BioWorld Today – No snooze button: Galleon advances drug therapy for sleep apnea

BioWorld Today

NEWCO NEWS

By Marie Powers, Staff Writer, Monday, April 14, 2014

When investors think about funding investigative treatments for sleep apnea, the last thing they're likely to consider is a pill. But that's exactly what Galleon Pharmaceuticals Inc. is pursuing for the indication, which is estimated to affect up to 40 million individuals in the U.S. and 100 million worldwide.

The concept certainly perked up the ears of listeners at the J.P. Morgan Healthcare Conference in January, according to Jim Mannion, Galleon's founder, president and CEO. "It was amazing to learn how many bankers have sleep apnea," Mannion said. "We didn't have to explain the condition to them at all."

Galleon was founded in 2005 and quickly latched on to drug technology discovered at the University of Virginia designed to replace caffeine in helping premature infants to breathe more easily.

"I wondered, if you could help premature babies to breathe, could you help mature adults with sleep apnea to breathe better?" recalled Mannion, who has a background in clinical development, drug safety and regulatory affairs at big pharma and served as president of Epigenesis Pharmaceuticals Inc., which was developing drugs to treat asthma. (See BioWorld Today, March 1, 2001.) The Horsham, Pa.-based company's initial funding came from Philadelphia biotech accelerator Bioadvance, allowing Galleon to refine a strategy for creating a drug discovery platform. At the time, the requisite chemistry and biology expertise "didn't really exist in the industry and mostly not in academia, either," Mannion said.

So, in 2007 the company closed a series A that brought in life science venture firms TPG Biotech, Morgenthaler Ventures and Healthcare Ventures LLC. The round added three scientists to Galleon's board and undisclosed funding sufficient to build the platform for what the company calls "breathing control disorders."

The company hunkered down for five years to focus on the science, deliberately avoiding publications and conference presentations. Although Galleon's long-term goal was always to design a pill to treat sleep apnea, "we thought there were some potential indications along that road which would benefit from breathing control drugs," Mannion said. But, since no company had attempted to develop drug therapies for sleep apnea, "we thought we needed a very solid foundation because our drugs would raise a lot of questions," he added.

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Respiratory drugs are commonly associated with asthma or chronic obstructive pulmonary disease, but "that's not what we're doing," Mannion told BioWorld Today. Rather than mimicking mechanisms of action in what he characterized more as inflammatory conditions, Galleon's technology combines neuroscience principles and respiratory mechanics. "It turns out there are some nice analogies between how the body controls heart rate and heart rhythm and how the body controls breathing rate and breathing rhythm," he explained.

Lead program, GAL-021, is a small molecule delivered intravenously, that completed phase I studies. In 2012, the company reported that GAL-021 increased minute ventilation – the capacity measure of air supplied to the lungs – compared to placebo at different dose levels in two studies that enrolled a total of 48 healthy adults. The compound was well tolerated.

Because the company envisioned GAL-021 to prevent and treat postsurgical respiratory insufficiency in apnea and other high-risk patients, Galleon then simulated postsurgical conditions. In a double-blind, placebo-controlled crossover study, 12 people with both normal and elevated carbon-dioxide levels were given two doses of the analgesic alfentanil along with two dose levels of GAL-021. Findings showed that GAL-021 protected against opioid-induced respiratory depression without affecting analgesia. The effect was statistically and clinically significant both at low and high doses of alfentanil.

“That gave us confidence that we potentially had a drug for these surgical type patients and that our models were accurately predicting what would happen in man,” Mannion said. “Because this was a new area, those were unknown questions. You can get fooled by animals.”

Once Galleon completes toxicology studies, the company will move GAL-021 into a phase II study in surgical patients. Mannion envisions the drug as “a pharmacologic safety net for respiratory complications,” giving physicians greater flexibility to control pain in the post-op setting while avoiding pulmonary complications for patients. In the end, patients, physicians and payers all win, he said.

Working with GAL-021 also gave Galleon scientists better insight into developing an oral drug for chronic sleep apnea. The technology involves regulating the respiratory drive – the signal that controls breathing – as well the signal from the brain to the upper airway. Both are lowered during sleep, Mannion explained.

In “normal” individuals, the airway remains open and they continue to breathe naturally, despite the decreased signaling. But in some people, when the lowered signals fall below a critical level, the upper airway collapses and causes an obstruction – an effect Mannion likened to trying to sip liquid through a collapsed paper straw.

Researchers also have learned that, in some individuals with sleep apnea, the body simply forgets to breathe, he added.

“We thought that, if you could make a drug that would affect both of those neurochemical targets, it should work for many sleep apnea patients,” Mannion said.

The company created hundreds of additional molecules before finding its Goldilocks compound, GAL-160, which has been in preclinical development for about a year. Based on promising animal studies, last month Galleon’s board green-lighted the company’s plans to ramp up for clinical development. Mannion expects to file an investigational new drug (IND) application or investigational medicinal product dossier in about a year.

GAL-160 won’t help certain groups who suffer from sleep apnea, including the morbidly obese and those with facial architecture abnormalities that affect the airways.

“We very quickly concede that a drug is not for everybody,” Mannion said. “But we think a drug might make sense for 30 to 50 percent of the population, and when your denominator is 40 million and there’s essentially no competition, that’s a pretty big number.”

With 16 employees, mostly on the science side, Galleon is seeking to progress both compounds simultaneously, though “in the short term, we will try to have GAL-160 catch up a bit,” he said. “We think both of them are valuable products for different markets.”

The company recently launched a series B round, seeking to raise $20 million to accelerate GAL-160 into the clinic. “We’ve done a lot of the preparatory work, and we can move quite quickly,” Mannion said, noting the company completed 28-day toxicology studies so it could advance post haste into IND-enabling studies.

Although GAL-021 is a “relatively compact program” that Galleon potentially could manage internally through approval and commercialization, the company will seek to partner the oral program during or at the conclusion of phase II studies.

“Given that pharma is interested in novel approaches for big markets, we think there will be significant interest in what we’re doing once we show them GAL-016 works in people,” Mannion said. “Sleep apnea is often seen in conjunction with high blood pressure, diabetes and heart disease, so the idea of treating sleep apnea can be adjacent to franchises they already have.”