

‘Backpacking’ to the next generation of I-O

‘Deep-Priming’ technology adds new ‘Torque’ to cancer immunotherapy

By Marie Powers, News Editor

Torque Therapeutics Inc. emerged from the deep, disclosing a series A by Flagship Pioneering that was opened in conjunction with its founding in 2015 and, with a second tranche pulled down in August, amounts to \$25 million.

The Cambridge, Mass.-based company’s “Deep-Priming” technology platform is designed to anchor stimulatory cytokines, antibodies and small molecules directly to immune cells to direct their activity and increase their efficacy and durability in the tumor microenvironment without the systemic exposure that has torpedoed some immuno-oncology (I-O) approaches.

In short, the startup hopes to make a big footprint in a dynamic field by creating a new class of cellular immunotherapies.

Co-founders Bart Henderson, CEO, and Ulrik Nielsen, president and founder chairman, were long-time acquaintances who were “looking for the next thing,” Henderson said, after leaving their previous posts as president and founder of Rhythm Pharmaceuticals Inc. and co-founder and chief scientific officer of Merrimack Pharmaceuticals Inc., respectively. They were quickly intrigued by work that Darrell Irvine, professor of materials science and engineering and biological engineering at the Massachusetts Institute of Technology and an investigator of the Howard Hughes Medical Institute, was conducting to apply engineering tools to problems in cellular immunology and to develop materials for vaccine and drug delivery.

“Darrell has been working on this technology for 10 years and was ahead of his time in the whole approach of anchoring biotherapeutics directly to immune cells to direct the immune response in the local tumor microenvironment,” Henderson told *BioWorld*.

The two added Irvine as co-founder and chairman of the company’s scientific advisory board. Flagship served as founding investor, with Doug Cole, general partner, stepping in as lead director on Torque’s board.

Co-founder Thomas Lars Andresen, professor and group leader of the colloids and biological interfaces group at DTU Nanotech, serves as head of discovery at Torque, while Becker Hewes, a biopharma veteran who most recently was executive medical director at Novartis Institute for Biomedical Research, is the company’s chief medical officer.

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Ulrik Nielsen, Co-founder and President
Torque Therapeutics

‘CAR T has shown the way’

As its name suggests, Torque – the name harkens both to the company’s force and to its engineering roots – has been in constant motion for two years. Already at 30 employees, Torque is applying its Deep-Priming platform across a range of immune cell therapeutic classes: CAR T, TCR therapeutics, NK cells and tumor-associated antigen, or TAA-specific T cells. The premise is that, in hematologic cancers, the technology may improve on the initial success of CAR T therapeutics, enabling more durable responses with less toxicity. Deep-Priming also offers the potential to show efficacy against solid tumors that are sheltered in hostile microenvironments not readily penetrated by current immune cell therapies.

“With two approvals now, CAR T has shown the way in terms of what’s possible with cell therapy,” Nielsen explained. “The challenge is and has been taking those to a broader patient population and, particularly, into solid tumors, where you have an overwhelming amount of immune suppression and other mechanisms that keep the CAR T cells from succeeding. By using the Deep-Priming approach, we can actually define the microenvironment around the T cell after infusion into the patient.”

Deep-Priming technology uses clusters of biotherapeutics, or so-called “backpacks,” engineered either to act on the carrier cell itself, as an autocrine signaling loop, to release the drug at the cell surface where it binds to the receptors, or to deliver a drug that activates other immune cells in the microenvironment, as a paracrine signaling loop, to boost the immune response by recruiting other immune cells for durable antitumor efficacy.

“By controlling the microenvironment, we can overcome, we

think, a lot of the immune suppression that would be present in the patient's tumor," Nielsen told *BioWorld*. "We've shown this now in a number of preclinical models and we look to bring this forward in several different cell therapy contexts."

The company has four active programs. Lead candidate Deep IL-15, an IL-15-anchored autologous T-cell therapy, is completing pre-IND studies and expected to enter the clinic, with trials in both hematologic and solid tumors, in mid-2018. The company is advancing small-molecule TLR/STING agonists and Deep IL-12 to target innate immunity to amplify the immune response for greater durability and retention, with lead candidates in those programs expected to emerge next year. Lastly, Torque is pursuing several approaches to develop Deep checkpoint inhibition.

Torque is working closely with the FDA and plans to conduct initial trials in the U.S.

"This is a good time for the field because we've already had the first approvals, which laid the foundation for this next generation of products," Henderson said.

"We're the first company to work at this interface between biotherapeutics and cell therapy and to combine them into a single package," Nielsen added. "But so far we've had a very warm reception from potential collaborators and also during our initial interaction with the agency."

The series A was sized to take Deep IL-15 into the clinic and to enable the company to identify follow-on candidates. Torque plans another fundraising to finance trials of the next set of candidates, but those details remain under wraps, according to Henderson.

While advancing its Deep-Priming programs internally, Torque is keeping an eye on I-O therapeutics that might provide attractive partnering options and keeping its options open on an endgame.

"The opportunity for us is universal in the sense that we can apply Deep-Priming to every type of immune cell therapeutics," Henderson said. "We'll do a blend of partnerships with companies that have immune cell therapeutics. We'll also develop our own to exploit the technology to its fullest." ♦