LIGAND PHARMACEUTICALS INC
Form POS AM
April 12, 2006

Table of Contents

As filed with the Securities and Exchange Commission on April 12, 2006
Registration No. 333-131029

UNITED STATES SECURITIES AND EXCHANGE COMMISSION
Washington, D.C. 20549

Post Effective Amendment No. 1
to
FORM S-1
REGISTRATION STATEMENT
Under
The Securities Act of 1933

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

Delaware	**2834**	**77-0160744**
(State or other jurisdiction of incorporation or organization)	**(Primary Standard Industrial Classification Code Number)**	**(I.R.S. Employer Identification Number)**

10275 Science Center Drive
San Diego, CA 92121
(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, CA 92121
(858) 550-7500
(Name, address, including zip code, and telephone number, including area code, of agent for service)

Copies to:

Faye H. Russell, Esq.	**Warner R. Broaddus, Esq.**
Latham & Watkins LLP	**Ligand Pharmaceuticals Incorporated**
12636 High Bluff Drive, Suite 400	10275 Science Center Drive
San Diego, CA 92130	San Diego, CA 92121
(858) 523-5400	(858) 550-7500

Approximate date of commencement of proposed sale to the public: As soon as practicable after the effective date of this Registration Statement.

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, check the following box. þ

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

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. o

If this Form is a post-effective amendment filed pursuant to Rule 462(d) 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. o

If delivery of the prospectus is expected to be made pursuant to Rule 434, please check the following box. o

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 or until the Registration Statement shall become effective on such date as the Commission, acting pursuant to said Section 8(a), may determine.

Table of Contents

7,988,793 SHARES OF COMMON STOCK

This prospectus relates to the offer and sale of up to 7,790,974 shares to be issued pursuant to awards granted or to be granted under our 2002 Stock Incentive Plan, or our 2002 Plan, and up to 147,510 shares to be issued pursuant to our 2002 Employee Stock Purchase Plan, or our 2002 ESPP.

This prospectus also relates to the offer and sale of up to 50,309 shares of our common stock which may be offered from time to time by the selling stockholders identified on page 110 of this prospectus for their own accounts. Each of the selling stockholders named in the prospectus acquired the shares of common stock upon exercise of options previously granted to them as an employee, director or consultant of Ligand or as restricted stock granted to them as a director of Ligand, in each case under the terms of our 2002 Plan.

It is anticipated that the selling stockholders will offer shares for sale at prevailing prices on the date of sale or in negotiated transactions. We will not receive any of the proceeds from the sale of the shares of our common stock by the selling stockholders under this prospectus. We are paying the expenses incurred in registering the shares, but all selling and other expenses incurred by each of the selling stockholders will be borne by that selling stockholder.

Among the shares of common stock there are shares which are restricted securities under the Securities Act before their sale under this prospectus. This prospectus has been prepared in part for the purpose of registering the shares of common stock under the Securities Act to allow for future sales by the selling stockholders, on a continuous or delayed basis, to the public without restriction. Each selling stockholder and any participating broker or dealer may be deemed to be an underwriter within the meaning of the Securities Act, in which event any profit on the sale of shares by the selling stockholder and any commissions or discounts received by those brokers or dealers may be deemed to be underwriting compensation under the Securities Act.

Our common stock is quoted on The Pink Sheets LLC under the symbol LGND. On April 10, 2006, the last reported sale price of our common stock was $13.05 per share.

AN INVESTMENT IN THE SHARES OFFERED BY THIS PROSPECTUS IS SPECULATIVE AND SUBJECT TO RISK OF LOSS. SEE RISK FACTORS BEGINNING ON PAGE 7 AND THE TABLE OF CONTENTS ON PAGE i.

NEITHER THE SECURITIES AND EXCHANGE COMMISSION NOR ANY STATE SECURITIES COMMISSION HAS APPROVED OR DISAPPROVED OF THE SECURITIES OR DETERMINED IF THIS PROSPECTUS IS TRUTHFUL OR COMPLETE. ANY REPRESENTATION TO THE CONTRARY IS A CRIMINAL OFFENSE.

THE DATE OF THIS PROSPECTUS IS _____ __, 2006.

TABLE OF CONTENTS

EXHIBIT 23.1

You should rely only on the information contained in this prospectus. We have not authorized anyone to provide you with information different from that contained in this prospectus. The information contained in this prospectus is accurate only as of the date of this prospectus, regardless of the time of delivery of this prospectus or of any sale of our common stock.

Table of Contents

PROSPECTUS SUMMARY

This summary highlights information contained elsewhere in this prospectus and does not contain all of the information that you should consider in making your investment decision. Before investing in our common stock, you should carefully read this entire prospectus, including our consolidated financial statements and the related notes included in this prospectus and the information set forth under the headings Risk Factors and Management s Discussion and Analysis of Financial Condition and Results of Operations.

The Company

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® gel (alitretinoin) 0.1%, ONTAK® (denileukin diftitox) and Targretin® (bexarotene) capsules, each of which was approved by the Food and Drug Administration, or FDA, in 1999; and Targretin® (bexarotene) gel 1%, which was approved by the FDA in 2000. Our fifth and newest product, AVINZA®, is a treatment for chronic, moderate-to-severe pain that was approved by the FDA in March 2002. In Europe, the European Commission, or EC, granted a Marketing Authorization, or MA, for Panretin gel in October 2000 and an MA for Targretin capsules in March 2001. We also continue efforts to acquire or in-license other products, like ONTAK and AVINZA, 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, or NSCLC, chronic lymphocytic leukemia, or CLL, non-Hodgkin s lymphoma, or NHL, and hand dermatitis.

We have formed research and development collaborations with numerous global pharmaceutical companies, including Abbott Laboratories, Allergan, Inc., Bristol-Myers Squibb, Eli Lilly & Company, GlaxoSmithKline, Organon (Akzo Nobel), Parke-Davis, Pfizer Inc., TAP Pharmaceutical Products, Inc. (TAP), and Wyeth. As of December 31, 2005, our corporate partners had 13 Ligand products in human development and numerous compounds on an Investigational New Drug Application, or IND, track or in preclinical and research stages. These corporate partner products are being studied for the treatment of large market indications such as osteoporosis, diabetes, contraception and cardiovascular disease. One of these partner products, lasofoxifene, is being developed by Pfizer for osteoporosis and other indications. Pfizer filed a New Drug Application, or NDA, with the FDA in August 2004 for the use of lasofoxifene in the prevention of osteoporosis and then filed a supplemental NDA in December 2004 for the use of lasofoxifene in the treatment of vaginal atrophy. Three of these partner products are in pivotal Phase III clinical trials: bazedoxifene, which is being developed by Wyeth as monotherapy for osteoporosis and in combination with Wyeth s PREMARIN for osteoporosis prevention, and vasomotor symptoms of menopause. A third partner product, eltrombopag (SB47115), being developed by Glaxo SmithKline for thrombocytopenia, recently advanced to Phase III in February 2006. A fourth partner product, LY519818, is being developed by Eli Lilly & Company for the treatment of type 2 diabetes. Lilly has announced plans to advance this product into Phase III registration studies after completion of two-year carcinogenicity studies and appropriate consultation with the FDA. Another Lilly product, LY674 has recently advanced into Phase II development for atherosclerosis and LY929 is in Phase I development for type 2 diabetes. An additional partner product being developed by GlaxoSmithKline is in Phase II: GSK516 for cardiovascular disease and dislipidemia. Other partner products in Phase II include pipendoxifene (formerly ERA-923) being developed by Wyeth for breast cancer and NSP-989 for contraception and NSP-989 combo for contraception in Phase I. In June 2005, GlaxoSmithKline commenced Phase I studies of SB-449448, a second product for thrombocytopenia and in April 2005, TAP

1

Table of Contents

commenced Phase I studies for LGD 2941 for the treatment of osteoporosis and frailty. Additionally, in September 2005 and February 2006, respectively, Pfizer announced the receipt of non-approvable letters from the FDA for the prevention of osteoporosis and vaginal atrophy. However, lasofoxifene continues in Phase III clinical trials by Pfizer for the treatment of osteoporosis.

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. Panretin gel, Targretin capsules, and Targretin gel as well as our corporate partner products currently on human development track are modulators of gene transcription, working through key cellular or intracellular receptor targets discovered using our Intracellular Receptor, or IR, technology.

On January 17, 2006, we signed an agreement with Organon that terminates the AVINZA co-promotion agreement between the two companies and returns AVINZA rights to us. The effective date of the termination agreement is January 1, 2006, however the parties have agreed to continue to cooperate during a transition period ending September 30, 2006 to promote the product. The transition period co-operation includes a minimum number of product sales calls per quarter (100,000 for Organon and 30,000 for us with an aggregate of 375,000 and 90,000 respectively for the transition period) as well as the transition of ongoing promotions, managed care contracts, clinical trials and key opinion leader relationships to us. During the transition period, we will pay Organon an amount equal to 23% of AVINZA net sales as reported by us. We will also pay and be responsible for the design and execution of all clinical, advertising and promotion expenses and activities. Additionally, in consideration of the early termination and return of rights under the terms of the agreement, we will unconditionally pay Organon $37.75 million on or before October 15, 2006 and will further pay Organon $10.0 million on or before January 15, 2007, provided that Organon has made its minimum required level of sales calls. Under certain conditions, including change of control, the cash payments will accelerate. In addition, after the termination, we will make quarterly royalty payments to Organon equal to 6.5% of AVINZA net sales through December 31, 2012 and thereafter 6% through patent expiration, currently anticipated to be November of 2017. See Business Strategy Ligand Marketed Products AVINZA Co-Promotion Agreement with Organon.

Corporate Information

We were incorporated in Delaware in 1987. 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 address is http://www.ligand.com. The information on, or accessible through, our website is not part of this prospectus. Unless the context requires otherwise, references in this prospectus to the Company, Ligand, we, us and our refer to Lig Pharmaceuticals Incorporated.

Our trademarks, trade names and service marks referenced in this prospectus include Ligand, ONTAK, Panretin, Targretin, and AVINZA. Each other trademark, trade name or service mark appearing in this prospectus belongs to its owner.

Table of Contents

THE OFFERING

Common stock offered	Up to 7,988,793 shares, assuming the issuance of all shares of common stock reserved for issuance under the 2002 Plan and the 2002 ESPP. The amount also includes 50,309 shares previously issued under the 2002 Plan which may be offered from time to time by the selling stockholders.
Common stock to be outstanding after this offering	Up to 82,014,997 shares, assuming the issuance of all shares of common stock reserved for issuance under the 2002 Plan and 2002 ESPP. The amount also includes 50,309 shares previously issued under the 2002 Plan which may be offered from time to time by the selling stockholders.
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 under this prospectus. We will receive proceeds in connection with option exercises under the 2002 Plan and shares issued under the 2002 ESPP which will be based upon each granted option exercise price or purchase price, as applicable. The exercise price under our 2002 Plan is generally based upon the fair market value of our shares at the option grant date. The purchase price of the common stock acquired under our 2002 ESPP is equal to 85% of the lower of the fair market value per share of common stock on the start date of the offering period in which the individual is enrolled or the fair market value on the quarterly purchase date. Any proceeds received by us will be used for working capital and general corporate purposes. See Use of Proceeds and Capitalization.

The number of shares of common stock that will be outstanding after this offering is based on shares outstanding as of December 31, 2005.

Table of Contents

SELECTED CONSOLIDATED FINANCIAL DATA

Set forth below are highlights from Ligand s consolidated financial data as of and for the years ended December 31, 2000 through 2005. Our selected statement of operations data set forth below for each of the five years ended December 31, 2005, 2004, 2003, 2002, and 2001 (unaudited), and the balance sheet data as of December 31, 2005, 2004, 2003, 2002 (unaudited), and 2001 (unaudited), are derived from our consolidated financial statements.

The selected consolidated financial data should be read in conjunction with Management s Discussion and Analysis of Financial Condition and Results of Operations and our and annual consolidated financial statements and related notes included elsewhere in this prospectus.

Table of Contents

	Years Ended December 31,				
	2005	2004	2003	2002	2001 (Unaudited)
	(in thousands, except share and loss per share data)				
Consolidated Statement of Operations Data:					
Product sales (1)	$ 166,081	$ 120,335	$ 55,324	$ 30,326	$ 32,038
Sale of royalty rights, net (2)		31,342	11,786	17,600	
Collaborative research and development and other revenues	10,527	11,835	14,008	23,843	30,718
Cost of products sold (1)	39,847	39,804	26,557	14,738	11,582
Research and development expenses	56,075	65,204	66,678	59,060	49,427
Selling, general and administrative expenses	74,656	65,798	52,540	41,825	35,072
Co-promotion expense (3)	32,501	30,077	9,360		
Loss from operations	(26,471)	(37,371)	(74,017)	(43,854)	(33,325)
Loss before cumulative effect of change in accounting principles	(36,399)	(45,141)	(94,466)	(52,257)	(53,305)
Cumulative effect of changing method of accounting for variable interest entity (4)			(2,005)		
Net loss	(36,399)	(45,141)	(96,471)	(52,257)	(53,305)
Basic and diluted per share amounts:					
Loss before cumulative effect of change in accounting principles	$ (0.49)	$ (0.61)	$ (1.33)	$ (0.76)	$ (0.90)
Cumulative effect of changing method of accounting for variable interest entity (4)			(0.03)		
Net loss	$ (0.49)	$ (0.61)	$ (1.36)	$ (0.76)	$ (0.90)
Weighted average number of common shares	74,019,501	73,692,987	70,685,234	69,118,976	59,413,270
Pro forma amounts assuming the changed method of accounting for variable interest entity is applied retroactively (4):					
Net loss			$ (94,352)	$ (52,456)	$ (53,600)

Basic and diluted net loss per share	$ (1.34)	$ (0.76)	$ (0.90)

	December 31,				
	2005	**2004**	**2003**	**2002 (Unaudited)**	**2001 (Unaudited)**
	(in thousands)				
Consolidated Balance Sheet Data:					
Cash, cash equivalents, short-term investments and restricted investments	$ 88,756	$ 114,870	$ 100,690	$ 74,894	$ 40,058
Working capital (deficit) (5)	(102,244)	(48,505)	(16,930)	18,370	2,375
Total assets	314,619	332,466	314,046	287,709	126,898
Current portion of deferred revenue, net	157,519	152,528	105,719	48,609	27,152
Long-term obligations (excludes long-term portion of deferred revenue, net)	173,280	174,214	173,851	162,329	138,837
Long-term portion of deferred revenue, net	4,202	4,512	3,448	3,595	4,164
Common stock subject to conditional redemption/repurchase	12,345	12,345	14,595	34,595	14,595
Accumulated deficit	(831,059)	(794,660)	(749,519)	(653,048)	(600,791)
Total stockholders equity (deficit)	(110,419)	(75,317)	(37,554)	8,925	(86,849)

(footnotes on next page)

Table of Contents

(1) We began selling ONTAK and Panretin gel in 1999 and Targretin capsules and Targretin gel in 2000. AVINZA was approved by the FDA in March 2002 and subsequently launched in the U.S. in June 2002.

(2) Represents the sale of rights to royalties. See Note 12 to our consolidated financial statements included elsewhere in this prospectus.

(3) Represents expense related to our AVINZA co-promotion agreement with Organon Pharmaceuticals USA, Inc. entered into in February 2003. See Note 9 to our consolidated financial statements included elsewhere in this prospectus. On January 17, 2006, we signed an agreement with Organon USA, Inc. that terminates the

AVINZA® co-promotion agreement between the two companies and returns AVINZA rights to us. The effective date of the termination agreement is January 1, 2006; however, the parties have agreed to continue to cooperate during a transition period ending September 30, 2006 to promote the product. See Management s Discussion and Analysis of Financial Condition and Results of Operations Overview ; Business Overview; and Business Overview-Ligand Marketed Products AVINZA Co-Promotion Agreement with Organon.

(4) In December 2003, we adopted Financial Accounting Standard Board Interpretation No. 46 (revised December 2003) (FIN46(R)), *Consolidation of Variable Interest*

Entities, an interpretation of ARB No. 51. Under FIN 46(R), we were required to consolidate the variable interest entity from which we leased our corporate headquarters. Accordingly, as of December 31, 2003, we consolidated assets with a carrying value of $13.6 million, debt of $12.5 million, and a non-controlling interest of $0.6 million. In connection with the adoption of FIN 46(R), we recorded a charge of $2.0 million as a cumulative effect of the accounting change on December 31, 2003. In April 2004, we acquired the portion of the variable interest entity that we did not previously own. The acquisition resulted in Ligand assuming the existing loan against the property and making a payment of approximately $0.6 million to the entity s other

shareholder. See Note 2 to our consolidated financial statements included elsewhere in this prospectus.

(5) Working capital (deficit) includes deferred product revenue recorded under the sell-through revenue recognition method.

Table of Contents

RISK FACTORS

The following is a summary description of some of the many risks we face in our business. You should carefully review these risks in evaluating an investment in our common stock.

The restatement of our consolidated financial statements has had a material adverse impact on us, including increased costs, the increased possibility of legal or administrative proceedings, and delisting from the NASDAQ National Market.

We determined that our consolidated financial statements for the years ended December 31, 2002 and 2003, and as of and for the quarters of 2003, and for the first three quarters of 2004, as described in more detail in our 2004 10-K, should be restated. As a result of these events, we have become subject to a number of additional risks and uncertainties, including:

§ We incurred substantial unanticipated costs for accounting and legal fees in 2005 in connection with the restatement. Although the restatement is complete, we expect to continue to incur such costs as noted below.

§ We have been named in a number of lawsuits that began in August 2004 and an additional lawsuit filed in October 2005 claiming to be class actions and shareholder derivative actions. As a result of our restatement the plaintiffs in these lawsuits may make additional claims, expand existing claims and/or expand the time periods covered by the complaints. Other plaintiffs may bring additional actions with other claims, based on the restatement. If such events occur, we may incur additional substantial defense costs regardless of their outcome. Likewise, such events might cause a diversion of our management s time and attention. If we do not prevail in any such actions, we could be required to pay substantial damages or settlement costs.

§ The Securities and Exchange Commission (SEC) has instituted a formal investigation of the Company s consolidated financial statements. This investigation will likely divert more of our management s time and attention and cause us to incur substantial costs. Such investigations can also lead to fines or injunctions or orders with respect to future activities, as well as further substantial costs and diversion of management time and attention.

§ The need to reconsider our accounting treatment and the restatement of our consolidated financial statements caused us to be late in filing our required reports on Form 10-K for December 31, 2004 and Forms 10-Q for the quarters ended March 31, 2005 and June 30, 2005, respectively, which caused us to be delisted from NASDAQ National Market in September 2005. See Our common stock was delisted from the NASDAQ National Market which may reduce the price of our common stock and the levels of liquidity available to our stockholders and cause confusion among investors for additional discussion regarding the NASDAQ delisting.

Material weaknesses or deficiencies in our internal control over financial reporting could harm stockholder and business confidence on our financial reporting, our ability to obtain financing and other aspects of our business.

Maintaining an effective system of internal control over financial reporting is necessary for us to provide reliable financial reports. As disclosed in the Company s 2004 Annual Report on Form 10-K and in its Quarterly Reports on Form 10-Q for each of the first three quarters of 2005, management s assessment of the Company s internal control over financial reporting identified material weaknesses in the Company s internal controls surrounding the accounting for revenue recognition, shipments of short-dated product, record keeping and documentation, accounting personnel, accruals and cut-off, and financial statement close procedures.

During the year ended December 31, 2005, the Company was not able to fully execute the remediation plans that were established to address the material weaknesses surrounding the accounting for revenue recognition, record keeping and documentation, accounting personnel, and financial statement close procedures. As a result, these material weaknesses were not fully remediated as of December 31, 2005. Additionally, during the assessment process, management identified four additional material weaknesses relating to the Company s internal control over financial reporting: 1) the inability of the Company to maintain an effective independent Internal Audit

Table of Contents

Department; 2) the existence of ineffective spreadsheet controls used in connection with the Company s financial processes, including review, testing, access and integrity controls; 3) the existence of accounting system access rights granted to certain members of the Company s accounting and finance department that are incompatible with the current roles and duties of such individuals (i.e., segregation of duties); and 4) the inability of management to properly maintain the Company s documentation of the internal control over financial reporting during 2005 or to substantively commence the process to update such documentation and assessment until December 2005. As a result of the unremediated and new material weaknesses, management concluded that we did not maintain effective internal control over financial reporting as of December 31, 2005.

Because we have concluded that our internal control over financial reporting is not effective and our independent registered public accountants issued a disclaimer opinion on the effectiveness of our internal controls, and to the extent we identify future weaknesses or deficiencies, there could be material misstatements in our consolidated financial statements and we could fail to meet our financial reporting obligations. As a result, our ability to obtain additional financing, or obtain additional financing on favorable terms, could be materially and adversely affected, which, in turn, could materially and adversely affect our business, our strategic alternatives, our financial condition and the market value of our securities. In addition, perceptions of us could also be adversely affected among customers, lenders, investors, securities analysts and others. Current material weaknesses or any future weaknesses or deficiencies could also hurt confidence in our business and consolidated financial statements and our ability to do business with these groups.

Our revenue recognition policy has changed to the sell-through method which is currently not used by most companies in the pharmaceutical industry which will make it more difficult to compare our results to the results of our competitors.

Because our revenue recognition policy has changed to the sell-through method which reflects products sold through the distribution channel, we do not recognize revenue for the domestic product shipments of AVINZA, ONTAK, Targretin capsules and Targretin gel. Under our previous method of accounting, product sales were recognized at time of shipment.

Under the sell-through revenue recognition method, future product sales and gross margins may be affected by the timing of certain gross to net sales adjustments including the cost of certain services provided by wholesalers under distribution service agreements, and the impact of price increases. Cost of products sold and therefore gross margins for our products may also be further impacted by changes in the timing of revenue recognition. Additionally, our revenue recognition models incorporate a significant amount of third party data from our wholesalers and IMS Health Incorporated, or IMS. Such data is subject to estimates and as such, any changes or corrections to these estimates identified in later periods, such as changes or corrections occurring as a result of natural disasters or other disruptions, including Hurricane Katrina, could affect the revenue that we report in future periods.

As a result of our change in revenue recognition policy and the fact that the sell-through method is not widely used by our competitors, it may be difficult for potential and current stockholders to assess our financial results and compare these results to others in our industry. This may have an adverse effect on our stock price.

Table of Contents

Our new revenue recognition models under the sell-through method are extremely complex and depend upon the accuracy and consistency of third party data as well as dependence upon key finance and accounting personnel to maintain and implement the controls surrounding such models.

We have developed revenue recognition models under the sell-through method that are unique to the Company s business and therefore are highly complex and not widely used in the pharmaceutical industry. The revenue recognition models incorporate a significant amount of third party data from our wholesalers and IMS. To effectively maintain the revenue recognition models, we depend to a considerable degree upon the timely and accurate reporting to us of such data from these third parties and our key accounting and finance personnel to accurately interpolate such data into the models. If the third party data is not calculated on a consistent basis and reported to us on an accurate or timely basis or we lose any of our key accounting and finance personnel, the accuracy of our consolidated financial statements could be materially affected. This could cause future delays in our earnings announcements, regulatory filings with the SEC, and potential delays in relisting or delisting with the NASDAQ.

Our common stock was delisted from the NASDAQ National Market which may reduce the price of our common stock and the levels of liquidity available to our stockholders and cause confusion among investors.

Our common stock was delisted from the NASDAQ National Market on September 7, 2005. Unless and until the Company s common stock is relisted on NASDAQ, our common stock is expected to be quoted on the Pink Sheets. The quotation of our common stock on the Pink Sheets may reduce the price of our common stock and the levels of liquidity available to our stockholders. In addition, the quotation of our common stock on the Pink Sheets may materially adversely affect our access to the capital markets, and any limitation on liquidity or reduction in the price of our common stock could materially adversely affect our ability to raise capital through alternative financing sources on terms acceptable to us or at all. Stocks that are quoted on the Pink Sheets are no longer eligible for margin loans, and a company quoted on the Pink Sheets cannot avail itself of federal preemption of state securities or blue sky laws, which adds substantial compliance costs to securities issuances, including pursuant to employee option plans, stock purchase plans and private or public offerings of securities. Our delisting from the NASDAQ National Market and quotation on the Pink Sheets may also have other negative implications, including the potential loss of confidence by suppliers, customers and employees, the loss of institutional investor interest and fewer business development opportunities.

While we have applied to have our common stock relisted on the NASDAQ National Market, our common stock may not ultimately be relisted. Even if we are successful in getting our common stock relisted on NASDAQ, the relisting may cause confusion among investors who have become accustomed to our being quoted on the Pink Sheets as they seek to determine our stock price or trade in our stock.

Our strategic alternatives exploration process is subject to a number of uncertainties and may or may not result in any expected transaction(s).

In November 2005, we announced that we would be exploring strategic alternatives for the Company and its assets in order to enhance shareholder value. This process is ongoing and is subject to a number of risks and uncertainties. For example, we may not decide to or be able to complete any strategic transaction or series of transactions on any given timeframe, or at all. Any transactions we do complete may not be the type of transaction or may not be on terms that some stockholders or members of the investing public may prefer. Any of these risks or uncertainties could harm our stock price.

Our small number of products and our dependence on partners and other third parties 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, as well as higher than expected total rebates, returns or discounts.

Table of Contents

In particular, AVINZA our pain product, now accounts for a majority of our product revenues and we expect AVINZA revenues will continue to grow over the next several years. Thus any setback with respect to AVINZA could significantly impact our financial results and our share price. AVINZA was licensed from Elan Corporation which is currently its sole manufacturer. We have contracted with Cardinal to provide additional manufacturing capacity and expect to source product from Cardinal in 2006. However, we expect Elan will continue to be a significant supplier over the next several years. Any problems with Elan s or Cardinal s manufacturing operations or capacity could reduce sales of AVINZA, as could any licensing or other contract disputes with these suppliers.

Similarly, our co-promotion partner executes a large part of the marketing and sales efforts for AVINZA and those efforts may be affected by our partner s organization, operations, activities and events both related and unrelated to AVINZA. Our co-promotion efforts have encountered and continue to encounter a number of difficulties, uncertainties and challenges, including sales force reorganizations and lower than expected sales call and prescription volumes, which have hurt and could continue to hurt AVINZA sales growth. The negative impact on the product s sales growth in turn has caused and may continue to cause our revenues and earnings to be disappointing. Any failure to fully optimize this co-promotion arrangement and the AVINZA brand, by either partner, could also cause AVINZA sales and our financial results to be disappointing and hurt our stock price. Any disputes with our co-promotion partner over these or other issues could harm the promotion and sales of AVINZA and could result in substantial costs to us. In addition, in January 2006 we announced that we were terminating the co-promotion arrangement with a nine-month transition period. Failure to successfully transition our partner s efforts and functions back to Ligand and/or failure to repartner or otherwise replace our partner s sales activities for AVINZA after the transition could adversely affect the sales of the product.

AVINZA is a relatively new product and therefore the predictability of its commercial results is relatively low. Higher than expected discounts (especially PBM/GPO rebates and Medicaid rebates, which can be substantial), returns and chargebacks and/or slower than expected market penetration could reduce sales. Other setbacks that AVINZA could face in the sustained-release opioid market include product safety and abuse issues, regulatory action, intellectual property disputes and the inability to obtain sufficient quotas of morphine from the Drug Enforcement Agency (DEA) to support our production requirements.

In particular, with respect to regulatory action and product safety issues, the FDA recently requested that we expand the warnings on the AVINZA label to alert doctors and patients to the dangers of using AVINZA with alcohol. We have made changes to the label. The FDA also requested clinical studies to investigate the risks associated with taking AVINZA with alcohol. We have submitted protocols to the FDA and are awaiting their comments on these protocol designs. These additional warnings, studies and any further regulatory action could have significant adverse affects on AVINZA sales.

Our product development and commercialization involve 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, 2005, our accumulated deficit was approximately $831.1 million. We began receiving revenues from the sale of pharmaceutical products in 1999. To consistently be profitable, we must successfully develop, clinically test, market and sell our products. Even if we consistently 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 developed with our partners will be approved for marketing. For example, lasofoxifene (Oporia), a partner product being developed by Pfizer recently received a non-approvable decision from the FDA and trials of our market product Targretin failed to meet endpoints in Phase III trials in which we were studying its use in non small cell lung cancer. 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:

Table of Contents

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

Any product development failures for these or other reasons, whether with our products or our partners products, may reduce our expected revenues, profits, and stock price.

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

Sales of prescription drugs depend significantly on access to the formularies, or lists of approved prescription drugs, of third-party payers such as government and private insurance plans, as well as the availability of reimbursement to the consumer from these third party payers. 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, may not be added to formularies 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 formulary access, discounts and reimbursement rates for our drugs, including AVINZA. We may not be able to negotiate favorable reimbursement rates and formulary status for our products or may have to pay significant discounts to obtain favorable rates and access. Only one of our products, ONTAK, is currently eligible to be reimbursed by Medicare (reimbursement for Targretin is being provided to a small group of patients by Medicare through December 2005 as part of the Medicare Replacement Drug Demonstration Project). Recently enacted changes by Medicare to the hospital outpatient payment reimbursement system may adversely affect reimbursement rates for ONTAK. Beginning in 2004 we have also experienced a significant increase in ONTAK units that are sold through Disproportionate Share Hospitals or DSHs. These hospitals are part of the federal government s procurement system and thus receive significantly higher rebates than non-government purchasers of our products. As a result, our net revenues for ONTAK could be substantially reduced if this trend continues.

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 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 approximately 113 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 and billing and customer reimbursement assistance. In Europe, we currently rely 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

Table of Contents

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, which is currently in transition, any revenues we receive will depend substantially on the marketing and sales efforts of others, which may or may not be successful.

The cash flows from our product shipments may significantly fluctuate each period based on the nature of our products.

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 130 locations throughout the United States. The purchasing and stocking patterns of our wholesaler customers for all our products are influenced by a number of factors that vary from product to product, including but not limited to overall level of demand, periodic promotions, required minimum shipping quantities and wholesaler competitive initiatives. As a result, the overall level of product in the distribution channel may average from two to six months worth of projected inventory usage. Although we have distribution services contracts in place to maintain stable inventories at our major wholesalers, if any of them were to substantially reduce the inventory they carry in a given period, e.g. due to circumstances beyond their reasonable control, or contract termination or expiration, our shipments and cash flow for that period could be substantially lower than historical levels.

We have entered into fee-for-service or distributor services agreements for each of our products with the majority of our wholesaler customers. Under these agreements, in exchange for a set fee, the wholesalers have agreed to provide us with certain services. Concurrent with the implementation of these agreements we will no longer routinely offer these wholesalers promotional discounts or incentives. The agreements typically have a one-year initial term and are renewable.

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

Ø the effectiveness of our commercialization activities.

We currently estimate our research and development expenditures over the next 3 years to range between $180 million and $225 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

Table of Contents

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.

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 April 2002 and September 2003 we issued an aggregate of 7.7 million shares of our common stock in private placement offerings. 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. In January 2006, holders of notes with a face value of $24.1 million (approximately 15% of total outstanding notes) converted their notes into approximately 3.9 million 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.

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, including lasofoxifene for which Pfizer announced receipt of non-approval letters from the FDA, and two products in Phase III trials by one of our partners involving bazedoxifene. 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.

In particular, we announced top-line data, or a summary of significant findings from our Phase III trials for Targretin capsules in NSCLC in late March of 2005. The data analysis showed that the trials did not meet their endpoints of improved overall survival and projected two-year survival. However, in both trials, additional subset analyses completed after the initial intent to treat results are being analyzed. We have been evaluating data from current and prior Phase II studies to see if they show a similar correlation between hypertriglyceridemia and increased survival. The data will further shape our future plans for Targretin. If further studies are justified they will be conducted on our own or with a partner or cooperative group. These analyses may not be favorable and may not be completed or demonstrate any hypothesis or endpoint. If these analyses or subsequent data fails to show safety or effectiveness, our stock price could be harmed. In addition, subsequent data may be inconclusive or mixed and could be delayed. The FDA may not approve Targretin for this new indication, or may delay approval, even if the data appears to be favorable. Any of these events could depress our stock price.

Table of Contents

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 involved approximately 600 patients and required significant time and investment to complete enrollments. Delays in patient enrollment for our other trials 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 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, L.P. s Duragesic, aai Pharma s Oramorph SR, Alpharma s Kadian, and generic sustained release morphine sulfate, oxycodone and fentanyl. New generic, A/B substitutable or other competitive products may also come to market and compete with our products, reducing our market share and revenues. Many of our existing or potential competitors, particularly large drug companies, have greater financial, technical and human resources than we do and may be better equipped to develop, manufacture and market products. Many of these companies also have extensive experience in preclinical testing and human clinical trials, obtaining FDA and other regulatory approvals and manufacturing and marketing pharmaceutical products. 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.

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

14

Table of Contents

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.

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 technology. Even though there are marketed drugs that act through IRs, some aspects of our IR technologies have not been used to produce marketed products. Much remains to be learned about the function of IRs. If we are unable to apply our IR and Signal Transducer and Activator of Transcription (or STAT) technologies to the development of our potential products, we may not be successful in discovering or developing new products.

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

Table of Contents

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.

Hoffmann-La Roche Inc. has received a US patent, has made patent filings and has issued patents in foreign countries that relate to our Panretin gel products. While we were unsuccessful in having certain claims of the US patent awarded to Ligand in interference proceedings, we continue to believe that any relevant claims in these Hoffman-La Roche patents in relevant jurisdictions are invalid and that our current commercial activities and plans relating to Panretin are not covered by these Hoffman-La Roche patents in the US or elsewhere. In addition, we have our own portfolio of issued and pending patents in this area which cover our commercial activities, as well as other uses of 9-*cis* retinoic acid, in the US, Europe and elsewhere. However, if the claims in these Hoffman-La Roche patents are not invalid and/or unenforceable, they might block the use of Panretin gel in specified cancers, not currently under active development or commercialization by us.

Novartis AG has filed an opposition to our European patent that covers the principal active ingredient of our ONTAK drug. We have received a favorable preliminary opinion from the European Patent Office, however this is not a final determination and Novartis has filed a response to the preliminary opinion that argues our patent is invalid. 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 possible future 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, some 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 active pharmaceutical ingredient for us, Raylo manufactures Targretin active pharmaceutical ingredient, and Cardinal Health manufactures Targretin capsules for us. We also recently entered into contracts with and received regulatory approval during 2005 for Cardinal Health to manufacture and package AVINZA and with Hollister-Stier for the filling and finishing of ONTAK. Any delays or failures of the manufacturing or packaging process could cause inventory problems or product shortages.

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 at acceptable cost and in sufficient quantities to meet product growth demands. Any extended or unplanned manufacturing shutdowns, shortfalls or delays could be expensive and could result in inventory and product shortages. If we are unable to reliably manufacture our products 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 translate our core technologies or other technologies into drugs that can be manufactured 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.

Table of Contents

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 $0.7 million. 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.

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.

Table of Contents

SPECIAL NOTE REGARDING FORWARD-LOOKING STATEMENTS

This prospectus contains forward-looking statements, including statements regarding the demand for our marketed products, the diligence of our corporate partners in continuing development of product candidates for which they are responsible, the progress and timing of clinical trials, whether conducted by us or by our corporate partners, the safety and efficacy of our products and product candidates, the goals of our development activities, estimates of the potential markets for our product candidates, the success of our previously announced strategic alternatives evaluation, our operations and expenditures and projected cash needs. The forward-looking statements are contained principally in the sections entitled Prospectus Summary, Risk Factors, Management s Discussion and Analysis of Financial Condition and Results of Operations and Business. These statements relate to future events or our future financial performance and involve known and unknown risks, uncertainties and other factors that could cause our actual results, levels of activity, performance or achievement to differ materially from those expressed or implied by these forward-looking statements. These risks and uncertainties include, among others:

- our ability to successfully complete clinical development of our product candidates on expected timetables, or at all, which includes enrolling sufficient patients in our clinical trials and demonstrating the safety and efficacy of our product candidates in such trials;
- our ability to ensure continued supply of sufficient quantities of our products and product candidates to support market demand and for clinical trials;
- our ability to obtain, maintain and successfully enforce adequate patent and other intellectual property protection of our currently marketed products and product candidates that may be approved for sale;
- the content and timing of submissions to and decisions made by the FDA and other regulatory agencies, including demonstrating to the satisfaction of the FDA the safety and efficacy of product candidates we or our corporate partners are developing;
- our ability to develop a sufficient sales and marketing force or enter into agreements with third parties to sell and market any of our products or product candidates that may be approved for sale;
- the success of our competitors;
- our ability to obtain reimbursement for any of our products or product candidates that may be approved for sale from third-party payors, and the extent of such coverage;
- our ability to successfully complete our previously announced strategic alternatives evaluation; and
- our ability to raise additional funds in the capital markets, through arrangements with corporate partners or from other sources.

Forward-looking statements include all statements that are not historical facts. In some cases, you can identify forward-looking statements by terms such as may, will, should, could, would, expects, plans, anticipates, estimates, projects, predicts, potential, or the negative of those terms, and similar expressions and comparable terminology intended to identify forward-looking statements. These statements reflect our current views with respect to future events and are based on assumptions and subject to risks and uncertainties. Given these uncertainties, you should not place undue reliance on these forward-looking statements. These forward-looking statements represent our estimates and assumptions only as of the date of this prospectus and, except as required by law, we undertake no obligation to update or revise publicly any forward-looking statements, whether as a result of new information, future events or otherwise after the date of this prospectus. The forward-looking statements contained in this prospectus are excluded from the safe harbor protection provided by the Private Securities Litigation Reform Act of 1995 and Section 27A of the Securities Act of 1933, as amended.

18

Table of Contents

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 under this prospectus. We will receive proceeds in connection with option exercises under the 2002 Plan and shares issued under the 2002 ESPP which will be based upon each granted option exercise price or purchase price, as applicable. The exercise price under our 2002 Plan is generally based upon the fair market value of our shares at the option grant date. The purchase price of the common stock acquired under our 2002 ESPP is equal to 85% of the lower of the fair market value per share of common stock on the start date of the offering period in which the individual is enrolled or the fair market value on the quarterly purchase date. Any proceeds received by us will be used for working capital and general corporate purposes. See Use of Proceeds and Capitalization.

DIVIDEND POLICY

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.

Table of Contents

CAPITALIZATION

The following table sets forth our cash, cash equivalents and short-term investments and our capitalization as of December 31, 2005:

on an actual basis; and

on a pro forma as adjusted basis to reflect the proceeds from (a) the exercise of all currently outstanding options and (b) the future grant and exercise of all options/shares currently reserved for future issuance under the 2002 ESPP and 2002 Plan as follows:

- 7,001,657 shares of common stock issuable upon the exercise of options outstanding as of December 31, 2005 at a weighted average exercise price of $11.76 per share.

- The addition of 595,617 shares of common stock issuable upon the exercise of options that were granted in January and February 2006 under the 2002 Plan at a weighted average exercise price of $11.96 per share.

- The addition of 194,581 shares of our common stock reserved for future issuance under the 2002 Plan at an estimated exercise price of $13.30 per share. The estimated per share price is based upon the current market value of our common stock on March 27, 2006.

- The addition of 147,510 shares of common stock reserved for issuance under our 2002 ESPP at an estimated purchase price of $11.31 per share. The estimated purchase per share price is based upon 85% of the purchase price of our common stock on March 27, 2006.

- The addition of 15,566 shares of restricted stock awarded on January 4, 2006 under the 2002 Plan to certain outside directors. The stock value is based upon the fair market value on January 4, 2006, the award date, which was $11.56 per share. We received no proceeds from the issuances of such shares of restricted stock. See Selling Stockholders.

You should read this table together with Management s Discussion and Analysis of Financial Condition and Results of Operations and our consolidated financial statements and the related notes appearing elsewhere in this prospectus. As described above, the pro forma capitalization assumes that all of the stock options or shares previously granted or reserved for future issuance will be exercised or issued. However, not all of such options or shares may be issued, exercised or granted. Additionally, subsequent to December 31, 2005, certain holders of the Company s outstanding 6% convertible subordinated notes converted notes with a face value of $26.1 million into approximately 4.2 million shares of common stock. This table does not reflect such conversion. See Management s Discussion and Analysis of Financial Condition and Results of Operations Recent Developments Conversion of 6% Convertible Subordinated Notes.

Table of Contents

	December 31, 2005	
	Actual	Pro Forma As Adjusted (Unaudited)
	(in thousands, except share and par value data)	
Cash, cash equivalents, short-term investments and restricted investments	$ 88,756	$ 182,475
Common stock subject to conditional redemption; 997,568 shares issued and outstanding at December 31, 2005	$ 12,345	$ 12,345
Stockholders deficit:		
Convertible preferred stock, $0.001 par value; 5,000,000 shares authorized; no shares issued or outstanding pro forma as adjusted	$	$
Common stock, $0.001 par value; 200,000,000 shares authorized; 73,136,340 and 81,091,271 shares issued and outstanding pro forma as adjusted	73	81
Additional paid-in capital	720,988	814,879
Accumulated other comprehensive income	490	490
Accumulated deficit	(831,059)	(831,239)
Treasury stock, at cost; 73,842 shares	(911)	(911)
Total stockholders deficit	$ (110,419)	$ (16,700)

Table of Contents

SELECTED CONSOLIDATED FINANCIAL DATA

Set forth below are highlights from Ligand s consolidated financial data as of and for the years ended December 31, 2000 through 2005. Our selected statement of operations data set forth below for each of the five years ended December 31, 2005, 2004, 2003, 2002, and 2001 (unaudited), and the balance sheet data as of December 31, 2005, 2004, 2003, 2002 (unaudited), and 2001 (unaudited), are derived from our consolidated financial statements.

The selected consolidated financial data should be read in conjunction with Management s Discussion and Analysis of Financial Condition and Results of Operations and our annual consolidated financial statements and related notes included elsewhere in this prospectus.

Table of Contents

	Years Ended December 31,				
	2005	2004	2003	2002	2001 (Unaudited)
	(in thousands, except share and loss per share data)				
Consolidated Statement of Operations Data:					
Product sales (1)	$ 166,081	$ 120,335	$ 55,324	$ 30,326	$ 32,038
Sale of royalty rights, net (2)		31,342	11,786	17,600	
Collaborative research and development and other revenues	10,527	11,835	14,008	23,843	30,718
Cost of products sold (1)	39,847	39,804	26,557	14,738	11,582
Research and development expenses	56,075	65,204	66,678	59,060	49,427
Selling, general and administrative expenses	74,656	65,798	52,540	41,825	35,072
Co-promotion expense (3)	32,501	30,077	9,360		
Loss from operations	(26,471)	(37,371)	(74,017)	(43,854)	(33,325)
Loss before cumulative effect of change in accounting principles	(36,399)	(45,141)	(94,466)	(52,257)	(53,305)
Cumulative effect of changing method of accounting for variable interest entity (4)			(2,005)		
Net loss	(36,399)	(45,141)	(96,471)	(52,257)	(53,305)
Basic and diluted per share amounts:					
Loss before cumulative effect of change in accounting principles	$ (0.49)	$ (0.61)	$ (1.33)	$ (0.76)	$ (0.90)
Cumulative effect of changing method of accounting for variable interest entity (4)			(0.03)		
Net loss	$ (0.49)	$ (0.61)	$ (1.36)	$ (0.76)	$ (0.90)
Weighted average number of common shares	74,019,501	73,692,987	70,685,234	69,118,976	59,413,270
Pro forma amounts assuming the changed method of accounting for variable interest entity is applied					

retroactively (4):			
Net loss	$ (94,352)	$ (52,456)	$ (53,600)
Basic and diluted net loss per share	$ (1.34)	$ (0.76)	$ (0.90)

	2005	2004	December 31, 2003	2002 (Unaudited)	2001 (Unaudited)
			(in thousands)		
Consolidated Balance Sheet Data:					
Cash, cash equivalents, short-term investments and restricted investments	$ 88,756	$ 114,870	$ 100,690	$ 74,894	$ 40,058
Working capital (deficit) (5)	(102,244)	(48,505)	(16,930)	18,370	2,375
Total assets	314,619	332,466	314,046	287,709	126,898
Current portion of deferred revenue, net	157,519	152,528	105,719	48,609	27,152
Long-term obligations (excludes long-term portion of deferred revenue, net)	173,280	174,214	173,851	162,329	138,837
Long-term portion of deferred revenue, net	4,202	4,512	3,448	3,595	4,164
Common stock subject to conditional redemption/repurchase	12,345	12,345	14,595	34,595	14,595
Accumulated deficit	(831,059)	(794,660)	(749,519)	(653,048)	(600,791)
Total stockholders equity (deficit)	(110,419)	(75,317)	(37,554)	8,925	(86,849)

(footnotes on next page)

Table of Contents

(1) We began selling ONTAK and Panretin gel in 1999 and Targretin capsules and Targretin gel in 2000. AVINZA was approved by the FDA in March 2002 and subsequently launched in the U.S. in June 2002.

(2) Represents the sale of rights to royalties. See Note 12 to our consolidated financial statements included elsewhere in this prospectus.

(3) Represents expense related to our AVINZA co-promotion agreement with Organon Pharmaceuticals USA, Inc. entered into in February 2003. See Note 9 to our consolidated financial statements included elsewhere in this prospectus. On January 17, 2006, we signed an agreement with Organon USA, Inc. that terminates the

AVINZA® co-promotion agreement between the two companies and returns AVINZA rights to us. The effective date of the termination agreement is January 1, 2006; however, the parties have agreed to continue to cooperate during a transition period ending September 30, 2006 to promote the product. See Management s Discussion and Analysis of Financial Condition and Results of Operations Overview ; Business Overview; and Business Overview-Ligand Marketed Products AVINZA Co-Promotion Agreement with Organon.

(4) In December 2003, we adopted Financial Accounting Standard Board Interpretation No. 46 (revised December 2003) (FIN46(R)), *Consolidation of Variable Interest*

Entities, an interpretation of ARB No. 51. Under FIN 46(R), we were required to consolidate the variable interest entity from which we leased our corporate headquarters. Accordingly, as of December 31, 2003, we consolidated assets with a carrying value of $13.6 million, debt of $12.5 million, and a non-controlling interest of $0.6 million. In connection with the adoption of FIN 46(R), we recorded a charge of $2.0 million as a cumulative effect of the accounting change on December 31, 2003. In April 2004, we acquired the portion of the variable interest entity that we did not previously own. The acquisition resulted in Ligand assuming the existing loan against the property and making a payment of approximately $0.6 million to the entity s other

shareholder. See Note 2 to our consolidated financial statements included elsewhere in this prospectus.

(5) Working capital (deficit) includes deferred product revenue recorded under the sell-through revenue recognition method.

Table of Contents

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 in Risk Factors. This outlook represents our current judgment on the future direction of our business. These statements include those related to our products, product sales and other revenues, expenses, our revenue recognition models and policies, our 2005 restatement, material weaknesses or deficiencies in internal control over financial reporting, revenue recognition, the potential relisting of the Company s securities on NASDAQ, and our evaluation of strategic alternatives. Actual events or results may differ materially from Ligand s expectations. For example, there can be no assurance that our product sales efforts or recognized revenues or expenses will meet any expectations or follow any trend(s), that our internal control over financial reporting will be effective or produce reliable financial information on a timely basis, that we will be relisted on the NASDAQ on any given timeframe or at all, or that our strategic evaluation process will be successful or yield preferred results. We cannot assure you that the Company will be able to successfully remediate any identified material weakness or significant deficiencies, or that the sell-through revenue recognition models will not require adjustment and not result in a subsequent restatement. In addition, the Company s ongoing or future litigation (including private securities litigation and the SEC investigation) may have an adverse effect on the Company, and our corporate or partner pipeline products may not gain approval or success in the market. Such risks and uncertainties, and others, could cause actual results to differ materially from any future performance suggested. We undertake no obligation to release publicly the results of any revisions to these forward-looking statements to reflect events or circumstances arising after the date of this prospectus. This caution is made under the safe harbor provisions of Section 21E of the Securities Exchange Act of 1934 as amended.

Overview

We discover, develop and market drugs that address patients critical unmet medical needs in the areas of cancer, pain, men s and women s health or hormone-related health issues, skin diseases, osteoporosis, blood disorders 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, a type of sensor or switch inside cells that turns genes on and off, and Signal Transducers and Activators of Transcription, also known as STATs, which are another type of gene switch.

We currently market five products in the United States: AVINZA, for the relief of chronic, moderate to severe pain; ONTAK, for the treatment of patients with persistent or recurrent cutaneous T-cell lymphoma (or CTCL); Targretin capsules, for the treatment of CTCL in patients who are refractory to at least one prior systemic therapy; Targretin gel, for the topical treatment of cutaneous lesions in patients with early stage CTCL; and Panretin gel, for the treatment of Kaposi s sarcoma (or KS) in AIDS patients. In Europe, we have marketing authorizations for Panretin gel and Targretin capsules and are currently marketing these products under arrangements with local distributors. In 2003, we withdrew our ONZAR (ONTAK in the U.S.) marketing authorization application 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 (EMEA) for the first generation product would be better spent on acceleration of the second generation ONTAK formulation development. We expect to resubmit the ONZAR application with the second generation product in 2007.

In February 2003, we entered into an agreement for the co-promotion of AVINZA with Organon Pharmaceuticals USA Inc. (Organon). Under the terms of the agreement, Organon committed to a specified minimum number of primary and secondary product calls delivered to certain high prescribing physicians and hospitals beginning in March 2003. Organon s compensation through 2005 was structured as a percentage of net sales, which paid Organon for their efforts and also provided Organon an economic incentive for performance and results. In exchange, we paid Organon a percentage of AVINZA net sales based on the following schedule:

Table of Contents

Annual Net Sales of AVINZA	% of Incremental Net Sales Paid to Organon by Ligand
$0-35 million (2003 only)	0% (2003 only)
$0-150 million	30%
$150-300 million	40%
$300-425 million	50%
> $425 million	45%

On January 17, 2006, we signed an agreement with Organon that terminates the AVINZA® co-promotion agreement between the two companies and returns AVINZA rights to Ligand. The effective date of the termination agreement is January 1, 2006, however the parties have agreed to continue to cooperate during a transition period ending September 30, 2006 (the Transition Period) to promote the product. The Transition Period co-operation includes a minimum number of product sales calls per quarter (100,000 for Organon and 30,000 for Ligand with an aggregate of 375,000 and 90,000 respectively for the Transition Period) as well as the transition of ongoing promotions, managed care contracts, clinical trials and key opinion leader relationships to Ligand. During the Transition Period, Ligand will pay Organon an amount equal to 23% of AVINZA net sales as reported by Ligand. Ligand will also pay and be responsible for the design and execution of all AVINZA clinical, advertising and promotion expenses and activities.

As previously disclosed, Organon and Ligand were in discussions regarding the calculation of prior co-promote fees under the co-promotion agreement. Through the third quarter of 2005, such fees were determined based on net sales calculated under the sell-in method of revenue recognition. In connection with the termination of the co-promotion agreement, the companies resolved their disagreement concerning prior co-promote fees and Ligand paid Organon $14.75 million in January 2006. Resolution of this matter resulted in no material adjustment to amounts previously recorded in 2005 for co-promotion expenses. The companies also agreed that Organon s compensation for the fourth quarter of 2005 would be calculated based on Ligand s reported AVINZA net sales determined in accordance with U.S. GAAP.

Additionally, in consideration of the early termination and return of rights under the terms of the agreement, we will unconditionally pay Organon $37.75 million on or before October 15, 2006. We will further pay Organon $10.0 million on or before January 15, 2007, provided that Organon has made its minimum required level of sales calls. Under certain conditions, including change of control, the cash payments will accelerate. In addition, after the termination, we will make quarterly royalty payments to Organon equal to 6.5% of AVINZA net sales through December 31, 2012 and thereafter 6.0% through patent expiration, currently anticipated to be November 2017.

The termination and return of rights transaction with Organon requires the analysis of several complex accounting alternatives. Accordingly, we are still in the process of determining the appropriate accounting treatment for the transaction in 2006 and going forward. Certain of these alternatives, however, could result in the recognition of significant additional expense in our consolidated statement of operations for the first quarter of 2006. We expect to complete our determination of the appropriate accounting by the time we file our first quarter 2006 Form 10-Q.

We are currently involved in the research phase of a research and development collaboration with TAP Pharmaceutical Products Inc. (or TAP). Collaborations in the development phase are being pursued by Eli Lilly and Company, GlaxoSmithKline, Organon, Pfizer, TAP 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.

We have been unprofitable since our inception on an annual basis. We achieved quarterly net income of $17.3 million during the fourth quarter of fiscal 2004, which was primarily the result of recognizing approximately $31.3 million from the sale of royalty rights to Royalty Pharma. However, for the year ended December 31, 2005, we incurred a net loss of approximately $36.4 million and expect to incur net losses in future periods. To consistently be profitable, we must successfully develop, clinically test, market and sell our products. Even if we consistently 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

26

Table of Contents

differences in the timing of revenues earned from product sales, expenses incurred, collaborative arrangements and other sources. Some of these fluctuations may be significant.

Recent Developments

Acceleration of Stock Options

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

On January 31, 2005, we accelerated the vesting of certain unvested and out-of-the-money stock options previously awarded to the executive officers and other employees under the Company s 1992 and 2002 stock option plans which had an exercise price greater than $10.41, the closing price of our stock on that date. Options to purchase approximately 1.3 million shares of common stock (of which approximately 450,000 shares were subject to options held by the executive officers) were accelerated. Options held by non-employee directors were not accelerated. Since the stock options were out-of-the-money, no compensation expense was recognized.

Holders of incentive stock options (ISOs) within the meaning of Section 422 of the Internal Revenue Code of 1986, as amended, were given the election to decline the acceleration of their options if such acceleration would have the effect of changing the status of such option for federal income tax purposes from an ISO to a non-qualified stock option. In addition, the executive officers plus other members of senior management agreed that they will not sell any shares acquired through the exercise of an accelerated option prior to the date on which the exercise would have been permitted under the option s original vesting terms. This agreement does not apply to a) shares sold in order to pay applicable taxes resulting from the exercise of an accelerated option or b) upon the officers retirement or other termination of employment.

The purpose of the acceleration was to eliminate any future compensation expense the Company would have otherwise recognized in its consolidated statement of operations with respect to these options upon the implementation of Statement of Financial Accounting Standards (SFAS) 123 ®, Share-Based Payment (SFAS 123R).

Restructuring of ONTAK Royalty

In November 2004, Ligand and Eli Lilly and Company (Lilly) agreed to amend their ONTAK royalty agreement to add options in 2005 that if exercised would restructure our royalty obligations on net sales of ONTAK. Under the revised agreement, we and Lilly each obtained two options. Our options, which were exercised in January 2005 and April 2005, provide for the buy down of a portion of our ONTAK royalty obligation on net sales in the United States for total consideration of $33.0 million. Lilly also had two options exercisable in July 2005 and October 2005 to trigger the same royalty buy-downs for total consideration of up to $37.0 million dependent on whether we have exercised one or both of our options.

Our first option, providing for a one-time payment of $20.0 million to Lilly in exchange for the elimination of our ONTAK royalty obligations in 2005 and a reduced reverse-tiered royalty scale on ONTAK sales in the U.S. thereafter, was exercised in January 2005. The second option, exercised in April 2005, provided for a one-time payment of $13.0 million to Lilly in exchange for the elimination of royalties on ONTAK net sales in the U.S. in 2006 and a reduced reverse-tiered royalty thereafter. Beginning in 2007 and throughout the remaining ONTAK patent life (2014), we will pay no royalties to Lilly on U.S. sales up to $38.0 million. Thereafter, Ligand would pay royalties to Lilly at a rate of 20% on net U.S. sales between $38.0 million and $50.0 million; at a rate of 15% on net U.S. sales between $50.0 million and $72.0 million; and at a rate of 10% on net U.S. sales in excess of $72.0 million.

Targretin Capsules Development Programs

In March 2005, we announced that the final data analysis for Targretin capsules in NSCLC showed that the trials did not meet their endpoints of improved overall survival and projected two year survival. We are continuing to

Table of Contents

analyze the data and apply it to the continued development of Targretin capsules in NSCLC. Failure to demonstrate the product s safety and effectiveness would delay or prevent regulatory approval of the product and could adversely affect our business as well as our stock price. See Risk Factors Our products face significant regulatory hurdles prior to marketing which could delay or prevent sales.

Additional Manufacturing Sources

In 2004, we entered into contracts with Cardinal Health to provide a second source for AVINZA, and with Hollister-Stier to fill and finish ONTAK. In July 2005, we announced that the FDA approved the Hollister-Stier facility for fill/finish of ONTAK. In August 2005, the FDA approved the production of AVINZA at the Cardinal Health facility which provides a second source of supply, thus diversifying the AVINZA supply chain and increasing production capacity.

Amended and Restated Research, Development and License Agreement with Wyeth

On December 1, 2005, we entered into an Amended and Restated Research, Development and License Agreement with Wyeth (formerly American Home Products Corporation). Under the previous agreement, effective September 2, 1994 as amended January 16, 1996, May 24, 1996, September 2, 1997 and September 9, 1999 (collectively the Prior Agreement), Wyeth and Ligand engaged in a joint research and development effort to discover and/or design small molecule compounds which act through the estrogen and progesterone receptors and to develop pharmaceutical products from such compounds. Wyeth sponsored certain research and development activities to be carried out by us and Wyeth may commercialize products resulting from the joint research and development subject to certain milestone and royalty payments. The Amended and Restated Agreement does not materially change the prior rights and obligations of the parties with respect to Wyeth compounds, currently in development, e.g. bazedoxifene, in late stage development for osteoporosis.

The parties agreed to amend and restate the Prior Agreement principally to better define, simplify and clarify the universe of research compounds resulting from the research and development efforts of the parties, combine and clarify categories of those compounds and related milestones and royalties and resolve a number of milestone payment issues that had arisen. Among other things, the Amended and Restated Agreement calls for Wyeth to pay Ligand $1.8 million representing the difference between amounts paid under the old compound categories versus the amounts due under the new, single category.

Termination of Organon Copromotion Agreement

On January 17, 2006, we signed an agreement with Organon that terminates the AVINZA® co-promotion agreement between the two companies and returns AVINZA rights to Ligand. The termination and return of rights transaction with Organon requires the analysis of several complex accounting alternatives. Accordingly, we are still in the process of determining the appropriate accounting treatment for the transaction in 2006 and going forward. Certain of these alternatives, however, could result in the recognition of significant additional expense in our consolidated statement of operations for the first quarter of 2006. We expect to complete our determination of the appropriate accounting by the time we file our first quarter 2006 Form 10-Q. For a discussion of this agreement, please see Management s Discussion and Analysis-Overview above.

Restructuring of AVINZA Sales Force

In January 2006, 18 Ligand sales representatives previously promoting AVINZA to primary care physicians were redeployed to call on pain specialists and all Ligand primary care territories were eliminated. In connection with this restructuring, 11 primary-care sales representatives were terminated. The AVINZA sales force restructuring was implemented to improve sales call coverage and effectiveness among high prescribing pain specialists.

Table of Contents

Conversion of 6% Convertible Subordinated Notes

In January 2006, certain holders of our outstanding 6% convertible subordinated notes converted notes with a face value of $24.1 million into 3,903,965 shares of common stock. Additionally, in March 2006, certain holders converted notes with a face value of $2.0 million into 323,980 shares of common stock.

Employee Retention Agreements

The Company has entered into letter agreements with approximately 67 of its key employees, including a number of its executive officers, dated as of March 1, 2006. The Compensation Committee of the Board of Directors has approved the Company s entry into these Agreements. The agreements provide for certain retention or stay bonus payments to be paid in cash and/or stock options under specified circumstances as an additional incentive to remain employed in good standing with the Company. The retention or stay bonus payments generally vest at the end of 2006 and total payments to employees of approximately $2.7 million would be made in January 2007 if all participants qualify for the payments. Stock options granted totaled approximately 122,000 and have an exercise price of $11.90. In accordance with the Statement of Financial Accounting Standard (SFAS) 146, *Accounting for Costs Associated with Exit or Disposal Activities*, the cost will ratably accrue over the term of the agreements, which is approximately 10 months.

Results of Operations

Total revenues for 2005 increased to $176.6 million compared to $163.5 million in 2004 and $81.1 million in 2003. Loss before cumulative effect of a change in accounting principle was $36.4 million ($0.49 per share) in 2005 compared to $45.1 million ($ 0.61 per share) in 2004, and $94.5 million ($1.33 per share) in 2003. Net loss for 2005 was $36.4 million ($0.49 per share) compared to $45.1 million ($0.61 per share) in 2004 and $96.5 million ($1.36 per share) in 2003. As more fully described in Note 2 of the notes to consolidated financial statements, results for 2003 reflect the implementation of FIN 46R, *Consolidation of Variable Interest Entities, an interpretation of ARB No. 51*, as revised December 2003, which required us to consolidate the entity from which we leased one of our corporate office buildings under a synthetic lease arrangement. The effect on 2003 results, recorded as a cumulative effect of a change in accounting principle, increased net loss by $2.0 million or $0.03 per share.

Product Sales

Our product sales for any individual period can be influenced by a number of factors including changes in demand for a particular product, competitive products, the level and nature of promotional activity, the timing of announced price increases, and the level of prescriptions subject to rebates and chargebacks. According to IMS data, AVINZA ended 2005 with a market share of prescriptions in the sustained-release opioid market of 4.4% compared to 3.9% at the end of 2004. Quarterly prescription market share for the three months ended December 31, 2005 and 2004 was 4.3% for both periods.

We expect that AVINZA prescription market share will reflect modest, if any, overall share growth in 2006 asmarket share increases in the commercial retail sector are increasingly offset by declines in the Medicaid segment as marginal Medicaid contracts are terminated. Quarter to quarter declines in prescriptions and overall market share, however, may result from more rapid declines in the Medicaid segment relative to increases in the commercial retail sector. We also continue to expect that demand for and sales of ONTAK will be positively impacted as further data is obtained from ongoing expanded-use clinical trials and the initiation of new expanded-use trials. The level and timing of any such increases, however, are influenced by a number of factors outside our control, including the accrual of patients and overall progress of clinical trials that are managed by third parties. We also expect that sales of ONTAK will benefit in 2006 from improving reimbursement rates under certain government reimbursement programs.

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 130 locations throughout the United States. The purchasing and stocking patterns of our wholesaler customers for all our products are influenced by a number of factors that vary from product to product. These factors include, but are

Table of Contents

not limited to, overall level of demand, periodic promotions, required minimum shipping quantities and wholesaler competitive initiatives. If any or all of our major wholesalers decide to reduce the inventory they carry in a given period (subject to the terms of our fee-for-service agreements discussed below), our shipments and cash flow for that period could be substantially lower than historical levels.

In the third and fourth quarters of 2004, we entered into one-year fee-for-service agreements (or distribution service agreements) for each of our products with the majority of our wholesaler customers. The principal fee-for-service agreements were subsequently renewed during the third quarter of 2005. In exchange for a set fee, the wholesalers have agreed to provide us with certain information regarding product stocking and out-movement; agreed to maintain inventory quantities within specified minimum and maximum levels; inventory handling, stocking and management services; and certain other services surrounding the administration of returns and chargebacks. In connection with implementation of the fee-for-service agreements, we no longer offer these wholesalers promotional discounts or incentives and as a result, we expect a net improvement in product gross margins as volumes grow. Additionally, we believe these arrangements will provide lower variability in wholesaler inventory levels and improved management of inventories within and between individual wholesaler distribution centers that we believe will result in a lower level of product returns compared to prior periods.

Certain of our products are included on the formularies (or lists of approved and reimbursable drugs) of many states health care plans, as well as the formulary for certain Federal government agencies. In order to be placed on these formularies, we generally sign contracts which provide discounts to the purchaser off the then-current list price and limit how much of an annual price increase we can implement on sales to these groups. As a result, the discounts off list price for these groups can be significant for products where we have implemented list price increases. We monitor the portion of our sales subject to these discounts, and accrue for the cost of these discounts at the time of the recognition of product sales. We believe that by being included on these formularies, we will gain better physician acceptance, which will then result in greater overall usage of our products. If the relative percentage of our sales subject to these discounts increases materially in any period, our sales and gross margin could be substantially lower than historical levels.

Net Product Sales

Our domestic net product sales for AVINZA, ONTAK, Targretin capsules and Targretin gel are determined on a sell-through basis less allowances for rebates, chargebacks, discounts, and losses to be incurred on returns from wholesalers resulting from increases in the selling price of the Company s products. We recognize revenue for Panretin upon shipment to wholesalers as our wholesaler customers only stock minimal amounts of Panretin, if any. As such, wholesaler orders are considered to approximate end-customer demand for the product. Revenues from sales of Panretin are net of allowances for rebates, chargebacks, returns and discounts. For international shipments of our product, revenue is recognized upon shipment to our third-party international distributors. In addition, we incur certain distributor service agreement fees related to the management of our product by wholesalers. These fees have been recorded within net product sales. For ONTAK, we also have established reserves for returns from end customers (i.e. other than wholesalers) after sell-through revenue recognition has occurred.

A summary of the revenue recognition policy used for each of our products and the expiration of the underlying patents for each product is as follows:

	Method	Revenue Recognition Event	Patent Expiration
AVINZA	Sell-through	Prescriptions	November 2017
ONTAK	Sell-through	Wholesaler out-movement	December 2014
Targretin capsules	Sell-through	Wholesaler out-movement	October 2016
Targretin gel	Sell-through	Wholesaler out-movement	October 2016
Panretin	Sell-in	Shipment to wholesaler	August 2016
International	Sell-in	Shipment to international distributor	February 2011 through April 2013

Table of Contents

For the years ended December 31, 2005, 2004, and 2003, net product sales recognized under the sell-through method represented 97%, 96%, and 94%, respectively, of total net product sales.

Our total net product sales for 2005 were $166.1 million compared to $120.3 million in 2004 and $55.3 million in 2003. A comparison of sales by product is as follows (in thousands):

	Year Ended December 31,		
	2005	**2004**	**2003**
AVINZA	$ 112,793	$ 69,470	$ 16,482
ONTAK	30,996	32,200	24,108
Targretin capsules	18,692	15,105	11,556
Other	3,600	3,560	3,178
Total product sales	$ 166,081	$ 120,335	$ 55,324

AVINZA

Sales of AVINZA were $112.8 million in 2005 compared to $69.5 million in 2004. This increase is due to higher prescriptions as a result of the increased level of marketing and sales activity under our co-promotion agreement with Organon, a shift in the mix of prescriptions to the higher doses of AVINZA, and the product s success in achieving state Medicaid and commercial formulary status. Formulary access removes obstacles to physicians prescribing the product and facilitates patient access to the product through lower co-pays. Demand for AVINZA as measured by prescription levels (or patient consumption for channels with no prescription requirements) increased by 27% in 2005 compared to 2004, as reported by IMS. Sales of AVINZA in 2005 also benefited from the full year impact of a 9.0% price increase effective July 1, 2004 and the partial year impact of a 7% price increase effective April 1, 2005. Note that under the sell-through revenue recognition method, price increases do not impact demand sales until the product sells through the distribution channel.

AVINZA sales for 2005 were negatively impacted by an increase in Medicaid rebates of approximately $4.4 million and an increase in managed care rebates of approximately $ 3.6 million, under contracts with pharmacy benefit managers (PBMs), group purchasing organizations (GPOs) and health maintenance organizations (HMOs).

Upon an announced price increase, we revalue our estimate of deferred product revenue to be returned to recognize the potential higher credit a wholesaler may take upon product return determined as the difference between the new price and the previous price used to value the allowance. AVINZA sales in 2005 reflect an approximate $3.5 million reduction in sales, recorded during the three months ended March 31, 2005, for losses expected to be incurred on product returns resulting from an AVINZA price increase which became effective April 1, 2005. For the year, the impact on sales of the April 1, 2005 price increase was partially offset by a reduction in the allowance for return losses of approximately $2.9 million recorded during the three months ended December 31, 2005. This reduction resulted from lower rates of return on lots that closed out in the fourth quarter of 2005, thereby lowering the historical weighted average rate of return used for estimating the allowance for return losses. This compares to a $2.6 million loss in 2004 on product returns, which was recorded during the three months ended June 30, 2004 for an AVINZA price increase which became effective July 1, 2004.

Lastly, product sales in 2005 and for the second half of 2004 are net of fees paid to our wholesaler customers under the fee for service agreements entered into during the third and fourth quarters of 2004.

As discussed above, we expect AVINZA demand to show modest, if any, growth in 2006 due to, for example, declines in the Medicaid segment, as evidenced by slower demand for AVINZA in the fourth quarter of 2005 as compared to the third quarter of 2005. Any changes to our estimates for Medicaid prescription activity or prescriptions written under our managed care contracts may have an impact on our rebate liability and a corresponding impact on AVINZA net product sales. For example, a 20% variance to our estimated Medicaid and managed care contract rebate accruals for AVINZA as of December 31, 2005 could result in adjustments to our Medicaid and managed care contract rebate accruals and net product sales of approximately $1.0 million and $0.5 million, respectively.

Table of Contents

Sales of AVINZA were $69.5 million in 2004 compared to $16.5 million in 2003. This increase is due to increasing prescriptions as a result of the increased level of marketing and sales activity under our co-promotion arrangement with Organon. Demand for AVINZA as measured by prescription levels (or patient consumption for channels with no prescription requirements) increased by 235.6% for 2004 compared to 2003, as reported by IMS. Sales in 2004 also benefited from a 9.9% price increase effective January 1, 2004 and a 9.0% price increase effective July 1, 2004.

AVINZA sales were negatively impacted during 2004 by an increase in Medicaid rebates of approximately $11.3 million, which significantly increased in the fourth quarter of 2003, driven by increased prescriptions in states where AVINZA (1) obtained preferred formulary status relative to competing products and (2) came onto the state formulary but not in a preferred position. AVINZA sales during 2004 compared to 2003 were also impacted by an increase in managed care rebates of approximately $4.6 million under contracts entered into in late 2003 and early 2004 with pharmacy benefit managers (PBMs), group purchasing organizations (GPOs) and health maintenance organizations (HMOs).

ONTAK

Sales of ONTAK were $31.0 million in 2005 compared to $32.2 million in 2004. ONTAK sales in 2005 compared to 2004 were negatively impacted by a 13% decrease in wholesaler out-movement due primarily to a decline in the office segment of the market, which has been impacted by negative changes in the Centers for Medicare and Medicaid Services reimbursement rates. Increases in the hospital segment have not been sufficient to offset the office segment trend. ONTAK sales for 2005 were also negatively impacted by a continued increase in chargebacks and rebates of approximately $1.5 million, due to changes in patient mix and the evolving reimbursement rates.

The decrease in ONTAK sales in 2005 was partially offset by the full year impact of a 9% price increase effective January 1, 2004, which under the sell-through revenue recognition method does not impact net product sales until the product sells through the distribution channel, and the partial year impact of a 7% price increase effective January 1, 2005 and a 4% price increase effective July 1, 2005. Net product sales for the 2004 periods are also net of promotional discounts and amounts paid to wholesalers for marketing support. In connection with the implementation of fee for service agreements in the third quarter of 2004, the Company no longer provides to wholesalers promotional discounts or marketing support payments. Accordingly, sales of ONTAK for 2005 reflect no such discounts compared to approximately $2.8 million for 2004. The impact of no discounts and marketing support payments in the 2005 periods on net product sales is offset by a full year of fees paid to wholesalers under the fee for service agreements for 2005 compared to only six months for the year ended December 31, 2004.

We continue to study changes to the Centers for Medicare and Medicaid Services reimbursement rates and expect improved reimbursement rates for 2006.

Sales of ONTAK were $32.2 million in 2004 compared to $24.1 million in 2003. Sales in 2004 were positively impacted by a 9% price increase effective January 1, 2004 and increasing use (impacted in part by expanded clinical data) in CTCL, CLL, and NHL. Demand for ONTAK as measured by shipments to end users as reported by our wholesalers increased by 28.0% for 2004 compared to 2003. Sales of ONTAK in 2004 were negatively impacted, however, by a continued increase in chargebacks and rebates of approximately $1.9 million due to changes in patient mix and evolving reimbursement rates.

Table of Contents

Targretin Capsules

Sales of Targretin capsules were $18.7 million in 2005 compared to $15.1 million in 2004. This increase reflects the full year impact of a 7% price increase effective January 1, 2004 which under the sell-through revenue recognition method does not impact net product sales until the product sells-through the distribution channel and therefore had only a limited impact on net sales for the same 2004 period, and the partial year impact of a 7% price increase effective January 1, 2005 and a 5% price increase effective July 1, 2005. Based on information provided by IMS, demand for Targretin capsules, as measured by product out-movement, increased by 8.2% in 2005 compared to 2004. Lastly, Targretin capsules product sales for 2005 are net of a full year of fees paid to our wholesaler customers under the fee for service agreements entered into during the third and fourth quarters of 2004.

In June 2004, the Centers for Medicare and Medicaid Services (CMS) announced formal implementation of the Section 641 Demonstration Program under the Medicare Modernization Act of 2003 including reimbursement under Medicare for Targretin for patients with CTCL. As a result, we continue to expect improved patient access for Targretin in 2006.

Sales of Targretin capsules were $15.1 million in 2004 compared to $11.6 million in 2003. This increase reflects a 7% price increase effective January 1, 2004 and the full year impact of a 15% price increase effective April 1, 2003. Additionally, demand for Targretin capsules as measured by product outmovement increased by 5.4% for 2004 compared to 2003, as reported by IMS.

Sale of Royalty Rights

Revenue from the sale of royalty rights represents the sale to third parties of rights and options to acquire future royalties we may earn from the sale of products in development with our collaborative partners. In those instances where we have no continuing involvement in the research or development of these products, sales of royalty rights are recognized as revenue in the period the transaction is consummated or the options are exercised or expire. See Note 2 to our consolidated financial statements for further discussion of our revenue recognition policy with respect to sales of royalty rights.

Sale of royalty rights recognized in 2004 and 2003 amounted to $31.3 million and $11.8 million, respectively, net of the deferral of offset rights of $1.4 million and $0.6 million, respectively, and the recognition in 2004 and 2003 of $0.2 million and $0.1 million, respectively, of option value deferred in previous periods. There was no sale of royalty rights in 2005.

In March 2002, we entered into an agreement with Royalty Pharma AG (Royalty Pharma), to sell a portion of our rights to future royalties from the net sales of three selective estrogen receptor modulator (SERM) products now in late stage development with two of our collaborative partners, Pfizer and Wyeth. The agreement provided for the initial sale of rights to 0.25% of such product net sales for $6.0 million and options to acquire up to an additional 1.00% of net sales for $50.0 million. Of the initial $6.0 million sale of rights, $0.2 million was attributed to the options and recorded as deferred revenue.

In July and December of 2002, the agreement was amended to replace the existing options with new options providing for the rights to acquire an additional 1.3125% of net sales for $63.8 million. Royalty Pharma exercised each of the three available 2002 options, as amended, acquiring rights to 0.4375% of net sales for $12.3 million. The fair value estimated for the amended options, $0.2 million, was recorded as deferred revenue.

In October 2003, the existing royalty agreement was amended and Royalty Pharma exercised an option for $12.5 million in exchange for 0.7% of potential future sales of the three SERM products for 10 years. Under the revised agreement, Royalty Pharma had three additional options to purchase up to 1.3% of such product net sales for $39.0 million.

In November 2004, Royalty Pharma agreed to purchase an additional 1.625% royalty on future sales of the SERM products for $32.5 million and cancel its remaining two options.

Table of Contents

Under the underlying royalty agreements, both Pfizer and Wyeth have the right to offset a portion of any future royalty payments owed to the Company. Accordingly, we deferred a portion of the revenue associated with each tranche of royalty right sold, including rights acquired upon the exercise of options, equal to the pro-rata share of the potential royalty offset. Such amounts associated with the offset rights against future royalty payments will be recognized as revenue upon receipt of future royalties from the respective partners.

Collaborative Research and Development and Other Revenue

Collaborative research and development and other revenues for 2005 were $10.5 million compared to $11.8 million for 2004 and $14.0 million for 2003. Collaborative research and development and other revenues include reimbursement for ongoing research activities, earned development milestones, and recognition of prior years up-front fees previously deferred in accordance with Staff Accounting Bulletin (SAB) No. 101 *Revenue Recognition*, as amended by SAB 104 (hereinafter referred to as SAB104). Revenue from distribution agreements includes recognition of up-front fees collected upon contract signing and deferred over the life of the distribution arrangement and milestones achieved under such agreements.

A comparison of collaborative research and development and other revenues is as follows (in thousands):

	Year Ended December 31,		
	2005	2004	2003
Collaborative research and development	$ 3,513	$ 7,843	$ 10,887
Development milestones	6,704	3,681	2,807
Other	310	311	314
	$ 10,527	$ 11,835	$ 14,008

Collaborative Research and Development. The decrease in ongoing research activities reimbursement revenue in 2005 compared to 2004 is due to the termination in November 2004 of our research arrangement with Lilly which contributed $4.0 million to revenue in 2004.

The decrease in ongoing research activities reimbursement revenue in 2004 compared to 2003 is due to lower funding from our research arrangement with Lilly, which contributed $4.0 million to revenue in 2004 compared to $5.7 million in 2003. Additionally, the decrease is due to the contractually agreed lower level of research activity and funding under our research arrangement with TAP, which contributed $3.4 million to revenue in 2004 compared to $4.2 million in 2003.

Development Milestones. Development milestones revenue in 2005 reflects net development milestones of $3.0 million earned from GlaxoSmithKline in connection with the commencement of Phase II studies of eltrombopag and Phase I studies of SB-559448 for the treatment of thrombocytopenia; $1.4 million, net for prior milestones received from Wyeth in connection with an agreement in the fourth quarter of 2005 to amend the research, development, and license agreement between Ligand and Wyeth; $1.2 million earned from Lilly in connection with the commencement of Phase II trials of LY674 for the treatment of atherosclerosis; and $1.1 million from TAP in connection with TAP s filing of an IND for LGD2941.

Development milestones revenue in 2004 includes net development milestones of $2.0 million from Pfizer as a result of Pfizer s filing with the FDA of a new drug application for lasofoxifene, $0.8 million earned from TAP in connection with TAP s selection of an additional selective androgen receptor modulator (SARM) as a second clinical candidate for development for the treatment of major androgen-related diseases, and $0.8 million earned from GlaxoSmithKline. Development milestone revenue in 2003 represents $0.9 million earned from Wyeth, a $1.1 million milestone from Lilly, and a $0.8 million milestone from GlaxoSmithKline.

Gross Margin

Gross margin on product sales was 76.0% in 2005 compared to 66.9% in 2004 and 52.0% in 2003. The increase in the margin in 2005 compared to 2004 is primarily due to the increase in sales of AVINZA. AVINZA represented 67.9% of net product sales for 2005 compared to 57.7% for 2004 and 30.0% for 2003. For both AVINZA and

Table of Contents

ONTAK we have capitalized license, royalty and technology rights recorded in connection with the acquisition of the rights to those products and accordingly, margins improve as sales of these products increase and there is greater coverage of the fixed amortization of the intangible assets. AVINZA cost of product sold includes the amortization of license and royalty rights capitalized in connection with the restructuring of our AVINZA license and supply agreement in November 2002. The total amount of capitalized license and royalty rights, $114.4 million, is being amortized to cost of product sold on a straight-line basis over 15 years. The total amount of ONTAK acquired technology, $45.3 million, is also amortized to cost of product sold on a straight-line basis over 15 years. ONTAK margins were also positively impacted during 2005 by lower royalties as a result of the restructuring of the Company s royalty obligation to Lilly as further discussed under Recent Development Restructuring of ONTAK Royalty. This restructuring resulted in no royalty liability owed to Lilly in 2005. This impact was partially offset by amortization of the $33.0 million paid to Lilly to restructure the ONTAK royalty and the recognition of deferred royalty expense previously paid to Lilly which under the sell-through revenue recognition method is recognized as the related product sales are recognized. The amount paid to restructure the ONTAK royalty is being amortized through 2014, the remaining life of the underlying patent, using the greater of the straight-line method or expense determined based on the tiered royalty schedule set forth under Restructuring of ONTAK Royalty above. In accordance with SFAS 142, *Goodwill and Other Intangibles* (SFAS 142), for both AVINZA and ONTAK, capitalized license, royalty and technology rights are amortized on a straight-line basis since the pattern in which the economic benefits of the assets are consumed (or otherwise used up) cannot be reliably determined. At December 31, 2005, acquired technology and products rights, net totaled $146.8 million.

Gross margins in 2005 were also favorably impacted by price increases on ONTAK, Targretin capsules and Targretin gel which became effective January 1, 2004 and July 1, 2005 and for AVINZA which became effective July 1, 2004 and April 1, 2005. Under the sell-through revenue recognition method, changes to prices do not impact net product sales and therefore gross margins until the product sells-through the distribution channel. Additionally, gross margin in 2004 reflects a charge to royalty expense in the amount of $3.0 million, recorded in the fourth quarter of 2004, for deferred royalties at the end of the contracted royalty period for which we did not have offset rights. Under the sell-through revenue recognition method, royalties paid based on unit shipments to wholesalers are deferred and recognized as royalty expense as those units are sold through and recognized as revenue. Royalties paid to technology partners are deferred as we have the right to offset royalties paid for product that are later returned against subsequent royalty obligations. Royalties for which we do not have the right to offset, however, (for example, at the end of the contracted royalty period) are expensed in the period the royalty obligation becomes due.

Gross margin in 2005 compared to 2004 was negatively impacted, however, by a higher proportionate level of AVINZA rebates and ONTAK chargebacks and rebates and the costs associated with our wholesaler distribution service agreements. Additionally, gross margin in 2005 compared to 2004 was negatively impacted by a $0.5 million write-off of ONTAK finished goods inventory due to the Company s updated assessment of the timing of certain clinical trials.

Gross margin on product sales was 66.9% in 2004 compared to 52.0% in 2003. The increase in the margin was primarily due to the increase in sales of AVINZA. Gross margin in 2004 was also favorably impacted by price increases on our products which became effective January 1, 2004 and July 1, 2004 and a lower level of promotional discounts paid to the Company s wholesaler customers. In the third and fourth quarters of 2004, we entered into distribution service agreements with the majority of our wholesaler customers. In connection with the implementation of these agreements, we no longer offer wholesalers promotional discounts or incentives. The cost of AVINZA product sold in 2004 also reflects the full-year impact of a reduction to the pricing of AVINZA purchases from Elan which occurred in prior periods. In November 2002, the Company and Elan agreed to amend the terms of the AVINZA license and supply agreement. Under the terms of the amended agreement, Elan s adjusted royalty and supply price of AVINZA was reduced to approximately 10% of the product s net sales, compared to approximately 30-35% in the prior agreement. Under the sell-through revenue recognition model, product shipped to the wholesaler is recorded as deferred cost of goods sold and subsequently recognized as cost of sales when it sells-through. Accordingly, the majority of product manufactured by Elan in 2002 at the higher contractual cost of production sold-through and was recognized as cost of sales in 2003. As a result, AVINZA gross margins for 2003 under

sell-through revenue recognition reflect this higher product cost compared to cost of product sold in 2004.

Table of Contents

Gross margin in 2004 compared to 2003 was negatively impacted, however, by a higher proportionate level of AVINZA rebates and ONTAK chargebacks and rebates and the costs associated with our wholesaler distribution service agreements. Additionally, as discussed above, gross margin in 2004 reflects a charge to royalty expense in the amount of $3.0 million for deferred royalties at the end of the contracted royalty period for which we did not have offset rights.

Overall, given the fixed level of amortization of the capitalized AVINZA license and royalty rights, we expect the AVINZA gross margin percentages in 2006 to continue to increase as sales of AVINZA increase.

Research and Development Expenses

Research and development expenses were $56.1 million in 2005 compared to $65.2 million in 2004 and $66.7 million in 2003. The major components of research and development expenses are as follows (in thousands):

	Years Ended December 31,		
	2005	**2004**	**2003**
Research			
Research performed under collaboration agreements	$ 3,611	$ 7,853	$ 10,535
Internal research programs	20,839	15,517	12,013
Total research	24,450	23,370	22,548
Development			
New product development	18,794	28,329	30,771
Existing product support (1)	12,831	13,505	13,359
Total development	31,625	41,834	44,130
Total research and development	$ 56,075	$ 65,204	$ 66,678

(1) Includes costs incurred to comply with post-marketing regulatory commitments.

Spending for research expenses amounted to $24.5 million for 2005 compared to $23.4 million for 2004. The overall increase in 2005 is due to an increased level of internal program research in the area of thrombopoietin (TPO) agonists. This increase is partially offset by a decrease in research performed under collaboration agreements due primarily to a lower contractual level of research funding under our agreement with TAP and lower research funding under the Lilly collaboration which concluded in November 2004.

Spending for development expenses decreased to $31.6 million for 2005 compared to $41.8 million for 2004. Such decrease reflects a lower level of expense for both new product development and existing product support. The decrease in expenses for new product development is due primarily to a reduced level of spending on Phase III clinical trials for Targretin capsules in NSCLC. In March 2005, we announced that the final data analysis for Targretin capsules in NSCLC showed that the trials did not meet their endpoints of improved overall survival and projected two-year survival. We are continuing to analyze the data and apply it to the continued development of Targretin in

NSCLC. The decrease in existing product support in 2005 as compared to 2004 is primarily due to lower expenses for Targretin capsules and ONTAK post-marketing regulatory studies.

Table of Contents

Overall, spending for research expenses remained relatively constant in 2004 compared to 2003, with increases in expenses for internal research programs offset by decreases in expenses for research performed under collaboration agreements. The decrease in expenses for research performed under collaboration agreements was due primarily to a lower contractual level of research funding under our agreement with TAP and a lower level of research funding agreed to with Lilly in connection with the November 2003 extension of our collaboration agreement through November 2004. The increase in internal research program expenses in 2004 compared to the 2003 period reflects an increased level of effort in the areas of thrombopoietin (TPO) agonists and peroxisome proliferation activated receptors (PPARs). The level of effort on selective androgen receptor modulators (SARMs) remained constant in 2004 as compared to 2003. Spending for development expenses decreased to $41.8 million in 2004 compared to $44.1 million in 2003 reflecting a lower level of expense for new product development. The decrease in expenses for new product development is due primarily to a reduced level of spending on Phase III clinical trials for Targretin capsules in NSCLC, which became fully enrolled in 2003. The decrease in 2004 as compared to 2003 is partially offset by a $1.1 million payment to The Salk Institute in March 2004 to buy out milestone payments, other payment sharing obligations and royalty payments due on future sales of lasofoxifene, a product under development by Pfizer. Pfizer filed an NDA for lasofoxifene with the FDA in August 2004.

A summary of our significant internal research and development programs is as follows:

Program	**Disease/Indication**	**Development Phase**
AVINZA	Chronic, moderate-to-severe pain	Marketed in U.S. Phase IV
ONTAK	CTCL	Marketed in U.S., Phase IV
	Chronic lymphocytic leukemia	Phase II
	Peripheral T-cell lymphoma	Phase II
	B-cell Non-Hodgkin s lymphoma	Phase II
	NSCLC third line	Phase II
Targretin capsules	CTCL	Marketed in U.S. and Europe
	NSCLC first-line	Phase III
	NSCLC monotherapy	Planned Phase II/III
	NSCLC second/third line	Planned Phase II/III
	Advanced breast cancer	Phase II
	Renal cell cancer	Phase II
Targretin gel	CTCL	Marketed in U.S.
	Hand dermatitis (eczema)	Planned Phase II/ III
	Psoriasis	Phase II
LGD4665 (Thrombopoietin oral mimic)	Idiopathic Thrombocytopenias (TCP), other TCPs	IND Track
LGD5552 (Glucocorticoid agonists)	Inflammation, cancer	IND Track
Selective androgen receptor modulator, e.g., LGD3303 (agonist/antagonist)	Male hypogonadism, female & male osteoporosis, male & female sexual dysfunction, frailty. Prostate cancer,	Pre-clinical

	hirsutism, acne, androgenetic alopecia.

We do not provide forward-looking estimates of costs and time to complete our ongoing research and development projects, as such estimates would involve a high degree of uncertainty. Uncertainties include our ability to predict the outcome of complex research, our ability to predict the results of clinical studies, regulatory requirements placed upon us by regulatory authorities such as the FDA and EMEA, our ability to predict the decisions of our collaborative partners, our ability to fund research and development programs, competition from other entities of which we may become aware in future periods, predictions of market potential from products that may be derived from our research and development efforts, and our ability to recruit and retain personnel or third-

Table of Contents

party research organizations with the necessary knowledge and skills to perform certain research. Refer to Risk Factors for additional discussion of the risks and uncertainties surrounding our research and development initiatives.

Selling, General and Administrative Expenses

Selling, general and administrative expenses were $74.7 million for 2005 compared to $65.8 million for 2004 and $52.5 million for 2003. The increase for 2005 reflects a higher level of costs associated with additional Ligand sales representatives hired in the second and third quarter of 2004 to promote AVINZA and higher advertising and promotion expenses for AVINZA, ONTAK and Targretin capsules. The 2005 period also reflects higher accounting and legal expenses incurred in connection with the Audit Committee s review of the Company s consolidated financial statements, the restatement and re-audits of the Company s consolidated financial statements and ongoing shareholder litigation. We expect selling, general and administrative expenses in 2006 to be higher than 2005 due to a continuing higher level of accounting expenses, including costs of compliance with the Sarbanes-Oxley Act, higher audit fees and consultant expenses, expected costs to be incurred in connection with employee retention agreements discussed under Recent Developments above, and higher AVINZA related clinical, advertising and promotion expenses Prior to the termination agreement with Organon, the companies shared equally all costs for AVINZA clinical, advertising, and promotion activities In connection with the termination of the Organon co-promotion agreement, however, starting in January 2006, we are now solely responsible for all such expenses. These increases are expected to be partially offset by lower sales force expenses as a result of the reduction in our AVINZA primary care sales force as discussed under Recent Developments above.

The increase in 2004 compared to 2003 is primarily due to costs associated with 36 additional Ligand sales representatives hired to promote AVINZA and higher advertising and promotion expenses for AVINZA in connection with our co-promotion activities with Organon which started in March 2003. The 36 additional sales representatives were hired in the second and third quarters of 2004 resulting in higher expenses in the third and fourth quarters of 2004 compared to the first two quarters of 2004 and the full year of 2003. Marketing expenses also increased in 2004 as a result of our increased emphasis on physician-attended product information and advisory meetings for AVINZA. Additionally, selling, general and administrative expenses reflect increased costs incurred in 2004 in connection with the development of an alternate source of supply (Cardinal Health PGS LLC or Cardinal) for AVINZA.

Co-promotion Expense

Co-promotion expense payable to Organon amounted to $32.5 million in 2005 compared to $30.1 million for 2004 and $9.4 million for 2003. Prior to the restatement of our revenues to the sell-through revenue recognition method and through the third quarter of 2005, prior to the termination of the co-promotion agreement as discussed under Overview, we calculated the amount owed to Organon using the sell-in revenue recognition method. Since revenues based on the sell-in revenue recognition method were higher than revenues based on the sell-through revenue recognition method for 2004 and 2003, the co-promotion expense for these years is higher than the contracted 30% rate. Likewise, the co-promotion expense for the nine months ended September 30, 2005 was determined using the sell-in revenue recognition method, which was lower than reported revenues based on sell-through revenue recognition. Accordingly, co-promotion expense for this period as a percentage of net AVINZA sales (28%) was lower than the contracted rate of 30%. As previously disclosed, the companies were in discussions regarding the calculation of prior co-promote fees under the co-promotion agreement. In connection with the termination of the co-promotion agreement, the companies resolved their disagreement concerning prior co-promote fees and as a result, we paid Organon $14.75 million in January 2006. Resolution of this matter resulted in no material adjustment to amounts previously recorded for co-promotion expense. Additionally, in connection with the termination agreement, the companies agreed that Organon would be paid 30% of reported U.S. GAAP net sales for the fourth quarter of 2005. This resulted in fourth quarter 2005 co-promotion expense of $10.0 million which was paid in February 2006. During the transition period of the termination agreement, the companies agreed that Organon would be paid 23% of reported U.S. GAAP net sales through September 30, 2006. After termination, Ligand will make quarterly royalty payments to Organon equal to 6.5% of AVINZA net sales through December 31, 2012 and thereafter 6.0% through patent expiration, currently anticipated to be November 2017. Additionally, as described above, Ligand will now pay 100% of all AVINZA related clinical, advertising, and promotion expenses.

Table of Contents

The termination and return of rights transaction with Organon requires the analysis of several complex accounting alternatives. Accordingly, we are still in the process of determining the appropriate accounting treatment for the transaction in 2006 and going forward. Certain of these alternatives, however, could result in the recognition of significant additional expense in our consolidated statement of operations for the first quarter of 2006. We expect to complete our determination of the appropriate accounting by the time we file our first quarter 2006 Form 10-Q.

Other Expenses, Net

Other expenses, net were $9.9 million for 2005 compared to $7.5 million for 2004 and $20.4 million for 2003.

Interest expense increased to $12.5 million for 2005 compared to $12.3 million for 2004 and $11.1 million for 2003. Interest expense in 2005, 2004, and 2003 primarily represents interest on the $155.3 million of 6% convertible subordinated notes that we issued in November 2002. The increase in interest expense in 2004 compared to 2003 is due primarily to interest on a note payable secured by one of our corporate office buildings. Effective December 31, 2003, the entity from which we leased the building (Nexus Equity VI LLC or Nexus) was consolidated in connection with the implementation of FIN 46® *Consolidation of Variable Interest Entities, an interpretation of Accounting Research Bulletin No. 51*. Prior to that, the lease arrangement with Nexus was treated as an operating lease. We subsequently acquired the portion of Nexus we did not previously own in April 2004.

Other, net reflects income of $0.7 million in 2005 compared to $3.7 million in 2004 and net expenses of $10.0 million in 2003. In September 2004, we agreed to vote our shares of X-Ceptor in favor of the acquisition of X-Ceptor by Exelixis Inc. (Exelixis). Exelixis acquisition of X-Ceptor was subsequently completed in October, 2004 and in connection therewith, Ligand received shares of Exelixis common stock. The shares were restricted securities for which a resale registration statement has been filed. Such shares are subject to trading restrictions for up to two years. Additionally, approximately 21% of the shares were placed in escrow for up to one year to satisfy indemnification and other obligations. As of December 31, 2005, there were no shares remaining in escrow. We recorded a net gain on the transaction in the fourth quarter of 2004 of approximately $3.7 million, based on the fair market value of the consideration received.

Other, net expenses of $10.0 million in 2003 include the March 2003 write-off of a $5.0 million one-time payment made in July 2002 to X-Ceptor Therapeutics, Inc. (or X-Ceptor) to extend Ligand s right to acquire the outstanding stock of X-Ceptor not already held by Ligand. In March 2003, we informed X-Ceptor that we would not exercise the purchase right and wrote-off the purchase right valued at $4.0 million that was recorded in 1999.

Cumulative Effect of Accounting Change

In January 2003, the Financial Accounting Standards Board (FASB) issued FASB Interpretation No. 46 (FIN 46), *Consolidation of Variable Interest Entities, an interpretation of ARB No. 51*, which was subsequently revised in December 2003 (FIN 46(R)). FIN 46(R) requires the consolidation of certain variable interest entities (VIEs) by the primary beneficiary of the entity if the equity investment at risk is not sufficient to permit the entity to finance its activities without additional subordinated financial support from other parties, or if the equity investors lack the characteristics of a controlling financial interest.

We implemented FIN 46 effective December 31, 2003, and consolidated the entity from which we leased one of our two corporate office buildings as of that date, as we determined that the entity was a VIE, as defined by FIN 46, and that we would absorb a majority of its expected losses if any, as defined by FIN 46(R). Accordingly, we consolidated the assets of the entity, which consist of land, the building, and related tenant improvements, with a total carrying value of $13.6 million, net of accumulated depreciation. Additionally, we consolidated the entity s debt of $12.5 million and non-controlling interest of $0.6 million. In connection with the implementation of FIN 46, we also recorded a $2.0 million charge ($0.03 per share) as a cumulative effect of the accounting change on December 31, 2003.

Table of Contents

Income Taxes

Income tax expense was $0.1 million for 2005 compared to approximately $0.2 million for 2004 and $0.1 million in 2003. At December 31, 2005, we have both federal and state net operating loss carryforwards of approximately $554.5 million and $73.2 million, respectively, which will begin expiring in 2006. The difference between the federal and California tax loss carryforwards is primarily due to the capitalization of research and development expenses for California income tax purposes and the 50% to 60% limitation on losses incurred prior to 2004 in California. We have $25.5 million of federal research and development credits carryforwards which will expire beginning in 2006, and $15.4 million of California research and development credits that have no expiration date.

Pursuant to Internal Revenue Code Sections 382 and 383, use of a portion of net operating loss and credit carryforwards related to Glycomed and Seragen will be limited because of cumulative changes in ownership of more than 50% that occurred within three periods during 1989, 1992, and 1996. Such tax net operating loss and credit carryforwards have been reduced, including the related deferred tax assets. The Company has also completed a 382 study for Ligand, excluding Glycomed and Seragen, and has determined that Ligand s net operating losses and credits are not currently subject to any limitations under Internal Revenue Code Sections 382 and 383. Future changes in ownership could result in limitations of utilization of Ligand s net operating losses and credits under Internal Revenue Code Sections 382 and 383.

The Company s research and development credits pertain to federal and California jurisdictions. These jurisdictions require that the Company create minimum documentation and support, such as done via a Research & Development Credit Study . In the absence of sufficient documentation and support these government jurisdictions may disallow some or all of the credits. Although the Company has not completed a formal study, the Company believes that it maintains sufficient documentation to support the benefiting of the credits in the consolidated financial statements. Prior to utilizing a significant portion of the credits to reduce taxes payable, the Company will review its documentation and support to determine if a formal study is necessary.

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, product sales, capital and operating lease transactions, accounts receivable factoring and equipment financing arrangements and investment income.

Working capital was a deficit of $102.2 million at December 31, 2005 compared to a deficit of $48.5 million at December 31, 2004. Cash, cash equivalents, short-term investments, and restricted investments totaled $88.8 million at December 31, 2005 compared to $114.9 million at December 31, 2004. We primarily invest our cash in United States government and investment grade corporate debt securities. Restricted investments at December 31, 2005 consist of certificates of deposit held with a financial institution as collateral under equipment financing and third-party service provider arrangements. Restricted investments at December 31, 2004 also included shares of Exelixis common stock, that had certain trading limitations, received in connection with the sale of our shares of X-Ceptor.

Operating Activities

Operating activities provided cash of $8.4 million in 2005, $5.8 million in 2004, and $0.3 million in 2003. Operating cash flow in 2005 benefited from increased product shipments primarily due to the growth of AVINZA and lower development expenses as a result of the conclusion of the clinical trials for Targretin capsules in NSCLC in March 2005. Operating cash was negatively impacted, however, by increased accounting and legal expenses in connection with the restatement of our prior period consolidated financial statements, SEC investigation, and shareholder litigation.

Non-cash operating items in 2005 increased $8.4 million compared to 2004 and decreased $8.7 million compared to 2003. The change compared to 2004 includes higher amortization of acquired technology and license rights of $3.0 million resulting from the capitalizaton of $33.0 million paid to Lilly in connection with the

Table of Contents

restructuring of the Company s ONTAK royalty agreement. Additionally, non-cash operating items in 2004 included a development milestone of approximately $2.0 million received from Pfizer, in connection with Pfizer s filing with the FDA of a new drug application for lasofoxifene, paid in stock in September 2004, and a net gain on sale of equity investments totaling $3.7 million. Non-cash operating items in 2003 include the $9.0 million write-off of the $5.0 million X-Ceptor payment to extend our X-Ceptor purchase right and capitalization of the purchase right of $4.0 million in March 2003, in connection with our decision to not acquire X-Ceptor, and the non-cash cumulative effect of the change in accounting principle (approximately $2.0 million) recognized in connection with the implementation of FIN 46(R).

Changes in operating assets and liabilities provided cash of $26.6 million in 2005 primarily due to increases in accounts payable and accrued liabilities of $13.7 million, deferred revenue of $4.7 million, decreases in accounts receivable, net of $9.9 million, and decreases in other current assets of $2.0 million, partially offset by an increase in inventories of $3.4 million. This compares to cash provided by changes in operating assets and liabilities of $41.2 million in 2004 primarily due to increases in deferred revenue of $47.9 million and accounts payable and accrued liabilities of $9.8 million, partially offset by increases in accounts receivable and inventories of $11.9 million and $3.3 million, respectively. For 2003, cash provided by changes in operating assets and liabilities provided cash of $69.9 million primarily due to increases in deferred revenue of $57.0 million and accounts payable and accrued liabilities of $24.2 million, partially offset by increases in accounts receivable and inventories of $6.5 million and $3.5 million, respectively.

The increase in deferred revenue in each period reflects shipments of product into the wholesale and retail distribution channels offset in part by end-customer product demand recognized as revenue under the sell-through revenue recognition method. The decrease in accounts receivable in the 2005 period reflects a decrease in gross accounts receivable at quarter-end as wholesalers are now purchasing product more consistently throughout each quarter in accordance with the requirements of the distribution services agreements. The increase in accounts receivable in 2004 and 2003 reflects increasing wholesaler purchases in connection with the growth of product demand, primarily AVINZA for which co-promotion activities with Organon started in 2003. Likewise, the increase in accounts payable and accrued liabilities for each year primarily reflects the growth in Medicaid rebates and government chargebacks in connection with the growth in demand of AVINZA and ONTAK. Additionally, the increase in accrued liabilities in the 2005 period reflects the delay in payment of co-promotion expenses to Organon for the second and third quarters of 2005 to the first quarter of 2006 in connection with the terminationof the co-promotion agreement, as further discussed under Recent Developments above. Operating cash flows in 2003 also benefited from the impact of the accounts receivable factoring arrangement which was entered into in the second quarter of 2003.

In connection with the termination of the co-promotion agreement, we will pay Organon $37.75 million on or before October 15, 2006 and $10.0 million on or before January 15, 2007, provided that Organon has made its minimum required level of sales calls. Additionally, we agreed to pay Organon 23% of AVINZA net sales for co-promotion activities through September 30, 2006 (the transition period), and a 6.5% royalty on AVINZA net sales through December 31, 2012 and thereafter a 6.0% royalty through patent expiration.

Investing Activities

Investing activities used cash of $33.7 million in 2005 and provided cash of $19.6 million in 2004 and used cash of $14.2 million in 2003. The use of cash in 2005 reflects $33.0 million of payments for the buy-down of ONTAK royalty payments in connection with the amended royalty agreement entered into in November 2004 between the Company and Lilly, and $2.6 million of purchases of property and equipment. Additionally, the use of cash in 2005 was partially offset by the net proceeds from the sale of short-term investments of $1.9 million.

Cash provided by investing activities for 2004 reflects net proceeds of $14.1 million from the sale of short-term investments and $9.2 million from the maturing of restricted investments which was used to pay interest on our 6% convertible subordinated notes. The use of cash for investing activities in 2004 reflects $3.6 million for purchases for property and equipment. The use of cash in 2003 reflects the net purchase of short-term investments of $18.0 million, a $4.1 million payment to Elan in connection with the November 2002 restructuring of the AVINZA license and supply agreement and capital purchases of $2.8 million. Cash provided by investing activities for 2003 includes

41

Table of Contents

$10.4 million from the maturing of restricted investments which was subsequently used to pay interest on our 6% convertible subordinated notes.

Financing Activities

Financing activities used cash of $0.2 million in 2005 compared to cash provided of $7.9 million in 2004 and $32.1 million in 2003. Cash used in financing activities in 2005 reflects repayment of long-term debt and net payments under equipment financing arrangements of $0.3 million and $0.8 million, respectively, partially offset by net proceeds from the exercise of employee stock options and stock purchases under the Company s employee stock purchase plan of $0.9 million.

Cash provided by financing activities in 2004 includes net proceeds of $6.6 million from the exercise of employee stock options and stock purchases under our employee stock purchase plan and $1.8 million of net proceeds received under equipment financing arrangements. Cash provided by financing activities in 2003 includes net proceeds of $45.0 million from the issuance of common stock through a private placement of 3,483,593 shares of our common stock, $4.5 million from the exercise of employee stock options and employee stock purchases, and $1.1 million from equipment financing arrangements. These proceeds were offset by the $15.9 million repurchase and retirement of approximately 2.2 million shares of our outstanding common stock held by an affiliate of Elan in connection with a November 2002 share repurchase agreement completed in February 2003, and payments of $2.5 million on equipment financing arrangements.

Certain of our property and equipment is pledged as collateral under various equipment financing arrangements. As of December 31, 2005, $5.8 million was outstanding under such arrangements with $2.4 million classified as current. Our equipment financing arrangements have terms of three to five years with interest ranging from 4.73% to 9.33%.

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 including during the transition period of our AVINZA co-promotion agreement with Organon, which will conclude September 30, 2006; 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. We will also consider additional equipment financing arrangements similar to arrangements currently in place.

Leases and Off-Balance Sheet Arrangements

We lease certain of our 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%.

Table of Contents

Contractual Obligations

As of December 31, 2005, future minimum payments due under our contractual obligations are as follows (in thousands):

		Payments Due by Period			
	Total	Less than 1 year	1-3 years	3-5 years	After 5 years
Capital lease obligations (1)	$ 6,513	$ 2,777	$ 3,408	$ 328	$ ¾
Operating lease obligations	20,370	2,995	3,860	3,833	9,682
Loan payable to bank (2)	14,000	1,191	12,809	¾	¾
6% Convertible Subordinated Notes (3)	173,880	9,315	164,565	¾	¾
Other liabilities (4)	3,600	3,098	502	¾	¾
Distribution service agreements	5,865	5,865	¾	¾	¾
Consulting agreements	855	855	¾	¾	¾
Manufacturing agreements	10,731	10,731	¾	¾	¾
Total contractual obligations	$ 235,814	$ 36,827	$ 185,144	$ 4,161	$ 9,682

(1) Includes $0.7 million of interest payments.

(2) Includes interest of $ 0.8 million and $1.3 million for 2006 and for the period from 2007 to 2008, respectively.

(3) Includes interest of $9.3 million and $9.3 million for 2006 and 2007, respectively.

(4) Other liabilities include merger contingencies and a liability under a royalty financing arrangement. Deferred revenues are

excluded because they have no effect on future liquidity.

As of December 31, 2005, we have net open purchase orders (defined as total open purchase orders at year end less any accruals or invoices charged to or amounts paid against such purchase orders) totaling approximately $14.5 million. In the next 12 months, we also plan to spend approximately $3.2 million on capital expenditures.

In March 2004, we entered into a five-year manufacturing and packaging agreement with Cardinal Health PTS, LLC (Cardinal) under which Cardinal will manufacture AVINZA at its Winchester, Kentucky facility. Under the terms of the agreement, we committed to certain minimum annual purchases ranging from approximately $1.6 million to $2.3 million. In August 2005, the FDA approved the production of AVINZA at the Cardinal facility.

In January 2006, we signed an agreement with Organon that terminated the AVINZA co-promotion agreement between the two companies and returns AVINZA rights to Ligand. In connection with this agreement, we will pay Organon $37.75 million on or before October 15, 2006 and $10.0 million on or before January 15, 2007, provided that Organon has made its minimum required level of sales calls. After termination, we will make quarterly royalty payments to Organon equal to 6.5% of AVINZA net sales through December 31, 2012 and thereafter 6.0% through patent expiration, currently anticipated to be November 2017. The termination and return of rights transaction with Organon requires the analysis of several complex accounting alternatives. Accordingly, we are still in the process of determining the appropriate accounting treatment for the transaction in 2006 and going forward. Certain of these alternatives, however, could result in the recognition of significant additional expense in our consolidated statement of operations for the first quarter of 2006. We expect to complete our determination of the appropriate accounting by the time we file our first quarter 2006 Form 10-Q.

In March 2006, we entered into employee retention agreements with approximately 67 of our key employees, including a number of our executive officers. The agreements provide for certain retention or stay bonus payments to be paid in cash and/or stock options under specified circumstances as an additional incentive to remain employed in good standing with the Company. The retention or stay bonus generally vest at the end of 2006 and total payments to employees of approximately $2.7 million would be made in January 2007 if all the participants qualify for the payments. Stock options granted totaled approximately 122,000 and have an exercise price of $11.90.

Critical Accounting Policies

Certain of our policies require the application of management judgment in making estimates and assumptions that affect the amounts reported in the consolidated financial statements and disclosures made in the accompanying

Table of Contents

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 judgment in determining such estimates and assumptions is by nature, subject to a degree of uncertainty. Accordingly, actual results could differ materially from the estimates made. Our critical accounting policies are as follows:

Revenue Recognition

The Company generates revenue from product sales, collaborative research and development arrangements, and other activities such as distribution agreements, royalties, and sales of technology rights. 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.

The Company recognizes product revenue in accordance with SAB 104 and SFAS 48 *Revenue Recognition When Right of Return Exists* (SFAS 48). SAB 104 states that revenue should not be recognized until it is realized or realizable and earned. Revenue is realized or realizable and earned when all of the following criteria are met: (1) persuasive evidence of an arrangement exists; (2) delivery has occurred or services have been rendered; (3) the seller s price to the buyer is fixed and determinable; and (4) collectibility is reasonably assured. SFAS 48 states that revenue from sales transactions where the buyer has the right to return the product shall be recognized at the time of sale only if (1) the seller s price to the buyer is substantially fixed or determinable at the date of sale, (2) the buyer has paid the seller, or the buyer is obligated to pay the seller and the obligation is not contingent on resale of the product, (3) the buyer s obligation to the seller would not be changed in the event of theft or physical destruction or damage of the product, (4) the buyer acquiring the product for resale has economic substance apart from that provided by the seller, (5) the seller does not have significant obligations for future performance to directly bring about resale of the product by the buyer, and (6) the amount of future returns can be reasonably estimated.

Product sales

The Company has determined that domestic shipments made to wholesalers for AVINZA, ONTAK, Targretin capsules and Targretin gel do not meet the revenue recognition criteria of SFAS 48 and SAB 104 at the time of shipment, and therefore such shipments are accounted for using the sell-through method. Under the sell-through method, the Company does not recognize revenue upon shipment of product to the wholesaler. For these product sales, the Company invoices the wholesaler, records deferred revenue at gross invoice sales price less estimated cash discounts and for ONTAK, end-customer returns, and classifies the inventory held by the wholesaler as deferred cost of goods sold within Other current assets. At that point, the Company makes an estimate of units that may be returned and records a reserve for those units against the deferred cost of goods sold account. The Company recognizes revenue when such inventory is sold through (as defined hereafter), on a first-in first-out (FIFO) basis. Sell through for ONTAK, Targretin capsules and Targretin gel are considered to be at the point of out movement from the wholesaler to the wholesaler s customer. Sell through for AVINZA is considered to be at the prescription level or at the point of patient consumption for channels with no prescription requirements.

Table of Contents

A summary of the revenue recognition policy used for each of our products and the expiration of the underlying patents for each product is as follows:

	Method	Revenue Recognition Event	Patent Expiration
AVINZA	Sell-through	Prescriptions	November 2017
ONTAK	Sell-through	Wholesaler out-movement	December 2014
Targretin capsules	Sell-through	Wholesaler out-movement	October 2016
Targretin gel	Sell-through	Wholesaler out-movement	October 2016
Panretin	Sell-in	Shipment to wholesaler	August 2016
International	Sell-in	Shipment to international distributor	February 2011 through April 2013

For the years ended December 31, 2005, 2004, and 2003, net product sales recognized under the sell-through method represented approximately 97%, 96% and 94%, respectively, of total net product sales.

Additionally under the sell-through method, royalties paid based on unit shipments to wholesalers are deferred and recognized as royalty expense as those units are sold through and recognized as revenue. Royalties paid to technology partners are deferred as the Company has the right to offset royalties paid for product that are later returned against subsequent royalty obligations. Royalties for which the Company does not have the ability to offset (for example, at the end of the contractual royalty period) are expensed in the period the royalty obligation becomes due.

The Company estimates sell-through based upon (1) analysis of third-party information, including information obtained from certain wholesalers with respect to their inventory levels and sell-through to customers, and third-party market research data, and (2) the Company s internal product movement information. To assess the reasonableness of third-party demand (i.e. sell-through) information, the Company prepares separate demand reconciliations based on inventory in the distribution channel. Differences identified through these reconciliations outside an acceptable range will be recognized as an adjustment to the third-party reported demand in the period those differences are identified. This adjustment mechanism is designed to identify and correct for any material variances between reported and actual demand over time and other potential anomalies such as inventory shrinkage at wholesalers. The Company s estimates are subject to the inherent limitations of estimates that rely on third-party data, as certain third-party information is itself in the form of estimates. The Company s sales and revenue recognition under the sell-through method reflect the Company s estimates of actual product sold through the channel.

We use information from external sources to estimate our gross product sales under the sell-through revenue recognition method and significant gross to net sales adjustments. Our estimates include product information with respect to prescriptions, wholesaler out-movement and inventory levels, and retail pharmacy stocking levels, and our own internal information. We receive information from IMS, a supplier of market research to the pharmaceutical industry, which we use to estimate sell-through demand for our products and retail pharmacy inventory levels. We also receive wholesaler out-movement and inventory information from our wholesaler customers that is used to support and validate our demand-based, sell-through revenue recognition estimates. Additionally, we use wholesaler provided out-movement information to estimate ONTAK sell-through revenue as this data is not available from IMS. The inventory information received from wholesalers is a product of their record-keeping process and their internal controls surrounding such processes.

We recognize revenue for Panretin upon shipment to wholesalers as our wholesaler customers only stock minimal amounts of Panretin, if any. As such, wholesaler orders are considered to approximate end-customer demand for the product. Revenues from sales Panretin are net of allowances for rebates, chargebacks and discounts. For international shipments of our product, revenue is recognized upon shipment to our third-party international distributors.

Table of Contents

Sale of Royalty Rights

Revenue from the sale of royalty rights represents the non-refundable sale to third parties of rights for and exercise of options to acquire future royalties the Company may earn from the sale of products in development with its collaborative partners. If the Company has no continuing involvement in the research, development or marketing of these products, sales of royalty rights are recognized as revenue in the period the transaction is consummated or the options are exercised or expired. If the Company has significant continuing involvement in the research, development or marketing of the product, proceeds received for the sale of royalty rights are accounted for as a financing arrangement in accordance with EITF 88-18: *Sales of Future Revenues*.

Collaborative Research and Development and Other Revenues

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. Payments received in advance of performance or delivery are recorded as deferred revenue and subsequently recognized over the period of performance or upon delivery.

Net Product Sales

The Company s net product sales represent total product sales less allowances for rebates, chargebacks, discounts, promotions, and losses to be incurred on returns from wholesalers resulting from increases in the selling price of the Company s products. In addition, the Company incurs certain distributor service agreement fees related to the management of its product by wholesalers. These fees have been recorded within net revenues. For ONTAK, the Company also has established reserves for returns from end customers after sell-through revenue recognition has occurred. Due to estimates and assumptions inherent in determining the amount of returns, chargebacks, and rebates, the actual amount of product returns and claims for chargeback and rebates may be materially different from our estimates.

Table of Contents

The following summarizes the activity in the accrued liability accounts related to allowances for loss on returns, rebates, chargebacks, other discounts, and ONTAK end-customer and Panretin returns (in thousands):

	Losses on Returns Due to Changes in Price	Medicaid Rebates	Managed Care Rebates and Other Rebates	Charge-backs	Other Discounts	ONTAK End-customer and Panretin Returns	Total
Balance at January 1, 2003	$ 974	$ 207	$ 31	$ 117	$ 826	$ 1,797	$ 3,952
Provision	4,229	2,724	852	2,184	9,035	1,547	20,571
Payments	¾	(1,239)	(457)	(2,123)	(9,344)	¾	(13,163)
Charges	(856)	¾	¾	¾	¾	(1,308)	(2,164)
Balance at December 31, 2003	4,347	1,692	426	178	517	2,036	9,196
Provision	5,018	14,430	5,773	3,962	6,495	3,015	38,693
Payments	¾	(11,074)	(4,455)	(3,684)	(7,008)	¾	(26,221)
Charges	(3,025)	¾	¾	¾	¾	(2,492)	(5,517)
Balance at December 31, 2004	6,340	5,048	1,744	456	4	2,559	16,151
Provision	1,801(1)	18,852	10,592	5,874	¾	3,439	40,558
Payments	¾	(18,552)	(8,869)	(6,130)	(4)	¾	(33,555)
Charges	(4,103)	¾	¾	¾	¾	(3,322)	(7,425)
Balance at December 31, 2005	$ 4,038	$ 5,348	$ 3,467	$ 200	$ ¾	$ 2,676	$ 15,729

(1) The provision for losses on returns in 2005 is net of a $2.9 million reduction in the allowance for such losses recorded in the fourth quarter of 2005. This adjustment resulted from lower rates of return on lots of AVINZA that

closed out in the fourth quarter of 2005, thereby lowering the historical weighted average rate of return used for estimating the allowance.

Allowance for Return Losses

Product sales are net of adjustments for losses resulting from price increases the Company may experience on product returns from its wholesaler customers. Our policy for returns allows customers, primarily wholesale distributors, to return our oncology products three months prior to and six months after expiration. For ONTAK, customers are generally allowed to return product in exchange for replacement ONTAK vials. Our policy for returns of AVINZA allows customers to return the product six months prior to and six months after expiration. Upon an announced price increase, typically in the quarter prior to when a price increase becomes effective, the Company revalues its estimate of deferred product revenue to be returned to recognize the potential higher credit a wholesaler may take upon product return determined as the difference between the new price and the previous price used to value the allowance. Due to estimates and assumptions inherent in determining the amount of return losses, the actual amount of product returns may be materially different from our estimates. In addition, because of the inherent difficulties of predicting possible changes to the estimates and assumptions used to determine losses to be incurred on returns from price changes due to, among other factors, changes in future prescription levels and wholesaler inventory practices, we are unable to quantify an estimate of the reasonably likely effect of any such changes on our results of operations or financial position. For reference purposes, a 10% to 20% variance to our estimated allowance for return losses as of December 31, 2005 would result in an approximate $0.4 million to $0.8 million adjustment to net product sales.

ONTAK End-Customer Returns

Under the sell-through method of revenue recognition, the estimate of product returns from the wholesalers does not result in a gross to net sales adjustment since the shipment of product to the wholesalers does not result in revenue recognition. For ONTAK, revenue is recognized when product is shipped from wholesalers to end-customers, primarily hospitals and clinics that have the capability to administer the product to patients. These customers have the right to return expired product to the wholesaler who in turn can return the product to the Company. In accordance with SFAS 48, we record a return provision upon sell-through of ONTAK by establishing

Table of Contents

a reserve in an amount equal to our estimate of sales recorded but for which the related products are expected to be returned by the end customer. Estimates of the sales return accrual are based on historical experience. Due to the estimates and assumptions inherent in determining the amount of ONTAK end-customer returns, the actual amount of product returns may be materially different from our estimates. However, based on our experience with returns of ONTAK from end-customers, we do not believe that a material change to our estimated allowance for ONTAK end-customer returns is reasonably likely.

Medicaid Rebates

Our products are subject to state government-managed Medicaid programs whereby discounts and rebates are provided to participating state governments. We account for Medicaid rebates by establishing an accrual in an amount equal to our estimate of Medicaid rebate claims attributable to sales recognized in that period. We determine our estimate of the Medicaid rebates accrual primarily based on historical experience regarding Medicaid rebates, as well as current and historical prescription activity provided by external sources, current contract prices and any expected contract changes. We additionally consider any legal interpretations of the applicable laws related to Medicaid and qualifying federal and state government programs and any new information regarding changes in the Medicaid programs regulations and guidelines that would impact the amount of the rebates. We adjust the accrual periodically throughout each period to reflect actual experience, expected changes in future prescription volumes and any changes in business circumstances or trends. In addition, because of the inherent difficulties of predicting the impact on our estimates and assumptions of rapidly evolving state Medicaid programs and regulations, we are unable to quantify an estimate of the reasonably likely effect of any such changes on our results of operations or financial position. For reference purposes, a 10% to 20% variance to our estimated allowance for state Medicaid rebates as of December 31, 2005 would result in an approximate $0.6 million to $1.2 million adjustment to net product sales.

Government Chargebacks

Our products are subject to certain programs with federal government entities and other parties whereby pricing on products is extended below wholesaler list price to participating entities. These entities purchase products through wholesalers at the lower vendor price, and the wholesalers charge the difference between their acquisition cost and the lower vendor price back to us. We account for chargebacks by establishing an accrual in an amount equal to our estimate of chargeback claims. We determine our estimate of the chargebacks primarily based on historical experience regarding chargebacks and current contract prices under the vendor programs. We consider vendor payments and our claim processing time lag and adjust the accrual periodically throughout each period to reflect actual experience and any changes in business circumstances or trends. Due to estimates and assumptions inherent in determining the amount of government chargebacks, the actual amount of claims for chargebacks may be materially different from our estimates. Based on our experience with government chargebacks, however, we do not believe that a material change to our estimated allowance for chargebacks is reasonably likely.

Managed Health Care Rebates and Other Contract Discounts

We offer rebates and discounts to managed health care organizations and to other contract counterparties such as hospitals and group purchasing organizations in the U.S. We account for managed health care rebates and other contract discounts by establishing an accrual in an amount equal to our estimate of managed health care rebates and other contract discounts. We determine our estimate of the managed health care rebates and other contract discounts accrual primarily based on historical experience regarding these rebates and discounts and current contract prices. We also consider the current and historical prescription activity provided by external sources, current contract prices and any expected contract changes and adjust the accrual periodically throughout each period to reflect actual experience and any changes in business circumstances or trends. Due to estimates and assumptions inherent in determining the amount of rebates and contract discounts, the actual amount of claims for rebates and discounts may be materially different from our estimates. In addition, because of the inherent difficulties of predicting the impact on our estimates and assumptions of rapidly evolving managed care programs, we are unable to quantify an estimate of the reasonably likely effect of any such changes on our results of operations or financial position. For reference purposes, a 10% to 20% variance to our estimated allowance for managed health care and other contract discounts as of December 31, 2005 would result in an approximate $0.2 million to $0.5 million adjustment to net product sales.

Table of Contents

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. If actual future demand or market conditions are less favorable than our estimates, then additional material inventory write-downs might be required.

Acquired Technology and Product Rights

Acquired technology and product rights represent payments related to our acquisition of ONTAK and license and royalty rights for AVINZA. In accordance with SFAS 142, these payments are amortized on a straight line basis since the pattern in which the economic benefit of these assets are consumed (or otherwise used up) cannot be reliably determined. Accordingly, acquired technology and product rights are amortized on a straight-line basis over 15 years, which approximated the remaining patent life at the time the assets were acquired and represents the period estimated to be benefited. Specifically, we are amortizing the ONTAK asset through June 2014, which is approximate to the expiration date of its U.S. patent of December 2014. The AVINZA asset is being amortized through November 2017, the expiration of its U.S. patent.

Impairment of Long-Lived Assets

We review long-lived assets, including acquired technology and product rights and property and equipment, during the fourth quarter of each year, or whenever events or circumstances indicate that the carrying amount of the assets may not be fully recoverable. We measure the recoverability of assets to be held and used by comparing the carrying amount of an asset to the future undiscounted net cash flows expected to be generated by the asset. If an asset is considered to be impaired, the impairment to be recognized is measured as the amount by which the carrying amount of the asset exceeds its fair value. Fair value of our long-lived assets is determined using the expected cash flows discounted at a rate commensurate with the risk involved. Assumptions and estimates used in the evaluation of impairment may affect the carrying value of long-lived assets, which could result in impairment charges in future periods.

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, 2005. Our impairment assessment could be impacted by various factors including a more than insignificant disruption of supply, new competing products or technologies that could result in a significant decrease in the demand for or the pricing of our products, regulatory actions that require us to restrict or cease promotion of the products, a product recall to address regulatory issues, and/or patent claims by third parties.

Income Taxes

Income taxes are accounted for under the liability method. This approach requires the recognition of deferred tax assets and liabilities for the expected future tax consequences of differences between the tax basis of assets or liabilities and their carrying amounts in the consolidated financial statements. A valuation allowance is provided for deferred tax assets if it is more likely than not that these items will either expire before we are able to realize their benefit or if future deductibility is uncertain. Developing the provision for income taxes requires significant judgment and expertise in federal and state income tax laws, regulations and strategies, including the determination of deferred tax assets and liabilities and, if necessary, any valuation allowances that may be required for deferred tax assets. Our judgments and tax strategies are subject to audit by various taxing authorities. While we believe we have provided adequately for our income tax liabilities in our consolidated financial statements, adverse determinations by these taxing authorities could have a material adverse effect on our consolidated financial condition and results of operations.

Stock-Based Compensation

We grant stock options to our employees at an exercise price equal to the fair value of the shares at the date of grant and account for these stock option grants in accordance with APB Opinion No. 25, *Accounting for Stock*

Table of Contents

Issued to Employees (APB 25) and related interpretations. Under APB 25, when stock options are issued with an exercise price equal to the market price of the underlying stock on the date of grant, no compensation expense is recognized in the statement of operations. Refer to Note 3 of the notes to consolidated financial statements for pro-forma disclosures of the impact on our consolidated financial statements of accounting for stock options under the fair-value requirements of SFAS No. 123, *Accounting for Stock-based Compensation*.

New Accounting Pronouncements

In November 2005, the FASB issued Staff Position (FSPs) Nos. FSPs 115-1 and 124-1, *The Meaning of Other-Than-Temporary Impairment and Its Application to Certain Investments*, in response to Emerging Issues Task Force 03-1, *The Meaning of Other-Than-Temporary Impairment and Its Application to Certain Investments* (EITF 03-1). FSPs 115-1 and 124-1 provide guidance regarding the determination as to when an investment is considered impaired, whether that impairment is other-than-temporary, and the measurement of an impairment loss. FSPs 115-1 and 124-1 also include accounting considerations subsequent to the recognition of an other-than-temporary impairment and requires certain disclosures about unrealized losses that have not been recognized as other-than-temporary impairments. These requirements are effective for annual reporting periods beginning after December 15, 2005. Adoption of the impairment guidance contained in FSPs 115-1 and 124-1 is not expected to have a material impact on the Company s financial position or results of operations.

In December 2004, the FASB issued SFAS No. 123R (revised 2004), *Share-Based Payment* (SFAS 123R). SFAS 123R replaced SFAS No. 123, *Accounting for Stock-Based Compensation* (SFAS 123), and superseded Accounting Principles Board Opinion No. 25, *Accounting for Stock Issued to Employees* (APB 25). In March 2005, the U.S. Securities and Exchange Commission (SEC) issued SAB 107. Valuation of share-based payment arrangements for public companies, which expresses views of the SEC staff regarding the interaction between SFAS 123R and certain SEC rules and regulations, and provides the staff s views regarding the valuation of share-based payment arrangements for public companies. SFAS 123R will require compensation cost related to share-based payment transactions to be recognized in the financial statements. SFAS 123R required public companies to apply SFAS 123R in the first interim or annual reporting period beginning after June 15, 2005. In April 2005, the SEC approved a new rule that delays the effective date, requiring public companies to apply SFAS 123R in their next fiscal year, instead of the next interim reporting period, beginning after June 15, 2005. As permitted by SFAS 123, the Company elected to follow the guidance of APB 25, which allowed companies to use the intrinsic value method of accounting to value their share-based payment transactions with employees. SFAS 123R requires measurement of the cost of share-based payment transactions to employees at the fair value of the award on the grant date and recognition of expense over the requisite service or vesting period. SFAS 123R requires implementation using a modified version of prospective application, under which compensation expense of the unvested portion of previously granted awards and all new awards will be recognized on or after the date of adoption. SFAS 123R also allows companies to adopt SFAS 123R by restating previously issued financial statements, basing the amounts on the expense previously calculated and reported in their pro forma footnote disclosures required under SFAS 123. The Company will adopt SFAS 123R using the modified prospective method in the first interim period of fiscal 2006 and is currently evaluating the impact that the adoption of SFAS 123R will have on its results of operations and financial position.

In November 2004, the FASB issued SFAS No. 151, *Inventory Pricing* (SFAS 151). SFAS 151 amends the guidance in ARB No. 43, Chapter 4, Inventory Pricing, to clarify the accounting for abnormal amounts of idle facility expense, freight, handling costs, and wasted material (spoilage). This statement requires that those items be recognized as current-period charges. In addition, SFAS 151 requires that allocation of fixed production overheads to the costs of conversion be based on the normal capacity of the production facilities. The statement is effective for inventory costs incurred during fiscal years beginning after June 15, 2005. The adoption of SFAS No. 151 is not expected to have a material impact on our results of operations or financial position.

In December 2004, the FASB issued SFAS No. 153, *Exchanges of Nonmonetary Assets* (SFAS 153), to address the measurement of exchanges of nonmonetary assets. It eliminates the exception from fair value measurement for nonmonetary exchanges of similar productive assets in APB No. 29, *Accounting for Nonmonetary Transactions*, and replaces it with an exception for nonmonetary exchanges that do not have commercial substance. This statement specifies that a nonmonetary exchange has commercial substance if the future cash flows of the entity are expected to

change significantly as a result of the exchange. This statement is effective for nonmonetary asset exchanges

Table of Contents

occurring in fiscal periods beginning after June 15, 2005. The adoption of SFAS 153 did not have a material impact on our results of operations or financial position.

In May 2005, the FASB issued SFAS No. 154, *Accounting Changes and Error Corrections* (SFAS 154). SFAS 154 requires retrospective application to prior-period financial statements of changes in accounting principles, unless it is impracticable to determine either the period-specific effects or the cumulative effect of the change. SFAS 154 also redefines restatement as the revising of previously issued financial statements to reflect the correction of an error. This statement is effective for accounting changes and corrections of errors made in fiscal years beginning after December 15, 2005.

In February 2006, the FASB issued SFAS No. 155, *Accounting for Certain Hybrid Financial Instruments* (SFAS 155) which amends SFAS No. 133, *Accounting for Derivative Instruments and Hedging Activities* (SFAS 133) and SFAS 140, *Accounting or the Impairment or Disposal of Long-Lived Assets* (SFAS 140). Specifically, SFAS 155 amends SFAS 133 to permit fair value remeasurement for any hybrid financial instrument with an embedded derivative that otherwise would require bifurcation, provided the whole instrument is accounted for on a fair value basis. Additionally, SFAS 155 amends SFAS 140 to allow a qualifying special purpose entity to hold a derivative financial instrument that pertains to a beneficial interest other than another derivative financial instrument. SFAS 155 applies to all financial instruments acquired or issued after the beginning of an entity s first fiscal year that begins after September 15, 2006, with early application allowed. The adoption of SFAS 155 is not expected to have a material impact to our results of operations or financial position.

In March 2006, the FASB issued SFAS No. 156, *Accounting for Servicing of Financial Assets* (SFAS 156) to simplify accounting for separately recognized servicing assets and servicing liabilities. SFAS 156 amends SFAS No. 140, *Accounting for Transfers and Servicing of Financial Assets and Extinguishments of Liabilities*. Additionally, SFAS 156 applies to all separately recognized servicing assets and liabilities acquired or issued after the beginning of an entity s fiscal year that begins after September 15, 2006, although early adoption is permitted. The adoption of SFAS 156 is not expected to have a material impact on our results of operations or financial position.

Quantitative and Qualitative Disclosures About Market Risk

At December 31, 2005 and 2004, our investment portfolio included fixed-income securities of $18.5 million and $18.3 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. At December 31, 2005 and 2004, we also have certain equipment financing arrangements with variable rates of interest. Due to the relative insignificance of such arrangements, however, an immediate 10% change in interest rates would have no material impact on our financial condition, results of operations, or cash fows. 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.

Table of Contents

BUSINESS

Caution: This discussion and analysis may contain predictions, estimates and other forward-looking statements that involve a number of risks and uncertainties, including those discussed in Risk Factors. This outlook represents our current judgment on the future direction of our business. These statements include those related to our products, product sales and other revenue, expenses, our revenue recognition models and policies, our 2005 restatement, material weaknesses or deficiencies in internal control over financial reporting, revenue recognition, the potential relisting of the Company s securities on NASDAQ, and our evaluation of strategic alternatives. Actual events or results may differ materially from Ligand s expectations. For example, there can be no assurance that our product sales efforts, recognized revenues or expenses will meet any expectations or follow any trend(s), that our internal control over financial reporting will be effective or produce reliable financial information on a timely basis, that we will be relisted on the NASDAQ on any given timeframe or at all, or that our strategic evaluation process will be successful or yield preferred results. We cannot assure you that the Company will be able to successfully remediate any identified material weakness or significant deficiencies, or that the sell-through revenue recognition models will not require adjustment and not result in a subsequent restatement. In addition, the Company s ongoing or future litigation (including private securities litigation and the SEC investigation) may have an adverse effect on the Company, and our corporate or partner pipeline products may not gain approval or success in the market. Such risks and uncertainties, and others, could cause actual results to differ materially from any future performance suggested. We undertake no obligation to release publicly the results of any revisions to these forward-looking statements to reflect events or circumstances arising after the date of this prospectus. This caution is made under the safe harbor provisions of Section 21E of the Securities Exchange Act of 1934 as amended.

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 gel, ONTAK and Targretin capsules, each of which was approved by the FDA in 1999; and Targretin gel, which was approved by the FDA in 2000. Our fifth product, AVINZA, is a treatment for chronic, moderate-to-severe pain that was approved by the FDA in March 2002. In Europe, the EC granted an MA for Panretin gel in October 2000 and an MA for Targretin capsules in March 2001. We also continue efforts to acquire or in-license other products, like ONTAK and AVINZA, 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 NSCLC, CLL, NHL and hand dermatitis.

We have formed research and development collaborations with numerous global pharmaceutical companies, including Abbott Laboratories, Allergan, Inc., Bristol-Myers Squibb, Eli Lilly & Company, GlaxoSmithKline, Organon (Akzo Nobel), Parke-Davis, Pfizer Inc., TAP Pharmaceutical Products, Inc. (TAP), and Wyeth. As of December 31, 2005, our corporate partners had 13 Ligand products in human development and numerous compounds on an IND track or in preclinical and research stages. These corporate partner products are being studied for the treatment of large market indications such as osteoporosis, diabetes, contraception and cardiovascular disease. One of these partner products, lasofoxifene, is being developed by Pfizer for osteoporosis and other indications. Pfizer filed an NDA with the FDA in August 2004 for the use of lasofoxifene in the prevention of osteoporosis and then filed a supplemental NDA in December 2004 for the use of lasofoxifene in the treatment of vaginal atrophy. Three of these partner products are in pivotal Phase III clinical trials: bazedoxifene, which is being

Table of Contents

developed by Wyeth as monotherapy for osteoporosis and in combination with Wyeth s PREMARIN for osteoporosis prevention, and vasomotor symptoms of menopause. A third partner product, eltrombopag (SB47115), being developed by Glaxo SmithKline for thrombocytopenia, recently advanced to Phase III in February 2006. A fourth partner product, LY519818, is being developed by Eli Lilly & Company for the treatment of type 2 diabetes. Lilly has announced plans to advance this product into Phase III registration studies after completion of two-year carcinogenicity studies and appropriate consultation with the FDA. Another Lilly product, LY674 has recently advanced into Phase II development for atherosclerosis and LY929 is in Phase I development for type 2 diabetes. An additional partner product being developed by GlaxoSmithKline is in Phase II: GSK516 for cardiovascular disease and dislipidemia. Other partner products in Phase II include pipendoxifene (formerly ERA-923) being developed by Wyeth for breast cancer and NSP-989 for contraception and NSP-989 combo for contraception in Phase I. In June 2005, GlaxoSmithKline commenced Phase I studies of SB-449448, a second product for thrombocytopenia and in April 2005, TAP commenced Phase I studies for LGD 2941 for the treatment of osteoporosis and frailty. Additionally, in September 2005 and February 2006, respectively, Pfizer announced the receipt of non-approvable letters from the FDA for the prevention of osteoporosis and vaginal atrophy. However, lasofoxifene continues in Phase III clinical trials by Pfizer for the treatment of osteoporosis.

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. Panretin gel, Targretin capsules, and Targretin gel as well as our corporate partner products currently on human development track are modulators of gene transcription, working through key cellular or intracellular receptor targets discovered using our IR technology.

On January 17, 2006, we signed an agreement with Organon that terminates the AVINZA co-promotion agreement between the two companies and returns AVINZA rights to Ligand. The effective date of the termination agreement is January 1, 2006, however the parties have agreed to continue to cooperate during a transition period ending September 30, 2006 to promote the product. The transition period co-operation includes a minimum number of product sales calls per quarter (100,000 for Organon and 30,000 for Ligand with an aggregate of 375,000 and 90,000 respectively for the transition period) as well as the transition of ongoing promotions, managed care contracts, clinical trials and key opinion leader relationships to Ligand. During the transition period, Ligand will pay Organon an amount equal to 23% of AVINZA net sales as reported by Ligand. Ligand will also pay and be responsible for the design and execution of all clinical, advertising and promotion expenses and activities. Additionally, in consideration of the early termination and return of rights under the terms of the agreement, Ligand will unconditionally pay Organon $37.75 million on or before October 15, 2006. Ligand will further pay Organon $10.0 million on or before January 15, 2007, provided that Organon has made its minimum required level of sales calls. Under certain conditions, including change of control, the cash payments will accelerate. In addition, after the termination, Ligand will make quarterly royalty payments to Organon equal to 6.5% of AVINZA net sales through December 31, 2012 and thereafter 6% through patent expiration, currently anticipated to be November of 2017. See Business Strategy Ligand Marketed Products AVINZA Co-Promotion Agreement with Organon.

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 technology, our strategy is to generate cash flow primarily from the sale 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.

Our strategy with respect to specialty pharmaceutical products is to develop a product pipeline based on our IR 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. Our execution of this strategy to date has been implemented in the U.S., Europe and Latin America. We expect to address additional global markets when and where practicable. Ligand s current international distribution partners are Zeneus (principally in Western and Eastern Europe), Ferrer (in Spain, Portugal, Greece, Central and South America) and Sigma Tau (in Italy). In

Table of Contents

October 2005, the Italian distribution rights were transferred from Alfa Wasserman to Sigma Tau. In December 2005, Cephalon Inc., announced that it had acquired the outstanding share capital of Zeneus, which will operate as a wholly owned subsidiary of Cephalon.

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 currently being marketed or 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 annually in global sales.

We have entered into a number of collaborative arrangements with global pharmaceutical companies focusing on a broad range of disease targets. The table below lists those of our corporate partners which have one or more compounds identified in our collaborative research efforts moving through clinical development .

Corporate Collaborator	Initiation of Collaboration	Focus
Pfizer Inc.	May 1991	Osteoporosis, vaginal atrophy, breast cancer prevention
GlaxoSmithKline (Glaxo Wellcome plc)	September 1992	Cardiovascular diseases
Wyeth	September 1994	Women s health, oncology
GlaxoSmithKline (SmithKline Beecham)	February 1995	Blood disorders
Eli Lilly & Company	November 1997	Type II diabetes, metabolic and cardiovascular diseases
TAP Pharmaceutical Products, Inc.	June 2001	Men s and women s health, osteoporosis

In addition to the collaborations listed above, we have also entered into collaborations with Allergan, Inc. (in June 1992 focused on skin disorders), Abbott Laboratories (in July 1994 focused on inflammatory diseases) and Organon (in February 2000 in women s health). Allergan, Abbott and Organon retain the right to move compounds identified during our collaborative research activities forward into clinical development, although we believe none of them is currently doing so. Two other collaborative partners, Parke-Davis and Bristol-Myers Squibb, no longer have rights to move compounds forward into clinical development.

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. In some instances, we have sold a portion of our rights to future royalties to Royalty Pharma AG. See - Royalty Pharma Agreement.

Table of Contents

Ligand Marketed Products

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

Marketed Product	Approved Indication	European Status	Additional Indications Studied or in Development
AVINZA	Chronic, moderate-to-severe pain	N/A	None
ONTAK	CTCL	MAA withdrawn (ONZAR)	CLL, B-cell NHL, other T-cell lymphomas, NSCLC
Targretin capsules	CTCL	MA issued	NSCLC, renal cell cancer, breast, prostate/colon cancer and other solid tumors
Targretin gel	CTCL	MAA withdrawn	Hand dermatitis, psoriasis
Panretin gel	KS	MA issued	None

AVINZA. AVINZA was approved by the FDA in March 2002 for the once-daily treatment of moderate-to-severe pain in patients who require continuous, around-the-clock opioid therapy for an extended period of time. We launched the product in the second quarter of 2002. AVINZA consists of two components: an immediate-release component that rapidly achieves morphine concentrations in plasma, and an extended-release component that maintains plasma concentrations throughout a 24-hour dosing interval. This unique drug delivery technology makes AVINZA the first true once-daily sustained release opioid. AVINZA was developed by Elan, which licensed the U.S. and Canadian rights to us in 1998. The U.S. sustained-release opioid market grew to approximately $4.1 billion in 2004, the largest initial market we have entered. Because tens of thousands of U.S. physicians prescribe sustained-release opioids, our goal was to co-promote the product with another company to maximize its potential. Early in 2003, we finalized a co-promotion agreement with Organon, which was terminated effective January 1, 2006. However, the parties have agreed to continue to cooperate during a transition period ending September 30, 2006 to promote the product. The details of the termination agreement are discussed below under the caption AVINZA Co-Promotion Agreement with Organon .

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, Targretin capsules, and Targretin 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. ONTAK was approved by the FDA and launched in the U.S. in February 1999 as our first product for the treatment of patients with CTCL. ONTAK was the first treatment to be approved for CTCL in nearly 10 years. ONTAK has been studied or is currently in Phase II clinical trials for the treatment of patients with CLL, B-cell NHL, other T-cell lymphomas, NSCLC, and GVHD. Results from several of these studies were reported in 2002, 2003 and 2004. Ligand s top priorities for additional ONTAK development are B-cell NHL and T-cell NHL. We began a Phase II CLL study in 2003 which is still continuing as are Phase II studies in NHL. Clinical trials using ONTAK for the treatment of patients with psoriasis and rheumatoid arthritis also have been conducted, and further trials are being considered. These indications provide significantly larger market opportunities than CTCL. A European Marketing Authorization Application (or MAA) for CTCL was filed in December 2001, which we withdrew in April 2003. It

was our assessment that the cost of the additional clinical and technical information requested by the European Agency for the EMEA would be better spent on the acceleration of the second generation

Table of Contents

ONTAK formulation development. We expect to resubmit the ONZAR (the tradename for ONTAK in the EU) application with the second generation product in 2007.

Targretin capsules. We launched U.S. sales and marketing of Targretin capsules in January 2000 following receipt of FDA approval in December 1999. Targretin capsules offer the convenience of a daily oral dose administered by the patient at home. In March 2001, the EC 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 the fourth quarter of 2001 in Europe. We are developing Targretin capsules in a variety of larger market opportunities, including NSCLC and other solid tumors. In March 2005, we announced that the final data analysis for Targretin capsules in NSCLC showed that the trials did not meet their primary endpoints of improved overall survival and projected two-year survival. We are continuing to analyze the data and apply it to the continued development of Targretin in NSCLC. The details of the final data analysis for Targretin capsules in NSCLC are discussed below under Ligand Product Development Programs Targretin Capsules Development Program .

Targretin gel. We launched U.S. sales and marketing of Targretin gel in September 2000 following receipt of FDA approval in June 2000. Targretin gel offers patients with refractory, early stage CTCL a novel, non-invasive, self-administered treatment topically applied only to the affected areas of the skin. Targretin gel is currently in clinical development for hand dermatitis. In 2002 and early 2003, we reported positive Phase I/II data that showed nearly 40% of patients with chronic, severe hand dermatitis improved by 90% or more after being treated with Targretin gel monotherapy and nearly 80% responded with greater than 50% improvement. Based on these promising results, we intend to design and implement Phase II/III registration trials in hand dermatitis. We filed an MAA in Europe for CTCL in March of 2001, but withdrew it in 2002. Due to the small size of the European early stage CTCL market and the limited revenue potential of Targretin gel, we believed that the additional comparative clinical studies requested by the EMEA were not economically justified.

Panretin gel. Panretin gel was approved by the FDA and launched in February 1999 as the first FDA-approved patient-applied topical treatment for AIDS-related KS. Panretin gel represents a 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. 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.

AVINZA Co-Promotion Agreement with Organon. In February 2003, we entered into an agreement for the co-promotion of AVINZA with Organon Pharmaceuticals USA Inc. (Organon). Under the terms of the agreement, Organon committed to specified minimum numbers of primary and secondary product calls delivered to high prescribing physicians and hospitals beginning in March 2003 as well as additional sales calls as approved by the companies joint steering committee in annual marketing plans.

On January 17, 2006, we signed an agreement with Organon that terminates the AVINZA co-promotion agreement between the two companies and returns AVINZA rights to Ligand. The effective date of the termination agreement is January 1, 2006, however the parties have agreed to continue to cooperate during a transition period ending September 30, 2006 (the Transition Period) to promote the product. The Transition Period co-operation includes a minimum number of product sales calls per quarter (100,000 for Organon and 30,000 for Ligand with an aggregate of 375,000 and 90,000 respectively for the Transition Period) as well as the transition of ongoing promotions, managed care contracts, clinical trials and key opinion leader relationships to Ligand. During the Transition Period, Ligand will pay Organon an amount equal to 23% of AVINZA net sales as reported by Ligand. Ligand will also pay and be responsible for the design and execution of all clinical, advertising and promotion expenses and activities.

As previously disclosed, Organon and Ligand were in discussions regarding the calculation of prior co-promote fees under the co-promotion agreement. In connection with the termination of the co-promotion agreement, the companies resolved their disagreement concerning prior co-promote fees and Ligand paid Organon $14.75 million in January 2006. Resolution of this matter resulted in no material adjustment to amounts previously recorded in 2005 for co-promotion expense. The companies also agreed that Organon s compensation for the fourth quarter of 2005 would be calculated based on Ligand s reported AVINZA net sales determined in accordance with U.S. GAAP.

Table of Contents

Additionally, in consideration of the early termination and return of rights under the terms of the agreement, Ligand will unconditionally pay Organon $37.75 million on or before October 15, 2006. Ligand will further pay Organon $10.0 million on or before January 15, 2007, provided that Organon has made its minimum required level of sales calls. Under certain conditions, including change of control, the cash payments will accelerate. In addition, after the termination, Ligand will make quarterly royalty payments to Organon equal to 6.5% of AVINZA net sales through December 31, 2012 and thereafter 6% through patent expiration, currently anticipated to be November of 2017. The termination and return of rights transaction with Organon requires the analysis of several complex accounting alternatives. Accordingly, we are still in the process of determining the appropriate accounting treatment for the transaction in 2006 and going forward. Certain of these alternatives, however, could result in the recognition of significant additional expense in our consolidated statement of operations for the first quarter of 2006. We expect to complete our determination of the appropriate accounting by the time we file our first quarter 2006 Form 10-Q.

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 our IR technology. See Technology for a discussion of our IR technology and retinoids.

General 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 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 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 an optimal 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 concerns. Once a product has been approved, Phase IV post-market clinical studies may be performed to support the marketing of the product.

Table of Contents

Program	Disease/Indication	Development Phase
AVINZA	Chronic, moderate-to-severe pain	Marketed in U.S. Phase IV
ONTAK	CTCL	Marketed in U.S., Phase IV
	CLL	Phase II
	Peripheral T-cell lymphoma	Phase II
	B-cell NHL	Phase II
	NSCLC third line	Phase II
Targretin capsules	CTCL	Marketed in U.S. and Europe
	NSCLC first-line	Phase III
	NSCLC monotherapy	Planned Phase II/III
	NSCLC second/third line	Planned Phase II/III
	Advanced breast cancer	Phase II
	Renal cell cancer	Phase II
Targretin gel	CTCL	Marketed in U.S.
	Hand dermatitis (eczema)	Planned Phase II/III
	Psoriasis	Phase II
LGD4665 (Thrombopoietin oral mimic)	Idiopathic Thrombocytopenias, other TCPs	IND Track
LGD5552 (Glucocorticoid agonists)	Inflammation, cancer	IND Track
Selective androgen receptor modulators, e.g., LGD3303 (agonist/antagonist)	Male hypogonadism, female & male osteoporosis, male & female sexual dysfunction, frailty. Prostate cancer, hirsutism, acne, androgenetic alopecia.	Pre-clinical

AVINZA Development Programs

AVINZA (oral morphine sulfate extended-release capsules) is the first true once-a-day treatment for chronic moderate-to-severe pain in patients who require continuous, around-the-clock opioid therapy for an extended period of time. Approved by the FDA in March 2002, AVINZA consists of two components: an immediate-release component that rapidly achieves morphine concentrations in plasma, and an extended-release component that maintains plasma concentrations throughout a 24-hour dosing interval.

In a poster presented at the American Pain Society (APS) annual meeting in March of 2005, AVINZA showed better control of chronic pain and improved sleep in a large study comparing once-daily AVINZA (once-a-day morphine sulfate extended-release capsules) to twice-daily OxyContin® (oxycodone hydrochloride controlled-release). The results of the first phase of the study, with 265 evaluable patients (132 in the AVINZA arm and 133 in the oxycodone CR arm) followed through two months, showed that at lower, mean morphine-equivalent doses, patients receiving AVINZA once daily demonstrated statistically significant better around the clock pain control (evaluated using the Brief Pain Inventory assessment instrument), statistically significant better quality of sleep (evaluated using the Pittsburgh Sleep Quality Index assessment instrument), and a statistically significant reduction in the total number of rescue medications. The final study results for all patients enrolled are expected to be published in 2006. The results from an additional four-month treatment phase to collect long-term comparator data are to be reported at the APS

meeting in 2006.

A second poster at the March 2005 APS meeting presented the initial results of a study evaluating AVINZA s effects on various sleep measures for patients with chronic, moderate-to-severe osteoarthritis pain of the hip or knee who self-report trouble sleeping. This was a 29-patient, placebo/baseline-controlled, single blind study using both polysomnography and subjective sleep measurements to assess and better quantify sleep parameters. Preliminary results demonstrated AVINZA s ability to provide improved quality and quantity of sleep as well as improved pain control. Final results are expected to be reported in 2006.

Table of Contents

A third study of AVINZA, involving 507 patients, extends the findings of previously published controlled studies. The primary objective of this study was to measure the efficacy of once-daily AVINZA when used according to the package insert in patients with chronic non-cancer pain. Patients were recruited by office-based physicians. They were interviewed 4 times over a period of 3 months using questionnaires assessing pain, sleep, functional status, and rescue medication use. Measures were collected at baseline and at Month 1, 2, and 3. Interviews were conducted by phone or via the internet. The interim analysis, presented in a poster session at the College on Problems of Drug Dependence in June of 2005, showed that for patients who continue to take AVINZA for 3 months, 88% report their pain to be better compared to baseline and 88% rate AVINZA as effective or extremely effective. Full results are expected to be reported in 2006.

ONTAK Development Programs

ONTAK is a fusion protein that represents the first of a new class of targeted cytotoxic biologic agents. Rights to ONTAK were acquired from Eli Lilly in 1997 and in the acquisition of Seragen in 1998. ONTAK is marketed in the U.S. for patients with CTCL, which affects approximately 16,000 people in the U.S. In addition to ongoing CTCL trials, we have conducted, or are conducting clinical trials with ONTAK in patients with CLL, peripheral T-cell lymphoma, B-cell NHL, NSCLC, and GVHD, indications that represent significantly larger market opportunities than CTCL.

In early 1999, ONTAK entered Phase II trials for the treatment of patients with NHL. NHL affects approximately 300,000 people in the U.S. and Ligand estimates that more than 50,000 of these patients would be candidates for ONTAK therapy. One multicenter study conducted by the Eastern Cooperative Oncology Group (ECOG) assessed 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. The study results were presented at ASCO 2005 and showed the efficacy of ONTAK in patients with small cell lymphocytic lymphoma. A second multicenter trial evaluated ONTAK in 54 patients with relapsed/refractory low or intermediate grade lymphoma. The results of this study are being analyzed and are expected to be presented in 2006.

Separately, a Phase II study of ONTAK in 45 patients with relapsed/refractory B-cell NHL was conducted by researchers from the MD Anderson Cancer Center and published in 2004 in the Journal of Clinical Oncology. The study enrolled late-stage, heavily pretreated patients (median of 4 prior treatments) and showed that 25% of the patients achieved a complete or partial response and an additional 20% achieved stabilization of disease. Furthermore, this study showed that ONTAK could be administered in patients with low blood platelet counts, a patient population that cannot tolerate treatment with chemotherapy or radio-immunotherapy. On the basis of these favorable findings, two Phase II studies of ONTAK in relapsed/refractory B-cell lymphoma were launched in 2004. One multicenter trial conducted by Ligand is evaluating ONTAK on a weekly regimen in patients with poor blood platelet counts at entry and another study conducted by investigators at MD Anderson Cancer Center is evaluating ONTAK plus Rituxan® (a monoclonal antibody marketed for the treatment of relapsed low grade lymphoma) in patients who have failed prior treatment with Rituxan. The interim results of the latter study were presented at ASH in 2005. Of the 39 patients enrolled, 36 are evaluable for response. The overall response rate was 33.3% and another 19% had stable disease. All of the responders but four had disease refractory to previous rituximab treatment. The objective response rate in the subset of patients with relapsed/refractory follicular lymphoma was 64%. Based on these favorable results, Ligand plans to launch two new studies of ONTAK plus rituximab in this patient population.

Investigators at MD Anderson Cancer Center also conducted a Phase II study on ONTAK in relapsed/refractory T-cell NHL. The final results of this study, which enrolled a total of 26 patients, were presented at ASH in 2005, which showed an overall 50% response rate. Of the 13 patients whose tumors positively expressed the CD25 component of the IL-2 receptor, 61.5% showed a complete or positive response. The other 13 patients, which were not positive for CD25, showed a response rate of 45%. We are also conducting a multicenter Phase II study of ONTAK plus a chemotherapy regimen designated as CHOP as first line treatment of patients with T-cell NHL. Although the CHOP chemotherapy regimen is considered as the standard of care for patients with T-cell NHL, about 50% of patients fail to achieve a complete response and, of those who respond, over 50% relapse within 2 years. The trial is designed to demonstrate whether the addition of ONTAK to CHOP will increase the response rate and the duration of response. Interim results of the trial are expected in 2006. Additional studies are being planned to

59

Table of Contents

better define the role of ONTAK in combination with chemotherapy in the treatment of newly diagnosed and relapsed T-cell NHL.

ONTAK is also being evaluated to treat CLL, which affects more than 60,000 people in the U.S. Researchers from Wake Forest University conducted a multicenter Phase II study of ONTAK in patients with CD25-positive CLL who have failed prior treatment with fludarabine. The results of this pilot study were published in the journal Clinical Cancer Research in 2003 and showed that ONTAK reduced CLL in blood cells, lymph nodes and bone marrow. In the study, nine of 10 patients who received at least three courses of ONTAK experienced reductions in peripheral CLL cells, with three of these patients showing reductions of at least 99%. In addition, six of 10 patients showed reductions in the diameter of their cancerous lymph nodes, with one patient showing an 80% reduction. One of 12 evaluable patients showed a partial remission, with 80% node shrinkage and 100% clearance of CLL cells from bone marrow. Based on these encouraging results, three multicenter Phase II studies were launched in 2003 to further evaluate the role of ONTAK in patients with relapsed/refractory CLL. Preliminary results from one study of 16 patients conducted by investigators from Wake Forest University were reported at ASH in 2004 , and showed there was a 27% response rate among the 11 evaluable patients with fludarabine-refractory B-cell chronic lymphocytic leukemia. The investigators concluded that ONTAK has activity in CLL with toxicities that can be managed with adequate premedication and close monitoring. The final results of this study and another study conducted by the Hoosier Oncology Group are expected to be published in 2006. The Company conducted a third trial which is nearing completion.

Clinical trials with ONTAK have demonstrated benefits in patients with steroid-resistant acute graft-versus-host disease (GVHD) after allogeneic bone marrow transplantation. One Phase I-II study conducted by investigators from the Dana Farber Cancer Center in Boston enrolled 30 patients and the results were published in the journal Blood in 2004. The study established a dose of ONTAK that is safe in this patient population and showed that ONTAK resulted in a 71% response rate. Another multicenter Phase I-II study conducted by investigators from the Texas Transplant Institute enrolled 21 patients and the results were published in the journal Biology of Blood and Marrow Transplantation in 2005. The study confirmed that ONTAK can be safely administered in this patient population and that ONTAK achieved a 47% response rate at Day 36 of treatment with an additional 31% of patients achieving a response by Day 100. On the basis of these promising results, a randomized 4-arm study is being conducted by the Bone Marrow Transplant Network with NCI funding to evaluate the efficacy and safety of ONTAK and three other investigational agents in the primary treatment of acute GVHD.

A multicenter Phase II study exploring the use of ONTAK as a monotherapy for patients with relapsed/refractory advanced NSCLC was conducted by investigators from the University of Cincinnati and completed in late 2004. The preliminary study results reported at the American Society of Clinical Oncology (ASCO) meeting in May of 2005 showed that ONTAK resulted in an unconfirmed partial response or disease stabilization in 40% of patients and noted an association between disease stabilization and an increase in a subset of T-lymphocytes in the circulation, suggesting that ONTAK s effect could be ascribed to an activation of the immune system. These findings were consistent with the results of a study conducted by investigators from Duke University and presented at an oral session at ASCO in 2004 which showed that ONTAK significantly activated the immune system in patients with solid tumors receiving ONTAK in combination with an investigational anti-tumor vaccine.

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. The studies were designed to support a supplemental indication for Targretin capsules for first-line treatment of patients with advanced NSCLC. One of

these multicenter studies evaluated Targretin in combination with the chemotherapy

Table of Contents

drugs cisplatin and vinorelbine, and was conducted primarily in Europe and Latin America. The other multicenter study examined Targretin in combination with carboplatin and paclitaxel, and was conducted mainly in the U.S. Both studies were randomized with approximately 600 patients each, and had survival as the primary endpoint. Patient enrollments were completed in August and September 2003, respectively. The final statistical plan, as agreed with the FDA, specified the analysis trigger to be at the 456th death event or 18 months of follow-up from the date the last patient was entered into each study, whichever occurs later. Based on enrollment dates, that 18-month time point was reached in mid-March, 2005. This modification resulted in the majority of patients having between 1.5 and 2.5 years of follow-up observation based upon actual accrual rates.

We publicly released top-line data within approximately two weeks after the commencement of final data analysis showing that the trials did not meet their endpoints of improved overall survival and projected two-year survival. For both studies, the primary endpoint was overall survival and the secondary endpoint was Kaplan-Meier projected two-year survival. No statistically significant differences in primary or secondary endpoints in the intent to treat population were seen in either trial. In both trials, additional subset analysis completed after the initial intent to treat results were analyzed revealed a significant correlation between high-grade (grade 3 and 4) hypertriglyceri-demia in response to Targretin and increased survival, potentially identifying a large subgroup patient population that may receive significant survival benefit of added Targretin treatment in first line therapy. Pooled survival analysis from both SPIRIT trials showed that those patients on Targretin with high hypertriglyceridemia, 40% of Targretin-treated patients, had an overall survival of 12.3 months versus 9.5 months in the chemo arm, which was statistically significant ($p < 0.025$). Data from both trials was presented during the plenary session at the 2005 annual ASCO meeting. Review of data from current and prior Phase II studies shows a similar correlation between hypertriglyceridemia and increased survival. The data will further shape our future plans for Targretin. Any further studies will be conducted with a partner or cooperative group.

In 2003 we also began a Phase II study of Targretin as monotherapy for late-stage lung cancer patients who have failed at least two prior treatments with chemotherapy and/or biologic therapy. A poster presentation at the 2005 annual meeting of ASCO reported on the interim analysis of data covering all 146 patients enrolled at that point. Patients in the study were heavily pre-treated, having received a median of three prior treatments, and 54% of these patients had already failed treatment with Iressa. Overall median survival was five months and overall one-year survival was 15 percent. The data was also analyzed to evaluate the survival of patients based on the triglyceride response to Targretin treatment, in view of the SPIRIT results reported earlier at this meeting that showed an improved survival in patients who showed high grade triglyceridemia after Targretin administration. With this subanalysis, two populations of patients were identified. Those with increased triglyceridemia (grade 1 4) had a median survival of 7 months ($p<0.0001$) and a projected 1 year survival of 23%, compared with those with no hypertriglyceridemia who had a median survival of 2 months and a projected 1 year survival of 5%. The data from this study provides new information for Targretin monotherapy for patients with third-line treatment or beyond and also adds additional support to the subgroup analysis that resulted from our SPIRIT trials about a triglyceride biomarker that may identify patients with the potential to benefit from Targretin therapy. This information will factor into our evolving plans for further studies.

The American Cancer Society estimates that approximately 170,000 Americans are diagnosed with lung cancer each year; of those approximately 80% were diagnosed with NSCLC.

Targretin Gel Development Program

Targretin gel is marketed in the U.S. for patients with refractory CTCL. In 2002 and early 2003, we reported Phase I/II data that showed 39% of patients with chronic, severe hand dermatitis improved by 90% or more after being treated with Targretin gel monotherapy. In addition, 79% of patients improved by at least 50%. Fifty-five patients with a history of chronic severe hand dermatitis for at least six months were enrolled in the 22-week, randomized, open-label study, which was designed to evaluate safety, tolerability and activity. Patients were treated with Targretin alone, Targretin in combination with a medium potency topical steroid, and Targretin in combination with a low potency topical steroid. Based on these promising results, we intend to design and initiate Phase II/III registration trials in hand dermatitis in 2007. There are many subtypes of hand dermatitis, and many causes. Most hand dermatitis is caused by contact with irritating environmental substances, such as chemicals, soaps and cleaning fluids, and some

cases are caused by allergic reactions to a wide variety of environmental substances. We estimate that more than 4 million people in the United States have hand dermatitis and seek treatment.

Table of Contents

We filed an MAA for Targretin gel in Europe for CTCL in March of 2001, but withdrew it in 2002. Due to the small size of the European early stage CTCL market and the limited revenue potential of Targretin gel, we believed that the additional comparative clinical studies requested by the EMEA were not economically justified.

Thrombopoietin (TPO) Research Programs

In our TPO program, we seek to develop our own drug candidates that mimic the activity of thrombopoietin (TPO) for use in the treatment or prophylaxis of thrombocytopenia with indications in a variety of conditions including cancer and disorders of blood cell formation. In 2005, we selected a TPO mimetic, LGD4665, as a clinical candidate. Our goal is to complete the preclinical studies necessary for filing an IND for this in 2006. Our partner GlaxoSmithKline (GSK) has two TPO mimics that were part of our collaboration with GSK in clinical trials: Eltrombopag in Phase III and SB-559448 in Phase I. For a discussion of these clinical trials, see Collaborative Research and Development Programs TPO/Inflammatory Disease/Oncology Collaborative Program GlaxoSmithKline Collaboration.

Selective Glucocorticoid Receptor Modulators 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. When the research phase of the collaboration ended in July 1999, Abbott retained rights to certain Selective Glucocorticoid Receptor Modulators (or SGRMs). We retained rights to all other compounds discovered through the collaboration, as well as recapturing technology rights. We subsequently initiated an internal effort to develop SGRMs for inflammation, oncology and other therapeutic applications. As a result of that effort, in 2001, we moved several SGRMs into late preclinical development. During 2003, LGD5552 was designated a clinical candidate. Phase I studies are being planned for LGD5552 to evaluate pharmakinetic (PK) and pharmacodynamic (PD) of the oral formulation under an exploratory IND. These non-steroidal SGRM 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.

Another group of SGRMs from this program, selected from a different chemical class, are being targeted for the treatment of multiple myeloma and other blood cancers. The profile of these molecules is to have activity equal to dexamethasone but a significant reduction in side effects, particularly in bone and other parameters affecting quality of life.

SARM Programs

We are pioneering the development of tissue selective SARMs, a novel class of non-steroidal, orally active molecules that selectively modulate the activity of the Androgen Receptor (or 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 hormone therapy (or HT) and the treatment of patients with male hypogonadism, female & male osteoporosis, male & female sexual dysfunction, frailty, prostate cancer, hirsutism, acne, androgenetic alopecia, 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.

SARM programs have been one of our largest programs over the past several years. We have assembled an extensive SARM compound library and, we believe, 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.

Table of Contents

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. In December 2004, we announced the second extension of this collaboration for an additional year through June 2006. Please see the Collaborative Research and Development Programs/Sex Hormone Modulators Collaborative Programs/TAP Collaboration section below for more details on this alliance.

As part of the TAP alliance, we exercised an option to select for development one compound and a back-up, LG 123303 and LG 123129, out of a pool of compounds available for development in the TAP field. The SARM agonist which we now refer to as LGD3303 was designated a clinical candidate in late 2004. Preclinical studies indicate that the compound may have utility for osteoporosis, male and female sexual dysfunction, frailty and male hypogonadism. *In vivo* studies in rodents indicate a favorable profile with anabolic effects on bone, but an absence of the prostatic hypertrophy that occurs with the currently marketed androgens.

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 technologies. These collaborations focus on several large market indications as estimated (as of 2004, except contraception, which is as of 2002) in the table below.

Indication	**Estimated U.S. Prevalence**
Menopausal symptoms	50 million
Osteoporosis/osteopenia (men and women)	55 million
Dyslipidemias	109 million
Contraception	38 million
Type II diabetes	18 million
Breast cancer	.8 million

As of December 31, 2005, 13 of our collaborative product candidates were in human development - lasofoxifene, bazedoxifene, bazedoxifene CE (PREMARIN combo), pipendoxifene, NSP989, NSP989 combo, LGD2941, GW516, LY818, LY929, LY674, SB497115, and SB559448. Please see Note 16 of the 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 summary of these programs.

Table of Contents

Program	Disease/Indication	Development Phase	Marketing Rights
SEX HORMONE MODULATORS			
SERMs			
Lasofoxifene (1)	Osteoporosis prevention, vaginal atrophy	NDA and SNDA filed (1)	Pfizer
Lasofoxifene	Breast cancer prevention, Osteoporosis treatment	Phase III	Pfizer
Bazedoxifene	Osteoporosis	Phase III	Wyeth
Bazedoxifene CE	Osteoporosis prevention Vasomotor symptoms	Phase III	Wyeth
Pipendoxifene (formerly ERA-923)(2)	Breast cancer	Phase II	Wyeth
PR modulators			
NSP-989 (PR agonist) (3)	Contraception	Phase II	Wyeth
NSP-989 combo (PR agonist) (3)	Contraception	Phase I	Wyeth
SRMs			
LGD 2941 (androgen agonist)	Osteoporosis, frailty, HT and sexual dysfunction	Phase I	TAP
METABOLIC/CARDIOVASCULAR DISEASES			
PPAR modulators			
GW516	Cardiovascular disease, dyslipidemia	Phase II	GlaxoSmithKline
LY818 (naveglitazar) (4)	Type II diabetes	Phase II	Lilly
LY929 (5)	Type II diabetes, metabolic diseases, dyslipidemia	Phase I	Lilly
LY674	Atherosclerosis/dyslipidemia	Phase II	Lilly
LYWWW (6)(7)	Atherosclerosis	IND track	Lilly
Selective PPAR modulators(7)	Type II diabetes, metabolic diseases, dyslipidemia	IND track	Lilly
LYYYY (6)(7)	Atherosclerosis	Pre-clinical	Lilly
INFLAMMATORY DISEASES, ONCOLOGY			
Eltrombopag (formerly SB-497115)	Thrombocytopenia	Phase III	GlaxoSmithKline

(TPO agonist)			
SB-559448 (TPO agonist)	Thrombocytopenia	Phase I	GlaxoSmithKline

(1) In September 2005 and February 2006, respectively, Pfizer announced receipt of non-approvable letters from the FDA for the prevention of osteoporosis and vaginal atrophy.

(2) Pipendoxifene development has been terminated for oncology; it is currently on hold as a potential back-up to bazedoxifene.

(3) On internal hold; strategic alternatives for Phase III development being explored.

(4) Lilly decision to advance to Phase III announced March 2004; timing of initiation delayed by new FDA guidelines.

(5) Product placed on internal hold.

(6) Compound number not disclosed.

(7) Rights subject to IND filing. See Eli Lilly Collaboration below.

Table of Contents

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 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 Progesterone Receptor (or PR), the Estrogen Receptor (or ER) and the AR. Through our collaborations with Pfizer and Wyeth, three SERM compounds are in development for osteoporosis, breast cancer, vaginal atrophy and vasomotor symptoms of menopause. 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.

Pfizer Collaboration. In May 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. Portions of these royalty rights have been sold to Royalty Pharma AG. See Royalty Pharma Agreement.

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 1,800 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. In January 2003, Pfizer disclosed that this large, 7,500-patient risk-reduction study was fully enrolled.

In August 2004, Pfizer submitted an NDA to the FDA for lasofoxifene for the prevention of osteoporosis in postmenopausal women. We earned a development milestone of approximately $2.0 million from Pfizer in connection with the filing. Under the terms of the agreement between Ligand and Pfizer, payment of milestones can occur in either cash or shares of Ligand common stock held by Pfizer. Pfizer elected to pay the milestone in stock and subsequently tendered 181,818 shares to the Company. We retired the tendered shares in September 2004. In September 2005, Pfizer announced the receipt of a non-approvable letter from the FDA for the prevention of osteoporosis. However, lasofoxifene continues in Phase III clinical trials by Pfizer for the treatment of osteoporosis.

In December 2004, Pfizer filed a supplemental NDA for the use of lasofoxifene for the treatment of vaginal atrophy for which no additional milestone was due. In February 2006, Pfizer announced the receipt of a non-approval letter from the FDA for this indication.

Wyeth Collaboration. In September 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 HT, 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

Table of Contents

advanced chemical compound series from its internal ER-osteoporosis program to the collaboration. The research phase of the collaboration ended in August 1998.

In December 2005, the Company entered into an Amended and Restated Agreement with Wyeth to better define, simplify and clarify the universe of research compounds resulting from the research and development efforts of the parties, combine and clarify categories of those compounds and related milestones and royalties and resolve a number of milestone payment issues.

Wyeth has ongoing clinical studies with two SERMs from the collaboration. Wyeth is developing bazedoxifene (TSE-424) and bazedoxifene CE for the treatment of post-menopausal osteoporosis. We have milestone and royalty rights for bazedoxifene (TSE-424) and bazedoxifene CE. Portions of these royalty rights have been sold to Royalty Pharma AG. See Royalty Pharma Agreement.

Phase III trials for bazedoxifene (TSE-424) and bazedoxifene CE were initiated in June 2001. In late 2002, Wyeth disclosed that it had completed enrollment in a Phase III osteoporosis prevention trial, and that it expected enrollment in a bazedoxifene fracture prevention trial to finish in 2003, and that bazedoxifene is on track for regulatory submission in 2005. In January 2005, Wyeth indicated that it is now targeting the bazedoxifene regulatory submission for the first half of 2006. Wyeth has reiterated its commitment to developing bazedoxifene CE as a progesterone-free treatment for menopausal symptoms in the wake of the well-publicized Women s Health Initiative (WHI) study of hormone therapies. Ligand believes it is important to recognize that bazedoxifene is a synthetic drug that was specifically designed to increase bone density and reduce cholesterol levels while at the same time protecting breast and uterine tissue. In other words, bazedoxifene may represent a potential solution to some of the side effects associated with progestin in the WHI study.

Wyeth also has conducted Phase II studies of pipendoxifene (formerly ERA 923) for the treatment of breast cancer. In 2003, Wyeth began Phase II studies of NSP-989, a progesterone agonist that may be useful in contraception. These studies were completed in 2004. Wyeth also continues to do preclinical work in the area of PR antagonists.

Organon (Akzo Nobel) 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 was 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 therapy, oral contraception, reproductive diseases, and other hormone-related disorders. The initial research phase concluded in February 2002.

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), sexual dysfunction, male and female osteoporosis, frailty, and male HT related diseases. The three-year collaboration carries an option to extend by up to two additional one-year terms. In December 2004, we announced the second extension of this collaboration for an additional year through June 2006.

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 HT related diseases and other indications not retained by Ligand. We may also receive milestones and up to double-digit royalties as compounds are developed and commercialized. LGD 2941, an androgen agonist targeting osteoporosis and frailty, commenced Phase I development in April 2005. 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, we had 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. We recently exercised our option to select one compound and a back-up for development, LG 123303 and LG 123129, out of a pool of compounds available for development in the TAP field. TAP retains

Table of Contents

certain royalty rights and an option to negotiate to co-develop and co-promote such compounds with us up to the end of Phase II development.

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®. 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 Retinoid X Receptors (or 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 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 four compounds in clinical development.

GlaxoSmithKline Collaboration. In September 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 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. GW516 is currently in Phase II 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 IR technology with broad applications in the fields of metabolic diseases, including diabetes, obesity, dyslipidemia, insulin resistance and cardiovascular diseases associated with insulin resistance and obesity. Under the collaboration, Lilly received: (1) worldwide, exclusive rights to our compounds and technology associated with the RXR receptor in the field; (2) rights to use our technology to develop an RXR compound in combination with a SERM in cancer; (3) worldwide, exclusive rights in certain areas to our PPAR technology, along with rights to use PPAR research technology with the RXR technology; and (4) exclusive rights to our HNF-4 receptor and 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. In April 2002, Lilly and Ligand announced the companies would extend the collaboration until November of 2003. In May 2003, the companies announced the second and final extension of the collaboration through November 2004.

Under the Lilly collaboration, we retained or received: (1) exclusive rights to independently research, develop and commercialize Targretin and other RXR compounds in the fields of cancer and dermatology; (2) an option to obtain selected rights to one of Lilly s specialty pharmaceutical products; and (3) rights to receive milestones,

Table of Contents

royalties and options to obtain certain co-development and co-promotion rights for the Lilly-selected RXR compound in combination with a SERM.

Our rights under the initial agreements have changed. In connection with the acquisition of Seragen in 1998, we obtained from Lilly its rights to ONTAK in satisfaction of our option to obtain selected rights to one of Lilly s specialty pharmaceutical products. In November 2004, Ligand and Lilly agreed to amend the ONTAK royalty agreement to add options in 2005 that if exercised would restructure our royalty obligations on net sales of ONTAK. Under the revised agreement, Ligand and Lilly each had two options. We received options exercisable in January 2005 and April 2005 to buy down a portion of the Company s ONTAK royalty obligation on net sales in the United States for total consideration of $33.0 million. Lilly received two options exercisable in July 2005 and October 2005 to trigger the same royalty buy-downs for total consideration of up to $37.0 million dependent on whether we have exercised one or both of our options.

In January 2005 we exercised the first option which provided for a one-time payment of $20.0 million to Lilly in exchange for the elimination of our ONTAK royalty payment obligations in 2005 and a reduced reverse-tiered royalty scale on ONTAK sales in the U.S. thereafter. The second option, exercised in April 2005, provided for a one-time payment of $13.0 million to Lilly in exchange for the elimination of royalties on ONTAK net sales in the U.S. in 2006 and a reduced reverse-tiered royalty thereafter. Since both options were exercised, beginning in 2007 and throughout the remaining ONTAK patent life (2014), we will pay no royalties to Lilly on U.S. sales up to $38.0 million. Thereafter, we will pay royalties to Lilly at a rate of 20% on net U.S. sales between $38.0 million and $50.0 million; at a rate of 15% on net U.S. sales between $50.0 million and $72.0 million; and at a rate of 10% on net U.S. sales in excess of $72.0 million.

In 1999, we agreed to focus our collaborative efforts on the RXR modulator second-generation program, which has compounds with improved therapeutic indices relative to the three first-generation compounds, and on co-agonists of the PPAR receptor program. In early 1999, Lilly opted not to proceed with the development of certain first-generation compounds, including Targretin, in the RXR program for diabetes. As a result of this decision, all rights to the oral form of Targretin reverted to us, and LGD1268 and LGD1324 returned to the pool of eligible RXR modulators for possible use in oncology in combination with a SERM under the collaboration agreement between Ligand and Lilly.

In September 2001, we announced that we had earned a milestone from Lilly as a result of Lilly s filing with the FDA an IND for LY818 (naveglitazar), a PPAR modulator for type II diabetes and metabolic diseases. Naveglitazar entered Phase II studies early in 2003, resulting in a $1.5 million milestone payment. In March 2004, Lilly announced their decision to move naveglitazar into Phase III registration studies. Shortly afterwards, the FDA provided new guidance regarding preclinical and clinical safety assessments for current and future PPAR molecules in clinical development. Accumulated rodent data reviewed by the agency for a number of PPAR agonists (gamma, alpha or dual agonists), but not including naveglitazar, showed carcinogenicity findings that did not demonstrate adequate margins of safety to support continued clinical development with some members of this class of compounds. Based on this information, the new guidance provided by the FDA for all compounds in this class indicates that clinical studies longer than six months in duration cannot be initiated until two-year rodent carcinogenicity studies are completed and submitted for agency review. Any proposed studies of greater than six months duration have been placed on clinical hold until carcinogenicity data are reviewed and adequate margins of safety are demonstrated.

Two-year carcinogenicity studies on naveglitazar are ongoing and data for evaluation should be available in 2006. While the full impact of these guidelines on naveglitazar clinical development plans and timelines is being reviewed, it is clear that, based on the timing of the completion of the carcinogenicity studies and subsequent FDA review of the data allowing the initiation of long-term safety studies, there will be an estimated delay of 18-24 months in the initiation of clinical studies of greater than six months duration. Lilly will review and revise their naveglitazar Phase III development plan accordingly.

In June 2002, we announced that we had earned a $1.1 million milestone payment as a result of Lilly s filing with the FDA an IND for LY929, a PPAR modulator for the treatment of Type II diabetes, metabolic diseases and dyslipidemias. In November 2002, we announced that we had earned a $2.1 million milestone payment as a result of Lilly s filing with the FDA an IND for LY674, a PPAR modulator for the treatment of atherosclerosis. In July

Table of Contents

2005, we announced that we had earned a $1.6 million milestone payment as a result of LY674 entering Phase II studies. We will receive additional milestones if these products continue through the development process, and royalties on product sales if the products receive marketing approval. Lilly also has two other PPAR compounds on IND track, the compound numbers for which have not been disclosed. If IND s are filed by May 2006, the Company will continue to qualify for milestones and royalties.

Inflammatory Disease Collaborative Program

Abbott Collaboration. In July 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 was 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.

When the research phase of the collaboration ended in July 1999, Abbott retained rights to certain selective glucorcorticoid receptor modulators, or SGRMs, whose development has now been slowed or halted. We retained rights to all other compounds discovered through the collaboration, as well as recaptured technology rights. Abbott will make milestone and royalty payments on products targeted at inflammation resulting from the collaboration. Each party will be responsible for the development, registration, and commercialization of the products in its respective field.

TPO / Inflamatory Disease / Oncology Collaborative Program

GlaxoSmithKline Collaboration. In February 1995, we entered into a research and development collaboration with SmithKline Beecham (now GlaxoSmithKline) to use our proprietary expertise 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