

ATRIX LABORATORIES INC

Form 10-K

March 03, 2004

Table of Contents

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

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**FORM 10-K**

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

**For the Fiscal Year Ended December 31, 2003**

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

**For the transition period from            to**

Commission File Number 0-18231

**ATRIX LABORATORIES, INC.**

(Exact name of registrant as specified in its charter)

**Delaware**  
(State or other jurisdiction of  
incorporation or organization)

**84-1043826**  
(I.R.S. Employer  
Identification No.)

**2579 Midpoint Drive, Fort Collins, Colorado**  
(Address of principal executive office)

**80525**  
(Zip Code)

Registrant's telephone number, including area code: (970) 482-5868

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

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

Common Stock, \$0.001 par value

(Title of Class)

Series A Preferred Stock Purchase Rights

(Title of Class)

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

## Edgar Filing: ATRIX LABORATORIES INC - Form 10-K

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

Indicate by check mark whether the registrant is an accelerated filer (as defined in Rule 12b-2 of the Exchange Act).    Yes ☒ p    No ☐ o

The aggregate market value of voting stock held by non-affiliates of the registrant as of June 30, 2003 was approximately \$360.2 million based upon the closing sale price on The Nasdaq National Market for that date. This calculation excludes shares of common stock held by registrant's officers and directors and each person known by the registrant to beneficially own more than 5% of the registrant's outstanding common stock, as such persons may be deemed to be affiliates. This determination of affiliate status should not be deemed conclusive for any other purpose.

The number of shares outstanding of the registrant's common stock as of March 1, 2004, was 21,629,018.

### DOCUMENTS INCORPORATED BY REFERENCE

The information required by Part III of this report, to the extent not set forth in Part III, is incorporated by reference from the registrant's definitive proxy statement for its Annual Meeting of Stockholders scheduled to be held on May 2, 2004.

### TABLE OF CONTENTS

	<u>Page</u>
<b>PART I</b>	1
<u>Item 1.</u> <u>Business</u>	1
<u>Item 2.</u> <u>Properties</u>	31
<u>Item 3.</u> <u>Legal Proceedings</u>	31
<u>Item 4.</u> <u>Submission of Matters to a Vote of Security Holders</u>	31
<b>PART II</b>	32
<u>Item 5.</u> <u>Market for the Registrant's Common Equity, Related Stockholder Matters and Issuer Purchases of Equity Securities</u>	32
<u>Item 6.</u> <u>Selected Financial Data</u>	33
<u>Item 7.</u> <u>Management's Discussion and Analysis of Financial Condition and Results of Operations</u>	35
<u>Item 7A.</u> <u>Quantitative and Qualitative Disclosures About Market Risk</u>	51
<u>Item 8.</u> <u>Financial Statements and Supplementary Data</u>	52
<u>Item 9.</u> <u>Changes in and Disagreements with Accountants on Accounting and Financial Disclosure</u>	52
<u>Item 9A.</u> <u>Controls and Procedures</u>	52
<b>PART III</b>	53
<u>Item 10.</u> <u>Directors and Executive Officers of the Registrant</u>	53
<u>Item 11.</u> <u>Executive Compensation</u>	53
<u>Item 12.</u> <u>Security Ownership of Certain Beneficial Owners and Management and Related Stockholder Matters</u>	53
<u>Item 13.</u> <u>Certain Relationships and Related Transactions</u>	53
<u>Item 14.</u> <u>Principal Accountant Fees and Services</u>	53
<b>PART IV</b>	55
<u>Item 15.</u> <u>Exhibits, Financial Statement Schedules, and Reports on Form 8-K</u>	55
<u>Consent of Deloitte &amp; Touche LLP</u>	
<u>Rule 13a-14(a) Certification of the CEO</u>	
<u>Rule 13a-14(a) Certification of the CFO</u>	
<u>Section 1350 Certification of CEO</u>	
<u>Section 1350 Certification of CFO</u>	



**Table of Contents**

**FORWARD-LOOKING INFORMATION**

*Statements in this report that are not descriptions of historical facts are forward-looking statements provided under the safe harbor protection of the Private Securities Litigation Reform Act of 1995. These statements are made to enable a better understanding of our business, but because these forward-looking statements are subject to many risks, uncertainties, future developments and changes over time, actual results may differ materially from those expressed or implied by such forward-looking statements. Examples of forward-looking statements are statements about anticipated financial or operating results, financial projections, business prospects, future product performance, future research and development results, anticipated regulatory filings and approvals, and other matters that are not historical facts. Such statements often include words such as believes, expects, anticipates, intends, plans, estimates or similar expressions.*

*These forward-looking statements are based on the information that was currently available to us, and the expectations and assumptions that were deemed reasonable by us, at the time the statements were made. We do not undertake any obligation to update any forward-looking statements in this report or in any of our other communications, except as required by law, and all such forward-looking statements should be read as of the time the statements were made, and with the recognition that these forward-looking statements may not be complete or accurate at a later date.*

*Many factors may cause or contribute to actual results or events being materially different from those expressed or implied by forward-looking statements. Although it is not possible to predict or identify all such factors, they include those set forth under Factors Affecting Our Business and Prospects below. These risk factors include, but are not limited to, the results of research and development efforts, the results of preclinical and clinical testing, the effect of regulation by the U.S. Food and Drug Administration, or FDA, and other agencies, the impact of competitive products, product development, commercialization and technology difficulties, the results of financing efforts, the effect of our accounting policies and other risks detailed in our filings with the Securities and Exchange Commission.*

**PART I**

**Item 1. Business.  
Overview**

Atrix Laboratories, Inc. and its subsidiaries are collectively referred to herein as Atrix, the Company, we, our or us. Incorporated in Delaware in 1986, we are an emerging specialty pharmaceutical company focused on advanced drug delivery. With unique patented drug delivery technologies, we are currently developing a diverse portfolio of products, including proprietary oncology and dermatology products. We also form strategic alliances with a variety of pharmaceutical and biotechnology companies to develop products utilizing our various drug delivery systems and/or to commercialize our products. Current significant strategic alliances include, Sanofi-Synthelabo Inc., Fujisawa Healthcare, Inc., Sandoz Inc. (formerly Geneva Pharmaceuticals, Inc.), Pfizer Inc., Sosei Co. Ltd., MediGene AG and Yamanouchi, Mayne Pharma, Tecnofarma, Han All Pharmaceutical Co., Ltd. and CollaGenex Pharmaceuticals, Inc.

Our drug delivery systems deliver controlled amounts of drugs in various time frames to address a range of therapeutic and patient needs. Atrigel is our original proprietary sustained release biodegradable polymer drug delivery system. We believe that the Atrigel system may provide benefits over traditional methods of drug administration such as safety and effectiveness, ease of applications, site-specific or systemic delivery, customized release rates and biodegradability. Our four additional drug delivery systems are SMP™, MCA™, BCP™ and BEMA™.

## **Table of Contents**

### **Our Strategy**

Our primary objective is to be a leading specialty pharmaceutical company focused on advanced drug delivery to improve the effectiveness of existing pharmaceuticals and new chemical entities, including proteins, peptides and small molecules. Key elements to our strategy include:

*Expanding our portfolio of products through internal development.* We intend to develop our own pharmaceutical product candidates and undertake human clinical development ourselves. We are applying our drug delivery technologies to novel applications and formulations of approved pharmaceutical products seeking to improve their delivery and effectiveness.

*Maximizing the value of products by entering into late-stage collaborative relationships.* We believe that advancing our products through late-stage development before seeking commercialization partners allows us to license our products on more favorable terms than would be available earlier in the development cycle.

*Licensing our technologies to major pharmaceutical and biotechnology companies.* We are focused on developing partnerships with pharmaceutical and biotechnology companies to utilize our drug delivery systems for new chemical entities and life cycle management products. We also conduct preclinical feasibility studies with various companies.

*Pursuing acquisitions of complementary drug delivery technologies.* We are pursuing opportunities that further strengthen our delivery technologies. We believe that if we are able to increase the number of delivery systems in our portfolio we can increase our attractiveness as a product development partner with other pharmaceutical and biotechnology companies. In addition, we believe that pursuit of this strategy will strengthen our internal product development efforts.

*Acquiring or in-licensing proprietary compounds.* To expand our pipeline, we seek to identify drug candidates that may benefit from the application of our drug delivery technologies. These compounds generally have entered or are about to enter human clinical trials.

*Forward integration.* We intend to pursue a strategy of forward integration to include sales and marketing of our own products either through internal development or acquisition of late-stage products.

### **2003 Highlights and Recent Developments**

The following discussion highlights significant events for our company during the year ended December 31, 2003 and thereafter:

#### *Atrisone Acne Product*

In January 2004, we announced successful completion of two pivotal Phase III clinical efficacy studies for our Atrisone acne product. Over 3,000 patients were enrolled in these double-blind, randomized, vehicle-controlled studies, which were conducted in over 100 centers around the United States and Canada. We expect to file a New Drug Application, or NDA, with the FDA for the Atrisone acne product by mid-2004.

#### *Eligard 30-mg Four-Month Product*

We received approval from the FDA for our Eligard 30-mg four-month product in February 2003. In March 2003, Sanofi-Synthelabo Inc. launched the product into the U.S. market, and we received a \$6.0 million milestone payment in April 2003 for the first commercial sale.

#### *Eligard 45-mg Six-Month Product*

In November 2003, we announced the completion of the pivotal Phase III clinical study for the Eligard 45-mg six-month product. In February 2004, we submitted an NDA to the FDA for this product.

**Table of Contents**

*Eligard International*

In January 2003, we entered into an exclusive licensing agreement with Sosei Co., Ltd. to develop and commercialize our Eligard products in Japan. Sosei paid us a one-time non-refundable license fee of \$1.0 million. We may receive additional payments for research and development support and payments for specific regulatory and sales milestones. Additionally, we will receive royalty payments based on sales of the Eligard products if the products are approved for marketing by the Japanese Ministry of Health, Labor and Welfare, or MHLW. Sosei will be responsible for any preclinical and clinical studies required for approval and will be responsible for submission of the necessary documents to obtain marketing authorization from the MHLW. In December 2003, Sosei entered into a co-promotion agreement with Nippon Organon K.K. to market our Eligard products. We will manufacture the Eligard products for Sosei and will earn manufacturing margins.

In February 2003, Tecnofarma received approval to market the Eligard 7.5-mg one-month and 22.5-mg three-month products in Argentina. Tecnofarma launched the Eligard 7.5-mg one-month product in May 2003. In January 2004, Tecnofarma received approval to market the Eligard 7.5-mg one-month and 22.5-mg three-month products in Mexico.

In November 2003, Sanofi-Synthelabo Canada received a notice of compliance from the Therapeutic Products Directorate of Health Canada for our Eligard 7.5-mg one-month and 22.5-mg three-month products. Sanofi-Synthelabo Canada will be responsible for marketing the products in Canada. Sanofi-Synthelabo launched the Eligard 7.5-mg one-month and 22.5-mg three-month products in December 2003. In February 2004, Sanofi-Synthelabo Canada received a notice of compliance from the Therapeutic Products Directorate of Health Canada for our Eligard 30-mg four-month product.

In December 2003, MediGene AG, our European licensee, received marketing authorization from the German pharmaceutical regulatory authority, Bundesinstitut für Arzneimittel und Medizinprodukte, or BfArM, for our Eligard 7.5-mg one-month product. MediGene received marketing authorization from BfArM for our Eligard 22.5-mg three-month product in January 2004. Also, in January 2004 we entered into an agreement with MediGene and Yamanouchi, naming Yamanouchi as our pan-European marketing partner.

In November 2003, Mayne Pharma, our Australian licensee, received marketing approval of Eligard 7.5-mg one-month, 22.5-mg three-month and 30-mg four-month products in Australia from the Australian Drug Evaluation Committee. Mayne Pharma launched the Eligard 7.5-mg one-month, 22.5-mg three-month and 30-mg four-month products in February 2004.

In January 2004, we entered into an exclusive licensing agreement with Han All Pharmaceutical Co., Ltd. to develop and commercialize our Eligard products in Korea. Han All paid us a one-time non-refundable license fee of \$0.3 million in January 2004, and we may receive additional payments for research and development support. Additionally, we will receive royalty payments based on sales of the Eligard products if the products are approved for marketing in Korea. Han All will be responsible for any preclinical and clinical studies required for approval and will be responsible for submission of the necessary documents to obtain marketing authorization. We will manufacture the Eligard products for Han All and will earn manufacturing margins.

*Other Products*

In January 2004, we announced that Pfizer Inc. completed the initial phase of clinical testing of a novel bone growth product formulated in our Atrigel sustained-release drug delivery system and is advancing the product into additional human clinical testing.

In August 2003, we submitted an investigational new drug application, or IND, to the FDA for an Atrigel formulation of octreotide, which is designed to deliver the pharmaceutical over a 30-day period for the long term treatment of severe diarrhea and flushing episodes associated with carcinoid tumors.

**Table of Contents**

We received approval from the FDA for our Abbreviated New Drug Application, or ANDA, for lidocaine/prilocaine cream in August 2003, and our partner, Sandoz, subsequently commenced marketing of this product. Our product is the AB-rated generic to EMLA--Registered Trademark-- Anesthetic Cream (lidocaine 2.5% and prilocaine 2.5%).

In August 2003, we received a non-approval letter from the FDA indicating that a generic dermatology product was not approved. We are currently appealing this action through the FDA; however, we cannot provide any assurance that our appeal will be successful.

We received approval from the FDA for our ANDA for mometasone furoate ointment USP, 0.1% in November 2003, and our partner, Sandoz, subsequently commenced marketing of this product. Our product is the AB-rated generic to Elocon--Registered Trademark-- brand of mometasone furoate ointment 0.1%.

In December 2003, we received tentative approval from the FDA for mometasone furoate topical solution, USP, 0.1%, an AB-rated generic of Elocon--Registered Trademark-- lotion 0.1%, which is currently protected by a patent until 2007. Sandoz intends to market this product upon expiration of the patent in 2007.

In January 2004, we announced approval from the FDA for our ANDA for betamethasone dipropionate cream, USP, 0.05% (Augmented), and our partner, Sandoz, subsequently commenced marketing of this product. Our product is an AB-rated generic to Diprolene--Registered Trademark-- AF Cream 0.05% brand augmented betamethasone dipropionate, which is marketed by Schering Plough Corporation.

In January 2004, we announced that we submitted three ANDAs to the FDA for approval of generic formulations of undisclosed dermatology products. With these applications, we currently have six ANDA submissions under FDA review.

In September 2003, we reached an agreement to terminate our joint venture with a subsidiary of Elan Corporation. Termination of the joint venture returns the BEMA-fentanyl product to us. Upon termination, we acquired Elan's ownership interest in the joint venture, Transmucosal Technologies Ltd., in exchange for Elan receiving a portion of any consideration we receive from the licensing of BEMA-fentanyl and a royalty based on net sales of BEMA-fentanyl if the product is commercialized.

**Our Marketed Products and Products Under Development**

The following table details certain information about our marketed pharmaceutical products and products under development:

Pharmaceutical Products and Product Candidates	Delivery System	Indication	Status	Collaborative Partner(s)
Eligard 7.5-mg one-month	Atrigel	Prostate cancer	Marketed	Sanofi-Synthelabo
			U.S. launch, May 2002	Tecnofarma
			Argentina launch, May 2003	Sanofi-Synthelabo
			Canada launch, Dec 2003	Mayne Pharma
			Australia launch, Feb 2004	MediGene/Yamanouchi
			Approval in Germany, Dec 2003	Tecnofarma
			Approval in Mexico, Jan 2004	
			Pending approval in Korea, Israel, Latin America and South Africa	Han All, Luxembourg Pharma, Tecnofarma and Key Oncologics
Eligard 3.75-mg three-month	Atrigel	Prostate cancer	Bioequivalence clinical trials	Sosei





**Table of Contents**

<b>Pharmaceutical Products and Product Candidates</b>	<b>Delivery System</b>	<b>Indication</b>	<b>Status</b>	<b>Collaborative Partner(s)</b>
Eligard 22.5-mg three-month	Atrigel	Prostate cancer	Marketed U.S. launch, Sept. 2002 Canada launch, Dec 2003 Australia launch, Feb 2004 Approval in Argentina, Feb 2003 Approval in Germany, Jan 2004 Approval in Mexico, Jan 2004 Pending approval in Korea, Israel, Latin America and South Africa	Sanofi-Synthelabo  Sanofi-Synthelabo  Mayne Pharma  Tecnofarma  MediGene/ Yamanouchi Tecnofarma  Han All, Luxembourg Pharma, Tecnofarma and Key Oncologics
Eligard 11.25-mg three-month	Atrigel	Prostate cancer	In development	Sosei
Eligard 30-mg four-month	Atrigel	Prostate cancer	Marketed U.S. launch, March 2003 Australia launch, Feb 2004 Canada approval, Feb 2004 Pending approval in Korea, Israel, Latin America and South Africa	Sanofi-Synthelabo  Mayne Pharma  Sanofi-Synthelabo  Han All, Luxembourg Pharma, Tecnofarma and Key Oncologics
Eligard 45-mg six-month formulation	Atrigel	Prostate cancer	NDA submitted Feb 2004	Sanofi-Synthelabo, MediGene/ Yamanouchi, Mayne Pharma, Han All, and Luxembourg Pharma
One- and three-month leuprolide products for endometriosis	Atrigel	Endometriosis	Preclinical	None
Atrisone	SMP <sup>TM</sup>	Acne vulgaris  Other indications (rosacea, atopic dermatitis, other)	Phase III Completed Preclinical/ Phase I/ II	Fujisawa Healthcare  Fujisawa Healthcare
Bone growth product	Atrigel	Bone regeneration	Completed Phase I	Pfizer
Octreotide	Atrigel	Symptoms of carcinoid syndrome	INDA submitted Phase I	None
Lidocaine 2.5%/ Prilocaine 2.5% Cream an AB-rated generic to	N/A	Topical anesthetic	Marketed U.S. launch, Sept	Sandoz



**Table of Contents**

Pharmaceutical Products and Product Candidates	Delivery System	Indication	Status	Collaborative Partner(s)
Mometasone Ointment, 0.1% an AB-rated generic to Elocon® Ointment 0.1%	N/A	Topical corticosteroid	Marketed U.S. launch, Dec 2003	Sandoz
Betamethasone Dipropionate Cream USP, 0.05% (augmented) an AB-rated generic to Diprolene® AF Cream 0.05%	N/A	Topical corticosteroid	Marketed U.S. launch, Jan 2004	Sandoz
Mometasone Furoate Topical Solution USP, 0.1% an AB-rated generic of Elocon® lotion 0.1%	N/A	Topical corticosteroid	Tentative approval, currently on patent until 2007	Sandoz
Growth hormone releasing peptide-1.	Atrigel	Renal insufficiency	Phase I	Tulane University Health Science Center
Atrigel- <sup>125</sup> IUDR MICRaS	Atrigel	Treatment of solid tumors	Preclinical	None
Atrigel-Risperidone	Atrigel	Schizophrenia	Preclinical	None
BEMA-fentanyl	BEMA	Chronic and breakthrough cancer pain	Phase I	Terminated Elan joint venture agreement Sept 2003

The following table details certain information about our marketed dental and OTC products:

Dental/OTC Products	Delivery System	Indication	Status	Collaborative Partner(s)
Atridox	Atrigel	Antibiotic therapy for chronic periodontitis	Marketed Launched 1998	CollaGenex, PharmaScience,
Atrisorb-Doxycycline FreeFlow GTR Barrier	Atrigel	Tissue regeneration and infection reduction following periodontal surgery	Marketed Launched 2002	CollaGenex, Pharmascience
Atrisorb FreeFlow GTR Barrier	Atrigel	Tissue regeneration following periodontal surgery	Marketed Launched 1998	CollaGenex, Pharmascience
Doxirobe® Gel	Atrigel	Periodontitis in companion animals	Marketed Launched 1997	Pfizer Animal Health
Orajel-Ultra®	MCA™	Canker sores	Marketed OTC	



**Table of Contents**

***Marketed Pharmaceutical Products and Product Candidates***

***Eligard Products***

Our proprietary Eligard products for prostate cancer incorporate a leutinizing hormone-releasing hormone, or LHRH, agonist with our proprietary Atrigel drug delivery system. The Atrigel technology allows for sustained delivery of leuprolide acetate for periods ranging from one month to six months.

Clinical trials have demonstrated that the sustained release of a LHRH agonist decreases testosterone levels to suppress tumor growth in patients with hormone-responsive prostate cancer. The Phase III results for the Eligard 7.5-mg one-month, 22.5-mg three-month, 30-mg four-month and 45-mg six-month products revealed low testosterone levels with 99% of completing patients achieving and maintaining castrate suppression by the conclusion of the studies.

Our Eligard products are injected subcutaneously as a liquid with a small gauge needle. The polymers precipitate after injection, forming a solid implant in the body that slowly releases the leuprolide as the implant is bioabsorbed. We believe our Eligard products, which use a small needle and are injected subcutaneously, are safe and effective in treating prostate cancer.

Net sales and royalties for our Eligard products for the years ended December 31, 2003 and 2002 were \$14.1 million and \$2.1 million, respectively. There were no sales of Eligard products in 2001.

***Eligard 7.5-mg One-Month Product***

We received FDA approval for our Eligard 7.5-mg one-month product in January 2002, and Sanofi-Synthelabo commenced U.S. marketing of this product in May 2002.

In November 2001, MediGene submitted a Marketing Authorization Application, or MAA, for our Eligard 7.5-mg one-month product to the German pharmaceutical regulatory authority, BfArM, as a Reference Member State under a Mutual Recognition Procedure. MediGene received marketing authorization from the BfArM for our Eligard 7.5-mg one-month product in December 2003. In January 2004, we announced that we and MediGene named Yamanouchi as its pan-European marketing partner. We anticipate Yamanouchi will submit a modified MAA to specific Concerned Member States in the European Union for marketing approval in other key countries.

Tecnofarma launched Eligard 7.5-mg in Argentina in May 2003 and received approval in Mexico in January 2004.

Mayne Pharma submitted a General Marketing Authorization, or GMA, with the Australian regulatory authority in August 2002 for our Eligard 7.5-mg one-month product. In November 2003, Mayne Pharma received marketing approval of our Eligard 7.5-mg one-month product from the Australian Drug Evaluation Committee and launched the product in February 2004.

Sanofi-Synthelabo Canada filed a New Drug Submissions, or NDS, with the Canadian regulatory authority in December 2001 for our Eligard 7.5-mg one-month product. In November 2003, Sanofi-Synthelabo Canada received notice of compliance from the Therapeutic Products Directorate of Health Canada for our Eligard 7.5-mg one-month product and launched the product in December 2003.

***Eligard 22.5-mg Three-Month Product***

In July 2002, we received approval from the FDA for our Eligard 22.5-mg three-month product, and Sanofi-Synthelabo commenced marketing in the United States in September 2002.

In April 2002, MediGene submitted an MAA for our Eligard 22.5-mg three-month product to the German pharmaceutical regulatory authority, BfArM, as a Reference Member State under a Mutual Recognition Procedure and in January 2004, received marketing authorization. Yamanouchi intends to submit a modified MAA to specific Concerned Member States in the European Union for marketing approval in other key countries.



## **Table of Contents**

Tecnofarma received approval for Eligard 22.5-mg three-month product in Argentina in February 2003 and received approval in Mexico in January 2004.

Mayne Pharma submitted a GMA with the Australian regulatory authority in August 2002 for our Eligard 22.5-mg three-month product and received marketing approval from the Australian Drug Evaluation Committee in November 2003. Mayne Pharma launched the Eligard 22.5-mg three-month product in February 2004.

Sanofi-Synthelabo Canada filed an NDS with the Canadian regulatory authority in December 2001 for our Eligard 22.5-mg three-month product. In November 2003, Sanofi-Synthelabo Canada received notice of compliance from the Therapeutic Products Directorate of Health Canada for our Eligard 22.5-mg three-month product and launched the product in December 2003.

### *Eligard 30-mg Four-Month Product*

In February 2003, we received FDA approval for Eligard 30-mg four-month product, and Sanofi-Synthelabo commenced U.S. marketing of this product in March 2003.

Mayne Pharma submitted a GMA with the Australian regulatory authority in August 2002 for our Eligard 30-mg four-month product and received marketing approval from the Australian Drug Evaluation Committee in November 2003.

Sanofi-Synthelabo Canada filed an NDS with the Canadian regulatory authority in November 2002 for our Eligard 30.0-mg three-month product and received a notice of compliance from the Therapeutic Products Directorate of Health Canada for our Eligard 30-mg four-month product in February 2004.

### *Eligard 45-mg Six-Month Product*

Our Eligard 45-mg six-month product for prostate cancer completed Phase III clinical trials in November 2003, and we submitted an NDA to the FDA in the February 2004.

### *One- and Three-Month Leuprolide Products for Endometriosis*

In November 2002, we entered into an exclusive North American marketing agreement with EmerGen, Inc. for a one-month and a three-month leuprolide product for the treatment of endometriosis. The new leuprolide products for endometriosis involve the development and clinical testing of half-strength dose versions of Eligard 7.5-mg one-month and Eligard 22.5-mg three-month products. In July 2003, we received the rights back from EmerGen for these products. Currently, these products are in the preclinical stage of development.

### *Atrisone*

We are currently developing Atrisone, our proprietary product for the treatment of acne, rosacea, atopic dermatitis and additional indications. Atrisone incorporates dapsone, an anti-inflammatory and antimicrobial drug, with our proprietary SMP drug delivery system. Dapsone is a potent antibiotic with a separate anti-inflammatory activity, which may reduce inflammation associated with acne. The goal for Atrisone is topical application to the acne lesion so as to reduce any potential side effects, such as anemia. After topical application, the blood levels of dapsone are 500 to 1,000 times less than found when the compound is administered orally, thus significantly reducing the potential for systemic side effects.

In January 2004, we announced successful completion of two pivotal Phase III clinical efficacy studies for our Atrisone acne product. Over 3,000 patients were enrolled in these double-blind, randomized, vehicle-controlled studies, which were conducted in over 100 centers around the United States and Canada. We expect to file an NDA with the FDA for the Atrisone acne product in mid-2004.



**Table of Contents**

*Generic Dermatology Products*

We received approval from the FDA for our ANDA for lidocaine/prilocaine cream in August 2003. Our product is the AB-rated generic to EMLA Anesthetic Cream (lidocaine 2.5% and prilocaine 2.5%) and is being marketed by our partner, Sandoz.

We received approval from the FDA for our ANDA for mometasone furoate ointment USP, 0.1% in November 2003. Our product is an AB-rated generic of Elocon® brand of mometasone furoate ointment USP, 0.1% and is being marketed by our partner, Sandoz.

In December 2003, we received tentative approval from the FDA for mometasone furoate topical solution USP, 0.1%, an AB-rated generic of Elocon® lotion 0.1% currently on patent until 2007. Sandoz intends to market this product upon patent expiration.

We received approval from the FDA for our ANDA for betamethasone dipropionate cream USP, 0.05% (augmented) in January 2004. Our product is an AB-rated generic to Diprolene® AF Cream 0.05% brand augmented betamethasone dipropionate, which is marketed by Schering Plough Corporation.

In January 2004, we announced that we submitted three ANDAs to the FDA for approval of generic formulations of undisclosed dermatology products. With these applications, we currently have six ANDA submissions under FDA review. Of the generic topical products approved thus far, we were in each case, the second or later approval, thus sales to date have been minimal.

*Bone Growth Product*

In January 2004, we announced that Pfizer completed the initial phase of clinical testing of a novel bone growth product, formulated in our proprietary Atrigel sustained-release drug delivery system and is advancing the product into additional human clinical testing. Pfizer plans to conduct all clinical trials of the Atrigel formulation. We will continue to support this product through production of clinical supplies and consultation.

*Octreotide*

In August 2003, we submitted an IND to the FDA for an Atrigel formulation of octreotide, which is designed to deliver the pharmaceutical over a 30-day period for the long term treatment of severe diarrhea and flushing episodes associated with carcinoid tumors. We are currently in development stages for this product.

*BEMA-Fentanyl*

Through our joint venture with Elan, we were developing BEMA-fentanyl, which uses our proprietary BEMA drug delivery system with fentanyl, an opiate analgesic, for breakthrough cancer pain and potentially the management of chronic pain. The BEMA delivery system is a polymer-based system designed to deliver systemic levels of drugs across oral mucosal tissues. The system consists of a thin, semi-soft bioerodible multi-layer disc of various polymers, which adheres readily to the mucosal tissues. The BEMA disc softens upon contact with moisture and erodes away over approximately 10 to 20 minutes as it delivers the drug. In late 2001, we submitted an IND to the FDA and subsequently commenced a Phase I clinical safety study for BEMA-fentanyl. In September 2003, we reached an agreement to terminate our joint venture with a subsidiary of Elan Corporation. Termination of the joint venture returns the BEMA-fentanyl product to us. Upon termination, we acquired Elan's ownership interest in the joint venture, Transmucosal Technologies Ltd., in exchange for Elan receiving a portion of any consideration we receive from the licensing of BEMA-fentanyl and a royalty based on net sales of BEMA-fentanyl if the product is commercialized.

**Table of Contents*****Marketed Dental and Over-The-Counter Products and Product Candidates******Dental Products***

We have a number of approved products that target the dental market. Atridox, which combines the Atrigel system and the antibiotic doxycycline, is a minimally invasive treatment intended to control the bacteria that cause periodontal disease. Atridox was awarded the American Dental Association Seal of Acceptance that signifies a dental product's safety, effectiveness and the scientific validity of its health benefits.

Our Atrisorb-D product also uses the Atrigel system with the antibiotic doxycycline to address infections following periodontal surgery and thereby improve healing. Atrisorb-D is a biodegradable polymer that utilizes the Atrigel system to aid in the guided tissue regeneration of a tooth's support following osseous flap surgery or other periodontal procedures.

In addition to these dental products, Pfizer Animal Health currently has the worldwide marketing right of our Doxirobe Gel product, a periodontal disease treatment for companion animals.

Net sales and royalties for our dental products in the years ended December 31, 2003, 2002 and 2001 were \$4.2 million, \$2.6 million and \$2.4 million, respectively.

***Over-The-Counter Products***

Orajel-Ultra Mouth Sore Medicine is an over-the-counter product that utilizes our proprietary MCA drug delivery system and is currently marketed by Del Laboratories. We will receive royalties on the net sales of this product through October 2016.

**Our Drug Delivery Technologies**

The following chart provides a brief description of our drug delivery systems:

<b>Technology</b>	<b>Description</b>	<b>Application</b>
Atrigel System	Biodegradable sustained release implant for local or systemic delivery	Delivery of drugs from days to months
Solvent Microparticle System (SMP)	Topical gel providing two-stage delivery through the skin	Delivery of water insoluble drugs through the skin
Mucocutaneous Absorption System (MCA)	Water resistant topical gel providing sustained delivery	Film for either wet or dry surfaces
Biocompatible Polymer System (BCP)	Non-cytotoxic gel/liquid for topical delivery ( non-cytotoxic means the material does not kill cells or tissue in the body)	Protective gel film for wound healing and liquid formulation for wound washing
Bioerodible Mucoadhesive Disc System (BEMA)	Bioerodible disc for local or systemic delivery	Delivery of drugs through mucosal membranes

***Atrigel System***

The Atrigel drug delivery system consists of biodegradable polymers, similar to those used in biodegradable sutures, dissolved in biocompatible carriers. Pharmaceuticals may be blended into this liquid delivery system at the time of manufacturing or, depending upon the product, may be added later by the physician at the time of use. When the liquid product is injected subcutaneously or intramuscularly through a

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small gauge needle or placed into accessible tissue sites through a cannula, displacement of the carrier with water in the tissue fluids causes the polymer to precipitate, forming a solid film or implant. The drug encapsulated within the implant is then released in a controlled manner as the polymer matrix biodegrades with time. Depending upon the patient's medical needs, the Atrigel system can deliver small molecules, peptides or proteins over a period ranging from days to months.

## **Table of Contents**

The delivery system containing the suspended drug is injected into the patient. Once injected, the solvent diffuses out as water diffuses into the delivery system with the suspended drug. This process leads to solidification of the polymer to form an implant. Rapid release of a portion of the drug during the initial diffusion of the solvent is called the burst phase. Once the implant is formed, the drug is slowly released in a controlled manner for the specified time period.

We believe that the Atrigel system addresses many of the limitations associated with traditional drug delivery technologies. Most drugs are administered orally or by injection at intermittent and frequent doses. These routes of administration are not optimal for several reasons, including:

destruction of the compound in the gastrointestinal system,

difficulty in maintaining uniform drug levels over time,

problems with toxicity and side effects,

high costs due to frequent administration, and

poor patient compliance.

Furthermore, innovations in biotechnology have led to an increase in the number of protein and peptide drugs under development. These therapeutics, because of their larger molecular size and susceptibility to degradation in the gastrointestinal tract, often are required to be administered by multiple injections, usually in a hospital or other clinical setting.

We believe that the Atrigel system may provide benefits over traditional methods of drug administration such as tablets or capsules, injections and continuous infusion as a result of the following properties:

*Broad Applicability* The Atrigel system is compatible with a broad range of pharmaceutical compounds, including water soluble and insoluble compounds and high and low molecular weight compounds, including peptides and proteins.

*Site Specific Drug Delivery* The Atrigel system can be delivered directly to a target area, thus potentially achieving higher drug concentrations at the desired site of action to minimize systemic side effects.

*Systemic Drug Delivery* The Atrigel system can also be used to provide sustained drug release into the systemic circulation.

*Customized Continuous Release and Degradation Rates* The Atrigel system can be designed to provide continuous release of incorporated pharmaceuticals over a targeted time period thereby reducing the frequency of drug administration.

*Biodegradability* The Atrigel system will biodegrade and does not require removal when the drug is depleted.

*Ease of Application* The Atrigel system can be injected or inserted as flowable compositions, such as solutions, gels, pastes, and putties, by means of ordinary needles and syringes, or can be sprayed or painted onto tissues.

*Safety* All current components of the Atrigel system are biocompatible and have independently established safety and toxicity profiles. The polymers used in the system are members of a class of polymers, some of which have previously been approved by the FDA for human use in other applications.

### ***Solvent/ Microparticle System***

The Solvent/ Microparticle, or SMP, technology consists of a two-stage system designed to provide topical delivery of highly water-insoluble drugs to the skin. The combination of dissolved drug with a microparticle suspension of the drug in a single formulation allows a controlled amount of the dissolved

## **Table of Contents**

drug to permeate into the epidermal layer of the skin, while a high level of the microparticle drug is maintained just above the outermost layer of the skin for later delivery. The consistent microparticle size and distribution maximize drug delivery while minimizing crystal growth over the shelf life of the product.

### ***Mucocutaneous Absorption System***

The Mucocutaneous Absorption, or MCA, delivery system can be formulated as either alcohol-based gels or as aerosols for the localized delivery of drugs to the skin or mucosal tissues. The MCA formulations can be applied to dry, damp or even wet skin or mucosal surfaces. Because of the novel blend of cellulose polymers dissolved in alcohol, they quickly dry to form moisture-resistant films that can deliver drugs and/or promote healing. Depending on the desired application, the MCA products can be formulated to form opaque films to highlight the area of treatment, or to transparent films that are more cosmetically acceptable. The MCA formulations can be easily flavored to mask the taste of active ingredients for oral products and are compatible with liquid spray applicators.

### ***Biocompatible Polymer System***

The Biocompatible Polymer, or BCP system, composed of polymers, solvents and actives carefully selected for their low toxicity to skin cells, can be formulated as either film-forming gels or liquids for topical applications. The BCP gels are non-greasy, non-staining formulations that can be applied to wounded or denuded skin to deliver a drug, such as an antibiotic, and then dry to form a non-constricting, protective film over the wound. We believe the gels have the unique property of maintaining an ideal wound-healing environment by removing excess moisture from exudative wounds and transferring moisture from the gel into wounds that are too dry. The liquid BCP formulations are designed to provide effective cleansing of topical wounds or denuded skin without causing further trauma to the skin, thereby promoting faster healing with minimal scarring.

### ***Bioerodible Mucoadhesive System***

The Bioerodible Mucoadhesive, or BEMA, system is a proprietary polymer-based system designed to deliver systemic levels of drugs across oral or vaginal mucosal tissues. The semi-soft BEMA disc adheres readily to the mucosa, where it softens further on contact with moisture, becoming unnoticeable as it delivers the drug and erodes away. The BEMA system is versatile and can incorporate a wide variety of drugs, including proteins and peptides. The compound can be loaded into the mucoadhesive layer for delivery into the mucosal tissue, while minimizing drug release into surrounding tissues or cavities. The drug may also be loaded into the backing layer to provide more controlled release into the oral cavity.

Various properties of the BEMA products, such as residence time, bioerosion kinetics, taste, shape and thickness can be modified to the desired level to customize drug delivery to the medical need and patient needs. The BEMA technology has potential applications in pain management, anti-migraine compounds and anti-emetics.

## **Research and Development**

Our strategic goal is to devote substantial resources to our medical research and development efforts with the expectation of quickly moving products from the development stage to commercialization. During the year ended December 31, 2003, we continued to devote significant resources to the research and development of our Eligard, Atrisone and octreotide products. Currently, we have multiple compounds in various stages of preclinical development, a number of which are being developed through partnerships with a variety of external companies. Most of these projects are preliminary in nature and we cannot predict whether any of them will be commercialized.

Our research and development expenses were \$36.4 million, \$32.7 million and \$28.6 million for the years ended December 31, 2003, 2002 and 2001, respectively.

## **Table of Contents**

### **Collaborative Arrangements**

Our business strategy includes forming collaborations to provide technological, financial, marketing and other resources. We have entered into a number of such collaborative arrangements with a variety of pharmaceutical and biotechnology companies utilizing our various drug delivery systems and/or to commercialize our products. Current significant strategic alliances include Sanofi-Synthelabo Inc., Fujisawa Healthcare, Inc., Sandoz Inc., Pfizer Inc., Sosei Co. Ltd., MediGene AG and Yamanouchi, Mayne Pharma, Tecnofarma, Han All Pharmaceutical Co., Ltd. and CollaGenex Pharmaceuticals, Inc.

#### ***Sanofi-Synthelabo, Inc.***

In December 2000, we entered into an exclusive North American marketing agreement with Sanofi-Synthelabo for our Eligard one-month, three-month, and four-month prostate cancer treatment products. Under the terms of the agreement, we will manufacture the Eligard products and receive an agreed upon transfer price from Sanofi-Synthelabo as well as royalties from sales. In addition, we received an up-front license fee of \$8.0 million. As part of the agreement, Sanofi-Synthelabo purchased 824,572 shares of our common stock for \$15.0 million. The Sanofi-Synthelabo agreement provides for payments of up to \$60.0 million, including the purchase of our common stock, license fees and payments for clinical, regulatory and sales milestones for the Eligard products. In April 2003, we received a \$6.0 million milestone payment for the first commercial sale of our Eligard 30-mg four-month product. In January 2002, Sanofi-Synthelabo exercised its right to develop a six-month formulation of Eligard. Under the terms of the agreement, we receive reimbursement for research and development expenses related to the development of this six-month formulation. Additionally, we will receive payments for certain regulatory and sales milestones, a royalty based on sales of the product and will manufacture the six-month product at our facility. A Phase III clinical study for Eligard 45-mg six-month product was completed in November 2003, and we submitted an NDA to the FDA in February 2004.

#### ***Fujisawa Healthcare, Inc.***

In October 2001, we entered into a collaboration, license and supply agreement with Fujisawa for the exclusive North American marketing and distribution rights of our Atrisone acne treatment product. The Fujisawa agreement provides for payments of up to \$25.0 million for an up-front license fee, research and development support and certain milestone payments. Additionally, we will receive a royalty on net sales of the Atrisone product and a manufacturing margin. In October 2001, we received a \$2.0 million license fee upon signing of the agreement. In December 2002, Fujisawa exercised its option to explore additional indications for topical Atrisone. Similar to the original agreement, Fujisawa will be responsible for a significant portion of any research and development costs that arise for development of Atrisone for these additional indications.

In January 2004, we announced successful completion of our two pivotal Phase III clinical efficacy studies for our Atrisone acne product. Over 3,000 patients were enrolled in these double-blind, randomized, vehicle-controlled studies, which were conducted in over 100 centers around the United States and Canada. We expect to file an NDA with the FDA for the Atrisone acne product by mid-2004.

We received no milestone or license fee payments from Fujisawa for the year ended December 31, 2003.

#### ***Sandoz, Inc. (formerly Geneva Pharmaceuticals, Inc.)***

In August 2000, we entered into a development and supply agreement with Sandoz, Inc. (formerly Geneva Pharmaceuticals, Inc.), a subsidiary of Novartis, to conduct research and development activities on a collaborative basis to develop designated generic topical prescription dermatology products. Under the terms of the agreement, we will be responsible for validation, formulation, development and required clinical studies of selected products. This collaboration extends to the United States, although additional territories may be added at a later date. Sandoz will be responsible for market research and

## **Table of Contents**

commercialization of the products. Sandoz will reimburse us for 50% of the research and development expenses we incur, and both parties will share equally in the net profits from the sale of the products.

We received approval from the FDA for our ANDA for lidocaine/prilocaine cream in August 2003, and Sandoz subsequently commenced marketing of this product. Our product is the AB-rated generic to EMLA Anesthetic Cream (lidocaine 2.5% and prilocaine 2.5%).

We received approval from the FDA for our ANDA for mometasone furoate ointment USP, 0.1% in November 2003. The AB-rated generic to Elocon® brand of mometasone furoate ointment USP Ointment 0.1% will be marketed by Sandoz.

In December 2003, we received tentative approval from the FDA for mometasone furoate topical solution USP, 0.1%, an AB-rated generic of Elocon® lotion 0.1% currently on patent until 2007. Sandoz will market this product upon patent expiration.

In January 2004, we announced approval from the FDA for our ANDA for betamethasone dipropionate cream USP, 0.05% (augmented), an AB-rated generic to Diprolene® AF Cream 0.05% brand augmented betamethasone dipropionate, which is marketed by Schering Plough Corporation.

In January 2004, we announced that we submitted three ANDAs to the FDA for approval of generic formulations of undisclosed dermatology products. With these applications, we currently have six ANDA submissions under FDA review.

### ***Pfizer, Inc.***

In August 2000, we executed a non-exclusive comprehensive research and worldwide licensing agreement with Pfizer to provide broad-based access to our proprietary drug delivery systems in the development of new products. Pfizer will provide funding to develop and commercialize selected compounds developed by Pfizer using our patented drug delivery technologies. We retained co-manufacturing rights and will receive royalties on the sales of products that are successfully developed and commercialized under this agreement. Pfizer purchased 447,550 shares of our common stock for \$5.0 million as part of the agreement.

In January 2004, we announced that Pfizer completed the initial phase of clinical testing of a novel bone growth product, formulated in our Atrigel sustained-release drug delivery system and is advancing the product into additional human clinical testing.

As of December 31, 2003, all other products under the Pfizer agreement were in preclinical stages of development.

### ***MediGene AG/ Yamanouchi***

In April 2001, we entered into an exclusive European marketing agreement with MediGene AG, a German biotechnology company, to market our Eligard one-month, three-month and four-month products. MediGene also has the right to develop the Eligard 45-mg six-month product. Under the terms of the agreement, we will manufacture the Eligard products and we will receive additional payments for certain clinical, regulatory and sales milestones and royalties on sales. Pursuant to the agreement, we received an up-front license fee of \$2.0 million and MediGene purchased 233,918 shares of our common stock for \$3.8 million. Additionally, MediGene will provide funding to conduct clinical, research and regulatory activities associated with seeking European marketing approvals. The MediGene agreement provides for payments of up to \$16.0 million including MediGene's purchase of our common stock, the license fee and payments for certain clinical, regulatory and sales milestones.

In November 2001, MediGene submitted an MAA for our Eligard 7.5-mg one-month product to the German regulatory authority, BfArM, as a Reference Member State under a Mutual Recognition Procedure. In April 2002, MediGene submitted an MAA for our Eligard 22.5-mg three-month product to BfArM, as a Reference Member State under a Mutual Recognition Procedure. MediGene received marketing authorization from BfArM for our Eligard 7.5-mg one-month and Eligard 22.5-mg three-month

## **Table of Contents**

products in December 2003 and January 2004, respectively. The MAAs submitted by MediGene utilized data for the U.S. dosage strengths of Eligard, which is twice the strength of competing leuprolide acetate products used in Europe for the palliative treatment of hormone-sensitive advanced prostate cancer.

In January 2004, we entered into an agreement with MediGene and Yamanouchi, naming Yamanouchi as our pan-European marketing partner. We anticipate Yamanouchi will submit a modified MAA to specific Concerned Member States in the European Union for marketing approval in other key countries. We received no milestone or license fee payments from MediGene or Yamanouchi for the year ended December 31, 2003.

### ***CollaGenex Pharmaceuticals, Inc.***

In August 2001, we licensed the exclusive U.S. marketing rights of our dental products to CollaGenex, following the reacquisition of the sales and marketing rights from Block Drug Company. Under the terms of the CollaGenex agreement, we received \$1.0 million for an up-front license fee. Additionally, we receive a royalty on product sales and a manufacturing margin. As part of the transaction, we purchased 330,556 shares of CollaGenex's common stock for \$3.0 million. CollaGenex commenced U.S. marketing of Atridox and Atrisorb FreeFlow in November 2001 and Atrisorb-D in January 2002.

## **International Operations**

In February 2000, our wholly owned registered subsidiary, Atrix Laboratories GmbH, based in Bad Homburg, Germany, commenced operations. Atrix Laboratories GmbH was organized to conduct our European dental operations. Atrix Laboratories GmbH manages our business relationships with European distributors for the dental products and in 2002 commenced promoting Atridox directly to dentists in Germany. Atrix Laboratories GmbH currently holds the marketing authorizations for European sales of Atridox. To date, we have received individual marketing authorizations in sixteen European countries. In 2003, we reorganized our European operations and initiated the closing of our wholly owned subsidiary, Atrix Laboratories Limited in the United Kingdom, which we expect to complete in 2004.

In March 2002, we entered into an exclusive licensing agreement with Luxembourg Pharmaceuticals for the Israeli marketing rights of our four Eligard products. We also entered into exclusive licensing agreements in the third quarter of 2002 with the following marketing partners for our four Eligard products: Tecnofarma for Latin America (including Mexico) and Key Oncologics in South Africa. Each company will be responsible for regulatory submissions necessary to gain approval in their respective territories, and we will manufacture the products and will earn manufacturing margins and royalties on sales.

In November 2003, Mayne Pharma received marketing authorization from the Australian Drug Evaluation Committee for our Eligard one-month, three-month, and four-month products.

Sanofi-Synthelabo submitted NDSs in Canada for our Eligard 7.5-mg one-month and our Eligard 22.5-mg three-month products in December 2001, and an NDS was filed in Canada for our Eligard 30.0-mg four-month product in November 2002. In November 2003, Sanofi-Synthelabo received marketing authorization in Canada for our Eligard 7.5-mg one-month and Eligard 22.5-mg three-month products. In February 2004, Sanofi-Synthelabo received marketing authorization in Canada for our Eligard 30-mg four-month product.

In January 2003, we entered into an exclusive licensing agreement with Sosei Co., Ltd. to develop and commercialize our Eligard 3.75-mg and 11.25-mg products in Japan. Sosei will be responsible for submission of the necessary documents to obtain marketing authorization from the Japanese Ministry of Health, Labor and Welfare. We received \$1.0 million in January 2003 for an up-front license fee less \$0.1 million for taxes withheld. In December 2003, Sosei entered into a co-promotion agreement with Nippon Organon K.K. for the Eligard products in Japan.

In January 2004, we entered into an exclusive licensing agreement with Han All Pharmaceutical Company, Ltd. to develop and commercialize our four Eligard products in Korea. Han All will be



**Table of Contents**

responsible for submission of the necessary documents to obtain market authorization. We will earn manufacturing margins on sales.

Our revenues from foreign sources, including the joint venture with Elan, were \$4.5 million, \$3.1 million and \$5.5 million for the fiscal years ended December 31, 2003, 2002 and 2001, respectively.

**Patents and Trademarks**

We consider patent protection and proprietary position to be significant to our business. As of December 31, 2003, we held 58 United States patents and 160 foreign patents, and 17 United States and 102 foreign patent applications are pending. A number of the claims contained in these patents and pending patent applications cover certain aspects of our drug delivery technologies, including the Atrigel, SMP, MCA, BCP and BEMA drug delivery technologies and products based upon these technologies, including the Eligard, Atrisone, Atridox, Atrisorb-D, Atrisorb FreeFlow and Atrisorb GTR Barrier products.

Notwithstanding our pursuit of patent protection, others may develop delivery systems, compositions and/or methods that infringe our patent rights resulting from outright ownership or non-revocable exclusive licensure of patents that relate to our delivery systems, composition and/or methods. In that event, such delivery systems, compositions and methods may compete with our systems, compositions and methods and may adversely affect our operations. Furthermore, patent protection may not afford adequate protection against competitors with similar systems, composition or methods, and our patents may be infringed or circumv