Seagen®

DISITAMAB VEDOTIN

An investigational antibody-drug conjugate directed to HER2

Key Attributes

- Binds to a distinct epitope on subdomain IV of the HER2 extracellular domain[1,4]
- Optimized for enhanced internalization and delivery of cytotoxic MMAE to target cells

Anti-HER2 antibody

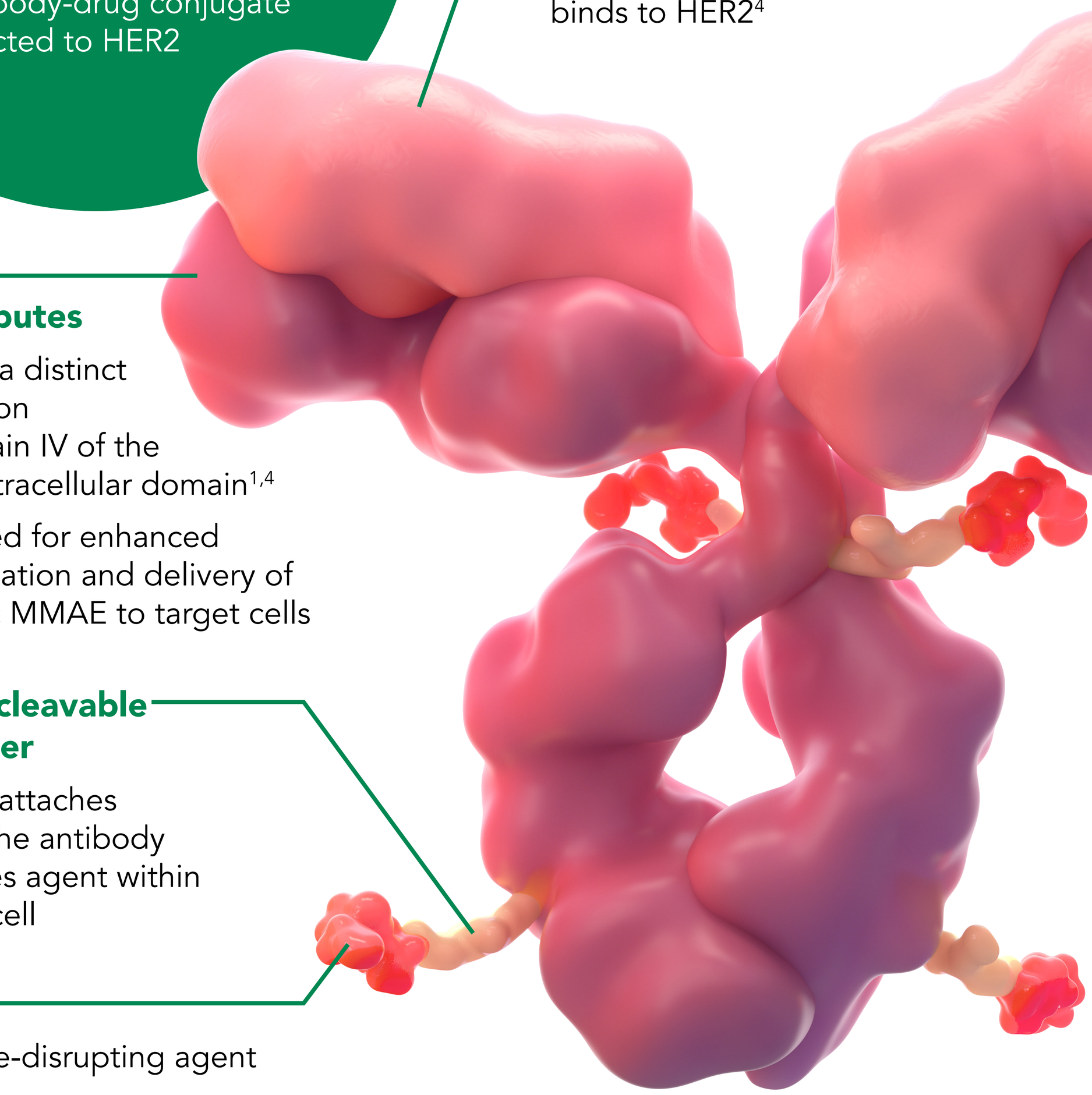
Recombinant, humanized, high-affinity IgG1 monoclonal antibody that binds to HER2[4]

Protease-cleavable mc-vc linker

Covalently attaches MMAE to the antibody and releases agent within the target cell

MMAE

Microtubule-disrupting agent



Target: HER2

- A receptor tyrosine kinase that regulates cell proliferation and differentiation[2]
- Overexpressed or amplified in multiple cancers (breast, gastroesophageal, bladder, colon, head and neck, ovarian, endometrial, lung etc)[3]
- Clinically validated as an oncogenic driver and/or therapeutic target in select cancers (breast, gastric, colon, and non-small cell lung cancer)[9,10]

Proposed Mechanism of Action[1,4-8,a]

- Direct cytotoxicity
- Bystander effect
- Immunogenic cell death
- HER2 signaling inhibition
- Antibody-dependent cellular cytotoxicity

HER2: human epidermal growth factor receptor 2; **mc-vc**: maleimidocaproyl-valine-citrulline; **MMAE**: monomethyl auristatin E

[a]Based on preclinical data

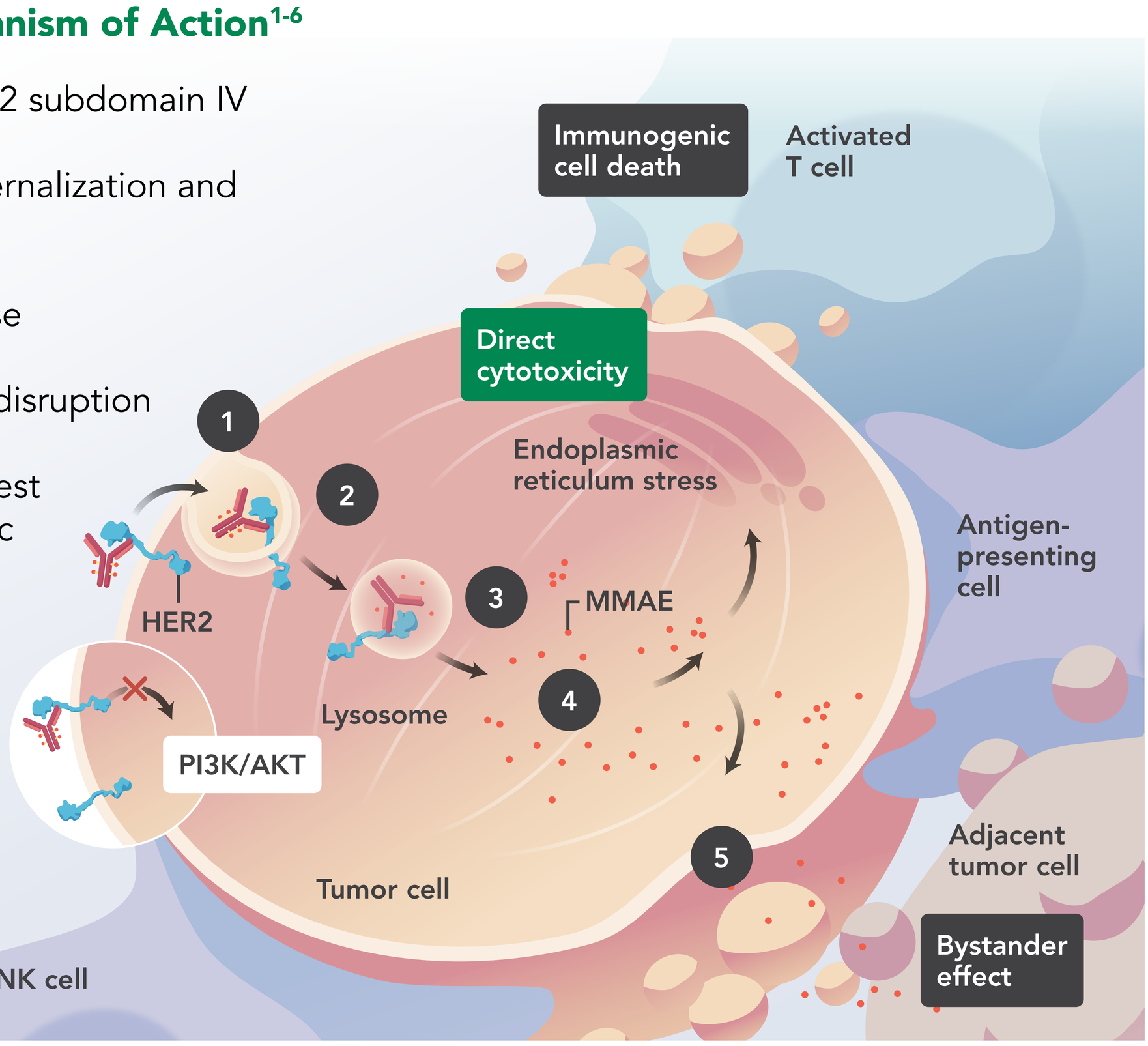
1. Yao X. Breast Cancer Res Treat. 2015: 123-33. 2. Olayioye MA. Breast Cancer Res. 2001: 385-9. 3. Scholl S. Ann Oncol. 2001: S81-7. 4. Li H. Cancer Biol Ther. 2016: 346-54. 5. Jiang J. Eur J Pharm Sci. 2016: 274-86. 6. Li L. Eur Rev Med Pharmacol Sci. 2020: 12929-37. 7. Klussman K. SITC virtual 2020: Poster 618. 8. Cao AT. AACR 2017: Abstract 5588. 9. Iqbal N. Mol Biol Int. 2014: 852748. 10. Strickler JH. ESMO GI 2022: Abstract LBA 2.

The safety and efficacy of this agent(s), or use in this setting, has not been established or is subject to confirmation. For an agent(s) whose safety and efficacy has not been established or confirmed, future regulatory approval or commercial availability is not guaranteed.

DISITAMAB VEDOTIN

Proposed Mechanism of Action[1-6]

1. Binds to HER2 subdomain IV
2. Complex internalization and trafficking
3. MMAE release
4. Microtubule disruption
5. Cell cycle arrest and apoptotic cell death



AKT: protein kinase; **HER2**: human epidermal growth factor receptor 2; **MMAE**: monomethyl auristatin E; **NK**: natural killer; **PI3K**: phosphoinositide 3-kinase

1. Yao X. Breast Cancer Res Treat. 2015: 123-33. 2. Li H. Cancer Biol Ther. 2016: 346-54. 3. Jiang J. Eur J Pharm Sci. 2016: 274-86. 4. Li L. Eur Rev Med Pharmacol Sci. 2020: 12929-37. 5. Klussman K. SITC virtual 2020: Poster 618. 6. Cao AT. AACR 2017: Abstract 5588.

Clinical Trials

	Phase 1	Phase 2	Phase 3
RECRUITING	**SGNDV-001[a]: Urothelial cancer with HER2 expression** (NCT05911295) Disitamab vedotin + pembrolizumab vs chemotherapy		
RECRUITING	**RC48 G001[b]: Locally advanced or metastatic urothelial cancer with HER2 expression** (NCT04879329) Disitamab vedotin ± pembrolizumab		
RECRUITING	**SGNDV-005: Locally advanced or metastatic solid tumors with HER2 expression** (NCT06003231) Disitamab vedotin alone		
ACTIVE, NOT YET RECRUITING	**SGNDV-004[c]: Locally advanced or metastatic breast cancer and gastric cancer with HER2 expression** (NCT########) Disitamab vedotin ± tucatinib		

FPO

[a]Trial in collaboration with RemeGen Co., Ltd. and Merck Sharp & Dohme LLC, a subsidiary of Merck & Co., Inc., Rahway, NJ, USA (MSD)
[b]Trial in collaboration with MSD
[c]Phase 1b/2

Clinical trial information retrieved from clinicaltrials.gov, accessed Oct 2023.

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