BGB-B2033 (GPC3 x 4-1BB Bispecific Antibody)

Disclaimer: This fact sheet is intended for media professionals only.
BGB-B2033 is an investigational drug for which safety and efficacy have not been established.

WHAT IS BGB-B2033?

BGB-B2033 is an investigational, potentially first-in-class bispecific antibody designed to target GPC3 and mediate engagement of 4-1BB. BeOne Medicines is developing BGB-B2033 for patients with hepatocellular carcinoma (HCC), the most common form of liver cancer, and other GPC3-expressing cancers.

THE TARGET: GPC3 AND 4-1BB

GPC3 (glypican-3) is a protein found on many cancer cells, and in HCC particularly, but is minimally expressed in most normal adult tissues.

4-1BB is a receptor found on activated immune cells, including T cells and natural killer (NK) cells. When activated, 4-1BB helps these immune cells become stronger and more effective at attacking cancer cells.

By targeting both GPC3 and 4-1BB, BGB-B2033 is designed to limit tumor growth, while helping direct the body's immune response toward cancer cells.

SIGNIFICANT UNMET NEED IN HCC

- Hepatocellular carcinoma (HCC), the most common type of liver cancer, remains a significant global health challenge. It is the sixth most common cancer worldwide and the third leading cause of cancer-related death.[i]
- Many patients are diagnosed at an advanced stage, with more than half presenting with advanced disease across major regions of the world.[ii] In the United States alone, approximately 30,000 people will be diagnosed with HCC in 2026.[iii]
- Although immunotherapies and tyrosine kinase inhibitors (TKIs) have improved treatment options and are now considered the standard of care for many patients, long-term outcomes remain poor. Treatment-related toxicities and compromised liver function often limit patients' ability to access or remain on current therapies.
- The five-year survival rate for patients with metastatic disease is approximately 4%, highlighting the continued need for new treatment approaches for patients with HCC.[iv]

HOW DOES BGB-B2033 WORK?

BGB-B2033 is designed to act as a bridge between cancer cells and immune cells.

CANCER CELL

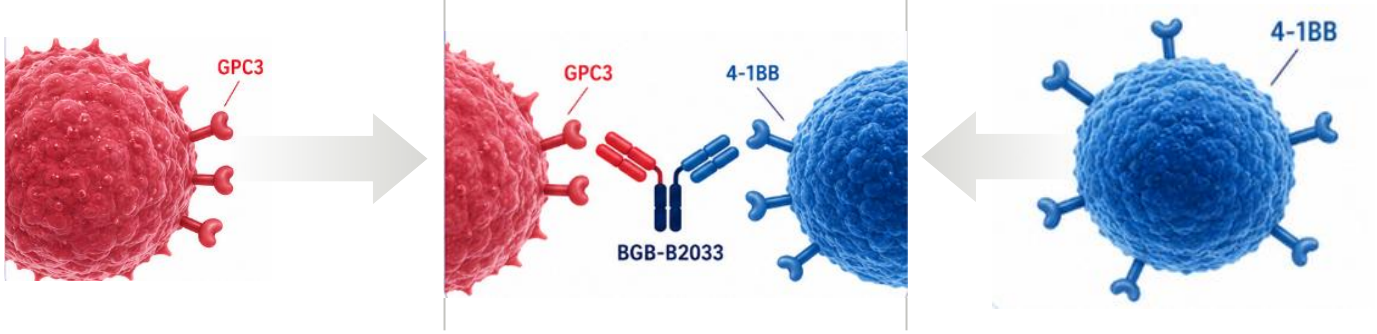
Many tumors express GPC3 on their surface.

WITH BGB-B2033

BGB-B2033 binds to both GPC3 on the cancer cell and 4-1BB on the immune cell.

IMMUNE CELL

Activated T-cells and NK cells express 4-1BB, a receptor that can increase immune activity when stimulated.



This brings immune cells into close proximity with the tumor and activates 4-1BB signaling directly within the tumor environment. **As a result, immune cells may become more effective at recognizing and destroying cancer cells.**

DIFFERENTIATION: TUMOR-DIRECTED IMMUNE ACTIVATION

Scientists have long been interested in activating 4-1BB because it can produce strong anti-cancer immune responses. However, earlier approaches sometimes activated immune cells throughout the body, which could lead to safety concerns.

BGB-B2033 was designed to activate 4-1BB only when it is attached to a GPC3-expresing tumor cell.

TUMOR-DIRECTED ACTIVATION	IMMUNE CELL STIMULATION	POTENTIALLY SAFETY ADVANTAGE	COMBINATION POTENTIAL
BGB-B2033 requires GPC3 engagement before strong 4-1BB signaling occurs. This helps focus on immune activation within the tumor microenvironment.	**The molecule was designed to enhance T-cell and NK-cell activity against cancer cells expressing GPC3.**	**By limiting the activations to GPC3-expressing tumors, BGB-B2033 aims to reduce unwanted immune activation outside the tumor microenvironment.**	**Early clinical data suggest BGB-B2033 may work well in combination with PD-1 inhibitors such as tislelizumab by further enhancing anti-tumor immune responses.**

Disclaimer. The clinical significance of data based on non-clinical studies has not been established

DEVELOPMENT HIGHLIGHTS

BGB-B2033 is currently being evaluated in a **global clinical development program in patients with advanced or metastatic hepatocellular carcinoma.** It has been granted **Fast Track Designation** and **Orphan Drug Designation** by the U.S. FDA and **Innovation Passport Designation** from the UK's MHRA.



Early Phase Clinical Data

- BGB-B2033 is currently being evaluated in a Phase 1 trial in patients with solid tumors.
- Results presented at the 2026 American Society of Clinical Oncology (ASCO) Annual Meeting demonstrated a favorable safety and tolerability profile, along with promising anti-tumor activity in heavily pretreated patients with hepatocellular carcinoma (HCC).[v]
- Additional data from this Phase 1 study was accepted as a proffered paper session at the 2026 European Society for Medical Oncology (ESMO) Annual Meeting.

Pivotal Development Trials

- Building on the Phase 1 results, BeOne has expanded the clinical study of BGB-B2033 to focus on patients whose disease has progressed after immunotherapy and tyrosine kinase inhibitor (TKI) treatment, helping support a potential regulatory pathway. The company also plans to initiate a global Phase 3 trial in patients whose cancer has progressed after first-line treatment, including immunotherapy, by the end of 2026. As development continues, future studies will explore the potential of BGB-B2033 in earlier lines of treatment.

---

[i] Samant H, Amiri HS, Zibari GB. Addressing the worldwide hepatocellular carcinoma: epidemiology, prevention and management. J Gastrointest Oncol. 2021 Jul;12(Suppl 2):S361-S373. doi: 10.21037/jgo.2020.02.08. PMID: 34422400; PMCID: PMC8343080.

[ii] Park JW, et al. Global patterns of hepatocellular carcinoma management from diagnosis to death: the BRIDGE Study. Liver International. 2015.

[iii] American Cancer Society's Cancer Facts & Figures 2026. https://www.cancer.org/content/dam/cancer-org/research/cancer-facts-and-statistics/annual-cancer-facts-and-figures/2026/2026-cancer-facts-and-figures.pdf

[iv] https://www.mayoclinic.org/diseases-conditions/hepatocellular-carcinoma/survival-rates/gnc-20589115

[v] Chon HJ, et all; Poster Presentation at ASCO 2026; Rapid Oral Abstract: 3016