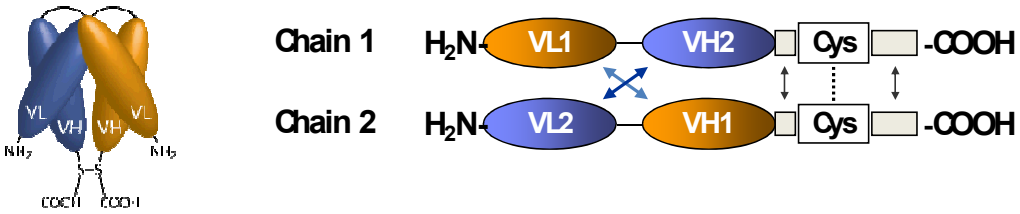
S.1.2 STRUCTURE (MGD006)

MGD006 is a CD123 x CD3 Dual Affinity Re-Targeting (DART®) protein produced in CHO cells. DART proteins are bi-specific, antibody-based molecules that can bind two distinct antigens simultaneously (**Figure S.1.2-1**). MGD006 is designed to target CD123-positive cells for recognition and elimination by CD3-expressing T lymphocytes as effector cells.

Figure S.1.2-1. DART Protein Schematic and Assembly



Johnson et al. *J. Mol. Biol.* **399**: 436-349, 2010

MGD006 is a heterodimeric protein composed of two chains that are covalently linked by a disulfide bond near the C-terminus of each chain. Following the Cys residues on the respective chains that form the interchain disulfide are oppositely charged coiled-coil sequences designated as E-coil (Chain 1) and K-coil (Chain 2) that promote and stabilize formation of the heterodimer. The two chains are held together by the disulfide bond and by non-covalent forces.

Chain 1, shown in **Figure S.1.2-2**, comprises the variable region light chain (VL) of the humanized anti-CD3 monoclonal antibody (mAb) hXR32 linked to the variable region heavy chain (VH) of the anti-CD123 mAb h7G3, followed by a short linker sequence (GGCGGG) containing the Cys residue that forms the interchain disulfide, and the E-coil sequence. Chain 2, shown in **Figure S.1.2-3**, comprises the VL of h7G3 linked to the VH of hXR32, followed by a short linker sequence containing a single Cys residue, and the K-coil sequence. Short linker sequences (GGGSGGGG) between the VL and VH segments promote 'diabody'-type association. The E- and K-coils promote the desired heterodimeric bispecific diabody structure. The interchain disulfide stabilizes the desired structure.

Chain 1 has a reduced molecular weight (MW) of 28577.9 Da (with pyroglutamic acid on the N-terminus). Chain 2 has a reduced MW of 30329.6 Da. The MW of the intact molecule, with 5 disulfide bridges, is 58897.4 Da. Locations of the disulfide bridges are shown in **Section S.3.1.1**. MGD006 has no predicted sites of glycosylation.

Figure S.1.2-2. Protein Sequence of MGD006 Chain 1

```
1   QAVVTQEPSLTVSPGGTVTLTCRSSTGAVTTSNYANWVQQKPGQAPRGLI
51  GGTNKRAPWTPARFSGSLLGGKAALTITGAQAEDEADYYCALWYSNLWVF
101 GGGTKLTVLGGGGSGGGGEVQLVQSGAELKKPGASVKVSCKASGYTFTDY
151 YMKWVRQAPGQGLEWIGDIIPSNGATFYNQKFKGRVTITVDKSTSTAYME
201 LSSLRSEDTAVYYCARSHLLRASWFAYWGQGTLVTVSSGGCGGGEVAALE
251 KEVAALEKEVAALEKEVAALEK
```

N-terminal glutamine of Chain 1 is modified to pyroglutamic acid.

Figure S.1.2-3. Protein Sequence of MGD006 Chain 2

```
1   DFVMTQSPDSLAVSLGERVTMSCKSSQSLLNSGNQKNYLTWYQQKPGQPP
51  KLLIYWASTRESGVPDRFSGSGSGTDFTLTISSLQAEDVAVYYCQNDYSY
101 PYTFGQGTKLEIKGGGSGGGGEVQLVESGGGLVQPGGSLRLSCAASGFTF
151 STYAMNWVRQAPGKGLEWVGRIRSKYNNYATYYADSVKDRFTISRDDSKN
201 SLYLQMNSLKTEDTAVYYCVRHGNFGNSYVSWFAYWGQGTLVTVSSGGCG
251 GGKVAALKEKVAALKEKVAALKEKVAALKE
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