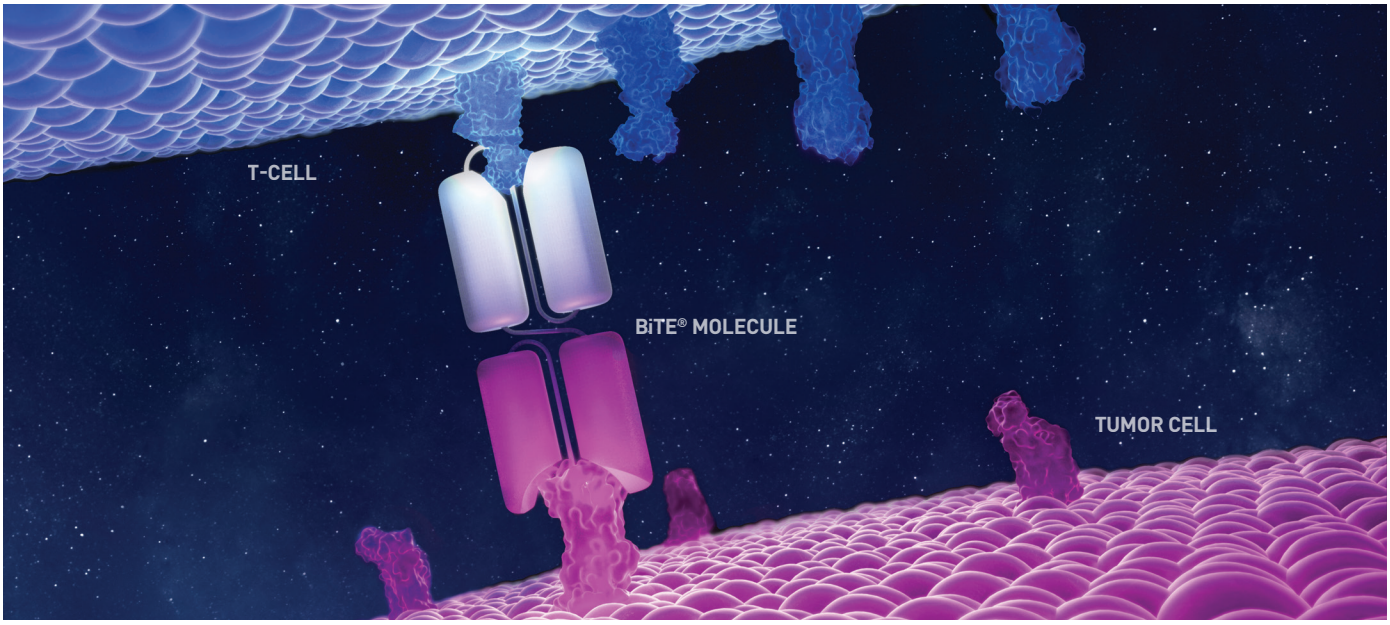
THE BiTE® IMMUNO-ONCOLOGY PLATFORM

- Despite recent advances in immuno-oncology, there remains a need for new therapies across a broad range of hematologic and solid tumor malignancies
- The Bispecific T-cell Engager (BiTE®) platform has the potential to bring T-cell innovation to more patients, including those with rare and aggressive cancers

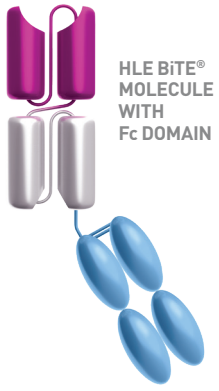
How BiTE® technology targets cancer

- BiTE® technology is designed to overcome cancer cells' evasion of the body's immune system by engaging patients' own T-cells to directly target cancer cells[1]
- Cancer cells can be recognized and eliminated through T-cell–mediated immune surveillance. Over time, cancer cells are able to develop mechanisms to evade immune system detection, including the downregulation or loss of major histocompatibility complex class I (MHC-I)[1-3]
- BiTE® molecules are engineered with a CD3-targeting domain that binds to any T-cell, while the tumor-targeting domain can be designed to target any tumor-associated antigen[1]
- BiTE® molecules mediate the engagement of a T-cell to a cancer cell without the need for MHC-I presentation and signaling, leading to the formation of an immune synapse. Perforin and granzymes are then released, initiating apoptosis of the cancer cell[4,5]
- Following apoptosis, activated T-cells can target surrounding cancer cells, resulting in serial lysis. Sustained activation leads to local proliferation and expansion of polyclonal memory T-cells[1,4]



BiTE® technology continues to evolve to harness the promise of immuno-oncology

- HLE BiTE® molecules include an Fc domain to slow their clearance, providing the potential for more flexible dosing options to enhance patient convenience[5,6]
- Additional formats of the BiTE® molecule are designed using a human heavy chain antibody platform and Fc domain[6,7]



BiTE® technology is engineered to deliver off-the-shelf therapies and is currently being investigated across both hematologic and solid tumor malignancies[8]

CD, cluster of differentiation; Fc, fragment crystallizable; HLE, half-life extended.

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The versatility of the BiTE® platform:

Solid tumor malignancies

	Cancer Type	Target
	Small Cell Lung Cancer (SCLC)[7,9]	**DLL3:** Minimally expressed in normal tissue; overexpressed on the surface of SCLC tumor cells
	Prostate Cancer[7,10,11]	**DLL3:** Absent in benign prostate cancer cells, but expressed in most neuroendocrine prostate cancer cells **PSMA:** Normally expressed on the surface of prostate cancer epithelial cells, PSMA is upregulated in most prostate tumors and its expression levels further increase with progression to advanced disease
	Gastric or Gastroesophageal Junction Cancer[7,12,13]	**MUC17:** Overexpressed in up to half of the patients with gastric cancer; expression is significantly higher in gastric cancer tissue compared with the surrounding normal gastrointestinal mucosal epithelial cells

Hematologic malignancies

	Cancer Type	Target
	Acute Lymphoblastic Leukemia (ALL)[7,8]	**CD19:** Expressed on B-cells at all stages of development and is a reliable B-cell biomarker
	Acute Myeloid Leukemia (AML)[7,14]	**FLT3:** Expressed in bone marrow cells, with increased expression in leukemic blast cells in the majority of patients with AML
	Multiple Myeloma (MM)[7,15]	**BCMA:** Normally expressed in late-stage B-cells and plasma cells, overexpressed in MM cells

BCMA, B-cell maturation antigen; CD, cluster of differentiation; DLL3, delta-like ligand 3; FLT3, FMS-like tyrosine kinase 3; MUC17, mucin 17; PSMA, prostate-specific membrane antigen.

Amgen is committed to bringing T-cell innovation to patients, including those with rare and aggressive cancers

Scan the QR code to visit the BiTE® Interactive Pipeline or, for more information, visit:
amgenoncology.com/bite-platform.html

References: 1. Baeuerle PA, et al. *Curr Opin Mol Ther*. 2009;11:22-30. **2.** Ferrone S, et al. *Surg Oncol Clin N Am*. 2007;16:755-774. **3.** Töpfer K, et al. *J Biomed Biotechnol*. 2011;2011:918471. **4.** Nagorsen D, et al. *Exp Cell Res*. 2011;317:1255-1260. **5.** Arvedson TL, et al. *Cancer Res*. 2017;77(suppl 13). Abstract 55. **6.** Weidle UH, et al. *Cancer Genomics Proteomics*. 2013;10:1-18. **7.** Amgen Pipeline. https://www.amgenpipeline.com/-/media/Themes/Amgen/amgenpipeline-com/amgenpipeline-com/PDF/amgen-pipeline-chart.pdf. Accessed April 14, 2022. **8.** Yuraszeck T, et al. *Clin Pharmacol Ther*. 2017;101:634-645. **9.** Giffin MJ, et al. *Clin Cancer Res*. 2021;27:1526-1537. **10.** Ben Jemaa A, et al. *J Exp Clin Cancer Res*. 2010;29:171. **11.** Puca L, et al. *Sci Transl Med*. 2019;11:eaav0891. **12.** Yang B, et al. *J Exp Clin Cancer Res*. 2019;38:283. **13.** Wang K, et al. *Nat Genet*. 2014;46:573-582. **14.** Gilliland DG, et al. *Blood*. 2002;100:1532-1542. **15.** Sanchez E, et al. *Br J Haematol*. 2012;158:727-738.

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