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# Anchors aweigh: Catamaran Bio sets sail with $42M to develop allogeneic CAR-NK cell therapies

*By Cormac Sheridan, Staff Writer*

When the first chimeric antigen receptor T-cell (CAR T) therapy, Kymriah (tisagenlecleucel), was approved in 2016 for treating B-cell acute lymphoblastic leukemia, its developer, Novartis AG, confined the initial rollout to just 20 treating centers. Its label carried a black box warning, because of the risk of life-threatening cytokine release syndrome, and Basel, Switzerland-based Novartis put in place a comprehensive risk evaluation and mitigation system to ensure its safe use. Catamaran Bio Inc., a Boston-based startup that has raised $42 million in seed and series A financing, is considering the administration of similarly engineered natural killer cells in walk-in clinics. "If the product is safe, it can be given as an out-patient treatment," Chief Scientific Officer Vipin Suri told *BioWorld*. "As a field, this absolutely has to be our ambition."

Vipin Suri, chief scientific officer, Catamaran

That is, obviously, a long-term vision. Right now, the young company is in mid-lead-optimization with its two initial programs, which target a solid tumor indication and a hematological malignancy. But preliminary data from other sources suggest that allogeneic CAR-NK therapy could be a whole lot safer than CAR T therapy, while offering similar levels of efficacy. Once manufacturing scale-up is achieved, engineered NK cells should also be far more flexible – and cheaper – to produce than autologous CAR T therapies.

The company – and its founding investors – have taken inspiration from interim data from an ongoing phase I/II study, led by Katy Rezvani, of MD Anderson Cancer Center in Houston, in which eight of 11 patients (73%) with either CD19-positive non-Hodgkin's lymphoma or CD19-positive chronic lymphocytic leukemia achieved a response to a CD19-directed CAR-NK therapy. Seven of the eight responses were classified as complete remissions – and none of the treated patients experienced cytokine release syndrome, graft-vs.-host disease, neurotoxicity or any increase in inflammatory cytokines. The data were published on Feb. 6, 2020, in *The New England Journal of Medicine*.

Rezvani's program is already partnered, with Tokyo-based Takeda Pharmaceutical Co. Ltd. The latter's venture capital arm, Takeda Ventures, is part of Catamaran Bio's investor syndicate. The series A round was co-led by founding investor SV Health Investors and Lightstone Ventures. Astellas Capital Management, the corporate venture arm of Tokyo-based Astellas Pharma Inc., also participated. The company emerged from an 18-month process initiated by SV Health Investors, which sought to assemble a set of technologies and people to develop end-to-end capabilities in developing and manufacturing allogeneic highly engineered CAR-NK cells. "We looked at all four corners of the globe," Houman Ashrafian, managing partner at London-and-Boston based SV Health Investors, told *BioWorld*.

The company's scientific founders are Catherine Bollard, director of the Center for Cancer and Immunology at the Children's National Research Institute, Washington, and a professor at George Washington University, who has developed potency-boosting switches for NK cells, and Branden Moriarity, an assistant professor at the University of Minnesota's Masonic Cancer Research Center, an expert in nonviral cell engineering. The other two founders come from SV Health Investors: Kevin Pojasek, who is executive chairman, and Tim Harris, who leads the company's scientific advisory board. "We are not in it for a quick exit," said Ashrafian, who has also taken a board seat. "Our commitment to this space is substantial."

Houman Ashrafian, managing partner, SV Health Investors

The company is not disclosing details about what Ashrafian described as "the Boolean components" of its CAR-NK designs at this point. "We always start with the patient and the tumor and work backwards," Suri said. That includes informatics analyses of the cancer and the immune response to it, as well as patient samples. Its therapies are designed, ab initio, to modulate the tumor microenvironment as well as to kill cancer cells. "We weigh them almost equally," Suri said. CAR T developers have, so far, been unable to penetrate the immunosuppressive defenses

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erected by solid tumors. "Solid tumors have this force field around them designed to quiesce the immune response to the cancer cells," he said.

Because the cells will contain multiple synthetic biology switches, the company has opted to avoid using viral vectors to transduce its target cells. Suri, as co-founder of Cambridge, Mass.-based Obsidian Therapeutics Inc., brings considerable experience of industrializing synthetic biology innovations in cell and gene therapy. Moriarity has developed transposon-based gene transfer systems, which Catamaran Bio will use for delivering the genetic payloads that will encode the biological instruction set. "Transposons do not have the capacity constraints that viral vectors have," Suri said. They also enable multiplex gene transfer. Capturing the therapeutic potential of engineered NK cells also requires a robust manufacturing process, which includes a cryopreservation step, to ensure that the resulting therapy will be truly off the shelf. "The MD Anderson study was done with a fresh product – it's not going to be off the shelf," Suri said.

Catamaran Bio is still a number of years from clinical trials. Several longer-established competitors are further advanced. Nkarta Inc., of South San Francisco, recently started a phase I trial of NKX-101 in patients with either relapsed or refractory acute myeloid leukemia (AML) or high-risk myelodysplastic syndromes. The therapy comprises NK cells expressing a CAR directed at NKG2D, an activating receptor expressed on wild-type NK cells which recognizes stress ligands expressed by many tumor cells.

Celularity Inc., of Florham Park, N.J., is also developing allogeneic CAR-NK therapies, but its lead NK cell therapy, CYNK-001, comprises unengineered NK cells, derived from placental hematopoietic stem cells. It is currently in clinical trials in multiple myeloma, AML, glioblastoma multiforme and COVID-19. Cyad SA, of Mont-Saint-Guibert, Belgium, is harnessing NK cell biology with a CAR T. CYAD-101, which is in a phase I trial in patients with metastatic colorectal cancer, comprises allogeneic T cells expressing the NKG2D receptor, as well as TIM, which knocks down T-cell receptor signaling. Sanofi SA's pending €308 million (US$367 million) acquisition of Kiadis Pharma BV, which brings in a pipeline of three clinical-stage NK cell therapies, is evidence of big pharma interest in NK cell biology.

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