ORPHAN MEDICAL INC
Form 10-K/A
August 27, 2004

SECURITIES AND EXCHANGE COMMISSION
WASHINGTON, D.C. 20549

FORM 10-K/A
(Amendment No. 4)

(Mark One)

[X] Annual Report pursuant Section 13 or 15(d) of the Securities Exchange Act of 1934 [No Fee Required]
For the fiscal year ended December 31, 2003

or

Transition report pursuant to section 13 or 15(d) of the Securities Exchange Act of 1934 [No Fee Required]
[ ] For the transition period from _____ to _____

Commission File Number 0-24760

Orphan Medical, Inc.

(Exact name of registrant as specified in its charter)

DELAWARE	**41-1784594**
(State or other jurisdiction of incorporation organization)	(I.R.S. Employer Identification Number)
13911 Ridgedale Drive, Suite 250, Minnetonka, MN 55305	**(952) 513-6900**
(Address of principal executive offices and zip code)	(Registrant s telephone number, including area code)

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, and (2) has been subject to such filing requirements for the past 90 days. Yes [**X**] No [ ]

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

Aggregate market value of common stock held by non-affiliates of Registrant, based upon the last sale price of the Common Stock reported on the Nasdaq National Market tier of The Nasdaq Stock Market on June 30, 2003 was $83,493,000 based on approximately 9,135,000 shares held by non-affiliates at that date.

As of April 30, 2004 the Company had 10,841,296 shares of Common Stock outstanding.

Documents Incorporated By Reference

Portions of the Registrant s Definitive Proxy Statement filed with the Securities and Exchange Commission in connection with the solicitation of proxies for the Registrant s Annual Meeting of Shareholders to be held on June 15, 2004 are incorporated by reference in Part III, Items 10, 11, 12, 13 and 14 of this Form 10-K.

EXPLANATORY NOTE

This Form 10-K/A Amendment No. 4 amends the Registrant s Annual Report on Form 10-K for the year ended December 31, 2003 filed on March 15, 2004, as previously amended on March 19, 2004, June 9, 2004 and July 20, 2004.

PART I.

This Annual Report contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended. All forward-looking statements are inherently uncertain as they are based on current expectations and assumptions concerning future events or future performance of the Company. Readers are cautioned not to place undue reliance on these forward-looking statements, which are only predictions and speak only as of the date hereof. Forward-looking statements are not descriptions of historical facts. The words or phrases will likely result , look for , may result , will continue , is anticipated , expect , pro similar expressions are intended to identify forward-looking statements, and are subject to numerous known and unknown risks and uncertainties. Actual results could differ materially from those currently anticipated due to a number of factors, including those identified in the Cautionary Statements filed as an Exhibit to this Annual Report on Form 10-K, and in the Company s other filings with the Securities and Exchange Commission. The Company undertakes no obligation to update or publicly announce revisions to any forward-looking statements to reflect future events or developments.

Antizol®, Antizol-Vet®, Cystadane®, Xyrem®, MedExpand , The Orphan Drug Company , Xyrem Success Program , Orphan Medical, Inc.® and Dedicated to Patients with Uncommon Diseases® are trademarks of the Company.

ITEM 1. BUSINESS

Overview

Orphan Medical, Inc. is a specialty pharmaceutical company focused primarily on sleep disorders, pain and other central nervous system (CNS) disorders. We seek to acquire, develop and market pharmaceutical products that are prescribed by physician specialists and offer a major improvement in the safety or efficacy of patient treatment and have no substantially equivalent substitute.

The Company s lead product, Xyrem® (sodium oxybate) solution is approved for the treatment of cataplexy, a debilitating symptom of narcolepsy, a sleep disorder. The Company markets Xyrem using a 37 person specialty sales force that focuses its selling efforts on physicians specializing in the treatment of sleep disorders. Clinical trials conducted in accordance with United States Food and Drug Administration (FDA) approved protocols have shown that Xyrem consolidates sleep and increases sleep continuity and non-REM sleep, particularly Stages III and IV, which stages are known as slow-wave sleep. Stages III and IV are the stages in which the body experiences the greatest level of restoration. Although currently marketed hypnotics, as well as those in late stage clinical trials, facilitate sleep onset and maintenance, they tend to reduce rather than increase slow-wave sleep. The active ingredient of Xyrem, sodium oxybate or gamma hydroxybutyrate, has also been shown to have other activity that may have therapeutic significance.

Recognizing the significant long-term potential of Xyrem, the Company has initiated a range of clinical development and product development programs. Two clinical trials that are near completion may demonstrate that Xyrem treats excessive daytime sleepiness (EDS) and other symptoms of narcolepsy. If the results of these trials are positive, Xyrem could be marketed to the entire narcolepsy market, which is estimated to affect approximately .05% of the population or 100,000 to 140,000 persons in the United States. We also expect to begin a clinical trial in the first half of 2004 to assess Xyrem in treating the symptoms of Fibromyalgia Syndrome (FMS). FMS is a chronic condition characterized by widespread muscular pain, musculoskeletal discomfort, fatigue, and systemic symptoms. FMS is estimated to affect over 4 million Americans. If Xyrem demonstrates efficacy in treating certain FMS symptoms, additional trials will be conducted in order to obtain FDA approval to market Xyrem to physicians treating this condition.

We are assessing another product, butamben (butyl-p-amino benzoate), as a treatment for intractable cancer pain and, depending on its safety and efficacy profile, other chronic pain conditions as well. Butamben is a unique long-acting ester local anesthetic that is selective for afferent pain fibers with no measurable residual sensory or motor effects. It also appears to provide long-lasting effects, averaging about 6 months in humans in studies to date. We expect to begin clinical trials after meeting with the FDA to present our development plan for butamben.

In addition to expanding the labeling of Xyrem and developing Butamben, we plan to build our presence in specialty CNS markets through the acquisition of both development stage compounds and marketed products. The Company generally seeks to develop products that (1) have some clinical history, (2) have a straightforward formulation that can be readily manufactured with established technologies, and (3) do not require excessive specialized processes for development or manufacture. We do not conduct extensive basic research to discover new chemical entities.

In 2003, we sold all rights to three of our products in order to concentrate resources on Xyrem and enhance our focus on sleep, pain and specialty CNS markets. Medicines developed or acquired in the future may hold orphan drug status, although we may develop or acquire products that do not hold such status if we can obtain appropriate proprietary protection through patents or otherwise. A drug that has orphan drug designation and which is the first product to receive marketing approval for its product claim, indication or application, receives orphan drug status and is entitled to a seven-year exclusive marketing period in the United States for that product claim and a 10-year exclusive period in Europe for that product claim, indication or application, subject to certain limitations.

Since its inception, the Company has obtained New Drug Application (NDA) approvals from the United States Food and Drug Administration (FDA) for six specialty pharmaceutical products. Each of the NDAs was granted Orphan Drug Status by the FDA. We currently market three FDA approved drugs:

Xyrem® (sodium oxybate) oral solution, for the treatment of cataplexy associated with narcolepsy; Antizol® (fomepizole) Injection, an antidote for ethylene glycol or suspected ethylene glycol ingestion in humans and an antidote for methanol or suspected methanol ingestion in humans; and Cystadane® (betaine anhydrous for oral solution), for homocystinuria, a genetic disease. Antizol-Vet® (fomepizole) for injection, an antidote for ethylene glycol or suspected ethylene glycol ingestion in dogs was approved using a New Animal Drug Application (NADA). The Company continues to market Antizol, Antizol-Vet, and Cystadane, to treat disorders outside of CNS to help reduce losses since they have attractive gross and operating margins. In the second quarter of 2003, the Company sold its rights to three products, Busulfex, Sucraid and Elliotts B Solution.

Our activities have consisted primarily of obtaining the rights for pharmaceutical products, hiring the personnel required to implement our business plan, managing the development of these products, preparing for the commercial introduction of these products and raising capital to

support our business operations.

Orphan Medical, Inc. was incorporated on June 17, 1994 as a Minnesota corporation to carry on the business previously conducted by the Orphan Medical division of Chronimed, Inc. The business was reincorporated as a Delaware corporation on September 1, 2000. We have not generated sufficient levels of revenue from our approved products to date to fund our operating activities and have sustained significant operating losses each year since inception. We expect operating losses to continue at least through 2004. Our operations to date have not been profitable and as of March 31, 2004 we have an accumulated deficit of $60.8 million since inception.

The Company continues to market two smaller market products that treat conditions outside of CNS disorders. These products are maintained to help reduce losses since they have attractive gross and operating margins.

Our corporate offices are located at 13911 Ridgedale Drive, Suite 250, Minnetonka, Minnesota 55305. Our telephone number is 952-513-6900 and our website is www.orphan.com. The information on our website is not incorporated into and is not intended to be a part of this report. We make available free of charge on or through our website our annual report on Form 10-K, quarterly reports on Form 10-Q, current reports on Form 8-K and amendments to those reports filed or furnished pursuant to Section 13(a) or 15(d) of the Exchange Act as soon as reasonably practible after we electronically file such material with, or furnish it to, the United States Securities and Exchange Commission. Unless the context otherwise indicates, all references to the Registrant , the Company , or Orphan Medical in this Form 10-K relate to Orphan Medical, Inc.

Our Strategy

Orphan Medical has set its strategic vision on becoming an integrated CNS specialty pharmaceutical company. In this regard, the Company has decided to focus its development and commercial efforts, at least initially, in the areas of sleep disorders and pain. Other CNS disorders will be considered as the Company progresses with its CNS specialty pharmaceutical strategy.

The sleep disorders market is a large therapeutic area affecting an estimated 70 million to 100 million (Source: 2002 National Sleep Foundation Sleep in America Poll) adults in the United States, yet sleep disorders is still a market with significant unmet needs. Moreover, there is increasing recognition of the role of sleep across a range of diseases and its role in health is becoming broadly recognized. Sleep disorders have been underdiagnosed since symptoms are vague and often are missed by physicians. Therefore, sleep disorders or related illnesses may go undiagnosed and untreated for a number of years. The broader specialty CNS area is one of significant opportunities. Outside the major therapeutic areas of depression and schizophrenia, there is a wide range of diseases with unmet medical needs. Our lead product, Xyrem, has the potential to address a number of specialty CNS diseases including narcolepsy, insomnia and fibromyalgia syndrome and the Company has built unique development and commercial capabilities to address several of these opportunities. Epidemiolody studies (including NSF 2002 and Epidemiology Catchment Assessment; Mattson, Jack 4/22/2002) estimate a prevalence for insomnia exceeding 40% of the adult population in the United States. This is approximately 80 million people. According to the Mayo Clinic in a publication dated April 22, 2003, fibromyalgia affects three to eight million people in the United States. The market opportunity associated with each of these indications exceeds $1.0 billion on an annual basis. Other specialty CNS areas of high strategic interest to the Company include Parkinson s disease, epilepsy, movement disorder, Huntington s disease, sleep apnea, Alzheimer s disease and mild cognitive impairment. Building on its current capabilities and expertise, the Company believe it could develop a meaningful presence in these therapeutic areas with key specialist audiences, i.e., sleep specialists, neurologists and psychiatrists.

Xyrem and butamben are the cornerstones of our strategy. Xyrem is currently approved for cataplexy associated with narcolepsy and has application in several other sleep-related disorders. It also has potential utility in fibromyalgia, an increasingly recognized pain disorder. Butamben is expected to be developed for chronic cancer pain, and possibly chronic pain from other causes.

Orphan Medical believes it can apply its competitive advantages to build a specialty pharmaceutical company focused on diseases of the CNS. The Company aims to:

- Avoid large market CNS diseases and concentrate on unmet needs in diseases that are treated by neurologists, psychiatrists, sleep specialists and pain specialists
- Build on the Company s expertise in, and the science of, Gamma Hydroxybutyrate (GHB)

- Expand the Company s marketing and sales presence in the sleep community in order to market other high value products that treat sleep disorders
- Assess and develop products that address pain treated by specialist physicians

- Acquire marketed as well as development stage products that can be marketed through the Company s sales organization and distribution systems

As in all industries, companies that survive and grow long-term must have sustainable uniqueness. The factors of success in the specialty segment of the pharmaceutical industry are:

- A strong and experienced management team
- The capability to develop medicines as well as the ability to acquire drugs in therapeutic areas that the Company has scientific and clinical expertise
- A marketing and sales presence that reaches a concentrated set of prescribers
- Products with growth potential that address unmet medical needs
- An ability to address regulatory issues
- Having good access to capital markets

Products

The following tables summarize certain information relating to the Company s products:

Marketed Products

Approved Product	Application	NDA Approval Date	Orphan Drug Status**
Xyrem® (sodium oxybate) oral solution	For the treatment of cataplexy associated with narcolepsy	July 2002	Granted
Antizol® (fomepizole) Injection	Antidote for ethylene glycol (antifreeze) or suspected ethylene	December 1997	Granted

Approved Product	Application	NDA Approval Date	Orphan Drug Status**
	Antidote for methanol poisoning and suspected methanol ingestion in humans	December 2000	Granted
Cystadane® (betaine anhydrous for oral solution)	Homocystinuria, a genetic disease	October 1996	Granted
Antizol-Vet® (fomepizole) for injection	Antidote for ethylene glycol (antifreeze) or suspected ethylene glycol ingestion in dogs	November 1996	Five year period of exclusivity

Products Under Development

Investigational Product	Proposed Application	Phase of Development*	Orphan Drug Designation**
Xyrem® (sodium oxybate) oral solution	EDS/Narcolepsy	III(b)	
Xyrem® (sodium oxybate) oral solution	Fibromyalgia	IND	
Butamben***	Cancer Pain	II	

* Development Phases are discussed under Business The Regulatory Process .

** Orphan Drug Designation and Status are discussed under Business Proprietary Rights .

*** The Company holds an inactive investigational new drug application (IND) at the FDA. If the IND is reactivated, we will begin Phase II trials at that time. See discussion under PRODUCTS UNDER DEVELOPMENT.

Approved Products

Xyrem® (sodium oxybate) oral solution

Narcolepsy is a chronic neurologic sleep disorder in which sleep is fragmented, and does not occur in an integrated and cohesive manner. This fragmentation results in excessive daytime sleepiness (EDS), unavoidable daytime sleep attacks, cataplexy (a sudden loss of muscle control provoked by emotions), sleep paralysis (brief periods of muscle paralysis) and hallucinations (vivid and sometimes frightening dreaming when falling asleep or waking up). Other related symptoms include broken nighttime sleep, disturbances of auditory and visual perception, and lapses of consciousness and memory problems. These symptoms can lead to a variety of complications, such as limitations on education and employment opportunities, driving or machine accidents, difficulties at work resulting in disability, forced retirement or job dismissal, and depression. Based on published epidemiology studies, including Ohayon, MM. Prevalence of Narcolepsy Symptomology and Diagnosis in European General Population, *Neurology* 2002; 58:1826-1833; Roln, 1998; Mignot, 1998; Hublin et al., 1994c; Dement, et al., 1973 and Aldriaon, 1992, narcolepsy is thought to affect approximately 100,000 to 140,000 persons in the United States.

The second most common symptom of narcolepsy is cataplexy. Cataplexy is the most specific feature of narcolepsy and its presence is diagnostic. Published epdemiology studies, including Basseth, C. Narcolepsy *Neurology Clinics* 1996; 14(3): 545-550; Overcem, S. *Journal of Clinical Neurophysiology* 2001; 18(2): 78-105; and Chaud Harg, M.D. *The Journal of Family Practice* 1993; 36(2): 207-213, suggest that the prevalence of cataplexy in narcolepsy ranges from 60% to 90%. However, according to published studies and our proprietary market research, only about one-fourth to one-third of persons who are diagnosed with narcolepsy are also diagnosed with, and treated for, cataplexy.

Estimating the number of patients with narcolepsy who seek treatment is challenging. Utilizing national insurance databases, it is estimated that approximately 55% or about 55,000 to 75,000 patients with narcolepsy are diagnosed and treated. Furthermore, it is estimated that about one-third of the 55,000 to 75,000-treated narcolepsy patients, or 18,500-25,000 patients, are also diagnosed with and treated for cataplexy. The one-third treatment rate contrasts with the 60% to 90% prevalence rate of cataplexy in patients with narcolepsy. We estimate that the average revenue per patient with Xyrem is approximately $4,000 annually. Accordingly, we estimate the market for cataplexy associated with narcolepsy to approach $100 million and could exceed $100 million if treatment rates for those diagnosed with cataplexy increase in the future.

As discussed below under the heading Xrem® (sodium oxybate) oral solution-Excessive Daytime Sleepiness we are conducting clinical trials to expand the indication for Xyrem for the treatment of EDS associated with narcolepsy. If approved for EDS, the potential market for Xyrem could be in the range of $200 million to $300 million based on estimates of the number of people with narcolepsy in the U.S.

The standard treatment for excessive daytime sleepiness and sleep attacks in patients with narcolepsy are stimulants or wakefulness promoting agents. The symptoms of cataplexy, sleep paralysis and hypnagogic hallucinations have typically been treated with tricyclic antidepressants (TCAs) or selective serotonin reuptake inhibitors (SSRIs). These treatment regimens, in addition to limited efficacy, are often unsatisfactory for a number of other reasons. Amphetamines and other stimulants often cause undesirable side effects such as insomnia, hypertension, palpitations, irritability and, at higher doses, may mimic the symptoms of schizophrenia. Patients often build tolerance to the TCAs and SSRIs and doses are increased to obtain clinical effectiveness. These medications can cause the side effects of dry mouth, impotence, loss of libido, and increased heart rate. Clinical results with Xyrem suggest that it is effective in the treatment of narcolepsy symptoms. Administered at night, it is believed to consolidate sleep and has been shown to reduce cataplexy attacks, and to reduce the severity of daytime sleepiness when used in combination with stimulants during the day. Following initial clinical trials and subsequent commercial use, thousands of narcolepsy patients have been exposed to clinical doses with an acceptable side effect profile. Xyrem does not appear to have the side effects associated with TCAs and SSRIs. Narcoleptic patients could be treated with Xyrem at night and, if needed, with stimulants during waking hours.

The Company submitted its NDA for Xyrem on October 2, 2000 and was granted approval on July 17, 2002. The product is indicated for the treatment of cataplexy associated with narcolepsy. The Company began shipping product in September 2002 and the commercial launch commenced on October 7, 2002. Through December 31, 2003 over 4,000 patients have been prescribed Xyrem by over 1,200 physicians.

Gamma hydroxybutyrate (GHB), also known as sodium oxybate, is the active ingredient in Xyrem. Illicitly produced GHB has been reported to be a drug of abuse. On February 18, 2000, President Clinton signed PL 106-172, a public law that makes GHB a Schedule I substance. Schedule I is the designation by which illegal drugs are controlled. The bill further delineates GHB products being studied under Food and Drug Administration (FDA) approved protocols or approved for commercial sale as Schedule III substances.

Each state has the ability to schedule products more strictly or equivalent to the federally designated schedule. Most states have adopted, either administratively or legislatively, the I/III schedule as described above. The Company continues its efforts to promote consistency of scheduling across all states.

Sodium oxybate (GHB) is a known compound and is not patentable. The Company has received orphan drug status for its indicated use of Xyrem in the U.S. There are no license fees or royalty payments associated with Xyrem revenues. FDA orphan drug status extends through July 17, 2009. Upon expiration of orphan drug status, our products might be subject to competition from other pharmaceutical companies. The Company has an issued formulation patent, which expires

on December 22, 2019. Other patents are pending. The Company has contracted with third-party bulk drug and drug product manufacturers for the production of Xyrem under Good Manufacturing Practices (GMP) conditions.

Antizol® (fomepizole) Injection

Antizol received marketing clearance from the FDA in December 1997 for suspected or confirmed ethylene glycol poisonings and December 2000 for suspected or confirmed methanol poisonings. We commenced shipping Antizol in December 1997. Antizol is primarily used in a hospital setting and is distributed for us by an affiliate of Cardinal Health. When ingested by humans, ethylene glycol (found in antifreeze) and methanol (found in windshield wiper fluid) can lead to death or permanent and serious physical damage. Based on recent revenue trends, we believe that hospital pharmacies will continue to stock Antizol because it is important to treat poisoned patients very quickly in order to improve the chances of successful recovery. For 2003, Antizol contributed approximately 41% of our total revenues. We estimate that over one-third of all hospitals with emergency rooms currently stock the product. Antizol has become the standard of care for toxic alcohol poisoning and guidelines issued by the American Academy of Clinical Toxicologists recommended Antizol as the drug of choice for such poisonings. Since not every hospital will stock antidotes, we expect to see limited incremental stocking by hospitals in 2004. Future sales will be based more on usage as stocking levels are expected remain constant. We have also received marketing approval for Antizol in Canada for the treatment of

suspected or confirmed ethylene glycol poisonings.

We have obtained orphan drug status for Antizol as an antidote to treat ethylene glycol and methanol poisonings, which provides marketing exclusivity to us through December 2004 for ethylene glycol and December 2007 for methanol. We have contracted with a third party for the production of Antizol under GMP conditions. Through a sublicense agreement with Mericon Investment Group, Inc. (MIG), we have an exclusive, worldwide license to develop and market Antizol, which expires in July 2013, subject to a five year renewal through July 2018 exercisable by MIG at our request. This agreement includes a royalty that is paid quarterly.

Cystadane® (betaine anhydrous for oral solution)

Cystadane received marketing clearance from the FDA in October 1996. The first commercial sales of Cystadane occurred in December 1996. Cystadane is distributed by an affiliate of Cardinal Health to patients in the United States through retail pharmacies. It is the first agent approved by the FDA for the treatment of homocystinuria, an inherited metabolic disease. The clinical consequences are wide-ranging and include dislocation of the ocular lens, early (under age 30) thromboembolism, developmental and mental retardation and reduced life span related to elevated plasma homocysteine levels. Based on published epidemiology studies, it has been estimated that homocystinuria occurs approximately once in every 200,000 live births worldwide (Sources: Sokalova et al., 2001; Linnabank et al., 2001; Yap, 2003) and that there are estimated to be 1,000 patients with homocystinuria in the United States. Based on the Company s historical domestic revenue growth rate of 10-15% for this product, the Company estimates that the annual market potential for Cystadane may approach $1.0-$1.5 million in the United States. The Company receives sales revenue generated outside of the United States through its licensees. Cystadane revenues met the Company s expectations in 2003 and are expected to grow slightly in subsequent periods. The Company believes that the small size of the market and the high medical value of Cystadane justify the limited resources required by the Company to continue making this product available to patients.

The Company obtained orphan drug status for Cystadane for the treatment of homocystinuria, which provided marketing exclusivity to the Company through October 2003. The Company does not expect the expiration of orphan drug protection to significantly impact the sales of Cystadane in 2004 given the relatively small market size. The Company has contracted with a third party for the production of Cystadane under GMP conditions. No license was required for the Company to develop and market Cystadane.

The Company is not currently sponsoring any clinical trials with/for Cystadane but is aware of, and supporting through unrestricted grants, clinical trials being conducted by independent investigators affiliated with major hospitals to assess the safety and efficacy of Cystadane as a stand alone or adjunctive therapy for the following indications: Non-alcoholic steatohepatitis, Rett syndrome, rheumatoid arthritis and hyperhomocystinemia. The Company does not expect that the results of any of these clinical trials will significantly enhance or decrease the current limited market potential for Cystadane in the near future. Depending on the results, these trials may result in potential long-term opportunities for us.

Antizol-Vet® (fomepizole) for injection

In November 1996, the Center for Veterinary Medicine of the FDA approved Antizol-Vet as a treatment for dogs that have ingested or are suspected of having ingested ethylene glycol. The first commercial sales of Antizol-Vet occurred in January 1997. The earlier an ethylene glycol poisoned dog is treated with Antizol-Vet, the more likely that there will be a positive

outcome. The annual market potential for Antizol-Vet is expected to be under $300,000. We have found that stocking of this product has been limited due to its high cost, but it is ordered when a poisoning occurs. Antizol-Vet revenues met our expectations in 2003 and are expected to remain constant or decline in subsequent periods. Revenues from this product have not been nor will they be material to our product revenue.

Federal law provided us with a marketing exclusivity period through November 2001 for the use of Antizol-Vet in dogs for the approved indication. We have contracted with a third party for the production of Antizol-Vet under GMP conditions.

We have partnered with several leading regional and national veterinary wholesalers to distribute Antizol-Vet to veterinary clinics. It is believed that the current partners effectively and efficiently encompass the entire country with limited sales territory overlap, thus helping prevent downward retail pricing pressures. We do not anticipate adding additional distribution partners. These agreements do not result in material revenue.

Disposition of products

On June 10, 2003, we announced the disposition of Busulfex® (busulfan) Injection to ESP Pharma, Inc. for $29.3 million plus the book value of inventory, approximately $0.2 million. We announced the sale of the product Sucraid® (sacrosidase) oral solution to a specialty pharmaceutical company on May 6, 2003 for $1.5 million. We also divested a third product, Elliotts B Solution® to the same specialty company for proceeds that were not material. Proceeds from these dispositions will be used for further development and marketing of Xyrem and for the creation of a

stronger presence in the sleep and central nervous system (CNS) markets.

Products Under Development

We incurred $10.8 million, $8.7 million and $7.0 million of Product Development expenses for the years ended December 31, 2003, 2002 and 2001, respectively. We had $14.7 million of outstanding commitments for spending associated with product development spending for the following development projects at December 31, 2003.

Sleep Disorders Investigational Products

Xyrem® (sodium oxybate)® oral solution-Excessive Daytime Sleepiness

We are conducting two Phase III (b) clinical trials for Xyrem. These controlled clinical trials assess the efficacy of Xyrem in treating excessive daytime sleepiness (EDS) related to narcolepsy. These trials continue to progress toward completion in early 2004 with the data to be compiled into a supplemental New Drug Application (sNDA) to the FDA expected in the second half of-2004. We expect that the FDA will take action on this sNDA in mid 2005. If approved, this sNDA may provide an expanded indication which could increase the market opportunity for the product. We expect to incur approximately $5.0 million of expenses in 2004 for the completion of these trials. We incurred expenses related to these trials of $5.0 million, $2.5 million and $1.5 million in the fiscal years ended December 31, 2003, 2002 and 2001, respectively.

Xyrem® (sodium oxybate)® oral solution-Fibromyalgia

Fibromyalgia is a syndrome characterized by widespread pain that cannot be explained by an inflammatory or degenerative musculoskeletal disorder. Fatigue, depression, and somatic symptoms are also often present. The prevalence of fibromyalgia has been reported in several epidemiological studies. The estimated prevalence ranges from 1-4% of the adult population, a prevalence rate of 2% is most commonly cited in the literature. Accordingly, about 4.2 million Americans over the age of 18 have fibromyalgia.

We plan to initiate a proof-of-principle trial at an estimated cost of $3.0 million to $4.0 million to be incurred in 2004 and 2005 to assess the efficacy of Xyrem in the treatment of the symptoms of fibromyalgia. Patient enrollment in this trial is expected to begin in the second quarter of 2004. Data from this trial is expected to be available in mid 2005. At that time we will determine whether or not to pursue a development program in support of a regulatory application. The nature and scope of a potential development program cannot be determined until this trial is complete and the data is available. Therefore, the total costs and timing of a potential development program are uncertain at this time.

Butamben (butyl-p-amino benzoate)

Butamben is a new treatment for pain. It is intended to provide physicians with an effective adjunct for their patients who require long-term management of moderate-to-severe chronic pain. Butamben is a unique, material-based, long-acting local anesthetic that is delivered by epidural injection. It selectively blocks pain afferentation by blocking transmission in A delta and C fibers in peripheral nerves. Butamben blocks fast-sodium ion channels, which leads to hyperpolarization of the neuronal membrane and long-term pain control. It is non-neurolytic and non-narcotic. In previous clinical experiences under an investigator IND, butamben appeared to provide long-term relief from pain, with no motor blockade when accurately placed in the site appropriate to the sequential afferentation of pain. These experiences were published in several articles, including Schulman, M et al., *Regional Anesthesia and Pain Medicine* 23(4):395-401,1998; Schulman, Harris, Lubenow, Nath, and Ivankovich, *The Clinical Journal of Pain* 16:304-309, 2000; and Korsten et al., *Anesthesiology* 75: 950-959, 1991. To date, however, butamben's efficacy has not been conclusively proven. Therefore, we cannot assure you that the efficacy of butamben will ever be proven, or that butamben will be approved by the U.S. Food and Drug Administration for sale.

Orphan Medical s butamben is a new patented formulation for use as a long acting pain medication. This new indication will require a full development program under the IND to support a future NDA. The product will be used initially in patients who either have pain that is not alleviated by escalating doses of oral analgesics or need relief from the side effects that accompany these escalating doses. Treatment with butamben may allow patients to reduce their doses of oral analgesics, and thereby reduce dose-related analgesic side effects. Should we initiate a development program, we will begin Phase II trials at that time. We hold an inactive IND at the FDA for butamben. We acquired the previous IND as part of a transaction with a pharmaceutical company that had discontinued clinical development and voluntarily converted its IND to inactive status. We are in the process of defining the manufacturing process for butamben and, if successful, will submit a new chemistry and manufacturing package to the FDA and then expect to meet with the FDA to review a development program for this product. At that time, if we pursue a product development program, we will take action to reactivate the IND at the FDA. Human clinical trials will not begin until after we meet with the FDA to review the proposed development program. Because the nature and scope of the potential development program cannot be determined until after the currently unscheduled meeting with the FDA, the costs and timing of a development program are uncertain at this time. The total expected cost of defining the manufacturing process and other related costs in determining whether or not to pursue a development program is approimately $0.5 million, most of which will be incurred in 2004. We currently expect to determine by the end of the first quarter of fiscal 2005 whether to initiate a development program for butamben. We do not expect any revenue from this product until at least 2008.

Product Development Risk Management

Our product strategy has been designed, in part, to mitigate its overall business risk. We have pursued multiple distinct therapeutic areas within CNS such as sleep and pain pharmaceuticals rather than concentrating financial, development and marketing resources on a single therapeutic area or a single platform technology. To reduce its product development risk, we generally seek to develop products that (1) have

some clinical history, (2) have a straightforward formulation that can be readily manufactured with established technologies, and (3) do not require excessive specialized processes for development or manufacture. In addition, we generally seek to acquire products that are already in Phase II or Phase III clinical trials, or in an earlier stage of development with proof of concept established. When a product is licensed without the equivalent of Phase II or III data, we may conduct one or more proof of concept trials to better assess the likelihood of efficacy or safety. Each such pilot trial is narrowly defined. We do not conduct extensive basic research to discover new chemical entities. We may also purchase rights to approved products. To reduce its marketing risk, we generally attempt to obtain some form of proprietary protection, such as patent protection, orphan drug status, exclusive licensing agreements, or sole supplier agreements.

Proprietary Rights

We believe it is important that our products receive patent protection or orphan drug status or have other factors that limit potential competition. When available and appropriate, we will seek orphan drug status to enhance or provide proprietary protection to a product. A drug that has orphan drug designation and which is the first product to receive marketing approval for its product claim, indication or application, receives orphan drug status and is entitled to a seven-year exclusive marketing period in the United States for that product claim and a 10-year exclusive period in Europe for that product claim, indication or application, subject to certain limitations. We have two products with orphan drug status. Applications for orphan drug designation will be made when and where appropriate and available for any additional indications or products that may be licensed in the future.

Orphan drug protection is available in Japan and the European Union under requirements similar to those in the United States. An important distinction in the European Union is the ten-year period of marketing exclusivity for products designated as orphan drugs, compared to seven years of exclusivity in the United States. The period of exclusivity in the European Union also begins upon marketing approval.

With respect to additional products we may license in the future, if any, we expect that such licenses would include, if such rights are available, an assignment of the licensor s proprietary rights with respect to the licensed product. We also seek foreign patent protection for our products and have applied for patents outside the U.S. for Xyrem. We have licensed two patents related to butamben, a product that is being evaluated for development. We are in the process of defining the manufacturing process for butamben and, if successful, expect to have a second meeting with the FDA to finalize a development program for this product. We evaluate the desirability of registering approved patents or other forms of protection for our products in individual foreign markets based on the expected costs and relative benefits of attaining such protection.

The Regulatory Process

Pharmaceutical products intended for therapeutic use in humans are governed by extensive FDA and other federal regulations in the United States and by comparable regulations in foreign countries. The process of seeking and obtaining FDA approval for a previously unapproved new human pharmaceutical product generally takes many years and involves the expenditure of substantial resources and considerable risk.

Before a drug product can be investigated or marketed in the United States, the following general steps are required: (i) pre-clinical laboratory and animal safety tests, (ii) the submission to the FDA of an IND, (iii) clinical and other studies to assess safety and parameters of use, (iv) adequate and well-controlled clinical trials to establish the safety and effectiveness of the drug product, (v) the submission to the FDA of an NDA, (vi) FDA approval of the NDA prior to any commercial sale or shipment of the product, (vii) marketing of the drug, and (viii) post-approval safety and risk monitoring.

Typically, pre-clinical studies are conducted in the laboratory and in animal model systems to gain preliminary information on the product s pharmacology and toxicology and to identify any potential safety problems that would preclude testing in humans. The results of these studies, together with the general investigative plan, protocols for specific human studies and other information, are submitted to the FDA as part of the IND application. The FDA regulations do not, by their terms, require FDA approval of an IND. Rather, if the FDA does not notify the sponsor to the contrary within 30 days of receipt of the IND, they allow a clinical investigation to commence. As a practical matter, however, FDA approval is often sought before a company commences clinical investigations. That approval may come within 30 days of IND receipt, but may involve substantial delays if the FDA requests additional information.

The initial phase of clinical testing (Phase I) is conducted to evaluate the metabolism and pharmacological actions of the experimental product in humans, as well as the side effects associated with increasing doses, and, if possible, to gain early evidence of possible effectiveness. Phase I studies can also evaluate various dosages, methods and schedules of product administration. These studies generally involve a small number of healthy volunteer subjects, but may be conducted in people with the disease that the product is intended to treat. The total number of subjects is generally in the range of 20 to 80. A demonstration of therapeutic benefit is not required in order to complete Phase I trials successfully. If acceptable product safety is demonstrated, Phase II trials may be initiated.

Phase II trials are designed to evaluate the effectiveness of the product in the treatment of a given disease and involve patients with the disease under study. These trials often are well-controlled, closely monitored studies involving a relatively small number of subjects, usually no more than several hundred. The optimal dosages, methods and schedules of administration are determined in these studies. If Phase II trials are successfully completed, Phase III trials are often commenced, although Phase III trials are not always required, particularly for drugs of high medical value intended for smaller patient populations.

Phase III trials are expanded, controlled trials that are performed after preliminary evidence of the effectiveness of the experimental product has been obtained. These trials are intended to gather the additional information about safety and effectiveness needed to evaluate the overall risk/benefit relationship of the experimental product. In addition, these trials provide the substantial evidence of both effectiveness and safety necessary for product approval. Phase III trials usually involve from several hundred to several thousand subjects.

A clinical trial may combine the elements of more than one phase (i.e., a Phase I/II or II/III trial) and typically two or more Phase III studies are required for FDA approval. A company s designation of a clinical trial as being of a particular Phase is not necessarily indicative that such a trial will be sufficient to satisfy the FDA requirements of that Phase because this determination cannot be made until the protocol and data have been submitted to and reviewed by the FDA. In addition, a clinical trial may contain elements of more than one Phase notwithstanding the designation of the trial as being of a particular Phase. The FDA closely monitors the progress of the Phases of clinical testing and may, at its discretion, re-evaluate, alter, suspend or terminate the testing based on the data accumulated and its assessment of the risk/benefit ratio to patients. It is not possible to predict with certainty the time required to complete Phase I, II and III studies with respect to a given product.

Upon the successful completion of clinical testing, a marketing application (i.e., NDA) is submitted to the FDA for approval. This application requires detailed data on the results of pre-clinical testing, clinical testing and the composition of the product; proposed labeling to be used with the drug; information on manufacturing methods; and samples of the product in some cases. Since the passage of the Prescription Drug User Fee Act (PDUFA), the FDA typically takes from six to eighteen months to review an NDA after it has been accepted for filing. Following its review of a marketing application, the FDA typically raises questions or requests additional information. The NDA approval process can, accordingly, be very lengthy. Further, there is no assurance that the FDA will ultimately approve an NDA. The FDA can also determine that a drug is approvable contingent on satisfactory review of additional information requested by the FDA. We cannot assure you that such requests by the FDA for additional information can be fulfilled in a timely manner, if at all. If the FDA approves the NDA, the new product may be marketed for the applications or

treatments that have been approved by the FDA. The claims with which a product can be marketed are also subject to review and approval by the Division of Drug Marketing, Advertising and Communications (DDMAC), the FDA s marketing surveillance department within the Center for Drugs. The FDA often clears a product for marketing with a modification, or restriction to the proposed label claims or requires that post-marketing surveillance, or Phase IV testing, to be conducted. The method and system of a drug s distribution can also be controlled by the FDA if approved under Subpart H.

Operating Functions

We have structured each of its operating functions to support its strategy. Following is a general explanation of the typical steps in our processes of product acquisition, development and marketing.

Product Acquisition

We actively search for product licensing opportunities. The continual acquisition of products for development and/or commercialization is a key element of our growth strategy. We attract product acquisition proposals through a network of customer and industry contacts, licensing brokers and a growing awareness of its activities by governmental, academic and industry sources. Since its inception, we have evaluated many product opportunities. To date, seventeen products have been acquired and, of these, three products were developed, marketed and subsequently divested (Busulfex, Sucraid, and Elliotts B Solution) and four products (Xyrem, Antizol, Cystadane and Antizol-Vet) have been developed and are currently being marketed by us. In addition, Xyrem is also currently under development for other indications.

We seek to acquire pharmaceutical products within CNS markets that, in our opinion, generally:

- Are of high medical value as defined by the customer (physician or patient) within a therapeutic area;
- Treat diseases that affect distinct patient populations;
- Are prescribed by physician specialists;
- Can be marketed with a focused, specialized sales team to health care specialists, health care institutions, and patients;
- Are likely to be eligible for reimbursement by third-party payors;

- Have, or are candidates for, patent protection, orphan drug designation or have other characteristics that enhance our competitive position;
- Treat diseases that have clinical endpoints (i.e., signs or symptoms) that are readily measured;
- Are conventional pharmaceutical products that are relatively straightforward in formulation and development, and do not involve the application of new technologies;
- Are in Phase II or Phase III clinical trials and have a relatively high likelihood of obtaining the approval of the FDA within three to five years of acquisition;
- Offer attractive potential financial returns with relatively low development costs;
- Complement our other products in order to leverage existing talent and resources.

In selecting additional products for potential inclusion in its portfolio, we generally focus on acquiring rights to medicines that serve niche or defined patient populations served by specialty physicians. Major drug companies are less likely to address these niche markets because they do not believe these markets will produce acceptable revenues and returns. This reluctance limits the number of potential sources of competition. In addition, a product designed for smaller patient populations may be eligible for orphan drug designation. By obtaining orphan drug designation, we are granted exclusive marketing rights or status in the United States for seven years, subject to certain limitations, after an NDA for a product is approved, if we are the first to receive approval for the designated drug and indication.

We seek to acquire potential products that already have, or will not require, a substantial quantity of clinical data to demonstrate their relative efficacy and safety. We also search for product candidates that represent new delivery methods or dosage forms of previously approved or known compounds because we believe these types of products are more likely to be quickly approved by the FDA and accepted by the medical community. In addition, we attempt to develop medicines where clear clinical endpoints can demonstrate their effectiveness. Generally, we seek to acquire products that can be developed to the point of FDA approval within three to five years of their acquisition. Typically, we also focus our development efforts on one

indication and, when possible, one dosage form to minimize development costs. Potential additional indications or dosage forms may be evaluated, but only after the primary NDA is submitted and/or approved.

An additional element of our product development strategy is to acquire products that have or can have a degree of proprietary protection. Generally, this goal is accomplished by selecting products that are covered by patents, are eligible for orphan drug designation, or are the subject of an exclusive license from a sole supplier or a manufacturer with specialized or proprietary processes. The likely availability of adequate levels of reimbursement from third-party payors is also an important factor in product acquisition decisions.

Product Development

Pharmaceutical product development is one of the Company s principal activities. We have incurred in excess of $60 million in expenses for research and development activities through December 31, 2003. In addition, the Company estimates that it will need to incur at least an additional $14.7 million of expense in research and development activities over the next four quarters relating to the products it currently markets, including obtaining any potential additional Xyrem indications. Although we believe we have sufficient cash available for currently anticipated clinical trials, we may need additional capital to fund clinical trials related to products that we may acquire or develop in the future or for trials related to new indicators of existing products.

A major element of the Company s product development strategy is to use third-parties or contract research organizations (CROs) to assist in the conduct of safety and efficacy testing and clinical studies, to assist the Company in guiding products through the FDA review and approval process, and to manufacture and distribute any FDA approved products. The Company believes that maintaining a limited infrastructure will enable it to develop products efficiently and cost effectively.

The Company believes the use of third-parties to develop and manufacture its products has several advantages. This approach generally allows a greater pool of resources to be concentrated on a product than if these functions were performed by internal personnel who were required to support all of the Company s products. Although this approach will allow the Company to avoid the expense associated with developing a large internal infrastructure to support its product development efforts, it will result in the Company being dependent on the ability of outside parties to perform critical functions for the Company. Over time, the Company expects to build internal capabilities to replace certain development functions now contracted to outside parties.

This contract approach to product development requires project management by professionals with substantial industry experience. The Company believes it has in-house experts in areas of critical importance to all of its proposed products who can be consulted by the development teams. These areas include regulatory affairs, marketing and sales, quality assurance, manufacturing, clinical trials management, finance,

information systems and general management.

The product development process is designed to identify problems associated with a proposed product s safety and effectiveness. The Company attempts to reduce the risk that a proposed product will not be accepted in the marketplace by conducting market research and defining commercial strategy with a product s development. A drug development portfolio cannot be completely insulated from potential clinical and marketing failures. It is likely that some proposed products selected for development by the Company will not produce the clinical or revenue results expected. To date, the Company has discontinued development activities with respect to eleven proposed products because either the products were deemed unapprovable or the estimated financial returns of these proposed products were unacceptable. In May and June 2003, the Company divested three products from its commercially marketed product portfolio resulting in a net gain of $30.3 million.

Manufacturing

The Company does not have and does not intend to establish any internal product testing, drug or chemical synthesis of bulk drug substance, and manufacturing capability for drug product. Manufacturers of the Company s products are subject to applicable GMP as required by FDA regulations or other rules and regulations prescribed by foreign regulatory authorities. The Company is negotiating or has entered into bulk drug supply and drug product manufacturing agreements with third-parties for all of its FDA approved products and is dependent on such third parties for continued compliance with GMP and applicable foreign standards. The Company believes that qualified manufacturers will continue to be available in the future, at a reasonable cost to the Company, although there can be no assurance that this will be the case.

Due to FDA mandated dating requirements and the limited market size for the Company s approved products, the Company may be subject to complex manufacturing logistics, minimum order quantities that could result in excess inventory as determined under the Company s accounting policy, unsalable inventory as a result of product expiring prior to use, and competition with others for manufacturing services when needed or expected. The Company has a production-planning program to assess and manage the manufacturing logistics amongst the vendors supplying the required finished product components of bulk drug substance, drug product and packaging.

We generally use a single contract drug product manufacturer for each of our products. The Company is in the process of changing manufacturers of Cystadane which is the reason two manufacturers are listed for that product. These manufacturers have been approved by the FDA for the production of our approved products. Following is a listing of the Company s contract drug product manufacturers:

Contract Drug Product Manufacturer	Marketed and Proposed Products
An affiliate of Boehringer Ingelheim	Antizol, Antizol-Vet
Ropack, Inc.; ProClinical Inc.	Cystadane
DSM Pharmaceuticals, Inc.	Xyrem

In addition to the contract drug product manufacturers, we use single suppliers for the bulk drug substance for Antizol, Antizol-Vet and Xyrem. Ash Stevens, Inc. is the Company s sole supplier of bulk drug substance for the manufacture of Antizol and Antizol-Vet; while Lonza, Inc. is the Company s sole supplier of bulk drug substance for the manufacture of Xyrem.

The loss of either a bulk drug supplier or drug product manufacturer would require us to obtain regulatory clearance in the form of a pre-approval submission and incur validation and other costs associated with the transfer of the bulk drug or drug product manufacturing process. We believe that it could take as long as two years for the FDA to approve such a submission. Because our products are targeted to relatively small markets and our manufacturing production runs are small by industry standards, we have not incurred the added costs to certify and maintain secondary sources of supply for bulk drug substance or backup product manufacturers for some products. Should we lose either a bulk drug supplier or a drug product manufacturer, we could run out of salable product to meet market demands or investigational product for use in clinical trials, while we wait for the FDA approval of a new bulk drug supplier or drug product manufacturer.

We believe that the foregoing risks regarding the possible loss of a manufacturer or supplier could be mitigated in a number of ways. First, the Company s currently effective manufacturing and supply agreement provide for relatively long termination periods, ranging from one to two years, during which the manufacturer or supplier is required to continue to perform its obligations under its agreement with us. During this time period, the Company would actively search for an alternate manufacturing or supply source and it is management s current belief that, given the relatively long time period, an alternate source could be obtained during that period.

Second, during the termination period, we expect that we would increase our inventory levels in order to safeguard against delay in implementing a new manufacturing or supply relationship. Given the longer expiration periods for the Company s current products, the Company currently expects it would be able to sell increased inventory levels prior to the expiration dates of the increased inventory. Expiration periods for our products generally range from two to five years from the date of manufacture. Given the foregoing, we believe that there are alternate manufacturing and supply sources that would be available both on acceptable terms and on a timely basis for our products.

Despite our expectation that we would be able to take steps to mitigate the risk of loss of one or more manufacturing or supply relationships, we cannot assure you that the change of a bulk drug supplier or drug product manufacturer and the transfer of the processes to another third party would be approved by the FDA, and if approved, in a timely manner. Therefore, despite our efforts to mitigate risk, we may experience additional costs and delay while switching providers, which in turn could adversely affect sales revenue.

Marketing United States

As part of its marketing efforts, the Company identifies and defines appropriate therapeutic areas, identifies customer needs within each therapeutic area, identifies specific product acquisition candidates within each therapeutic area, works with the development team to insure clinical data are collected that supports the desired indication and marketing claims, and if FDA approval is obtained, designs and implements marketing plans for each of its approved products. Market research is conducted to analyze the potential of products prior to their acquisition. Once a product is acquired and is being developed, further market research is completed and, based on this analysis; the product s marketing plan is developed and appropriate pre-launch programs are initiated. Upon submission of the NDA to the FDA, the product management responsibilities transition from the development team to the Company s commercialization staff. The development group continues to provide support where needed to enhance marketing and sales efforts. This group is responsible for all aspects of a product s marketing and sales, including product forecasting, positioning, price, promotion and physical distribution to successfully launch and commercialize the product. Senior sales and marketing employees lead a cross functional team of internal and external personnel to implement a product s marketing and commercialization plan. In addition, marketing and sales staff also supports the Company s international sales efforts through support of and interfacing with international partners.

Marketing Foreign

In general, the Company expects to out-license foreign marketing, sales and distribution rights after an NDA is submitted or approved in the United States. The Company contracts with foreign companies (usually pharmaceutical companies) to market and distribute its products. The Company considers Europe and Japan to be its most attractive foreign markets. The Company has entered into marketing, sales and distribution agreements for Antizol and Cystadane in Europe, Cystadane in Australia and New Zealand, Cystadane in Israel, Antizol and Cystadane in Canada.

In October 2003, the Company announced that it has licensed European sales and marketing rights for Xyrem to Celltech Pharmaceuticals, a division of Celltech Group plc. Under the terms of the agreement, Celltech will be responsible for the registration, marketing and sales of Xyrem in Europe. The licensing agreement includes the use of Xyrem in narcolepsy and provides Celltech with rights to negotiate for other potential future indications including fibromyalgia syndrome.

The Company s historical practice is to negotiate contracts with foreign distributors that generally provide for minimum order and sales performance. Minimum fees negotiated with foreign parties to date are not material and are not refundable, nor subject to future performance criteria. The foreign contracting party is responsible for obtaining

marketing approval for the Company s product to which the agreement relates and the Company is responsible for providing selected U.S regulatory information to the foreign party on request. The Company cannot unilaterally terminate these agreements without established evidence of default, but these agreements do expire over a defined period of time and the Company may seek other foreign parties to provide comparable services upon expiration if not satisfied with the performance of its partners. The principal benefit a foreign party receives from entering into these agreements with the Company and paying the minimum fees, if any, is a contracted price for acquisition of product from the Company because the Company is the sole supplier of its approved products on a worldwide basis.

Distribution

In the foreseeable future, the Company does not intend to develop internal physical distribution capabilities because the Company believes its relatively low-volume products can be more economically and efficiently distributed through third-party distribution organizations. Cystadane, principally delivered to patients through retail pharmacies, and Antizol, primarily used in a hospital setting, are distributed by an affiliate of Cardinal Health. This distribution system allows the sale of these products directly into hospitals or, if customers prefer, through their primary wholesaler. Antizol-Vet is a product used in veterinary clinics and is distributed by an affiliate of Cardinal Health to individual veterinary clinics and a network of veterinary wholesalers.

The Company has a contract with a central pharmacy, Express Scripts Specialty Distribution Services, Inc., to distribute Xyrem in the United States. Xyrem is classified as a Schedule III controlled substance and approved under Subpart H of the FDA s review and approval process, and distribution is strictly controlled. A specialty pharmacy is the only source through which Xyrem can be obtained. Distribution is governed by the FDA s Subpart H regulations and complies with the risk-management controls jointly developed by Orphan Medical, the Drug Enforcement Agency and law enforcement agencies. Every shipment of Xyrem is subject to stringent safeguards to ensure it reaches only individuals for whom it has been legitimately prescribed. The Company s agreement with the central pharmacy calls for fees to be paid based on the number of

bottles shipped to patients and is for a term of three years, ending September 2005. This agreement may be terminated for cause or noncompliance with appropriate notice given according to the provisions of the agreement.

While we believe that there are other third parties that can provide these distribution services, we cannot assure you that our distribution agreements with these entities or other third parties would be available, or continue to be available to us on commercially acceptable terms. Nonetheless, we do not believe the loss of a distributor or the failure to renew agreements with our existing distributors would have a material adverse effect on our sales revenue.

Competition

Potential competitors in the United States are numerous and include pharmaceutical, chemical and biotechnology companies. The Company will experience competition in several specific areas, including, but not limited to, those described below.

Product Acquisition The Company will compete with other entities in acquiring product rights from other companies, universities, other research institutions, as well as from other potential licensors.

Product Development Resources The Company will compete for certain resources, such as the services of clinical investigators, contract manufacturers, advisors and other consultants. The Company will generally have little or no control over the allocation of such resources.

Orphan Drug Designation The Company is aware of another company that filed for and received orphan drug designation on a product similar to one of its products. Teva (formerly Biocraft) had been granted orphan drug designations for their sodium oxybate. Sodium oxybate is the equivalent of the Company s Xyrem product. In 1999, the Company entered into an agreement with Teva that, in effect, transfers Teva s development data to the Company. While the Company is not aware of others holding or seeking orphan drug designation for products that would compete with the Company s products for NDA approval, there can be no assurance that the Company s products will not have such competition from another formulation or drug of materially different composition from being approved, with or without orphan drug status, for the same indication.

Marketing And Sales Each of the Company s current products will face competition from other products or from other therapeutic alternatives. The Company s products may compete against products whose marketers have substantially greater resources, including large specialized sales forces, than the Company. The following is a description of competition that our products face.

Xyrem: for the cataplexy symptoms of narcolepsy, tricyclic and SSRI antidepressants are used although they are not approved for this use.

Xyrem: for excessive daytime sleepiness associated with narcolepsy, Provigil® / modafinil (Cephalon) is approved as a wakefulness-promoting drug. Stimulant drugs are also used for this symptom although not specifically approved for narcolepsy. Xyrem may not be directly competitive with these agents as its use in combination with modafinil or stimulants may be additive or, in fact, synergistic.

Antizol: prior to the introduction of Antizol, ethanol has been used for many years for the treatment of ethylene glycol and methanol poisonings. Although not approved for this use, it continues to be used in some hospitals.

Cystadane: no competitors.

Manufacturing The Company may also compete for limited manufacturing capacity or availability.

Government Regulation

General

Political, economic and regulatory influences are subjecting the health care industry in the United States to fundamental change. Several potential approaches are under consideration, including mandated basic health care benefits, controls on health care spending through limitations on the growth of private health insurance premiums and Medicare and Medicaid spending, price discounts from drug manufacturers, the creation of large purchasing groups and other significant changes to the health care delivery system. In addition, some states have adopted or are considering price controls and various health care reform proposals. The Company anticipates that Congress and state legislatures will

continue to review and assess alternative health care delivery systems and payment methods and that public debate of these issues will likely continue in the future. Because of uncertainties regarding the ultimate features of reform initiatives and their enactment and implementation, the Company cannot predict which, if any, of such reform proposals will be adopted, when they may be adopted or what impact they may have on the Company or its prospects.

Reimbursement

Employers, through payments to their employee benefit plans, bear a significant share of the health care costs of their employees. These plans are typically administered by insurance companies, health maintenance organizations, preferred provider organizations and other third-party payors. Health care services and products, including pharmaceutical products, are also paid for by government agencies such as Medicaid. Employers and the payors involved in providing or administering health care benefits are increasingly turning to managed care systems to control health care costs. Under these systems, the administrative requirements and standards of care are established by the health care purchasers and providers and the benefit level depends on the negotiated price. Managed care systems usually limit treatment options to approved therapeutic regimens and formularies, or lists of approved drugs and medical products.

Inclusion or listing on the formularies of managed care groups is important to the commercial success of most prescription medicines. A pharmaceutical must be included on a third-party payor s formulary or must be deemed medically necessary to be eligible for reimbursement by that payor. In deciding whether a drug is to be included on a formulary, payors will generally consider its therapeutic value and cost in comparison to other available treatments. The Company believes that the proprietary nature and medical usefulness of its products should assist it in its efforts to have its products approved for reimbursement. No assurance can be given, however, that the Company s products will be approved for reimbursement by third-party payors at acceptable levels, or at all.

Product Approvals

The Company s products require FDA approval in the United States and comparable approvals in foreign markets before they can be marketed. The development of investigational products and the marketing and supply of approved products require continuing compliance with FDA regulations on the part of the Company as well as its manufacturers and distributors.

Scheduled Products

Products that are designated controlled substances also require compliance with regulations administered by the U.S. Drug Enforcement Agency (DEA), and similar regulations administered by state regulatory agencies. On February 28, 2000 President Clinton signed PL 106-172, a public law that makes gamma hydroxybutyrate (GHB) a Schedule I substance. Schedule I is the designation by which illegal and non-approved drugs are controlled. The bill further delineates GHB products being studied under Food and Drug Administration (FDA) approved protocols or approved for commercial sale by the FDA as Schedule III substances.

Each state has the ability to schedule products more strictly or equivalent to the federally designated schedule. Most states have adopted, either administratively or legislatively, the bifurcated I/III schedule as described above. The Company continues its efforts to ensure consistency of scheduling across all states.

Manufacturing Regulation

All facilities and manufacturing processes used to manufacture products for clinical use or sale in the United States must be operated in conformity with Good Manufacturing Practices (GMP). These represent the FDA requirements governing the production of pharmaceutical products. FDA approval is required before a contract manufacturer can implement most changes in manufacturing procedures for any of the Company s approved products. The Company has established a quality assurance program to monitor third-party manufacturers of its products to promote compliance by such manufacturers with domestic and foreign regulations (based on country of use). In addition, FDA approval is required to change contract manufacturers of approved products. Obtaining the FDA s approval for a change in manufacturing procedures or change in manufacturers could cause production delays and loss of revenue.

Foreign Regulation

Products marketed outside of the United States are subject to regulatory approval requirements similar to those required in the United States, although the requirements governing the conduct of clinical trials, product licensing, pricing and reimbursement vary widely from country to country. No action can be taken to market any product in a country until an

appropriate application has been approved by the regulatory authorities in that country. The current approval process varies from country to country, and the time spent in gaining approval varies from that required for FDA approval. In certain European countries, the price of a product must also be approved. The pricing review period often begins after market approval is granted. The Company intends to use foreign partners to apply for foreign marketing approvals.

Insurance

Providing health care products entails an inherent risk of liability. In recent years, participants in the health care industry have been subject to a large number of lawsuits alleging malpractice, product liability or related legal theories, many of which involve large claims and significant defense costs. The Company may from time to time be subject to such suits as a result of the nature of its business. The Company carries product

liability insurance coverage in the aggregate amount of $30 million. The Company also carries a $10 million general business insurance policy. The Company does not carry any insurance to cover the financial risks associated with a potential FDA mandated recall of an approved product. There can be no assurance, however, that such insurance policies will be sufficient to fully indemnify the Company against any asserted claims or that such insurance will continue to be available.

Human Resources
The Company has 79 full-time and six part-time employees. The Company believes that its relationship with its employees is good. None of the Company s employees is represented by a labor union.

Trade Secrets
The Company also relies on trade secrets and proprietary knowledge to protect certain of its technologies and potential products. The Company requires employees, consultants and advisors to enter into confidentiality agreements that prohibit disclosure to any third-party or use of such secrets and knowledge for commercial purposes. Company employees also agree to disclose and assign to the Company all methods, improvements, modifications, developments, discoveries and inventions conceived during their employment that relate to the Company s business. We cannot assure, however, that these agreements will be observed to prevent disclosure or that they will provide adequate protection for the Company s confidential information and inventions.

Grants
Previously the Company used both FDA Office of Orphan Drug Products (orphan drug grants) and the Small Business Administration (SBIR grants) to assist in funding product development programs. The Company collected approximately $1.6 million in grant proceeds to product development expenses for certain products. The Company currently has no active grants. The Company does not intend to use grants as a primary source of funding for product development activities in the future.

Discontinued Development Products
Through December 31, 2003, the Company discontinued development activities on a total of eleven proposed products. There can be no assurance that the Company s license rights and/or any clinical data related to a discontinued product have any value to a third party and, if such rights or clinical data have value, there can be no assurance that the Company can come to terms with a third party for the sale of such rights or clinical data.

ITEM 2. PROPERTIES

The Company currently occupies approximately 15,000 square feet of leased office space at a monthly rent of approximately $25,000, including operating expenses. This lease expires on October 31, 2004.

ITEM 3. LEGAL PROCEEDINGS

None.

ITEM 4. SUBMISSION OF MATTERS TO VOTE OF SECURITY HOLDERS

None.

ITEM 4A. EXECUTIVE OFFICERS OF THE REGISTRANT

The executive officers of the Company and their ages as of March 1, 2004.

Name	Age	Title
John Howell Bullion	52	Chief Executive Officer and Chairman of the Board

William Houghton, M.D	61	Executive Vice President and Chief Scientific and Medical Officer
Mark Perrin	47	Executive Vice President and Chief Commercial Officer
Timothy G. McGrath	39	Vice President and Chief Financial Officer
Dayton T. Reardan, Ph.D	48	Vice President of Regulatory Affairs
Pamela J. Stahl	38	Vice President of Commercial Operations