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Fast-Dissolving Delivery Systems

IN THIS ISSUE



INTERVIEW WITH
INOVIO BIOMEDICAL'S
PRESIDENT & CEO

AVTAR DHILLON, MD

**ClickSoft™
Microinjection** 22
Pankaj Modi, PhD, MD

**Ocular
Delivery** 34
Misty Hughes

**Adhesives
Evolution** 40
William G. Meathrel, PhD

**Osmotic
Tablets** 45
Jayvadan Patel, PhD

FEATURING

SPECIALTY 
Strategies For
Business Development **PHARMA**

**CRO
Trends** 64
Cindy H. Dubin

**Insomnia
Market** 69
Gary Cupit, PharmD

The science & business of drug development in specialty pharma, biotechnology, and drug delivery



**Derrek G.
Hennecke,
MBA**

Growth or Recession:
Selling Solutions is the
Answer



**Bill
Martineau,
MBA**

A Look at Fast-
Dissolving Drug
Delivery Systems



**Anil K.
Philip, PhD**

Colon-Specific
Delivery:
Histomorphological
Analysis &
Targeted Prodrug
Approach

Executive Summary



Gary Cupit
CEO
Somnus Therapeutics

Somnus Therapeutics: Taking On the Top Unmet Need in the Blockbuster Insomnia Market

Early in 2007, venture capitalists at Care Capital found a new controlled-release formulation of a successful insomnia drug that was nearing patent expiry. Somnus Therapeutics, based in Bedminster, New Jersey, was formed to exploit this opportunity, and is developing an improved therapeutic to address the top need of insomnia patients: preventing mid-night awakenings without next-day hangovers. In June 2007, Somnus licensed the SKP-1041 formulation of zaleplon (Sonata, Starnoc) from SkyePharma, PLC, a company that applies drug delivery to improve and extend the life-cycle of existing drugs. Gary Cupit, CEO, tells *Specialty Pharma* magazine that while the company's focus is on the insomnia market, these economic times call for a broader view of product development.

Q: *What makes Somnus unique as a specialty pharmaceutical developer?*

A: From the beginning, our business model was designed to emphasize efficiency, accelerate product development, and reduce costs to increase return on investment. We had in-licensed an off-patent entity from the most successful class of current insomnia drugs, and intended to use technical advances in formulation, controlled-release, and clinical testing to develop a better product faster and less expensively to address a big underserved market segment. Our business model is to develop through Phase II and

partner the drug for commercialization.

So we recruited a virtual team of 20-year experienced pharmaceutical executives, and leveraged their abilities with outsourced capabilities from our scientific advisory board, contract research organizations, and consultants. Indeed, we have been able to move quickly, and since establishing our development team in October 2007, we have designed, conducted, and completed the first SKP-1041 Phase I trial in 14 months. In keeping with this nimble approach, we plan to commercialize the product through an established pharmaceutical partner.

Q: *Why has Somnus Therapeutics chosen the insomnia market?*

A: Insomnia is a huge market, estimated to total \$3.5 billion within the United States and \$4.6 billion worldwide. It's a growing market with sales estimated to be \$7 billion in 2012. Growth is driven by an aging population, travel across time zones, ubiquitous artificial light at night, and shift work. Around the world, sleep disturbances are prevalent: with estimates ranging from a low of 7% in Japan, to more than 30% in some European countries, depending on methodology and definitions.

Remarkably, market research indicates that fewer than 12% of people with insomnia make use of prescription medications. Because it's such an underpenetrated market, we believe better therapeutics will not only capture market share but also drive market penetration. In particular, we believe improvements in drug delivery, dosing, and development can produce a more effective product faster with a lower cost to market.

We also focused on the biggest unmet need in the insomnia market: middle-of-the-night (MOTN) awakening. Our market research confirms that some two-thirds of insomnia sufferers find staying asleep a major problem, making it the most frequent complaint of insomnia patients. MOTN insomnia is strongly associated with daytime fatigue and cognitive impairment and thus with reduced job productivity and safety. Mid-night awakenings are more prevalent in women and increase with age for both sexes. A recent study showed a significant association with comorbidities, including obesity, mood disorders, and chronic pain, which may be exacerbated by nocturnal awakenings. All in all, it's a big unmet need.

Because the developers of earlier generations of insomnia therapeutics generally focused on falling asleep, this sector is less competitively crowded. However, as an indication, sleep maintenance calls for a differentiated approach to product design. Avoiding next-day hangover side effects is one challenge when

treating nocturnal awakenings, but one amenable to a controlled-release approach. Furthermore, our market research found that medical practitioners and patients prefer a single dose at bedtime to maintain restful sleep. Thus, a delayed-release formulation of a short-acting drug struck us as a product design with great market potential. An independent third-party forecast has determined the market potential to be greater than \$600 million on the low end.

Q: *What advantages does reformulating an approved drug have over the new chemical classes of drugs in development?*

A: Zaleplon is a chemical entity from a successful, established chemical class with a big safety database and an excellent track-record over many years. All that knowledge mitigates our development risk going forward compared to developing a drug from a novel chemical class. New chemical entities have a longer path to market and entail higher risk, as less is known about real-world safety and patient response.

Non-benzodiazepine GABA agonists have been one of the most successful classes of insomnia drugs. Zaleplon, and two other so-called Z-drugs, were the first of this class to reach the market, and in their patented forms (Sonata[®], Ambien[®], Lunesta[®]) were blockbusters among the most successful insomnia product introductions. The zaleplon patent expired in 2008, dovetailing nicely with our clinical timeline.

Interestingly, the biggest shortcoming of zaleplon (its 1.5-hour half-life) makes it a superior candidate for a controlled-release version with improved pharmacokinetics and pharmacodynamics as well as for fine-tuning the dosing specifically for the MOTN awakening market. All in all, zaleplon is an ideal candidate for use with the Geoclock[™] controlled-release technology.

Q: *How does controlled-release technology work in this product?*

A: The SKP-1041 tablet uses two of SkyePharma's controlled-release technologies, Geoclock and Geomatrix™. The Geoclock layer combines a hydrophobic wax with a material that enables a pH-independent (important in the high-acid environment of the stomach) drug delivery at a predetermined release rate. The inner payload uses the Geomatrix technology, a multilayered tablet of hydrophilic polymers with surface-controlling barrier layers. These barrier layers control the active loaded-core surface that releases when exposed to fluid.

The tablet opens like a clamshell to deliver the inner payload with a precisely calibrated delay before delivery. That makes possible the single bedtime dosing we are aiming for, allows the patient to experience normal deep levels of delta sleep before the drug is delivered, and the drug metabolizing completely before the sleeper awakens for the morning.

So, the patient will swallow one tablet at bedtime, fall asleep normally, and then 3 to 5 hours into the sleep period, the tablet releases the zaleplon, which will prevent mid-night awakening but be out of the patient's system by morning. This approach is user-friendly for patients, consistent with providers' preferences, and should minimize next-day cognitive impairment and fatigue.

Q: *What is your clinical strategy?*

A: There are three major elements to our clinical strategy aimed at speeding product development while keeping costs down to increase return on investment. First, we licensed in a molecule with an excellent performance, safety, and sales record that went off patent as we completed Phase I. This means we can pursue accelerated development through the 505(b)2 pathway for known chemical entities. Furthermore, we are taking advantage of SkyePharma's superior

formulation and proven controlled-release technology to rapidly develop an improved product.

Second, as discussed previously, we targeted an underserved indication, sleep maintenance, in a large market (insomnia), in which we thought an improved product would capture share and may increase the market.

Third, we took advantage of the growing body of biochemical and pharmacological knowledge about sleep, building particularly on the clinical expertise of our SAB, who are guiding the clinical study design. A key aspect of the clinical strategy is leveraging advanced technology. In Phase I, our international CRO, FORENAP Pharma in Rouffach, France, used their state-of-the-art sleep-monitoring instrumentation and cognitive testing capabilities to provide high-tech evaluation of sleep patterns and next-day alertness that improved the efficiency of our clinical trials.

We plan to add US clinical sites in 2009 for Phase II, and to that end have filed an IND with the FDA. Both in Europe and the US, we will be using the MSLT (Multiple Sleep Latency Test) to screen clinical subjects to reduce statistical "noise" in the data sets. We will also pursue studies in specific sub-populations, like the elderly and shift-workers, to keep the data clean and allow us to fine-tune the dosing if that produces better outcomes.

Q: *What's next for the company?*

A: Beyond SK-1041, our strategic focus is on CNS indications. Especially in this financial environment, our accelerated development model is attractive to both investors and licensors, so we are looking at a number of opportunities to pursue next. ■