

CLAIMS

What is claimed is:

1. Use of an antibody that specifically binds to human PSGL-1 in the manufacture of a medicament for use in combinatorial therapy for treating or preventing (a) a T-cell mediated inflammatory disease or (b) cancer in a subject in need thereof, wherein said medicament is to be administered in combination with a Janus kinase (JAK) inhibitor.
2. The use of claim 1, wherein the JAK inhibitor:
 - (a) inhibits JAK1 and/or JAK2;
 - (b) inhibits JAK1 and/or JAK3;
 - (c) is ruxolitinib; or
 - (d) is tofacitinib.
3. The use of any one of claims 1-2, wherein the antibody that specifically binds to human PSGL-1 comprises a heavy chain comprising a heavy chain variable (VH) domain and a light chain comprising a light chain variable (VL) domain; wherein:
 - (a) the VH domain comprises a CDR-H1 comprising the amino acid sequence SFGMH (SEQ ID NO:8), a CDR-H2 comprising the amino acid sequence YINGGSSTIFYANAVKG (SEQ ID NO:9), and a CDR-H3 comprising the amino acid sequence YASYGGGAMDY (SEQ ID NO:10); and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence RSSQSIVHNDGNTYFE (SEQ ID NO:5), a CDR-L2 comprising the amino acid sequence KVSNRFS (SEQ ID NO:6), and a CDR-L3 comprising the amino acid sequence FQGSYVPLT (SEQ ID NO:7);
 - (b) the VH domain comprises a CDR-H1 comprising the amino acid sequence AYYIH (SEQ ID NO:24), a CDR-H2 comprising the amino acid sequence RVNPNTGGTSYNPKFKG (SEQ ID NO:25), and a CDR-H3 comprising the amino acid sequence SGSPYYRYDD (SEQ ID NO:26); and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence RASSTVNSTYLH (SEQ ID NO:28), a CDR-L2

comprising the amino acid sequence GSSNLAS (SEQ ID NO:29), and a CDR-L3 comprising the amino acid sequence QQYSGYPLT (SEQ ID NO:30); or

(c) the VH domain comprises a CDR-H1 comprising the amino acid sequence TNAMN (SEQ ID NO:32), a CDR-H2 comprising the amino acid sequence RIRSKSNNYATYYADSVKD (SEQ ID NO:33), and a CDR-H3 comprising the amino acid sequence GGSYWYFDV (SEQ ID NO:34); and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence RSSQSIVNSNGNTYLE (SEQ ID NO:36), a CDR-L2 comprising the amino acid sequence KVSNRFS (SEQ ID NO:37), and a CDR-L3 comprising the amino acid sequence FQGSHVPWT (SEQ ID NO:38).

4. The use of any one of claims 1-3, wherein the antibody is a humanized antibody.

5. The use of any one of claims 1-4, wherein:

(a) the VH domain comprises the amino acid sequence of SEQ ID NO:4, and the VL domain comprises the amino acid sequence of SEQ ID NO:3;

(b) the heavy chain comprises the amino acid sequence of SEQ ID NO:27, and the light chain comprises the amino acid sequence of SEQ ID NO:31;

(c) the heavy chain comprises the amino acid sequence of SEQ ID NO:35, and the light chain comprises the amino acid sequence of SEQ ID NO:39.

6. The use of any one of claims 1-4, wherein the heavy chain further comprises an antibody constant domain; optionally wherein the constant domain is a human IgG4 constant domain; and optionally wherein the constant domain is a human IgG4 constant domain comprising an S228P amino acid substitution at position 228, wherein the numbering is according to EU numbering.

7. The use of any one of claims 1-6, wherein the light chain is a human kappa light chain.

8. The use of any one of claims 1-4, wherein the heavy chain comprises the amino acid sequence of SEQ ID NO:2, and the light chain comprises the amino acid sequence of SEQ ID NO:1.

9. The use of any one of claims 1-4, wherein the antibody that specifically binds to human PSGL-1 comprises the amino acid sequence of SEQ ID NO:23.
10. The use of any one of claims 1-9, wherein the T-cell mediated inflammatory disease is graft-versus-host disease (GVHD) or transplantation rejection; optionally wherein the T-cell mediated inflammatory disease is acute GVHD, steroid-refractory acute GVHD (SR-aGVHD), treatment-refractory acute GVHD (TR-aGVHD), or chronic GVHD.
11. The use of any one of claims 1-9, wherein the T-cell mediated inflammatory disease is selected from the group consisting of: a skin disorder, multiple sclerosis, rheumatoid arthritis, juvenile arthritis, type I diabetes, lupus, inflammatory bowel disease, Crohn's disease, myasthenia gravis, immunoglobulin nephropathies, myocarditis, psoriasis, ankylosing spondylitis, arthritis, diabetes mellitus, systemic lupus erythematosus, dermatitis, Sjogren's Syndrome, ulcerative colitis, asthma, allergic asthma, scleroderma, autoimmune uveitis, Stevens-Johnson syndrome, vitiligo, alopecia areata, cytokine release syndrome, hidradenitis suppurativa, sarcoidosis, primary biliary cirrhosis, uveitis posterior, allergies, and autoimmune thyroid disorder.
12. The use of any one of claims 1-9, wherein the cancer is a T-cell leukemia or T-cell lymphoma; optionally wherein the T-cell leukemia or lymphoma is adult T cell leukemia/lymphoma (ATLL), anaplastic large cell lymphoma (ALCL), or cutaneous T-cell lymphoma (CTCL).
13. The use of any one of claims 1-12, wherein human PSGL-1 comprises the amino acid sequence of SEQ ID NO:11 or SEQ ID NO:22.
14. The use of any one of claims 1-13, wherein the subject is a human.
15. The use of any one of claims 1-14, wherein the antibody is to be administered by intravenous infusion.
16. The use of any one of claims 1-15, wherein the antibody is a monoclonal antibody.
17. The use of any one of claims 1-16, wherein the JAK inhibitor is to be administered to the subject before, after, or simultaneous with administration of the antibody; optionally wherein the JAK inhibitor is to be administered orally to the subject.

18. The use of any one of claims 1-17, wherein the subject has been treated with a corticosteroid.
19. A kit comprising an antibody that specifically binds to human PSGL-1 and a package insert comprising instructions for using the antibody in combination with a Janus kinase (JAK) inhibitor for treating or preventing a T-cell mediated inflammatory disease in a subject.
20. A kit comprising an antibody that specifically binds to human PSGL-1 and a package insert comprising instructions for using the antibody in combination with a Janus kinase (JAK) inhibitor for treating or preventing cancer in a subject.
21. The kit of claim 19 or claim 20, further comprising the JAK inhibitor.
22. The kit of any one of claims 19-21, wherein the antibody comprises a heavy chain comprising a heavy chain variable (VH) domain and a light chain comprising a light chain variable (VL) domain; wherein:
- (a) the VH domain comprises a CDR-H1 comprising the amino acid sequence SFGMH (SEQ ID NO:8), a CDR-H2 comprising the amino acid sequence YINGGSSTIFYANAVKG (SEQ ID NO:9), and a CDR-H3 comprising the amino acid sequence YASYGGGAMDY (SEQ ID NO:10); and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence RSSQSIVHNDGNTYFE (SEQ ID NO:5), a CDR-L2 comprising the amino acid sequence KVSNRFS (SEQ ID NO:6), and a CDR-L3 comprising the amino acid sequence FQGSYVPLT (SEQ ID NO:7);
- (b) the VH domain comprises a CDR-H1 comprising the amino acid sequence AYYIH (SEQ ID NO:24), a CDR-H2 comprising the amino acid sequence RVNPNTGGTSYNPKFKG (SEQ ID NO:25), and a CDR-H3 comprising the amino acid sequence SGSPYYRYDD (SEQ ID NO:26); and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence RASSTVNSTYLH (SEQ ID NO:28), a CDR-L2 comprising the amino acid sequence GSSNLAS (SEQ ID NO:29), and a CDR-L3 comprising the amino acid sequence QQYSGYPLT (SEQ ID NO:30); or
- (c) the VH domain comprises a CDR-H1 comprising the amino acid sequence TNAMN (SEQ ID NO:32), a CDR-H2 comprising the amino acid sequence

RIRSKSNNYATYYADSVKD (SEQ ID NO:33), and a CDR-H3 comprising the amino acid sequence GGSYWYFDV (SEQ ID NO:34); and wherein the VL domain comprises a CDR-L1 comprising the amino acid sequence RSSQSIVNSNGNTYLE (SEQ ID NO:36), a CDR-L2 comprising the amino acid sequence KVSNRFS (SEQ ID NO:37), and a CDR-L3 comprising the amino acid sequence FQGSHVPWT (SEQ ID NO:38).