BY ELISABETH PENA

Orphan Medical's development of **Xyrem**, a 40-year-old compound, is providing relief to thousands of people who suffer from **cataplexy**, a debilitating sleep disorder

AWAKENINGS

CATAPLEXY, a symptom of the chronic sleep disorder narcolepsy, is an alarming condition, resulting in sudden, brief episodes of muscle weakness or paralysis brought on by strong emotions such as laughter, anger, surprise, or anticipation. In severe attacks, the patient may collapse and be unable to move for up to several minutes.

Until recently, there were no approved treatments for people with this condition. That changed July 17, 2002, when the Food and Drug Administration approved Xyrem (sodium oxybate) oral solution for the treatment of cataplexy. Xyrem is the only drug approved for treating cataplexy. Of the estimated 140,000 Americans who suffer from narcolepsy, between 60% and 90% experience cataplexy. Orphan Medical Inc. developed Xyrem under the FDA's Orphan Drug Act of 1983, which provides market exclusivity to companies that develop products for small, underserved patient populations.

While the Orphan Drug Act provides some financial advantages to the developing company in the form of tax credits, which are available for testing expenses for drugs, vaccines, diagnostic drugs, or preventive drugs used to treat rare diseases or conditions, bringing Xyrem to market wasn't an easy task. Xyrem is a formulation of the chemical compound gamma hydroxybutyrate, or GHB, which has been around since the 1960s. GHB, a central nervous system depressant, was developed as an anesthetic and hypnotic for use in humans in Europe, but was soon withdrawn due to adverse side effects. Later, GHB gained notoriety because of its potential for abuse and illicit use.

The journey for Orphan Medical began in 1994 when the FDA approached the company to gauge its interest in developing GHB as a treatment for narcolepsy. The drug previously had been under development for narcolepsy by

As part of our overall commercialization efforts, there is a large medical education component ... we will undertake a major CME initiative in the understanding of narcolepsy.

another company, but had been dropped. After researching the proposal, executives at Orphan Medical expressed interested in developing GHB, but were concerned about the proprietary situation. Full support was given to the project after it was discovered that the drug was eligible to receive orphan drug status. Orphan Medical has created a niche in the industry by acquiring, developing, and marketing pharmaceuticals of high medical value for inadequately treated and uncommon diseases treated by specialist physicians.

"GHB is a compound that has been around since the early 1960s, and only now has been approved by the FDA for a therapeutic use," says John Bullion, CEO and chairman of Orphan Medical. "Since the compound has been in the public domain, no pharma company was willing to develop it. Were it not for the protection afforded by the Orphan Drug Act, we wouldn't have developed the drug either."

Orphan drug status is given to medications that treat a rare disease or condition — defined as one that affects less than 200,000 persons in the U.S. (for more information see box on page 58).

Soon after Orphan Medical began developing GHB, serious concerns emerged because of an explosion of reports surrounding abuse.

"When we began development, one thing we considered was the abuse characteristic of the drug," Mr. Bullion says. "Most GHB abuse appeared to be in the weight-lifting and bodybuilding community because it had been reported to be a growth-hormone-releasing agent."

The compound GHB originated about 40 years ago when it was synthesized as a peripherally administered agonist of the inhibitory neurotransmitter, gamma-aminobutyric acid. It was used as an alternative anesthetic to aid in surgery because of its ability to induce sleep and reversible coma. However, it had little analgesic effect, and onset of coma often was associated with seizure activity, including tonic-clonic jerking movements of the limbs or face.

During the 1980s, GHB was sold in health-food stores, training gyms, fitness centers, and on the Internet. In addition, it was promoted as a natural treatment for insomnia and to induce weight loss.

In 1990, the FDA issued a press release warning against GHB, stating that it was illegal and dangerous. Illicit GHB use has been associated in combination with ecstasy and other illegal drugs as a euphoric drug, and in reported date rapes as a sedative. The drug is odorless and colorless, making it impossible to detect when added to a drink.

According to the Drug Abuse Warning Network, a division of the Substance Abuse and Mental Health Services Administration, the number of patients treated for GHB overdose or GHB-related problems in hospital emergency departments in 1994, when Orphan Medical began developing the drug, was 55. By 1998, the number was 1,282 and by 1999, the number of GHB-related medical emergencies was reported at 2,973. More than 70% of emergency department episodes involving GHB were found to involve more than one drug; alcohol was the most frequent substance mentioned in combination episodes. The substance has been linked to about 60 deaths, mostly in combination with alcohol.

The significant increase in the incidence of GHB abuse led to a movement to petition Congress to make the compound a Schedule I drug — drugs that have a high potential for abuse, that require greater storage security, and have a quota on manufacturing, among other restrictions. Schedule I drugs are only available for research and have no approved medical use.

After learning of this petition, company executives began working with Congress and the FDA to find a way to resolve the situation.

"We got wind of the bill and approached those in Congress seeking to make GHB a Schedule 1 compound," Mr. Bullion says. "We explained that the compound had shown significant efficacy in the treatment of narcolepsy, and Congress ultimately approved the FDA's proposed bifurcated schedule."

In February 2000, the passage of the Hillory J. Farias and Samantha Reid Date-Rape Drug Prohibition Act of 2000, named for two teenagers who died after the substance was slipped into their soft drinks, amended the Controlled Substances Act and created a bifurcated schedule for GHB, the first for any drug. According to the bifurcated schedule, when intended for abuse or misuse, GHB is a Schedule I agent. If it is used as an approved medication, such as Xyrem, it is classified in the Schedule III category. Schedule III and Schedule IV drugs are available by prescription, may have five refills in six months, and may be ordered orally. In addition, Xyrem's distribution is governed by Subpart H of the Food, Drug & Cosmetic Act. Subpart H provides for restrictions on the marketing, distribution, and risk management of pharmaceuticals.

"The bifurcated schedule for GHB was a very appropriate response to the situation — allowing patients access to the medication for treatment of a serious, debilitating disease, and providing an appropriate penalty to anyone abusing the drug," Mr. Bullion says. "We worked with Congress to shape that legislation and we think

Market Facts

- Americans with narcolepsy: Approximately **140,000 Americans**, however, only about 75,000 are diagnosed and treated, with some reports suggesting diagnosis is as low as 50,000 people.
- Narcoleptics with cataplexy: **60% to 90%**.
- The mean number of years between the onset of symptoms and correct diagnosis: **14 years**.
- Age and gender factors: Narcolepsy occurs in both men and women at any age, although **symptoms are usually first noticed in teenagers or young adults** between the ages of 15 and 30.
- Heredity factor: **8% to 12% of people** with narcolepsy have a close relative with the disease.
- Economic impact: Sleep deprivation and untreated sleep disorders are estimated to **cost more than $100 billion annually** in lost productivity, medical expenses, sick leave, and property and environmental damage.

it is a perfect balance between needed patient therapy and potential abuse."

In addition to working with Congress and the FDA to create the bifurcated scheduling, the company worked with law enforcement agencies to make it difficult for potential abusers to get hold of the product.

"Throughout the development program we consulted with institutions such as the DEA, law enforcement agencies, and the toxicology community — people who deal with the abusing populations," says Bill Houghton, M.D., VP, chief medical officer, and chief scientific officer of Orphan Medical. "As a result, we proposed, as part of the approval process, a very restricted distribution program for the post-approval availability of Xyrem so that we could proactively ensure that the patients who really needed the drug had it, at the same time making it as impossible as we could for misplacement or diversion of the drug."

Restricted Access

In an effort to ensure that only narcoleptic patients would receive Xyrem, Orphan Medical created a limited distribution plan known as the Xyrem Success Program. Under the arrangement, Xyrem only is available to prescribers through a single centralized pharmacy. Orphan Medical is making Xyrem available to the public through an exclusive distribution arrangement with Express Scripts' Specialty Distribution Services (SDS) subsidiary.

Once Xyrem is manufactured it is shipped to Express Scripts' SDS, which will provide pharmacy services to patients, collect patient-registry information, provide reimbursement support, distribute informational materials, and serve as a resource for product and educational program information. Prescriptions written for

Understanding Narcolepsy

THE APPEAL OF A DRUG LIKE XYREM IS APPARENT, GIVEN THE DEVASTATING IMPACT NARCOLEPSY, AND THE CONDITION CATAPLEXY, CAN HAVE ON THE LIFE OF THE AFFECTED INDIVIDUAL.

Narcolepsy is a disabling neurological disorder of sleep regulation that affects the control of sleep and wakefulness.

Normally, when an individual is awake, brain waves show a regular rhythm. When a person first falls asleep, the brain waves become slower and less regular, a sleep state called non-rapid eye movement (NREM) sleep. After about an hour and a half of NREM sleep, the brain waves begin to show a more active pattern again, even though the person is in a deep sleep, a state called rapid eye movement (REM) sleep, which is when dreaming occurs.

In narcolepsy, the order and length of NREM and REM sleep periods are disturbed, with REM sleep occurring at sleep onset instead of after a period of NREM sleep. Also, some of the aspects of REM sleep that normally occur only during sleep — lack of muscle tone, sleep paralysis, and vivid dreams — occur at other times in people with narcolepsy. It can be described as an intrusion of the dreaming state of sleep, REM, into the waking state.

Symptoms generally appear in people between 15 years old and 30 years old. The four classic symptoms of the disorder are excessive daytime sleepiness, sleep paralysis, hypnagogic hallucinations, and cataplexy — sudden, brief episodes of muscle weakness or paralysis often brought on by strong emotions such as laughter, anger, surprise, or anticipation. For patients with severe cataplexy, the episodes can happen frequently throughout the day and with little provocation.

140,000 people have narcolepsy. While 100% of people with narcolepsy suffer from the excessive daytime sleepiness symptom of narcolepsy, about 60% to 90% of those patients also have cataplexy.

"I have cataplexy quite severely, and without any medication I can have anywhere from 20 to 40 complete collapses in a day," says Mali Einen, clinical research coordinator at the Center for Narcolepsy Research in the Stanford Sleep Disorders Center and a Xyrem patient. "Even thinking almost anything can cause a collapse, it doesn't necessarily take extreme emotion. Instead cataplexy can be triggered by any proactive thought, if I see somebody I recognize, I can have a complete loss of muscle tone and collapse."

In the U.S., about 140,000 people have narcolepsy. While 100% of people with narcolepsy suffer from the excessive daytime sleepiness symptom of narcolepsy, about 60% to 90% of those patients also have cataplexy.

Cataplexy comes on as an immediate attack that lasts for minutes. The patient can lose control of multiple muscle groups including neck, arms, and legs during an attack. The brief attacks can occur frequently enough to prevent patients from carrying on a normal life, since any social interaction can cause attacks. This can lead to many patients withdrawing from any situation where they may experience emotion.

"Before taking Xyrem, I was on the brink of disability," says Bob Cloud, executive director of Narcolepsy Network and a Xyrem patient. "I couldn't leave the office without fear of falling down in the streets. Sometimes I couldn't hold a telephone. I fell every place imaginable. That was the reason I began taking Xyrem, and after several weeks the cataplexy symptoms disappeared by about 90%."

The usual treatment for narcolepsy includes symptomatic treatment of excessive daytime sleepiness and sleep attacks with stimulants or drugs such as Cephalon Inc.'s Provigil, a wakefulness-promoting agent that was approved in December 1998 for the treatment of excessive day-

Xyrem only can be filled by Express Scripts, which verifies that the physicians are in good standing, makes sure that the physician has received the Xyrem physician-education program, verifies that the patient has received a patient-education program, contacts the patient to ensure that they are prepared to receive the drug, and then ships the product to the patient using a courier service.

"The single, mail-order pharmacy will capture patient names and data in a patient registry as well as data on the physicians," Mr. Bullion says. "Impropriety should be readily apparent and that information will be available to law enforcement agencies. This is quite different from having upwards of 100,000 retail pharmacy distribution points. This is a very direct distribution system: from manufacturer to pharmacy to patient."

Orphan Medical executives believe the system not only will help prevent the drug from getting into the wrong hands, but will help educate patients and physicians, as well as provide the company with important prescribing data and trends. "We view this program as a very nice continuum," says Mark Perrin, executive VP and chief commercial officer for Orphan Medical. "Even though the distribution program was set up as part of a risk-management system, one that clearly fulfills our obligations, it is a highly comprehensive patient and physician education program that provides us with a clear understanding of how the product is being prescribed as well with other valuable information."

While GHB has been the subject of negative publicity, and doctors will need to go through a rigorous prescribing process for Xyrem, those in the medical community don't believe the drug's success will be hampered.

BOB CLOUD

Before taking Xyrem, I was on the brink of disability. I couldn't leave the office without fear of falling down in the streets. Sometimes I couldn't hold a telephone. I fell every place imaginable. That was the reason I began taking Xyrem, and after several weeks the cataplexy symptoms disappeared by about 90%.

time sleepiness associated with narcolepsy. Provigil, however, is not indicated for, and does not treat, the other symptoms of narcolepsy.

Before the approval of Xyrem, the symptoms of cataplexy, sleep paralysis, and hypnagogic hallucinations were typically treated with anticataplectics — tricyclic antidepressants or selective serotonin reuptake inhibitors used off label. Patients suffering from narcolepsy that experience cataplexy typically take a combination of stimulants and antidepressants.

For cataplexy, treatment with antidepressants is used because the drugs are known to suppress REM sleep. Cataplexy is a pathological equivalent of REM sleep atonia unique to narcolepsy. Although antidepressants suppress REM sleep, the drugs have a significant side-effect profile.

"With Xyrem I don't have the side effects that the various antidepressants caused, such as dry mouth, gastric complications, and bumps on my eyeballs from dry eyes," Ms. Einen says. "I don't have any of these side effects with Xyrem and more of my cataplexy is curbed as well."

Xyrem, while not side-effect free, was found to have fewer and more tolerable side effects than commonly used anticataplectics. The primary side effects associated with Xyrem are confusion, dizziness, nausea, occasional vomiting, occasional bedwetting, and occasional sleepwalking. The FDA's Center for Drug Evaluation and Research drug information also lists trouble breathing while asleep, abnormal thinking, depression, and loss of consciousness.

"Certainly Xyrem has side effects," says Bill Houghton, M.D., VP, chief medical officer, and chief scientific officer of Orphan Medical. "But these are balanced by very strong clinical efficacy and the benefits in treating narcolepsy, so it certainly represents a satisfactory side-effect profile."

Xyrem also has been found to have an excellent tolerance profile. With antidepressant treatments, in addition to the side effects, patients often build tolerance to the antidepressants and doses are increased to obtain clinical effectiveness.

Also, in studies with Xyrem, the drug was not found to cause any addictive behavior or withdrawal symptoms when used in a controlled manner.

"In clinical research, there was no evidence of the development or resurfacing of symptoms at any given dose over time," says Jed Black, M.D., director of the Stanford Sleep Disorders Clinic. "One of the ways to get a sense for tolerance is to record how much rebound occurs when the medication is withdrawn. The abrupt discontinuation of GHB does not result in any rebound cataplexy, unlike any other anticatapletic medication. With Xyrem there is no evidence of withdrawal symptoms."

"At this point, I think the medical community has respect for the agent and wants to monitor it closely to make sure there is no misuse or illicit use," says Jed Black, M.D., director of the Stanford Sleep Disorders Clinic. "There's been no abuse of the drug within the narcolepsy patient population. There doesn't appear to be any addiction potential in these patients and there have been no dose escalation problems, so

The Orphan Drug Act

The term "orphan drug" refers to a product that treats a rare disease affecting fewer than 200,000 Americans or affecting more than 200,000 persons in the U.S., but there is no reasonable expectation that the cost of developing and making available a drug for disease or condition will be recovered from sales in the U.S. of such a drug.

The Orphan Drug Act was signed into law Jan.4, 1983, to stimulate the research, development, and approval of products that treat rare diseases.

This mission is accomplished through several mechanisms, including:

1. Pharmaceutical company sponsors are **granted seven years of marketing exclusivity** after approval of its orphan drug product.

2. Pharmaceutical company sponsors are **granted tax incentives for clinical research** they have undertaken.

3. The FDA's Office of Orphan Products Development **coordinates research study design assistance** for sponsors of drugs for rare diseases.

4. The Office of Orphan Products Development, division of the Food and Drug Administration, **encourages sponsors to conduct open protocols**, allowing patients to be added to ongoing studies.

5. **Grant funding is available** to defray costs of qualified clinical testing expenses incurred in connection with the development of orphan products.

Recently Approved Orphan Drugs

From 1983 to 2000, there have been 1,063 orphan designations, and 218 orphan marketing approvals — 20.5% of tested orphan products received FDA marketing approval.

2002

Orfadin (nitisinone) for treating tyrosinemia type 1 — Swedish Orphan AB

Remodulin (treprostinil) for treating pulmonary arterial hypertension — United Therapeutics Corp.

Synthetic porcine secretin for use in conjunction with diagnostic procedures for pancreatic disorders to increase pancreatic fluid secretion and for use in the diagnosis of gastrinoma associated with Zollinger-Ellison syndrome — ChiRhoClin Inc.

Xyrem (sodium oxybate) for treating cataplexy — Orphan Medical Inc.

Zevalin (ibritumomab tiuxetan) for treating B-cell non-Hodgkin's lymphoma — Idec Pharmaceuticals Corp.

2001

Campath (alemtuzumab) for the treatment of chronic lymphocytic leukemia — Millennium and Ilex Partners LP

Gleevec (imatinib mesylate) for treating chronic myeloid leukemia — Novartis

Topamax (topiramate) — for the treatment of Lennox-Gastaut syndrome — Johnson & Johnson

Tracleer (bosentan) for treating pulmonary arterial hypertension — Actelion Ltd.

Zometa (zoledronic acid) for treating excess calcium in the blood caused by tumors — Novartis

2000

CroFab (antivenin,crotalidae polyvalent immune Fab (ovine)) for the treatment of envenomations inflicted by North American crotalid snakes — Protherics Inc.

Gonal-F (follitropin alfa, recombinant) for the induction of spermatogenesis in men with primary and secondary hypogonadotropic hypogonadism in whom the cause of infertility is not due to primary testicular failure — Serono Laboratories Inc.

Mylotarg (gemtuzumab ozogamicin) for treating CD33-positive acute myeloid leukemia in patients 60 years or older who have relapsed for the first time and are not suitable candidates for the standard but poorly tolerated cytotoxic therapy — Wyeth

NeuroBloc (botulinum toxin type B) for the treatment of cervical dystonia — Elan Pharmaceuticals Inc.

Norditropin (somatropin, recombinant) for the long-term treatment of children who have growth failure due to inadequate secretion of endogenous growth hormone — Novo Nordisk

Trisenox (arsenic trioxide) for treating acute promyelocytic leukemia, a cancer of white blood cells, in patients whose disease has recurred or who have failed to respond to standard therapy — Cell Therapeutics Inc.

I think the medical community feels pretty good about Xyrem."

Analysts believe the focus will be on the benefits of the drug. In clinical trials, Xyrem has been shown to reduce cataplexy attacks by 70% and is able to maintain its effect long term.

"Most physicians who are in a position to prescribe the drug are well-aware of the therapeutic benefits and they are just waiting for this drug to be launched," says Donald Ellis, Pharm.D., partner at Thomas Weisel Partners LLC.

Waking Up the Market

Orphan Medical plans to launch Xyrem in mid-October of this year with the backing of a dedicated salesforce of more than 30 experienced sales representatives that the company has hired specifically to detail the compound.

"Given the sophisticated nature of the drug, the launch is going to be challenging, yet very rewarding," Mr. Perrin says. "The company evaluated options on how to best commercialize Xyrem and we elected to hire a dedicated group of specialty representatives. We're fielding a team of about 36 people and they will be solely responsible for Xyrem, they won't be involved in any of Orphan Medical's other products."

The Xyrem salesforce will target the nearly 600 accredited sleep centers across the U.S. Orphan Medical has compiled a proprietary database of physicians who have high numbers of patients with sleep disorders. The salesforce also will target these 3,000 to 4,000 physicians who comprise three specialty groups: neurologists, psychiatrists, and pulmonologists.

In addition, the company will supplement salesforce calls with traditional non-personal detailing, including direct mail and journal advertising. Because the product is a Subpart H drug with a black-box warning, the company is prohibited from doing any direct-to-consumer advertising.

In addition, Orphan Medical has plans to partner with a major university to undertake a comprehensive CME initiative to help the prescribing community better understand narcolepsy and the debilitating effects of cataplexy.

The company plans to continue to align itself closely with patient advocacy groups, which the company worked with throughout Xyrem's development.

"When working with Congress, we also worked very closely with patient groups such as the Narcolepsy Network, the National Sleep Foundation, and other patient groups," Mr. Bullion says. "Early on we began working with


John Bullion

Were it not for the protection of the Orphan Drug Act of 1983, we wouldn't have developed the drug.

these groups to learn more about the condition, the patients, and the idiosyncrasies of the marketplace. We've worked closely with patient groups to discover what their other needs may be. Patient groups are going to be very important by letting the narcolepsy community know that Xyrem is available for cataplexy."

Xyrem currently is the only treatment approved for treating cataplexy.

Analysts believe that Xyrem will be well-received and have a strong uptake by cataplexy patients. Furthermore, industry experts expect that patients currently being treated with other remedies, such as antidepressants, will convert to Xyrem and that the market will expand because of the drug's strong efficacy and safety profile.

"We believe that Xyrem's efficacy and side-effect profile should support uptake of the drug upon its launch among this population," says Andrew Forman, senior analyst and managing director in the healthcare research group of Friedman, Billings, Ramsey & Co. "Xyrem likely will increase the size of the market as patients with milder symptoms, who currently choose not to take antidepressants due to their side effects, decide to try Xyrem as an advancement in the treatment of cataplexy. We forecast the cataplexy market will be more than $100 million, in which Xyrem would be the only approved treatment."

According to analyst forecasts, Xyrem is expected to generate sales of $11 million in 2003, $31 million in 2004, $54 million in 2005, and $81.9 million in 2006.

Another factor that encourages analysts is Orphan Medical's development of Xyrem for an additional indication: the treatment of excessive daytime sleepiness in narcolepsy.

"While we had very positive results in the reduction of cataplexy, we were surprised to see positive efficacy results in the management of excessive daytime sleepiness," Mr. Bullion says. "Xyrem appeared to provide a positive effect in reducing excessive daytime sleepiness, incrementally to the effect provided by stimulants. Since we used a subjective, though validated measurement, as a secondary endpoint in our pivotal study, we are conducting another trial using objective measures of the primary endpoint: the reduction of excessive daytime sleepiness."

A Phase IIIb study is under way and expected to be completed by the end of 2003, with a supplemental new drug application filing in 2004 and potential approval in 2005.

"The addition of this indication to the drug's label would broaden Xyrem's utility to all narcolepsy patients," Mr. Forman says. "While there would be significant overlap with the cataplexy market, we conservatively estimate that an excessive daytime sleepiness indication could expand the market by 20% or more. We believe the opportunity for patients to treat two of their symptoms with one drug will help drive growth."

This additional indication would also be covered under the Orphan Drug Act.

Xyrem only is approved for marketing in the U.S., however, the company is actively seeking marketing partners in Europe and Japan.

Upon the U.S. launch of Xyrem, Orphan Medical will have seven orphan drugs on the market: Antizol for ethylene glycol or methanol poisoning, or for use in suspected ethylene glycol or methanol ingestion, either alone or in combination with hemodialysis in humans; Antizol-Vet for ethylene glycol or suspected ethylene glycol ingestion in dogs; Busulfex for use in combination with cyclophosphamide as a conditioning regimen prior to allogenic hematopoietic cell transplantation for chronic myelogenous leukemia; Cystadane for homocystinuria, a genetic disease; Elliotts B Solution, for intrathecal administration of methotrexate sodium and cytarabine for the prevention or treatment of meningeal leukemia or lymphocytic lymphoma; and Sucraid for sucrase deficiency, a genetic disease. ✦

PharmaVoice welcomes comments about this article. E-mail us at feedback@pharmalinx.com.

Experts on this topic

JED BLACK, M.D. Director, Stanford Sleep Disorders Clinic, Stanford University Sleep Research Center, Stanford, Calif.; The Stanford Sleep Disorders Clinic was founded to diagnose and treat patients who have difficulties falling asleep or staying asleep at night, problems with excessive daytime sleepiness, or other medical problems that may occur during, or be exacerbated, during sleep

JOHN BULLION. Chairman and CEO, Orphan Medical Inc., Minnetonka, Minn.; Orphan Medical acquires, develops, and markets pharmaceuticals of high medical value for inadequately treated and uncommon diseases treated by specialist physicians

BOB CLOUD. Executive director, Narcolepsy Network, Cincinnati; Narcolepsy Network is a national, non-profit, patient-based organization whose mission is to educate the public and healthcare professionals about narcolepsy

MALI EINEN. Clinical research coordinator, Center for Narcolepsy Research in the Stanford Sleep Disorders Center, Stanford, Calif.; The Stanford Center for Narcolepsy Research, founded in the 1980s, is the world's leader in narcolepsy research

DONALD ELLIS, PHARM.D. Partner, Thomas Weisel Partners LLC, San Francisco; Thomas Weisel Partners is a merchant bank providing institutional brokerage, private client services, private equity, and asset management

ANDREW FORMAN. Senior analyst and managing director, healthcare research group, Friedman, Billings, Ramsey & Co., Arlington, Va.; FBR & Co. is a financial holding company that focuses capital and financial expertise on six industry sectors: financial services, real estate, technology, energy, healthcare, and diversified industries

BILL HOUGHTON, M.D. VP, chief medical officer, chief scientific officer, Orphan Medical Inc., Minnetonka, Minn.; Orphan Medical acquires, develops, and markets pharmaceuticals of high medical value for inadequately treated and uncommon diseases treated by specialist physicians

MARK PERRIN. Executive VP, chief commercial officer, Orphan Medical Inc.; Minnetonka, Minn., Orphan Medical acquires, develops, and markets pharmaceuticals of high medical value for inadequately treated and uncommon diseases treated by specialist physicians