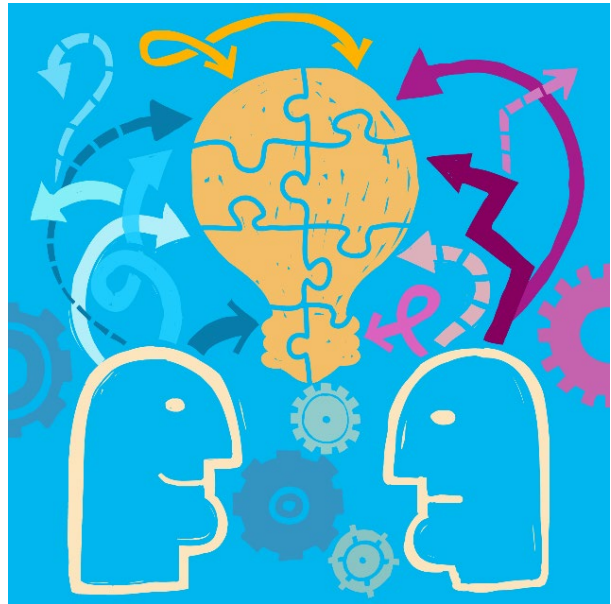


Solid Tumors, Meet Off-the-Shelf CAR-NK Cell Therapies. Biotech World, Meet Catamaran Bio.



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by **Mark Boshar, JD (COO) and Vipin Suri, PhD, MBA (CSO)**

Early generations of immune cell therapies blazed new trails as cancer treatments, and their success to date has been in the form of autologous products for treating certain blood cancers. Cell therapies have not yet successfully reached the frontier of combatting solid tumors. Catamaran Bio was founded to pioneer the development of allogeneic cell therapies that can safely and effectively treat solid tumors. We are charting a new course for cell therapies to harness the natural cancer-fighting properties of natural killer (NK) cells.

Our research approach, and indeed the whole cell therapy field, is built on the foundation of CAR-T treatments that have made it to the market—Novartis’ Kymriah, and Yescarta and Tecartus from Gilead’s Kite Pharma. Each of these autologous CAR-T products targets a specific B-cell surface marker associated with certain blood cancers. These treatments involve removing T cells from individual patients, engineering them to recognize and kill specific antigen expressing cancer cells, and then re-introducing the engineered CAR-T cells into the patient. This is a complex and costly process that can take three to four weeks from initial collection of patient cells by leukapheresis to infusion of the final product into the patient.

While the remarkable efficacy of CAR-T therapies in treating B-cell malignancies is clear, equally obvious are their current limitations: the complexity and delay of autologous cell therapy, well-recognized safety challenges, and the lack of success reaching solid tumors.

Setting the bar for the next generation of cell therapies.

by Mark

The holy grail for the next generation of cell therapies is a highly potent “off-the-shelf” product that is based on healthy donor-derived cells and can effectively treat solid tumors—all without causing the safety concerns observed with CAR-T therapies. A team at SV Health Investors embarked on an effort in 2019 to think about how best to build a next-gen cell therapy company focused on reaching this holy grail. Over the course of several months, this team, led by Kevin Pojasek, Houman Ashrafian and Tim Harris, conducted a deep survey of the space and had lots of conversations with scientific and clinical KOLs, companies and other investors active in the cell therapy space.

The months of research and exploration led to an evening gathering for drinks at a trendy bar in Boston on a cold, snowy day in December 2019. Several weeks earlier, Kevin had introduced me (Mark) to Houman and he had also reacquainted Vipin Suri, who had immersed himself in the cell therapy space for five years, as part of his nearly two decades in innovative drug development. Joining Kevin, Houman, Vipin and me was Branden Moriarity of the University of Minnesota. Branden had deep expertise in engineering immune cells using a variety of advanced technologies, combined with a highly productive academic lab with very relevant NK cell experience.

Everyone around the table had a different and valuable perspective about the cell therapy field. Top on everyone’s mind was the recent clinical study from MD Anderson showing that CAR-NK cells have anti-cancer activity, along with a very attractive safety profile. The promise of CAR-NK cell therapies was coming into clear view. After a long and lively discussion that took many twists and turns, our conversation converged on a single ‘lightbulb moment:’ the ‘ideal’ cell therapy approach would come from a holistic approach – not a single linchpin technology – in order to make progress beyond the limitations of early generation products.

Catamaran was born as an NK cell therapy company based on this realization that next-gen cell therapy would require a platform which integrated a unique set of innovative technologies, while also building on the great work and important accomplishments to date in the cell therapy space. Technology and know-how from Branden’s lab addressed key elements of an NK cell platform. The team also recognized that a cell therapy approach to address the tumor microenvironment (TME) was also a necessary element to achieve solid tumor efficacy, and Dr. Catherine Bollard of Children’s National/George Washington University was brought into the team soon after the December gathering. Cath is one of the deepest thinkers in the TME space, especially with NK cells, and she also brought a critical patient-facing perspective as an ideal complement to the founding group.

As we further assembled the pieces and refined the company concept to form Catamaran, all of our research and expert insights led to a clear definition of the characteristics of the next generation of cancer-fighting cell therapies:

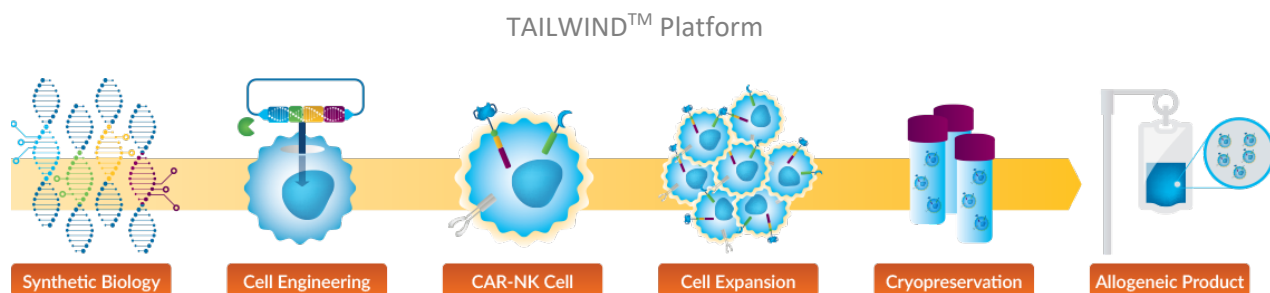
- **Make the product allogeneic:** The key challenge to using donor derived T-cells is the risk of graft-vs-host disease (GVHD), as the mismatched donor T-cells can potentially recognize a recipient's cells as foreign and launch a T-cell response, a process that is driven by T-cell receptors found on the donated cells. NK cells do not have a T-cell receptor, and donor NK cells have been safely infused into hundreds of patients without any incidence of GVHD. This progress and new scientific insights are paving the way to develop cell therapy products that do not rely on first harvesting cells from the cancer patient but are made from donor cells. In this way, an off-the-shelf product (likely stored in a freezer) can be available on demand, ready to be administered to any patient without delay.
- **Function in the tumor microenvironment:** As those of us in cancer drug development know well, the TME, the hostile milieu created by and surrounding the tumor, is highly immunosuppressive and a major barrier for cancer therapies to effectively eliminate solid tumors. Immunosuppressive factors, like PD-L1 and TGF β , produced by the tumor or stromal cells and resident in the TME, suppress the activity of our immune cells – limiting our immune systems' ability to put up the good fight against the invading cancer. Recently, clinical studies have been initiated with CAR-T cell therapies designed to reach solid tumors, and a number of research efforts in the field are focusing on allogeneic and off-the-shelf cell therapy solutions.
- **Achieve favorable safety profile:** The early generation of CAR-T therapies encountered several safety concerns, such as cytokine release syndrome (CRS) and neurological toxicity. More recently, clinical studies testing CAR-NK cells in certain hematologic malignancies have demonstrated impressive clinical responses with minimal incidence of CRS or neurological toxicity. This early clinical work with engineered NK cells provides a reason to believe in the promise of CAR-NK cells as a safer class of cell therapies.

So far, no group has yet brought all the functional and safety components together in one cell therapy modality to reach this holy grail.

Purpose built to set a new mark. Catamaran sets sail.

By Vipin

After a year in the making, Catamaran officially launched today. We were founded with a clear vision: deliver on the therapeutic potential of cell therapy by very deliberately solving the limitations of current cell therapy modalities. We started with the end in mind by defining the attributes of an ideal cell therapy. Then, we methodically created and assembled an integrated set of capabilities, know-how and tools – with proprietary technologies for key components – to achieve the end goal: a highly potent allogeneic and off-the-shelf product with the power to reach solid tumors and without the safety concerns of CAR-T cell therapies.



Our assets are a combination of ‘home grown’ tools and know-how developed by the Catamaran team and third-party technologies that we have integrated in our TAILWIND™ Platform. Here are the key components that differentiate our platform and set Catamaran apart in the cell therapy field:

For our cellular chassis, we chose NK cells, which can be engineered to express chimeric antigen receptors (CARs) for antigen targeting and other functional effectors. NK cells are cancer-fighting cells which are inherently allogeneic. In fact, they are our body’s first line of defense against cancer. In short, NK cells are a natural cancer fighting cell with an established safety profile which can be engineered to express a CAR – so, we believe we have the right cellular chassis.

Using synthetic biology, we are powering our CAR-NK cells to reach solid tumors by using “sense and respond” switches that neutralize the bad actors in the tumor microenvironment or, in some cases, convert signals that would have otherwise been inhibitory into NK cell activation signals to enhance the anti-tumor of our CAR-NK cells. Cath Bollard, one of our scientific co-founders, has made important discoveries for potency-boosting switches for NK cells. We are privileged to have her insight and her unique ability to bridge early research to transformative cell therapies through innovative synthetic biology and protein engineering, cell therapy manufacturing, and clinical innovation in the effective use of cell therapies to improve patient outcomes.

To deliver large genetic payloads and efficiently manufacture our cell therapies, we are advancing leading-edge, non-viral NK cell engineering using transposon systems. Our scientific co-founder, Branden Moriarity, is an expert in the field of genome engineering and an inventor of leading-edge DNA transposon systems. The transposon technology will differentiate our CAR-NK cell therapies because it enables multiplex cell engineering and will provide a more cost-effective, streamlined manufacturing process.

In a mere 9 months, our platform and our enormously talented and creative cell therapy research team has brought us from concept to reality, allowing us to advance two programs into lead optimization in a remarkably fast timeframe. Supporting our progress and our ambitious goals is a syndicate of investors who have a track record for investing in breakthrough science as well as a deep understanding of the cell therapy space and a commitment to finding next generation solutions.

Our Series A financing was co-led by Sofinnova Partners and Lightstone Ventures and joined by SV Health Investors, our founding investor, and two strategic investors, Takeda Ventures and

Astellas Venture Management. Of note, Takeda and Astellas represent a special caliber of investors in cell therapies, given Takeda's early and comprehensive efforts in CAR-NK therapies with MD Anderson and Astellas' world-class investments in the cell therapy field. We were also fortunate to attract early investment support from Discovery Capital at the University of Minnesota given Branden Moriarity's involvement.

We deeply believe that one of the hallmarks of Catamaran that will define our success is the talented team that we have assembled, with a breadth of experience and talent to give rise to transformative CAR-NK cell therapies.

The time is right for this journey.

The cell therapy field has rapidly evolved and shown tremendous treatment potential for cancer patients. We now understand that the most effective therapeutic approaches will harness our body's own immune system by applying powerful cell engineering technologies that tune and augment how immune cells target solid tumors. Catamaran is on the leading edge of this wave, and we have our sights set on creating a new generation of allogeneic cell therapies for patients.