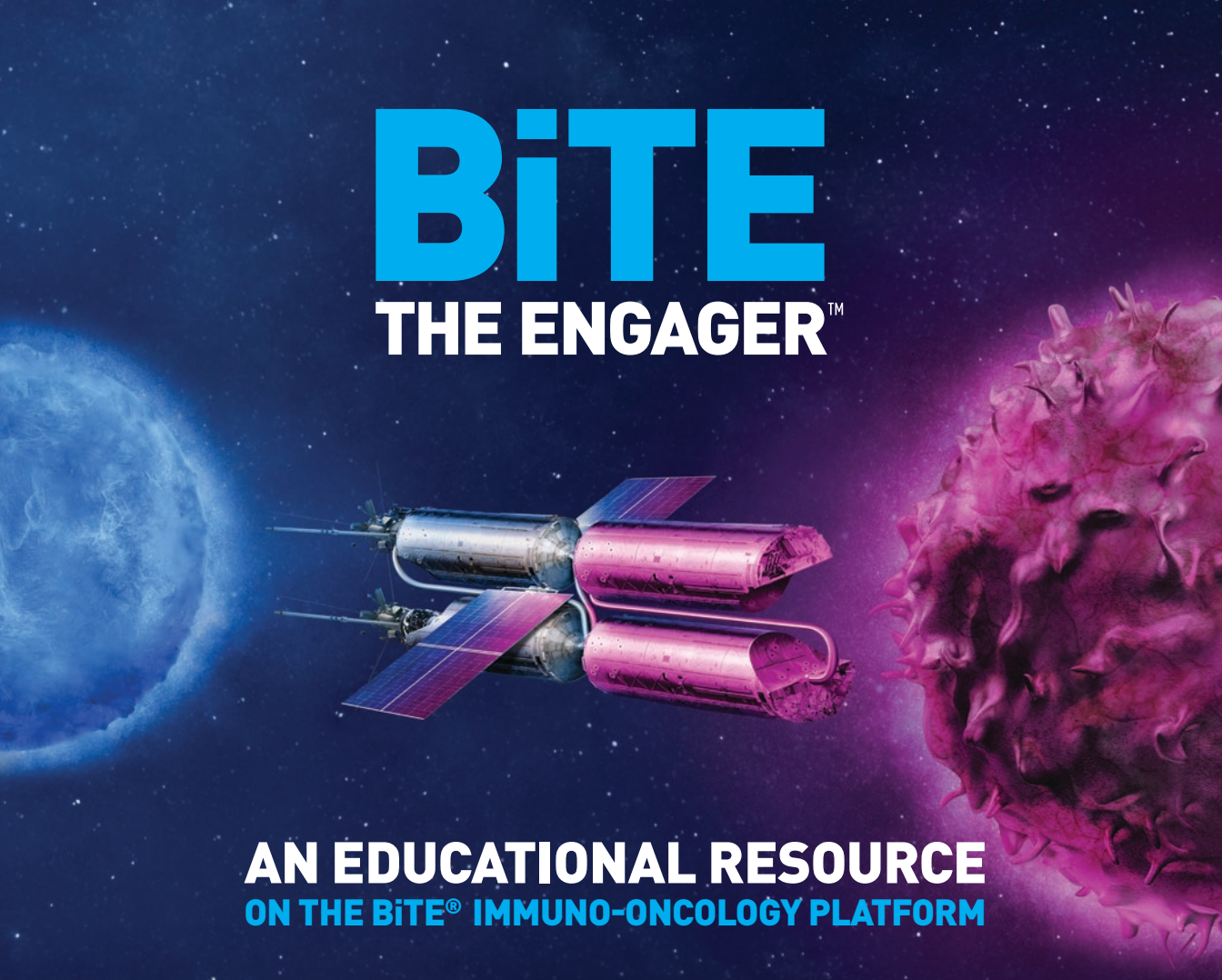
BiTE
THE ENGAGER™



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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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 patients[1]
- Ensure broad patient access[2]
- Management of treatment and patient care costs[3]
- Limit the impact of burden of care[4]

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]

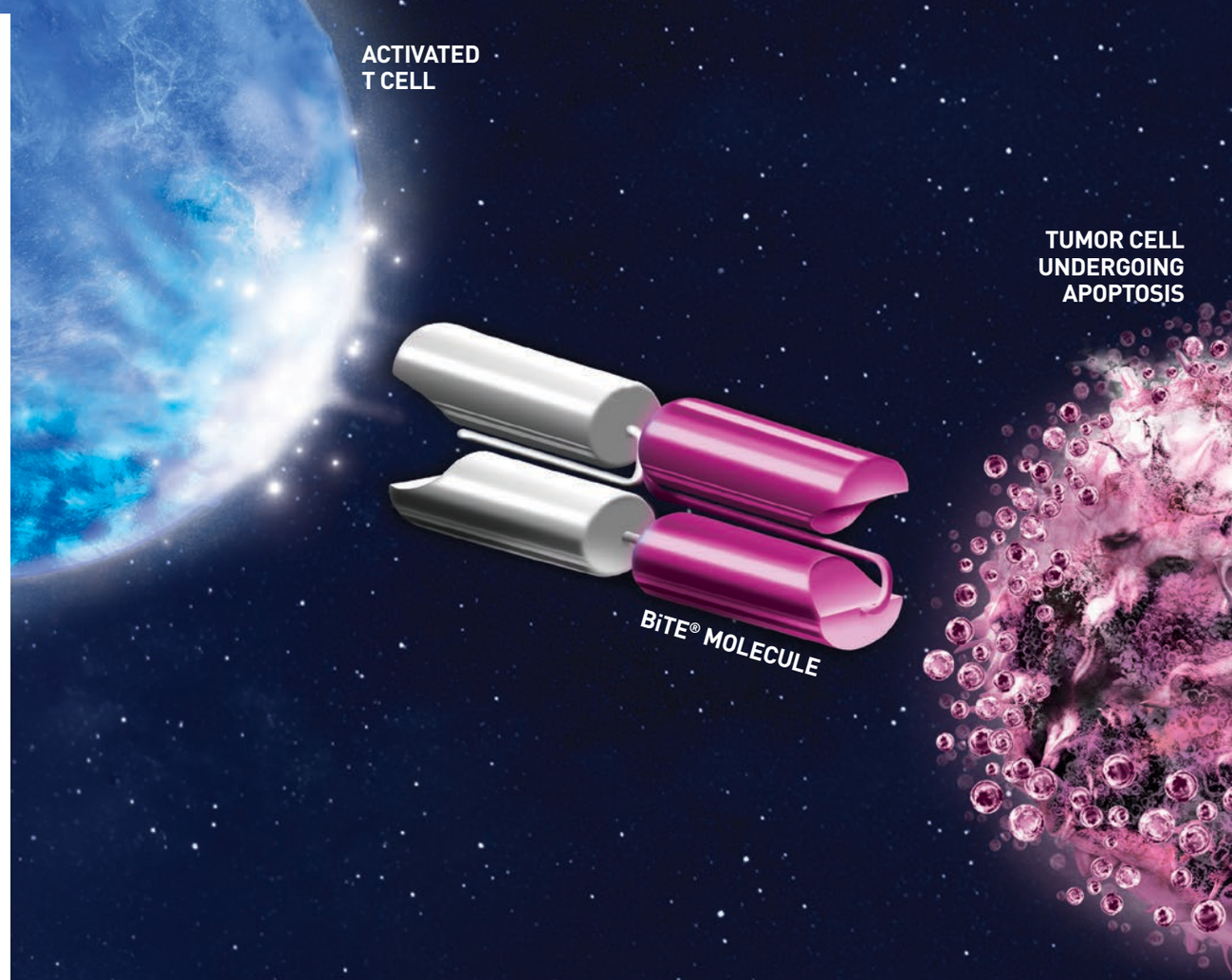
The BiTE® molecule is designed to activate the cytotoxic potential of T cells with the goal of eliminating cancer cells.[6]

- 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 granzymes[6]
- Fusion of perforin with the cancer cell membrane allows granzymes, released by the cytotoxic T cell, to enter the cancer cell to induce apoptosis[6]

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 cell[6]
- Sustained activation of a single activated cytotoxic T cell theoretically results in local proliferation and expansion of polyclonal memory T cells[2,6]



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CD, cluster of differentiation.

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

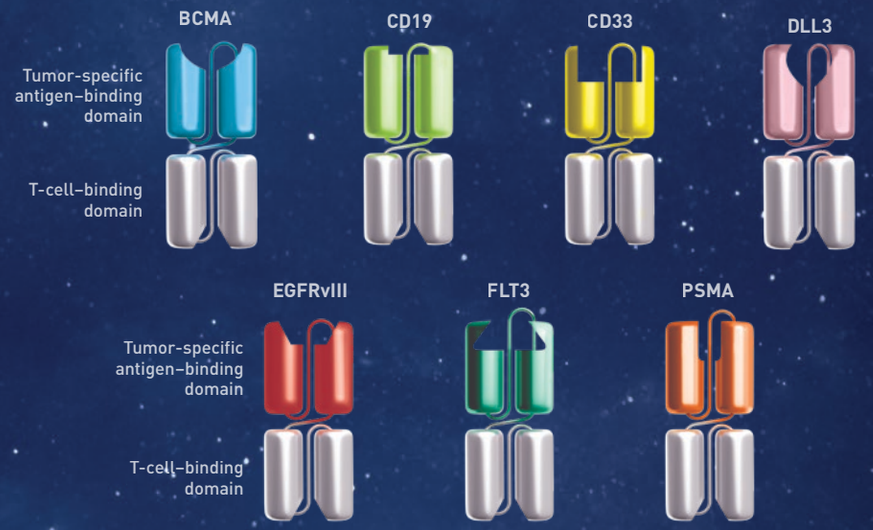
The BiTE® immuno-oncology platform offers versatility to potentially target any tumor-specific antigen

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]:



BCMA, B-cell maturation antigen; DLL3, delta like canonical Notch ligand 3; EGFRvIII, epidermal growth factor receptor variant III; FLT3, FMS-like tyrosine kinase 3; PSMA, prostate-specific membrane antigen.

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

- Designed to target tumor-specific antigens[2]
- Being investigated across a broad range of solid and hematologic malignancies[2]
- 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]

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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

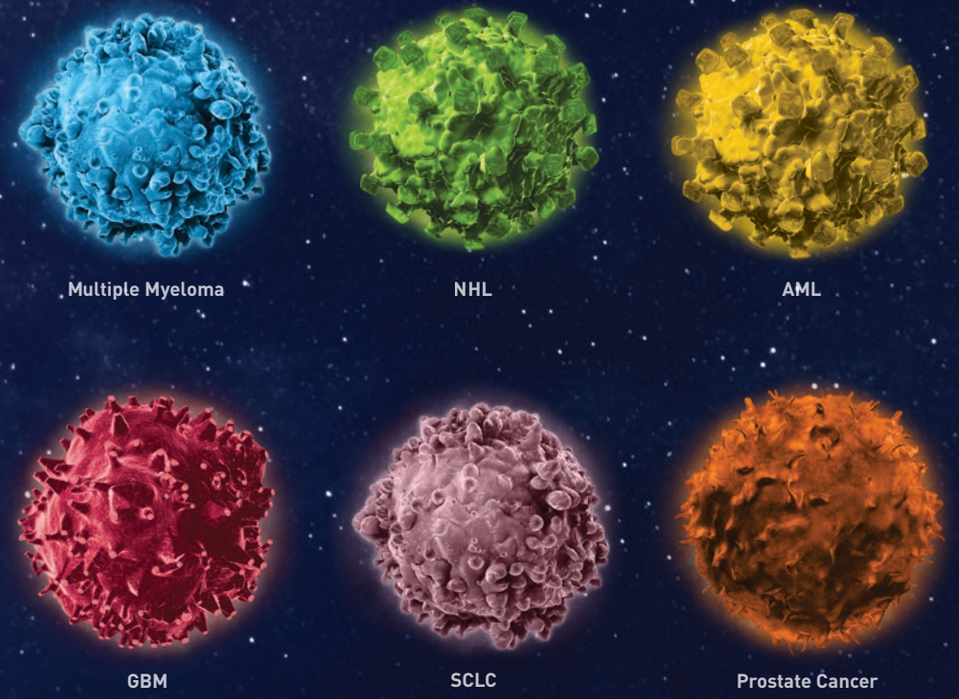
Amgen is a pioneer in immuno-oncology and developed the first approved BiTE® molecule. The BiTE® immuno-oncology platform continues to be investigated across multiple different hematologic malignancies and solid tumors.[8]

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 survival[14-16]

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® platform[9]



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

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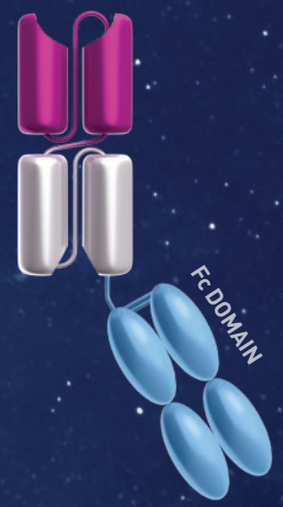
AMGEN IS COMMITTED TO BRINGING T CELL INNOVATION TO PATIENTS

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 pipeline[9]

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

*HLE BiTE® platform.

References:

1. Gomes-Silva D, Ramos CA. *Biotechnol J.* 2018;13. doi:10.1002/biot.201700097. **2.** Baeuerle PA, Kufer P, Bargou R. *Curr Opin Mol Ther.* 2009;11:22-30. **3.** Hartmann J, Schüßler-Lenz M, Bondanza A, et al. *EMBO Mol Med.* 2017;9:1183-1197. **4.** Frankel SR, Baeuerle PA. *Curr Opin Chem Biol.* 2013;17:385-392. **5.** Ferrone S, Whiteside TL. *Surg Oncol Clin N Am.* 2007;16:755-774. **6.** Nagorsen D, Baeuerle PA. *Exp Cell Res.* 2011;317:1255-1260. **7.** Baeuerle PA, Reinhardt C. *Cancer Res.* 2009;69:4941-4944. **8.** Yuraszeck T, Kasichayanula S, Benjamin JE. *Clin Pharmacol Ther.* 2017;101:634-645. **9.** Q4 2018 pipeline, Amgen. https://www.amgenpipeline.com/~/media/amgen/full/www-amgenpipeline-com/charts/amgen-pipeline-chart.ashx. Accessed March 4, 2019. **10.** ClinicalTrials.gov. https://clinicaltrials.gov/ct2/show/NCT02879695. Accessed May 13, 2019. **11.** Data on file, Amgen; 2019. **12.** Berry DA. *Clin Pharmacol Ther.* 2016;99:82-91. **13.** Amgen Science. https://www.amgenscience.com/features/a-strategy-for-making-clinical-trials-more-successful. Accessed May 13, 2019. **14.** Gökbuget N, Dombret H, Bonifacio M, et al. *Blood.* 2018;131:1522-1531. **15.** Hoelzer D. *Haematologica.* 2015;100:855-858. **16.** Harousseau JL, Avet-Loiseau H. *J Clin Oncol.* 2017;35:2863-2865. **17.** Weidle UH, Tiefenthaler G, Weiss EH, et al. *Cancer Genomics Proteomics.* 2013;10:1-18. **18.** Raum T, Münz M, Brozy J, inventors. US Patent 2017/0218077 A1. August 3, 2017.

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

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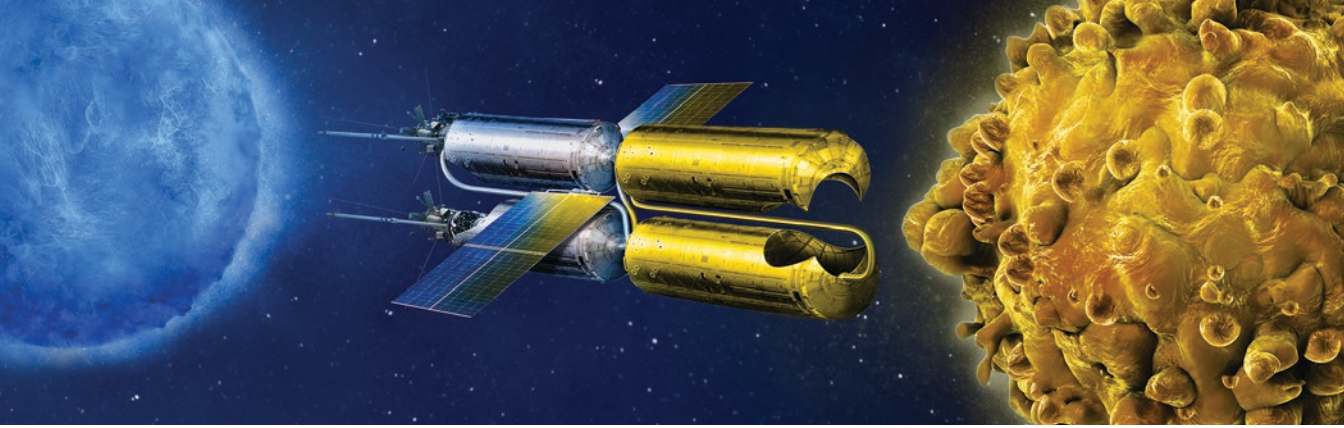

BiTE: THE ENGAGER™

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

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