ANTI-STEAP1 ANTIGEN-BINDING MOLECULES AND USES THEREOF

SEQUENCE LISTING

The instant application contains a Sequence Listing which has been submitted electronically in XML format and is hereby incorporated by reference in its entirety. Said XML copy, created on July 18, 2023, is named “50474-301WO2_Sequence_Listing” and is 170,087 bytes in size.

TECHNICAL FIELD

The present invention relates to antigen-binding molecules that bind to STEAP1, including monospecific and multispecific antibodies, compositions thereof, and methods for treating diseases such as cancer.

BACKGROUND

Cancer is a heterogeneous disease which evolves at the genetic, phenotypic, and pathological levels. Current therapies include chemotherapy, radiation therapy, surgery, hormone therapy, targeted therapy, immunotherapy, and stem cell transplant. Targeted therapy and immunotherapy have shown promise in mediating potent killing of tumor cells. However, the presence of intratumoral heterogeneity, cancer subtypes, and mutations leading to acquired resistance present challenges in target selection. There remains a need for developing therapeutic agents that recognize one or more targets shared among the different cancer subtypes and those that acquired resistance driving by mutations.

SUMMARY

At least one example of the disclosure described herein relates to a multispecific antigen-binding molecule comprising: (A) a first antigen-binding domain that binds to STEAP1 and comprises an anti-STEAP1 heavy chain variable region (VH) comprising CDR-H1, CDR-H2, and CDR-H3 of a VH sequence selected from SEQ ID NOs: 7, 17-25, 30-34, 38 and 68; and an anti-STEAP1 light chain variable region (VL) comprising CDR-L1, CDR-L2, and CDR-L3 of a VL sequence selected from SEQ ID NOs: 8, 26-29, 39 and 69; and (B) a second antigen-binding domain that binds to a T cell receptor.

At least another example of the disclosure described herein relates to a multispecific antigen-binding molecule comprising: (A) a first antigen-binding domain that binds to STEAP1 and comprises an anti-STEAP1 heavy chain variable region (VH) comprising CDR-H1, CDR-H2, and CDR-H3; and an anti-STEAP1 light chain variable region (VL) comprising CDR-L1, CDR-L2, and CDR-L3; and (B) a second antigen-binding domain that binds to a T cell receptor; wherein:

CDR-H1 comprises Xaa^1Xaa^2YMA (SEQ ID NO: 35); wherein Xaa^1 is Asp (D) or Asn (N); and Xaa^2 is His (H), Tyr (Y), or Phe (F);

CDR-H2 comprises $YIXaa^3YDGXaa^4Xaa^5TXaa^6YGDSVKG$ (SEQ ID NO: 36); wherein Xaa^3 is Asp (D) or Ser (S); Xaa^4 is Gly (G), Asp (D), or Leu (L); Xaa^5 is Ser (S), Asp (D), or Asn (N); and Xaa^6 is Ser (S) or Tyr (Y);

CDR-H3 comprises RSGXaa^{7}YHVGYAMXaa^{8}Xaa^{9} (SEQ ID NO: 37); wherein Xaa^{7} is Phe (F) or Tyr (Y); Xaa^{8} is Asn (N) or Asp (D); and Xaa^{9} is Ala (A) or Gly (G);

CDR-L1 comprises the amino acid sequence of SEQ ID NO: 4; CDR-L2 comprises the amino acid sequence of SEQ ID NO: 5; and CDR-L3 comprises the amino acid sequence of SEQ ID NO: 6.

In some examples, the CDR-H1 comprises the amino acid sequence of SEQ ID NO: 10, 1, or 9.

In some examples, the CDR-H2 comprises the amino acid sequence of SEQ ID NO: 2, 11, 12, or 13.

In some examples, the CDR-H3 comprises the amino acid sequence of SEQ ID NO: 16, 3, 14, or 15.

In some examples, the first antigen-binding domain comprises: CDR-H1 comprising the amino acid sequence of SEQ ID NO: 10; CDR-H2 comprising the amino acid sequence of SEQ ID NO: 2; CDR-H3 comprising the amino acid sequence of SEQ ID NO: 16; CDR-L1 comprising the amino acid sequence of SEQ ID NO: 4; CDR-L2 comprising the amino acid sequence of SEQ ID NO: 5; and CDR-L3 comprising the amino acid sequence of SEQ ID NO: 6.

In some examples, the first antigen-binding domain comprises: CDR-H1 comprising the amino acid sequence of SEQ ID NO: 1; CDR-H2 comprising the amino acid sequence of SEQ ID NO: 2; CDR-H3 comprising the amino acid sequence of SEQ ID NO: 3; CDR-L1 comprising the amino acid sequence of SEQ ID NO: 4; CDR-L2 comprising the amino acid sequence of SEQ ID NO: 5; and CDR-L3 comprising the amino acid sequence of SEQ ID NO: 6.

In some examples, the first antigen-binding domain comprises: CDR-H1 comprising the amino acid sequence of SEQ ID NO: 9; CDR-H2 comprising the amino acid sequence of SEQ ID NO: 11; CDR-H3 comprising the amino acid sequence of SEQ ID NO: 3; CDR-L1 comprising the amino acid sequence of SEQ ID NO: 4; CDR-L2 comprising the amino acid sequence of SEQ ID NO: 5; and CDR-L3 comprising the amino acid sequence of SEQ ID NO: 6.

In some examples, the first antigen-binding domain comprises: CDR-H1 comprising the amino acid sequence of SEQ ID NO: 9; CDR-H2 comprising the amino acid sequence of SEQ ID NO: 12; CDR-H3 comprising the amino acid sequence of SEQ ID NO: 3; CDR-L1 comprising the amino acid sequence of SEQ ID NO: 4; CDR-L2 comprising the amino acid sequence of SEQ ID NO: 5; and CDR-L3 comprising the amino acid sequence of SEQ ID NO: 6.

In some examples, the first antigen-binding domain comprises: CDR-H1 comprising the amino acid sequence of SEQ ID NO: 9; CDR-H2 comprising the amino acid sequence of SEQ ID NO: 12; CDR-H3 comprising the amino acid sequence of SEQ ID NO: 14; CDR-L1 comprising the amino acid sequence of SEQ ID NO: 4; CDR-L2 comprising the amino acid sequence of SEQ ID NO: 5; and CDR-L3 comprising the amino acid sequence of SEQ ID NO: 6.

In some examples, the first antigen-binding domain comprises: CDR-H1 comprising the amino acid sequence of SEQ ID NO: 10; CDR-H2 comprising the amino acid sequence of SEQ ID NO: 13; CDR-H3 comprising the amino acid sequence of SEQ ID NO: 15; CDR-L1 comprising the

amino acid sequence of SEQ ID NO: 4; CDR-L2 comprising the amino acid sequence of SEQ ID NO: 5; and CDR-L3 comprising the amino acid sequence of SEQ ID NO: 6.

In some examples, the multispecific antigen-binding molecule is a humanized antibody.

In some examples, the first antigen-binding domain and the second antigen-binding domain each independently comprises an IgG framework region, optionally an IgG1 or IgG4 framework region.

In some examples, the first antigen-binding domain comprises an anti-STEAP1 heavy chain variable region comprising a VH sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 7, 17-25, 30-34, 38, or 68.

In some examples, the first antigen-binding domain comprises an anti-STEAP1 light chain variable region comprising a VL sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 8, 26-29, 39, or 69.

In some examples, the first antigen-binding domain comprises an anti-STEAP1 heavy chain variable region comprising a VH sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 68, and an anti-STEAP1 light chain variable region comprising a VL sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 69.

In some examples, the first antigen-binding domain comprises an anti-STEAP1 heavy chain variable region comprising a VH sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 34, and an anti-STEAP1 light chain variable region comprising a VL sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 27.

In some examples, the first antigen-binding domain comprises an anti-STEAP1 heavy chain variable region comprising a VH sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 30, and an anti-STEAP1 light chain variable region comprising a VL sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 27.

In some examples, the first antigen-binding domain comprises an anti-STEAP1 heavy chain variable region comprising a VH sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 31, and an anti-STEAP1 light chain variable region comprising a VL sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 27.

In some examples, the first antigen-binding domain comprises an anti-STEAP1 heavy chain variable region comprising a VH sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 32, and an anti-STEAP1 light chain variable region comprising a VL sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 27.

In some examples, the first antigen-binding domain comprises an anti-STEAP1 heavy chain variable region comprising a VH sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 33, and an anti-STEAP1 light chain variable region comprising a VL sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 27.

In some examples, the T cell receptor is cluster of differentiation 3 (CD3).

In some examples, the second antigen-binding domain that binds to CD3 comprises an anti-CD3 heavy chain variable region (VH) comprising CDR-H1, CDR-H2, and CDR-H3, and an anti-

CD3 light chain variable region (VL) comprising CDR-L1, CDR-L2, and CDR-L3, wherein the CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprise the sequences of SEQ ID NOs: 48-53, respectively.

In some examples, the second antigen-binding domain that binds to CD3 comprises an anti-CD3 heavy chain variable region comprising a VH sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 54, and a VL sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 55.

In some examples, the second antigen-binding domain that binds to CD3 comprises an anti-CD3 heavy chain variable region (VH) comprising CDR-H1, CDR-H2, and CDR-H3, and an anti-CD3 light chain variable region (VL) comprising CDR-L1, CDR-L2, and CDR-L3, wherein the CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprise the sequences of SEQ ID NO: 40-45, respectively.

In some examples, the second antigen-binding domain that binds to CD3 comprises an anti-CD3 heavy chain variable region comprising a VH sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 46, and an anti-CD3 light chain variable region comprising a VL sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 47.

In some examples, the multispecific antigen binding molecule comprises one or more heavy chain constant domains, wherein the one or more heavy chain constant domains are selected from a first CH1 ($CH1_1$) domain, a first CH2 ($CH2_1$) domain, a first CH3 ($CH3_1$) domain, a second CH1 ($CH1_2$) domain, a second CH2 ($CH2_2$) domain, and a second CH3 ($CH3_2$) domain.

In some examples, at least one of the one or more heavy chain constant domains is paired with another heavy chain constant domain.

In some examples, the $CH3_1$ and $CH3_2$ domains each comprise a protuberance or cavity, and wherein the protuberance or cavity in the $CH3_1$ domain is positionable in the cavity or protuberance, respectively, in the $CH3_2$ domain.

In some examples, the $CH3_1$ and $CH3_2$ domains meet at an interface between said protuberance and cavity.

In some examples, the $CH2_1$ and $CH2_2$ domains each comprise a protuberance or cavity, and wherein the protuberance or cavity in the $CH2_1$ domain is positionable in the cavity or protuberance, respectively, in the $CH2_2$ domain.

In some examples, the $CH2_1$ and $CH2_2$ domains meet at an interface between said protuberance and cavity.

In some examples, the first antigen-binding domain comprises an anti-STEAP1 heavy chain constant region sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 83 and an anti-STEAP1 light chain constant region sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 82; and the second antigen-binding domain comprises an anti-CD heavy chain constant region sequence having at least 80%, 85%, 90%, 95%, or

100% sequence identity to SEQ ID NO: 85 and an anti-CD light chain constant region sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 84.

In some examples, the antigen-binding molecule comprises an anti-STEAP1 heavy chain constant region sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 85 and an anti-STEAP1 light chain constant region sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 84; and the second antigen-binding domain comprises an anti-CD3 heavy chain constant region sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 83 and an anti-CD3 light chain constant region sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 82.

In some examples, the multispecific antigen-binding molecule comprises an anti-STEAP1 heavy chain comprising SEQ ID NO: 73, an anti-STEAP1 light chain comprising SEQ ID NO: 72, an anti-CD3 heavy chain comprising SEQ ID NO: 79, and an anti-CD3 light chain comprising SEQ ID NO: 78.

In some examples, the multispecific antigen-binding molecule comprises an anti-STEAP1 heavy chain comprising SEQ ID NO: 73, an anti-STEAP1 light chain comprising SEQ ID NO: 72, an anti-CD3 heavy chain comprising SEQ ID NO: 81, and an anti-CD3 light chain comprising SEQ ID NO: 80.

In some examples, the multispecific antigen-binding molecule comprises an anti-STEAP1 heavy chain comprising SEQ ID NO: 71, an anti-STEAP1 light chain comprising SEQ ID NO: 70, an anti-CD3 heavy chain comprising SEQ ID NO: 79, and an anti-CD3 light chain comprising SEQ ID NO: 78.

In some examples, the multispecific antigen-binding molecule comprises an anti-STEAP1 heavy chain comprising SEQ ID NO: 71, an anti-STEAP1 light chain comprising SEQ ID NO: 70, an anti-CD3 heavy chain comprising SEQ ID NO: 81, and an anti-CD3 light chain comprising SEQ ID NO: 80.

In some examples, the antigen-binding molecule is a single-chain Fv (scFv), trispecific (Fab3), bispecific (Fab2), diabody ((VL-VH)2 or (VH-VL)2), triabody (trivalent), tetrabody (tetravalent), minibody ((scFV-CH)2), bispecific single-chain Fv (Bis-scFv), IgGdeltaCH2, scFv-Fc, or (scFv)2-Fc.

In some examples, the multispecific antigen-binding molecule is a multispecific antibody, preferably a bispecific or trispecific antibody.

In some examples, the multispecific antigen-binding molecule further comprises a third antigen-binding domain that binds to a tumor-associated antigen. In some examples, the tumor-associated antigen is a receptor expressed on a prostate cancer cell or Ewing sarcoma. In some examples, the tumor-associated antigen is prostate-specific membrane antigen (PSMA), STEAP2, prostate stem cell antigen (PSCA), epithelial cell adhesion molecule (EpCAM), prostate-specific antigen (PSA), prostatic acid phosphatase (PAP), or HBA-71.

In some examples, the multispecific antigen-binding molecule binds to human STEAP1, cynomolgus monkey STEAP1, or a combination thereof, preferably wherein the multispecific antigen-binding molecule binds to the human STEAP1 of SEQ ID NO: 65.

In some examples, the first antigen-binding domain binds to at least one, at least two, at least three, at least four, or at least five residue selected from Ser101, His102, Gln103, Trp195, Gln198, Gln202, and Lys281 of STEAP1, wherein the residue positions 101, 102, 103, 195, 198, 202, and 281 correspond to positions 101, 102, 103, 195, 198, 202, and 281 set forth in SEQ ID NO: 65. In some examples, the first antigen-binding domain binds to Ser101, His102, Gln103, Trp195, Gln198, Gln202, and Lys281 of STEAP1. In some examples, the heavy chain variable region of the first antigen-binding domain forms a hydrogen bond with at least one, at least two, at least three, at least four, or at least five residue selected from Ser101, His102, Gln103, Trp195, Gln198, Gln202, and Lys281 of STEAP1. In some examples, at least one, at least two, at least three, at least four, or at least five residue selected from Leu56, Ser73, Asn74, Gly101, Tyr103, and Tyr107 of the heavy chain variable region of the first antigen-binding domain forms a hydrogen bond with at least one, at least two, at least three, at least four, or at least five residue selected from Ser101, His102, Gln103, Trp195, Gln198, Gln202, and Lys281 of STEAP1, wherein the residue positions of the heavy chain variable region of the first antigen-binding domain correspond to positions 56, 73, 74, 101, 103, and 107 set forth in SEQ ID NO: 18.

In some examples, the first antigen-binding domain binds to at least one, at least two, or at least three residue selected from Gln201, Gln202, Asn203 and Lys204 of STEAP1, wherein the residue positions 201, 202, 203 and 204 correspond to positions 201, 202, 203 and 204 set forth in SEQ ID NO: 65. In some examples, the first antigen-binding domain binds to Gln201, Gln202, Asn203 and Lys204 of STEAP1. In some examples, the light chain variable region of the first antigen-binding domain forms a hydrogen bond with at least one residue selected from Gln201 and Gln202 of STEAP1. In some examples, at least one residue selected from Tyr53 and Tyr54 of the light chain variable region of the first antigen-binding domain forms a hydrogen bond with at least one residue selected from Gln201 and Gln202, wherein the residue positions of the light chain variable region of the first antigen-binding domain correspond to positions 53 and 54 set forth in SEQ ID NO: 18. In some examples, a residue of the light chain variable region of the first antigen-binding domain forms Van der Waals interactions with at least one residue selected from Asn203 and Lys204 of STEAP1.

In some examples, the multispecific antigen-binding molecule has a C_{max} of about 11, 11.5, 12, 12.6, 13, 13.5, 15, 18, 20, 23.4, 25, 27.9, 29.1, or 30 µg/mL.

In some examples, the multispecific antigen-binding molecule has a C_{max} of about 11 µg/mL to about 30 µg/mL.

In some examples, the multispecific antigen-binding molecule has a C_{max} of about 20 µg/mL to about 28 µg/mL.

In some examples, the multispecific antigen-binding molecule has a C_{max} of about 24 µg/mL.

In some examples, the multispecific antigen-binding molecule has an EC_{50} of about 0.6, 0.56, 0.5, 0.45, 0.4, 0.35, 0.3, 0.25, 0.2, 0.15, 0.1, 0.09, 0.05, or lower.

In some examples, the multispecific antigen-binding molecule has an EC_{50} of about 0.05 to about 0.8.

In some examples, the EC_{50} is determined in a cell killing assay at 72 hours with human CD8+ T cells and STEAP1-expressing LNCaP-X1.2 cells, and the EC_{50} is about 0.05 to about 0.4.

In some examples, the EC_{50} is about 0.08 or about 0.3.

In some examples, the EC_{50} is determined in a cell killing assay at 72 hours with human CD8+ T cells and STEAP1-expressing LNCaPX1.2KO3-13 cells, and the EC_{50} is about 0.1 to about 0.8.

In some examples, the EC_{50} is about 0.1 or about 0.7.

In some examples, the multispecific antigen-binding molecule binds to STEAP1 monovalently.

At least another aspect of the disclosure described herein relates to an antigen-binding molecule that binds to STEAP1, comprising an anti-STEAP1 heavy chain variable region (VH) comprising CDR-H1, CDR-H2, and CDR-H3 of a VH sequence selected from SEQ ID NOs: 7, 17-25, 30-34, 38, and 68; and an anti-STEAP1 light chain variable region (VL) comprising CDR-L1, CDR-L2, and CDR-L3 of a VL sequence selected from SEQ ID NOs: 8, 26-29, 39, and 69.

At least another aspect of the disclosure described herein relates to an antigen-binding molecule that binds to STEAP1, comprising: an anti-STEAP1 heavy chain variable region (VH) comprising CDR-H1, CDR-H2, and CDR-H3; and an anti-STEAP1 light chain variable region (VL) comprising CDR-L1, CDR-L2, and CDR-L3; wherein

CDR-H1 comprises Xaa^1Xaa^2YMA (SEQ ID NO: 35); wherein Xaa^1 is Asp (D) or Asn (N); and Xaa^2 is His (H), Tyr (Y), or Phe (F);

CDR-H2 comprises $YIXaa^3YDGXaa^4Xaa^5TXaa^6YGDSVKG$ (SEQ ID NO: 36); wherein Xaa^3 is Asp (D) or Ser (S); Xaa^4 is Gly (G), Asp (D), or Leu (L); Xaa^5 is Ser (S), Asp (D), or Asn (N); and Xaa^6 is Ser (S) or Tyr (Y);

CDR-H3 comprises $RSGXaa^7YHVGYAMXaa^8Xaa^9$ (SEQ ID NO: 37); wherein Xaa^7 is Phe (F) or Tyr (Y); Xaa^8 is Asn (N) or Asp (D); and Xaa^9 is Ala (A) or Gly (G);

CDR-L1 comprises the amino acid sequence of SEQ ID NO: 4; CDR-L2 comprises the amino acid sequence of SEQ ID NO: 5; and CDR-L3 comprises the amino acid sequence of SEQ ID NO: 6.

In some examples, the CDR-H1 comprises the amino acid sequence of SEQ ID NO: 10, 1, or 9. In some examples, the CDR-H2 comprises the amino acid sequence of SEQ ID NO: 2, 11, 12, or 13. In some examples, the CDR-H3 comprises the amino acid sequence of SEQ ID NO: 16, 3, 14, or 15.

In some examples, the antigen-binding molecule comprises: CDR-H1 comprising the amino acid sequence of SEQ ID NO: 10; CDR-H2 comprising the amino acid sequence of SEQ ID NO: 2; CDR-H3 comprising the amino acid sequence of SEQ ID NO: 16; CDR-L1 comprising the amino acid sequence of SEQ ID NO: 4; CDR-L2 comprising the amino acid sequence of SEQ ID NO: 5; and CDR-L3 comprising the amino acid sequence of SEQ ID NO: 6.

In some examples, the antigen-binding molecule comprises: CDR-H1 comprising the amino acid sequence of SEQ ID NO: 1; CDR-H2 comprising the amino acid sequence of SEQ ID NO: 2; CDR-H3 comprising the amino acid sequence of SEQ ID NO: 3; CDR-L1 comprising the amino acid sequence of SEQ ID NO: 4; CDR-L2 comprising the amino acid sequence of SEQ ID NO: 5; and CDR-L3 comprising the amino acid sequence of SEQ ID NO: 6.

In some examples, the antigen-binding molecule comprises: CDR-H1 comprising the amino acid sequence of SEQ ID NO: 9; CDR-H2 comprising the amino acid sequence of SEQ ID NO: 11; CDR-H3 comprising the amino acid sequence of SEQ ID NO: 3; CDR-L1 comprising the amino acid sequence of SEQ ID NO: 4; CDR-L2 comprising the amino acid sequence of SEQ ID NO: 5; and CDR-L3 comprising the amino acid sequence of SEQ ID NO: 6.

In some examples, the antigen-binding molecule comprises: CDR-H1 comprising the amino acid sequence of SEQ ID NO: 9; CDR-H2 comprising the amino acid sequence of SEQ ID NO: 12; CDR-H3 comprising the amino acid sequence of SEQ ID NO: 3; CDR-L1 comprising the amino acid sequence of SEQ ID NO: 4; CDR-L2 comprising the amino acid sequence of SEQ ID NO: 5; and CDR-L3 comprising the amino acid sequence of SEQ ID NO: 6.

In some examples, the antigen-binding molecule comprises: CDR-H1 comprising the amino acid sequence of SEQ ID NO: 9; CDR-H2 comprising the amino acid sequence of SEQ ID NO: 12; CDR-H3 comprising the amino acid sequence of SEQ ID NO: 14; CDR-L1 comprising the amino acid sequence of SEQ ID NO: 4; CDR-L2 comprising the amino acid sequence of SEQ ID NO: 5; and CDR-L3 comprising the amino acid sequence of SEQ ID NO: 6.

In some examples, the antigen-binding molecule comprises: CDR-H1 comprising the amino acid sequence of SEQ ID NO: 10; CDR-H2 comprising the amino acid sequence of SEQ ID NO: 13; CDR-H3 comprising the amino acid sequence of SEQ ID NO: 15; CDR-L1 comprising the amino acid sequence of SEQ ID NO: 4; CDR-L2 comprising the amino acid sequence of SEQ ID NO: 5; and CDR-L3 comprising the amino acid sequence of SEQ ID NO: 6.

In some examples, the antigen-binding molecule is a humanized antibody.

In some examples, the antigen-binding molecule comprises an IgG framework region, optionally an IgG1 framework region.

In some examples, the antigen-binding molecule comprises an anti-STEAP1 heavy chain variable region comprising a VH sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 7, 17-25, 30-34, 38, or 68.

In some examples, the antigen-binding molecule comprises an anti-STEAP1 light chain variable region comprising a VL sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 8, 26-29, 39, or 69.

In some examples, the antigen-binding molecule comprises an anti-STEAP1 heavy chain variable region comprising a VH sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 68, and an anti-STEAP1 light chain variable region comprising a VL sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 69.

In some examples, the antigen-binding molecule comprises an anti-STEAP1 heavy chain variable region comprising a VH sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 34, and an anti-STEAP1 light chain variable region comprising a VL sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 27.

In some examples, the antigen-binding molecule comprises an anti-STEAP1 heavy chain variable region comprising a VH sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 30, and an anti-STEAP1 light chain variable region comprising a VL sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 27.

In some examples, the antigen-binding molecule comprises an anti-STEAP1 heavy chain variable region comprising a VH sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 31, and an anti-STEAP1 light chain variable region comprising a VL sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 27.

In some examples, the antigen-binding molecule comprises an anti-STEAP1 heavy chain variable region comprising a VH sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 32, and an anti-STEAP1 light chain variable region comprising a VL sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 27.

In some examples, the antigen-binding molecule comprises an anti-STEAP1 heavy chain variable region comprising a VH sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 33, and an anti-STEAP1 light chain variable region comprising a VL sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 27.

In some examples, the antigen-binding molecule comprises an anti-STEAP1 heavy chain constant region sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 83 and an anti-STEAP1 light chain constant region sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 82.

In some examples, the antigen-binding molecule comprises an anti-STEAP1 heavy chain constant region sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 85 and an anti-STEAP1 light chain constant region sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 84.

In some examples, the antigen-binding molecule comprises an anti-STEAP1 heavy chain comprising SEQ ID NO: 73 and an anti-STEAP1 light chain comprising SEQ ID NO: 72. In some examples, the antigen-binding molecule comprises an anti-STEAP1 heavy chain comprising SEQ ID NO: 71 and an anti-STEAP1 light chain comprising SEQ ID NO: 70.

In some examples, the antigen-binding molecule is a full-length antibody or a fragment thereof.

In some examples, the antigen-binding molecule is a Fab, Fab', F(ab')2, Fv, Fd, single-chain Fv (scFv), trispecific (Fab3), bispecific (Fab2), diabody ((VL-VH)2 or (VH-VL)2), triabody (trivalent), tetrabody (tetravalent), minibody ((scFV-CH)2), bispecific single-chain Fv (Bis-scFv), IgGdeltaCH2, scFv-Fc, or (scFv)2-Fc.

In some examples, the antigen-binding molecule is a multispecific antibody, preferably wherein the antigen-binding molecule is a bispecific antibody or a trispecific antibody.

In some examples, the antigen-binding molecule further comprises an antigen-binding domain that binds to a T cell receptor. In some examples, the T cell receptor is cluster of differentiation 3 (CD3).

In some examples, the antigen-binding domain that binds to CD3 comprises an anti-CD3 heavy chain variable region (VH) comprising CDR-H1, CDR-H2, and CDR-H3, and an anti-CD3 light chain variable region (VL) comprising CDR-L1, CDR-L2, and CDR-L3, wherein CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprise the amino acid sequences of SEQ ID NOs: 48-53, respectively.

In some examples, the antigen-binding domain that binds to CD3 comprises an anti-CD3 heavy chain variable region comprising a VH sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 54, and an anti-CD3 light chain variable region comprising a VL sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 55.

In some examples, the antigen-binding domain that binds to CD3 comprises an anti-CD3 heavy chain variable region (VH) comprising CDR-H1, CDR-H2, and CDR-H3, and an anti-CD3 light chain variable region (VL) comprising CDR-L1, CDR-L2, and CDR-L3, wherein CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprise the amino acid sequences of SEQ ID NO: 40-45, respectively.

In some examples, the antigen-binding domain that binds to CD3 comprises an anti-CD3 heavy chain variable region comprising a VH sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 46, and an anti-CD3 light chain variable region comprising a VL sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 47.

In some examples, the antigen-binding molecule further comprises an additional antigen-binding domain that binds to a tumor-associated antigen. In some examples, the tumor-associated antigen is a receptor expressed on a prostate cancer cell or Ewing sarcoma. In some examples, the tumor-associated antigen is prostate-specific membrane antigen (PSMA), STEAP2, prostate stem cell antigen (PSCA), epithelial cell adhesion molecule (EpCAM), prostate-specific antigen (PSA), prostatic acid phosphatase (PAP), or HBA-71.

In some examples, the antigen-binding molecule binds to human STEAP1, cynomolgus monkey STEAP1, or a combination thereof, preferably wherein the antigen-binding molecule binds to the human STEAP1 of SEQ ID NO: 65.

In some examples, the antigen-binding molecule binds to at least one, at least two, at least three, at least four, or at least five residue selected from Ser101, His102, Gln103, Trp195, Gln198, Gln202, and Lys281 of STEAP1, wherein the residue positions 101, 102, 103, 195, 198, 202, and 281 correspond to positions 101, 102, 103, 195, 198, 202, and 281 set forth in SEQ ID NO: 65. In some examples, the antigen-binding molecule binds to Ser101, His102, Gln103, Trp195, Gln198, Gln202, and Lys281 of STEAP1. In some examples, the heavy chain variable region of the antigen-binding molecule forms a hydrogen bond with at least one, at least two, at least three, at

least four, or at least five residues selected from Ser101, His102, Gln103, Trp195, Gln198, Gln202, and Lys281 of STEAP1. In some examples, at least one, at least two, at least three, at least four, or at least five residues selected from Leu56, Ser73, Asn74, Gly101, Tyr103, and Tyr107 of the heavy chain variable region of the antigen-binding molecule forms a hydrogen bond with at least one, at least two, at least three, at least four, or at least five residues selected from Ser101, His102, Gln103, Trp195, Gln198, Gln202, and Lys281 of STEAP1, wherein the residue positions of the heavy chain variable region of the antigen-binding molecule correspond to positions 56, 73, 74, 101, 103, and 107 set forth in SEQ ID NO: 18.

In some examples, the antigen-binding molecule binds to at least one, at least two, at or at least three residue selected from Gln201, Gln202, Asn203 and Lys204 of STEAP1, wherein the residue positions 201, 202, 203 and 204 correspond to positions 201, 202, 203 and 204 set forth in SEQ ID NO: 65. In some examples, the antigen-binding molecule binds to Gln201, Gln202, Asn203 and Lys204 of STEAP1. In some examples, the light chain variable region of the antigen-binding molecule forms a hydrogen bond with at least one residue selected from Gln201 and Gln202 of STEAP1. In some examples, at least one residue selected from Tyr53 and Tyr54 of the light chain variable region of the antigen-binding molecule forms a hydrogen bond with at least one residue selected from Gln201 and Gln202, wherein the residue positions of the light chain variable region of the antigen-binding molecule correspond to positions 53 and 54 set forth in SEQ ID NO: 18. In some examples, a residue of the light chain variable region of the antigen-binding molecule forms Van der Waals interactions with at least one residue selected from Asn203 and Lys204 of STEAP1.

In some examples, the antigen-binding molecule binds to STEAP1 monovalently.

At least another example of the disclosure described herein relates to an antibody comprising a first antigen-binding domain that binds to human STEAP1 at one or more residues selected from Ser101, His102, Gln103, Trp195, Gln198, Gln202, and Lys281, wherein the residue positions 101, 102, 103, 195, 198, 202, and 281 correspond to positions 101, 102, 103, 195, 198, 202, and 281 set forth in SEQ ID NO: 65.

In some examples, the first antigen-binding domain binds to at least one, at least two, at least three, at least four, or at least five residue selected from Ser101, His102, Gln103, Trp195, Gln198, Gln202, and Lys281 of SEQ ID NO: 65. In some examples, the first antigen-binding domain binds to Ser101, His102, Gln103, Trp195, Gln198, Gln202, and Lys281 of SEQ ID NO: 65. In some examples, the heavy chain variable region of the first antigen-binding domain forms a hydrogen bond with at least one, at least two, at least three, at least four, or at least five residues selected from Ser101, His102, Gln103, Trp195, Gln198, Gln202, and Lys281 of STEAP1. In some examples, at least one, at least two, at least three, at least four, or at least five residues selected from Leu56, Ser73, Asn74, Gly101, Tyr103, and Tyr107 of the heavy chain variable region of the first antigen-binding domain forms a hydrogen bond with at least one, at least two, at least three, at least four, or at least five residues selected from Ser101, His102, Gln103, Trp195, Gln198, Gln202, and Lys281 of STEAP1, wherein the residue positions of the heavy chain variable region of the first

antigen-binding domain correspond to positions 56, 73, 74, 101, 103, and 107 set forth in SEQ ID NO: 18.

In some examples, the first antigen-binding domain comprises an anti-STEAP1 heavy chain variable region (VH) comprising CDR-H1, CDR-H2, and CDR-H3 of a VH sequence selected from SEQ ID NO: 7, 17-25, 30-34, 38, and 68; and three CDRs of an anti-STEAP1 light chain variable region (VL) comprising CDR-L1, CDR-L2, and CDR-L3 of a VL sequence selected from SEQ ID NO: 8, 26-29, 39, and 69.

In some examples, the first antigen-binding domain comprises an anti-STEAP1 heavy chain variable region comprising a VH sequence comprising at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 7, 17-25, 30-34, 38, or 68.

In some examples, the first antigen-binding domain comprises an anti-STEAP1 light chain variable region comprising a VL sequence comprising at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 8, 26-29, 39, or 69.

In some examples, the antibody further comprises a second antigen-binding domain that binds to a T cell receptor. In some examples, the T cell receptor is cluster of differentiation 3 (CD3).

In some examples, the second antigen-binding domain that binds to CD3 comprises an anti-CD3 heavy chain variable region (VH) comprising CDR-H1, CDR-H2, and CDR-H3, and an anti-CD3 light chain variable region (VL) comprising CDR-L1, CDR-L2, and CDR-L3, wherein the CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprise the amino acid sequences of SEQ ID NO: 48-53, respectively.

In some examples, the second antigen-binding domain that binds to CD3 comprises an anti-CD3 heavy chain variable region comprising a VH sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 54 and an anti-CD3 light chain variable region comprising a VL sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 55.

In some examples, the second antigen-binding domain that binds to CD3 comprises an anti-CD3 heavy chain variable region (VH) comprising CDR-H1, CDR-H2, and CDR-H3, and an anti-CD3 light chain variable region (VL) comprising CDR-L1, CDR-L2, and CDR-L3, wherein the CDR-H1, CDR-H2, CDR-H3, CDR-L1, CDR-L2, and CDR-L3 comprise the amino acid sequences of SEQ ID NO: 40-45, respectively.

In some examples, the second antigen-binding domain that binds to CD3 comprises an anti-CD3 heavy chain variable region comprising a VH sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 46 and an anti-CD3 light chain variable region comprising a VL sequence having at least 80%, 85%, 90%, 95%, or 100% sequence identity to SEQ ID NO: 47.

In some examples, the multispecific antigen-binding molecule further comprises a third antigen-binding domain that binds to a tumor-associated antigen. In some examples, the tumor-associated antigen is a receptor expressed on a prostate cancer cell. In some examples, the

tumor-associated antigen is prostate-specific membrane antigen (PSMA), STEAP2, prostate stem cell antigen (PSCA), epithelial cell adhesion molecule (EpCAM), prostate-specific antigen (PSA), or prostatic acid phosphatase (PAP).

At least another example of the disclosure described herein relates to one or more isolated nucleic acids individually or together encoding the multispecific antigen-binding molecule described herein, the antigen-binding molecule described herein, or the antibody described herein.

At least another example of the disclosure described herein relates to one or more vectors individually or together comprising the isolated nucleic acid(s) described herein.

At least another example of the disclosure described herein relates to one or more host cells individually or together comprising the isolated nucleic acid(s) described herein or the vector(s) described herein. In some examples, the host cell is a mammalian cell. In some examples, the mammalian cell is a Chinese hamster ovary (CHO) cell. In some examples, the host cell is an insect cell. In some examples, the host cell is a prokaryotic cell.

At least another example of the disclosure described herein relates to a method of producing the multispecific antigen-binding molecule described herein, the antigen-binding molecule described herein, or the antibody described herein, comprising culturing the host cell(s) described herein in a culture medium. In some examples, the method further comprises harvesting the multispecific antigen-binding molecule described herein, the antigen-binding molecule described herein, or the antibody described herein from the host cell(s) or the culture medium.

At least another example of the disclosure described herein relates to a pharmaceutical composition comprising the multispecific antigen-binding molecule described herein, the antigen-binding molecule described herein, or the antibody described herein. In one aspect, the disclosure refers to a pharmaceutical composition comprising the antigen-binding molecule as disclosed herein, and a pharmaceutically acceptable carrier, excipient, or diluent. In some examples, the pharmaceutical composition further comprises a pharmaceutically acceptable carrier, excipient, or diluent.

In some examples, the pharmaceutical composition is for use as a medicament. In some examples, the pharmaceutical composition is for use in treating or delaying progression of a STEAP1 expressing cancer. In some examples, the pharmaceutical composition is for use in treating or delaying progression of prostate cancer or Ewing sarcoma.

At least another example of the disclosure described herein relates to use of the multispecific antigen-binding molecule described herein, the antigen-binding molecule described herein, or the antibody described herein for use in treating or delaying progression of a STEAP1-expressing cancer in a subject in need thereof.

At least another example of the disclosure described herein relates to use of the multispecific antigen-binding molecule described herein, the antigen-binding molecule described herein, or the antibody described herein for use in inhibiting or reducing the proliferation of a STEAP1 expressing cancer cell.

In some examples, the STEAP1-expressing cancer is a solid tumor.

In some examples, the STEAP1-expressing cancer is prostate cancer or Ewing sarcoma.

In some examples, the multispecific antigen-binding molecule described herein, the antigen-binding molecule described herein, or the antibody described herein is to be used in combination with an additional therapeutic agent or an additional therapeutic regimen.

In some examples, the additional therapeutic agent comprises a chemotherapeutic agent, an immunotherapeutic agent, a targeted therapy, radiation therapy, or a combination thereof.

In some examples, the additional therapeutic agent comprises a first-line, second-line, or third-line therapy.

In some examples, the additional therapeutic regimen comprises surgery.

In some examples, the multispecific antigen-binding molecule described herein, the antigen-binding molecule described herein, or the antibody described herein and the additional therapeutic agent are to be administered simultaneously.

In some examples, the multispecific antigen-binding molecule described herein, the antigen-binding molecule described herein, or the antibody described herein and the additional therapeutic agent are to be administered sequentially.

In some examples, the multispecific antigen-binding molecule described herein, the antigen-binding molecule described herein, or the antibody described herein is to be administered first prior to administering the additional therapeutic agent.

In some examples, the multispecific antigen-binding molecule described herein, the antigen-binding molecule described herein, or the antibody described herein is to be administered after administering the additional therapeutic agent.

In some examples, the multispecific antigen-binding molecule described herein, the antigen-binding molecule described herein, or the antibody described herein is to be administered systemically.

In some examples, the multispecific antigen-binding molecule described herein, the antigen-binding molecule described herein, or the antibody described herein is to be administered locally.

In some examples, the multispecific antigen-binding molecule described herein, the antigen-binding molecule described herein, or the antibody described herein is to be administered by parenteral administration.

In some examples, the multispecific antigen-binding molecule described herein, the antigen-binding molecule described herein, or the antibody described herein is to be administered intravenously or subcutaneously.

In some examples, the subject is a human.

At least another example of the disclosure described herein relates to use of the multispecific antigen-binding molecule described herein, the antigen-binding molecule described herein, or the antibody described herein in the manufacture of a medicament for treating or delaying progression of a STEAP1 expressing cancer, optionally for treating or delaying progression of prostate cancer or Ewing sarcoma. In one aspect, the disclosure refers to use of the antigen-binding molecule as disclosed herein in the manufacture of a medicament for treating or delaying progression of a STEAP1-expressing cancer selected from solid tumor, prostate cancer and Ewing sarcoma, in a subject in need thereof.

At least another example of the disclosure described herein relates to use of the multispecific antigen-binding molecule described herein, the antigen-binding molecule described herein, or the antibody described herein in the manufacture of a medicament for inhibiting or reducing the proliferation of a STEAP1 expressing cancer cell, optionally a prostate cancer cell or Ewing sarcoma cell.

At least another example of the disclosure described herein relates to a method for treating or delaying progression of a STEAP1-expressing cancer in a subject in need thereof, comprising administering to the subject an effective amount of the multispecific antigen-binding molecule described herein, the antigen-binding molecule described herein, or the antibody described herein.

In some examples, the STEAP1 expressing cancer is a solid tumor. In some examples, the STEAP1 expressing cancer is prostate cancer or Ewing sarcoma.

In some examples, the method further comprises administering to the subject an additional therapeutic agent or an additional therapeutic regimen. In some examples, the additional therapeutic agent comprises a chemotherapeutic agent, an immunotherapeutic agent, a targeted therapy, radiation therapy, or a combination thereof. In some examples, the additional therapeutic agent comprises a first-line, second-line, or third-line therapy. In some examples, the additional therapeutic regimen comprises surgery.

In some examples, the additional therapeutic agent are administered simultaneously with the multispecific antigen-binding molecule described herein, the antigen-binding molecule described herein, or the antibody described herein.

In some examples, the additional therapeutic agent are administered sequentially with the multispecific antigen-binding molecule described herein, the antigen-binding molecule described herein, or the antibody described herein.

In some examples, the multispecific antigen-binding molecule described herein, the antigen-binding molecule described herein, or the antibody described herein is administered first prior to administering the additional therapeutic agent.

In some examples, the multispecific antigen-binding molecule described herein, the antigen-binding molecule described herein, or the antibody described herein is administered after administering the additional therapeutic agent.

In some examples, the multispecific antigen-binding molecule described herein, the antigen-binding molecule described herein, or the antibody described herein is administered systemically. In some examples, the multispecific antigen-binding molecule described herein, the antigen-binding molecule described herein, or the antibody described herein is administered locally. In some examples, the multispecific antigen-binding molecule described herein, the antigen-binding molecule described herein, or the antibody described herein is administered by parenteral administration. In some examples, the multispecific antigen-binding molecule described herein, the antigen-binding molecule described herein, or the antibody described herein is administered intravenously or subcutaneously.

In some examples, the subject is a human.

At least another example of the disclosure described herein relates to a method of inhibiting or reducing the proliferation of a STEAP1 expressing cell, comprising contacting the cell with , the multispecific antigen-binding molecule described herein, the antigen-binding molecule described herein, or the antibody described herein for a time sufficient to inhibit proliferation of the cell.

In some examples, the cell is a prostate cancer cell or Ewing sarcoma cell. In some examples the method is an *in vivo* method. In some examples the method is an *in vitro* or an *ex vivo* method.

At least another example of the disclosure described herein relates to a kit comprising the multispecific antigen-binding molecule described herein, the antigen-binding molecule described herein, the antibody described herein, the isolated nucleic acid(s) described herein, the vector(s) described herein, the host cell(s) described herein, or the pharmaceutical composition described herein, optionally comprising a set of instructions.

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1A illustrates screening of select rat monoclonal antibodies for specific binding to STEAP1-expressing cells. The rat monoclonal antibodies are STEAP1-44, STEAP1-45, STEAP1-81, STEAP1-75, STEAP1-103, STEAP1-10, STEAP1-23, STEAP1-67, STEAP1-34, STEAP1-19, and STEAP1-92.

FIG. 1B illustrates screening of select rat monoclonal antibodies for specific binding to STEAP1-expressing cells. The rat monoclonal antibodies are STEAP1-48, STEAP1-15, STEAP1-28, STEAP1-95, STEAP1-54, STEAP1-69, STEAP1-2, STEAP1-59, STEAP1-49, and STEAP1-62. Ab120 is the control antibody.

FIG. 1C shows binding of antibody STEAP1-44 in a titration assay. Arrows indicate the minimal concentration in which binding of STEAP1-44 to 293-hSTEAP1, PC3-hSTEAP1, LNCaP X1.2, and 22Rv1 cells was observed, which was 0.39 nM, 6.25 nM, 3.125 nM, and 12.5 nM, respectively.

FIG. 2 illustrates variable region sequences of antibody STEAP1-44 and STEAP1-44 clonal variants obtained by deep sequencing aligned to closest rat germline segment sequences (top sequences). For the clonal variants obtained by deep sequencing (“NGS”) only heavy chains are available. These were combined with the STEAP1-44 light chain to produce full-length antibodies and thus share light chains. Presumed somatic mutations are shown in black background. CDR boundaries according to the Kabat and Chothia systems shown above the alignments, with Kabat CDRs boundaries underlined. Residue numbering is according to the Kabat system. Dots represent sequence gaps introduced by aligning software. Germline segment names are shown in the alignments. The SEQ ID NOs for the Kabat CDRs and the VH and VL sequences are shown in Table 1. The SEQ ID NOs for the Chothia CDRs are shown in Table 2.

FIG. 3 illustrates scoring of somatic mutations in the STEAP1-44 clonotype group in the deep sequencing dataset. Sequence read counts with each of the amino acid mutations are shown for