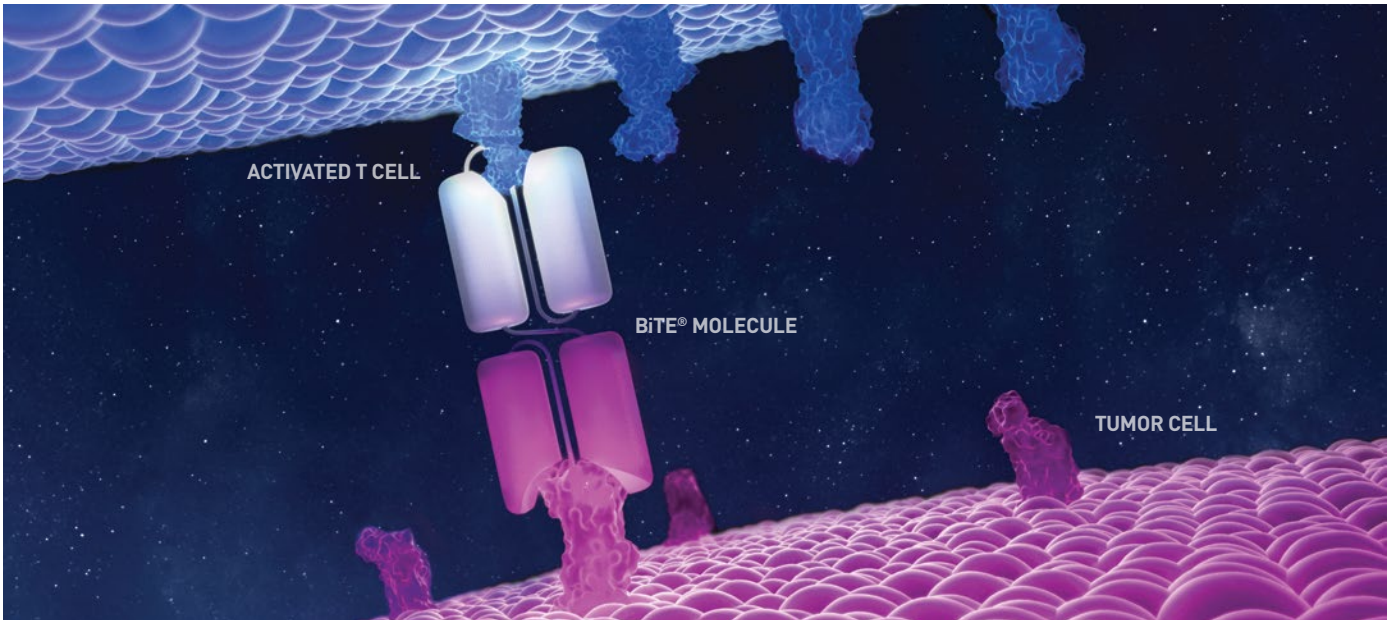
THE BiTE® IMMUNO-ONCOLOGY PLATFORM

- Despite recent advances in immuno-oncology, not enough patients benefit from current treatments. New therapies are needed across a broad range of solid and hematologic malignancies
- The BiTE® platform has potential to bring T cell innovation to more patients, including those with rare and aggressive diseases

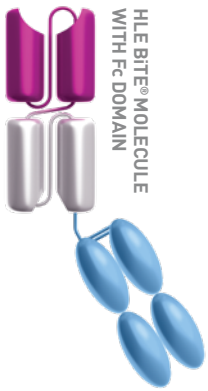
How BiTE® (Bispecific T Cell Engager) technology targets cancer

- BiTE® technology is designed to overcome cancer cells' evasion of the 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 (MHCI)[1-3]
- BiTE® molecules are engineered with a CD3-targeting domain that binds to the T cell, while the second domain can be designed to target any tumor-associated antigen[1,4]
- BiTE® molecules mediate the engagement of a T cell to a cancer cell regardless of the presence of MHCI, leading to the formation of an immune synapse. Perforin and granzymes are then released, initiating apoptosis of the cancer cell[5,6]
- 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[1,5]



BiTE® technology continues to deliver on the promise of immuno-oncology

- BiTE® molecules are engineered in both canonical and half-life extended (HLE) constructs for additional versatility[7]
- Canonical BiTE® molecules are relatively small fusion proteins with a short half-life of only a few hours[1,6-8]
- HLE BiTE® molecules include an Fc region to extend the amount of time before they are cleared from the body, with the potential for more flexible dosing options to enhance patient convenience[7,9]



BiTE® technology is engineered to deliver off-the-shelf therapies and is currently being investigated across both solid and hematologic malignancies[1,4,6,10,11]

CD, cluster of differentiation; Fc, fragment crystallizable.

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The versatility of the BiTE® platform:

Hematologic malignancies

	Disease state	Target
	Acute Lymphoblastic Leukemia (ALL)/Non-Hodgkin's Lymphoma (NHL)[6,10,11]	CD19: Expressed on B cells at all stages of development and is a reliable B-cell biomarker
	Acute Myeloid Leukemia (AML)[11-15]	CD33: Expressed on normal myeloid progenitors and in the majority of patients with AML
		FLT3: Expressed in bone marrow cells and overexpressed in leukemic blast cells in the majority of patients with AML
	Multiple Myeloma (MM)[11,16]	BCMA: Normally expressed in late-stage B cells and plasma cells, overexpressed on multiple myeloma cells

Solid tumors

	Disease state	Target
	Gastric or Gastroesophageal Junction Cancer[11,17-22]	CLDN18.2: Normal expression limited to differentiated epithelial cells of the gastric mucosa and small intestine; highly expressed in a significant number of primary gastric cancers
		MUC17: Expressed in normal gastrointestinal mucosal epithelial cells, but overexpressed in up to half of patients with gastric cancer, with expression being significantly higher in gastric cancer tissue compared with the surrounding normal tissue
	Glioblastoma[11,23]	EGFRvIII: Expressed in many patients with EGFR-amplified glioblastoma and is exclusively expressed in tumor cells
	Prostate Cancer[11,24]	PSMA: Normally expressed on prostate epithelial cells, overexpressed by virtually all prostate cancers. Its expression is progressively upregulated during disease progression
	Small Cell Lung Cancer (SCLC)[11,25]	DLL3: Minimally expressed in normal tissue, overexpressed on the surface of SCLC tumor cells

BCMA, B-cell maturation antigen; CLDN18.2, Claudin-18 isoform 2; DLL3, delta-like protein 3; EGFRvIII, epidermal growth factor receptor variant III; 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 diseases

For more information, visit **amgenoncology.com/bite-platform.html**

References: 1. Baeuerle PA, Kufer P, Bargou R. *Curr Opin Mol Ther*. 2009;11:22-30. **2.** Ferrone S, Whiteside TL. *Surg Oncol Clin N Am*. 2007;16:755-774. **3.** Töpfer K, Kempe S, Muller N, et al. *J Biomed Biotechnol*. 2011;2011:918471. **4.** Frankel SR, Baeuerle PA. *Curr Opin Chem Biol*. 2013;17:385-392. **5.** Nagorsen D, Baeuerle PA. *Exp Cell Res*. 2011;317:1255-1260. **6.** Yuraszeck T, Kasichayanula S, Benjamin JE. *Clin Pharmacol Ther*. 2017;101:634-645. **7.** Arvedson TL, Balazs M, Bogner P, et al. *Cancer Res*. 2017;77(suppl 13): Abstract 55. **8.** Thakur A, Huang M, Lum LG. *Blood Rev*. 2018;32:339-347. **9.** Weidle UH, Tiefenthaler G, Weiss EH, et al. *Cancer Genomics Proteomics*. 2013;10:1-18. **10.** Stieglmaier J, Benjamin J, Nagorsen D. *Expert Opin Biol Ther*. 2015;15:1093-1099. **11.** Amgen. Amgen pipeline. https://www.amgenpipeline.com/-/media/themes/amgen/amgenpipeline-com/amgenpipeline-com/pdf/amgen-pipeline-chart.pdf. Accessed April 29, 2020. **12.** Laszlo GS, Estey EH, Walter RB. *Blood Rev*. 2014;28:143-153. **13.** Krupka C, Kufer P, Kischel R, et al. *Blood*. 2014;123:356-365. **14.** Gilliland DG, Griffin JD. *Blood*. 2002;100:1532-1542. **15.** Carow CE, Levenstein M, Kaufmann SH, et al. *Blood*. 1996;87:1089-1096. **16.** Sanchez E, Li M, Kitto A, et al. *Br J Haematol*. 2012;158:727-738. **17.** ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT04260191. Accessed April 29, 2020. **18.** Zhu G, Foletti D, Liu X, et al. *Sci Rep*. 2019;9:8420. **19.** Gum JR, Crawley SC, Hicks JW, et al. *Biochem Biophys Res Commun*. 2002;291:466-475. **20.** Yang B, Wu A, Hu Y, et al. *J Exp Clin Cancer Res*. 2019;38:283. **21.** Lin S, Zhang Y, Hu Y, et al. *Gastric Cancer*. 2019;22:941-954. **22.** Wang K, Yuen ST, Xu J, et al. *Nat Genet*. 2014;46:573-582. **23.** Keller S, Schmidt MHH. *Int J Mol Sci*. 2017;18. doi:10.3390/ijms18061295. **24.** Ben Jemaa A, Bouraoui Y, Sallami S, et al. *J Exp Clin Cancer Res*. 2010;29:171. **25.** Sharma SK, Pourat J, Abdel-Atti D, et al. *Cancer Res*. 2017;77:3931-3941.

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