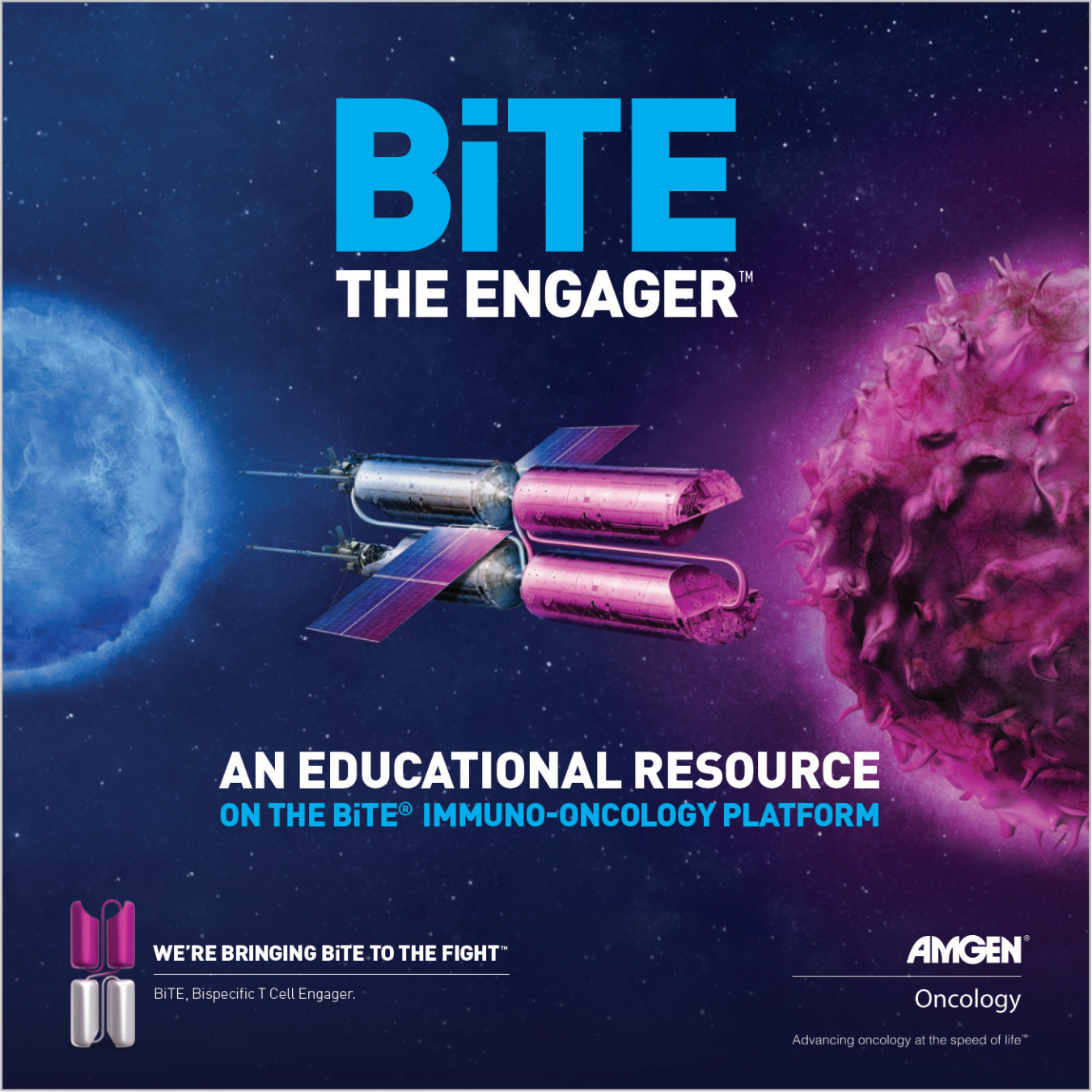
BiTE
THE ENGAGER™



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. Additional immuno-oncology options are needed to address both hematologic malignancies and solid tumors.

- Certain immuno-oncology therapies and chemotherapy do not target tumor-specific antigens[1,2]
- Not enough patients experience long-term benefits, and with the potential cost of high toxicity[2,3]

Considerations for addressing the unmet need[4,5]

- Avoid a lengthy, individualized manufacturing process, which can delay treatment
- Broader patient access
- Manage high treatment and patient care costs
- Limit the burden of care

Amgen is 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.[6-8]

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 specifically for a selected tumor antigen and the other specifically for CD3 found on T cells.[6,9-11]

The BiTE® molecule is designed to activate the cytotoxic potential of T cells with the goal of eliminating cancer cells.[6,12]

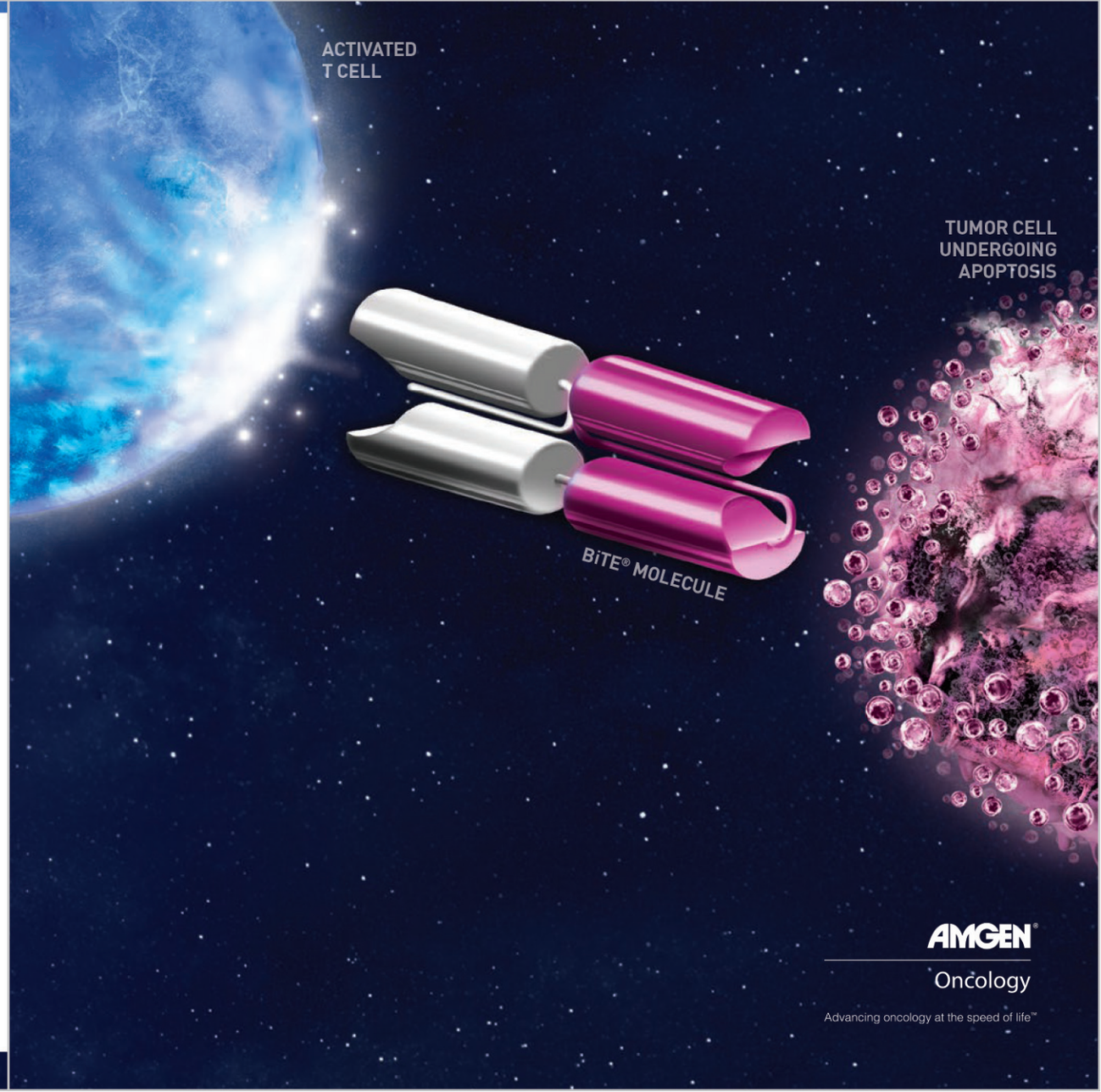
- Recruitment of a T cell to a cancer cell leads to the formation of a cytolytic synapse, triggering T-cell activation and the release of perforin and granzymes[6,12]
- Fusion of perforin with the cancer cell membrane allows granzymes, released by the cytotoxic T cell, to enter the cancer cell to induce apoptosis[10,12]

The goal of BiTE® technology is to eliminate cancer

Once T cells are activated by a BiTE® molecule, the T cells may induce further T-cell proliferation and cytokine production.[6,10,12]

- 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[6,12,13]
- Sustained activation of a single activated cytotoxic T cell theoretically results in local proliferation and expansion of polyclonal memory T cells[6,12,14]

CD, cluster of differentiation.



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

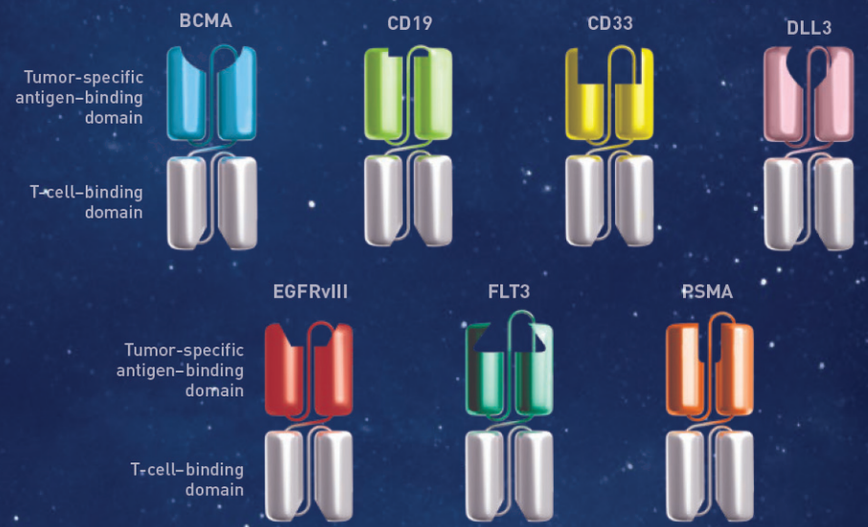
The BiTE® immuno-oncology platform offers versatility to potentially target any tumor-specific antigen

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.[6,9]

This approach is being studied across a wide range of settings[6,9,11]:

- 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[6]:



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® technology has the potential to be ready when patients need it

- Engineered to deliver off-the-shelf therapies to enable patients, including those with aggressive tumors, to initiate treatment immediately[6,9]
- Does not depend on ex vivo manipulation of patient's cells[6,9]
- Investigated for use as monotherapies and in combination with other treatments[10,11]

The goal of the BITE® immuno-oncology platform is to make innovative T-cell therapies available to more healthcare providers and their patients[6,9,11]

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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.[15]

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

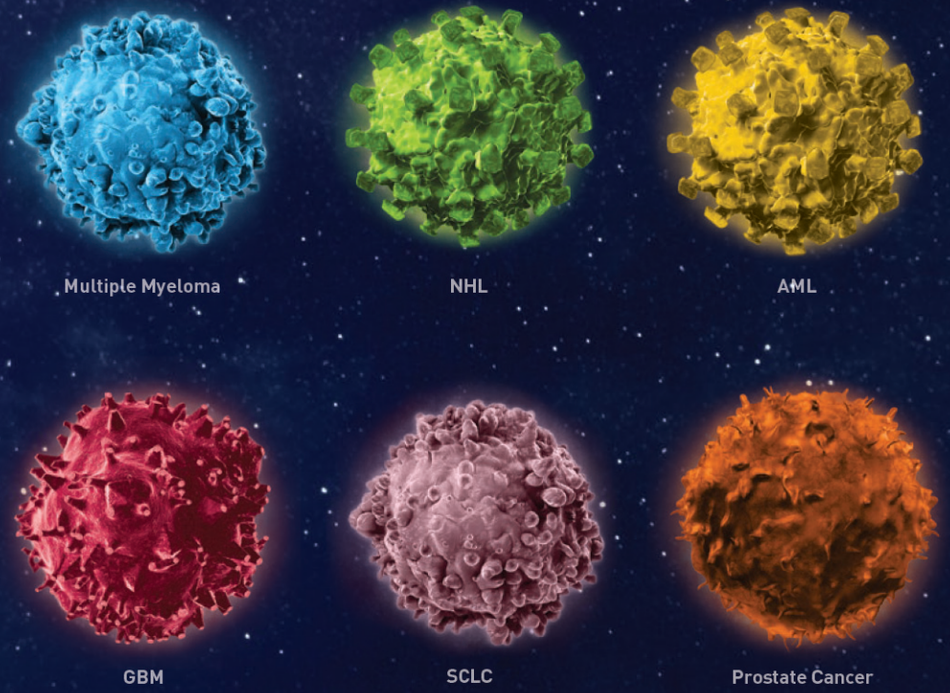
Amgen is a pioneer in the development of immuno-oncology therapies and has brought the first approved BiTE® molecule to the market. The BiTE® immuno-oncology platform continues to be investigated across multiple different hematologic malignancies and solid tumors.[11]

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.[16-19]

- Leveraging innovative trial designs
- Using clinically relevant endpoints and outcomes such as MRD negativity and long-term survival

BiTE® therapies are being investigated for use as monotherapies and in combination with other treatments[10,11]

Current and investigational cancers being targeted by the BiTE® platform



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

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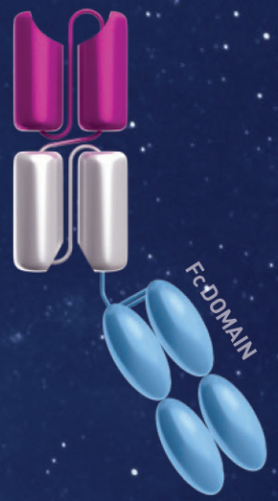
AMGEN IS COMMITTED TO BRINGING T-CELL INNOVATION TO MORE PATIENTS

Enhancing features of the BiTE® platform



Canonical BiTE® molecules are designed to be relatively small recombinant proteins that are cleared through the kidney, with the goal of a serum half-life of a few hours. Currently, the protein engineers at Amgen are designing BiTE® molecules with enhanced features, including a half-life extended (HLE) BiTE® molecule containing a fragment-crystallizable (Fc) domain. Adding an Fc portion to the BiTE® molecule is designed to extend the amount of time before it is eliminated from the body.[6,9,11,20-22]

It is anticipated that these HLE BiTE® molecules could potentially be infused less frequently.[22,23]

The growing BiTE® immuno-oncology pipeline[24]

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.

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

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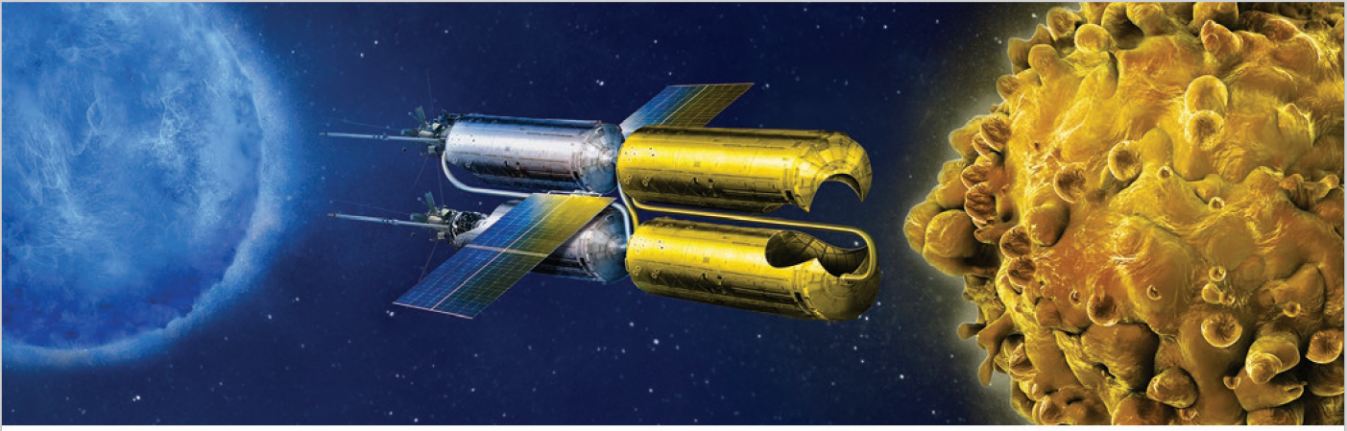

BiTE: THE ENGAGER™

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[6,9-11]
- Is being investigated in more than a thousand patients and continues to be investigated across multiple different hematologic malignancies and solid tumors[15,24]
- Pioneered by Amgen, who continues to accelerate the investigation of BiTE® technology with the goal of enhancing patient experience and therapeutic potential[10,11]

Learn more at amgenoncology.com

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