LIGAND PHARMACEUTICALS INC
Form S-3/A
October 08, 2003

AS FILED WITH THE SECURITIES AND EXCHANGE COMMISSION ON OCTOBER 8, 2003
REGISTRATION STATEMENT NO. 333-109172

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SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

AMENDMENT NO. 1
TO
FORM S-3
REGISTRATION STATEMENT
UNDER THE SECURITIES ACT OF 1933

LIGAND PHARMACEUTICALS INCORPORATED

(Exact Name of Registrant as Specified in its Charter)

DELAWARE
(State or Other Jurisdiction of Incorporation or Organization)

77-0160744
(I.R.S. Employer Identification Number)

10275 Science Center Drive, San Diego, California 92121-1117
(858) 550-7500
(Address, Including Zip Code, and Telephone Number, Including Area Code, of Registrant's Principal Executive Offices)

David E. Robinson
President and Chief Executive Officer
LIGAND PHARMACEUTICALS INCORPORATED

10275 Science Center Drive, San Diego, California 92121-1117
(858) 550-7500
(Name, Address, Including Zip Code, and Telephone Number, Including Area Code, of Agent for Service)

Copies to:
Faye H. Russell, Esq.
CLIFFORD CHANCE US LLP
3811 Valley Centre Drive, Suite 200
San Diego, California 92130
(858) 720-3500

Approximate date of commencement of proposed sale to the public: From time to time after the effective date of this registration statement.

If the only securities being registered on this form are being offered pursuant to dividend or interest reinvestment plans, please check the following box: [ ]

If any of the securities being registered on this form are to be offered on a delayed or continuous basis pursuant to Rule 415 under the Securities Act of 1933, other than securities offered only in connection with dividend or interest reinvestment plans, check the following box: [x]

If this form is filed to register additional securities for an offering pursuant to Rule 462(b) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering: [ ]

If this form is a post-effective amendment filed pursuant to Rule 462(c) under the Securities Act, check the following box and list the Securities Act registration statement number of the earlier effective registration statement for the same offering: [ ]

If delivery of the prospectus is expected to be made pursuant to Rule 434, please check the following box: [ ]

THE REGISTRANT HEREBY AMENDS THIS REGISTRATION STATEMENT ON SUCH DATE OR DATES AS MAY BE NECESSARY TO DELAY ITS EFFECTIVE DATE UNTIL THE REGISTRANT SHALL FILE A FURTHER AMENDMENT WHICH SPECIFICALLY STATES THAT THIS REGISTRATION STATEMENT SHALL THEREAFTER BECOME EFFECTIVE IN ACCORDANCE WITH SECTION 8(A) OF THE SECURITIES ACT OF 1933, AS AMENDED, OR UNTIL THE REGISTRATION STATEMENT SHALL BECOME EFFECTIVE ON SUCH DATE AS THE SEC, ACTING PURSUANT TO SAID SECTION 8(A), MAY DETERMINE.

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THE INFORMATION IN THIS PROSPECTUS IS NOT COMPLETE AND MAY BE CHANGED. WE MAY NOT SELL THESE SECURITIES UNTIL THE REGISTRATION STATEMENT FILED WITH THE SECURITIES AND EXCHANGE COMMISSION IS EFFECTIVE. THE PRELIMINARY PROSPECTUS IS NOT AN OFFER TO SELL THESE SECURITIES AND IS NOT SOLICITING AN OFFER TO BUY THESE SECURITIES IN ANY STATE WHERE THE OFFER OR SALE IS NOT PERMITTED.

SUBJECT TO COMPLETION, DATED OCTOBER 8, 2003

PRELIMINARY PROSPECTUS

LIGAND PHARMACEUTICALS INCORPORATED

3,483,593 SHARES OF COMMON STOCK

This prospectus relates to the public offering, which is not being underwritten, of 3,483,593 shares of our common stock, which is held by some of our current stockholders. These stockholders acquired the shares directly from us in a private placement completed on September 11, 2003.

Our common stock is traded on The Nasdaq Stock Market under the symbol "LGND." On October 7, 2003, the average of the high and low sales prices for our common stock was $12.62.

THE COMMON STOCK OFFERED INVOLVES A HIGH DEGREE OF RISK. SEE "RISK FACTORS" COMMENCING ON PAGE 7 FOR A DISCUSSION OF SOME IMPORTANT RISKS YOU SHOULD CONSIDER BEFORE BUYING ANY OF OUR COMMON STOCK.

NEITHER THE SECURITIES AND EXCHANGE COMMISSION NOR ANY STATE SECURITIES COMMISSION HAS APPROVED OR DISAPPROVED THESE SECURITIES, OR PASSED UPON THE ACCURACY OR ADEQUACY OF THIS PROSPECTUS. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

The date of this prospectus is _____, ____

PROSPECTUS SUMMARY

THE FOLLOWING IS A SUMMARY HIGHLIGHTING SELECTED INFORMATION APPEARING ELSEWHERE IN THIS PROSPECTUS AND MAY NOT CONTAIN ALL OF THE INFORMATION THAT IS IMPORTANT TO YOU. THIS PROSPECTUS INCLUDES INFORMATION ABOUT THE SECURITIES WE ARE OFFERING, AS WELL AS INFORMATION REGARDING OUR BUSINESS AND DETAILED FINANCIAL DATA. WE ENCOURAGE YOU TO READ THIS PROSPECTUS IN ITS ENTIRETY, INCLUDING THE DOCUMENTS INCORPORATED BY REFERENCE.

OUR COMPANY

We are a biopharmaceutical company involved in the discovery, development and commercialization of new drugs that address critical unmet medical needs in the areas of cancer, pain, men's and women's health or hormone related health issues, skin diseases, osteoporosis and metabolic, cardiovascular and inflammatory diseases. Our marketed products and products in development are designed to be safer, more effective, more convenient (taken orally or topically administered) and more cost efficient than existing therapies.

We currently market five products and are developing, either exclusively or with our collaboration partners, 24 selected additional products in development for multiple therapeutic indications, as summarized in the table below. Our five marketed products are Avinza(R), ONTAK(R), Targretin(R) capsules, Targretin(R) gel and Panretin(R) gel. Our efforts are directed toward building a profitable biopharmaceutical company that generates income from biopharmaceutical products that we develop and market, and from research, milestone and royalty revenues from our collaborations with large pharmaceutical partners.

PRODUCT SUMMARY BY THERAPEUTIC AREA (LIGAND AND COLLABORATIVE PARTNERS)

MARKETED PRODUCTS	CLINICAL PROGRAMS	PRE-CLINICAL

(5 PRODUCTS)	(4 PHASE III/7 PHASE II/6 PHASE I PRODUCTS IN DEVELOPMENT)	(7 PRODUCTS
Cancer	Cancer	Aging and fr
Moderate/Severe Pain	Hormone replacement therapy	Autoimmune d
	Osteoporosis	Dermatology
	Dermatology	Diabetes
	Diabetes	Hormone repl
	Inflammation	Inflammatory
	Thrombocytopenia	Sexual dysfu
	Dyslipidemia	
	Contraception	

OUR MARKETED PRODUCTS

PRODUCT	US APPROVED INDICATION	EUROPEAN STA
Avinza.....	Once-daily treatment of chronic moderate-to-severe pain	Not applicab
ONTAK.....	Cutaneous T-cell lymphoma	MAA withdraw
Targretin capsules.....	Cutaneous T-cell lymphoma	MA issued
Targretin gel.....	Cutaneous T-cell lymphoma	MAA withdraw
Panretin gel.....	Kaposi's sarcoma	MA issued

AVINZA. Avinza is marketed for the once-daily treatment of chronic moderate-to-severe pain to patients who require continuous, around-the-clock opioid therapy. We launched US sales and marketing of Avinza with distribution in June 2002 and national promotion in July 2002 following receipt of FDA approval in March 2002. We licensed exclusive rights to Avinza in the United States and Canada from Elan Corporation plc in 1998. Avinza is an oral once-daily morphine product and has a more rapid onset and more stable pharmocokinetic profile with less peak-to-trough fluctuation than other competing sustained release products. The sustained-release opioid market was estimated at $2.8 billion in the United States in 2002.

ONTAK. ONTAK is marketed for the treatment of patients with persistent or recurrent cutaneous T-cell lymphoma, or CTCL. ONTAK was approved by the FDA and launched in the United States in February 1999 as our first product for the treatment of patients with CTCL. ONTAK was the first treatment to be approved for CTCL in nearly 10 years. ONTAK is currently in three Phase II clinical trials for the treatment of patients with B-cell Non-Hodgkin's lymphoma. Clinical trials using ONTAK for the treatment of patients with psoriasis, rheumatoid arthritis and chronic lymphocytic leukemia, or CLL, have also been conducted, and further trials are being considered. There are physician-sponsored Phase II trials ongoing in CLL, peripheral T-cell lymphoma and graft versus host disease. We believe that these indications provide significantly larger market opportunities than CTCL. A European MAA for CTCL was filed in December 2001. In April 2003, we withdrew our MAA in Europe for our first generation product. It was our assessment that the cost of the additional clinical and technical information requested by the European Agency for the Evaluation of Medicinal Products for the first generation product would be

better spent on acceleration of the second generation ONTAK development. We expect to resubmit the MAA in Europe with the second generation product in 2004 or early 2005.

TARGRETIN CAPSULES. Targretin capsules are marketed for the treatment of patients with CTCL. We launched US sales and marketing of Targretin capsules in January 2000 following receipt of FDA approval in December 1999. Targretin capsules offer the convenience of a daily oral dose administered by the patient at home. We are developing Targretin capsules for a variety of larger market opportunities, including non-small cell lung cancer, or NSCLC, and moderate-to-severe plaque psoriasis. In March 2001, the European Commission granted marketing authorization for Targretin capsules in Europe for the treatment of patients with CTCL, and our network of distributors began marketing the drug in Europe in the fourth quarter of 2001.

TARGRETIN GEL. Targretin gel is marketed for the treatment of patients with CTCL. We launched US sales and marketing of Targretin gel in September 2000 following receipt of FDA approval in June 2000. Targretin gel offers patients with refractory, early-stage CTCL a novel, non-invasive, self-administered treatment topically applied only to the affected areas of the skin. Preliminary data presented at the American Academy of Dermatology meeting in March 2001 showed that Targretin gel produced an overall response rate of 75% in patients with untreated, early-stage CTCL. Targretin gel is currently in clinical development for hand dermatitis, and we released interim Phase I/II data from a 55-patient trial in September 2002.

PANRETIN GEL. Panretin gel is marketed for the treatment of patients with AIDS-related Kaposi's sarcoma, or KS. Panretin gel was approved by the FDA and launched in February 1999 as the first FDA-approved patient-applied topical treatment for AIDS-related Kaposi's sarcoma. Panretin 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 United States and Europe. Panretin 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.

SALES AND MARKETING

As of June 30, 2003, our marketing and selling organization consisted of approximately 120 people. Since 1998, we had assembled a 25-person sales force for the United States focused on specialty cancer sales and selling ONTAK, Targretin capsules, Targretin gel and Panretin gel. We have also formed a separate sales force of approximately 70 representatives to market only Avinza by targeting pain specialists and general pain centers not currently served by our specialty cancer representatives. Since a relatively small number of physicians are responsible for writing a majority of prescriptions in our target markets, we believe that the size of our sales force is appropriate to reach our target physicians.

In addition, in February 2003 we entered into an agreement with Organon Pharmaceuticals USA Inc., a business unit of Akzo Nobel N.V., under which we co-promote Avinza with Organon's primary care, hospital (anesthesiology) and specialty (pain centers) sales forces, which together consist of more than 700 sales representatives.

COLLABORATIVE RESEARCH AND DEVELOPMENT PROGRAMS

We are currently involved in the research phase of research and development collaborations with Eli Lilly and TAP Pharmaceuticals. Collaborations in the development phase are being pursued by Abbott Laboratories, Allergan, GlaxoSmithKline, Organon (Akzo-Nobel), Pfizer and Wyeth (formerly American Home Products). Currently, our corporate partners have 11 Ligand products in human development, three products moving toward regulatory filings for human clinical trials and numerous compounds in research and pre-clinical stages. These products are being studied for the treatment of health problems in large markets such as osteoporosis, diabetes, contraception and cardiovascular disease. Three of these partner products are being tested in three separate pivotal Phase III clinical trial programs: lasofoxifene, which is being developed by Pfizer for osteoporosis and breast cancer prevention; and bazedoxifene (formerly TSE-424), which is being developed by Wyeth both as monotherapy for osteoporosis and in combination with Wyeth's Premarin as hormone replacement therapy, or HRT.

PROPRIETARY TECHNOLOGY PLATFORM

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, a technology for regulating how genes control cellular activity. Our proprietary technologies involve two natural mechanisms that regulate gene activity: hormone-activated intracellular receptors, or IRs, a type of sensor or switch inside cells that turns genes on and off and alters the production of proteins in response to hormones, and Signal Transducers and Activators of Transcription, or STATs, another type of protein production switch. Targretin capsules, Targretin gel, Panretin gel and all but one of our corporate partner products currently on human development track were discovered using our IR technology.

PRODUCT PIPELINE SUMMARY

We are developing several proprietary products for which we have worldwide rights for a variety of cancers, skin diseases and other indications, as summarized in the table below. 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. In addition to our proprietary product pipeline, our collaborative partners have multiple products in human development, as well as numerous compounds in research and pre-clinical stages.

PRODUCT PIPELINE SUMMARY (CONTINUED)

PRODUCT	CLINICAL INDICATION	DEVELOPMENT STATUS	COMME
OUR MARKETED PRODUCTS AND DEVELOPMENT PROGRAMS			
Avinza.....	Chronic pain (moderate-to-severe)	Marketed	Unite
ONTAK.....	Cutaneous T-cell lymphoma	Marketed	World
	Peripheral T-cell lymphoma	Phase II	
	Chronic lymphocytic leukemia	Phase II	

	B-cell Non-Hodgkin's lymphoma	Phase II	
	Psoriasis (severe)	Phase II	
Targretin capsules.....	Cutaneous T-cell lymphoma	Marketed	World
	Non-small cell lung cancer (combination and monotherapy)	Phase III	
	Psoriasis (moderate to severe)	Phase II	
	Advanced breast cancer	Phase II	
	Renal cell cancer	Phase II	
Targretin gel.....	Cutaneous T-cell lymphoma	Marketed	World
	Hand dermatitis	Phase II	
	Psoriasis	Phase II	
Panretin gel.....	Kaposi's sarcoma	Marketed	World
Panretin capsules.....	Kaposi's sarcoma, bronchial metaplasia	Phase II	World
LGD 1550.....	Advanced cancers	Phase II	World
	Acne, psoriasis	Pre-clinical	
LGD 1331.....	Acne, prostate cancer, androgenetic alopecia, hirsutism	Pre-clinical	World
Glucocorticoid agonist.....	Inflammation, cancer	Pre-clinical	World
Mineralocorticoid receptor modulators.....	Congestive heart failure, hypertension	Research	World
OUR COLLABORATIVE RESEARCH AND DEVELOPMENT PROGRAMS			
Lasofoxifene.....	Osteoporosis and breast cancer prevention	Phase III	Pfize
Bazedoxifene (TSE424).....	Osteoporosis	Phase III	Wyeth
Bazedoxifene + Premarin....	Hormone replacement therapy	Phase III	Wyeth
ERA 923.....	Breast cancer	Phase II	Wyeth
NSP 989.....	Contraception, hormone replacement therapy	Phase I	Wyeth
NSP 989 combo.....	Contraception	Phase I	Wyeth
GW 516 (501516).....	Dyslipidemia	Phase I	Glaxo
LY 929.....	Type II diabetes, dyslipidemia	Phase I	Lilly
LY 818.....	Type II diabetes	Phase II	Lilly
SB-497115.....	Thrombocytopenia	Phase I	Glaxo
LY 674.....	Dyslipidemia, atherosclerosis	Phase I	Lilly
LGD 2226/back-ups.....	Sexual dysfunction--hypogonadism	IND Track	TAP
LY YYY.....	Type II diabetes, dyslipidemia	IND Track	Lilly
LY WWW.....	Dyslipidemia	IND Track	Lilly

Our principal executive offices are located at 10275 Science Center Drive, San Diego, California 92121, and our telephone number is (858) 550-7500. Our website is located at WWW.LIGAND.COM. The information on our website is not a part of this prospectus.

Our trademarks, trade names and service marks referenced in this document include Ligand(R), Avinza(R), ONTAK(R), Panretin(R) and Targretin(R). Each other trademark, trade name or service mark appearing in this document belongs to its holder.

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

RECENT DEVELOPMENTS

UPDATES ON PATIENT ENROLLMENT IN PIVOTAL STUDIES OF TARGRETIN CAPSULES IN LUNG

CANCER

On August 14, 2003, we announced that we had exceeded our 600-patient enrollment goal in the first of two pivotal Phase III studies of Targretin capsules in front-line combination therapy to treat advanced NSCLC, and on September 18, 2003, we announced that we had exceeded our 600-patient enrollment goal in the second of these studies.

These randomized trials are known as SPIRIT I and II (Studies Providing Investigational Research in Targretin). SPIRIT I is being conducted at 94 sites worldwide and is designed to evaluate whether adding Targretin to front-line cisplatin/vinorelbine chemotherapy extends the lives of patients with advanced NSCLC. SPIRIT II is being conducted at 165 sites worldwide, more than 80% of which are in North America, and is designed to evaluate whether adding Targretin to front-line carboplatin/paclitaxel chemotherapy extends the lives of patients with advanced NSCLC.

RISK FACTORS

IN ADDITION TO THE OTHER INFORMATION IN THIS PROSPECTUS, YOU SHOULD CAREFULLY CONSIDER THE FOLLOWING RISKS AND UNCERTAINTIES BEFORE PURCHASING OUR SECURITIES. EACH OF THESE RISKS AND UNCERTAINTIES COULD ADVERSELY AFFECT OUR BUSINESS, OPERATING RESULTS AND FINANCIAL CONDITION, AS WELL AS THE VALUE OF AN INVESTMENT IN OUR SECURITIES.

RISKS RELATED TO US AND OUR BUSINESS

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 June 30, 2003, our accumulated deficit was approximately $651 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;

>> regulatory or governmental authorities may apply restrictions to our products, which could adversely affect their commercial success; or

>> the proprietary rights of other parties may prevent us or our partners from marketing the products.

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 US sales force of about 95 people. We also rely on third-party distributors to distribute our products. The distributors are responsible for providing many marketing support services, including customer service, order entry, shipping, 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. Our reliance on these third parties means our results may suffer if any of them are unsuccessful or fail to perform as expected. 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. With respect to our co-promotion or licensing arrangements, for example our co-promotion agreement for Avinza, any revenues we receive will depend substantially on the marketing and sales 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 five products approved for marketing and a handful of other products/indications that have made significant progress through development. 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 prices for our securities. Setbacks could include problems with shipping, distribution, manufacturing, product safety, marketing, government licenses and approvals, intellectual property rights and physician or patient acceptance of the product.

SALES OF OUR SPECIALTY PHARMACEUTICAL PRODUCTS MAY SIGNIFICANTLY FLUCTUATE EACH PERIOD BASED ON THE NATURE OF OUR PRODUCTS, OUR PROMOTIONAL ACTIVITIES AND WHOLESALER PURCHASING AND STOCKING PATTERNS.

Excluding Avinza, our products are small-volume specialty pharmaceutical products that address the needs of cancer patients in relatively small niche markets with substantial geographical fluctuations in demand. To ensure patient access to our drugs, we maintain broad distribution capabilities with inventories held at approximately 150 locations throughout the United States. Furthermore, the purchasing and stocking patterns of our wholesaler customers are influenced by a number of factors that vary with each product, including but

not limited to overall level of demand, periodic promotions, required minimum shipping quantities and wholesaler competitive initiatives. As a result, the level of product in the distribution channel may average from two to six months' worth of projected inventory usage. If any or all of our major distributors decide to substantially reduce the inventory they carry in a given period, our sales for that period could be substantially lower than historical levels.

OUR DRUG DEVELOPMENT PROGRAMS WILL REQUIRE SUBSTANTIAL ADDITIONAL FUTURE FUNDING WHICH COULD HURT OUR OPERATIONAL AND FINANCIAL CONDITION.

Our drug development programs require substantial additional capital to successfully complete them, arising from costs to:

>> conduct research, preclinical testing and human studies;

>> establish pilot scale and commercial scale manufacturing processes and facilities; and

>> establish and develop quality control, regulatory, marketing, sales and administrative capabilities to support these programs.

Our future operating and capital needs will depend on many factors, including:

>> the pace of scientific progress in our research and development programs and the magnitude of these programs;

>> the scope and results of preclinical testing and human studies;

>> the time and costs involved in obtaining regulatory approvals;

>> the time and costs involved in preparing, filing, prosecuting, maintaining and enforcing patent claims, competing technological and market developments;

>> our ability to establish additional collaborations;

>> changes in our existing collaborations;

>> the cost of manufacturing scale-up; and

>> the effectiveness of our commercialization activities.

We currently estimate our research and development expenditures over the next 3 years to range between $200 million and $275 million. However, we base our outlook regarding the need for funds on many uncertain variables. Such uncertainties include regulatory approvals, the timing of events outside our direct control such as product launches by partners and the success of such product launches, negotiations with potential strategic partners and other factors. Any of these uncertain events can significantly change our cash requirements as they determine such one-time events as the receipt of major milestones and other payments.

While we expect to fund our research and development activities from cash generated from internal operations to the extent possible, if we are unable to do so we may need to complete additional equity or debt financings or seek other external means of financing. If additional funds are required to support our operations and we are unable to obtain them on terms favorable to us, we may be required to cease or reduce further development or commercialization of our

products, to sell some or all of our technology or assets or to merge with another entity.

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.

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 may not 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, in February and March 2002 we issued to Elan an aggregate of 6.3 million shares upon the conversion of zero coupon convertible senior notes held by Elan, and in April 2002 and September 2003 we issued an aggregate of 7.7 million shares of our common stock in private placements. These transactions have resulted in the issuance of significant numbers of new shares. In addition, in November 2002 we issued in a private placement $155.3 million in aggregate principal amount of our 6% convertible subordinated notes due 2007, which could be converted into 25,149,025 shares of our common stock.

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

OUR PRODUCTS FACE SIGNIFICANT REGULATORY HURDLES PRIOR TO MARKETING WHICH COULD DELAY OR PREVENT SALES. EVEN AFTER APPROVAL, GOVERNMENT REGULATION OF OUR BUSINESS IS EXTENSIVE.

Before we obtain the approvals necessary to sell any of our potential products, we must show through preclinical studies and human testing that each product is safe and effective. We and our partners have a number of products moving toward or currently in clinical trials, the most significant of which are our Phase III trials for Targretin capsules in NSCLC and three Phase III trials by our partners involving bazedoxifene and lasofoxifene. 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. For example, each of our Phase III Targretin clinical trials will involve approximately 600 patients and may require significant time and investment to complete, including enrollment of patients and the gathering and analyzing of data. 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.

In addition, the manufacturing and marketing of approved products is subject to extensive government regulation, including by the FDA, Drug Enforcement Agency (or DEA) and state and other territorial authorities. The FDA administers processes to assure that marketed products are safe, effective, consistently of uniform, high quality and marketed only for approved indications. For example, while our products are prescribed legally by some physicians for unapproved uses, we may not market our products for such uses. Failure to comply with applicable regulatory requirements can result in sanctions up to the suspension of regulatory approval as well as civil and criminal sanctions.

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. The principal products competing with our products targeted at the cutaneous t-cell lymphoma market are Supergen/Abbott's Nipent and interferon, which is marketed by a number of companies, including Schering-Plough's Intron A. Products that compete with Avinza include Purdue Pharma L.P.'s OxyContin and MS Contin, Janssen Pharmaceutica Products, L.P.'s Duragesic, Elan's Oramorph SR, Faulding's Kadian and generic sustained release morphine sulfate. 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. For example, we have current and recurring discussions with insurers regarding reimbursement rates for our drugs, including Avinza. We may not be able to negotiate favorable reimbursement rates for our products or may have to pay significant discounts to obtain favorable rates. Only one of our products, ONTAK, is currently eligible to be reimbursed by Medicare. Recently-enacted changes by Medicare to the hospital outpatient payment reimbursement system may adversely affect reimbursement rates for ONTAK.

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, including price caps and controls for pharmaceuticals. These proposals could reduce and/or cap the prices for our products or reduce government reimbursement rates for products such as ONTAK. 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, INCLUDING RESEARCH FUNDING AND MILESTONE PAYMENTS.

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 and related revenue, if any.

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, US 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. While we routinely receive communications or have conversations with the owners of other patents, none of these third parties have directly threatened an action or claim against us. 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 licenses on acceptable terms, or at all. Any failure to obtain such licenses could delay or prevent us from pursuing the development or commercialization of our potential products.

We have had and will continue to have discussions with our current and potential collaborators regarding the scope and validity of our patents 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 US patent and has made patent filings in foreign countries that relate to our Panretin capsules and gel products. We filed a patent application with an earlier filing date than Hoffmann-La Roche's patent, which we believe is broader than, but overlaps in part with, Hoffmann-La Roche's patent. We 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 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 drug. We are currently investigating the scope and merits of this opposition. If the opposition is successful, we could lose our ONTAK patent protection in Europe which could substantially reduce our future ONTAK 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. Elan manufactures Avinza for us, Cambrex manufactures ONTAK for us and Cardinal Health and Raylo manufacture Targretin capsules for us.

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. While we believe that we would be able to develop our own facilities or contract with others for manufacturing services with respect to all of our products, if we are unable to do so 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 believe that we carry reasonably adequate insurance for product liability claims.

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. Our annual cost of compliance with these regulations is approximately $600,000. 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. We believe that we carry reasonably adequate insurance for toxic tort claims.

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. For example, in 2002, the intraday sale price of our common stock on The Nasdaq National Market was as high as $20.50 and as low as $4.64. Future announcements concerning us or our competitors as well as other companies in our industry and other public companies 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 our competitors;

>> our failure to receive regulatory approvals for products under development;

>> developments concerning proprietary rights;

>> litigation or public concern about the safety of our products; or

>> intent to sell or actual sale of our stock held by our corporate partners.

AS A NEW INVESTOR, YOU MAY EXPERIENCE IMMEDIATE AND SUBSTANTIAL DILUTION.

The offering price of our common stock may be substantially higher than the net tangible book value per share of our common stock. If you purchase common stock in this offering from a selling stockholder for the per-share purchase price of $12.62, which is the average of the high and low sales prices per share of the common stock on October 7, 2003 as reported on The Nasdaq Stock Market, you will incur immediate dilution in net tangible book value of approximately $14.29 per share, based on our net tangible book value of $(1.67) per share at June 30, 2003.

FUTURE SALES OF OUR SECURITIES MAY DEPRESS THE PRICE OF OUR SECURITIES.

Sales of substantial amounts of our securities in the public market could seriously harm prevailing market prices for our securities. 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 SECURITIES OTHER THAN THROUGH THE SALE OF YOUR SECURITIES.

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 on any of our securities in the foreseeable future.

OUR SHAREHOLDER RIGHTS PLAN AND CHARTER DOCUMENTS MAY HINDER OR PREVENT CHANGE OF CONTROL TRANSACTIONS.

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

CAUTIONARY NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus may contain forward-looking statements that involve substantial risks and uncertainties regarding future events or our future performance within the meaning of Section 27A of the Securities Act of 1933, as

amended, and Section 21E of the Securities Exchange Act of 1934, as amended. You can identify these statements by forward-looking words such as "may," "will," "expect," "intent," "anticipate," "believe," "estimate" and "continue" or similar words. You should read statements that contain these words carefully because they discuss our future expectations, contain projections of our future results of operations or of our financial condition or state other "forward-looking" information. We believe that it is important to communicate our future expectations to our investors. However, there may be events in the future that we are not able to accurately predict or control. The factors listed in the section captioned "Risk Factors," as well as any cautionary language included in this prospectus or incorporated by reference, provide examples of risks, uncertainties and events that may cause our actual results to differ materially from the expectations we describe in our forward-looking statements. Before you invest in our common stock, you should be aware that the occurrence of the events described in the "Risk Factors" section and elsewhere in this prospectus could have a material adverse effect on our business, operating results and financial condition. All subsequent written and oral forward-looking statements attributable to us or persons acting on our behalf are expressly qualified in their entirety by these statements.

WHERE YOU CAN FIND MORE INFORMATION

We file annual, quarterly and special reports, proxy statements and other information with the SEC. You may read and copy any document we file at the SEC's public reference rooms at 450 Fifth Street, N.W., Washington, D.C. 20549. Please call the SEC at 1-800-SEC-0330 for further information on the public reference rooms. Our SEC filings are also available to the public on the SEC's website at http://www.sec.gov.

INFORMATION INCORPORATED BY REFERENCE

The SEC allows us to incorporate by reference the information we file with them, which means that we can disclose important information to you by referring you to those documents. The information incorporated by reference is considered to be part of this prospectus, and later information filed with the SEC will update and supersede this information. We incorporate by reference the documents listed below and any future filings we make with the SEC under Section 13(a), 13(c), 14, or 15(d) of the Securities Exchange Act of 1934 from the date of the initial registration statement until the completion of the offering of the securities covered by this prospectus:

- Our annual report on Form 10-K for the fiscal year ended December 31, 2002,
- Our quarterly reports on Form 10-Q for the quarterly periods ended March 31, 2003 and June 30, 2003,
- Our current reports on Form 8-K filed February 25, 2003, April 2, 2003, May 15, 2003, September 12, 2003, and October 3, 2003,
- The description of our common stock, contained in our registration statement on Form 8-A filed on November 21, 1994, including any amendments or reports filed for the purpose of updating such descriptions, and
- The description of our preferred stock purchase rights, contained in our registration statement on Form 8-A filed on September 30, 1996, including any amendments or reports filed for the purpose of updating such

descriptions.

The reports and other documents that we file after the date of this prospectus will update and supersede the information in this prospectus.

Notwithstanding the foregoing, reports or documents or portions thereof furnished to but not filed with the SEC and not otherwise incorporated by reference are not and will not be incorporated by reference into this registration statement.

You may request a copy of these filings, at no cost, by writing or telephoning us at:

Ligand Pharmaceuticals Incorporated
Attn: Investor Relations
10275 Science Center Road
San Diego, California 92121-1117
(858) 550-7500

YOU SHOULD RELY ONLY ON THE INFORMATION PROVIDED OR INCORPORATED BY REFERENCE IN THIS PROSPECTUS OR ANY RELATED PROSPECTUS SUMMARY. WE HAVE NOT AUTHORIZED ANYONE TO PROVIDE YOU WITH DIFFERENT INFORMATION. YOU SHOULD NOT ASSUME THAT THE INFORMATION IN THIS PROSPECTUS OR ANY RELATED PROSPECTUS SUMMARY IS ACCURATE AS OF ANY DATE OTHER THAN THE DATE ON THE FRONT OF THE DOCUMENT.

DILUTION

The net tangible book value of Ligand at June 30, 2003 was $(116,137,000), or approximately $(1.67) per share of common stock. Net tangible book value per share represents the amount of our tangible assets less total liabilities, divided by the number of our outstanding shares of common stock.

Net tangible book value dilution per share represents the difference between the amount per share paid by purchasers of shares of common stock from selling stockholders in the offering made hereby and the pro forma net tangible book value per share of common stock immediately after completion of the offering. Assuming that the sales of 3,483,593 shares of common stock in the offering are made at an offering price of $12.62 per share, which is the average of the high and low sales prices per share of the common stock on October 7, 2003 as reported on The Nasdaq Stock Market, and that we will receive none of the net proceeds therefrom, the purchasers of common stock from the selling stockholders would experience an immediate dilution in net tangible book value of $14.29 per share, as illustrated in the following table:

Assumed public offering price per share.....	$ 12.62
Net tangible book value per share as of June 30, 2003 (1)..	$(1.67)
Pro forma dilution per share to new investors.....	$ 14.29

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(1) Because the shares being offered and sold by the selling stockholders are

issued and outstanding and we will receive none of the proceeds from the offering of the common stock by the selling stockholders, net tangible book value per share will not change as a result of such offering.

USE OF PROCEEDS

We will not receive any of the proceeds from the sale of the shares of our common stock by the selling stockholders.

PLAN OF DISTRIBUTION

We are registering on the registration statement of which this prospectus forms a part all 3,483,593 shares of our common stock on behalf of the selling stockholders. We issued all of the shares to the selling stockholders in a private placement transaction completed in September 2003. The selling stockholders named in the table below or pledgees, donees, transferees or other successors in interest selling shares received from a named selling stockholder as a gift, pledge, partnership distribution or other non-sale related transfer after the date of this prospectus may sell the shares from time to time. The selling stockholders will act independently of us in making decisions regarding the timing, manner and size of each sale. The sales may be made on The Nasdaq Stock Market or in the over-the-counter market or otherwise, at prices and at terms then prevailing or at prices related to the then-current market price, or in negotiated transactions. The selling stockholders may effect these transactions by selling the shares to or through broker-dealers. Except as otherwise provided in the Stock Purchase Agreements by which we originally issued the shares, the shares may be sold by one or more of, or a combination of, the following:

- a block trade in which the broker-dealer will attempt to sell the shares as agent but may position and resell a portion of the block as principal to facilitate the transaction,
- purchases by a broker-dealer as principal and resale by such broker-dealer for its account under this prospectus,
- an exchange distribution in accordance with the rules of the respective exchange,
- ordinary brokerage transactions and transactions in which the broker solicits purchasers,

- an over-the-counter distribution in accordance with the rules of The Nasdaq National Market,
- in privately negotiated transactions, and
- in options transactions.

To the extent required, this prospectus may be amended or supplemented from time to time to describe a specific plan of distribution. In effecting sales, broker-dealers engaged by the selling stockholders may arrange for other broker-dealers to participate in the resales.

Except as otherwise provided in the Stock Purchase Agreements by which we originally issued the shares, the selling stockholders may enter into hedging transactions with broker-dealers or other financial institutions in connection with distributions of the shares or otherwise. In connection with these

transactions, broker dealers or other financial institutions may engage in short sales of the shares in the course of hedging the positions they assume with selling stockholders. Except as otherwise provided in the Stock Purchase Agreements by which we originally issued the shares, the selling stockholders also may sell shares short and redeliver the shares to close out such short positions. The selling stockholders may enter into option or other transactions with broker-dealers which require the delivery to the broker-dealer of the shares. The broker-dealer may then resell or otherwise transfer such shares covered by this prospectus (as supplemented or amended to reflect such transaction). The selling stockholders also may loan or pledge the shares to a broker-dealer or other financial institution. The broker-dealer or such other financial institution may sell the shares so loaned, or upon a default the broker-dealer may sell the pledged shares under this prospectus (as supplemented or amended to reflect such transaction). Broker-dealers or agents may receive compensation in the form of commissions, discounts or concessions from selling stockholders. Broker-dealers or agents may also receive compensation from the purchasers of the shares for whom they act as agents or to whom they sell as principals, or both. Compensation as to a particular broker-dealer might be in excess of customary commissions and will be in amounts to be negotiated in connection with the sale. Broker-dealers or agents and any other participating broker-dealers or the selling stockholders may be deemed to be underwriters within the meaning of Section 2(11) of the Securities Act of 1933, as amended, in connection with sales of the shares. Accordingly, any such commission, discount or concession received by them and any profit on the resale of the shares purchased by them may be deemed to be underwriting discounts or commissions under the Securities Act. Because selling stockholders may be deemed to be underwriters within the meaning of Section 2(11) of the Securities Act, the selling stockholders will be subject to the prospectus delivery requirements of the Securities Act. In addition, any securities covered by this prospectus which qualify for sale in compliance with Rule 144 promulgated under the Securities Act may be sold under Rule 144 rather than under this prospectus. The selling stockholders have advised us that they have not entered into any agreements, understandings or arrangements with any underwriters or broker-dealers regarding the sale of their securities. There is no underwriter or coordinating broker acting in connection with the proposed sale OF shares by the selling stockholders.

The shares will be sold only through registered or licensed brokers or dealers if required under applicable state securities laws. In addition, in certain states the shares may not be sold unless they have been registered or qualified for sale in the applicable state or an exemption from the registration or qualification requirement is available and is complied with.

Under applicable rules and regulations under the Securities Exchange Act of 1934, as amended, persons engaged in the distribution of the shares may be limited in their ability to engage in market activities with respect to such shares. In addition, each selling stockholder will be subject to applicable provisions of the Securities Exchange Act and the associated rules and regulations under the Securities Exchange Act, including Regulation M, which provisions may limit the timing of purchases and sales of shares of our common stock by the selling stockholders. We will make copies of this prospectus available to the selling stockholders and have informed them of the need to deliver copies of this prospectus to purchasers at or prior to the time of any sale of the shares.

We will file a supplement to this prospectus, if required, to comply with Rule 424(b) under the Securities Act, upon being notified by a selling stockholder that any material arrangements have been entered into with a broker-dealer for the sale of shares through a block trade, special offering, exchange distribution or secondary distribution or a purchase by a broker or dealer. Such supplement will disclose:

- the name of each such selling stockholder and of the participating broker-dealer(s),
- the number of shares involved,
- the price at which such shares were sold,
- the commissions paid or discounts or concessions allowed to such broker-dealer(s), where applicable,
- that such broker-dealer(s) did not conduct any investigation to verify the information set out or incorporated by reference in this prospectus, and
- other facts material to the transaction.

In addition, upon being notified by a selling stockholder that a donee or pledgee intends to sell more than 500 shares, if required we will file a supplement to this prospectus.

We will bear all costs, expenses and fees in connection with the registration of the shares, other than fees and expenses, if any, of counsel or other advisers to the selling stockholders. In addition, the selling stockholders will bear all commissions and discounts, if any, attributable to the sales of the shares. The selling stockholders may agree to indemnify any broker-dealer or agent that participates in transactions involving sales of the shares against various liabilities, including liabilities arising under the Securities Act. We have agreed to indemnify the selling stockholders against various liabilities in connection with the offering of the shares, including liabilities arising under the Securities Act. The selling stockholders have agreed to indemnify us, our directors and officers who sign the registration statement of which this prospectus forms a part, and control persons against various liabilities in connection with the offering of the shares, including liabilities arising under the Securities Act.

We have agreed with the selling stockholders to keep the registration statement of which this prospectus constitutes a part effective until the earlier of (i) September 11, 2005, (ii) the date on which the selling stockholders may sell all shares covered by this prospectus without restriction pursuant to Rule 144(k) under the Securities Act or (iii) such time as all shares covered by this prospectus have been sold pursuant to and in accordance with the registration statement.

SELLING STOCKHOLDERS

The following table sets forth the number of shares owned by each of the selling stockholders. These stockholders acquired the shares directly from us in a private placement completed in September 2003. This registration statement also shall cover any additional shares of common stock which become issuable in connection with the shares registered for sale hereby by reason of any stock dividend, stock split, recapitalization or other similar transaction effected without the receipt of consideration which results in an increase in the number of our outstanding shares of common stock.

The investment advisor for UBS Juniper Crossover Fund LLC is a joint venture between OrbiMed Advisors LLC and an affiliate of UBS Securities, Inc. UBS Securities, Inc. is a current advisor to the Company on financial matters and transactions and acted as the placement agent for the private placement of the shares acquired by the selling stockholders. Among other matters, UBS Securities, Inc. also acted as the initial purchaser for the offering of our 6% Convertible Subordinated Notes Due 2007 that was completed in November 2002.

None of the selling stockholders has had a material relationship with us within the past three years other than as a result of the ownership of the shares or other securities of ours.

We do not know when or in what amounts the selling stockholders may offer shares for sale. The selling stockholders may decide not to sell all or any of the shares that this prospectus covers. The shares offered by this prospectus may be offered from time to time by the selling stockholders named below. Because the selling stockholders may offer all or some of the shares pursuant to this offering, and because there are currently no agreements, arrangements or understandings with respect to the sale of any of the shares that the selling stockholders will hold after completion of the offering, we cannot estimate the number of shares that the selling stockholders will hold after completion of the offering.

The percentages of common stock beneficially owned and being offered are calculated based on 69,355,579 shares of common stock issued and outstanding as of July 31, 2003.

	SHARES OWNED PRIOR TO THIS OFFERING		NUM
NAME OF SELLING STOCKHOLDER	NUMBER	PERCENTAGE OF COMMON STOCK OUTSTANDING	RE
Acqua Wellington Opportunity I Limited Shirlaw House 87 Shirley Street Nassau, Bahamas	500,000	*	
Adage Capital Partners, L.P. 200 Clarendon Street 52nd Floor Boston, MA 02116	592,593	*	
Eaton Vance Variable Trust c/o OrbiMed Advisors LLC 767 Third Avenue 30th Floor New York, NY 10017	20,000	*	

SHARES OWNED PRIOR

	TO THIS OFFERING		NUM
NAME OF SELLING STOCKHOLDER	NUMBER	PERCENTAGE OF COMMON STOCK OUTSTANDING	RE
Eaton Vance Worldwide Health Sciences c/o OrbiMed Advisors LLC 767 Third Avenue 30th Floor New York, NY 10017	2,150,000	3.1	
Eaton Vance Emerald Worldwide Health Sciences c/o OrbiMed Advisors LLC 767 Third Avenue 30th Floor New York, NY 10017	69,000	*	
S.A.C. Capital Associates, LLC c/o S.A.C. Capital Advisors, LLC 72 Cummings Point Road Stamford, CT 06902	560,000	*	
S.A.C. Healthco Fund, LLC c/o S.A.C. Capital Advisors, LLC 72 Cummings Point Road Stamford, CT 06902	375,000	*	
UBS Juniper Crossover Fund LLC c/o OrbiMed Advisors LLC 767 Third Avenue 30th Floor New York, NY 10017	80,000	*	
TOTAL:	4,346,593		

* Indicates less than 1%

LEGAL MATTERS

The validity of the securities offered hereby will be passed upon by Clifford Chance US LLP, San Diego, California.

EXPERTS

The consolidated financial statements as of December 31, 2002 and 2001, and for the years ended December 31, 2002, 2001 and 2000, incorporated in this prospectus by reference from our Annual Report on Form 10-K for the year ended December 31, 2002 have been audited by Deloitte & Touche LLP, independent auditors, as stated in their report, which is incorporated herein by reference (which report expresses an unqualified opinion and includes an explanatory paragraph referring to a change in accounting principle), and have been so incorporated in reliance upon the report of such firm given upon their authority

as experts in accounting and auditing.

WE HAVE NOT AUTHORIZED ANY PERSON TO MAKE A STATEMENT THAT DIFFERS FROM WHAT IS IN THIS PROSPECTUS. IF ANY PERSON DOES MAKE A STATEMENT THAT DIFFERS FROM WHAT IS IN THIS PROSPECTUS, YOU SHOULD NOT RELY ON IT. THIS PROSPECTUS IS NOT AN OFFER TO SELL, NOR IS IT AN OFFER TO BUY, THESE SECURITIES IN ANY STATE IN WHICH THE OFFER OR SALE IS NOT PERMITTED. THE INFORMATION IN THIS PROSPECTUS IS COMPLETE AND ACCURATE AS OF ITS DATE, BUT THE INFORMATION MAY CHANGE AFTER THAT DATE.

3,483,593 SHARES

LIGAND PHARMACEUTICALS INCORPORATED

COMMON STOCK

Prospectus

_____, _____

PART II
INFORMATION NOT REQUIRED IN PROSPECTUS

ITEM 14. OTHER EXPENSES OF ISSUANCE AND DISTRIBUTION.

The following table sets forth all expenses, other than underwriting discounts and commissions, payable by the registrant in connection with the sale of the common stock being registered. All the amounts shown are estimates, except for the SEC registration fee.

SEC registration fee.....	$3,553.78
Printing and engraving expenses.....	5,000.00
Legal fees and expenses.....	15,000.00

Accounting fees and expenses.....	5,000.00
Transfer agent and registrar fee.....	30,000.00
Miscellaneous expenses.....	10,000.00
TOTAL	$68,553.78

ITEM 15. INDEMNIFICATION OF OFFICERS AND DIRECTORS.

Under Section 145 of the Delaware General Corporation Law, we have broad powers to indemnify our officers, directors and third parties acting on our behalf against liabilities they may incur in such capacities, including liabilities under the Securities Act.

Our amended and restated certificate of incorporation provides for the indemnification of all of our officers, directors and third parties acting on our behalf to the fullest extent permissible under Delaware law.

Our amended and restated by-laws provide for the indemnification of officers, directors and third parties acting on our behalf if such person acted in good faith and in a manner reasonably believed to be in and not opposed to our best interest, and, with respect to any criminal action or proceeding, the indemnified party had no reason to believe his or her conduct was unlawful.

We maintain directors and officers insurance providing indemnification for certain of our directors and officers for certain liabilities.

We also entered into indemnification agreements between us and our directors and officers, which may be sufficiently broad to permit indemnification of our officers and directors for liabilities arising under the Securities Act.

In the Stock Purchase Agreements between us and the selling stockholders dated as of September 10, 2003 entered into in connection with our September 2003 private placement, the selling stockholders agreed to indemnify us and our directors, officers and controlling persons, as defined in the Securities Act, against certain liabilities, including liabilities arising under the Securities Act, in connection with matters specifically provided in writing by the selling stockholders for inclusion in the Registration Statement.

Insofar as indemnification for liabilities arising under the Securities Act may be permitted to directors, officers or persons controlling us pursuant to the foregoing provisions, we have been informed that in the opinion of the SEC such indemnification is against public policy as expressed in the Securities Act and is therefore unenforceable.

ITEM 16. EXHIBITS.

(A) EXHIBITS.

EXHIBIT NO.	DESCRIPTION
4.1	Instruments defining the rights of stockholders.

	Reference is made to our Form 8-A registration statement filed on November 21, 1994 (incorporated into this registration statement by reference), the Amended and Restated Certificate of Incorporation (incorporated into this registration statement by reference to Exhibit 3.2 to our Form S-4 registration statement filed on July 9, 1998), the Bylaws (incorporated into this registration statement by reference to Exhibit 3.3 of our Form S-4 registration statement, filed on July 9, 1998), the Amended Certificate of Designation of Rights, Preferences and Privileges of Series A Participating Preferred Stock (incorporated into this registration statement by reference to Exhibit 3.3 to our quarterly report on Form 10-Q for the period ended March 31, 1999) and our Form 8-A registration statement filed on September 30, 1996 (incorporated into this registration statement by reference to Exhibit 4.1 filed with our registration statement filed on April 16, 1992), including any amendments or reports filed for the purposes of updating such descriptions
4.2(1)	Form of Stock Purchase Agreement dated as of September 10, 2003 between the Company and the investors listed on Exhibit A.
5.1(1)	Opinion of Clifford Chance US LLP
23.1	Consent of Deloitte & Touche LLP, Independent Auditors
23.2(1)	Consent of Clifford Chance US LLP. Included in the Opinion of Clifford Chance US LLP filed as Exhibit 5.1
24.1(1)	Power of Attorney

(1) Previously filed

ITEM 17. UNDERTAKINGS.

The undersigned registrant hereby undertakes:

(1) To file, during any period in which offers or sales are being made, a post-effective amendment to this registration statement:

(i) to include any prospectus required by Section 10(a)(3) of the Securities Act of 1933;

(ii) to reflect in the prospectus any facts or events arising after the effective date of the registration statement (or the most recent post-effective amendment thereof) which, individually or in the aggregate, represent a fundamental change in the information set forth in the registration statement. Notwithstanding the foregoing, any increase or decrease in volume of securities offered (if the total dollar value of securities offered would not exceed that which was registered) and any deviation from the low or high end of the estimated maximum offering range may be reflected in the form of prospectus filed with the Commission pursuant to Rule 424(b) if, in the aggregate, the changes in volume and price represent no more than 20 percent change in the maximum aggregate offering price set forth in the "Calculation of Registration Fee" table in the effective registration statement; and

(iii) to include any material information with respect to the plan of distribution not previously disclosed in the registration statement or any material change to such information in the registration statement;

(2) That, for the purpose of determining any liability under the Securities Act of 1933, each such post-effective amendment shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof;

(3) To remove from registration by means of a post-effective amendment any of the securities being registered which remain unsold at the termination of the offering.

The undersigned registrant hereby undertakes that, for purposes of determining any liability under the Securities Act of 1933, each filing of the registrant's annual report pursuant to Section 13(a) or Section 15(d) of the Securities Exchange Act of 1934 (and, where applicable, each filing of an employee benefit plan's annual report pursuant to Section 15(d) of the Securities Exchange Act of 1934) that is incorporated by reference in the registration statement shall be deemed to be a new registration statement relating to the securities offered therein, and the offering of such securities at that time shall be deemed to be the initial bona fide offering thereof.

Insofar as indemnification for liabilities arising under the Securities Act of 1933 may be permitted to directors, officers and controlling persons of the registrant pursuant to the foregoing provisions, or otherwise, the registrant has been advised that in the opinion of the Securities and Exchange Commission such indemnification is against public policy as expressed in the Act and is, therefore, unenforceable. In the event that a claim for indemnification against such liabilities (other than the payment by the registrant of expenses incurred or paid by a director, officer, or controlling person of the registrant in the successful defense of any action, suit, or proceeding) is asserted by such director, officer, or controlling person in connection with the securities being registered, the registrant will, unless in the opinion of its counsel the matter has been settled by controlling precedent, submit to a court of appropriate jurisdiction the question of whether such indemnification by it is against public policy as expressed in the Act and will be governed by the final adjudication of such issue.

SIGNATURES

Pursuant to the requirements of the Securities Act of 1933, the registrant certifies that it has reasonable grounds to believe that it meets all of the requirements for filing on Form S-3 and has duly caused this registration statement to be signed on its behalf by the undersigned, thereunto duly authorized, in the City of San Diego, State of California, on October 8, 2003.

LIGAND PHARMACEUTICALS INCORPORATED

By: /S/ DAVID E. ROBINSON

David E. Robinson, President
and Chief Executive Officer

Pursuant to the requirements of the Securities Act of 1933, this Registration Statement has been signed by the following persons in the capacities and on the dates indicated:

SIGNATURE	TITLE
/S/ DAVID E. ROBINSON David E. Robinson	President and Chief Executive Officer (Principal Executive Officer)
/S/ PAUL V. MAIER Paul V. Maier	Senior Vice President and Chief Financial Officer (Principal Financial and Accounting Officer)
* Henry F. Blissenbach	Director
* Alexander D. Cross	Director
* John Groom	Director
* Irving S. Johnson, Ph.D.	Director
* John W. Kozarich	Director
* Carl C. Peck	Director
* Michael A. Rocca	Director

* By: /S/ PAUL V. MAIER
Paul V. Maier
Attorney-in-Fact

EXHIBIT INDEX

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