BiTE
THE ENGAGER

AN EDUCATIONAL RESOURCE
ON THE BiTE® IMMUNO-ONCOLOGY PLATFORM

WE’RE BRINGING
BiTE TO THE FIGHT™

BiTE, Bispecific T-cell Engager.
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.
The BiTE® molecule is designed to activate the cytotoxic potential of T cells with the goal of eliminating cancer cells.

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

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.

- 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.
- Sustained activation of a single activated cytotoxic T cell theoretically results in local proliferation and expansion of polyclonal memory T cells.

CD, cluster of differentiation.
The BiTE® immuno-oncology platform offers versatility to potentially target any tumor-associated antigen

The CD3-targeting domain is designed to bind to the T cell, while the other domain can be engineered to target tumor-associated antigens across both solid and hematologic malignancies.2 This approach is being studied across a wide range of settings:2,4

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

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

- Designed to target tumor-associated 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 cells2,4
- Investigated for use as monotherapies and in combination with other treatments7,8,12

The goal of the BiTE® immuno-oncology platform is to make innovative T-cell therapies available to more healthcare providers and their patients2,4

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

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
- Investigating 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

AML, acute myeloid leukemia; GBM, glioblastoma; MRD, minimal residual disease; NHL, non-Hodgkin’s lymphoma; SCLC, small cell lung cancer.
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. Currently, Amgen is designing BiTE® molecules with additional 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.

The growing BiTE® immuno-oncology pipeline

<table>
<thead>
<tr>
<th>Investigational BiTE® molecule</th>
<th>Tumor-associated antigen target</th>
<th>Cancer type</th>
</tr>
</thead>
<tbody>
<tr>
<td>AMG 160,* AMG 212</td>
<td>PSMA</td>
<td>Prostate cancer</td>
</tr>
<tr>
<td>AMG 199*</td>
<td>MUC17</td>
<td>Gastric or gastroesophageal junction cancer</td>
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<tr>
<td>AMG 330, AMG 673*</td>
<td>CD33</td>
<td>Acute myeloid leukemia</td>
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<tr>
<td>AMG 701*</td>
<td>BCMA</td>
<td>Multiple myeloma</td>
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<tr>
<td>AMG 427*</td>
<td>FLT3</td>
<td>Acute myeloid leukemia</td>
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<tr>
<td>AMG 562*</td>
<td>CD19</td>
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<tr>
<td>AMG 596</td>
<td>EGFRVIII</td>
<td>Glioblastoma</td>
</tr>
<tr>
<td>AMG 757*</td>
<td>DLL3</td>
<td>Small cell lung cancer</td>
</tr>
<tr>
<td>AMG 910*</td>
<td>CLDN18.2</td>
<td>Gastric or gastroesophageal junction cancer</td>
</tr>
</tbody>
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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™

The BiTE® universe is expanding

The BiTE® immuno-oncology platform:

- Engages patients’ own T cells to identified tumor-associated 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\(^10,13\)
- Pioneered by Amgen, which 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