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Bolt Biotherapeutics Nabs \$93.5M to Push Provenge Inventor's New Idea Deeper in the Clinic

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A cancer-fighting concept from the inventor of the first cancer vaccine is nearing prime time, and its biotech developer has received a significant new infusion of cash to get it there.

Bolt Biotherapeutics announced a \$93.5 million Series C round led by Sofinnova Investments and joined by more than 9 others, including Pfizer Ventures and RA Capital Management. That money will go toward pushing the San Francisco biotech's platform of innate immune-boosting warheads through its first trial on metastatic solid tumors and into several more.



Randy Schatzman

It's "a fairly elegant but simple molecule," CEO Randy Schatzman told Endpoints News. "It's basically an off-the-shelf therapeutic that physicians can call on to treat their patients without all the personalization and manufacturing difficulties that many of the I/O approaches have today."

The experimental drug is what Bolt calls an immune-stimulating antibody conjugate. It's based on a concept from Stanford immunologist Edgar Engleman, who invented the first cancer vaccine in Provenge, a treatment for prostate cancer. That vaccine involves a multi-step process where innate immune cells called dendritic cells are extracted, exposed to a protein from the patients' own tumors (as you would expose the immune system to a viral or bacterial protein in a traditional vaccine) and then reinfused.

Bolt's platform is designed to directly activate dendritic cells around tumors without the need for removal, treatment and re-infusion. The therapy is an antibody drug conjugate similar to those produced by Seattle Genetics, ADC Therapeutics, and Immunomedics, each of which contain an antibody to guide the therapy like a warhead to the tumor. The difference is that instead of strapping a chemical to the antibody that will kill cells in the area, Bolt's drug has an agonist that will bind to receptors on the dendritic cells and activate them to attack the tumor.

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If it works, the drug would turn the environment around the tumor from an immuno-suppressive to one that could not only kill the tumors once but prevent recurrence. Their first candidate uses a Herceptin biosimilar to target HER2, but in theory, Schatzman said, it should work with an antibody targeted at any oncogene and Bolt is exploring those options, both internally and with partnerships.

In February, five years after the company's foundation, they launched their first trial, putting the drug — known as BDC-1001 — into a Phase I/II trial for metastatic tumors that are HER2+, including gastric and breast cancer. That trial will test the drug both as a single-agent therapy and in combination with Merck's Keytruda. The idea is that activating the immune system in two different ways might make for a more effective treatment.



Despite some early concerns, Schatzman says, the company has not seen any delays in that trial from Covid-19.

After the first data emerge from the Phase I/II trial, the company will move into trials specifically for gastric and breast cancer, looking to see if it can not only clear cancers initially but also, by keeping the immune system on guard, ward off recurrence, an event that can come quickly for patients with these late-stage tumors.

"We're going to see some quick answers in going past what is the current standard of care," Schatzman said. "I'd like to think it will take a long time to know where the end of this is, because in that sense, we'll have been very effective at treating these patients."

Edgar Engleman