to Employees*, and FASB Interpretation No. 44, *Accounting for Certain Transactions Involving Stock Compensation*.

### *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. 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.

### *Recent Accounting Pronouncements*

In July 2001, the Financial Accounting Standards Board ("FASB") issued SFAS No. 141, *Business Combinations*, which requires the use of the purchase method of accounting for all business combinations initiated after June 30, 2001 and eliminates the pooling-of-interests method. The adoption of SFAS No. 141 did not have a material impact on the Company's operations or financial position.

In July 2001, the FASB issued SFAS No. 142, *Goodwill and Other Intangible Assets*, which requires that goodwill and other intangible assets with indefinite lives no longer be amortized, but instead tested for impairment at least annually. In addition, the standard includes provisions for the reclassification of certain existing intangibles as goodwill and reassessment of the useful lives of existing recognized intangibles. SFAS No. 142 is effective for fiscal years beginning after December 31, 2001.

In October 2001, the FASB issued SFAS No. 144, *Accounting for the Impairment or Disposal of Long-Lived Assets*, which establishes one accounting model to be used for long-lived assets to be disposed of by sale and broadens the presentation of discontinued operations to include more disposal transactions. SFAS No. 144 supercedes SFAS No. 121, *Accounting for the Impairment of Long-Lived Assets and for Long-Lived Assets to Be Disposed Of*, and the accounting and reporting provisions of APB No. 30. SFAS No. 144 is effective for fiscal years beginning after December 15, 2001.

The adoption of SFAS No. 142 and SFAS No. 144 effective January 1, 2002 did not have a material effect on the Company's operations or financial position.

*Reclassifications*

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, 2001.

3. Investments

The following table summarizes the various investment categories at December 31, 2001 and 2000 (in thousands):

	<u>Cost</u>	<u>Gross unrealized gains (losses)</u>	<u>Estimated fair value</u>
<b>December 31, 2001</b>			
U.S. government securities .....	\$ 2,295	\$ 30	\$ 2,325
Corporate obligations.....	13,039	124	13,163
Certificates of deposit .....	<u>1,459</u>	<u>—</u>	<u>1,459</u>
	16,793	154	16,947
Certificates of deposit - restricted .....	<u>2,370</u>	<u>—</u>	<u>2,370</u>
	<u>\$ 19,163</u>	<u>\$ 154</u>	<u>\$ 19,317</u>
<b>December 31, 2000</b>			
U.S. government securities .....	\$ 2,290	\$ 21	\$ 2,311
Corporate obligations.....	9,955	104	10,059
Certificates of deposit .....	<u>2,069</u>	<u>—</u>	<u>2,069</u>
	14,314	125	14,439
Certificates of deposit - restricted .....	<u>1,434</u>	<u>—</u>	<u>1,434</u>
	<u>\$ 15,748</u>	<u>\$ 125</u>	<u>\$ 15,873</u>

There were no material realized gains or losses on sales of available-for-sale securities for the years ended December 31, 2001 and 1999. Net realized gains for the year ended December 31, 2000 were \$426,000.

The amortized cost and estimated fair value of investments at December 31, 2001 and 2000, 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.

	<u>December 31, 2001</u>		<u>December 31, 2000</u>	
	<u>Cost</u>	<u>Estimated Fair Value</u>	<u>Cost</u>	<u>Estimated Fair Value</u>
Due in one year or less .....	\$ 11,112	\$ 11,117	\$ 9,601	\$ 9,617
Due after one year through three years.....	8,051	8,200	5,522	5,620
Due after three years .....	<u>—</u>	<u>—</u>	<u>625</u>	<u>636</u>
	<u>\$ 19,163</u>	<u>\$ 19,317</u>	<u>\$ 15,748</u>	<u>\$ 15,873</u>

4. Other Balance Sheet Details

Accounts receivable consist of the following (in thousands):

	<u>December 31,</u>	
	<u>2001</u>	<u>2000</u>
Trade accounts receivable .....	\$ 13,239	\$ 3,540
Less allowances.....	<u>(3,441)</u>	<u>(716)</u>
	<u>\$ 9,798</u>	<u>\$ 2,824</u>

Other assets consist of the following (in thousands):

	<u>December 31,</u>	
	<u>2001</u>	<u>2000</u>
Technology license.....	\$ 4,000	\$ 4,000
Prepaid royalty buyout.....	3,400	3,672
Deferred rent.....	3,204	3,373
Investment in X-Ceptor.....	2,448	3,378
Other.....	908	1,020
	<u>\$ 13,960</u>	<u>\$ 15,443</u>

Accrued liabilities consist of the following (in thousands):

	<u>December 31,</u>	
	<u>2001</u>	<u>2000</u>
ONTAK® obligation.....	\$ —	\$ 5,000
Compensation.....	2,786	2,412
Interest.....	1,942	1,985
Royalties.....	2,736	1,122
Payment to licensor (Note 7).....	2,500	—
Other.....	2,281	2,156
	<u>\$ 12,245</u>	<u>\$ 12,675</u>

### 5. Strategic Alliance with Elan Corporation

The Company and Elan Corporation, plc ("Elan") are parties to a number of agreements that provided financing to the Company and a license to Elan's product Avinza™ (formerly named Morphelan™). Significant provisions 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.

In December 2001, Elan agreed to convert Notes of \$50 million plus accrued interest of \$11.8 million into 4,406,010 shares of Ligand common stock. The conversion occurred in February 2002 subsequent to regulatory approval. In connection with the conversion, Ligand provided Elan with a \$5.0 million conversion incentive through the issuance in December 2001 of 274,843 shares of the Company's common stock. After giving effect to the conversion, Elan continues to hold Notes with a face value of \$20 million and accrued interest of \$4.3 million as of December 31, 2001. The Notes and accrued interest are convertible into common stock at \$14.00 per share.

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 all outstanding Notes and exercise of outstanding warrants as of December 31, 2001, Elan would own approximately 19.2% of Ligand's common stock 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 Avinza™ (formerly Morphelan™), a form of morphine for chronic, moderate-to-severe pain. For the rights to Avinza™ 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 Avinza™ phase III clinical trials. In June 2000, as a result of Elan's submission of the Avinza™ NDA, the Company made a \$4 million payment through the issuance of 367,183 shares of the Company's common stock. Upon approval of Avinza™ by the FDA the Company will be required to pay Elan up to \$5 million. The Company is also committed to spend not less than \$7 million (of which more than 50% has been incurred through December 31, 2001) through May 2003 to undertake additional clinical activities related to the commercialization of Avinza™. In the event the Company does not spend this amount, any shortfall 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 \$1.5 million up-front fee at contract inception, and \$4.5 million in milestone payments upon the subsequent submission of a European Union ("EU") application for Marketing Authorization Approval ("MAA") for Targretin gel, the grant of an EU MAA for Targretin capsules and the submission of an EU MAA for ONTAK. The Company may receive additional payments as products are submitted and approved in the territories.

### *6. Seragen*

#### *Merger*

In 1998, the Company completed a merger with Seragen. Under the terms of the merger agreement, Ligand paid merger consideration of \$31.7 million at closing and \$34.1 million in 1999 subsequent to final FDA approval of ONTAK. 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.

In connection with the Seragen merger, the Company acquired substantially all the assets of Marathon Biopharmaceuticals, LLC ("Marathon"), which provided manufacturing services to Seragen, for \$8 million. In 2000, Ligand sold the contract manufacturing assets 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 for the manufacture of ONTAK and the performance of certain development work for Seragen's next-generation ONTAK product. Purchases under the agreement amounted to \$2.1 million and \$2.6 million in 2001 and 2000, respectively.

#### *Arrangement With Lilly*

In conjunction with the Seragen merger, Eli Lilly and Company ("Lilly") assigned to Ligand certain rights and obligations under its agreements with Seragen, including its sales and marketing rights to ONTAK. The agreement provides for milestone payments of \$5 million to Lilly upon FDA approval of ONTAK and upon 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 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 2000, cumulative net sales of ONTAK reached \$20 million. The Company issued 412,504 shares of its common stock to Lilly in 2001 as payment for this \$5 million milestone. Revenues recognized for reimbursement of clinical and other costs for the years ended December 31, 2001, 2000 and 1999 were \$206,000, \$1.1 million and \$1.0 million, respectively.

## 7. Commitments and Contingencies

### *Payment to Licensor*

The Company and one of its licensors have been in discussions concerning the clarification and amendment of an existing license agreement. While the exact payments by and to the licensor are still being discussed, the Company has recorded a fourth quarter 2001 charge of \$2.5 million to non-operating expenses based on an estimate of the amount ultimately expected to be paid to the licensor.

### *Equipment Financing*

The Company has entered into capital lease and equipment note payable agreements that require monthly payments through December 2005 including interest ranging from 4.85% to 10.66%. The carrying value of equipment under these agreements at December 31, 2001 and 2000 was \$13.1 million and \$18.8 million, respectively. At December 31, 2001 and 2000, related accumulated amortization was \$7.5 million and \$8.1 million, respectively. The underlying equipment is used as collateral under the equipment notes payable.

### *Property Leases*

The Company leases its corporate headquarters from a limited liability company (the "LLC") in which Ligand holds a 1% ownership interest. The lease terminates in 2014 and can be extended for a period of five years. The lease agreement provides for increases in annual rent of 4%. Ligand also has an option to either purchase the LLC or the leased premises from the LLC at a purchase price equal to the outstanding debt on the property plus a calculated return on the investment made by the LLC's other shareholder.

In accordance with existing accounting standards, the lease is treated as an operating lease for financial reporting purposes. The FASB, however, is considering modifications to existing accounting principles that under certain conditions could result in consolidation of such entities or treatment of such lease arrangements as capital leases. If Ligand were required to treat such lease arrangement as a financing obligation, the Company's consolidated balance sheet as of December 31, 2001 would reflect additional property and equipment of \$14.1 million and additional debt of \$13.0 million. The impact of such treatment on the Company's 2001, 2000 and 1999 operating results would not be significant.

The Company leases its other office and research facilities under operating lease arrangements with varying terms through July 2015. The agreements provide for increases in annual rents based on changes in the Consumer Price Index or fixed percentage increases ranging from 3% to 7%.

Total rent expense under all office leases for 2001, 2000 and 1999 was \$3.4 million, \$3.4 million, and \$3.2 million, respectively.

At December 31, 2001, annual minimum payments due under the Company's office and equipment lease obligations are as follows (in thousands):

	<b>Obligations under capital leases and equipment notes payable</b>	<b>Operating leases</b>
2002.....	\$ 3,324	\$ 3,029
2003.....	2,179	3,013
2004.....	1,097	3,070
2005.....	397	3,130
2006.....	—	3,170
Thereafter.....	—	26,053
Total minimum lease payments.....	<u>6,997</u>	<u>\$ 41,465</u>
Less amounts representing interest.....	<u>(776)</u>	
Present value of minimum lease payments ....	6,221	
Less current portion.....	<u>(2,867)</u>	
	<u>\$ 3,354</u>	

### *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 \$50 million 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 \$2.5 million convertible note was issued in connection with the Company's collaborative arrangement with SmithKline Beecham Corporation (see Note 9). The note is convertible, at the option of SmithKline Beecham, 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 (4.75% at December 31, 2001).

### *Royalty Agreements*

The Company has royalty obligations under various technology license agreements. During 2001, royalties were accrued ranging from 1% to 18% of net sales. Royalty expense for the years ended December 31, 2001, 2000 and 1999 was \$7.8 million, \$3.5 million, and \$967,000, respectively.

In September 1999, the Company 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 2002 through 2004. 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**

#### *Stock Issuance*

In January 2001, the Company raised net proceeds of \$22.4 million in a private placement of 2 million shares of its common stock.

#### *Warrants*

At December 31, 2001, the Company had outstanding warrants to purchase 1,191,406 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, 2001.

### Stock Plans

The Company's 1992 Stock Option Stock Issuance Plan provides for the issuance of options to purchase up to 8,430,815 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 465,000 shares of the Company's common stock.

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

	<u>Shares</u>	<u>Weighted average exercise price</u>
Balance at January 1, 1999 .....	5,045,019	10.56
Granted .....	894,792	10.67
Exercised .....	(228,991)	8.29
Canceled .....	<u>(405,361)</u>	<u>11.82</u>
Balance at December 31, 1999 .....	5,305,459	10.58
Granted .....	1,156,481	12.90
Exercised .....	(511,872)	9.25
Canceled .....	<u>(285,519)</u>	<u>11.63</u>
Balance at December 31, 2000 .....	5,664,549	11.11
Granted .....	1,010,299	12.14
Exercised .....	(573,531)	10.11
Canceled .....	<u>(702,951)</u>	<u>12.22</u>
Balance at December 31, 2001 .....	<u>5,398,366</u>	<u>\$ 11.27</u>

Following is a further breakdown of the options outstanding as of December 31, 2001:

<u>Range of exercise prices</u>	<u>Options outstanding</u>			<u>Options exercisable</u>	
	<u>Options outstanding</u>	<u>Weighted average remaining life in years</u>	<u>Weighted average exercise price</u>	<u>Number exercisable</u>	<u>Weighted average exercise price</u>
\$ 4.58 - \$ 9.31 .....	1,330,118	4.59	\$ 8.15	1,144,342	\$ 8.09
9.50 - 10.75 .....	1,143,233	6.65	10.25	632,170	10.09
11.06 - 12.13 .....	1,381,210	6.58	11.70	1,028,270	11.73
12.50 - 16.06 .....	1,117,534	6.80	13.54	753,349	13.66
16.38 - 16.40 .....	426,271	8.70	16.39	120,232	16.38
	<u>5,398,366</u>	<u>6.32</u>	<u>\$ 11.27</u>	<u>3,678,363</u>	<u>\$ 10.86</u>

At December 31, 2001, 848,343 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 2001, 2000 and 1999 was \$7.48, \$8.32, and \$6.73 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 2001, 2000 and 1999:

	<u>2001</u>	<u>2000</u>	<u>1999</u>
Risk free interest rates.....	4.30%	4.75%	6.30%
Dividend yields.....	—	—	—
Volatility.....	70%	75%	70%
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 that 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):

	<u>Year ended December 31,</u>		
	<u>2001</u>	<u>2000</u>	<u>1999</u>
Net loss as reported.....	\$ (42,995)	\$ (72,376)	\$ (74,719)
Net loss pro forma.....	(48,566)	(78,714)	(80,549)
Net loss per share as reported.....	(0.72)	(1.30)	(1.58)
Net loss per share pro forma.....	(0.82)	(1.41)	(1.71)

#### *Shareholder Rights Plan*

In 1996, the Company's Board of Directors adopted a preferred shareholder rights plan (the "Shareholder Rights Plan"), 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 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 TAP Pharmaceutical Products Inc., Organon Company, Pfizer, Inc., Eli Lilly and Company, GlaxoSmithKline, Wyeth (formerly American Home Products), and Abbott Laboratories. 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 significant collaborative arrangements that were in the research phase during the years ended December 31, 2001, 2000 and 1999.

#### *TAP*

In June 2001, the Company entered into a research and development collaboration with TAP Pharmaceutical Products Inc. ("TAP") to focus on the discovery and development of selective androgen receptor modulators ("SARMs"). SARMs contribute to the prevention and treatment of certain diseases, including hypogonadism, male and female sexual dysfunction, male and female osteoporosis, frailty, and male hormone replacement therapy. Collaborative research revenues recognized under the agreement for the year ended December 31, 2001 were \$4.3 million.

#### *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. In June 2001, Bristol-Myers Squibb terminated this collaboration. Collaborative research revenues recognized under the agreement for the years ended December 31, 2001 and 2000 were \$3.7 million and \$2 million, respectively.

#### *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 research phase was completed in February 2002. Collaborative research revenues recognized under the agreement for the years ended December 31, 2001 and 2000 were \$3.1 million and \$2.7 million, respectively.

#### *Pfizer*

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 & Company*

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, 2001, 2000 and 1999 were \$13.7 million, \$13.7 million and \$9.1 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, 2001, 2000 and 1999 were \$52,000, \$820,000 and \$2.7 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 that agreement for the years ended December 31, 2000 and 1999 were \$240,000 and \$1 million, respectively.

#### *Wyeth*

In September 1994, the Company entered into a research and development collaboration with Wyeth-Ayerst Laboratories (now Wyeth Pharmaceuticals), the pharmaceutical division of Wyeth (formerly American Home Products), to discover and develop drugs which interact with the estrogen or progesterone receptors. The research phase was completed in September 1998.

#### *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 year ended December 31, 1999 were \$600,000.

#### *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 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. 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 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. In the event Ligand does not exercise its option to acquire the remaining shares of X-Ceptor at June 30, 2002 or extend the option, X-Ceptor can require the Company to purchase up to 2.5 million shares of X-Ceptor preferred stock at a price per share of \$1.00.

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 for 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, 2001, 2000 and 1999 was \$1.4 million, \$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, 2001, 2000 and 1999 were \$804,000, \$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.

## 11. Income Taxes

At December 31, 2001, the Company had consolidated federal and combined California income tax net operating loss carryforwards of approximately \$483 million and \$76 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. The federal tax loss carryforwards will begin to expire in 2002, unless previously utilized. The California tax loss carryforwards began expiring in 1998. At December 31, 2001, the Company also had consolidated federal and combined California research tax credit carryforwards of approximately \$22 million and \$9 million, respectively, which will begin to expire in 2002 unless 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% that 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.

Significant components of the Company's deferred tax assets and liabilities as of December 31, 2001 and 2000 are shown below. A valuation allowance has been recognized to fully offset the net deferred tax assets as of December 31, 2001 and 2000 as realization of such assets is uncertain.

	<u>December 31,</u>	
	<u>2001</u>	<u>2000</u>
	(in thousands)	
Deferred tax liabilities:		
Acquired subordinated debt .....	\$ 1,065	\$ 2,345
Purchased intangible assets .....	<u>11,656</u>	<u>11,375</u>
Total deferred tax liabilities .....	<u>12,721</u>	<u>13,720</u>
Deferred tax assets:		
Net operating loss carryforwards .....	168,761	166,156
Research and development credits .....	28,174	24,729
Capitalized research and development .....	8,893	11,859
Accrued expenses .....	3,565	3,232
Fixed assets and intangibles .....	8,533	8,226
Deferred revenue .....	5,136	5,743
Other, net .....	<u>870</u>	<u>2,267</u>
Total deferred tax assets .....	<u>223,932</u>	<u>222,212</u>
Net deferred tax assets .....	211,211	208,492
Valuation allowance for deferred tax assets ..	<u>(211,211)</u>	<u>(208,492)</u>
	<u>\$ —</u>	<u>\$ —</u>

As of December 31, 2001, approximately \$4.2 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

In February 2002, pursuant to an agreement reached in December 2001, the Company converted \$50 million in issue price of zero coupon convertible senior notes and \$11.8 million of accrued interest owed to Elan into 4,406,010 shares of common stock (see Note 5).

### 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, 2001 and 2000 (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.

	Quarter ended			
	March 31	June 30	September 30	December 31
<b>2001</b>				
Total revenues .....	\$ 17,035	\$ 17,489	\$ 19,174	\$ 22,643
Cost of products sold .....	2,839	3,077	3,645	4,386
Research and development costs .....	12,405	13,191	12,882	12,626
Total operating costs and expenses .....	25,401	25,154	23,733	25,190
Net loss .....	(11,581)	(10,615)	(7,744)	(13,055)
Basic and diluted net loss per share .....	\$ (0.20)	\$ (0.18)	\$ (0.13)	\$ (0.22)
Weighted average number of common shares .....	58,854	59,380	59,581	59,747
<b>2000 (Restated for SAB No. 101)</b>				
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 .....	<u>\$ (28,907)</u>	<u>\$ (17,360)</u>	<u>\$ (13,405)</u>	
<b>Basic and diluted per share amounts:</b>				
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 .....	<u>\$ (0.54)</u>	<u>\$ (0.31)</u>	<u>\$ (0.24)</u>	

## Corporate Information

### BOARD OF DIRECTORS

**Henry F. Blissenbach, Pharm.D.**  
Chairman, President and Chief Executive Officer,  
Chronimed, Inc.

**Alexander D. Cross, Ph.D.**  
Chairman and Chief Executive Officer,  
Cytopharm, Inc.

**John Groom**  
President and Chief Operating Officer, Retired,  
Elan Corporation, plc

**Irving S. Johnson, Ph.D.**  
Biomedical Research Consultant  
Vice President of Research, Retired,  
Eli Lilly and Company

**Carl C. Peck, M.D.**  
Professor of Pharmacology and Medicine,  
Director, Center for Drug Development Science,  
Georgetown University Medical Center

**David E. Robinson**  
Chairman, President and Chief Executive Officer,  
Ligand Pharmaceuticals Incorporated

**Michael A. Rocca**  
Financial Consultant

### CORPORATE HEADQUARTERS

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Chairman, President, Chief Executive Officer

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

**Andrés Negro-Vilar, M.D., Ph.D.**  
Senior Vice President, Research and Development  
and Chief Scientific Officer

**William A. Pettit**  
Senior Vice President, Human Resources and  
Administration

**Thomas H. Silberg**  
Senior Vice President, Commercial Operations

**Giambattista Aliprandi**  
Vice President, Senior Corporate Controller

**Warner R. Broaddus**  
Vice President, General Counsel and Secretary

**Philip A. Duffy**  
Vice President, Technical Operations

**Eric S. Groves, M.D., Ph.D.**  
Vice President, Project Management

**Howard T. Holden, Ph.D.**  
Vice President, Regulatory Affairs and Compliance

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### SEC FORM 10-K

A copy of the Company's annual report on Form 10-K is available without charge via Ligand's web site at [www.ligand.com](http://www.ligand.com) or upon written request to:  
Investor Relations

Ligand Pharmaceuticals Incorporated  
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San Diego, California 92121

### PRICE RANGE OF COMMON STOCK\*

2000	1st Qtr	2nd Qtr	3rd Qtr	4th Qtr
High	26.500	18.688	14.000	16.313
Low	12.500	9.688	10.000	10.500

2001	1st Qtr	2nd Qtr	3rd Qtr	4th Qtr
High	14.750	14.040	11.750	19.100
Low	7.813	8.063	7.300	8.730

\*Prices are intraday highs/lows.

### MARKET INFORMATION

The Company's Common Stock trades on the NASDAQ National Market under the symbol LGND. No cash dividends have been paid on the Common Stock and the Company does not anticipate paying any cash dividends in the foreseeable future. As of February 28, 2002, there were approximately 2,164 shareholders of record of the Company's Common Stock.

### PRODUCT INFORMATION

Full prescribing information for Ligand products may be obtained from Ligand Professional Services by calling toll free at (800) 964-5836 or by visiting Ligand's web site at [www.ligand.com](http://www.ligand.com). For more information about placing orders for Ligand products, contact Ligand Customer Service toll free at (877) 4 Ligand (877-454-4263).

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