

CLAIMS

1. An isolated antibody ~~or antibody fragment thereof comprising an antigen binding region that specifically binds to human V-domain Ig Suppressor of T cell Activation (human VISTA),~~ which antibody comprises an FcR binding human IgG2 Fc or constant region, wherein the antibody or antibody fragment agonizes or promotes one or more of the suppressive effects of VISTA on T cell immunity- and in the absence of said FcR binding human IgG2 Fc or constant region or when it comprises a human Ig Fc or constant region other than an FcR binding human IgG2 Fc or constant region the antibody antagonizes or inhibits the suppressive effects of VISTA on T cell immunity; and which antibody:
 - (i) comprises the VH CDRs of SEQ ID NO:120, 121 and 122 and the VL CDRs of SEQ ID NO:123, 124 and 125;
 - (ii) comprises the VH CDRs of SEQ ID NO:140, 141 and 142 and the VL CDRs of SEQ ID NO:143, 144 and 145;
 - (iii) comprises the VH CDRs of SEQ ID NO:370, 371 and 372 and the VL CDRs of SEQ ID NO:373, 374 and 375;
 - (iv) comprises the VH CDRs of SEQ ID NO:380, 381 and 382 and the VL CDRs of SEQ ID NO:383, 384 and 385;
 - (v) comprises the VH CDRs of SEQ ID NO:400, 401 and 402 and the VL CDRs of SEQ ID NO:403, 404 and 405;
 - (vi) comprises the VH CDRs of SEQ ID NO:470, 471 and 472 and the VL CDRs of SEQ ID NO:473, 474 and 475;
 - (vii) comprises the VH CDRs of SEQ ID NO:500, 501 and 502 and the VL CDRs of SEQ ID NO:503, 504 and 505;
 - (viii) comprises the VH CDRs of SEQ ID NO:740, 741 and 742 and the VL CDRs of SEQ ID NO:743, 744 and 745; or
 - (ix) comprises the VH CDRs of SEQ ID NO:770, 771 and 772 and the VL CDRs of SEQ ID NO:773, 774 and 775.

~~2.—The isolated antibody of claim 1, which comprises a human IgG2 constant or human IgG2-Fc region.~~

~~3-2.~~ The isolated antibody of claim 2, wherein the human IgG2 constant or Fc region binds to Fc gamma receptors including human CD32A.

~~4-3.~~ The isolated antibody of claim 1 or 2, wherein the IgG2 constant or Fc region comprises native human IgG2 binding to Fc gamma receptors.

~~5-4.~~ The isolated antibody of claim 43 wherein said FcγRs include one or more of hFcγRI (CD64), FcγRIIA or hFcγRIIB, (CD32 or CD32A) and FcγRIIIA (CD16A) or FcγRIIIB (CD16B).

~~6-5.~~ The isolated antibody or antibody fragment of any one of claims 1-54 which competes with or binds for binding to a VISTA epitope which includes or overlaps with the epitope bound by human VISTA any of the anti-human VISTA antibodies having the identical variable sequences as any of Figure 4. the anti-human VISTA antibodies having the following sequences:

(i) comprises the VH polypeptide of SEQ ID NO:126 and the VL polypeptide of SEQ ID NO:128;

(ii) comprises the VH polypeptide of SEQ ID NO:146 and the VL polypeptide of SEQ ID NO:148;

(iii) comprises the VH polypeptide of SEQ ID NO:376 and the VL polypeptide of SEQ ID NO:378;

(iv) comprises the VH polypeptide of SEQ ID NO:386 and the VL polypeptide of SEQ ID NO:388;

(v) comprises the VH polypeptide of SEQ ID NO:406 and the VL polypeptide of SEQ ID NO:408;

(vi) comprises the VH polypeptide of SEQ ID NO:476 and the VL polypeptide of SEQ ID NO:478;

(vii) comprises the VH polypeptide of SEQ ID NO:506 and the VL polypeptide of SEQ ID NO:508;

~~6.—The isolated antibody or antibody fragment of any one of claims 1-6 which binds or interacts with one of more residues of an epitope comprising residues of LLDSGLYCCLVVEIRHHHSEHRVH.~~

~~6.—The isolated antibody or antibody fragment of any one of claims 1-6 which binds or interacts with one of more residues of an epitope comprising one or more residues of ⁷⁹EVQTCSERRPIR₉₀₋₁₄₈NVTLTCRL⁶⁰⁻¹⁵³LPV⁶⁰⁻¹⁵³HHHSEHRVHGAM¹⁶⁴⁻¹⁶⁷LT¹⁶⁴⁻¹⁶⁷CRLLGPV⁶⁰⁻¹⁶⁷LLGPV⁵⁶⁻¹¹³VDKGHDVTFYK⁷⁰⁻¹¹³LAQRHGLESASDHHG¹²⁷⁻¹⁵³HHHSEHRVHGAM¹⁶⁴⁻¹⁶⁷~~

~~93-TFQDLHLHHGGHQAA₁₀₇₋₁₄₆CLVVEIRHHHSEH₁₅₈₋₅₃TCRLGPDVKG₆₃₋₁₂₃SDHHG₁₂₇
and/or₁₅₃HHHSEHRVHGAM₁₆₄~~

- ~~6. The isolated antibody or antibody fragment of any one of claims 1-6 which binds or interacts with one or more residues of an epitope comprising one or more residues of₇₉EVQTCSERRPIR₉₀.~~

~~(viii) The agonist comprises the VH polypeptide of SEQ ID NO:746 and the VL polypeptide of SEQ ID NO:748; or~~

~~(ix) comprises the VH polypeptide of SEQ ID NO:776 and the VL polypeptide of SEQ ID NO:778.~~

- ~~10-6. The anti-human VISTA antibody or antibody fragment of any one of Claims 1-95 which promotes or enhances at least one effect of human VISTA on immunity, e.g. its~~the~~ suppressive effect of VISTA on any one or more of T cell immunity, activation of monocytes, induction of T-cell proliferation; induction or suppression of cytokine expression, increased survival of monocytes, induction of antibody-dependent cell-mediated cytotoxicity (ADCC) in cells-expressing VISTA; and/or induction of antibody-dependent cellular phagocytosis (ADCP) in cells-expressing VISTA.~~

- ~~8. An isolated agonistic or antagonistic anti-human VISTA antibody or antibody fragment thereof comprising an antigen binding region that specifically binds to human VISTA, wherein the antibody or antibody fragment comprises variable heavy and light sequences having the identical CDR polypeptides as any one of the anti-human VISTA antibodies having the CDR and variable heavy and light polypeptides shown in Figure 4, with the proviso that if said antibody or fragment comprises an antagonist anti-human VISTA antibody or antibody fragment then the antibody or antibody fragment does not comprise the same CDRs as any one of VSTB112, VSTB116, VSTB95, VSTB50, VSTB53 or VSTB60.~~

- ~~9. The isolated antibody or antibody fragment of Claim 11, which comprises the same CDRs as an antibody selected from VSTB49-VSTB116, with the proviso that if said antibody or fragment comprises an antagonist anti-human VISTA antibody or fragment then the antibody or antibody fragment does not comprise the same CDRs as any one of VSTB112, VSTB116, VSTB95, VSTB50, VSTB53 or VSTB60.~~

- ~~10. The isolated antibody or antibody fragment of Claim 11 or 12, which comprises a variable heavy and/or variable light polypeptide having at least 90% sequence identity to those of an anti-human VISTA antibody selected from any one of VSTB49-VSTB116, wherein the variable heavy and light polypeptide sequences thereof are shown in Figure 4, with the proviso that if said antibody or fragment comprises an antagonist anti-human VISTA antibody or fragment then the antibody or antibody fragment does not comprise the same CDRs as any one of VSTB112, VSTB116, VSTB95, VSTB50, VSTB53 or VSTB60.~~

- ~~11. The isolated antibody or antibody fragment of Claim 11 or 12, which comprises a variable heavy and/or variable light polypeptide having at least 95% sequence identity to those of an anti-human VISTA antibody selected from any one of VSTB49-VSTB116, wherein the variable heavy and light polypeptide sequences thereof are shown in Figure 4, with the proviso that if said antibody or fragment comprises an antagonist anti-human VISTA antibody or antibody fragment then the antibody or antibody fragment does not comprise the same CDRs as any one of VSTB112, VSTB116, VSTB95, VSTB50, VSTB53 or VSTB60.~~
- ~~12. The isolated antibody or antibody fragment of Claim 11 or 12, which comprises a variable heavy and/or variable light polypeptide having at least 96-99% sequence identity to those of an anti-human VISTA antibody selected from any one of VSTB49-VSTB116, wherein the variable heavy and light polypeptide sequences thereof are shown in Figure 4, with the proviso that if said antibody or fragment comprises an antagonist anti-human VISTA antibody or antibody fragment then the antibody or antibody fragment does not comprise the same CDRs as any one of VSTB112, VSTB116, VSTB95, VSTB50, VSTB53 or VSTB60.~~
- ~~13. The isolated antibody or antibody fragment of Claim 11 or 12, which comprises a variable heavy and/or variable light polypeptide identical to those of an anti-human VISTA antibody selected from one of VSTB49-VSTB116, wherein the variable heavy and light polypeptide sequences thereof are shown in **Figure 4**, with the proviso that if said antibody or fragment comprises an antagonist anti-human VISTA antibody or antibody fragment then the antibody or antibody fragment does not comprise the same CDRs as any one of VSTB112, VSTB116, VSTB95, VSTB50, VSTB53 or VSTB60.~~
- ~~14. The isolated antibody or antibody fragment of any one of the foregoing Claims which antagonizes or blocks at least one effect of human VISTA on immunity.~~
- ~~15. The isolated antibody or antibody fragment of any one of the foregoing Claims which agonizes or blocks at least one effect of human VISTA on immunity.~~
- ~~16. The isolated antibody or antibody fragment of any one of the foregoing Claims which comprises a human constant domain.~~
- ~~17. The isolated antibody or antibody fragment of any one of the foregoing Claims which comprises a human constant domain selected from IgG1, IgG2, IgG3 and IgG4, which optionally is modified, e.g., by deletion, substitution or addition mutations or any combination of the foregoing.~~
- ~~18. The antibody or antibody fragment of any one of the foregoing Claims wherein the antibody fragment comprises or is a Fab, F(ab')₂, or scFv antibody fragment.~~
- ~~19. An antagonistic anti-human VISTA antibody or antibody fragment according to any of the foregoing claims which blocks or suppresses at least one of the effects of human VISTA on immunity, e.g., selected from its suppressive effect on T cell immunity, activation of monocytes, or T cell proliferation; induction or suppression of cytokine expression, increased survival of monocytes, suppression of antibody-dependent cell mediated cytotoxicity (ADCC) of cells expressing VISTA; and~~

~~suppression of antibody-dependent cellular phagocytosis (ADCP) of cells expressing VISTA.~~

- ~~20. An agonistic anti-human VISTA antibody or antibody fragment according to any of the foregoing claims which promotes or enhances at least one of the effects of human VISTA on immunity, e.g., selected from its suppressive effect T cell immunity, activation of monocytes, suppression of T cell proliferation; induction or suppression of cytokine expression, increased survival of monocytes, suppression of antibody-dependent cell-mediated cytotoxicity (ADCC) in cells expressing VISTA; and suppression of antibody-dependent cellular phagocytosis (ADCP) of cells expressing VISTA.~~
- ~~21. The agonist anti-human VISTA antibody or antibody fragment of Claim 23, which comprises a human IgG2 constant or Fc region.~~
- ~~22. The agonist anti-human VISTA antibody or antibody fragment of Claim 23 or 24 promotes or enhances the suppressive effect of human VISTA on immunity, e.g. its effect on any one or more of T cell immunity, activation of monocytes, T cell proliferation; cytokine expression, survival of monocytes, antibody-dependent cell-mediated cytotoxicity (ADCC) in cells expressing VISTA; and antibody-dependent cellular phagocytosis (ADCP) in cells expressing VISTA.~~
- ~~23. The agonist anti-human VISTA antibody or antibody fragment of any one of Claim 23-25, which inhibits T cell immunity and/or proinflammatory cytokine expression.~~
- ~~24. The agonist antibody or antibody fragment of any of the foregoing claims which is a human, humanized or chimeric antibody that comprises a human Fc region, e.g., human IgG1, IgG2, IgG3 and IgG4 or a chimera of any of the foregoing.~~
- ~~25. The agonist antibody of any of any of the foregoing claims which is chimeric, human or humanized.~~
- ~~26. The antibody of any of the foregoing claims which comprises a human IgG2 constant domain or Fc region which potentially may be mutated.~~
- ~~27. The agonist antibody of any of any of the foregoing claims which comprises a human IgG2 constant domain or fragment thereof or an hIgG1, hIgG3, hIgG4, IgA, IgD, IgE, or IgM, wherein the entire or substantially the entire hinge and CH1 domains of said antibody and optionally the entire or substantially the entire light chain constant region have been replaced with the corresponding entire or substantially the entire light chain, and the hinge and C_{H1} domains ("H2 regions" or "H2 domains") of hIgG2.~~
7. The agonist antibody of any of any of the foregoing claims which (i) comprises an IgG2 Fc region wherein The antibody of any one of Claims 1-6, wherein said human IgG2 Fc region comprises the following modifications:

- a. either or both of the heavy chain cysteine residue at position 127 and the light chain cysteine residue at position 214 (wherein numbering is according to Kabat) are deleted or changed to a different amino acid residue, resulting in an increase in the agonistic properties of the resultant modified antibody

relative to an antibody ~~wherein these residues are unchanged, (ii) lacking said~~
Fc modifications or

~~31.b.~~ the cysteine residue at position 214 in the H2 region of said
antibody IgG2 Fc region is mutated or substituted with another amino acid
and/or one or more of the cysteine residues at positions 127, 232 or 233 of
the heavy chain are deleted or substituted with another amino acid, ~~(iii) it~~
~~comprises a human IgG2 constant domain wherein at least one cysteine~~
~~residue is deleted or changed to another amino acid, (iv) it competes with or~~
~~binds to the same epitope on human VISTA as VSTB95 (variable heavy and~~
~~light sequences shown in Figure 4).~~ resulting in an increase in the agonistic
properties of the resultant modified antibody relative to an antibody lacking
said Fc modifications.

~~29. The antibody or antibody fragments of any one of the foregoing claims which:~~

- ~~(-) comprises the V_H-CDRs of SEQ ID NO:100, 101 and 102 and the V_L-CDRs of SEQ ID NO:103, 104 and 105;~~
- ~~(-) comprises the V_H-CDRs of SEQ ID NO:110, 111 and 112 and the V_L-CDRs of SEQ ID NO:113, 114 and 115;~~
- ~~(-) comprises the V_H-CDRs of SEQ ID NO:120, 121 and 122 and the V_L-CDRs of SEQ ID NO:123, 124 and 125;~~
- ~~(-) comprises the V_H-CDRs of SEQ ID NO:130, 131 and 132 and the V_L-CDRs of SEQ ID NO:133, 134 and 135;~~
- ~~(-) comprises the V_H-CDRs of SEQ ID NO:140, 141 and 142 and the V_L-CDRs of SEQ ID NO:143, 144 and 145;~~
- ~~(-) comprises the V_H-CDRs of SEQ ID NO:150, 151 and 152 and the V_L-CDRs of SEQ ID NO:153, 154 and 155;~~
- ~~(-) comprises the V_H-CDRs of SEQ ID NO:160, 161 and 162 and the V_L-CDRs of SEQ ID NO:163, 164 and 165;~~
- ~~(-) comprises the V_H-CDRs of SEQ ID NO:170, 171 and 172 and the V_L-CDRs of SEQ ID NO:173, 174 and 175;~~
- ~~(-) comprises the V_H-CDRs of SEQ ID NO:180, 181 and 182 and the V_L-CDRs of SEQ ID NO:183, 184 and 185;~~
- ~~(-) comprises the V_H-CDRs of SEQ ID NO:190, 191 and 192 and the V_L-CDRs of SEQ ID NO:193, 194 and 195;~~
- ~~(-) comprises the V_H-CDRs of SEQ ID NO:200, 201 and 202 and the V_L-CDRs of SEQ ID NO:203, 204 and 205;~~
- ~~(-) comprises the V_H-CDRs of SEQ ID NO:210, 211 and 212 and the V_L-CDRs of SEQ ID NO:213, 214 and 215;~~
- ~~(-) comprises the V_H-CDRs of SEQ ID NO:220, 221 and 222 and the V_L-CDRs of SEQ ID NO:223, 224 and 225;~~

- (-) — comprises the V_H-CDRs of SEQ ID NO:230, 231 and 232 and the V_L-CDRs of SEQ ID NO:233, 234 and 235;
- (-) — comprises the V_H-CDRs of SEQ ID NO:240, 241 and 242 and the V_L-CDRs of SEQ ID NO:243, 244 and 245;
- (-) — comprises the V_H-CDRs of SEQ ID NO:250, 251 and 252 and the V_L-CDRs of SEQ ID NO:253, 254 and 255;
- (-) — comprises the V_H-CDRs of SEQ ID NO:260, 261 and 262 and the V_L-CDRs of SEQ ID NO:263, 264 and 265;
- (-) — comprises the V_H-CDRs of SEQ ID NO:270, 271 and 272 and the V_L-CDRs of SEQ ID NO:273, 274 and 275;
- (-) — comprises the V_H-CDRs of SEQ ID NO:280, 281 and 282 and the V_L-CDRs of SEQ ID NO:283, 284 and 285;
- (-) — comprises the V_H-CDRs of SEQ ID NO:290, 291 and 292 and the V_L-CDRs of SEQ ID NO:293, 294 and 295;
- (-) — comprises the V_H-CDRs of SEQ ID NO:300, 301 and 302 and the V_L-CDRs of SEQ ID NO:303, 304 and 305;
- (-) — comprises the V_H-CDRs of SEQ ID NO:310, 311 and 312 and the V_L-CDRs of SEQ ID NO:313, 314 and 315;
- (-) — comprises the V_H-CDRs of SEQ ID NO:320, 321 and 322 and the V_L-CDRs of SEQ ID NO:323, 324 and 325;
- (-) — comprises the V_H-CDRs of SEQ ID NO:330, 331 and 332 and the V_L-CDRs of SEQ ID NO:333, 334 and 335;
- (-) — comprises the V_H-CDRs of SEQ ID NO:340, 341 and 342 and the V_L-CDRs of SEQ ID NO:343, 344 and 345;
- (-) — comprises the V_H-CDRs of SEQ ID NO:350, 351 and 352 and the V_L-CDRs of SEQ ID NO:353, 354 and 355;
- (-) — comprises the V_H-CDRs of SEQ ID NO:360, 361 and 362 and the V_L-CDRs of SEQ ID NO:363, 364 and 365;
- (-) — comprises the V_H-CDRs of SEQ ID NO:370, 371 and 372 and the V_L-CDRs of SEQ ID NO:373, 374 and 375;
- (-) — comprises the V_H-CDRs of SEQ ID NO:380, 381 and 382 and the V_L-CDRs of SEQ ID NO:383, 384 and 385;
- (-) — comprises the V_H-CDRs of SEQ ID NO:390, 391 and 392 and the V_L-CDRs of SEQ ID NO:393, 394 and 395;
- (-) — comprises the V_H-CDRs of SEQ ID NO:400, 401 and 402 and the V_L-CDRs of SEQ ID NO:403, 404 and 405;
- (-) — comprises the V_H-CDRs of SEQ ID NO:410, 411 and 412 and the V_L-CDRs of SEQ ID NO:413, 414 and 415;
- (-) — comprises the V_H-CDRs of SEQ ID NO:420, 421 and 422 and the V_L-CDRs of SEQ ID NO:423, 424 and 425;

- (-) — comprises the V_H-CDRs of SEQ ID NO:430, 431 and 432 and the V_L-CDRs of SEQ ID NO:433, 434 and 435;
- (-) — comprises the V_H-CDRs of SEQ ID NO:440, 441 and 442 and the V_L-CDRs of SEQ ID NO:443, 444 and 445;
- (-) — comprises the V_H-CDRs of SEQ ID NO:450, 451 and 452 and the V_L-CDRs of SEQ ID NO:453, 454 and 455;
- (-) — comprises the V_H-CDRs of SEQ ID NO:460, 461 and 462 and the V_L-CDRs of SEQ ID NO:463, 464 and 465;
- (-) — comprises the V_H-CDRs of SEQ ID NO:470, 471 and 472 and the V_L-CDRs of SEQ ID NO:473, 474 and 475;
- (-) — comprises the V_H-CDRs of SEQ ID NO:480, 481 and 482 and the V_L-CDRs of SEQ ID NO:483, 484 and 485;
- (-) — comprises the V_H-CDRs of SEQ ID NO:490, 491 and 492 and the VL CDR polypeptides of SEQ ID NO:493, 494 and 495;
- (-) — comprises the V_H-CDRs of SEQ ID NO:500, 501 and 502 and the VL CDR polypeptides of SEQ ID NO:503, 504 and 505;
- (-) — comprises the V_H-CDRs of SEQ ID NO:510, 511 and 512 and the VL CDR polypeptides of SEQ ID NO:513, 514 and 515;
- (-) — comprises the V_H-CDRs of SEQ ID NO:520, 521 and 522 and the VL CDR polypeptides of SEQ ID NO:523, 524 and 525;
- (-) — comprises the V_H-CDRs of SEQ ID NO:530, 531 and 532 and the VL CDR polypeptides of SEQ ID NO:533, 534 and 535;
- (-) — comprises the V_H-CDRs of SEQ ID NO:540, 541 and 542 and the VL CDR polypeptides of SEQ ID NO:543, 544 and 545;
- (-) — comprises the V_H-CDRs of SEQ ID NO:550, 551 and 552 and the VL CDR polypeptides of SEQ ID NO:553, 554 and 555;
- (-) — comprises the V_H-CDRs of SEQ ID NO:560, 561 and 562 and the V_L-CDRs of SEQ ID NO:563, 564 and 565;
- (-) — comprises the V_H-CDRs of SEQ ID NO:570, 571 and 572 and the V_L-CDRs of SEQ ID NO:573, 574 and 575;
- (-) — comprises the V_H-CDRs of SEQ ID NO:580, 581 and 582 and the V_L-CDRs of SEQ ID NO:583, 584 and 585;
- (-) — comprises the V_H-CDRs of SEQ ID NO:590, 591 and 592 and the V_L-CDRs of SEQ ID NO:593, 594 and 595;
- (-) — comprises the V_H-CDRs of SEQ ID NO:600, 601 and 602 and the V_L-CDRs of SEQ ID NO:603, 604 and 605;
- (-) — comprises the V_H-CDRs of SEQ ID NO:610, 611 and 612 and the V_L-CDRs of SEQ ID NO:613, 614 and 615;
- (-) — comprises the V_H-CDRs of SEQ ID NO:620, 621 and 622 and the V_L-CDRs of SEQ ID NO:623, 624 and 625;

- (~~-~~) — comprises the V_H-CDRs of SEQ ID NO:630, 631 and 632 and the V_L-CDRs of SEQ ID NO:633, 634 and 635;
- (~~-~~) — comprises the V_H-CDRs of SEQ ID NO:640, 641 and 642 and the V_L-CDRs of SEQ ID NO:643, 644 and 645;
- (~~-~~) — comprises the V_H-CDRs of SEQ ID NO:650, 651 and 652 and the V_L-CDRs of SEQ ID NO:653, 654 and 655;
- (~~-~~) — comprises the V_H-CDRs of SEQ ID NO:660, 661 and 662 and the V_L-CDRs of SEQ ID NO:663, 664 and 665;
- (~~-~~) — comprises the V_H-CDRs of SEQ ID NO:670, 671 and 672 and the V_L-CDRs of SEQ ID NO:673, 674 and 675;
- (~~-~~) — comprises the V_H-CDRs of SEQ ID NO:680, 681 and 682 and the V_L-CDRs of SEQ ID NO:683, 684 and 685;
- (~~-~~) — comprises the V_H-CDRs of SEQ ID NO:690, 691 and 692 and the V_L-CDRs of SEQ ID NO:693, 694 and 695;
- (~~-~~) — comprises the V_H-CDRs of SEQ ID NO:700, 701 and 702 and the V_L-CDRs of SEQ ID NO:703, 704 and 705;
- (~~-~~) — comprises the V_H-CDRs of SEQ ID NO:710, 711 and 712 and the V_L-CDRs of SEQ ID NO:713, 714 and 715;
- (~~-~~) — comprises the V_H-CDRs of SEQ ID NO:720, 721 and 722 and the V_L-CDRs of SEQ ID NO:723, 724 and 725;
- (~~-~~) — comprises the V_H-CDRs of SEQ ID NO:730, 731 and 732 and the V_L-CDRs of SEQ ID NO:733, 734 and 735;
- (~~-~~) — comprises the V_H-CDRs of SEQ ID NO:740, 741 and 742 and the V_L-CDRs of SEQ ID NO:743, 744 and 745;
- (~~-~~) — comprises the V_H-CDRs of SEQ ID NO:750, 751 and 752 and the V_L-CDRs of SEQ ID NO:753, 754 and 755;
- (~~-~~) — comprises the V_H-CDRs of SEQ ID NO:760, 761 and 762 and the V_L-CDRs of SEQ ID NO:763, 764 and 765;
- (~~-~~) — comprises the V_H-CDRs of SEQ ID NO:770, 771 and 772 and the V_L-CDRs of SEQ ID NO:773, 774 and 775;
- (~~-~~) — comprises the V_H-CDRs of SEQ ID NO:780, 781 and 782 and the V_L-CDRs of SEQ ID NO:783, 784 and 785;
- (~~-~~) — comprises the V_H-CDRs of SEQ ID NO:790, 791 and 792 and the V_L-CDRs of SEQ ID NO:793, 794 and 795;
- (~~-~~) — comprises the V_H-CDRs of SEQ ID NO:800, 801 and 802 and the V_L-CDRs of SEQ ID NO:803, 804 and 805;
- (~~-~~) — comprises the V_H-CDRs of SEQ ID NO:810, 811 and 812 and the V_L-CDRs of SEQ ID NO: 813, 814 and 815.

102. — ~~The antibody or antibody fragments of any one of the foregoing claims which:~~

- ~~(ciii) comprises the V_H-polypeptide of SEQ ID NO:106 and the V_L-polypeptide of SEQ ID NO:108;~~
- ~~(civ) comprises the V_H-polypeptide of SEQ ID NO:116 and the V_L-polypeptide of SEQ ID NO:118;~~
- ~~(cv)(i) comprises the V_H-polypeptide of SEQ ID NO:126 and the V_L-polypeptide of SEQ ID NO:128;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:136 and the V_L-polypeptide of SEQ ID NO:138;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:146 and the V_L-polypeptide of SEQ ID NO:148;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:156 and the V_L-polypeptide of SEQ ID NO:158;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:166 and the V_L-polypeptide of SEQ ID NO:168;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:176 and the V_L-polypeptide of SEQ ID NO:178;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:186 and the V_L-polypeptide of SEQ ID NO:188;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:196 and the V_L-polypeptide of SEQ ID NO:198;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:206 and the V_L-polypeptide of SEQ ID NO:208;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:216 and the V_L-polypeptide of SEQ ID NO:218;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:226 and the V_L-polypeptide of SEQ ID NO:228;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:236 and the V_L-polypeptide of SEQ ID NO:238;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:246 and the V_L-polypeptide of SEQ ID NO:248;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:256 and the V_L-polypeptide of SEQ ID NO:258;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:266 and the V_L-polypeptide of SEQ ID NO:268;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:276 and the V_L-polypeptide of SEQ ID NO:278;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:286 and the V_L-polypeptide of SEQ ID NO:288;~~

~~(cxxii) comprises the V_H-polypeptide of SEQ ID NO:296 and the V_L-polypeptide of SEQ ID NO:298;~~

~~(cxxiii) comprises the V_H-polypeptide of SEQ ID NO:306 and the V_L-polypeptide of SEQ ID NO:308;~~

~~(cxxiv) comprises the V_H-polypeptide of SEQ ID NO:316 and the V_L-polypeptide of SEQ ID NO:318;~~

~~(cxxv) comprises the V_H-polypeptide of SEQ ID NO:326 and the V_L-polypeptide of SEQ ID NO:328;~~

~~(cxxvi) comprises the V_H-polypeptide of SEQ ID NO:336 and the V_L-polypeptide of SEQ ID NO:338;~~

~~(cxxvii) comprises the V_H-polypeptide of SEQ ID NO:346 and the V_L-polypeptide of SEQ ID NO:348;~~

~~(cxxviii) comprises the V_H-polypeptide of SEQ ID NO:356 and the V_L-polypeptide of SEQ ID NO:358;~~

~~(cxxix) comprises the V_H-polypeptide of SEQ ID NO:366 and the V_L-polypeptide of SEQ ID NO:368;~~

~~(cxxx)(iii) comprises the V_H-polypeptide of SEQ ID NO:376 and the V_L-polypeptide of SEQ ID NO:378;~~

~~(cxxxi)(iii) comprises the V_H-polypeptide of SEQ ID NO:386 and the V_L-polypeptide of SEQ ID NO:388;~~

~~(cxxxii) comprises the V_H-polypeptide of SEQ ID NO:396 and the V_L-polypeptide of SEQ ID NO:398;~~

~~(cxxxiii)(v) comprises the V_H-polypeptide of SEQ ID NO:406 and the V_L-polypeptide of SEQ ID NO:408;~~

~~(-) comprises the V_H-polypeptide of SEQ ID NO:416 and the V_L-polypeptide of SEQ ID NO:418;~~

~~(-) comprises the V_H-polypeptide of SEQ ID NO:426 and the V_L-polypeptide of SEQ ID NO:428;~~

~~(-) comprises the V_H-polypeptide of SEQ ID NO:436 and the V_L-polypeptide of SEQ ID NO:438;~~

~~(-) comprises the V_H-polypeptide of SEQ ID NO:446 and the V_L-polypeptide of SEQ ID NO:448;~~

~~(-) comprises the V_H-polypeptide of SEQ ID NO:456 and the V_L-polypeptide of SEQ ID NO:458;~~

~~(-) comprises the V_H-polypeptide of SEQ ID NO:466 and the V_L-polypeptide of SEQ ID NO:468;~~

~~(-) comprises the V_H-polypeptide of SEQ ID NO:476 and the V_L-polypeptide of SEQ ID NO:478;~~

- ~~(cxli) comprises the V_H-polypeptide of SEQ ID NO:486 and the V_L-polypeptide of SEQ ID NO:488;~~
- ~~(cxlii) comprises the V_H-polypeptide of SEQ ID NO:496 and the V_L-polypeptide of SEQ ID NO:498;~~
- ~~(cxliii)(vii) comprises the V_H-polypeptide of SEQ ID NO:506 and the V_L-polypeptide of SEQ ID NO:508;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:516 and the V_L-polypeptide of SEQ ID NO:518;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:526 and the V_L-polypeptide of SEQ ID NO:528;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:536 and the V_L-polypeptide of SEQ ID NO:533, 534 and 535;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:546 and the V_L-polypeptide of SEQ ID NO:548;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:556 and the V_L-polypeptide of SEQ ID NO:558;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:566 and the V_L-polypeptide of SEQ ID NO:568;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:576 and the V_L-polypeptide of SEQ ID NO:578;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:586 and the V_L-polypeptide of SEQ ID NO:588;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:596 and the V_L-polypeptide of SEQ ID NO:598;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:606 and the V_L-polypeptide of SEQ ID NO:608;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:616 and the V_L-polypeptide of SEQ ID NO:618;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:626 and the V_L-polypeptide of SEQ ID NO:628;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:636 and the V_L-polypeptide of SEQ ID NO:638;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:646 and the V_L-polypeptide of SEQ ID NO:648;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:656 and the V_L-polypeptide of SEQ ID NO:658;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:666 and the V_L-polypeptide of SEQ ID NO:668;~~

- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:676 and the V_L-polypeptide of SEQ ID NO:678;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:686 and the V_L-polypeptide of SEQ ID NO:688;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:696 and the V_L-polypeptide of SEQ ID NO:698;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:706 and the V_L-polypeptide of SEQ ID NO:708;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:716 and the V_L-polypeptide of SEQ ID NO:718;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:726 and the V_L-polypeptide of SEQ ID NO:728;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:736 and the V_L-polypeptide of SEQ ID NO:738;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:746 and the V_L-polypeptide of SEQ ID NO:748;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:756 and the V_L-polypeptide of SEQ ID NO:758;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:766 and the V_L-polypeptide of SEQ ID NO:768;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:776 and the V_L-polypeptide of SEQ ID NO:778;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:786 and the V_L-polypeptide of SEQ ID NO:788;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:796 and the V_L-polypeptide of SEQ ID NO:798;~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:806 and the V_L-polypeptide of SEQ ID NO:808; and~~
- ~~(-) comprises the V_H-polypeptide of SEQ ID NO:816 and the V_L-polypeptide of SEQ ID NO: 818.~~

~~175. The antibody of Claim 32 or 33, which comprises a human IgG2 constant domain wherein optionally at least one cysteine residue is deleted or changed to another amino acid.~~

~~176. An agonistic anti human VISTA antibody or antibody fragment according to any of the foregoing claims which mediates any one or combination of at least one of the following immunoinhibitory effects: (i) decreases immune response, (ii) decreases T cell activation, (iii) decreases cytotoxic T cell activity, (iv) decreases natural killer (NK) cell activity, (v) decreases T-cell activity, (vi) decreases pro-inflammatory cytokine secretion, (vii) decreases IL-2 secretion; (viii) decreases interferon γ production, (ix) decreases Th1 response, (x) decreases Th2 response, (xi)~~

increases cell number and/or activity of regulatory T cells, (xii) increases regulatory cell activity and/or one or more of myeloid derived suppressor cells (MDSCs), iMCs, mesenchymal stromal cells, TIE2-expressing monocytes, (xiii) increases regulatory cell activity and/or the activity of one or more of myeloid derived suppressor cells (MDSCs), iMCs, mesenchymal stromal cells, TIE2-expressing monocytes, (xiii) increases M2 macrophages, (xiv) increases M2 macrophage activity, (xv) increases N2 neutrophils, (xvi) increases N2 neutrophils activity, (xvii) increases inhibition of T cell activation, (xviii) increases inhibition of CTL activation, (xix) increases inhibition of NK cell activation, (xx) increases T cell exhaustion, (xxi) decreases T cell response, (xxii) decreases activity of cytotoxic cells, (xxiii) reduces antigen specific memory responses, (xxiv) inhibits apoptosis or lysis of cells, (xxv) decreases cytotoxic or cytostatic effect on cells, (xxvi) reduces direct killing of cells, (xxvii) decreases Th17 activity, and/or (xxviii) reduces complement dependent cytotoxicity and/or antibody dependent cell mediated cytotoxicity, with the proviso that said anti VISTA antibody or antigen binding fragment may elicit an opposite effect to one or more of (i)-(xxviii) and optionally is used to treat autoimmunity, allergy, inflammation, transplant or sepsis.

8. A pharmaceutical composition comprising at least one agonistic antibody according to any one of claims 1-7 and a pharmaceutically acceptable carrier.

36-9. A diagnostic composition comprising at least one antagonistic or agonistic antibody or antibody fragment according to any one of the above claims 1-7 and a diagnostically acceptable carrier.

178. A method of treatment and/or diagnosis, or use of a composition containing at least one antagonistic antibody or antibody fragment according to any of the foregoing claims for diagnostic or therapeutic use, which method or use comprises the administration to a subject in need thereof at least one dosage or composition comprising a therapeutically or diagnostically effective amount of at least one at least one antagonistic antibody or antibody fragment according to any of the foregoing claims or composition containing according to any of the above claims.

179. The method of Use of the antibody according to any one of claims 1-7 or pharmaceutical composition according to claim 37 which is for the treatment of cancer or an infectious disorder.

180. The method of claim 38, wherein the cancer is a blood cancer or solid tumor, e.g., one surrounded by a tumor stroma comprising myeloid cells, T-cells, or a combination of myeloid cells and T-cells.

181. The method of claim 38, which is for the treatment of cancer selected from leukemia, lymphoma, myelodysplastic syndrome or myeloma, lung cancer or a combination thereof.

182. The method of claim 40, wherein the leukemia comprises acute lymphoblastic leukemia (ALL), chronic lymphocytic leukemia (CLL), acute myeloid (myelogenous) leukemia (AML), chronic myelogenous leukemia (CML); hairy cell

leukemia, T-cell prolymphocytic leukemia, large granular lymphocytic leukemia, or adult T-cell leukemia.

~~183. — A method of treatment and/or diagnosis, or use of a composition containing at least one agonistic antibody or antibody fragment according to any of the foregoing claims for diagnostic or therapeutic use, which method or use comprises the administration to a subject in need thereof at least one dosage or composition comprising a therapeutically or diagnostically effective amount of at least one at least one agonistic antibody or antibody fragment according to any of the foregoing claims or composition containing according to any of the above claims.~~

~~184. — A method or use of any agonistic antibody or antibody fragment according to any of the foregoing claims, for effecting in vitro and/or in vivo any one or combination of at least one of the following immunoinhibitory effects: (i) decreases immune response, (ii) decreases T cell activation, (iii) decreases cytotoxic T cell activity, (iv) decreases natural killer (NK) cell activity, (v) decreases T cell activity, (vi) decreases pro-inflammatory cytokine secretion, (vii) decreases IL-2 secretion; (viii) decreases interferon γ production, (ix) decreases Th1 response, (x) decreases Th2 response, (xi) increases cell number and/or activity of regulatory T cells, (xii) increases regulatory cell activity and/or one or more of myeloid derived suppressor cells (MDSCs), iMCs, mesenchymal stromal cells, TIE2-expressing monocytes, (xiii) increases regulatory cell activity and/or the activity of one or more of myeloid derived suppressor cells (MDSCs), iMCs, mesenchymal stromal cells, TIE2-expressing monocytes, (xiv) increases M2 macrophages, (xv) increases M2 macrophage activity, (xvi) increases N2 neutrophils, (xvii) increases N2 neutrophils activity, (xviii) increases inhibition of T cell activation, (xix) increases inhibition of CTL activation, (xx) increases inhibition of NK cell activation, (xxi) increases T cell exhaustion, (xxii) decreases T cell response, (xxiii) decreases activity of cytotoxic cells, (xxiv) reduces antigen-specific memory responses, (xxv) inhibits apoptosis or lysis of cells, (xxvi) decreases cytotoxic or cytostatic effect on cells, (xxvii) reduces direct killing of cells, (xxviii) decreases Th17 activity, and/or (xxviii) reduces complement dependent cytotoxicity and/or antibody dependent cell mediated cytotoxicity, with the proviso that said anti-VISTA antibody or antigen-binding fragment may elicit an opposite effect to one or more of (i) (xxviii) and optionally is used to treat autoimmunity, allergy, inflammation, transplant or sepsis.~~

~~44.10. — The method or use of any of claims 37-43, which is used in the treatment or prevention of allergy, autoimmunity, inflammation or sepsis or the treatment of a transplant, or gene therapy, inflammation, cancer, GVHD or sepsis, or to treat or prevent inflammatory, autoimmune, or allergic side effects associated with any of the foregoing therewith in a human subject recipient, wherein a therapeutically effective amount of at least one of the agonistic antibody is to be administered to a human subject in need thereof.~~

- ~~11. An anti-VISTA antibody or antigen-binding fragment or~~ The use of claim 10, which further comprises detecting VISTA expression in the subject optionally using a diagnostic composition, or method or use according to claim 9.
- ~~12. Use of an agonistic antibody according to any one of the foregoing claims 1-7 in the preparation of a medicament for suppressing T cell immunity and/or promoting the suppressive effects of human VISTA on immunity in a subject in need thereof.~~
- ~~13. Use of any agonistic antibody according to any one of claims 1-7 or a composition containing according to claim 8 in the manufacture of a medicament for suppressing T cell immunity and/or promoting the suppressive effects of human VISTA on immunity in a subject in need thereof, optionally wherein the subject has an autoimmune, inflammatory, allergic condition, and/or is at risk of developing an autoimmune, inflammatory or allergic response because the subject has or is to receive a transplant and/or the subject exhibits symptoms of an autoimmune, inflammatory or allergic response or sepsis.~~
- ~~45-14.~~ The use according to any one of claims 9-13, further comprising another immunomodulatory, immunoinhibitory antibody or immunoinhibitory fusion protein which is selected from immunoinhibitory antibodies or fusion proteins targeting one or more of CTLA4, PD-1, PDL-1, LAG-3, TIM-3, BTLA, B7-H4, B7-H3, VISTA, and/or agonistic antibodies or fusion protein targeting one or more of CD40, CD137, OX40, GITR, CD27, CD28 or ICOS to be administered.
- ~~15. The method or use of any one of the foregoing claims 10-14, which includes assaying~~
:
- ~~46-a.~~ VISTA protein expression by the individual's cells or in bodily fluids prior, concurrent and/or after treatment;
- ~~47. The method or use of any of the foregoing claims which includes assaying b.~~
VISTA expression levels on hematopoietic cells; and/or
- ~~48. The method or use of any of the foregoing claims which includes assaying VISTA c.~~
VISTA expression levels on hematopoietic cells selected from any one or more of myeloid lineage cells and/or a lymphocytes, monocyte or a neutrophils, T cells, B cells, a natural killer (NK) cells or a natural killer T (NKT) cells.
- ~~190. The method or use of any of the foregoing claims wherein the agonist anti-human VISTA antibody or fragment comprises the same CDRs as an antibody selected from VSTB49-VSTB116 and a human IgG2 Fc region which optionally may be mutated.~~
- ~~191. The method or use of claim 49 wherein the IgG2 constant or Fc region retains native FcR binding and/or the ability to bind CD32A.~~

~~51.16. The antibody, composition, method or use of any of the foregoing claims~~The antibody of any one of claims 1-7, or use of any one of claims 13-15, wherein the anti-human VISTA antibody or fragment comprises an affinity or K_D for human VISTA which is 50nM or less as determined by surface plasmon resonance at 37° C.;

~~The antibody, composition, method or use of any of the foregoing claims wherein the anti human VISTA antibody~~a. 50nM or less as determined by surface plasmon resonance at 37° C;~~or fragment comprises an affinity or K_D for human VISTA which is~~

~~52.b.~~1nM or less as determined by surface plasmon resonance at 37° C.

17. A pharmaceutical composition comprising a pharmaceutically effective amount of an antibody according to claim 16 and a pharmaceutically acceptable carrier.

18. A diagnostic composition comprising a pharmaceutically effective amount of an antibody according to claim 16 and a diagnostically acceptable carrier.

19. The agonistic antibody according to any one of claims 1-7 or pharmaceutical composition according to claim 8 for use in therapy.