CLAIMS:

1. An antibody that specifically binds to BST1, said antibody comprising:
   a) a heavy chain variable region comprising:
      i) a first vhCDR comprising SEQ ID NO:10;
      ii) a second vhCDR comprising a sequence selected from the group consisting of SEQ ID NO: 12 and SEQ ID NO: 51; and
      iii) a third vhCDR comprising SEQ ID NO:14; and
   b) a light chain variable region comprising:
      i) a first vlCDR comprising SEQ ID NO:16;
      ii) a second vlCDR comprising SEQ ID NO: 18; and
      iii) a third vlCDR comprising a SEQ ID NO:20.

2. An antibody that specifically binds to BST1, said antibody comprising:
   a) a heavy chain variable region comprising:
      j) a first vhCDR comprising SEQ ID NO:9;
      ii) a second vhCDR comprising SEQ ID NO: 11; and
      iii) a third vhCDR comprising SEQ ID NO:13; and
   b) a light chain variable region comprising:
      j) a first vlCDR comprising SEQ ID NO:15;
      ii) a second vlCDR comprising SEQ ID NO: 17; and
      iii) a third vlCDR comprising SEQ ID NO:19.

3. An antibody that specifically binds to BST1, said antibody comprising:
   a) a heavy chain variable region comprising:
      k) a first vhCDR comprising SEQ ID NO:56;
      ii) a second vhCDR comprising SEQ ID NO: 57; and
      iii) a third vhCDR comprising SEQ ID NO:58; and
   b) a light chain variable region comprising:
      k) a first vlCDR comprising SEQ ID NO:59;
      ii) a second vlCDR comprising SEQ ID NO: 60; and
      iii) a third vlCDR comprising SEQ ID NO:61.

4. A variant antibody comprising variant variable regions of a parent antibody, wherein the parent antibody comprises:

a) a first vhCDR comprising SEQ ID NO:10;

b) a second vhCDR comprising a sequence selected from the group consisting of SEQ ID NO: 12 and SEQ ID NO: 51;

c) a third vhCDR comprising SEQ ID NO:14;

d) a first vlCDR comprising SEQ ID NO:16;

e) a second vlCDR comprising SEQ ID NO: 18; and

f) a third vlCDR comprising a SEQ ID NO:20;

wherein said variant antibody have from one to four amino acid changes collectively in said first vhCDR, said second vhCDR, said third vhCDR, said first vlCDR, said second vlCDR and said third vlCDR.

5. A variant antibody comprising variant variable regions of a parent antibody, wherein the parent antibody comprises:

a) a first vhCDR comprising SEQ ID NO:9;

b) a second vhCDR comprising SEQ ID NO:11;

c) a third vhCDR comprising SEQ ID NO:13;

d) a first vlCDR comprising SEQ ID NO:115;

e) a second vlCDR comprising SEQ ID NO: 17; and

f) a third vlCDR comprising a SEQ ID NO:19;

wherein said variant antibody have from one to four amino acid changes collectively in said first vhCDR, said second vhCDR, said third vhCDR, said first vlCDR, said second vlCDR and said third vlCDR.

6. A variant antibody comprising variant variable regions of a parent antibody, wherein the parent antibody comprises:

a) a first vhCDR comprising SEQ ID NO:56;

b) a second vhCDR comprising SEQ ID NO: 57; and

c) a third vhCDR comprising SEQ ID NO:58;

d) a first vlCDR comprising SEQ ID NO:59;

e) a second vlCDR comprising SEQ ID NO:60; and

f) a third vlCDR comprising a SEQ ID NO:61;

wherein said variant antibody have from one to four amino acid changes collectively in said first vhCDR, said second vhCDR, said third vhCDR, said first vlCDR, said second vlCDR and said third vlCDR.

7. An antibody according to claim 1 or 4 comprising:
a) a heavy chain at least 95% identical SEQ ID NO: 2 and
a light chain at least 95% identical SEQ ID NO: 4.

8. An antibody according to claim 1 comprising:
a heavy chain variable region of SEQ ID NO: 2, and
a light chain variable region of SEQ ID NO: 4.

9. An antibody according to claim 2 or 5 comprising:
c) a heavy chain at least 95% identical SEQ ID NO: 1 and
d) a light chain at least 95% identical SEQ ID NO: 3.

10. An antibody according to claim 2 comprising:
e) a heavy chain variable region of SEQ ID NO: 1, and
f) a light chain variable region of SEQ ID NO: 3.

11. An antibody according to claim 1 or 4 comprising:
g) a heavy chain at least 95% identical SEQ ID NO: 45 and
h) a light chain at least 95% identical SEQ ID NO: 46.

12. An antibody according to claim 11 comprising:
i) a heavy chain variable region of SEQ ID NO: 45, and
j) a light chain variable region of SEQ ID NO: 46.

13. An antibody according to claim 3 or 6 comprising:
k) a heavy chain at least 95% identical SEQ ID NO: 52 and
l) a light chain at least 95% identical SEQ ID NO: 53.

14. An antibody according to claim 13 comprising:
m) a heavy chain variable region of SEQ ID NO: 52, and
n) a light chain variable region of SEQ ID NO: 53.

15. An isolated monoclonal antibody, or an antigen binding portion thereof, which binds an epitope on BST1 recognized by an antibody set forth in any of the preceding claims including DNA and amino acid changes that maintain at least 80% of the binding to BST1 of the original sequences.

16. An antibody or an antigen-binding portion thereof, according to any previous claim further comprising a covalently attached moiety.

17. An antibody or an antigen-binding portion thereof, according to claim 13 wherein said moiety is a drug.

18. An antibody or an antigen-binding portion thereof, according to claim 17 wherein said drug is selected from the group consisting of a maytansinoid, a dolastatin, an auristatin, a trichothecene, a calicheamicin, CC1065 and derivatives thereof.

19. An isolated antibody according to any of the claims 1-18, wherein said antibody induces antibody-dependent cell-mediated cytotoxicity (ADCC), complement dependent cytotoxicity (CDC) and/or T-cell cytotoxicity.

20. An isolated antibody according to claim 19, wherein the antibody is an engineered antibody having increased binding to Fc receptors and/or increased potency for ADCC, and/or a bispecific antibody.

21. An isolated antibody according to any previous claim, wherein the antibody is a bispecific or multispecific antibody which specificially binds to a first antigen comprising BST1 and a second antigen selected from the group consisting of CD3 antigen and CD5 antigen.

22. A nucleic acid encoding a heavy chain of the antibody of any of the preceding claims.

23. A nucleic acid encoding a light chain of the antibody of any of the preceding claims.

24. A host cell containing the nucleic acids of claim 22 and/or 23.

25. A method of making an antibody comprising culturing a host cell according to claim 24 under conditions where the antibody or an antigen-binding portion thereof, is expressed and optionally isolating the antibody or an antigen-binding portion thereof.

26. A method of treating disease comprising administering to a patient in need thereof an antibody or an antigen-binding portion thereof, of any of the claims 1-21 wherein the antibody or antigen-binding portion thereof, is internalized by a cell expressing BST1, said antibody comprising a covalently attached drug conjugate.

27. A method of treating disease comprising administering to a patient in need thereof an antibody of any of the claims 1-21 wherein the antibody induces antibody-dependent cell-mediated cytotoxicity (ADCC), complement dependent cytotoxicity (CDC) and/or T-cell cytotoxicity.

28. A method according to any of the claims 26-27 wherein said disease is cancer, including acute myeloid leukemia (AML), B-cell chronic lymphocytic leukemia, breast cancer, colorectal cancer, kidney cancer, head and neck cancer, lung cancer, ovarian cancer and pancreatic cancer.

29. A method according to any of the claims 26-27 wherein said disease is an inflammatory disease, including asthma, gout, crohns, lupus, multiple sclerosis, rheumatoid arthritis, psoriasis, diabetes and atherosclerotic.

30. An antibody as claimed in any one of claims 1-18 for use in therapy or for use as a medicament.

AMENDED CLAIMS
received by the International Bureau on 27 June 2013 (27.06.2013)

1. An antibody that specifically binds to BST1, said antibody comprising:
   a) a heavy chain variable region comprising:
      i) a first vhCDR comprising SEQ ID NO: 10;
      ii) a second vhCDR comprising a sequence selected from the group consisting of SEQ ID NO: 12 and SEQ ID NO: 51; and
      iii) a third vhCDR comprising SEQ ID NO: 14; and
   b) a light chain variable region comprising:
      i) a first vlCDR comprising SEQ ID NO: 16;
      ii) a second vlCDR comprising SEQ ID NO: 18; and
      iii) a third vlCDR comprising a SEQ ID NO: 20.

2. An antibody that specifically binds to BST1, said antibody comprising:
   a) a heavy chain variable region comprising:
      i) a first vhCDR comprising SEQ ID NO: 9;
      ii) a second vhCDR comprising SEQ ID NO: 11; and
      iii) a third vhCDR comprising SEQ ID NO: 13; and
   b) a light chain variable region comprising:
      i) a first vlCDR comprising SEQ ID NO: 15;
      ii) a second vlCDR comprising SEQ ID NO: 17; and
      iii) a third vlCDR comprising SEQ ID NO: 19.

3. An antibody that specifically binds to BST1, said antibody comprising:
   a) a heavy chain variable region comprising:
      i) a first vhCDR comprising SEQ ID NO: 56;
      ii) a second vhCDR comprising SEQ ID NO: 57; and
      iii) a third vhCDR comprising SEQ ID NO: 58; and
   b) a light chain variable region comprising:
      i) a first vlCDR comprising SEQ ID NO: 59;
      ii) a second vlCDR comprising SEQ ID NO: 60; and
      iii) a third vlCDR comprising SEQ ID NO: 61.

4. A variant anti-BST1 antibody comprising variant variable regions of a parent antibody, wherein the parent antibody comprises:

a) a first vhCDR comprising SEQ ID NO: 10;

b) a second vhCDR comprising a sequence selected from the group consisting of SEQ ID NO: 12 and SEQ ID NO: 51;

c) a third vhCDR comprising SEQ ID NO: 14;

d) a first vlCDR comprising SEQ ID NO: 16;

e) a second vlCDR comprising SEQ ID NO: 18; and

f) a third vlCDR comprising a SEQ ID NO: 20;

wherein said variant anti-BST1 antibody has from one to four amino acid changes collectively in said first vhCDR, said second vhCDR, said third vhCDR, said first vlCDR, said second vlCDR and said third vlCDR.

5. A variant anti-BST1 antibody comprising variant variable regions of a parent antibody, wherein the parent antibody comprises:

a) a first vhCDR comprising SEQ ID NO: 9;

b) a second vhCDR comprising SEQ ID NO: 11;

c) a third vhCDR comprising SEQ ID NO: 13;

d) a first vlCDR comprising SEQ ID NO: 15;

e) a second vlCDR comprising SEQ ID NO: 17; and

f) a third vlCDR comprising a SEQ ID NO: 19;

wherein said variant anti-BST1 antibody has from one to four amino acid changes collectively in said first vhCDR, said second vhCDR, said third vhCDR, said first vlCDR, said second vlCDR and said third vlCDR.

6. A variant anti-BST1 antibody comprising variant variable regions of a parent antibody, wherein the parent antibody comprises:

a) a first vhCDR comprising SEQ ID NO: 56;

b) a second vhCDR comprising SEQ ID NO: 57;

c) a third vhCDR comprising SEQ ID NO: 58;

d) a first vlCDR comprising SEQ ID NO: 59;

e) a second vlCDR comprising SEQ ID NO: 60; and

f) a third vlCDR comprising a SEQ ID NO: 61;

wherein said variant anti-BST1 antibody has from one to four amino acid changes collectively in said first vhCDR, said second vhCDR, said third vhCDR, said first vlCDR, said second vlCDR and said third vlCDR.

7. An antibody according to claim 1 or 4 comprising:
a heavy chain at least 95% identical SEQ ID NO: 2, and
a light chain at least 95% identical SEQ ID NO: 4.

8. An antibody according to claim 1 comprising:
a heavy chain variable region of SEQ ID NO: 2, and
a light chain variable region of SEQ ID NO: 4.

9. An antibody according to claim 2 or 5 comprising:
a heavy chain at least 95% identical SEQ ID NO: 1, and
a light chain at least 95% identical SEQ ID NO: 3.

10. An antibody according to claim 2 comprising:
a heavy chain variable region of SEQ ID NO: 1, and
a light chain variable region of SEQ ID NO: 3.

11. An antibody according to claim 1 or 4 comprising:
a heavy chain at least 95% identical SEQ ID NO: 46, and
a light chain at least 95% identical SEQ ID NO: 49.

12. An antibody according to claim 11 comprising:
a heavy chain variable region of SEQ ID NO: 46, and
a light chain variable region of SEQ ID NO: 49.

13. An antibody according to claim 3 or 6 comprising:
a heavy chain at least 95% identical SEQ ID NO: 52, and
a light chain at least 95% identical SEQ ID NO: 53.

14. An antibody according to claim 13 comprising:
a heavy chain variable region of SEQ ID NO: 52, and
a light chain variable region of SEQ ID NO: 53.

15. An isolated monoclonal antibody, or an antigen binding portion thereof, which binds an epitope on BST1 recognized by an antibody set forth in any of the preceding claims including DNA and amino acid changes that maintain at least 80% of the binding to BST1 of the original sequences.

16. An antibody as claimed in any one of claims 1 to 15, wherein the antibody is a full-length antibody of an IgG1, IgG2, IgG3 or IgG4 isotype.

17. An antibody or an antigen-binding portion thereof, according to any previous claim further comprising a covalently attached moiety.

18. An antibody or an antigen-binding portion thereof, according to claim 17 wherein said moiety is a drug.

19. An antibody or an antigen-binding portion thereof according to claim 18 wherein said drug is selected from the group consisting of a maytansinoid, a dolastatin, an auristatin, a trichothecene, a calicheamicin, CC1065 and derivatives thereof.

20. An isolated antibody according to any of the claims 1-19, wherein said antibody induces antibody-dependent cell-mediated cytotoxicity (ADCC), complement dependent cytotoxicity (CDC) and/or T-cell cytotoxicity.

21. An isolated antibody according to claim 20, wherein the antibody is an engineered antibody having increased binding to Fc receptors and/or increased potency for ADCC, and/or a bispecific antibody.

22. An isolated antibody according to any previous claim, wherein the antibody is a bispecific or multispecific antibody which specificially binds to a first antigen comprising BST1 and a second antigen selected from the group consisting of CD3 antigen and CD5 antigen.

23. A nucleic acid encoding a heavy chain of the antibody of any of the preceding claims.

24. A nucleic acid encoding a light chain of the antibody of any of the preceding claims.

25. A host cell containing the nucleic acids of claim 23 and/or 24.

26. A method of making an antibody comprising culturing a host cell according to claim 25 under conditions where the antibody or an antigen-binding portion thereof is expressed and optionally isolating the antibody or an antigen-binding portion thereof.

27. A method of treating a disease comprising administering to a patient in need thereof an antibody or an antigen-binding portion thereof of any of the claims 1-22 wherein the antibody or antigen-binding portion thereof is internalized by a cell expressing BST1, said antibody comprising a covalently attached drug conjugate.

28. A method of treating a disease comprising administering to a patient in need thereof an antibody of any of the claims 1-22 wherein the antibody induces antibody-dependent cell-mediated cytotoxicity (ADCC), complement dependent cytotoxicity (CDC) and/or T-cell cytotoxicity.

29. A method according to any of the claims 27-28 wherein said disease is cancer, including acute myeloid leukemia (AML), B-cell chronic lymphocytic leukemia, breast cancer, colorectal cancer, kidney cancer, head and neck cancer, lung cancer, ovarian cancer or pancreatic cancer.

30. A method according to any of the claims 27-28 wherein said disease is an inflammatory disease, including asthma, gout, crohns, lupus, multiple sclerosis, rheumatoid arthritis, psoriasis, diabetes or atherosclerotic.

31. An antibody as claimed in any one of claims 1-19 for use in therapy or for use as a medicament.

Claims

1. An antibody or antigen binding fragment thereof that specifically binds to BST1, said antibody or antigen binding fragment thereof comprising:

a) a heavy chain variable region comprising:

i) a first vhCDR comprising SEQ ID NO: 10;

ii) a second vhCDR comprising a sequence selected from the group consisting of SEQ ID NO: 12 and SEQ ID NO: 51; and

iii) a third vhCDR comprising SEQ ID NO: 14; and

b) a light chain variable region comprising:

i) a first vlCDR comprising SEQ ID NO: 16;

ii) a second vlCDR comprising SEQ ID NO: 18; and

iii) a third vlCDR comprising a SEQ ID NO: 20

wherein said antibody or antigen binding fragment thereof has from zero to four amino acid changes collectively in said first vhCDR, said second vhCDR, said third vhCDR, said first vlCDR, said second vlCDR and said third vlCDR.

2. The antibody or antigen binding fragment thereof according to claim 1 comprising:

a) a heavy chain variable region comprising:

i) a first vhCDR comprising SEQ ID NO: 10;

ii) a second vhCDR comprising a sequence selected from the group consisting of SEQ ID NO: 12 and SEQ ID NO: 51;

iii) a third vhCDR comprising SEQ ID NO: 14; and

b) a light chain variable region comprising:

i) a first vlCDR comprising SEQ ID NO: 16;

ii) a second vlCDR comprising SEQ ID NO: 18; and

iii) a third vlCDR comprising a SEQ ID NO: 20.

3. The antibody or antigen binding fragment thereof according to claim 1 or 2 comprising:

a heavy chain at least 95% identical SEQ ID NO: 2, and

a light chain at least 95% identical SEQ ID NO: 4.

4. The antibody or antigen binding fragment thereof according to claim 3 comprising:
a heavy chain variable region of SEQ ID NO: 2, and
a light chain variable region of SEQ ID NO: 4.

5. The antibody or antigen binding fragment thereof according to claim 1 or 2 comprising:
a heavy chain at least 95% identical SEQ ID NO: 46, and
a light chain at least 95% identical SEQ ID NO: 49.

6. The antibody or antigen binding fragment thereof according to claim 5 comprising:
a heavy chain variable region of SEQ ID NO: 46, and
a light chain variable region of SEQ ID NO: 49.

7. An isolated monoclonal antibody, or an antigen binding portion thereof, which competes for binding to BST1 with, or binds an epitope on BST1 recognized by, an antibody according to any preceding claim.

8. An antibody as claimed in any one of claims 1 to 7, wherein the antibody is a full-length antibody of an IgG1, IgG2, IgG3 or IgG4 isotype.

9. An antibody or an antigen-binding portion thereof, according to any previous claim further comprising a covalently attached moiety.

10. An antibody or an antigen-binding portion thereof, according to claim 9 wherein said moiety is a drug.

11. An antibody or an antigen-binding portion thereof according to claim 10 wherein said drug is selected from the group consisting of a maytansinoid, a dolastatin, an auristatin, a trichothecene, a calicheamicin, CC1065 and derivatives thereof.

12. An isolated antibody or antigen binding fragment thereof according to any of the claims 1-11, wherein said antibody induces antibody-dependent cell-mediated cytotoxicity (ADCC), complement dependent cytotoxicity (CDC) and/or T-cell cytotoxicity.

13. An isolated antibody or antigen binding fragment thereof according to claim 12, wherein the antibody is an engineered antibody having increased binding to Fc receptors and/or increased potency for ADCC, and/or a bispecific antibody.

14. An isolated antibody or antigen binding fragment thereof according to any previous claim, wherein the antibody is a bispecific or multispecific antibody which specificially binds to a first antigen comprising BST1 and a second antigen selected from the group consisting of CD3 antigen and CD5 antigen.

15. A nucleic acid encoding a heavy chain of the antibody of any of the preceding claims.

16. A nucleic acid encoding a light chain of the antibody of any of the preceding claims.

17. A host cell containing the nucleic acids of claim 15 and/or 16.

18. A method of making an antibody or antigen binding fragment thereof comprising culturing a host cell according to claim 17 under conditions where the antibody or an antigen-binding portion thereof is expressed and optionally isolating the antibody or an antigen-binding portion thereof.

18. The antibody drug conjugate of any one of claims 9 to 14 for use in the treatment of a disease wherein the antibody or antigen-binding portion thereof is internalized by a cell expressing BST1.

19. The antibody of any one of claims 1-14 for use in the treatment of a disease wherein the antibody induces antibody-dependent cell-mediated cytotoxicity (ADCC), complement dependent cytotoxicity (CDC) and/or T-cell cytotoxicity.

20. The use of the antibody drug conjugate of claim 18 or the antibody of claim 19 in the manufacture of a medicament for the treatment of cancer, including acute myeloid leukemia (AML), B-cell chronic lymphocytic leukemia, breast cancer, colorectal cancer, kidney cancer, head and neck cancer, lung cancer, ovarian cancer or pancreatic cancer.

21. An antibody or antigen binding fragment thereof as claimed in any one of claims 1-14 for use in therapy or for use as a medicament.