

CLAIMS

1. An anti-TCR delta variable 1 (anti-V δ 1) antibody or antigen-binding fragment thereof comprising:
a heavy chain variable region and a light chain variable region, the antibody or antigen-binding fragment thereof comprising:

a VHCDR1 comprising or consisting of an amino acid sequence having at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% identity to a sequence selected from the group consisting of: SEQ ID NOs: 51, 52 and 130;

a VHCDR2 comprising or consisting of an amino acid sequence having at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% identity to a sequence selected from the group consisting of: SEQ ID NO: 53 and 131; and

a VHCDR3 comprising or consisting of an amino acid sequence having at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% identity to a sequence selected from the group consisting of: SEQ ID NOs: 68, 55 to 67, 69 to 78 and 133 to 143; and/or

a light chain variable region comprising:

a VLCDR1 comprising or consisting of an amino acid sequence having at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% identity to a sequence selected from the group consisting of: SEQ ID NO: 79 and 144;

a VLCDR2 comprising or consisting of an amino acid sequence having at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% identity to a sequence selected from the group consisting of: SEQ ID NO: 80 and 145; and

a VLCDR3 comprising or consisting of an amino acid sequence having at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% identity to a sequence selected from the group consisting of: SEQ ID NOs: 95, 82 to 94, 96 to 105 and 147 to 157.

2. ~~The anti-V δ 1 antibody or antigen-binding fragment thereof of claim 1, comprising:~~

a. a VHCDR1, a VHCDR2 and a VHCDR3 comprising the amino acid sequences of SEQ ID NO: 51, 53 and 68, respectively, and a VLCDR1, a VLCDR2 and a VLCDR3 comprising the amino acid sequences of SEQ ID NOs: 79, 80 and 95, respectively;

b. a VHCDR1, a VHCDR2 and a VHCDR3 comprising the amino acid sequences of SEQ ID NO: 51, 53 and 55, respectively, and a VLCDR1, a VLCDR2 and a VLCDR3 comprising the amino acid sequences of SEQ ID NOs: 79, 80 and 82, respectively;

c. a VHCDR1, a VHCDR2 and a VHCDR3 comprising the amino acid sequences of SEQ ID NO: 51, 53 and 56, respectively, and a VLCDR1, a VLCDR2 and a VLCDR3 comprising the amino acid sequences of SEQ ID NOs: 79, 80 and 83, respectively;

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- ff. a VHCDR1, a VHCDR2 and a VHCDR3 comprising the amino acid sequences of SEQ ID NO: 130, 131 and 140, respectively, and a VLCDR1, a VLCDR2 and a VLCDR3 comprising the amino acid sequences of SEQ ID NOs: 144, 145 and 154, respectively;
- gg. a VHCDR1, a VHCDR2 and a VHCDR3 comprising the amino acid sequences of SEQ ID NO: 130, 131 and 141, respectively, and a VLCDR1, a VLCDR2 and a VLCDR3 comprising the amino acid sequences of SEQ ID NOs: 144, 145 and 155, respectively;
- hh. a VHCDR1, a VHCDR2 and a VHCDR3 comprising the amino acid sequences of SEQ ID NO: 130, 131 and 142, respectively, and a VLCDR1, a VLCDR2 and a VLCDR3 comprising the amino acid sequences of SEQ ID NOs: 144, 145 and 156, respectively; or
- ii. a VHCDR1, a VHCDR2 and a VHCDR3 comprising the amino acid sequences of SEQ ID NO: 130, 131 and 143, respectively, and a VLCDR1, a VLCDR2 and a VLCDR3 comprising the amino acid sequences of SEQ ID NOs: 144, 145 and 157, respectively.

2. The anti-TCR delta variable 1 (anti-V δ 1) antibody or antigen-binding fragment thereof of claim 1 comprising a heavy chain variable region and a light chain variable region, the antibody or antigen-binding fragment thereof comprising:

- a. a VHCDR1, a VHCDR2 and a VHCDR3 comprising the amino acid sequences of SEQ ID NO: 51, 53 and 68, respectively, and a VLCDR1, a VLCDR2 and a VLCDR3 comprising the amino acid sequences of SEQ ID NOs: 79, 80 and 95, respectively;
- b. a VHCDR1, a VHCDR2 and a VHCDR3 comprising the amino acid sequences of SEQ ID NO: 51, 53 and 58, respectively, and a VLCDR1, a VLCDR2 and a VLCDR3 comprising the amino acid sequences of SEQ ID NOs: 79, 80 and 85, respectively;
- c. a VHCDR1, a VHCDR2 and a VHCDR3 comprising the amino acid sequences of SEQ ID NO: 51, 53 and 60, respectively, and a VLCDR1, a VLCDR2 and a VLCDR3 comprising the amino acid sequences of SEQ ID NOs: 79, 80 and 87, respectively;
- d. a VHCDR1, a VHCDR2 and a VHCDR3 comprising the amino acid sequences of SEQ ID NO: 52, 53 and 61, respectively, and a VLCDR1, a VLCDR2 and a VLCDR3 comprising the amino acid sequences of SEQ ID NOs: 79, 80 and 88, respectively;
- e. a VHCDR1, a VHCDR2 and a VHCDR3 comprising the amino acid sequences of SEQ ID NO: 51, 53 and 62, respectively, and a VLCDR1, a VLCDR2 and a VLCDR3 comprising the amino acid sequences of SEQ ID NOs: 79, 80 and 89, respectively;
- f. a VHCDR1, a VHCDR2 and a VHCDR3 comprising the amino acid sequences of SEQ ID NO: 51, 53 and 65, respectively, and a VLCDR1, a VLCDR2 and a VLCDR3 comprising the amino acid sequences of SEQ ID NOs: 79, 80 and 92, respectively;
- g. a VHCDR1, a VHCDR2 and a VHCDR3 comprising the amino acid sequences of SEQ ID NO: 52, 53 and 66, respectively, and a VLCDR1, a VLCDR2 and a VLCDR3 comprising the amino acid sequences of SEQ ID Nos: 79, 80 and 93, respectively;
- h. a VHCDR1, a VHCDR2 and a VHCDR3 comprising the amino acid sequences of SEQ ID NO: 52, 53 and 74, respectively, and a VLCDR1, a VLCDR2 and a VLCDR3 comprising the amino acid sequences of SEQ ID NOs: 79, 80 and 101, respectively;

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- i. a VHCDR1, a VHCDR2 and a VHCDR3 comprising the amino acid sequences of SEQ ID NO: 51, 53 and 76, respectively, and a VLCDR1, a VLCDR2 and a VLCDR3 comprising the amino acid sequences of SEQ ID NOs: 79, 80 and 103, respectively;
- j. a VHCDR1, a VHCDR2 and a VHCDR3 comprising the amino acid sequences of SEQ ID NO: 51, 53 and 77, respectively, and a VLCDR1, a VLCDR2 and a VLCDR3 comprising the amino acid sequences of SEQ ID NOs: 79, 80 and 104, respectively;
- k. a VHCDR1, a VHCDR2 and a VHCDR3 comprising the amino acid sequences of SEQ ID NO: 51, 53 and 78, respectively, and a VLCDR1, a VLCDR2 and a VLCDR3 comprising the amino acid sequences of SEQ ID NOs: 79, 80 and 105, respectively;
- 10 l. a VHCDR1, a VHCDR2 and a VHCDR3 comprising the amino acid sequences of SEQ ID NO: 130, 131 and 138, respectively, and a VLCDR1, a VLCDR2 and a VLCDR3 comprising the amino acid sequences of SEQ ID NOs: 144, 145 and 152, respectively;
- m. a VHCDR1, a VHCDR2 and a VHCDR3 comprising the amino acid sequences of SEQ ID NO: 130, 131 and 142, respectively, and a VLCDR1, a VLCDR2 and a VLCDR3 comprising the amino acid sequences of SEQ ID NOs: 144, 145 and 156, respectively; or
- 15 n. a VHCDR1, a VHCDR2 and a VHCDR3 comprising the amino acid sequences of SEQ ID NO: 130, 131 and 143, respectively, and a VLCDR1, a VLCDR2 and a VLCDR3 comprising the amino acid sequences of SEQ ID NOs: 144, 145 and 157, respectively.

- 20 ~~3. The anti-TCR delta variable 1 (anti-Vδ1) antibody or antigen-binding fragment thereof of claim 1 or claim 2, comprising:~~
- ~~a heavy chain variable region comprising or consisting of a sequence having at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% identity to a sequence selected from the group consisting of SEQ~~
- 25 ~~ID NOs: 15, 2 to 14, 16 to 25 and 107 to 117; and/or~~
- ~~a light chain variable region comprising or consisting of a sequence having at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% identity to a sequence selected from the group consisting of SEQ~~
- 30 ~~ID NOs: 40, 27 to 39, 41 to 50 and 119 to 129.~~

- 4.3. The anti-Vδ1 antibody or antigen-binding fragment thereof of any preceding claim, comprising:
- a. a VH comprising an amino acid sequence having at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% sequence identity to SEQ ID NO: 15 and a VL comprising an amino acid sequence having at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% sequence identity to SEQ ID NO: 40;
- 35 b. a VH comprising an amino acid sequence having at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% sequence identity to SEQ ID NO: 2 and a VL comprising an amino acid sequence having at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at
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least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% sequence identity to SEQ ID NO: 42;

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least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% sequence identity to SEQ ID NO: 124;

ee. a VH comprising an amino acid sequence having at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% sequence identity to SEQ ID NO: 113 and a VL comprising an amino acid sequence having at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% sequence identity to SEQ ID NO: 125;

ff. a VH comprising an amino acid sequence having at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% sequence identity to SEQ ID NO: 114 and a VL comprising an amino acid sequence having at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% sequence identity to SEQ ID NO: 126;

gg. a VH comprising an amino acid sequence having at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% sequence identity to SEQ ID NO: 115 and a VL comprising an amino acid sequence having at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% sequence identity to SEQ ID NO: 127;

hh. a VH comprising an amino acid sequence having at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% sequence identity to SEQ ID NO: 116 and a VL comprising an amino acid sequence having at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% sequence identity to SEQ ID NO: 128; or

ii. a VH comprising an amino acid sequence having at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% sequence identity to SEQ ID NO: 117 and a VL comprising an amino acid sequence having at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% sequence identity to SEQ ID NO: 129.

4. The anti-TCR delta variable 1 (anti-V δ 1) antibody or antigen-binding fragment thereof of claim 3 comprising a heavy chain variable region and a light chain variable region, the antibody or antigen-binding fragment thereof comprising:

a. a VH comprising an amino acid sequence having at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% sequence identity to SEQ ID NO: 15 and a VL comprising an amino acid sequence having at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at

- least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% sequence identity to SEQ ID NO: 46;
- 5 i. a VH comprising an amino acid sequence having at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% sequence identity to SEQ ID NO: 23 and a VL comprising an amino acid sequence having at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% sequence identity to SEQ ID NO: 48;
- 10 j. a VH comprising an amino acid sequence having at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% sequence identity to SEQ ID NO: 24 and a VL comprising an amino acid sequence having at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% sequence identity to SEQ ID NO: 49;
- 15 k. a VH comprising an amino acid sequence having at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% sequence identity to SEQ ID NO: 25 and a VL comprising an amino acid sequence having at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% sequence identity to SEQ ID NO: 50;
- 20 l. a VH comprising an amino acid sequence having at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% sequence identity to SEQ ID NO: 112 and a VL comprising an amino acid sequence having at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% sequence identity to SEQ ID NO: 124;
- 25 m. a VH comprising an amino acid sequence having at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% sequence identity to SEQ ID NO: 116 and a VL comprising an amino acid sequence having at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% sequence identity to SEQ ID NO: 128; or
- 30 n. a VH comprising an amino acid sequence having at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% sequence identity to SEQ ID NO: 117 and a VL comprising an amino acid sequence having at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least 99% or 100% sequence identity to SEQ ID NO: 129.
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- 40 5. An anti-TCR delta variable 1 (anti-V δ 1) antibody or antigen-binding fragment thereof comprising:
- a. a VH comprising an amino acid sequence having at least 90%, at least 91%, at least 92%, at least 93%, at least 94%, at least 95%, at least 96%, at least 97%, at least 98%, at least

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5-7. The anti-V δ 1 antibody or antigen-binding fragment thereof of any preceding claim, wherein the antibody or antigen-binding fragment thereof comprises an amino acid residue other than serine at position 74 according to the IMGT kappa variable light chain sequence numbering system, optionally wherein the residue at position 74 according to the IMGT numbering system is a leucine residue.

6-8. An anti-TCR delta variable 1 (anti-V δ 1) antibody or antigen-binding fragment thereof, wherein the antibody or antigen-binding fragment thereof comprises:

- a. an HCDR1 sequence comprising the sequence of GDSVSSKSX₁A (SEQ ID NO: 158);
- b. an HCDR2 sequence comprising the sequence of SEQ ID NO: 53
- c. an HCDR3 sequence comprising the sequence of X₂WX₃X₄X₅X₆DX₇ (SEQ ID NO: 162), wherein the HCDR3 sequence is not SEQ ID NO: 54;
- d. an LCDR1 sequence comprising the sequence of SEQ ID NO: 79;
- e. an LCDR2 sequence comprising the sequence of SEQ ID NO: 80; and
- f. an LCDR3 sequence comprising the sequence of QQX₈YX₉X₁₀X₁₁X₁₂X₁₃T (SEQ ID NO: 166), wherein the LCDR3 sequence is not SEQ ID NO: 81;

wherein each of X₁ to X₁₃ is a naturally occurring amino acid.

or wherein the antibody or antigen-binding fragment thereof comprises:

- a. an HCDR1 sequence comprising the sequence of SEQ ID NO: 130
- b. an HCDR2 sequence comprising the sequence of SEQ ID NO: 131
- c. an HCDR3 sequence comprising the sequence of X₁X₂YX₃X₄AFDI, wherein the HCDR3 sequence is not SEQ ID NO: 132;
- d. an LCDR1 sequence comprising the sequence of SEQ ID NO: 144;
- e. an LCDR2 sequence comprising the sequence of SEQ ID NO: 145; and
- f. an LCDR3 sequence comprising the sequence of QQX₅X₆X₇X₈LX₉T, wherein the LCDR3 sequence is no SEQ ID NO: 146;

wherein each of X₁ to X₉ is a naturally occurring amino acid.

7-9. An anti-TCR delta variable 1 (anti-V δ 1) antibody or antigen-binding fragment thereof, wherein the anti-V δ 1 antibody or antigen-binding fragment thereof is an affinity matured variant of a parent anti-V δ 1 antibody or antigen-binding fragment thereof, wherein the parent anti-V δ 1 antibody or antigen-binding fragment thereof comprises:

- a. a VH comprising the amino acid sequence of SEQ ID NO: 1 and a VL sequence comprising the amino acid sequence of SEQ ID NO: 26;
- b. a VH comprising the amino acid sequence of SEQ ID NO: 106 and a VL sequence comprising the amino acid sequence of SEQ ID NO: 118;
- c. a VH comprising the amino acid sequence of SEQ ID NO: 273 and a VL comprising the amino acid sequence of SEQ ID NO: 282;
- d. a VH comprising the amino acid sequence of SEQ ID NO: 274 and a VL comprising the amino acid sequence of SEQ ID NO: 283;
- e. a VH comprising the amino acid sequence of SEQ ID NO: 275 and a VL comprising the amino acid sequence of SEQ ID NO: 284;

- f. a VH comprising the amino acid sequence of SEQ ID NO: 276 and a VL comprising the amino acid sequence of SEQ ID NO: 285;
- g. a VH comprising the amino acid sequence of SEQ ID NO: 277 and a VL comprising the amino acid sequence of SEQ ID NO: 286;
- h. a VH comprising the amino acid sequence of SEQ ID NO: 278 and a VL comprising the amino acid sequence of SEQ ID NO: 287;
- i. a VH comprising the amino acid sequence of SEQ ID NO: 279 and a VL comprising the amino acid sequence of SEQ ID NO: 288;
- j. a VH comprising the amino acid sequence of SEQ ID NO: 280 and a VL comprising the amino acid sequence of SEQ ID NO: 289;
- k. a VH comprising the amino acid sequence of SEQ ID NO: 281 and a VL comprising the amino acid sequence of SEQ ID NO: 290; or
- l. a VH comprising the amino acid sequence of SEQ ID NO: 312 and a VL comprising the amino acid sequence of SEQ ID NO: 313;

optionally wherein:

the affinity matured antibody has at least 20%, at least 30%, at least 40%, at least 50%, at least 100%, at least 500% or more preferably at least about 1000% greater affinity than the parental antibody for binding to a variable delta 1 (V δ 1) chain of a $\gamma\delta$ T cell receptor (TCR), for example as measured by the K_d;

the affinity matured anti-V δ 1 antibody or antigen-binding fragment thereof comprises VH and VL sequences that are at least 80%, at least 90%, at least 95% or at least 96% identical to the corresponding parental VH and VL sequences; and/or

the affinity matured anti-V δ 1 antibody or antigen-binding fragment comprises up to 20, for example up to 15, for example up to 10 amino acid substitutions compared to the parental antibody sequences.

8-10. An anti-V δ 1 antibody or antigen-binding fragment, wherein the antibody is a multispecific antibody that specifically binds:

- a. a first target epitope, wherein the first target epitope is an epitope of the variable delta 1 (V δ 1) chain of a $\gamma\delta$ T cell receptor (TCR); and
- b. a second target epitope;

wherein the multispecific antibody comprises SEQ ID NO: 385; SEQ ID NO: 386; SEQ ID NO: 387; SEQ ID NO: 314; ~~SEQ ID NO: 393~~; SEQ ID NO: 394; SEQ ID NO: 395; SEQ ID NO: 397; SEQ ID NO: 388; ~~SEQ ID NO: 315~~; SEQ ID NO: 316; SEQ ID NO: 378; SEQ ID NO: 379; SEQ ID NO: 380; SEQ ID NO: 382; SEQ ID NO: 383; SEQ ID NO: 384; SEQ ID NO: 393; SEQ ID NO: 396; SEQ ID NO: 398; SEQ ID NO: 399; ~~SEQ ID NO: 401~~; SEQ ID NO: 402; SEQ ID NO: 403; SEQ ID NO: 404; SEQ ID NO: 405; SEQ ID NO: 406; SEQ ID NO: 407; SEQ ID NO: 408; SEQ ID NO: 409; SEQ ID NO: 410; SEQ ID NO: 411; SEQ ID NO: 412; SEQ ID NO: 413; SEQ ID NO: 414 and SEQ ID NO: 415; SEQ ID NO: 414 and SEQ ID NO: 416; SEQ ID NO: 414 and SEQ ID NO: 419; SEQ ID NO: 414 and SEQ ID NO: 418; SEQ ID NO: 504 and SEQ ID NO: 415; SEQ ID NO: 504 and SEQ ID NO: 416; SEQ ID NO: 504 and SEQ ID NO: 419; SEQ ID NO: 504 and SEQ ID NO: 418; SEQ ID NO: 505 and SEQ ID NO: 415; SEQ ID NO: 505 and SEQ ID NO: 416;

SEQ ID NO: 505 and SEQ ID NO: 419; SEQ ID NO: 505 and SEQ ID NO: 418; SEQ ID NO: 421 and SEQ ID NO: 422; SEQ ID NO: 504 and SEQ ID NO: 422; SEQ ID NO: 423 and SEQ ID NO: 424; SEQ ID NO: 425 and SEQ ID NO: 426; SEQ ID NO: 421 and SEQ ID NO: 437; SEQ ID NO: 504 and SEQ ID NO: 437; SEQ ID NO: 423 and SEQ ID NO: 427; SEQ ID NO: 425 and SEQ ID NO: 428; SEQ ID NO: 421 and SEQ ID NO: 429; SEQ ID NO: 504 and SEQ ID NO: 429; SEQ ID NO: 423 and SEQ ID NO: 430; SEQ ID NO: 414 and SEQ ID NO: 431; SEQ ID NO: 414 and SEQ ID NO: 433; SEQ ID NO: 414 and SEQ ID NO: 434; SEQ ID NO: 414 and SEQ ID NO: 435; SEQ ID NO: 504 and SEQ ID NO: 431; SEQ ID NO: 504 and SEQ ID NO: 433; SEQ ID NO: 504 and SEQ ID NO: 434; SEQ ID NO: 504 and SEQ ID NO: 435; SEQ ID NO: 505 and SEQ ID NO: 431; SEQ ID NO: 505 and SEQ ID NO: 433; SEQ ID NO: 505 and SEQ ID NO: 434; SEQ ID NO: 505 and SEQ ID NO: 435; SEQ ID NO: 438 and SEQ ID NO: 417; or SEQ ID NO: 439 and SEQ ID NO: 420.

~~9. An anti-TCR delta variable 1 (anti-V δ 1) antibody or antigen-binding fragment thereof, characterised in that it:~~

- ~~a. causes downregulation of TCRs on V δ 1 T-cells to which it binds;~~
- ~~b. does not exhibit CDC or ADCC; and~~
- ~~c. does not deplete V δ 1 T-cells.~~

10.11. The anti-TCR delta variable 1 (anti-V δ 1) antibody or antigen-binding fragment thereof of any preceding claim, wherein the multispecific antibody causes a depletion of less than about 30%, or less than about 20%, or less than about 10% of the viable V δ 1 T+ cell population via ADCC and/or CDC.

11.12. The anti-TCR delta variable 1 (anti-V δ 1) antibody or antigen-binding fragment thereof of any preceding claim, wherein the antibody or antigen-binding fragment thereof binds to human TRVD1 with a KD of less than about 10 nM, optionally wherein the antibody or antigen-binding fragment thereof binds to cyno TRVD1 with a KD of less than about 100 nM.

~~12. An anti-TCR delta variable 1 (anti-V δ 1) antibody or antigen-binding fragment thereof that specifically binds to a human variable delta 1 (V δ 1) chain of a $\gamma\delta$ T cell receptor (TCR) with a KD of less than about 10 nM, optionally wherein the anti-V δ 1 antibody or antigen-binding fragment thereof binds to a cyno variable delta 1 (V δ 1) chain of a $\gamma\delta$ T cell receptor (TCR) with a KD of less than about 100 nM.~~

13. The anti-V δ 1 antibody or antigen-binding fragment thereof of any preceding claim, wherein the antibody or antigen-binding fragment thereof:

- a. binds to human TRDV1 (SEQ ID NOs 272 or 306) with a binding affinity (K_D , for example as measured by surface plasmon resonance) of less than about 100 nM (preferably less than about 50 nM);

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- b. optionally binds to cyno TRDV1 (SEQ ID NO 308) with a binding affinity (K_D , for example as measured by surface plasmon resonance) of less than about 100 nM (preferably less than about 50 nM);
 - c. has an IC_{50} for TCR downregulation of less than about 50nM (preferably less than about 10nM);
 - d. has an IC_{50} for THP-1 cell killing of less than about 10nM (preferably less than about 5 nM); and
 - e. has an IC_{90} for THP-1 cell killing of less than about 50nM.
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14. The anti-V δ 1 antibody or antigen-binding fragment thereof of any preceding claim, wherein the antibody or antigen-binding fragment thereof only binds to an epitope within amino acid residues 1-90 of SEQ ID NO: 272, SEQ ID NO: 306 and/or SEQ ID NO: 308.
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15. The anti-V δ 1 antibody or antigen-binding fragment thereof of any preceding claim, wherein the antibody or antigen-binding fragment thereof binds to an epitope within amino acid region
- (i) 3-20 of SEQ ID NO: 272, SEQ ID NO: 306 and/or SEQ ID NO: 308; and/or
 - (ii) 37-77 of SEQ ID NO: 272, SEQ ID NO: 306 and/or SEQ ID NO: 308.
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16. The anti-V δ 1 antibody or antigen-binding fragment thereof of any preceding claim, wherein the epitope is an activating epitope of a $\gamma\delta$ T cell, optionally wherein binding of the activating epitope:
- (i) downregulates the $\gamma\delta$ TCR; (ii) activates degranulation of the $\gamma\delta$ T cell; ~~and/or~~ (iii) promotes $\gamma\delta$ T cell mediated killing ; and/or upregulates expression of CD107a, CD25, CD69 and/or Ki67.
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- ~~17. The anti-V δ 1 antibody or antigen-binding fragment thereof of claim 16, wherein binding of the activating epitope upregulates expression of CD107a, CD25, CD69 and/or Ki67.~~
- 18.17. The anti-V δ 1 antibody or antigen-binding fragment thereof of any preceding claim, wherein the antibody is an IgG antibody, optionally wherein the antibody is an IgG1 antibody.
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- 19.18. The anti-V δ 1 antibody or antigen-binding fragment thereof of any preceding claim, wherein the antibody is a multispecific antibody that specifically binds a variable delta 1 (V δ 1) chain of a $\gamma\delta$ T cell receptor (TCR) and a second antigen, wherein the second antigen is a cancer antigen or a cancer-associated antigen, an immunomodulatory antigen, or a cluster of differentiation CD antigen.
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- 20.19. The anti-V δ 1 antibody or antigen-binding fragment thereof of claim ~~18~~19, wherein:
- the cancer antigen or cancer-associated antigen is selected from the group consisting of AFP, AKAP-4, ALK, alpha-fetoprotein, Androgen receptor, B7H3, BAGE, BCA225, BCAA, Bcr-abl, beta-Catenin, beta-HCG, beta-human chorionic gonadotropin, BORIS, BTAA, CA 125, CA 15-3, CA 195, CA 19-9, CA 242, CA 27.29, CA 72-4, CA-50, CAM 17.1, CAM43, Carbonic anhydrase IX, carcinoembryonic antigen, CD22, CD33/IL3Ra, CD68/VP1, CDK4, CEA, chondroitin sulfate proteoglycan 4 (CSPG4) , c-Met, CO-029, CSPG4, Cyclin B1, cyclophilin C-associated
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protein, CYP1B1, E2A-PRL, EGFR, EGFRVIII, ELF2M, EpCAM, EphA2, EphrinB2, Epstein Barr virus antigens EBVA , ERG (TMPRSS2ETS fusion gene), ETV6-AML, FAP, FGF-5, Fos-related antigen 1, Fucosyl GM1, G250, Ga733\EpCAM, GAGE-1, GAGE-2, GD2, GD3, glioma-associated antigen, GloboH, Glycolipid F77, GM3, GP 100, GP 100 (Pmel 17), H4-RET, HER-2/neu, HER-2/Neu/ErbB-2, high-molecular-weight melanoma-associated antigen (HMW-MAA), HPV E6, HPV E7, hTERT, HTgp-175, human telomerase reverse transcriptase, Idiotype, IGF-I receptor , IGF-II, IGH-IGK, insulin growth factor (IGF)-I, intestinal carboxyl esterase, K-ras, LAGE-1a, LCK, lectin-reactive AFP, Legumain, LMP2, M344, MA-50, Mac-2 binding protein, MAD-CT-1, MAD-CT-2, MAGE, MAGE A1, MAGE A3, MAGE-1, MAGE-3, MAGE-4, MAGE-5, MAGE-6, MART-1, MART-1/MelanA, M-CSF, melanoma-associated chondroitin sulfate proteoglycan (MCSP), Mesothelin, MG7-Ag, ML-IAP, MN-CA IX, MOV18, MUC1, Mum-1, hsp70-2, MYCN, MYL-RAR, NA17, NB/70K, neuron-glia antigen 2 (NG2), neutrophil elastase, nm-23H1, NuMa, NY-BR-1, NY-CO-1, NY-ESO, NY-ESO-1, NY-ESO-1, OY-TES1, p15, p16, p180erbB3, p185erbB2, p53, p53 mutant, Page4, PAX3, PAX5, PDGFR-beta, PLAC1, Polysialic Acid, prostate-carcinoma tumor antigen-1 (PCTA-1), prostate-specific antigen, prostatic acid phosphatase (PAP), Proteinase3 (PR1), PSA, PSCA, PSMA, RAGE-1, Ras, Ras-mutant, RCAS1, RGS5, RhoC, ROR1, RU1, RU2 (AS), SART3, SDCCAG16, sLe(a), Sperm protein 17, SSX2, STn, Survivin, TA-90, TAAL6, a TAG-72, telomerase, thyroglobulin, Tie 2, TLP, Tn, TPS, TRP-1, TRP-2, TRP-2, TSP-180, Tyrosinase, VEGF, VEGFR2, VISTA, WT1, XAGE 1, 43-9F, 5T4, and 791Tgp72;

the immunomodulatory antigen is be selected from the group consisting of B7-1 (CD80), B7-2 (CD86), B7-DC (CD273), B7-H1 (CD274), B7-H2 (CD275), B7-H3 (CD276), B7-H4 (VTCN1), B7-H5 (VISTA), BTLA (CD272), CD137, CD137L, CD24, CD27, CD28, CD38, CD40, CD40L (CD154), CD54, CD59, CD70, CTLA4 (CD152), CXCL9, GITR (CD357), HVEM (CD270), ICAM-1 (CD54), ICOS (CD278), LAG-3 (CD223), OX40 (CD134), OX40L (CD252), PD-1 (CD279), PD-L1 (CD274), TIGIT, CD314, CD334, CD335, CD337, and TIM-3 (CD366); or

the CD antigen is selected from the group consisting of CD1a, CD1b, CD1c, CD1d, CD1e, CD2, CD3, CD3d, CD3e, CD3g, CD4, CD5, CD6, CD7, CD8, CD8a, CD8b, CD9, CD10, CD11a, CD11b, CD11c, CD11d, CD13, CD14, CD15, CD16, CD16a, CD16b, CD17, CD18, CD19, CD20, CD21, CD22, CD23, CD24, CD25, CD26, CD27, CD28, CD29, CD30, CD31, CD32A, CD32B, CD33, CD34, CD35, CD36, CD37, CD38, CD39, CD40, CD41, CD42, CD42a, CD42b, CD42c, CD42d, CD43, CD44, CD45, CD46, CD47, CD48, CD49a, CD49b, CD49c, CD49d, CD49e, CD49f, CD50, CD51, CD52, CD53, CD54, CD55, CD56, CD57, CD58, CD59, CD60a, CD60b, CD60c, CD61, CD62E, CD62L, CD62P, CD63, CD64a, CD65, CD65s, CD66a, CD66b, CD66c, CD66d, CD66e, CD66f, CD68, CD69, CD70, CD71, CD72, CD73, CD74, CD75, CD75s, CD77, CD79A, CD79B, CD80, CD81, CD82, CD83, CD84, CD85A, CD85B, CD85C, CD85D, CD85F, CD85G, CD85H, CD85I, CD85J, CD85K, CD85M, CD86, CD87, CD88, CD89, CD90, CD91, CD92, CD93, CD94, CD95, CD96, CD97, CD98, CD99, CD100, CD101, CD102, CD103, CD104, CD105, CD106, CD107, CD107a, CD107b, CD108, CD109, CD110, CD111, CD112, CD113, CD114, CD115, CD116, CD117, CD118, CD119, CD120, CD120a, CD120b, CD121a, CD121b, CD122, CD123, CD124, CD125, CD126, CD127, CD129, CD130, CD131, CD132, CD133, CD134, CD135, CD136, CD137, CD138, CD139, CD140A, CD140B, CD141,

CD142, CD143, CD144, CDw145, CD146, CD147, CD148, CD150, CD151, CD152, CD153, CD154, CD155, CD156, CD156a, CD156b, CD156c, CD157, CD158, CD158A, CD158B1, CD158B2, CD158C, CD158D, CD158E1, CD158E2, CD158F1, CD158F2, CD158G, CD158H, CD158I, CD158J, CD158K, CD159a, CD159c, CD160, CD161, CD162, CD163, CD164, CD165, CD166, CD167a, CD167b, CD168, CD169, CD170, CD171, CD172a, CD172b, CD172g, CD173, CD174, CD175, CD175s, CD176, CD177, CD178, CD179a, CD179b, CD180, CD181, CD182, CD183, CD184, CD185, CD186, CD187, CD188, CD189, CD190, CD191, CD192, CD193, CD194, CD195, CD196, CD197, CDw198, CDw199, CD200, CD201, CD202b, CD203c, CD204, CD205, CD206, CD207, CD208, CD209, CD210, CDw210a, CDw210b, CD211, CD212, CD213a1, CD213a2, CD214, CD215, CD216, CD217, CD218a, CD218b, CD219, CD220, CD221, CD222, CD223, CD224, CD225, CD226, CD227, CD228, CD229, CD230, CD231, CD232, CD233, CD234, CD235a, CD235b, CD236, CD237, CD238, CD239, CD240CE, CD240D, CD241, CD242, CD243, CD244, CD245, CD246, CD247, CD248, CD249, CD250, CD251, CD252, CD253, CD254, CD255, CD256, CD257, CD258, CD259, CD260, CD261, CD262, CD263, CD264, CD265, CD266, CD267, CD268, CD269, CD270, CD271, CD272, CD273, CD274, CD275, CD276, CD277, CD278, CD279, CD280, CD281, CD282, CD283, CD284, CD285, CD286, CD287, CD288, CD289, CD290, CD291, CD292, CDw293, CD294, CD295, CD296, CD297, CD298, CD299, CD300A, CD300C, CD301, CD302, CD303, CD304, CD305, CD306, CD307, CD307a, CD307b, CD307c, CD307d, CD307e, CD308, CD309, CD310, CD311, CD312, CD313, CD314, CD315, CD316, CD317, CD318, CD319, CD320, CD321, CD322, CD323, CD324, CD325, CD326, CD327, CD328, CD329, CD330, CD331, CD332, CD333, CD334, CD335, CD336, CD337, CD338, CD339, CD340, CD344, CD349, CD351, CD352, CD353, CD354, CD355, CD357, CD358, CD360, CD361, CD362, CD363, CD364, CD365, CD366, CD367, CD368, CD369, CD370, and CD371.

~~21.20.~~ The anti-Vδ1 antibody or antigen-binding fragment thereof of any one of claims 1 to ~~1718~~, wherein the antibody is not a bispecific antibody or a multispecific antibody.

~~22.21.~~ The anti-Vδ1 antibody or antigen-binding fragment thereof of any one of claims 1 to ~~1920~~, wherein the antibody is a bispecific antibody and wherein:

- a. the second antigen is CD19, optionally wherein the antibody comprises SEQ ID NO: 314; SEQ ID NO: 315; SEQ ID NO: 316; SEQ ID NO: 396; SEQ ID NO: 397; SEQ ID NO: 421 and SEQ ID NO: 422; SEQ ID NO: 504 and SEQ ID NO: 422; or SEQ ID NO: 423 and SEQ ID NO: 424;
- b. the second antigen is Her2 (CD340), optionally wherein the antibody comprises SEQ ID NO: 393; SEQ ID NO: 394; SEQ ID NO: 395; SEQ ID NO: 398; SEQ ID NO: 414 and SEQ ID NO: 433; SEQ ID NO: 504 and SEQ ID NO: 433; SEQ ID NO: 505 and SEQ ID NO: 433; SEQ ID NO: 414 and SEQ ID NO: 434; SEQ ID NO: 504 and SEQ ID NO: 434; or SEQ ID NO: 505 and SEQ ID NO: 434;
- c. the second antigen is EGFR, optionally wherein the antibody comprises SEQ ID NO: 378; SEQ ID NO: 379; SEQ ID NO: 380; SEQ ID NO: 382; SEQ ID NO: 383; SEQ ID NO: 384; SEQ ID NO: 385; SEQ ID NO: 386; SEQ ID NO: 387; SEQ ID NO: 388~~++~~; SEQ ID NO: 399;

SEQ ID NO: 425 and SEQ ID NO: 426; SEQ ID NO: 421 and SEQ ID NO: 437; SEQ ID NO: 504 and SEQ ID NO: 437; SEQ ID NO: 423 and SEQ ID NO: 427; SEQ ID NO: 425 and SEQ ID NO: 428; SEQ ID NO: 421 and SEQ ID NO: 429; SEQ ID NO: 504 and SEQ ID NO: 429; SEQ ID NO: 423 and SEQ ID NO: 430; SEQ ID NO: 414 and SEQ ID NO: 431; SEQ ID NO: 414 and SEQ ID NO: 435; SEQ ID NO: 504 and SEQ ID NO: 431; SEQ ID NO: 504 and SEQ ID NO: 435; SEQ ID NO: 505 and SEQ ID NO: 431; or SEQ ID NO: 505 and SEQ ID NO: 435;

- d. the second antigen is FAP α , optionally wherein the antibody comprises SEQ ID NO: 401; SEQ ID NO: 402; SEQ ID NO: 414 and SEQ ID NO: 415; SEQ ID NO: 504 and SEQ ID NO: 415; or SEQ ID NO: 505 and SEQ ID NO: 415;
- e. the second antigen is MSLN, optionally wherein the antibody comprises SEQ ID NO: 403; SEQ ID NO: 404; SEQ ID NO: 414 and SEQ ID NO: 416; SEQ ID NO: 504 and SEQ ID NO: 416; or SEQ ID NO: 505 and SEQ ID NO: 416;
- f. the second antigen is PD-1, optionally wherein the antibody comprises SEQ ID NO: 405; SEQ ID NO: 406; or SEQ ID NO: 438 and SEQ ID NO: 417;
- g. the second antigen is 4-1BB, optionally wherein the antibody comprises SEQ ID NO: 407; SEQ ID NO: 408; or SEQ ID NO: 414 and SEQ ID NO: 418; SEQ ID NO: 504 and SEQ ID NO: 418; or SEQ ID NO: 505 and SEQ ID NO: 418;
- h. the second antigen is OX40, optionally wherein the antibody comprises SEQ ID NO: 409; SEQ ID NO: 410; SEQ ID NO: 414 and SEQ ID NO: 419; SEQ ID NO: 504 and SEQ ID NO: 419; or SEQ ID NO: 504 and SEQ ID NO: 419; or
- i. the second antigen is TIGIT, optionally wherein the antibody comprises SEQ ID NO: 411; SEQ ID NO: 412; or SEQ ID NO: 439 and SEQ ID NO: 420.

23.22. The anti-V δ 1 antibody or antigen-binding fragment thereof of any previous claim, wherein the antibody is Fc enabled.

24.23. A pharmaceutical composition comprising the antibody or antibody binding fragment thereof as defined in any one of claims 1 to 22 and a pharmaceutically acceptable diluent or carrier.

25.24. ~~Use of a method of treating a disease or disorder in a subject or a method of modulating an immune response in a subject, comprising administering to the subject~~ an anti-V δ 1 antibody or antibody binding fragment of any one of claims 1 to 22, or ~~the~~ pharmaceutical composition of claim 23 in the manufacture of a medicament for treating a disease or disorder in a subject, or modulating an immune response in a subject²⁴.

26.25. The ~~use method~~ of claim 24²⁵, wherein the disease or disorder is cancer, an infectious disease or an inflammatory disease, or wherein the subject in which an immune response is modulated has cancer, an infectious disease, or an inflammatory disease.

27.26. The ~~use method~~ of claim 24, wherein modulating an immune response in a subject comprises at least one selected from the group consisting of activating $\gamma\delta$ T cells, causing or

increasing proliferation $\gamma\delta$ T cells, causing or increasing expansion of $\gamma\delta$ T cells, causing or increasing $\gamma\delta$ T cell degranulation, causing or increasing $\gamma\delta$ T cell mediated killing activity, causing or increasing $\gamma\delta$ T cytotoxicity, causing or increasing $\gamma\delta$ T cell mobilization, increasing survival of $\gamma\delta$ T cells, and increasing resistance to exhaustion of $\gamma\delta$ T cells.

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~~28~~:27. The usemethod of any one of claims ~~24~~25 to ~~26~~27, wherein diseased cells are killed while healthy cells are spared.

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~~29~~:28. The anti-TCR delta variable 1 (anti-V δ 1) antibody or antigen-binding fragment thereof of any one of claims 1 to 22, or the pharmaceutical composition of claim ~~23~~24, for use in the treatment of cancer, an infectious disease, or an inflammatory disease.