

CLAIMS:

1. A multi-specific binding compound that binds to CD3, comprising:
a heavy chain variable region comprising:
 - (a) a CDR1 sequence having two or fewer substitutions in SEQ ID NO: 85; and/or
 - (b) a CDR2 sequence having two or fewer substitutions in SEQ ID NO: 86; and/or
 - (c) a CDR3 sequence having two or fewer substitutions in SEQ ID NO: 87; anda light chain variable region.
2. The multi-specific binding compound of claim 1, wherein said heavy chain CDR1, CDR2 and CDR3 sequences are present in a human VH framework.
3. The multi-specific binding compound of claim 1, comprising a heavy chain variable region comprising heavy chain CDR1, CDR2 and CDR3 sequences in a human VH framework, wherein each CDR sequence comprises a sequence with at least 85% identity to any one of SEQ ID NOs:85-87; and
a light chain variable region.
4. The multi-specific binding compound of claim 1, comprising:
a heavy chain variable region comprising:
 - (a) a CDR1 sequence having two or fewer substitutions in SEQ ID NO: 85; and
 - (b) a CDR2 sequence having two or fewer substitutions in SEQ ID NO: 86; and
 - (c) a CDR3 sequence having two or fewer substitutions in SEQ ID NO: 87; anda light chain variable region.
5. The multi-specific binding compound of claim 4, comprising:
a heavy chain variable region comprising a CDR1 sequence of SEQ ID NO: 85, a CDR2 sequence of SEQ ID NO: 86, and a CDR3 sequence of SEQ ID NO: 87; and
a light chain variable region.
6. The multi-specific binding compound of any one of claims 1-5, wherein the light chain variable region comprises a CDR1, CDR2 and CDR3 sequence in a human VL framework, wherein each CDR sequence comprises a sequence with 3 or fewer amino acid substitutions relative to a CDR sequence or set of CDR sequences in SEQ ID NO:92; or wherein the CDR sequences comprise a sequence with at least 85% identity to a CDR sequence or set of CDR sequences in SEQ ID NO:92.

7. The multi-specific binding compound of any one of claims 1-6, wherein the light chain variable region comprises a CDR1 sequence of SEQ ID NO: 88, a CDR2 sequence of SEQ ID NO: 89, and a CDR3 sequence of SEQ ID NO: 90.
8. The multi-specific binding compound of any one of claims 1-7, wherein the heavy chain variable region comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 91.
9. The multi-specific binding compound of any one of claims 1-7, wherein the heavy chain variable region comprises an amino acid sequence set forth in SEQ ID NO: 91.
10. The multi-specific binding compound of any one of claims 1-9, wherein the light chain variable region comprises an amino acid sequence having at least 95% identity to SEQ ID NO: 92.
11. The multi-specific binding compound of any one of claims 1-9, wherein the light chain variable region comprises an amino acid sequence of SEQ ID NO: 92.
12. A multi-specific binding compound comprising a first binding unit having binding affinity to CD22 and a second binding unit having binding affinity to CD3, wherein the first binding unit comprises:
- (a) a CDR1 having two or fewer substitutions in any of the amino acid sequences of SEQ ID NOs: 1 to 10; and/or
 - (b) a CDR2 having two or fewer substitutions in any of the amino acid sequences of SEQ ID NOs: 11 to 17; and/or
 - (c) a CDR3 having two or fewer substitutions in any of the amino acid sequences of SEQ ID NOs: 18 to 23.
13. The multi-specific binding compound of claim 12, wherein said CDR1, CDR2, and CDR3 sequences of the first binding unit are present in a human framework.
14. The multi-specific binding compound of any one of claims 12-13, wherein the first binding unit further comprises a heavy chain constant region sequence in the absence of a CH1 sequence.
15. The multi-specific binding compound of any one of claims 12 to 14, wherein the first binding unit comprises a heavy chain variable region comprising:

- (a) a CDR1 sequence selected from the group consisting of SEQ ID NOs: 1 to 10; and/or
 - (b) a CDR2 sequence selected from the group consisting of SEQ ID NOs: 11 to 17;
- and/or
- (c) a CDR3 sequence selected from the group consisting of SEQ ID NOs: 18 to 23.
16. The multi-specific binding compound of any one of claim 15, comprising:
- (a) a CDR1 sequence selected from the group consisting of SEQ ID NOs: 1 to 10; and
 - (b) a CDR2 sequence selected from the group consisting of SEQ ID NOs: 11 to 17; and
 - (c) a CDR3 sequence selected from the group consisting of SEQ ID NOs: 18 to 23.
17. The multi-specific binding compound of any one of claims 12 to 16, comprising:
- (a) a CDR1 sequence of SEQ ID NO: 1, a CDR2 sequence of SEQ ID NO: 11, and a CDR3 sequence of SEQ ID NO: 18;
 - (b) a CDR1 sequence of SEQ ID NO: 1, a CDR2 sequence of SEQ ID NO: 12, and a CDR3 sequence of SEQ ID NO: 19; or
 - (c) a CDR1 sequence of SEQ ID NO: 1, a CDR2 sequence of SEQ ID NO: 12, and a CDR3 sequence of SEQ ID NO: 20.
18. The multi-specific binding compound of claim 12, comprising a heavy chain variable region having at least 95% sequence identity to any one of the sequences of SEQ ID NOs: 24 to 84.
19. The multi-specific binding compound of claim 18, comprising a heavy chain variable region sequence selected from the group consisting of SEQ ID NOs: 24 to 84.
20. The multi-specific binding compound of claim 19, comprising a heavy chain variable region sequence of SEQ ID NO: 24.
21. A multi-specific binding compound comprising a first binding unit having binding affinity to CD22 and a second binding unit having binding affinity to CD3, wherein the first binding unit comprises
- a heavy chain variable region comprising:
- (a) a CDR1 sequence of the formula:
- $$G X_1 S I X_2 X_3 X_4 X_5 X_6 Y \text{ (SEQ ID NO: 104)}$$
- where
- X_1 is D or G;
 - X_2 is S, T, I or N;

X₃ is S or D;
 X₄ is G, S or N;
 X₅ is D, G or S; and
 X₆ is Y or H; and

(b) a CDR2 sequence of the formula:

X₇ X₈ Y X₉ G X₁₀ X₁₁ (SEQ ID NO: 105)

where

X₇ is I or V;
 X₈ is Y or H;
 X₉ is S or T;
 X₁₀ is A, V or S; and
 X₁₁ is T or A; and

(c) a CDR3 sequence of the formula:

X₁₂ R X₁₃ D S S X₁₄ W R S (SEQ ID NO: 106)

where

X₁₂ is T, A or K;
 X₁₃ is D or E; and
 X₁₄ is N or S.

22. A multi-specific binding compound comprising a first binding unit having binding affinity to CD22 and a second binding unit having binding affinity to CD3, wherein the first binding unit comprises
 a heavy chain variable region comprising CDR1, CDR2 and CDR3 sequences in a human VH framework, wherein the CDR sequences comprise a sequence having two or fewer substitutions in a CDR sequence selected from the group consisting of SEQ ID NOs: 1-23.

23. A multi-specific binding compound comprising a first binding unit having binding affinity to CD22 and a second binding unit having binding affinity to CD3, wherein the first binding unit comprises
 a heavy chain variable region comprising CDR1, CDR2 and CDR3 sequences in a human VH framework, wherein the CDR sequences are selected from the group consisting of SEQ ID NOs: 1-23.

24. A multi-specific binding compound comprising a first binding unit having binding affinity to CD22 and a second binding unit having binding affinity to CD3, wherein the first binding unit comprises
 a heavy chain variable region comprising:

- (a) a CDR1 sequence of SEQ ID NO: 1, a CDR2 sequence of SEQ ID NO: 11, and a CDR3 sequence of SEQ ID NO: 18; or
 - (b) a CDR1 sequence of SEQ ID NO: 1, a CDR2 sequence of SEQ ID NO: 12, and a CDR3 sequence of SEQ ID NO: 19; or
 - (c) a CDR1 sequence of SEQ ID NO: 1, a CDR2 sequence of SEQ ID NO: 12, and a CDR3 sequence of SEQ ID NO: 20,
in a human VH framework.
25. The multi-specific binding compound of claim 24, which is bispecific.
26. The multi-specific binding compound of any one of the preceding claims, which is in a CAR-T format.
27. A multi-specific binding compound comprising:
- (i) a heavy chain variable region having binding affinity to CD3, comprising a CDR1 sequence of SEQ ID NO: 85, a CDR2 sequence of SEQ ID NO: 86, and CDR3 sequence of SEQ ID NO: 87, in a human VH framework;
 - (ii) a light chain variable region comprising a CDR1 sequence of SEQ ID NO: 88, a CDR2 sequence of SEQ ID NO: 89, and CDR3 sequences of SEQ ID NO: 90, in a human VL framework;
and
 - (iii) an antigen-binding domain of an anti-CD22 heavy chain antibody, comprising a CDR1 sequence of SEQ ID NO: 1, a CDR2 sequence of SEQ ID NO: 11, and a CDR3 sequence of SEQ ID NO: 18, in a human VH framework.
28. A multi-specific binding compound comprising:
- (i) a heavy chain variable region having binding affinity to CD3, comprising a CDR1 sequence of SEQ ID NO: 85, a CDR2 sequence of SEQ ID NO: 86, and CDR3 sequence of SEQ ID NO: 87, in a human VH framework;
 - (ii) a light chain variable region comprising a CDR1 sequence of SEQ ID NO: 88, a CDR2 sequence of SEQ ID NO: 89, and CDR3 sequences of SEQ ID NO: 90, in a human VL framework;
and
 - (iii) an antigen-binding domain of an anti-CD22 heavy chain antibody, comprising a CDR1 sequence of SEQ ID NO: 1, a CDR2 sequence of SEQ ID NO: 12, and a CDR3 sequence of SEQ ID NO: 19, in a human VH framework.

29. A multi-specific binding compound comprising:
- (i) a heavy chain variable region having binding affinity to CD3, comprising a CDR1 sequence of SEQ ID NO: 85, a CDR2 sequence of SEQ ID NO: 86, and CDR3 sequence of SEQ ID NO: 87, in a human VH framework;
 - (ii) a light chain variable region comprising a CDR1 sequence of SEQ ID NO: 88, a CDR2 sequence of SEQ ID NO: 89, and CDR3 sequences of SEQ ID NO: 90, in a human VL framework; and
 - (iii) an antigen-binding domain of an anti-CD22 heavy chain antibody, comprising a CDR1 sequence of SEQ ID NO: 1, a CDR2 sequence of SEQ ID NO: 12, and a CDR3 sequence of SEQ ID NO: 20, in a human VH framework.
30. The multispecific binding compound of any one of claims 1-29, comprising a human IgG1 Fc region.
31. The multispecific binding compound of claim 30, wherein the human IgG1 Fc region is a silenced human IgG1 Fc region.
32. The multispecific binding compound of any one of claims 1-29, comprising a human IgG4 Fc region.
33. The multispecific binding compound of claim 32, wherein the human IgG4 Fc region is a silenced human IgG4 Fc region.
34. A pharmaceutical composition comprising a multi-specific binding compound of any one of claims 1 to 33.
35. A method for the treatment of a B-cell disorder characterized by expression of CD22, comprising administering to a subject with said disorder a multi-specific binding compound of any one of claims 1 to 33, or the pharmaceutical composition of claim 34.
36. Use of a multi-specific binding compound of any one of claims 1 to 33, in the preparation of a medicament for the treatment of a B-cell disorder characterized by expression of CD22.
37. A multi-specific binding compound of any one of claims 1 to 33 for use in the treatment of a B-cell disorder characterized by expression of CD22.

38. The method, use or multi-specific binding compound of any one of claims 35-37, wherein the disorder is diffuse large B cell lymphoma (DLBCL).
39. The method, use or multi-specific binding compound of any one of claims 35-37, wherein the disorder is non-Hodgkin's lymphoma (NHL).
40. The method, use or multi-specific binding compound of any one of claims 35-37, wherein the disorder is systemic lupus erythematosus (SLE).
41. The method, use or multi-specific binding compound of any one of claims 35-37, wherein the disorder is rheumatoid arthritis (RA).
42. The method, use or multi-specific binding compound of any one of claims 35-37, wherein the disorder is multiple sclerosis (MS).
43. A polynucleotide encoding a multi-specific binding compound of any of claims 1 to 33.
44. A vector comprising the polynucleotide of claim 43.
45. A cell comprising the vector of claim 44.
46. A method of producing a multi-specific binding compound of any of claims 1 to 33, comprising growing a cell according to claim 45 under conditions permissive for expression of the binding compound, and isolating the binding compound from the cell.
47. A method of making a multi-specific binding compound of any one of claims 1 to 33, comprising immunizing a UniRat animal with CD22 and identifying CD22-binding heavy chain sequences.
48. A method of treatment, comprising administering to an individual an effective dose of the multi-specific binding compound of any one of claims 1 to 33, or the pharmaceutical composition of claim 34.