

Aastrom Files SPA in Quest for First Cell Therapy in CLI

By Donna Young
Washington Editor

Hoping to ride Dendreon Corp.'s coattails to approval – now that the Provenge (sipuleucel-T) maker has forged a regulatory pathway for autologous cellular therapies – Aastrom Biosciences Inc. has taken a leap forward on its quest to market the first-of-its-kind expanded autologous cellular therapy for critical limb ischemia (CLI) by submitting a special protocol assessment (SPA) to the FDA for a Phase III study.

"We are very excited to be where we are right now," Aastrom CEO Tim Mayleben told *BioWorld Today*.

The company is far out front of any potential competitors in the race to find an effective therapy for CLI – the most severe form of peripheral artery disease, affecting about 400,000 people in the U.S., with about 160,000 of those undergoing a major limb amputation.

The disease kills a quarter of those patients within six to 12 months of a diagnosis, with two-thirds of CLI patients dying within four years.

"CLI is really a devastating disease for these patients," Mayleben said, adding that it has a higher mortality rate than most cancers.

"It is a relatively under-reported, unknown disease condition," he said. And while the patient population affected by CLI is not large, "it is a very high-risk population, for which there are no options."

About two-thirds of CLI patients are diabetic, Mayleben said. But the real root of the disease is atherosclerosis.

The condition also has other "collective" comorbidities, he added.

Mayleben noted that the gold standard treatment for patients with CLI is an open bypass graft procedure to attempt to restore blood flow to the affected extremity.

But some CLI patients are not healthy enough to endure that procedure, he said, adding that the surgery also sometimes fails, leaving those patients no other options.

There have been a number of gene therapies tested, but all of those so far have failed.

The most recent disappointment for a CLI gene therapy came just last month, when Vical Inc.'s and Sanofi-Aventis Group SA's NVIFGF failed to demonstrate superiority over a

placebo in preventing amputation or death in the firms' 525-patient Phase III TAMARIS trial. (See *BioWorld Today*, Sept. 23, 2010.)

"The reason that we had a much higher chance of success is that we had this mixed cell population that is a combination of CD14 cells, CD31 cells and CD90 cells," Mayleben explained. "This mixed cell combination provides all of the cells necessary to not only reduce the inflammation to grow new blood vessels, but to provide the stroma necessary, the foundation to the intercellular matrix to actually allow the therapy to be successful."

For Aastrom's autologous cellular therapy, a small amount, about 50 milliliters, of bone marrow stem cells is taken from the patient's hip in a 15-minute outpatient procedure, Mayleben explained.

Over about 12 days, Aastrom expands the naturally occurring populations of early stem and progenitor cells found in the extracted bone marrow. Two weeks after the initial visit, the cellular therapy is injected into the patient.

"It's simple; it's not invasive and very inexpensive, because it is done right in the physician's office without taking up an operating room," Mayleben said.

Interim results from Aastrom's Phase IIb trial reported in June in Boston at the annual meeting of the Society for Vascular Surgery demonstrated a 50 percent to 60 percent increase in amputation-free survival, Mayleben said.

The study had anticipated enrolling up to 150 patients, but given the "surprising" positive interim results in 86 patients, the trial's drug safety monitoring board advised discontinuing enrollment and moving forward to Phase III, he said.

The company also met in late June with the FDA, which "to our delight" encouraged Aastrom to submit an SPA for its Phase III program, Mayleben said.

"We were honestly on the fence as to whether to pursue the SPA," he said. "Certainly there are pros and cons. But with FDA's encouragement, we elected to do it, and we have been working for the last few months to draft the protocol and the statistical analysis plan."

The FDA has 45 days to respond to the company.

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"We do expect them to come back with questions and comments," Mayleben said.

He noted that the company had "very good interaction" with the FDA at its June meeting "and they provided us with a lot of guidance.

Aastrom also has received guidance and input from its clinical and regulatory advisers, he said.

"So we feel like we are on pretty firm ground," Mayleben said. "But of course, we will refine certain aspects of the program as we have this interaction with the FDA. But we are pretty confident going into it that we've listened well to the agency. We've listened well to those who have conducted

these kinds of trials and worked with the agency on these kinds of things before. So we don't expect major differences. We've had a very collegial relationship with the FDA throughout the process."

He noted that earlier this week, Aastrom received fast-track designation from the FDA for its expanded autologous cellular therapy, which has yet to be given a generic name.

Mayleben credited Aastrom's "very strong team," led by Chief Scientific Officer Ronnda Bartel, whom he said has been in cell therapies "since there was a cell therapy space," and Sharon Watling, clinical and regulatory vice president, for the firm's progress with its product. ■