

SPECIALTY PHARMA

Somnus Therapeutics Inc.

*Delivering controlled-release
sleep maintenance*

In early 2007, venture capitalists at Care Capital LLC identified a novel formulation of a known product that could fill an unmet medical need in patients with insomnia. Within weeks, they moved to establish the drug development firm **Somnus Therapeutics Inc.**, which, in turn, struck a deal with the licensor to bring the early-stage hypnotic to market.

The licensor was **SkyePharma PLC**, which was known to Care Capital for its record of applying novel drug delivery to approved products to add a clinical advantage or lengthen their life cycles. The product that caught their eye was zaleplon, the active ingredient in **King Pharmaceuticals Inc.**'s insomnia drug *Sonata*, which was about to become a generic.

Although zaleplon is currently approved for short-term difficulty in falling asleep, Somnus is developing a timed-release formulation known as SKP-1041, for approval as a first-in-class preventative with sleep maintenance as the primary indication. Zaleplon is a GABA (gamma-aminobutyric acid)-agonist, and is from a class that has been successful for sleep induction that also includes zolpidem (**Sanofi-Aventis'** *Ambien*). These therapeutics are not currently approved for sleep maintenance.

However, eszopiclone (**Sepracor Inc.**'s *Lunesta*) and extended-release zolpidem (**Sanofi-Aventis'** *Ambien CR*), also GABA-ag-

onists, are indicated for sleep maintenance. SKP-1041's advantage over these two drugs, according to CEO Gary Cupit, is that it is expected to offer patients an initial two hours of drug-free delta sleep, followed by the controlled release of a short-acting active ingredient, which may allow them to awaken more refreshed and alert.

Zaleplon works in the body by interacting with selective GABA receptors in the brain, which help control one's level of alertness or relaxation. Its selective activity targets only a certain type of GABA receptor that is believed to be more dedicated to promoting sleep. Because selective GABA medicines do not work on all the GABA receptors throughout the brain, they are thought to be relatively safer than benzodiazepines, the older drugs on which they are based, and to have less addictive potential.

Zaleplon has a short duration of action, explains Cupit, which allows patients to come on and off the medication with less drug hangover and drowsiness than others in the class with longer half-lives.

"We are not targeting the patient segment that has trouble going to sleep but those that have trouble staying asleep,"

Cupit emphasizes. A key aspect of the formulation is that it withholds release of the active ingredient for two hours after being taken by the patient, controlled by the proprietary *GeoClock* technology.

SKP-1401 is currently SkyePharma's only formulation that uses both its *GeoClock* and *Geomatrix* timed-release technologies in one tablet. The tablet consists of an outer and inner layer with each technology in control at different times.

Nearly two-thirds of insomnia patients have difficulty in sleep maintenance. That's the group that Somnus is targeting.

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Business: Therapeutics for sleep maintenance

Founded: June 2007

Founders: Gary Cupit; Care Capital LLC

Employees: 3

Financing to Date: Undisclosed

Investors: Care Capital LLP

Board of Directors: Gary Cupit; Linda Hogan (Somnus and Care Capital); David Ramsay (Care Capital); Jack W. Britts (CEO, Merz Pharmaceuticals)

Scientific Advisory Board: Charles A. Czeisler, PhD, MD, FRCP (Harvard Medical School); Gary Cutter, PhD (University of Alabama at Birmingham); Barbara Harris, PhD (PsyPharma Clinical Research, Phoenix, AZ); Remy Luthringer, PhD (FORENAP Institute for Research in Neurosciences & Neuropsychiatry, Rouffach, France); Thomas Roth, PhD (Henry Ford Hospital Sleep Disorders & Research Center, Detroit, MI); James K. Walsh, PhD (St Luke's Hospital Sleep Medicine and Research Center, Chesterfield, MO); Gary K. Zammit, PhD (Clinilabs)

The *GeoClock* layer consists of a mixture of hydrophobic wax and brittle material to obtain a pH-independent lag time prior to core drug delivery at a predetermined release rate. It works like a clamshell that opens only when initial absorption of liquid in the body initiates its separation, thereby releasing the contents.

The inner portion of the tablet uses the *Geomatrix* technology, which is applied to achieve customized levels of controlled release by constructing a multilayered table using hydrophilic polymers and surface-controlling barrier layers. These barrier layers control the active, loaded-core surface

that is available for drug release when exposed to fluid.

“We’re really very excited about our potential therapeutic,” Cupit says. “No other medication in the \$3.5 billion US hypnotic market has sleep maintenance as its primary indication, which is what we plan to seek, as 50 to 60% of insomnia patients experience awakenings during the night,” he adds.

Somnus has engaged a contract research organization to conduct the Phase I clinical trials currently underway for SKP-1041. “In designing our clinical trials, we’re trying to show that by not exposing patients to our drug for the first two hours, it will not affect delta wave sleep, the deepest sleep period,” says Cupit. As a result, patients will have “a more natural and restorative sleep.”

The Phase I clinical trial for SKP-1041 began in the second quarter of 2008 and is expected to be completed by the year’s end. An additional Phase I study will be conducted with elderly patients during the first half of 2009 to be followed by Phase II trials next summer. A meeting with the FDA is scheduled for the first quarter of 2009 to discuss the overall clinical program. An NDA filing is expected in 2011.

The fact that FDA will require only the submission of a 505(b)2—as the safety profile of the drug candidate is already known—will reduce the sponsor’s development risk and costs. The size of its Phase III trials can be reduced with their major focus on drug efficacy.

As to market potential, sources estimate current global sales for the insomnia market at \$4.6 billion, with sales growing to \$7 billion by 2012. Of the current

global market, \$3.5 billion is derived from the US, \$700 million from Europe, and \$460 million from Japan.

Annual sleep surveys on the prevalence of the condition show that one-third of the US population experiences insomnia and of that one-third, only 10 to 12% are treated with medication. Elderly people tend to have more sleep disturbances due to diseases or medications or to lack of structure in their lives. Another target population is those who do shift work or have jet lag.

Of the sleep issues that patients have, 29% of insomnia patients have trouble staying asleep, 35% falling asleep, and 36% both falling and staying asleep. In other words, nearly two-thirds of insomnia patients have difficulty with sleep maintenance, which is the group that Somnus is targeting.

Despite the positives, the market is not without its challenges. Somnus must be able to differentiate its hypnotic in a crowded market, notes Cupit. Many insomnia drugs are already losing patent protection, including *Ambien CR*, in 18 months’ time.

Somnus’ second biggest challenge is its single-product business model, says Cupit. It is looking for additional products to in-license for clinical development, possibly in the central nervous system or another specialty pharmaceutical area.

As to exit strategy, the firm would prefer to partner with a large organization on completion of Phase II, which would collaborate on Phase III trials and co-market to primary-care physicians. Following a US launch, the firm would seek an approval in Europe and eventually Japan.

Before joining Somnus, Gary Cupit was president of Enzo Therapeutics, and before that he was president and CEO of Sapphire Therapeutics, both specialty pharmaceutical firms. During his more than 20 years in the pharmaceutical industry, he has held key positions in licensing and global business and new product development at companies that include Novartis and SmithKline Beecham, with responsibility for several product launches.

Care Capital executives are represented on Somnus’ board of directors, providing strategic guidance on an ongoing basis. The recently announced scientific advisory board is also a significant asset that includes international sleep researchers and clinicians involved with sleep architecture.

Care Capital provided funding for the initial transaction with SkyePharma and also for establishing its Bedminster, NJ, headquarters. The agreement involved \$4 million up front to SkyePharma and a potential \$35 million in milestones and royalties later.

Somnus is reluctant to disclose the exact amount of financing that it has raised to date except to note that it is sufficient to cover Phase I trials. The current round of financing is still open, and the next round will begin in first quarter 2009.

CEO Cupit believes that “nothing makes a prescriber happier than using a medication about which his patients not only feel good but also give him good feedback.” He adds: “and there’s nothing else out there like ours.”

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—ANN ROBERTS BRICE