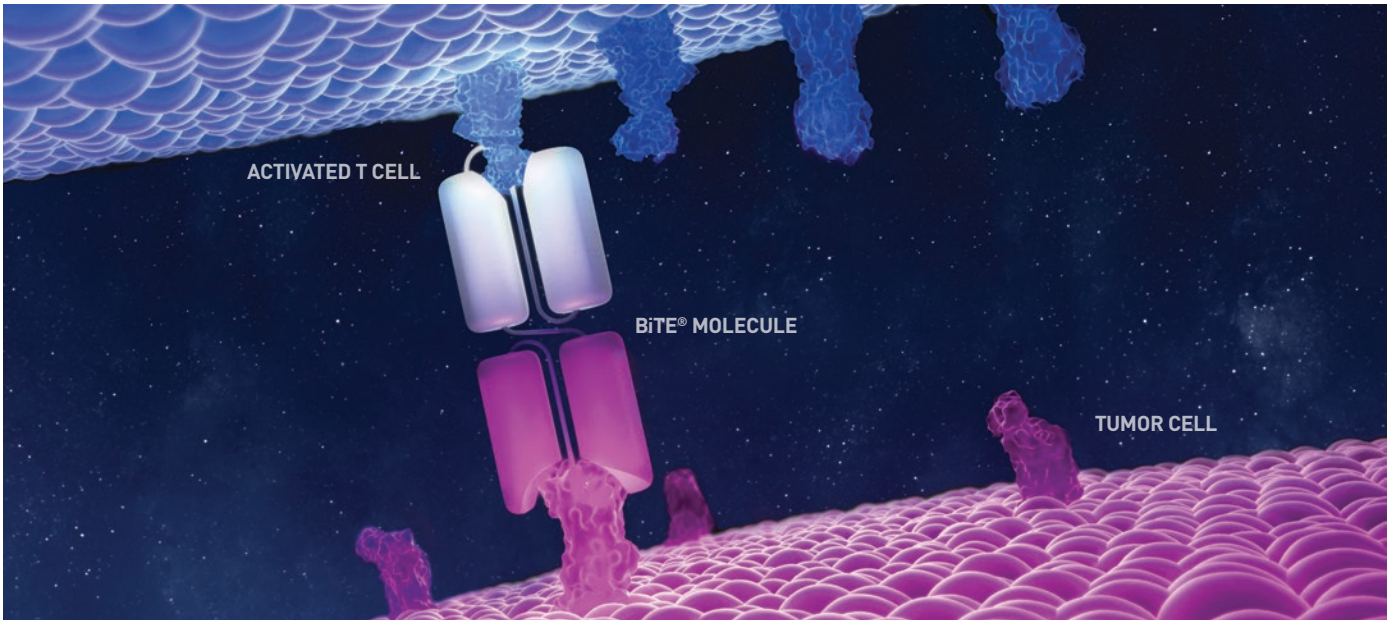
THE BiTE® IMMUNO-ONCOLOGY PLATFORM

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

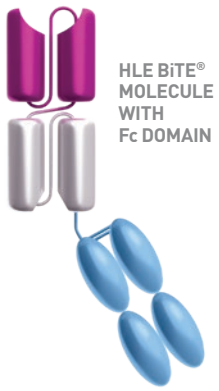
How BiTE® (Bispecific T-cell Engager) technology targets cancer

- BiTE® technology is designed to overcome cancer cells' evasion of the 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 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 MHC-I, 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 domain to extend the amount of time before they are cleared from the body, providing 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 hematologic and solid tumor 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)[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 increased expression 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 tumor malignancies

	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: Overexpressed in up to half of patients with gastric cancer; expression is significantly higher in gastric cancer tissue compared with the surrounding normal gastrointestinal mucosal epithelial cells
	Prostate Cancer[11,23-25]	PSMA: Normally expressed on the surface of prostate cancer epithelial cells, PSMA is upregulated in most prostate tumors and its expression levels increase with progression to advanced disease
		DLL3: Absent in benign prostate cancer cells, but expressed in most neuroendocrine prostate cancer cells
	Small Cell Lung Cancer (SCLC)[11,26,27]	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 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 diseases

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

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