

# Discover CAR T BCMA binders

Learn more about the 3 types of specifically engineered binding domains below.

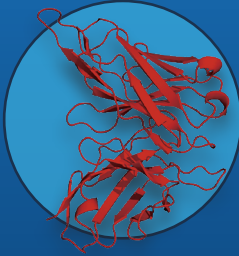


Image generated based on publicly available protein sequence using AlphaFold program.

## scFv

SINGLE-CHAIN  
VARIABLE FRAGMENT



Adapted from Buonato et al 2022.<sup>6</sup>

## D-Domain

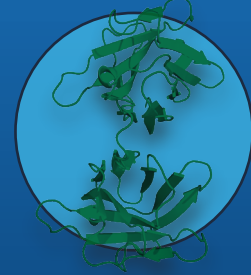


Image generated based on publicly available protein sequence using AlphaFold program.

## VHH

SINGLE-VARIABLE DOMAIN  
ON A HEAVY CHAIN

<b>SIZE</b> 28 kDa <sup>1</sup>	<b>SIZE</b> 8 kDa <sup>6</sup>	<b>SIZE</b> 30-35 kDa <sup>10,c</sup>
<b>SOURCE</b> Murine <sup>2</sup>	<b>SOURCE</b> Fully synthetic <sup>6</sup>	<b>SOURCE</b> Bivalent camelid <sup>11</sup>
<b>STRUCTURE</b> Variable light chain and variable heavy chain of an antibody connected by a flexible linker peptide <sup>3</sup>	<b>STRUCTURE</b> Triple-helical bundle held together with hydrophobic core <sup>6,7</sup>	<b>STRUCTURE</b> Variable domains of heavy-chain antibodies <sup>11</sup>
<b>CAR POSITIVITY</b> Median, 47%; range, 26%-79% <sup>4,a</sup>	<b>CAR POSITIVITY</b> Median, 82%; range, 72%-88% <sup>6,8,b</sup>	<b>CAR POSITIVITY</b> Median, 16%; range, 6%-28% <sup>12,d</sup>
<b>TRIAL STATUS</b> Phase 3 <sup>5</sup>	<b>TRIAL STATUS</b> Phase 2 <sup>9</sup>	<b>TRIAL STATUS</b> Phase 4 <sup>13</sup>

The safety and efficacy of this technology have not been established. This investigational technology has not been approved, cleared, or licensed.

<sup>a</sup>Phase 1 multicenter dose-escalation trial of an anti-BCMA CAR T in patients with relapsed or refractory multiple myeloma (n=21).<sup>4</sup>

<sup>b</sup>Preclinical study of a BCMA-directed CAR T (n=9).<sup>6,8</sup>

<sup>c</sup>Approximate size of 2 identical VHH domains connected by a linker peptide.<sup>10</sup>

<sup>d</sup>Translational data from a Phase 1b cohort of an ongoing Phase 1b/2 study of a BCMA-targeted CAR T in patients with relapsed or refractory multiple myeloma (n=25).<sup>12</sup>

Abbreviations: BCMA, B-cell maturation antigen; CAR T, chimeric antigen receptor T cell.



**References:** **1.** Bjerregaard-Andersen K, Johannesen H, Abdel-Rahman N, et al. Crystal structure of an L chain optimised 14F7 anti-ganglioside Fv suggests a unique tumour-specificity through an unusual H-chain CDR3 architecture. *Sci Rep.* 2018;8(1):10836. doi:10.1038/s41598-018-28918-5. **2.** Friedman KM, Garrett TE, Evans JW, et al. Effective targeting of multiple B-cell maturation antigen-expressing hematological malignancies by anti-B-cell maturation antigen chimeric antigen receptor T cells. *Hum Gene Ther.* 2018;29(5):585-601. doi:10.1089/hum.2018.001. **3.** Monnier PP, Vigoroux RJ, Tassew NG. In vivo applications of single chain Fv (variable domain) (scFv) fragments. *Antibodies.* 2013;2(2):193-208. doi:10.3390/antib2020193. **4.** Berdeja JG, Lin Y, Raje N, et al. Durable clinical responses in heavily pretreated patients with relapsed/refractory multiple myeloma: updated results from a multicenter study of bb2121 anti-Bcma CAR T cell therapy. *Blood.* 2017;130(suppl 1):740. doi:10.1182/blood.V130.Suppl\_1.740.740. **5.** A study to compare the efficacy and safety of idecabtagene vicleucel with lenalidomide maintenance therapy versus lenalidomide maintenance therapy alone in adult participants with newly diagnosed multiple myeloma who have suboptimal response after autologous stem cell transplantation (KarMMa-9). ClinicalTrials.gov website. Updated October 30, 2023. Accessed November 6, 2023. <https://classic.clinicaltrials.gov/ct2/show/NCT06045806>. **6.** Buonato JM, Edwards JP, Zaritskaya L, et al. Preclinical efficacy of BCMA-directed CAR T cells incorporating a novel D domain antigen recognition domain. *Mol Cancer Ther.* 2022;21(7):1171-1183. doi:10.1158/1535-7163.MCT-21-0552. **7.** Qin H, Edwards JP, Zaritskaya L, et al. Chimeric antigen receptors incorporating D domains targeting CD123 direct potent mono- and bi-specific antitumor activity of T cells. *Mol Ther.* 2019;27(7):1262-1274. doi:10.1016/j.ymthe.2019.04.010. **8.** Buonato JM, Edwards JP, Zaritskaya L, et al. Preclinical efficacy of BCMA-directed CAR T cells incorporating a novel D domain antigen recognition domain. Supplementary appendix. *Mol Cancer Ther.* 2022;21(7):1171-1183. Accessed November 6, 2023. [https://aacr.figshare.com/articles/journal\\_contribution/Supplementary\\_Figure\\_from\\_Preclinical\\_Efficacy\\_of\\_BCMA-Directed\\_CAR\\_T\\_Cells\\_Incorporating\\_a\\_Novel\\_D\\_Domain\\_Antigen\\_Recognition\\_Domain/22522623/1](https://aacr.figshare.com/articles/journal_contribution/Supplementary_Figure_from_Preclinical_Efficacy_of_BCMA-Directed_CAR_T_Cells_Incorporating_a_Novel_D_Domain_Antigen_Recognition_Domain/22522623/1). **9.** Study of CART-ddBCMA in relapsed or refractory multiple myeloma (iMMagine-1). ClinicalTrials.gov website. Updated September 29, 2023. Accessed November 13, 2023. <https://classic.clinicaltrials.gov/ct2/show/NCT05396885>. **10.** Bannas P, Hambach J, Koch-Nolte F. Nanobodies and nanobody-based human heavy chain antibodies as antitumor therapeutics. *Front Immunol.* 2017;8:1603. doi:10.3389/fimmu.2017.01603. **11.** Abebe EC, Shiferaw MY, Admasu FT, Dejenie TA. Ciltacabtagene autoleucel: The second anti-BCMA CAR T-cell therapeutic armamentarium of relapsed or refractory multiple myeloma. *Front Immunol.* 2022;13:991092. doi:10.3389/fimmu.2022.991092. **12.** Zudaire E, Madduri D, Usmani SZ, et al. Translational analysis from CARTITUDE-1, an ongoing phase 1b/2 study of JNJ-4528 BCMA-targeted CAR-T cell therapy in relapsed and/or refractory multiple myeloma (R/R MM), indicates preferential expansion of CD8+ T cell central memory cell subset. *Blood.* 2019;134(suppl 1):928. doi:10.1182/blood-2019-127309. **13.** A long-term study for participants previously treated with ciltacabtagene autoleucel. ClinicalTrials.gov website. Updated October 11, 2023. Accessed November 6, 2023. <https://clinicaltrials.gov/study/NCT05201781>.