

TORCell Takes Aim at AML Using Cancer-Killing T Cells

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Serious conditions attract serious attention. Acute myeloid leukemia (AML) is a devastating form of cancer with a poor prognosis and limited treatment options. Already, a raft of biotechs has thrown resources at the disease, but with more failure than success. Now, TORCell Therapeutics Inc., a biotech spun out of the Ontario Institute for Cancer Research (OICR) in Toronto, is taking aim at AML with a technology to boost a patient's own double-negative T cells (DNT) – a subpopulation of T lymphocytes that has potent anticancer properties, but comprises only 1 percent of a patient's peripheral blood mononuclear cells.

Patients with relapsed AML – especially those who are not eligible for a transplant – have exhausted viable treatment options, explained Frank Gleeson, a serial entrepreneur and venture capitalist who serves as TORCell's acting CEO.

Li Zhang, senior scientist at the University Health Network's Toronto General Research Institute, an OICR affiliate, found a promising immunotherapy approach for this group, and other AML patients, by demonstrating in vivo that a subpopulation of T cells had a powerful killing effect on leukemic blasts while sparing healthy bone marrow cells.

"We felt this was a technology that needed to advance into clinical development," said Gleeson, who also serves as executive-in-residence at OICR, which has invested seed funding in TORCell to bridge the company to a first-in-human trial, expected to begin early next year.

The injection of DNT cells back into patients may occur either alone or as an adjuvant therapy. Using a patient's own DNT cells reduces the risk of rejection or adverse reaction, Gleeson said. The ex vivo expanded DNT cells also were shown to kill human leukemia cells in a xenograft mouse model.

"Our whole focus is on creating the conditions under which this technology can get into humans," said Gleeson, former CEO of Canadian regenerative medicine firm Verio Therapeutics Inc., which was acquired last year by San Diego-based Fate Therapeutics Inc., and before that Toronto-based MDS Proteomics. (See *BioWorld Today*, April 4, 2010, and April 9, 2010.)

"We think we have the runway to enable that to happen.

This is a confluence of positive situations," Gleeson told *BioWorld Today*. "We have a very strong leukemia group at Princess Margaret Hospital, a world-renowned clinical center, and a significant patient population on which to draw – plus, the technology originated at the institute. We thought this shaped up very nicely for a newco formation."

Like most start-ups, the company is operating virtually. Although TORCell has contracted with a stable of experts, Gleeson splits his time as the only employee and as the acting CEO of DLVR ("deliver") Therapeutics Inc., an OICR spinout that is developing an RNAi delivery platform.

TORCell's DNT expansion method has been optimized to speed clinical application and regulatory approval, according to Gleeson. Once the company demonstrates proof of concept in humans, the goal is to move the immunotherapy into efficacy studies or broaden the indication, then partner with a larger biotech or pharma. In the short term, Gleeson is focused on positioning TORCell for a Series A financing next year.

The company faces numerous potential competitors in the AML space. Though forced to backpedal on an initial public offering, San Diego-based Ambit Biosciences Inc. recently attracted \$30 million in a Series D-2 round to support its ongoing Phase II pivotal trial of the AML drug AC220, a FLT3 inhibitor that is being developed with Astellas Pharma Inc., of Tokyo. (See *BioWorld Today*, June 13, 2011.)

Meanwhile, Sunesis Pharmaceuticals Inc., of South San Francisco, continues to focus resources on the ongoing, multinational Phase III VALOR trial for its lead candidate, vosaroxin, in combination with cytarabine in patients with relapsed or refractory AML. (See *BioWorld Today*, April 6, 2011.)

The FDA has granted fast-track designation for vosaroxin in relapsed or refractory AML and orphan drug designation for the treatment of AML.

In London, Chroma Therapeutics has forged a collaboration with Cell Therapeutics Inc. to co-develop Chroma's tosedostat, an inhibitor of aminopeptidases – a family of intracellular enzymes involved in generating

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amino acids that are essential for cell growth. (See *BioWorld Today*, March 15, 2011.)

And other biotechs are steaming full-speed ahead on AML treatments, among them Celator Pharmaceuticals Inc., of Princeton, N.J., Oxigene Inc., of South San Francisco, Stemline Therapeutics Inc., of New York, and EpiCept Corp., of Tarrytown, N.Y.

Gleeson is undeterred, noting that the TORCell technology is based on a simple and robust expansion method using active DNT cells that can be expanded from fresh or frozen samples. Moreover, the DNT cells can be expanded from patients after induction chemotherapy and consolidation therapies. The key is to enable the company to prove the technology in Phase I studies.

“We’re trying to create a new model – a type of virtual incubator – to build a bridge to true partner-ready

companies,” he explained. “We’re in a sweet spot – in sort of the million-dollar range – so we have meaningful amounts of capital, judiciously applied, at the right time. We also have the capacity in our community to syndicate this a little more broadly with other partners.”

Given the changing appetite of biotech investors for later-stage assets, emerging technologies must look at new financing mechanisms to survive the early years, Gleeson said.

“Players that are interested in early stage investments are looking for larger deal sizes, which suggests that people are looking for more profound opportunities that represent true innovation in some clinical paradigm,” he added. “In looking at those trends, we want to do whatever we can to take promising technology and move it to a point where its true potential can be demonstrated.” ■