

CLAIMS

1. Use of an anti-ICOS antibody or antigen-binding fragment thereof that binds the extracellular domain of human and/or mouse ICOS in the manufacture of a medicament for treating a disease or condition amenable to therapy by depleting regulatory T cells (Tregs) and/or increasing effector T cell (Teff) response in a subject in need thereof, wherein the anti-ICOS antibody or antigen-binding fragment thereof is to be administered to the subject at a dose of 0.8 mg to 240 mg.
2. The use according to claim 1, wherein the anti-ICOS antibody or antigen-binding fragment thereof comprises heavy chain complementary determining regions (HCDRs) HCDR1, HCDR2, and HCDR3, and light chain complementary determining regions (LCDRs) LCDR1, LCDR2, and LCDR3, wherein:
 - (a) HCDR1, HCDR2, and HCDR3 comprise the sequences having at least 85%, 90%, or 95% sequence identity to the amino acid sequences SEQ ID NO: 405, SEQ ID NO: 406, and SEQ ID NO: 407 and LCDR1, LCDR2, and LCDR3 comprise the sequences having at least 85%, 90%, or 95% sequence identity to the amino acid sequences SEQ ID NO: 412, SEQ ID NO: 413, SEQ ID NO: 414;
 - (b) HCDR1, HCDR2, and HCDR3 comprise sequences having at least 85%, 90%, or 95% sequence identity to the amino acid sequences SEQ ID NO: 363, SEQ ID NO: 364, and SEQ ID NO: 365 and LCDR1, LCDR2, and LCDR3 comprise sequences having at least 85%, 90%, or 95% sequence identity to the amino acid sequences SEQ ID NO: 370, SEQ ID NO: 371, SEQ ID NO: 372;
 - (c) HCDR1, HCDR2, and HCDR3 comprise the sequences having at least 85%, 90%, or 95% sequence identity to the amino acid sequences SEQ ID NO: 377, SEQ ID NO: 378, and SEQ ID NO: 379 and LCDR1, LCDR2, and LCDR3 comprise the sequences having at least 85%, 90%, or 95% sequence identity to the amino acid sequences SEQ ID NO: 384, SEQ ID NO: 385, SEQ ID NO: 386;
 - (d) HCDR1, HCDR2, and HCDR3 comprise the sequences having at least 85%, 90%, or 95% sequence identity to the amino acid sequences SEQ ID NO: 391, SEQ ID NO: 392, and SEQ ID NO: 393 and LCDR1, LCDR2, and LCDR3 comprise the sequences having at least 85%, 90%, or 95% sequence identity to the amino acid sequences SEQ ID NO: 398, SEQ ID NO: 399, SEQ ID NO: 400;

(e) HCDR1, HCDR2, and HCDR3 comprise the sequences having at least 85%, 90%, or 95% sequence identity to the amino acid sequences SEQ ID NO: 419, SEQ ID NO: 420, and SEQ ID NO: 421 and LCDR1, LCDR2, and LCDR3 comprise the sequences having at least 85%, 90%, or 95% sequence identity to the amino acid sequences SEQ ID NO: 426, SEQ ID NO: 427, SEQ ID NO: 428;

(f) HCDR1, HCDR2, and HCDR3 comprise the sequences having at least 85%, 90%, or 95% sequence identity to the amino acid sequences SEQ ID NO: 435, SEQ ID NO: 436, and SEQ ID NO: 437 and LCDR1, LCDR2, and LCDR3 comprise the sequences having at least 85%, 90%, or 95% sequence identity to the amino acid sequences SEQ ID NO: 442, SEQ ID NO: 443, SEQ ID NO: 444;

(g) HCDR1, HCDR2, and HCDR3 comprise the sequences having at least 85%, 90%, or 95% sequence identity to the amino acid sequences SEQ ID NO: 449, SEQ ID NO: 450, and SEQ ID NO: 451 and LCDR1, LCDR2, and LCDR3 comprise the sequences having at least 85%, 90%, or 95% sequence identity to the amino acid sequences SEQ ID NO: 456, SEQ ID NO: 457, SEQ ID NO: 458;

(h) HCDR1, HCDR2, and HCDR3 comprise the sequences having at least 85%, 90%, or 95% sequence identity to the amino acid sequences SEQ ID NO: 463, SEQ ID NO: 464, and SEQ ID NO: 465 and LCDR1, LCDR2, and LCDR3 comprise the sequences having at least 85%, 90%, or 95% sequence identity to the amino acid sequences SEQ ID NO: 470, SEQ ID NO: 471, SEQ ID NO: 472;

(i) HCDR1, HCDR2, and HCDR3 comprise the sequences having at least 85%, 90%, or 95% sequence identity to the amino acid sequences SEQ ID NO: 477, SEQ ID NO: 478, and SEQ ID NO: 479 and LCDR1, LCDR2, and LCDR3 comprise the sequences having at least 85%, 90%, or 95% sequence identity to the amino acid sequences SEQ ID NO: 484, SEQ ID NO: 485, SEQ ID NO: 486, or

(j) HCDR1, HCDR2, and HCDR3 comprise the sequences having at least 85%, 90%, or 95% sequence identity to the amino acid sequences SEQ ID NO: 491, SEQ ID NO: 492, and SEQ ID NO: 493 and LCDR1, LCDR2, and LCDR3 comprise the sequences having at least 85%, 90%, or 95% sequence identity to the amino acid sequences SEQ ID NO: 498, SEQ ID NO: 499, SEQ ID NO: 500.

3. The use according to claim 1 or claim 2, wherein the anti-ICOS antibody or antigen-binding fragment thereof comprises heavy chain complementary determining regions

(HCDRs) HCDR1, HCDR2, and HCDR3, and light chain complimentary determining regions (LCDRs) LCDR1, LCDR2, and LCDR3, wherein:

(a) HCDR1 comprises the amino acid sequence SEQ ID NO: 405, HCDR2 comprises the amino acid sequence SEQ ID NO: 406, HCDR3 comprises the amino acid sequence SEQ ID NO: 407, LCDR1 comprises the amino acid sequence SEQ ID NO: 412, LCDR2 comprises the amino acid sequence SEQ ID NO: 413, and LCDR3 comprises the amino acid sequence SEQ ID NO: 414;

(b) HCDR1 comprises the amino acid sequence SEQ ID NO: 363, HCDR2 comprises the amino acid sequence SEQ ID NO: 364, HCDR3 comprises the amino acid sequence SEQ ID NO: 365, LCDR1 comprises the amino acid sequence SEQ ID NO: 370, LCDR2 comprises the amino acid sequence SEQ ID NO: 371, and LCDR3 comprises the amino acid sequence SEQ ID NO: 372;

(c) HCDR1 comprises the amino acid sequence SEQ ID NO: 377, HCDR2 comprises the amino acid sequence SEQ ID NO: 378, HCDR3 comprises the amino acid sequence SEQ ID NO: 379, LCDR1 comprises the amino acid sequence SEQ ID NO: 384, LCDR2 comprises the amino acid sequence SEQ ID NO: 385, and LCDR3 comprises the amino acid sequence SEQ ID NO: 386;

(d) HCDR1 comprises the amino acid sequence SEQ ID NO: 391, HCDR2 comprises the amino acid sequence SEQ ID NO: 392, HCDR3 comprises the amino acid sequence SEQ ID NO: 393, LCDR1 comprises the amino acid sequence SEQ ID NO: 398, LCDR2 comprises the amino acid sequence SEQ ID NO: 399, and LCDR3 comprises the amino acid sequence SEQ ID NO: 400;

(e) HCDR1 comprises the amino acid sequence SEQ ID NO: 419, HCDR2 comprises the amino acid sequence SEQ ID NO: 420, HCDR3 comprises the amino acid sequence SEQ ID NO: 421, LCDR1 comprises the amino acid sequence SEQ ID NO: 426, LCDR2 comprises the amino acid sequence SEQ ID NO: 427, and LCDR3 comprises the amino acid sequence SEQ ID NO: 428;

(f) HCDR1 comprises the amino acid sequence SEQ ID NO: 435, HCDR2 comprises the amino acid sequence SEQ ID NO: 436, HCDR3 comprises the amino acid sequence SEQ ID NO: 437, LCDR1 comprises the amino acid sequence SEQ ID NO: 442, LCDR2 comprises the amino acid sequence SEQ ID NO: 443, and LCDR3 comprises the amino acid sequence SEQ ID NO: 444;

(g) HCDR1 comprises the amino acid sequence SEQ ID NO: 449, HCDR2 comprises the amino acid sequence SEQ ID NO: 450, HCDR3 comprises the amino acid sequence SEQ ID NO: 451, LCDR1 comprises the amino acid sequence SEQ ID NO: 456, LCDR2 comprises the amino acid sequence SEQ ID NO: 457, and LCDR3 comprises the amino acid sequence SEQ ID NO: 458;

(h) HCDR1 comprises the amino acid sequence SEQ ID NO: 463, HCDR2 comprises the amino acid sequence SEQ ID NO: 464, HCDR3 comprises the amino acid sequence SEQ ID NO: 465, LCDR1 comprises the amino acid sequence SEQ ID NO: 470, LCDR2 comprises the amino acid sequence SEQ ID NO: 471, and LCDR3 comprises the amino acid sequence SEQ ID NO: 472;

(i) HCDR1 comprises the amino acid sequence SEQ ID NO: 477, HCDR2 comprises the amino acid sequence SEQ ID NO: 478, HCDR3 comprises the amino acid sequence SEQ ID NO: 479, LCDR1 comprises the amino acid sequence SEQ ID NO: 484, LCDR2 comprises the amino acid sequence SEQ ID NO: 485, and LCDR3 comprises the amino acid sequence SEQ ID NO: 486; or

(j) HCDR1 comprises the amino acid sequence SEQ ID NO: 491, HCDR2 comprises the amino acid sequence SEQ ID NO: 492, HCDR3 comprises the amino acid sequence SEQ ID NO: 493, LCDR1 comprises the amino acid sequence SEQ ID NO: 498, LCDR2 comprises the amino acid sequence SEQ ID NO: 499, and LCDR3 comprises the amino acid sequence SEQ ID NO: 500.

4. The use according to claims 1-3, wherein the anti-ICOS antibody or antigen-binding fragment thereof comprises a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein:

(a) the VH domain comprises a sequence having at least 85%, 90%, or 95% sequence identity to the amino acid sequence SEQ ID NO: 408 and VL domain comprises a sequence having at least 85%, 90%, or 95% sequence identity to the amino acid sequence SEQ ID NO: 415;

(b) the VH domain comprises the amino acid sequence SEQ ID NO: 408 and the VL domain comprises the amino acid sequence SEQ ID NO: 415;

(c) the VH domain comprises a sequence having at least 85%, 90%, or 95% sequence identity to the amino acid sequence SEQ ID NO: 366 and the VL domain

comprises a sequence having at least 85%, 90%, or 95% sequence identity to the amino acid sequence SEQ ID NO: 373;

(d) the VH domain comprises a sequence having at least 85%, 90%, or 95% sequence identity to the amino acid sequence SEQ ID NO: 380 and the VL domain comprises a sequence having at least 85%, 90%, or 95% sequence identity to the amino acid sequence SEQ ID NO: 387;

(e) the VH domain comprises a sequence having at least 85%, 90%, or 95% sequence identity to the amino acid sequence SEQ ID NO: 394 and the VL domain comprises a sequence having at least 85%, 90%, or 95% sequence identity to the amino acid sequence SEQ ID NO: 401;

(f) the VH domain comprises a sequence having at least 85%, 90%, or 95% sequence identity to the amino acid sequence SEQ ID NO: 422 and the VL domain comprises a sequence having at least 85%, 90%, or 95% sequence identity to the amino acid sequence SEQ ID NO: 429;

(g) the VH domain comprises a sequence having at least 85%, 90%, or 95% sequence identity to the amino acid sequence SEQ ID NO: 438 and the VL domain comprises a sequence having at least 85%, 90%, or 95% sequence identity to the amino acid sequence SEQ ID NO: 445;

(h) the VH domain comprises a sequence having at least 85%, 90%, or 95% sequence identity to the amino acid sequence SEQ ID NO: 452 and VL domain comprises a sequence having at least 85%, 90%, or 95% sequence identity to the amino acid sequence SEQ ID NO: 459;

(i) the VH domain comprises a sequence having at least 85%, 90%, or 95% sequence identity to the amino acid sequence SEQ ID NO: 467 and the VL domain comprises a sequence having at least 85%, 90%, or 95% sequence identity to the amino acid sequence SEQ ID NO: 473;

(j) the VH domain comprises a sequence having at least 85%, 90%, or 95% sequence identity to the amino acid sequence SEQ ID NO 481: and the VL domain comprises a sequence having at least 85%, 90%, or 95% sequence identity to the amino acid sequence SEQ ID NO: 488;

(k) the VH domain comprises a sequence having at least 85%, 90%, or 95% sequence identity to the amino acid sequence SEQ ID NO: 494 and the VL domain

comprises a sequence having at least 85%, 90%, or 95% sequence identity to the amino acid sequence SEQ ID NO: 501;

(l) the VH domain comprises the amino acid sequence SEQ ID NO: 366 and the VL domain comprises the amino acid sequence SEQ ID NO: 373;

(m) the VH domain comprises the amino acid sequence SEQ ID NO: 380 and the VL domain comprises the amino acid sequence SEQ ID NO: 387;

(n) the VH domain comprises the amino acid sequence SEQ ID NO: 394 and the VL domain comprises the amino acid sequence SEQ ID NO: 401;

(o) the VH domain comprises the amino acid sequence SEQ ID NO: 408 and the VL domain comprises the amino acid sequence SEQ ID NO: 415;

(p) the VH domain comprises the amino acid sequence SEQ ID NO: 422 and the VL domain comprises the amino acid sequence SEQ ID NO: 429;

(q) the VH domain comprises the amino acid sequence SEQ ID NO: 438 and the VL domain comprises the amino acid sequence SEQ ID NO: 445;

(r) the VH domain comprises the amino acid sequence SEQ ID NO: 452 and the VL domain comprises the amino acid sequence SEQ ID NO: 459;

(s) the VH domain comprises the amino acid sequence SEQ ID NO: 467 and the VL domain comprises the amino acid sequence SEQ ID NO: 473;

(t) the VH domain comprises the amino acid sequence SEQ ID NO: 480 and the VL domain comprises the amino acid sequence SEQ ID NO: 487; or

(u) the VH domain comprises the amino acid sequence SEQ ID NO: 494 and the VL domain comprises the amino acid sequence SEQ ID NO: 501.

5. The use according to any one of claims 1-4, wherein the anti-ICOS antibody or antigen binding fragment thereof comprises heavy chain complementary determining regions (HCDRs) HCDR1, HCDR2, and HCDR3, and light chain complementary determining regions (LCDRs) LCDR1, LCDR2, and LCDR3 and a heavy chain variable (VH) domain and a light chain variable (VL) domain, wherein HCDR1 comprises the amino acid sequence SEQ ID NO: 405, HCDR2 comprises the amino acid sequence SEQ ID NO: 406, HCDR3 comprises the amino acid sequence SEQ ID NO: 407, LCDR1 comprises the amino acid sequence SEQ ID NO: 412, LCDR2 comprises the amino acid sequence SEQ ID NO: 413, and LCDR3 comprises the amino acid sequence SEQ ID NO: 414, optionally wherein the VH domain

comprises the amino acid sequence SEQ ID NO: 408 and the VL domain comprises the amino acid sequence SEQ ID NO: 415.

6. The use according to any one of claims 1-5, wherein the anti-ICOS antibody or antigen binding fragment thereof comprises a heavy chain and a light chain, wherein:

(a) the heavy chain comprises a sequence having at least 85%, 90%, or 95% sequence identity to the amino acid sequence SEQ ID NO: 410 and the light chain comprises a sequence having at least 85%, 90%, or 95% sequence identity to the amino acid sequence SEQ ID NO: 417;

(b) the heavy chain comprises the amino acid sequence SEQ ID NO: 410 and the light chain comprises the amino acid sequence SEQ ID NO: 417;

(c) the heavy chain comprises a sequence having at least 85%, 90%, or 95% sequence identity to the amino acid sequence SEQ ID NO: 368 and the light chain comprises a sequence having at least 85%, 90%, or 95% sequence identity to the amino acid sequence SEQ ID NO: 375;

(d) the heavy chain comprises a sequence having at least 85%, 90%, or 95% sequence identity to the amino acid sequence SEQ ID NO: 385 and the light chain comprises a sequence having at least 85%, 90%, or 95% sequence identity to the amino acid sequence SEQ ID NO: 389;

(e) the heavy chain comprises a sequence having at least 85%, 90%, or 95% sequence identity to the amino acid sequence SEQ ID NO: 396 and the light chain comprises a sequence having at least 85%, 90%, or 95% sequence identity to the amino acid sequence SEQ ID NO: 403;

(f) the heavy chain comprises a sequence having at least 85%, 90%, or 95% sequence identity to the amino acid sequence SEQ ID NO: 424 and the light chain comprises a sequence having at least 85%, 90%, or 95% sequence identity to the amino acid sequence SEQ ID NO: 432;

(g) the heavy chain comprises a sequence having at least 85%, 90%, or 95% sequence identity to the amino acid sequence SEQ ID NO: 440 and the light chain comprises a sequence having at least 85%, 90%, or 95% sequence identity to the amino acid sequence SEQ ID NO: 447;

(h) the heavy chain comprises a sequence having at least 85%, 90%, or 95% sequence identity to the amino acid sequence SEQ ID NO: 454 and the light chain comprises a sequence having at least 85%, 90%, or 95% sequence identity to the amino acid sequence SEQ ID NO: 461;

(i) the heavy chain comprises a sequence having at least 85%, 90%, or 95% sequence identity to the amino acid sequence SEQ ID NO: 468 and the light chain comprises a sequence having at least 85%, 90%, or 95% sequence identity to the amino acid sequence SEQ ID NO: 475;

(j) the heavy chain comprises a sequence having at least 85%, 90%, or 95% sequence identity to the amino acid sequence SEQ ID NO: 482 and the light chain comprises a sequence having at least 85%, 90%, or 95% sequence identity to the amino acid sequence SEQ ID NO: 489;

(k) the heavy chain comprises a sequence having at least 85%, 90%, or 95% sequence identity to the amino acid sequence SEQ ID NO: 496 and the light chain comprises a sequence having at least 85%, 90%, or 95% sequence identity to the amino acid sequence SEQ ID NO: 503;

(l) the heavy chain comprises the amino acid sequence SEQ ID NO: 368 and the light chain comprises the amino acid sequence SEQ ID NO: 375;

(m) the heavy chain comprises the amino acid sequence SEQ ID NO: 382 and the light chain comprises the amino acid sequence SEQ ID NO: 389;

(n) the heavy chain comprises the amino acid sequence SEQ ID NO: 396 and the light chain comprises the amino acid sequence SEQ ID NO: 403;

(o) the heavy chain comprises the amino acid sequence SEQ ID NO: 424 and the light chain comprises the amino acid sequence SEQ ID NO: 432;

(p) the heavy chain comprises the amino acid sequence SEQ ID NO: 440 and the light chain comprises the amino acid sequence SEQ ID NO: 447;

(q) the heavy chain comprises the amino acid sequence SEQ ID NO: 454 and the light chain comprises the amino acid sequence SEQ ID NO: 461;

(r) the heavy chain comprises the amino acid sequence SEQ ID NO: 468 and the light chain comprises the amino acid sequence SEQ ID NO: 475;

(s) the heavy chain comprises the amino acid sequence SEQ ID NO: 482 and the light chain comprises the amino acid sequence SEQ ID NO: 489; or

(t) the heavy chain comprises the amino acid sequence SEQ ID NO: 496 and the light chain comprises the amino acid sequence SEQ ID NO: 503.

7. The use according to any one of claims 1-6, wherein
 - i) the anti-ICOS antibody is a human IgG1 antibody; and/or
 - ii) the anti-ICOS antibody is KY1044.
8. The use according to any one of claims 1-7, wherein the anti-ICOS antibody or antigen-binding fragment thereof is to be administered to the subject at a dose of about 0.5 mg to about 10 mg, optionally wherein the anti-ICOS antibody or antigen-binding fragment thereof is to be administered to the subject at a dose of
 - i) 0.8 mg to 8 mg;
 - ii) about 8 mg (e.g., at a dose of 7.5 mg or less, at a dose of 7 mg or less);
 - iii) 0.8 mg to 2.4 mg;
 - iv) 2.4 mg to 8 mg;
 - v) about 0.8 mg;
 - vi) about 2.4 mg; or
 - vii) about 8 mg.
9. The use according to any one of claims 1-8, wherein the anti-ICOS antibody or antigen-binding fragment thereof is to be administered to the subject every 2-6 weeks, e.g., every 2 weeks, every 3 weeks, every 4 weeks, every 5 weeks, or every 6 weeks, optionally wherein the anti-ICOS antibody or antigen-binding fragment thereof is to be administered to the subject every 3 weeks, every 6 weeks, or monthly.
10. The use according to any one of claims 1-9, wherein the anti-ICOS antibody or antigen-binding fragment thereof is to be administered to the subject for at least 6 months, e.g., for 6 months, 12 months, or more than 12 months.
11. The use according to any one of claims 1-10, wherein a second therapeutic agent is to be administered to the subject, optionally wherein the second therapeutic comprises an anti-PD-L1 antibody or antigen-binding fragment thereof, optionally wherein the anti-PD-L1

antibody is atezolizumab, optionally wherein the anti-PD-L1 antibody or antigen-binding fragment thereof is to be administered to the subject at a dose of about 1200 mg.

12. The use according to claim 11, wherein the anti-PD-L1 antibody or antigen-binding fragment thereof is to be administered to the subject every 2-6 weeks, e.g., every 2 weeks, every 3 weeks, every 4 weeks, every 5 weeks, or every 6 weeks, optionally wherein the anti-PD-L1 antibody or antigen-binding fragment thereof is to be administered to the subject every 3 weeks or every 6 weeks.

13. The use according to claim 11, wherein the anti-PD-L1 antibody or antigen-binding fragment thereof is to be administered to the subject monthly, optionally wherein the anti-PD-L1 antibody or antigen-binding fragment thereof is to be administered to the subject for at least 6 months, e.g., for 6 months, 12 months, or more than 12 months.

14. The use according to claim 11, wherein the anti-PD-L1 antibody or antigen-binding fragment thereof is

a) to be co-administered to the subject with the anti-ICOS antibody or antigen-binding fragment thereof every 3 weeks, or

b) to be administered to the subject in alternating doses with the anti-ICOS antibody or antigen-binding fragment thereof, e.g., wherein the anti-PD-L1 antibody or antigen-binding fragment thereof is to be administered every 3 weeks and the anti-ICOS antibody or antigen-binding fragment thereof is to be administered every 6 weeks.

15. The use according to any one of claims 1-14, wherein the disease or condition amenable to therapy by depleting regulatory T cells (Tregs) and/or increasing effector T cell (Teff) response comprises a tumour, optionally wherein the disease or condition amenable to therapy by depleting regulatory T cells (Tregs) and/or increasing effector T cell (Teff) response comprises a cancer, optionally wherein the cancer comprises an advanced and/or metastatic cancer, optionally wherein the cancer comprises triple negative breast cancer, head and neck squamous cell carcinoma, penile cancer, pancreatic cancer, non-small cell lung cancer, hepatocellular carcinoma, esophageal cancer, gastric cancer, melanoma, renal cell carcinoma, and/or cervical cancer.