April 29, 2025

# BrightPath Presented the Preclinical Data of iPSC-derived HER2 CAR-iNKT cells at AACR 2025

**Tokyo, Japan - April 29, 2025**/ -- BrightPath Biotherapeutics ("BrightPath", TSE Growth 4954), a clinical-stage biopharmaceutical company focused on developing novel cancer therapeutics, today announced that the Company has presented preclinical data on iPS cell-derived HER2 CAR-iNKT ("HER2 CAR-ipsNKT") cells, at the American Association for Cancer Research Annual Meeting ("AACR 2025", April 25-30, Chicago). The abstract and the electronic poster have been posted on the website of BrightPath after AACR 2025 was held.

(Abstract Number 6105)
Title: iPSC-derived HER2 CAR-iNKT cells enhance the activity of immune cells against cancer cells
Date & Time: 2 p.m.-5 p.m. CDT on Tuesday, April 29, 2025

In hematologic malignancies, autologous CAR-T cell therapy has been established as a highly effective treatment option. To further enhance the accessibility of cell therapies, efforts have been made to develop allogeneic CAR-T cell therapies using T cells from healthy donors. However, successful clinical development has yet to be achieved. One of the main challenges is that allogeneic CAR-T cells are recognized and eliminated by the patient's immune system, leading to poor persistence and limited durability of clinical responses.

To address this challenge, BrightPath is pursuing an alternative approach that employs invariant natural killer T ("iNKT") cells derived from induced pluripotent stem ("iPS") cells, rather than conventional T cells, for its allogeneic CAR-T platform. Unlike conventional T cells, iNKT cells possess the unique ability not only to directly kill cancer cells but also to activate surrounding other immune cells, thereby enhancing antitumor immune responses.

Although allogeneic iPS cell-derived CAR-iNKT ("CAR-ipsNKT") cells are ultimately expected to be cleared by the patient's immune system, during their window of activity, they are anticipated to induce a response from the patient's endogenous antitumor immune cells, which are not subject to immune rejection. This mechanism may contribute to sustained clinical responses.

In this study, we demonstrated that the ability of native iNKT cells to activate other immune cells is preserved even after reprogramming to iPS cells, gene editing, and subsequent redifferentiation into CAR-ipsNKT cells in a tumor-bearing mouse model.

Activation of surrounding immune cells by iNKT cells requires prior activation of the iNKT cells themselves. Previous studies have shown that this activation is typically triggered through T-cell receptor (TCR) signaling. "Notably, for the first time, we demonstrated that CAR-ipsNKT cells differentiated from iPS cells can be activated via CAR signaling instead of TCR signaling, leading to subsequent activation of dendritic cells ("DCs") and tumor antigen-specific $CD8^+$ T cells in a xenograft mouse model. This finding goes beyond previous studies conducted in syngeneic models or using non-CAR-transfected cells," commented Kenichi Nagai, CEO of BrightPath.

Data from the study include the following findings:

- *In vitro*, HER2 CAR-ipsNKT cells were activated upon CAR engagement with the HER2, leading to

the activation and maturation of dendritic cells (DCs). Additionally, these cells stimulated monocytes, promoting their polarization into M1 macrophages with antitumor properties.

- In a xenograft tumor model transplanted with human PBMCs, HER2 CAR-ipsNKT cells, in the presence of DCs within hPBMCs, activated antigen-specific $CD8^+$T cells within the hPBMCs, leading to tumor regression.

Currently, BrightPath is advancing the development of BCMA CAR-ipsNKT (BP2202) as the first product of its CAR-ipsNKT platform and is preparing for a clinical trial in multiple myeloma.

More detailed results are available on the websites of BrightPath.

**About BrightPath Biotherapeutics:**

BrightPath is a clinical stage biopharmaceutical company focused on the development of novel cancer therapies to transform cancer treatment for refractory or progressive cancers that cannot be treated with conventional standard therapies. BrightPath is actively involved in developing cell therapies, currently in clinical trials, and immunomodulatory antibodies.

For more information, visit www.brightpathbio.com/English

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