ANTARES PHARMA INC
Form 10-K/A
August 24, 2005

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

FORM 10-K/A

[X] ANNUAL REPORT PURSUANT TO SECTION 13 OR 15 (D) OF
THE SECURITIES EXCHANGE ACT OF 1934
FOR THE FISCAL YEAR ENDED DECEMBER 31, 2004

[ ] TRANSITION REPORT PURSUANT TO SECTION 13 OR 15 (d) OF
THE SECURITIES EXCHANGE ACT OF 1934
For transition period from _____ to _____

Commission file number 0-20945

ANTARES PHARMA, INC.

(Exact name of registrant as specified in its charter)

Minnesota	41-1350192
State or other jurisdiction of incorporation or organization	(I.R.S. Employer Identification Number)

707 Eagleview Boulevard, Suite 414, Exton, PA 19341
(Address of principal executive offices) (Zip Code)

Registrant's telephone number, including area code: (610) 458-6200

SECURITIES REGISTERED PURSUANT TO SECTION 12 (b) OF THE ACT: None

SECURITIES REGISTERED PURSUANT TO SECTION 12 (g) OF THE ACT:
Common Stock, $.01 Par Value

Indicate by check mark whether the registrant (1) has filed all reports required to be filed by Section 13 or 15(d) of the Securities Exchange Act of 1934 during the preceding 12 months (or for such shorter period that the registrant was required to file such reports) and (2) has been subject to such filing requirements for the past 90 days.

YES __X__ NO ____

Indicate by check mark if disclosure of delinquent filers pursuant to Item 405 of Regulation S-K is not contained herein, and will not be contained, to the best of the 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. [X]

Indicate by check mark whether the registrant is an accelerated filer (as defined in Rule 12b-2 of the Act).

YES ____ NO __X__

Aggregate market value of the voting and non-voting common stock held by nonaffiliates of the registrant as of June 30, 2004, was approximately $25,682,223 (based upon the last reported sale price of $0.89 per share on June 30, 2004, on the Over the Counter Market).

There were 40,493,606 shares of common stock outstanding as of March 1, 2005.

Explanatory Note

This Annual Report on Form 10-K/A is being filed principally to include in Exhibits 31.1 and 31.2 language which was previously inadvertently omitted therefrom.

PART I

Item 1. BUSINESS

Overview

Antares Pharma, Inc. (Antares or the Company) is a specialty drug delivery/pharmaceutical company utilizing its experience and expertise in drug delivery systems to enhance the performance of established and developing pharmaceuticals. The Company currently has three primary delivery platforms (1) transdermal gels, (2) fast-melt tablets, and (3) injection devices. These technologies are summarized and briefly described below.

Technology Platforms

Transdermal Drug Delivery

Antares transdermal drug delivery platform is dedicated to developing gels that offer a cosmetically superior option to patches, while delivering medication efficiently with less potential for skin irritation and avoiding the initial gastrointestinal and liver uptake problems of some orally ingested drugs. The Company s gels consist of a hydro-alcoholic gel containing a combination of permeation enhancers to promote rapid drug absorption through the skin following application to the arms, shoulders, or abdomen. The Company s transdermal gel systems provide the options for delivery both systemically (penetrating into the subcutaneous tissues and then into the circulatory system) as well as locally (e.g. topically for skin and soft tissue injury, infection and local inflammation). Typically, the gel is administered daily, effective on a sustained release basis over a 24-hour duration. The Company s gel systems, known as our Advanced Transdermal Delivery (ATD) gels are currently being developed in the following areas:

ATD Single Gels, which are being developed to incorporate hormonal formulations to deliver testosterone for the treatment of hypogonadism in men and low libido in women, as well as an estradiol gel to treat hot flashes and vaginal atrophy. The Company has also announced development results for the treatment of overactive bladder syndrome (OAB) with (AP-1034), its oxybutynin ATD gel.

ATD Combination Gels, Antares is currently developing two transdermal, combination gel products for hormone therapy (HT), one containing estradiol and testosterone and one containing estradiol with the progestin, norethindrone acetate.

The Company s licensee principally in North America, BioSante Pharmaceuticals, Inc. (BioSante) a developer of male and female HT products, recently announced successful Phase II results for LibiGel , a transdermal testosterone gel utilizing Antares ATD gel for the treatment of female sexual dysfunction (FSD). Antares retains rights to the resulting clinical data of BioSante s LibiGel studies to enable the Company to file for approval to market in countries other than those licensed to BioSante. Antares is, therefore, exploring marketing alternatives for its own ATD testosterone gel product, possibly with marketing partners, in Europe and Japan. BioSante also has an estradiol gel (based on a license of Antares ATD gel), known as Bio-E-Gel , currently in Phase III clinical trials in the U.S. Antares again retains rights to the resulting clinical data to enable it to file for approval to market in territories not licensed to BioSante. The Company has licensed a combination gel of estradiol and the progestin, norethindrone acetate, to BioSante and Solvay Pharmaceuticals B.V. (Solvay) for hormone therapy, under which Solvay is designing the Phase III clinical trials for the U.S. market. Another combination gel, estradiol and testosterone, has also been licensed to BioSante for development.

Antares has developed and licensed a topical ibuprofen gel, under non-royalty bearing agreements in 11 countries, including Russia, New Zealand, and Australia, and is exploring options for the Canadian and U.S. markets. This product or other nonsteroidal anti-inflammatory drugs (NSAIDs) in a gel form are being explored as an alternative that could benefit from the safety concerns related to cyclooxygenase 2 (COX-2) medications, such as Vioxx, and the resulting need for safe and effective pain medication alternatives.

Fast-Melt Oral Tablets

Easy Tec fast-melt oral disintegrating tablets are designed to help patients who experience difficulty swallowing pills, tablets or capsules, while providing the same effectiveness as conventional oral dosage forms. Our tablet features a disintegrant addition that facilitates the disintegration of the oral drug to promote quick and easy administration in saliva without water. This could play a key role in Antares ability to target the pediatric market segment as well as the rapidly expanding geriatric market. Easy Tec tablets can be manufactured without specialized equipment and as the tablets are not effervescent (highly moisture sensitive), we believe it represents several significant processing and packaging advantages over conventional competitors. Our Easy Tec tablets may be of interest to pharmaceutical firms seeking line extensions in the marketplace and could also represent a key step in Antares evolution into a specialty pharmaceutical company with its own products.

Injection Devices

Antares injection device platform features three distinct products: reusable needle-free injectors, disposable mini-needle injectors, and its emerging vaccine intradermal injectors. Each product is briefly described below.

Reusable needle-free injectors deliver precise medication doses through high-speed, pressurized liquid penetration of the skin without a needle. These reusable, variable-dose devices are engineered to last for a minimum of two years and are designed for easy use, facilitating self-injection with a disposable syringe to assure safety and efficacy. The associated disposable, plastic needle-free syringe is designed to last for approximately one week.

The Company has sold the Medi-Jector VISION® for use in more than 30 countries to deliver either insulin or human growth hormone (hGH). The Medi-Jector VISION® employs a disposable plastic needle-free syringe, which offers high precision liquid medication delivery through an opening that is approximately half the diameter of a standard, 30-gauge needle. The product is available over-the-counter (OTC) or by prescription in the United States for use by patients with diabetes, and to date, we believe that more than 100 million such injections have been performed worldwide.

In September 2003, Antares entered into a collaborative agreement with Eli Lilly and Company (Lilly), under which Lilly has taken a license to develop and potentially market the Antares reusable needle-free technology in the fields of diabetes and obesity and has an option to use the technology in one other smaller field on a worldwide basis. To date, most of the development activities under this agreement have been focused on improving the

Company s reusable needle-free injector and evaluating market opportunities. Lilly currently holds approximately 70% of the domestic insulin market.

Disposable mini-needle injectors (Vibex) employ the same basic technology developed for the Medi-Jector VISION®, combining a low-energy power source with a tiny hidden needle in a disposable, single-use injection system compatible with conventional glass drug containers. The Vibex system is designed to economically provide highly reliable subcutaneous injection capabilities with reduced discomfort and improved convenience in conjunction with the enhanced safety of a shielded needle. After use, the device can be disposed of without the typical sharps disposal concerns. Antares and its potential partners have successfully tested the device in multiple patient preference and bioavailability tests, and the Company continues to explore product extensions within this category, including multiple dose, variable dose and user-fillable applications. Antares is also exploring opportunities to develop its own combination drug and device products incorporating the Vibex system.

Vaccine intradermal injectors are a variation of the Vibex disposable mini-needle injection technology and are being developed to deliver vaccines into the dermal and subdermal layers of the skin (a preferred method of administration in the vaccine industry). The Company believes that this proprietary device will offer easier and more rapid dosing compared with conventional needle-based devices.

History

On January 31, 2001, Antares Pharma, Inc. (formerly known as Medi-Ject Corporation or Medi-Ject) completed a business combination to acquire the three operating subsidiaries of Permatec Holding AG (Permatec), headquartered in Basel, Switzerland. Upon consummation of the transaction, the acquired Permatec subsidiaries were renamed Antares Pharma AG, Antares Pharma IPL AG and Permatec NV. Prior to the closing of the business combination, the Company did not have sufficient funds to continue operating and had determined that it was necessary to, among other things, either raise more capital or merge with another biopharmaceutical company. Medi-Ject was a company focused on delivering drugs across the skin using needle-free technology, and Permatec specialized in delivering drugs across the skin using transdermal patch and gel technologies as well as developing fast-melt tablet technology. Given that both groups were focused on delivering drugs across the skin, but with a focus on different sectors, it was believed that a business combination would be attractive to both pharmaceutical partners and to the Company s shareholders. The transaction was accounted for as a reverse acquisition, as Permatec s shareholders initially held approximately 67% of the outstanding stock of Antares. Accordingly, for accounting purposes, Permatec is deemed to have acquired Medi-Ject. Upon completion of the transaction the Company s name was changed from Medi-Ject Corporation to Antares Pharma, Inc.

From inception as a combined business entity, the Company had fifty-three employees with thirty-five research and development personnel, engineers, formulation chemists and technicians, engaged in designing, formulating and developing new products for the pharmaceutical industry. As of March 1, 2005, the Company has twenty-seven full-time and four part-time employees.

The U.S. operation, located in Minneapolis, Minnesota, develops, manufactures with partners and markets novel medical devices, called jet injectors or needle-free injectors, which allow people to self-inject drugs without using a needle. The Company makes a small reusable spring-action device and the attached disposable plastic needle-free syringes to hold the drug, known as the Medi-Jector VISION®. Using an adapter, the liquid drug is drawn from a conventional vial into the needle-free syringe, through a small hole at the end of the syringe. When the syringe is held against an appropriate part of the body and the spring is released, a piston drives the fluid stream into the tissues beneath the skin, from where the drug is dispersed into systemic circulation. A person may re-arm the device and repeat the process or attach a new sterile syringe between injections. The Company has also developed variations of the jet injector by adding a very small hidden needle to a pre-filled, single-use disposable injector, called the Vibex mini-needle injection system.

The Company was a pioneer in the invention of home use needle-free injection systems in the late 1970s. Prior to that, needle-free injection systems were powered by large air compressors or were relatively complex and expensive, so their use was limited to mass vaccination programs by the military, school health programs or for patients classified as needle phobic. Early injectors were painful in comparison to today s injectors, and their large size made home use difficult. The first home insulin injector was five times as heavy as the current injector, which weighs five ounces. Today s insulin injector sells at a retail price of $335 compared to $799 eight years ago. The first growth hormone

injector was introduced in Europe in 1994. This was the Company s first success in achieving distribution of its device through a license to a pharmaceutical partner, and it has resulted in continuing market growth and, the Company believes, a high degree of customer satisfaction. Distribution of growth hormone injectors has expanded through the Company s pharmaceutical company relationships to now include Japan and other Asian countries.

Antares is committed to other methods of drug delivery such as topical gel formulations. The Company believes that transdermal gels have advantages in cost, cosmetic elegance, ease of application and lack of irritancy compared with better-known transdermal patches and have applications in such therapeutic markets as hormone replacement therapy, osteoporosis therapy, cardiovascular therapy, pain management and central nervous system therapy. This drug delivery method is now a material part of the Company s business moving forward.

The Company s first transdermal and fast-melt tablet products were developed in Argentina under Permatec s name in the mid-1990s. Subsequently, the Argentine operations were moved to Basel, Switzerland, in late 1999. The transdermal product effort initially resulted in the commercialization of a seven-day estradiol patch in certain countries of South America in 2000. Over time, Permatec s research efforts moved away from the crowded transdermal patch field and focused on transdermal gel formulations, which allow the delivery of estrogens, progestins, testosterone and other drugs in a gel base without the need for occlusive or potentially irritating adhesive bandages. We believe the commercial potential for transdermal gels is attractive, and several licensing agreements with pharmaceutical companies of various sizes have led to successful clinical evaluation of Antares formulations. The Company is now also developing its own transdermal gel-based products for the market and has announced development results for AP-1034, its oxybutynin gel for OAB. The fast-melt tablet effort resulted in patents being issued in 2004 in the U.S. and Europe.

The Company operates in the specialized drug delivery sector of the pharmaceutical industry. Companies in this sector generally leverage technology and know-how in the area of drug formulation and/or delivery devices to pharmaceutical manufacturers through licensing and development agreements while continuing to develop their own products for the marketplace. The Company views pharmaceutical and biotechnology companies as primary customers. The Company has negotiated and executed licensing relationships in the growth hormone segment (needle-free devices in Europe and Asia) and the transdermal hormone gels segment (several development programs in place

worldwide, including the United States and Europe). In addition, the Company continues to market needle-free devices for the home administration of insulin in the U.S. market through distributors and has licensed its technology in the diabetes and obesity fields to Eli Lilly and Company. Antares has also announced its plans to develop its own products using its gel and fast-melt technology platforms and is exploring developing its own combination drug and device products with its disposable mini-needle injection technology platform.

The Company is a Minnesota corporation incorporated in February 1979. Principal executive offices are located at 707 Eagleview Boulevard, Exton, Pennsylvania 19341; telephone (610) 458-6200. The Company has wholly-owned subsidiaries in Switzerland (Antares Pharma AG and Antares Pharma IPL AG) and the Netherlands Antilles (Permatec NV).

Industry Trends

Based upon previous experience in the industry, the Company believes the following significant trends in healthcare have important implications for the growth of its business.

After a drug loses patent protection, the branded version of the drug often faces competition from generic alternatives. It is possible to preserve market share by altering the delivery method, e.g., a single daily controlled release dosage form rather than two to four pills a day. The Company expects pharmaceutical manufacturers will continue to seek differentiating delivery characteristics to defend against generic competition and to optimize convenience to patients. The altered delivery method may be an injection device or a novel oral or transdermal formulation that may offer therapeutic advantages, convenience or improved dosage schedules. Major companies now focus on life cycle management of their products to maximize return on investment and often consider phased product improvement opportunities to maintain competitiveness against other major companies or generic competition.

The increasing trend of pharmaceutical companies marketing directly to consumers, as well as the recent focus on patient rights may encourage the use of innovative, user-friendly drug delivery systems. Part of this trend involves offering patients a wider choice of dosage forms. The Company believes the patient-friendly attributes of its topical gels, fast-melt tablets and jet injection technologies meet these market needs.

The Company envisions its program with topical gel formulations as a second-generation technology, replacing the older transdermal patch products with more patient-friendly products. Topical gels offer patients more choices and added convenience with no compromise of efficacy. Although newer, our gel technology is based upon so-called GRAS (Generally Recognized as Safe) substances, meaning the toxicology profiles of the ingredients are known and widely used. We believe this approach has a major regulatory benefit and may reduce the cost and time of product development and approval.

Many drugs, including selected hormones and protein biopharmaceuticals, are destroyed in the gastrointestinal tract and may only be administered through the skin, the lung or by injection. Pulmonary delivery is complex and has not yet been commercialized for therapeutic proteins intended for systemic delivery. Injection remains the mainstay of protein delivery. Therefore, the growing number of protein biopharmaceuticals requiring injection may have limited commercial potential if patient compliance with conventional injection treatment is not optimal. The failure to take all prescribed injections can lead to increased health complications for the patient, decreased drug sales for pharmaceutical companies and increased healthcare costs for society. In addition, it is becoming increasingly recognized that conventional syringe needles require special and often costly disposal methods.

In addition to the increase in the number of drugs requiring self-injection, recommended changes in the frequency of insulin injections for the treatment of diabetes also may contribute to an increase in the number of self-injections. For many years, the standard treatment protocol was for insulin to be administered once or twice daily for the treatment of diabetes. However, according to major studies (the Diabetes Control and Complications Trial), tightly controlling the disease by, among other things, administration of insulin as many as four to six times a day, can decrease its debilitating effects. The Company believes that with the increasing incidence of diabetes coupled with an increasing awareness of this disease, the benefits of tightly controlling diabetes will become more widely known, and the number of insulin injections self-administered by people with diabetes will increase. The need to increase the number of insulin injections given per day may also motivate patients with diabetes to seek an alternative to traditional needles and syringes.

Due to the substantial costs involved, marketing efforts are not currently focused on drug applications administered by healthcare professionals. Jet injection systems, however, may be attractive to hospitals, doctors offices and clinics, and such applications may be explored in the future. The issues raised by accidental needle sticks and disposal of used syringes have led to the development of syringes with sheathed needles as well as the practice of administering injections through intravenous tubing to reduce the number of contaminated needles. In 1998, the State of California banned the use of exposed needles in hospitals and doctors offices, if alternatives exist, and several additional states have adopted similar legislation. In November 2000 the Federal Government issued guidelines encouraging institutions to replace needles wherever practical. The Company believes that needle-free injection systems may be attractive to healthcare professionals as a further means to reduce accidental needle sticks and the burdens of disposing of contaminated needles.

The importance of vaccines in industrialized and emerging nations is expanding as the prevalence of infectious diseases increases. New vaccines and improved routes of administration are the subject of intense research in the pharmaceutical industry. In the past, the Company had focused only upon the injection of medication in the home, but in 2000 the Company began to research the feasibility of using its devices for vaccines and new vaccine ingredients and is currently seeking collaboration with vaccine companies to support development of this application.

The Company s fast-melt technology also addresses industry trends by focusing on the needs of specific market segments such as geriatric and pediatric patients who often have difficulty swallowing conventional oral medications. We believe that better health outcomes can be expected when patients are compliant with recommended medication regimens. The Company s fast-melt technology offers consumers a potentially important alternative oral delivery system.

Market Opportunity

Drug delivery companies that compete with our technologies include Bioject Medical Technologies, Inc., Bentley Pharmaceuticals, Inc., Aradigm, Cellegy Pharmaceuticals, Inc., Cardinal Health, CIMA Laboratories, Laboratoires Besins-Iscovesco, MacroChem Corporation, NexMed, Inc. and Novavax, Inc., along with other companies. We also compete generally with other drug delivery, biotechnology and pharmaceutical companies engaged in the development of alternative drug delivery technologies or new drug research and testing.

According to one industry publication, worldwide hormone replacement revenues, the initial focus of the Company s transdermal gel formulation program, were expected to grow to $12.7 billion by 2005. Further growth in this sector may be achieved by the use of testosterone products in both male and female applications. The importance of gel products containing testosterone for men has been exemplified with the success of Androgel® (Unimed-Solvay) for treatment of male hypogonadism, where sales in the U.S. were recently estimated at approximately $500 million per year. A new market opportunity also exists with the use of low dose testosterone for treatment of FSD, a disorder that affects an estimated 30-50% of women and for which no drug is currently approved in the U.S. Antares Pharma, along with its U.S. partner BioSante, has a testosterone product in clinical trial for FSD. As evidenced in Europe and, more specifically, in France, the leading country in the use of transdermal hormone replacement therapy, the Company believes that patient demand for transdermal hormone therapy products will continue to increase. According to an industry report, 64.8% of treated menopausal women in France used either patch (44.7%) or gel (20.1%) therapy. It has also been suggested that the more physiological blood levels achieved when hormones are delivered across the skin may offer some advantage over oral therapy although currently there is no long-term evidence to support this contention. Gel products are also being formulated to address equally large opportunities in other sectors of the pharmaceutical industry, including cardiovascular, pain, infectious diseases, addiction and central nervous system therapies.

According to industry sources, oral drug delivery systems represented a $28 billion worldwide market in 2002 with fast-dissolving dosage forms being in excess of $1 billion of this market with a growth rate of more than 20% per year. There have been approximately 80 fast-dissolving dosage forms launched. This field of melt-in-the-mouth, or fast-dissolve, tablets clearly has a significant role to play in effective product administration to the elderly and to those who have difficulty swallowing. While many products have been developed to meet this need, many have disadvantages, including lack of applicability to all drug candidates, dose limitations, high cost of manufacturing, and product robustness issues that can challenge packaging and distribution systems. Using its Easy Tec technology, Antares has undertaken to develop products that could be applicable over a wide dose range, could be manufactured under conventional conditions and would meet the standards of performance necessary to provide the desired patient benefits of rapid dissolution, good mouth feel and ease of handling.

According to industry sources, an estimated 9 to 12 billion needles and syringes are sold annually worldwide. The Company believes that a significant portion of these are used for the administration of drugs that could be delivered using its injectors but only a small percentage of people who self-administer drugs currently use jet injection systems. The Company believes that this lack of market penetration is due to older examples of needle-free technology not meeting customer needs owing to cost and performance limitations as well as the small size of the companies directly marketing the technology to consumers not being able to gain a significant share of voice in the marketplace. The Company believes that its technology overcomes limitations of the past and that its business model of working with pharmaceutical company partners has the potential for improved market penetration. However, to date neither the Company nor its competitors have achieved substantial market penetration. The Company s largest customer is a pharmaceutical company (Ferring BV), and one of the Company s major competitors, Bioject Medical Technologies, Inc., has a pharmaceutical company (Serono) as its largest customer. Greystone Associates (www.greystoneassociates.org) in 2003 estimated that the needle-free injection market in the U.S. would grow from $10.2 million in 2002 to $425 million by 2007, of which self-administration of insulin is expected to account for 54% of the total market. In 2003, Antares licensed its needle-free injection technology to Eli Lilly and Company for use in the fields of diabetes and obesity.

Antares device focus is specifically on the market for delivery of self-administered injectable drugs. The largest and most mature segments of this market consist of the delivery of insulin for patients with diabetes and human growth hormone for children with growth retardation. In the U.S., over 3.2 million people inject insulin for the treatment of diabetes, resulting in an estimated 2.3 billion injections annually, and the Company believes that the number of insulin injections will increase with time as the result of new diabetes management techniques, which recommend more frequent injections. A second attractive market has developed with growth hormone; children and young adults suffering from

growth retardation take daily hormone injections for an average of five years. The number of children with growth retardation is small relative to diabetes, but most children are needle averse. The Company s pharmaceutical partner in Europe, Ferring BV (Ferring), has made significant inroads using its injectors in the hGH market, and the Company expects similar progress in other geographic regions where partnerships have already been established. Other injectable drugs that are presently self-administered and may be suitable for injection with the Company s systems include therapies for the prevention of blood clots and the treatment of multiple sclerosis, migraine headaches, inflammatory diseases, impotence, infertility, AIDS and hepatitis. Antares also believes that many injectable drugs currently under development will be administered by self-injection once they reach the market. It is estimated that there will be 190

biotechnology injectable drugs on the market in 2005, compared with 80 in 2000 and ten in 1990. This is supported by the continuing development of important chronic care products that can only be given by injection, the ongoing effort to reduce hospital and institutional costs by early patient release, and the gathering momentum of new classes of drugs that require injection. A partial list of such drugs introduced in recent years that all require home injection include Enbrel® (Amgen, Wyeth) for treatment of rheumatoid arthritis, Aranesp® (Amgen) for treatment of anemia, Kineret® (Amgen) for rheumatoid arthritis, Forteo (Lilly) for treatment of osteoporosis, Intron® A (Schering Plough) and Roferon® (Roche) for hepatitis C, Lantus® (Aventis Pharma) for diabetes, Rebif® (Serono) for multiple sclerosis, Copaxone® (Teva) for multiple sclerosis and Gonal-F® for fertility treatment. The dramatic increase in numbers of products for self-administration by injection and the breadth of therapeutic areas covered by this partial listing represents an opportunity for Antares device portfolio.

Products and Technology

Antares is leveraging its experience in drug delivery systems to enhance the product performance of established drugs as well as new drugs in development. The Company s current technology platforms include transdermal (Advanced Transdermal Delivery ATD) gels; fast-melt oral tablets (Easy Tec); disposable mini-needle injection systems (Vibex); and reusable needle-free injection systems (Medi-Jector VISION and Valeo).

Transdermal Drug Delivery

Transdermal drug delivery has emerged as a safe and patient-friendly method of drug delivery. The commercialization of transdermal patches for controlled drug delivery began over two decades ago and has resulted in the appearance of diverse products on the market. Among them are nitroglycerin for angina, scopolamine for motion sickness, fentanyl for pain control, nicotine for smoking cessation, estrogen for HT, clonidine for hypertension, lidocaine for topical anesthesia, testosterone for hypogonadism, and a combination of ethinyl estradiol and norelgestromin for contraception. Skin penetration enhancers are often used to enhance drug permeation through the dermal layers.

The primary goal of transdermal drug delivery is to effectively penetrate the surface of the skin via topical administration, such as a patch or gel. When successful, transdermal drug delivery provides an easy and painless method of administration. The protective capabilities of the skin, however, often act as a barrier to effective delivery. Since the primary role of the skin is to provide protection against infection and physical damage, the organ often prevents many pharmaceuticals from entering the body as well. Large molecules are not effectively absorbed by the skin and enter the body in prohibitively small amounts, significantly reducing their therapeutic potential. As a result, a limited number of active substances are able to cross the skin s surface.

Despite these limitations, transdermal drug delivery is still viewed as a highly attractive route of administration for certain therapeutics. As a high concentration of capillaries is located immediately below the skin, transdermal administration provides an easy means of access to systemic circulation. Transdermal systems can be designed to minimize absorption of the active drug in the blood circulation as is needed in topical applications. This allows a build-up of drug in the layers underlying the skin, leading to an increased residence time in the targeted tissue. Transdermal systems can also be designed to release an active ingredient over extended periods of time, providing benefits similar to depot injections and implants, without the need for an invasive procedure. If required, patients are also able to interrupt dosing by removing a patch or discontinuing the application of a gel. Finally, this delivery technology avoids first-pass metabolism by the liver as well as many of the gastrointestinal concerns of many orally ingested drugs.

Transdermal Gels

While transdermal patches remain an important aspect of the transdermal drug delivery market, transdermal gels have emerged as a viable means of administering a wide array of active pharmaceutical treatments. The concept of transdermal gels parallels that of the transdermal patch, in the creation of a drug reservoir to provide sustained delivery of therapeutic quantities of a drug. While a patch provides this from an external reservoir, gel formulations create a subdermal reservoir of the medication.

To address the penetration capabilities of transdermal products, Antares has developed its ATD (Advanced Transdermal Delivery) gel technology that utilizes a combination of permeation enhancers to further bolster a pharmaceutical agent s ability to penetrate the skin. This new

generation of products leads to a sustained plasma profile of the active agent, without the irritation and cosmetic concerns often associated with patches.

Gels also provide drug developers with an opportunity to explore a wide variety of potential applications. Due to the physicochemical properties of the excipients employed in gels, combined with the enhanced solubilization properties, a broad range of active agents can be formulated. These solubilization properties allow for higher concentrations of the active ingredient to be incorporated for delivery. The enhanced viscosity in gels further enhances the patient s ability to apply the product with little-to-no adverse cosmetic effect. There is also relatively little limitation in the surface area to which a gel can be applied, as opposed to patches, allowing greater quantities of drug to be transported if required. A summary of the benefits of transdermal gels is provided below.

Benefits of Transdermal Gels

Discrete
Easy application
Cosmetically appealing compared with patches
Reduced irritancy compared with patches
Application of once per day for most products
Potential for delivery of larger medication doses
Potential for delivery of multiple active drugs
Ability to be either systemic or topical

Antares Advanced Transdermal Delivery (ATD) System

Antares Advanced Transdermal Delivery (ATD) system has produced two transdermal drug delivery gels, both of which have demonstrated the ability to successfully penetrate the skin to deliver a variety of treatments. The gels consist of a hydro-alcoholic base including a combination of permeation enhancers. The gels are also designed to be absorbed quickly through the skin after application to the arms, shoulders, or abdomen. In comparison with commonly used patch delivery systems, the gels cause minimal skin irritation or occlusion following application and possess a distinct cosmetic advantage over other approaches. The following sections provide an overview of Antares ATD Single Gels and ATD Combination Gels.

ATD Single Drug Gels

Antares ATD single gels are single-drug transdermal gels that have demonstrated potential in a variety of therapeutic areas. Current ATD single drug gels in advanced development encompass a testosterone gel for men to treat hypogonadism, an estrogen gel for women to treat vasomotor symptoms associated with menopause, a low dose testosterone gel to treat low libido in women and an oxybutynin gel to treat overactive bladder syndrome (OAB). Antares has also licensed an ibuprofen gel in 11 countries for several years. ATD gels may be extended to a variety of fields, including the treatment of several central nervous system (CNS) disorders, cardiovascular disease and chronic pain, in which potent compounds may require alternatives to oral and injectable delivery for the following reasons:

- poor oral uptake;
- high first-pass effect;
- requirement for less frequent administration;
- desire to provide an alternative dosage form;
- reducing peak plasma levels to avoid side effects; and
- reduction in gastrointestinal side effects.

ATD Combination Drug Gels

Antares has also developed a transdermal combination gel product currently used in HT. This formulation has demonstrated the ability to deliver the following combinations of active agents as a means of HT, along with additional agents:

- Estradiol + Norethindrone Acetate;
- Estradiol + Testosterone;
- Estradiol + Levonorgestrel; and
- Ethinyl Estradiol + Levonorgestrel.

Currently the Company has ATD combination drug gels in advanced development with partners for HT including an estradiol/progestin combination product and estradiol/testosterone combination product.

Oral Delivery

Oral delivery remains the preferred method of dosage, with the majority of all drugs administered. Despite this method s widespread popularity, there remain limitations for those patients who have difficulty swallowing conventional oral dosage forms or where an underlying disease (for example, migraine, Parkinsonism or cancer) impacts a person s ability to swallow. Additionally, where patients are resistant to oral drug delivery, the phenomenon of cheeking (hiding a pill between the cheek and gum) and subsequent drug disposal is quite well known. New generations of oral product forms are being developed to address these issues.

Fast-Dissolving Tablets

Fast-dissolving tablet technology is an oral delivery method that offers an alternative to patients who experience difficulty ingesting conventional oral dosage forms. As a result, formulators are focusing on the development of tablet dosage formulations for oral administration that dissolve rapidly in saliva without need for the patient to drink any water. This formulation is easy to take and possesses similar therapeutic benefits to traditional oral technologies, thus appealing to a wide demographic population.

One of the primary realities influencing the development of fast-dissolving technologies is the increased life expectancy of a growing geriatric population. As many elderly individuals experience difficulty taking conventional oral dosage forms, such as solutions, suspensions, tablets and capsules, the need for more user-friendly formulations is expanding. While swallowing difficulties often affect the elderly population, many young individuals also experience difficulty as a result of underdeveloped muscular and nervous systems. Other groups, including the mentally ill, the developmentally disabled and uncooperative patients also require special attention. Other circumstances, such as motion sickness, allergic attacks and an unavailable source of water also necessitate fast-dissolving oral formulations.

The development of a fast-dissolving tablet also provides pharmaceutical companies with an opportunity for product line extensions. A wide range of drugs (e.g. neuroleptics, cardiovascular drugs, analgesics, antihistamines, and drugs for erectile dysfunction) may be considered candidates for this technology. Over 80 such products are currently marketed and generate sales in excess of $1 billion per year with growth rates projected at 20% per year.

Antares Easy Tec Fast-Melt Technology

Antares patented Easy Tec technology is based on the simultaneous use of two disintegrants in an oral formulation. Two primary advantages of Easy Tec over competing technologies are that Easy Tec tablets can be manufactured with conventional tableting equipment and that no unique packaging requirements are necessary. The Company also believes that Easy Tec possesses several other key advantages over competing fast-melt technologies; all of these advantages are listed below.

Easy Tec Competitive Advantages

- High drug dose loading is possible
- Friability within pharmaceutical specifications
- No need for special packaging
- Moisture sensitivity lower compared with many competitor products
- Blister packaging sufficient to prevent moisture uptake
- Cost-effective, easy, time-saving process
- Easily transferable to final product site
- Low cost of goods
- Uses conventional manufacturing equipment
- No specific facility required, compared to effervescent products
- Compendial and CFR listed excipients

Fast-melt technology has proven attractive to customers in both OTC and prescription product fields. Current market leadership is held by Cardinal Health s Zydis technology followed by CIMA s (now part of Cephalon Inc. DuraSolv technology. Marketed products include those for CNS disorders (for example, Zyprexa Zydis® from Eli Lilly and Company), and several products aimed at the treatment of gastrointestinal disorders.

In addition to being easy to take, such products are perceived as being fast acting because of rapid dispersion in the mouth. Antares believes that there may be attractive opportunities to develop its own fast-melt products using generic active ingredients as part of its specialty

pharmaceutical strategy and to achieve product approval based on an Abbreviated New Drug Application (ANDA) or 505(b)(2) filing in the United States and equivalent regulatory submissions in other parts of the world. Antares has formulated its first Easy Tec -based product and plans on filing, to seek market approval, with the Food and Drug Administration (FDA) sometime in 2005.

Needle-Free Injection

Needle-free injection is an emerging form of parenteral drug delivery that is also gaining acceptance among the medical community. Encompassing a wide variety of sizes and designs, this technology operates by using pressure to force the drug, in solution or suspension, through a minute perforation, creating an ultra-thin stream of liquid that penetrates the skin and deposits the drug into the subcutaneous tissue. Needle-free injection systems are being developed as small, pre-filled single-use devices, refillable devices for repeat usage and specialized systems for high throughput applications in mass immunization campaigns.

The future product portfolios of most pharmaceutical and biotechnology companies will contain a significant proportion of proteins and peptides derived from the so-called biotechnology revolution that began in the 1980s. This first generation of such products were bio-identical to natural proteins (for example, insulin and hGH) while future generations are expected to be novel macromolecules with construction based upon an understanding of specific targets supported by advanced research, such as that of the human genome project.

It is currently estimated that 350 biotechnology molecules are in clinical development. The most significant challenge beyond discovery of such molecules is how to effectively deliver them by means other than conventional injection technology. The majority of these molecules are not amenable to oral administration due to a combination of several factors, including breakdown in the gastrointestinal tract, fundamentally poor absorption, or high first pass metabolism. Many companies have expended considerable effort in searching for less invasive ways to deliver such molecules that may allow them to achieve higher market acceptance, particularly for those requiring patient self-administration.

Improving patient comfort through needle-free injection increases compliance and mitigates the problem of daily injections. Needle-free delivery eliminates the risk of needlestick injuries as well, which occur approximately 800,000 times annually in institutions in the U.S., and can result in disease transmission to healthcare workers. In response to concerns about needlestick injuries, the Occupational Safety and Health Administration (OSHA) issued a Bloodborne Pathogens Compliance Directive in November 1999 mandating the use of safer needles and requiring that healthcare facilities perform annual reviews of safety and compliance programs. The National Institute for Occupational Safety and

Health has also urged healthcare providers to avoid unnecessary use of needles where safe and effective alternatives are available.

One of the primary factors influencing development in the category of needle-free injection is the inherent problematic dependence on needles. It is also recognized that greater willingness to accept injection therapy could have a beneficial impact on disease outcomes. For example, patients with diabetes appear to be reluctant to engage in intensive disease management, at least in part because of concerns over increased frequency of injections. Similarly, patients with diabetes who are ineffectively managed with oral hypoglycemic agents are reluctant to transition to insulin injections in a timely manner because of injection concerns.

According to industry sources, an estimated 9-12 billion needles and syringes are sold each year. While the need for these components will always exist, burgeoning development efforts are focused on easing the dependence on needles in favor of more user-friendly injection systems. Currently available data suggest that injection with needle-free systems matches the performance of needle-based systems with regard to drug bioavailability, and offers benefits in the speed of injection and the lack of requirement for needle disposal.

Status of Existing Needle-Free Injection Devices On the Market and In Development

The advent of these technologies has, to date, had a minor influence within the injectable sector, and they have failed to produce the deep market penetration that many within the industry believe they are capable of gaining. Several factors are believed to contribute to this lack of market penetration, beginning with older needle-free injection systems. Many of the early needle-free injection systems had an assortment of drawbacks associated with both performance and cost efficiency. With potential consumers aware of these historical shortcomings, current technologies promising greater efficiency and lower prices have failed to gain wide acceptance in the industry. In spite of the relative minor market penetration within this sector to date, in June 2003, Greystone Associates predicted that the needle-free injection market would grow from $10.2 million in 2002 to $425 million by 2007 with 54% of these sales being insulin-based.

Several other companies are actively developing disposable, needle-free devices, reflecting the interest in this sector. These companies include BioValve, Aradigm Corp., Visionary Medical Products and Crossject. None of the products from these companies have yet been commercialized, but such products, if and when commercialized, could compete with Antares injection devices systems and/or its next generation of injection devices, which are in various stages of development. Other companies, such as The Medical House and Bioject, have

products in the marketplace and currently compete with Antares.

Antares Medi-Jector Series of Needle-Free Injectors

The Medi-Jector VISION® represents the seventh in a series of Medi-Jector devices, with each generation offering improvements over the previous versions. Antares pioneered the development of needle-free injection systems for individual use in 1979 and remains among the industry leaders as the technology continues to advance and is marketed worldwide. The Company s current revenue stream is derived primarily from sales of needle-free injectors.

Medi-Jector VISION® (MJ7)

The Medi-Jector VISION® has been sold for use in more than 30 countries to deliver either insulin or human growth hormone. The product features a reusable spring-based power source and disposable needle-free syringes, which eliminate the need for routine maintenance of the nozzle and allow for easy viewing of the medication dose prior to injection. The device s primary advantage over earlier devices is its ease of use and cost efficiency. The product permits variable dosing at the time of administration and has a maximum dosage volume of 0.5 ml per injection in 0.01 ml increments. The product is also reusable, with each device designed to last for approximately 3,000 injections (or approximately two years) while the needle-free syringe is disposable after approximately one week of continuous use.

Antares believes this method of administration is a particularly attractive alternative to the needle and syringe for the groups of patients described below.

Patient Candidates for Needle-Free Injection
Young adults and children
Patients looking for an alternative to needles
Patients mixing insulins
Patients unable to comply with a prescribed needle program
Patients transitioning from oral medication to insulin
New patients beginning an injection treatment program

Insulin Delivery

The Medi-Jector VISION® is primarily used in the U.S. to provide a needle-free means of administering insulin to patients with diabetes. The potential market for insulin injector products is significant. The World Health Organization (WHO) estimated the worldwide prevalence of patients with diabetes to be more than 170 million in 2000, expected to increase to more than 360 million by 2030. Of this population, approximately 40%, or 68 million patients require insulin. Within the U.S., WHO estimated 17.7 million people with diabetes in 2000, and the Centers for Disease Control reported that approximately 18% of patients with diabetes (more than 3 million) used insulin in 2002.

Patients with insulin-dependent diabetes are often required to make a life-long commitment to daily self-administration of insulin. In an effort to improve both the comfort and performance of this injected hormone, needle-free injection could become an important alternative method of choice for administration.

The Medi-Jector VISION® administers insulin by using a spring to push insulin in solution or suspension through a micro-fine opening in the needle-free syringe. The opening is approximately half the diameter of a standard 30-gauge needle. A fine liquid stream of insulin then penetrates the skin, and the insulin dose is dispersed into the layer of fatty, subcutaneous tissue. The insulin is subsequently distributed throughout the body, successfully producing the desired effect.

Development Efforts: MJ8 (Valeo) Needle-Free Injection Systems

In addition to the Medi-Jector VISION®, Antares is also developing a new reusable Medi-Jector device, the Medi-Jector MJ8 (Valeo) with unique needle-free injection capabilities. The Medi-Jector Valeo accepts a conventional drug cartridge to create a completely self-contained, multi-dose, needle-free injection system. With these improvements, the Medi-Jector Valeo aspires to provide more user-friendly capabilities than its predecessors and, if marketed, the Company believes it would be the smallest reusable needle-free injector produced. The maximum dosage volume is 0.3 ml per injection in 0.01 ml increments. Medi-Jector Valeo has been licensed worldwide to Eli Lilly and Company for use with its portfolio of diabetes and anti-obesity products.

Vibex Pre-filled, Disposable Mini-Needle Injector

Beyond Antares reusable needle-free injector technologies, the Company has designed disposable mini-needle devices to address acute medical needs, such as allergic reactions, migraine headaches, acute pain and other daily therapies, as well as for the delivery of vaccines. The Company s proprietary Vibex disposable mini-needle product combines a low-energy, spring-based power source with a small, hidden needle, which delivers the needed drug solution subcutaneously or, in the case of vaccines, subdermally.

In order to minimize the anxiety and perceived pain associated with injection-based technologies, the Vibex disposable mini-needle injector features a protective collar that shields the needle from view. The retracting collar springs back and locks in place as a protective needle guard after the injection, making the device safe for general disposal. In clinical studies, this device has outperformed other delivery methods in terms of completeness of injection, while limiting pain and bleeding. A summary of the unique benefits of the Vibex disposable mini-needle product is provided below.

Benefits of Vibex Disposable Mini-Needle Injectors

- Rapid injection
- Eliminates sharps disposal
- Ease of use in emergencies
- Reduces psychological barriers since the patient never sees the needle
- Highly dependable subcutaneous injection
- Designed around conventional cartridges or pre-filled syringes

The primary goal of the Vibex disposable mini-needle injector is to provide a fast, safe, and time-efficient method of self-injection that addresses the patient s need for immediate relief. This device is designed around conventional cartridges or pre-filled syringes, which are primary drug containers, offering ease of transition for potential pharmaceutical partners.

Disposable Mini-Needle Vaccine Delivery Device

Antares disposable vaccine delivery device is at an earlier stage and is derived from its mini-needle injector technology (see above section). The disposable device is designed to deliver vaccines to the intradermal and subdermal layers of the skin. Effective intradermal injection methods, using variants of conventional needles, depend extensively on the skill of the person administering the injection. Antares vaccine delivery technology simplifies the process for intradermal delivery, minimizing the dependence on the individual administering the injection, and providing for a more comfortable means of vaccine delivery.

Patents

When appropriate, the Company actively seeks protection for its products and proprietary information by means of U.S. and international patents and trademarks. With the injection device technology, the Company currently holds 24 patents and has an additional 74 applications pending in the U.S. and other countries. With the Company s topical delivery technologies, it holds five patents, and an additional 30 applications in various countries are pending. The patents have expiration dates ranging from 2013 to 2022. In addition to issued patents and patent applications, we are also protected by trade secrets in all of our technology platforms.

Some of the Company s technology is developed on its behalf by independent outside contractors. To protect the rights of its proprietary know-how and technology, Company policy requires all employees and consultants with access to proprietary information to execute confidentiality agreements prohibiting the disclosure of confidential information to anyone outside the Company. These agreements also require disclosure and assignment to the Company of discoveries and inventions made by such individuals while devoted to Company-sponsored activities. Companies with which Antares has entered into development agreements have the right to certain technology developed in connection with such agreements. Ownership of intellectual property developed under the Lilly Development and License Agreement will be governed by U.S. laws of inventorship except that intellectual property relating to compounds, which is assigned to Lilly.

Manufacturing

The Company is responsible for a U.S. device manufacturing facility in compliance with current Quality System Regulations (QSR) established by the Food and Drug Administration and by the centralized European regulatory authority (Medical Device Directive). Injector and disposable parts are manufactured by third-party suppliers and are assembled by a third-party supplier. Packaging is performed by a third-party supplier under the direction of the Company. Final quality control is performed by the Company.

The Company continues to have responsibility for the manufacturing of the product including the quality of all products and the release of all products produced by the supplier. The outsourcing agreement had an initial term of two years and continues with a six-month termination notice available to either party.

The Company pays Becton Dickinson royalties on sales of plastic components of certain injector systems. Such royalties will continue until the expiration of the last patent covering such plastic components.

The ATD Gel formulations for clinical studies have, in the past, been manufactured by contract under the Company s supervision. Early in 2005, Antares Pharma AG, our wholly owned subsidiary in Switzerland, received a GMP approval for the production and wholesaling of medicaments.

Marketing

The Company expects to market most of its products through the existing distribution systems of pharmaceutical and medical device companies while continuing direct-to-consumer marketing of its insulin injection devices and related disposable elements in the U.S.

During 2004, 2003 and 2002, international revenue accounted for 82%, 77% and 59% of total revenue, respectively. Europe (primarily Germany) accounted for 83%, 95% and 96% of international revenue in 2004, 2003 and 2002, respectively, with the remainder coming primarily from Asia. Ferring accounted for 47%, 62% and 49% of the Company s worldwide revenues in 2004, 2003 and 2002, respectively. BioSante Pharmaceuticals, Inc. accounted for 11%, 14% and 30% of the Company s worldwide revenues in 2004, 2003 and 2002, respectively. Revenue from Ferring resulted from sales of injection devices and related disposable components for its hGH formulation. Revenue from BioSante resulted from license fees, development fees, milestone payments and clinical testing supplies for hormone replacement therapy transdermal gel formulations.

Transdermal Delivery Products

Over the short term, the majority of revenues generated from topical drug formulation will continue to be through the fees generated by licensing and development agreements.

The following table describes existing pharmaceutical relationships in the transdermal delivery sector.

Pharmaceutical Company Partner	Compound	Market Segment	Technology
Solvay	Estradiol/NETA	Hormone replacement therapy (Worldwide, excluding North America, Japan and Korea)	ATD Gel
Solvay (sublicense agreement through BioSante)	Estradiol/NETA	Hormone replacement therapy (North America)	ATD Gel
BioSante	Estradiol	Hormone replacement therapy	ATD Gel
BioSante	Testosterone	Male and female sexual dysfunction, Male hypogonadism (North America, other countries)	ATD Gel
BioSante	Estradiol/Testosterone	Combination of HT and FSD (North America, other countries)	ATD Gel

The agreements in the table are license agreements under which the Company s partners are conducting clinical evaluation and development of the Company s transdermal products. For competitive reasons, the Company s partners may not divulge the exact stage of clinical development. The Company s two major agreements are with Solvay Pharmaceuticals and BioSante Pharmaceuticals, Inc. Under the Company s June 1999 agreement with Solvay, the Company granted an exclusive license to Solvay for the Company s transdermal gel technology for delivery of an estradiol/progestin combination for hormone replacement therapy. The exclusive license applies to all countries and territories in the world, except for North America, Japan and Korea. The agreement contains a development plan under which the Company and Solvay collaborate to bring the product to market. Solvay must pay the Company a license fee of $5 million in four separate payments, all of which are due upon completion of various phases of the development plan. To date, the Company has received $1.75 million of this fee. Once commercial sale of the product begins, Solvay

is required to, on a quarterly basis, pay the Company a royalty based on a percentage of sales. The royalty payments will be required for a period of 15 years or when the last patent for the product expires, whichever is later.

In June 2000, the Company granted an exclusive license to BioSante to allow BioSante to develop and commercialize three of the Company s gel technology products and one patch technology product for use in hormone replacement therapy in North America and other countries. Subsequently, the license for the patch technology product was returned to the Company in exchange for a fourth gel based product. BioSante paid the Company $1 million upon execution of the agreement and is also required to pay the Company royalty payments once commercial sales of the products have begun. The royalty payments are based on a percentage of sales of the products and must be paid for a period of 10 years following the first commercial sale of the products, or when the last patent for the products expires, whichever is later. The agreement also provides for milestone payments to the Company upon the occurrence of certain events related to regulatory filings and approvals.

In August 2001, BioSante entered into an exclusive agreement with Solvay in which Solvay has sublicensed from BioSante the U.S. and Canadian rights to the Company s estrogen/progestin combination transdermal hormone replacement gel product, one of the drug-delivery products the Company previously licensed to BioSante. Under the terms of this license agreement between the Company and BioSante, the Company received a portion of the up front payment made by Solvay to BioSante. The Company is also entitled to a portion of any milestone payments or royalties BioSante receives from Solvay under the sublicense agreement which included a $200,000 milestone payment in January of 2003.

Injection Devices

The Company markets needle-free injectors for insulin and growth hormone delivery through pharmaceutical companies and medical products distributors worldwide. Device and related disposable product sales in 2004 were approximately $1.8 million. Historical product development alliances have generated licensing and development fees and eventually sales of product.

Ferring is selling human growth hormone throughout Europe with a marketing campaign tied to the Antares needle-free delivery system. Ferring has been successful in establishing a user base of more than 3,000 children for its drug using the Antares needle-free system. In the Netherlands, where Ferring enjoys its largest market share, we understand that 22% of children taking growth hormone use Antares injector. During the past six years, a Japanese pharmaceutical company, JCR, has distributed small numbers of growth hormone injectors to hospital-based physicians in Japan. In 2004, JCR initiated a larger scale campaign to broaden its marketing efforts with our injector. In 1999, SciGen Pte Ltd. began distribution in Asia of Antares growth hormone injectors along with its drug, and in 2004 Shreya Life Sciences initiated a test market evaluation that resulted in limited distribution in India with insulin.

The table below summarizes the Company s current collaborative and distribution/supply agreements in the injection device sector.

Company	Market
Eli Lilly and Company	Development and license agreement Needle-free delivery Diabetes and Obesity plus an option for another therapeutic market (worldwide)
Wal-Mart Stores, Inc.	Insulin Distribution (United States)
Ferring BV	Growth Hormone (Europe)
JCR Pharmaceuticals Co., Ltd.	Growth Hormone (Japan)
SciGen Pte Ltd.	Growth Hormone (Asia/Pacific)
drugstore.com	Insulin Distribution E-Commerce (United States)
Care Service, Inc. (Diabetic Express)	Insulin Distribution E-Commerce (United States/Canada)

Distribution/supply agreements are arrangements under which the Company s products are supplied to end-users through the distributor or supplier. The Company provides the distributor/supplier with injection devices and related disposable components, and the distributor/supplier often receives a margin on sales. The Company currently has three distribution/supply agreements under which the distributors/suppliers sell the Company s injection devices and related disposable components for use with insulin.

Under the Company s growth hormone agreements, the Company sells its injection devices to partners who manufacture and/or market human growth hormone directly. The partners then market the Company s devices with human growth hormone. The Company typically receives

benefits from these agreements in the form of manufacturing margins and royalties on end-sales of the partner s products.

On January 22, 2003, the Company entered into a License Agreement with Ferring, under which the Company licensed certain of its intellectual property and extended the territories available to Ferring for use of certain of the Company s reusable needle-free injection devices to include all countries and territories in the world except Asia/Pacific. Specifically, the Company granted to Ferring an exclusive, perpetual, irrevocable, royalty-bearing license, within a prescribed manufacturing territory, to manufacture certain of the Company s reusable needle-free injector devices for the field of human growth hormone until the expiration of the last to expire of the patents in any country in the territory. The Company granted to Ferring similar non-exclusive rights outside of the prescribed manufacturing territory. In addition, the Company granted to Ferring a non-exclusive right to make and have made the equipment required to manufacture the licensed products, and an exclusive, perpetual, royalty-free license in a prescribed territory to use and sell the licensed products under certain circumstances. The Company also granted to Ferring a right of first offer to obtain an exclusive worldwide license to manufacture and sell the Company s AJ-1 device in a specified field.

Under the Company s December 1993 agreement with Ferring, the Company granted Ferring exclusive rights to use and market, throughout Europe and the former Soviet Union, the Company s reusable needle-free injection device for use with the administration of human growth hormone. Under the agreement, Ferring was required to pay the Company upon the occurrence of certain events, such as completion of certain clinical studies and receipt of regulatory approvals. The Company has received all such payments, and currently, the Company receives payments from Ferring for injectors and disposables supplied to Ferring. Unless Ferring exercises its option to renew the agreement for two-year periods, the agreement will terminate ten years following Ferring s receipt of technical and regulatory approvals to market the Company s injector devices in France, Germany, Italy and Spain. The last of such approvals was received December 1996. In 2004, 2003 and 2002, revenue from Ferring accounted for 62%, 82%, and 59%, respectively, of the Company s product sales. In 2004, revenue from JCR Pharmaceutical Co., Ltd and SciGen, Pte. Ltd. accounted for 9% and 13% of the Company s product sales, respectively, and in 2003 and 2002, revenue from these two companies accounted for 5% or less of product sales.

As consideration for the license grants, Ferring paid the Company EUR500,000 ($532,400) upon execution of the License Agreement, and paid an additional EUR1,000,000 ($1,082,098) on February 24, 2003. Ferring will also pay the Company royalties for each device manufactured by or on behalf of Ferring, including devices manufactured by the Company. Beginning on January 1, 2004, EUR500,000 ($541,049) of the license fee received on February 24, 2003, had been recorded as deferred revenue and will be credited against the royalties owed by Ferring, until such amount is exhausted. During 2004, $80,335 of the deferred revenue royalty fee was recorded as revenue. These royalty obligations expire, on a country-by-country basis, when the respective patents for the products expire, despite the fact that the License Agreement does not itself expire until the last of such patents expires.

Over the past few years, the Company has taken several steps to increase its U.S. insulin injector distribution. As a result, in March 2001, the Company granted non-exclusive U.S. distribution rights to Diabetic Express, a division of Care Services, Inc. Antares has concluded that the successful distribution of insulin devices will require additional physician support and the marketing power of a major insulin manufacturer. However, the Company s current effort will continue because its devices provide a vital service to certain patients and provide the Company with considerable information regarding the needs of people required to self-administer drugs by injection.

On September 12, 2003, the Company entered into a Development and License Agreement (the License Agreement) with Eli Lilly and Company . Under the License Agreement, the Company granted Lilly an exclusive license to certain of the Company s needle-free technology in the fields of diabetes and obesity. The Company also granted an option to Lilly to apply the technology in one additional therapeutic area, which option was extended on December 16, 2004, for a currently unnamed therapeutic area.

Competition

Competition in the pharmaceutical formulation sector is considerably large, mature and dominated by companies like ALZA Corporation, Elan Corporation plc, SkyePharma plc and Alkermes, Inc. Competition in the gel market includes companies like NexMed, Inc., Cellegy Pharmceuticals, Inc., Bentley Pharmaceuticals, Inc. and Novavax, Inc. Competition in the fast-melt market includes Eurand, CIMA Labs, Inc., Cardinal Health and Yamanouchi Pharmaceutical Co., Ltd. Competition in the disposable, single-use injector market includes, but is not limited to, OwenMumford Ltd., The Medical House and Innoject, Inc., while competition in the reusable needle-free injector market includes Bioject Medical Technologies Inc. and The Medical House. Most of these companies have substantially greater capital resources, more experienced research teams, larger facilities and a broader range of products and technologies.

Competition in the injectable drug delivery market is intensifying. The Company faces competition from traditional needle syringes, newer pen-like and sheathed needle syringes and other needle-free injection systems as well as alternative drug delivery methods including oral, transdermal and pulmonary delivery systems. Nevertheless, the vast majority of injections are still currently administered using needles. Because injections are typically only used when other drug delivery methods are not feasible, the needle-free injection systems may be made obsolete by the development or introduction of drugs or drug delivery methods which do not require injection for the treatment of conditions the Company has currently targeted. In addition, because the Company intends to, at least in part, enter into collaborative arrangements with pharmaceutical

companies, the Company s competitive position will depend upon the competitive position of the pharmaceutical company with which it collaborates for each drug application.

At least two companies currently sell injectors to the U.S. insulin market. Antares believes that it retained the largest market share in 2004, and competes on the basis of device size, price and ease of use. Equidyne, Inc. entered the worldwide insulin injector market in mid-2000 but was no longer operating in this area as of late 2003. Aradigm acquired the Weston medical injector technology and has financial resources to be a formidable competitor.

PowderMed Ltd (formerly Powderject Pharmaceuticals, plc), a British immunotherapeutics company, is developing a needle-free injection system based upon the principle of injecting a fine dry powder. Bioject and Powderject compete actively and successfully for licensing agreements with pharmaceutical manufacturers. Powderject has recently refocused exclusively on the use of its technology for vaccine delivery and licensed its technology for therapeutic applications to AlgoRx, a United States company.

The Company expects the needle-free injection market to expand, even though improvements continue to be made in needle syringes, including syringes with hidden needles and pen-like needle injectors. The Company expects to compete with existing needle injection methods as well as new delivery methods yet to be commercialized. For example, Nektar Therapeutics, in partnership with Pfizer, Inc. and Aventis Pharmaceuticals, has completed Phase III clinical testing of inhaled insulin that, if successful, could replace the use of injection for some patients, and in early March 2005, the companies announced the filing of a New Drug Application (NDA) in the U.S.

Government Regulation

We and our collaborative partners are subject to, and any potential products discovered, developed and manufactured by us or our collaborative partners must comply with, comprehensive regulation by the FDA in the United States and by comparable authorities in other countries. These national agencies and other federal, state, and local entities regulate, among other things, the pre-clinical and clinical testing, safety, effectiveness, approval, manufacture operations, quality, labeling, distribution, marketing, export, storage, record keeping, event reporting, advertising and promotion of pharmaceutical products and medical devices. Facilities and certain company records are also subject to FDA inspections. The FDA has broad discretion in enforcing the FD&C Act and the regulations thereunder, and noncompliance can result in a variety of regulatory steps ranging from warning letters, product detentions, device alerts or field corrections to mandatory recalls, seizures, injunctive actions and civil or criminal actions or penalties.

Transdermal and topical products indicated for the treatment of systemic or local treatments respectively are regulated by the FDA in the U.S. and other similar regulatory agencies in other countries as drug products. Transdermal and topical products are considered to be controlled release dosage forms and may not be marketed in the U.S. until they have been demonstrated to be safe and effective. The regulatory approval routes for transdermal and topical products include the filing of an NDA for new drugs, new indications of approved drugs or new dosage forms of approved drugs.

Alternatively, these dosage forms can obtain marketing approval as a generic product by the filing of an ANDA, providing the new generic product is bioequivalent to and has the same labeling as a comparable approved product or as a filing under Section 505(b)(2) where there is an acceptable reference product. Many topical products for local treatment do not require the filing of either an NDA or ANDA, providing that these products comply with existing OTC monographs. The combination of the drug, its dosage form and label claims, and FDA requirement will ultimately determine which regulatory approval route will be required.

The process required by the FDA before a new drug (pharmaceutical product) or a new route of administration of a pharmaceutical product may be approved for marketing in the United States generally involves:

- pre-clinical laboratory and animal tests;
- submission to the FDA of an IND application, which must be in effect before clinical trials may begin;
- adequate and well controlled human clinical trials to establish the safety and efficacy of the drug for its intended indication(s);

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