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# Charleston Ends Phase III Early: Opioid-Nausea Therapy Works

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**Staff Writer**

Although opioid-induced constipation (OIC) has gotten most of the press in recent years, Charleston Laboratories Inc. may be about to change all that, given Phase III success with CL-108, which provides the pain relief of hydrocodone without the side effects that are even more prevalent: nausea and vomiting (OINV).

Still in the memory of many is the potential $1.5 billion deal inked by San Francisco-based Nektar Therapeutics Inc. with Astrazeneca plc, of London, including $125 million up front, centered on OIC. (See *BioWorld Today*, Sept. 22, 2009.)

Now, Jupiter, Fla.-based Charleston has stopped early its Phase III trial with CL-108, which combines 12.5 mg of immediate-release promethazine, an anti-emetic, with 7.5 mg of the pain reliever hydrocodone and 325 mg of acetaminophen.

An independent data monitoring committee reviewed the safety and efficacy results in an interim analysis of the study, and notified Charleston that the study should be stopped at its midpoint because both efficacy endpoints of the study have been met.

Intellectual property related to the combination therapy, which brings about pharmacokinetic (PK) advantages not available when the drugs are given in separate pills, puts Charleston in "a very unique position as our company moves forward with our secondary pipeline," said Paul Bosse, president and CEO.

CL-108 yielded a significant ($P < 0.01$) effect on OINV compared to a commercial product that the company did not name, along with significant relief of moderate to severe pain.

Charleston said that it expects to file a new drug application next year.

Hydrocodone – still known to many by its brand name Vicodin, though it's long been available as a generic drug – is the most widely prescribed medication in the U.S., with more than 131 million prescriptions annually.

Just this week, the FDA approved Zohydro ER, an extended-release form designed by San Diego-based Zogenix Inc., despite an advisory panel's decisive thumbs-down last year. (See B*ioWorld Today*, Dec. 10, 2012.)

The Zogenix drug is the first pure hydrocodone to win marketing clearance in the U.S.; other versions have acetaminophen added, as does Charleston's CL-108 – in which the third ingredient, promethazine, heads off the opioid's unpleasant but common side effects.

Though the components in CL-108 all are available discretely, so that a patient could, theoretically, take two pills and get the same results, it doesn't work that way in practice.

"A patient would have to take an anti-emetic a pretty significant amount of time before taking their opioid, and when people are in pain, the pain prescription is what you need to take first," Bosse said.

"If you understand the dissolution of those products, it will make sense to you. We essentially reverse the curves. Our anti-emetic is absorbed and released very quickly, and we have somewhat of a modified release of the narcotic. It puts them in the proper order," he noted.

Better to have a preventive approach with the right PK, he said. "Physicians will tell you this is a no-brainer for them. It takes the guesswork out of their day. They're able to treat the pain without fear of side effects" that must be handled later, by way of another prescription, since nothing is available over the counter.

Founded in 2007, Charleston – so named because it started in the South Carolina city of that name – has five employees and is privately funded, with no venture capital backing.

Behind CL-108 in the pipeline is CL-HIT, a fixed-dose formulation of a triptan combined with an anti-emetic in a Charleston's release technology. CL-HIT will be investigated for treatment of migraine headaches and the reduction or elimination of migraine-induced nausea and vomiting.

"With migraines, 80 percent of people experience nausea and vomiting as part of the disease state," Bosse said.

"Interestingly enough, there is also a side effect similarly to an opioid's, although smaller. We recently had a pre-investigational new drug application meeting with the FDA, and we're very pleased with the outcome of that meeting," he said.

Earlier this month, Charleston disclosed a research program to evaluate anti-emetic effects on opioid-induced hyperalgesia and physical dependence with the Stanford School of Medicine. ■