

BiTE

THE ENGAGER™

**AN EDUCATIONAL RESOURCE
ON THE BiTE® IMMUNO-ONCOLOGY PLATFORM**



WE'RE BRINGING BiTE TO THE FIGHT™

BiTE, Bispecific T Cell Engager.

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Oncology

Advancing oncology at the speed of life™

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THE NEED FOR NEW THERAPEUTIC APPROACHES REMAINS HIGH

Despite recent advancements in immuno-oncology, not enough patients benefit from current treatments. Therefore, additional immuno-oncology options are needed to address both hematologic malignancies and solid tumors.

Considerations for addressing the unmet need



Designed to be readily available to patients¹



Ensure broad patient access²



Management of treatment and patient care costs³



Limit the impact of burden of care⁴

Amgen is committed to advancing the field of immuno-oncology

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BiTE® TECHNOLOGY IS DESIGNED TO ENGAGE THE NATURAL POWER OF T CELLS

Cytotoxic T cells play an important role in the body's immune defense by identifying and eliminating cancer cells; however, cancer cells can develop mechanisms to evade T cell recognition and destruction.^{2,5}

BiTE® technology is designed to overcome cancer cells' evasion of the immune system by engaging patients' own T cells to directly target cancer cells. BiTE® molecules are engineered from two flexibly linked, single-chain antibodies, with one that is specific for a selected tumor antigen and the other that is specific for CD3 found on T cells.^{2,4}

The BiTE® molecule is designed to activate the cytotoxic potential of T cells with the goal of eliminating cancer cells.⁶

- Recruitment of a T cell to a cancer cell leads to the formation of a cytolytic synapse, triggering T-cell activation and the release of perforin and granzymes⁶
- Fusion of perforin with the cancer cell membrane allows granzymes, released by the cytotoxic T cell, to enter the cancer cell to induce apoptosis⁶

The goal of BiTE® technology is to eliminate detectable cancer cells

Once T cells are activated by a BiTE® molecule, the T cells may induce further T-cell proliferation and cytokine production.^{6,7}

- Following cancer cell apoptosis, activated T cells release cytokines and produce additional perforin and granzymes that may allow T cells to target surrounding cancer cells, potentially resulting in the serial lysis of multiple cancer cells by a single T cell⁶
- Sustained activation of a single activated cytotoxic T cell theoretically results in local proliferation and expansion of polyclonal memory T cells^{2,6}

ACTIVATED
T CELL



TUMOR CELL
UNDERGOING
APOPTOSIS

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BiTE® TECHNOLOGY: POTENTIAL FOR OFF-THE-SHELF THERAPIES

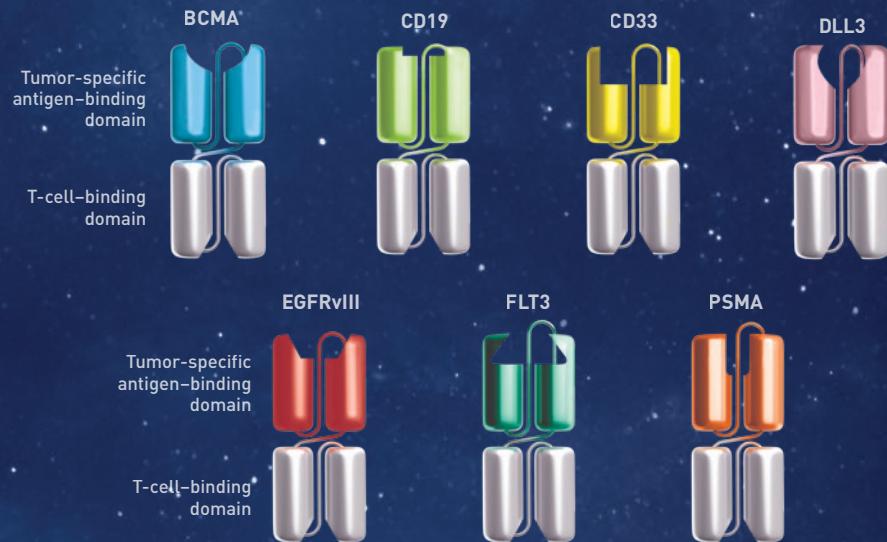
The BiTE® immuno-oncology platform offers versatility to potentially target any tumor-specific antigen

The CD3-targeting domain is designed to bind to the T cell, while the other domain can be engineered to target tumor-specific antigens across both solid and hematologic malignancies.²

This approach is being studied across a wide range of settings^{2,4,8}:

- In patients with high and low tumor burden
- In patients with rapidly progressing disease
- Across different treatment lines

BiTE® molecules under clinical investigation include the following targets^{2,9}:



BiTE® molecules are designed to bring T cell innovation to more patients

- Designed to target tumor-specific antigens²
- Being investigated across a broad range of solid and hematologic malignancies²
- Designed to lead to off-the-shelf therapies without the need for ex-vivo manipulation of patient's cells^{2,4}
- Investigated for use as monotherapies and in combination with other treatments^{7,8,10}

The goal of the BiTE® immuno-oncology platform is to make innovative T cell therapies available to more healthcare providers and their patients^{2,4,8}

**THE BiTE®
PLATFORM IS BEING
INVESTIGATED
ACROSS A BROAD
SET OF CANCERS**

The BiTE® immuno-oncology platform has been studied in thousands of patients, many of whom have been followed for up to 5 years.¹¹

Amgen is committed to developing innovative medicines that address important unmet needs

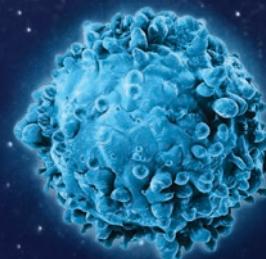
Amgen is a pioneer in immuno-oncology and developed the first approved BiTE® molecule. The BiTE® immuno-oncology platform continues to be investigated across multiple different hematologic malignancies and solid tumors.⁸

With the BiTE® immuno-oncology platform, Amgen is driven to push the boundaries of science to transform the standard of care for patients with cancer by:

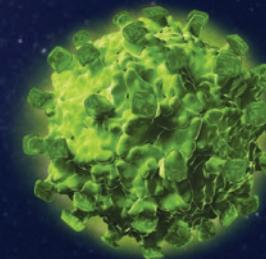
- Leveraging innovative trial designs^{12,13}
- Investigating clinically relevant endpoints and outcomes such as MRD negativity and long-term survival¹⁴⁻¹⁶

BiTE® therapies are being investigated for use as monotherapies and in combination with other treatments^{7,8,10}

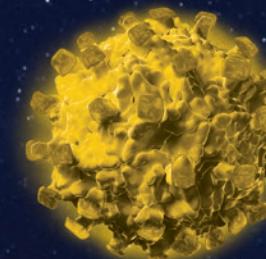
Investigational cancers being targeted by the BiTE® platform⁹



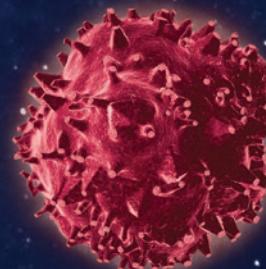
Multiple Myeloma



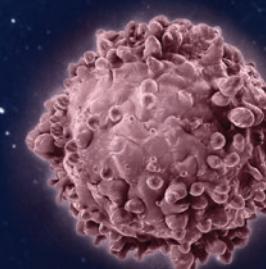
NHL



AML



GBM



SCLC



Prostate Cancer

AML, acute myeloid leukemia; GBM, glioblastoma; NHL, non-Hodgkin's lymphoma; SCLC, small cell lung cancer.

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AMGEN IS COMMITTED TO BRINGING T CELL INNOVATION TO PATIENTS

Features of the BiTE® platform

Canonical BiTE® molecules are designed to be relatively small recombinant proteins that are cleared through the kidney, with a typical serum half-life of a few hours.^{8,17} Currently, Amgen is designing BiTE® molecules with additional features, including a half-life extended (HLE)

BiTE® molecule containing a fragment-crystallizable (Fc) domain.¹⁸ Adding an Fc portion to the BiTE® molecule is designed to extend the amount of time before it is eliminated from the body.¹⁷



The growing BiTE® immuno-oncology pipeline⁹

Investigational BiTE® molecule	Tumor-specific antigen target	Cancer type
AMG 160,* AMG 212	PSMA	Prostate cancer
AMG 330, AMG 673*	CD33	Acute myeloid leukemia
AMG 420, AMG 701*	BCMA	Multiple myeloma
AMG 427*	FLT3	Acute myeloid leukemia
AMG 562*	CD19	Non-Hodgkin's lymphoma
AMG 596	EGFRvIII	Glioblastoma
AMG 757*	DLL3	Small cell lung cancer

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The BiTE® platform has the potential to bring hope to patients, including those with rare and aggressive diseases



BiTE: THE ENGAGER™

Designed to close the space between T cells and tumors

The BiTE® immuno-oncology platform:

- Engages patients' own T cells to identified tumor-specific antigens, with the goal of activating the cytotoxic potential of T cells to fight cancer^{2,4,7,8}
- Is being investigated in more than a thousand patients and continues to be investigated across multiple different hematologic malignancies and solid tumors^{9,11}
- Pioneered by Amgen, who continues to accelerate the investigation of BiTE® technology with the goal of enhancing patient experience and therapeutic potential^{7,8}

Learn more at [amgenoncology.com](https://www.amgenoncology.com)

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