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(54) Titre : ANTICORPS CONTRE ENTPD2, POLYTHÉRAPIES, ET PROCÉDES D'UTILISATION DES ANTICORPS ET DES POLYTHÉRAPIES
(54) Title: ENTPD2 ANTIBODIES, COMBINATION THERAPIES, AND METHODS OF USING THE ANTIBODIES AND COMBINATION THERAPIES

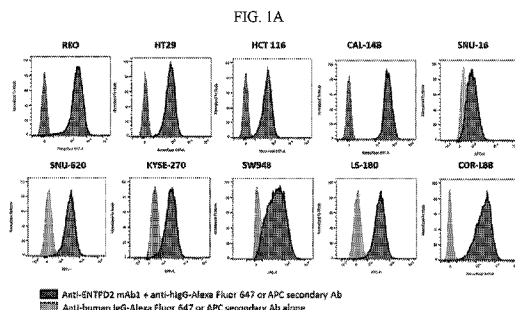


FIG. 1B
Table 20: ENTPD2 expression density across representative cancer cell lines

Cell Line	Source	Indication	Receptor Density
CAL-148	DSMZ (Germany)	Breast Adenocarcinoma	111,726
COR-188	ECACC (UK)	Small Cell Lung Cancer	90,000
RKO	ATCC (Manassas, VA)	Colorectal Cancer	51,208
LS-180	ATCC (Manassas, VA)	Colorectal Cancer	44,706
SW948	ATCC (Manassas, VA)	Colorectal Cancer	41,576
HT29	ATCC (Manassas, VA)	Colorectal Cancer	28,337
KYSE-270	DSMZ (Germany)	Esophageal Cancer	28,273
SNU-620	KCLB (South Korea)	Stomach Adenocarcinoma	19,646
HCT 116	ATCC (Manassas, VA)	Colorectal Cancer	18,697
SNU-16	ATCC (Manassas, VA)	Gastric Carcinoma	12,763

(57) **Abrégé/Abstract:**

Provided herein are antibodies or antigen-binding fragments thereof, e.g., monoclonal antibodies or antigen binding fragments thereof, that specifically bind to ENTPD2 (e.g., human ENTPD2 protein), and methods of using these antibodies or antigen-

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binding fragments. The present invention also relates to combination therapies comprising an anti-human ENTPD2 antibody or antigen binding fragment and at least one additional therapeutic agent, and methods of using these combination therapies.

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(54) Title: ENTPD2 ANTIBODIES, COMBINATION THERAPIES, AND METHODS OF USING THE ANTIBODIES AND COMBINATION THERAPIES

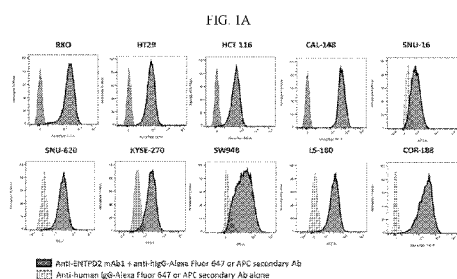


FIG. 1B

Table 20: ENTPD2 expression density across representative cancer cell lines

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CAL-148	DSMZ (Germany)	Breast Adenocarcinoma	111,726
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LS-180	ATCC (Manassas, VA)	Colorectal Cancer	44,708
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KYSE-270	DSMZ (Germany)	Esophageal Cancer	28,273
SNU-620	KCLB (South Korea)	Stomach Adenocarcinoma	19,646
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SNU-16	ATCC (Manassas, VA)	Gastric Carcinoma	32,763

(57) Abstract: Provided herein are antibodies or antigen-binding fragments thereof, e.g., monoclonal antibodies or antigen binding fragments thereof, that specifically bind to ENTPD2 (e.g., human ENTPD2 protein), and methods of using these antibodies or antigen-binding fragments. The present invention also relates to combination therapies comprising an anti-human ENTPD2 antibody or antigen binding fragment and at least one additional therapeutic agent, and methods of using these combination therapies.

[Continued on next page]

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DEMANDE OU BREVET VOLUMINEUX

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CECI EST LE TOME 1 DE 2
CONTENANT LES PAGES 1 À 284

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THIS SECTION OF THE APPLICATION/PATENT CONTAINS MORE THAN ONE VOLUME

THIS IS VOLUME 1 OF 2
CONTAINING PAGES 1 TO 284

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NOM DU FICHIER / FILE NAME :

NOTE POUR LE TOME / VOLUME NOTE:

ENTPD2 ANTIBODIES, COMBINATION THERAPIES, AND METHODS OF USING THE ANTIBODIES AND COMBINATION THERAPIES

CROSS-REFERENCE TO RELATED APPLICATIONS

[0001] This application claims the benefit of U.S. Provisional Application No. 62/677,850 filed May 30, 2018, the content of which are hereby incorporated by reference in its entirety.

TECHNICAL FIELD

[0002] The present invention provides antibodies or antigen-binding fragments thereof, e.g., monoclonal antibodies or antigen binding fragments thereof, that specifically bind to the ectoenzyme ectonucleoside triphosphate diphosphohydrolase 2 (ENTPD2) and methods of using these antibodies or antigen-binding fragments.

[0003] The present invention also relates to combination therapies comprising an anti-human ENTPD2 antibody or antigen-binding fragment thereof and at least one additional therapeutic agent.

SEQUENCE LISTING

[0004] The instant application contains a Sequence Listing which has been submitted electronically in ASCII format and is hereby incorporated by reference in its entirety. Said ASCII copy, created on April 5, 2019, is named PAT058145-WO-PCT_SL.txt and is 635,873 bytes in size.

BACKGROUND

[0005] Cellular stress and apoptosis trigger the release of ATP into the extracellular space. Increased ATP concentration promotes rapid inflammation, resulting in amplification of T-cell signaling, inhibiting regulatory T cells (Tregs), and promoting inflammasome activation in dendritic cells and macrophages. The ectoenzyme ectonucleoside triphosphate diphosphohydrolase 2 (ENTPD2) is part of the family of ecto-nucleosidases that hydrolyze 5'-triphosphates and is an integral membrane protein, which participates in purinergic signaling. ENTPD2 catalyzes the conversion of adenosine triphosphate (ATP) to adenosine diphosphate (ADP) and adenosine monophosphate (AMP). In turn, AMP is catalyzed by Cluster of Differentiation 73 (CD73), also known as ecto-5'-nucleotidase (ecto-5'NT), to adenosine. The molecule AMP interacts with several receptors, including the Adenosine A1, A2A, A2B, and A3 receptors. The A2A receptor has received particular attention due to its

broad expression on immune cells. AMP has pleiotropic effects in the tumor microenvironment, including expansion of regulatory T cells (Tregs), inhibition of effector T cell (Teff) responses mediated by interferon (IFN)- γ , and expansion of myeloid derived suppressor cells (MDSCs). See, e.g., Allard B, et al., *Curr Opin Pharmacol* 29:7-16 (2016) and Allard D, et al., *Immunotherapy* 8:145-163 (2016).

[0006] In a mouse model of hepatocellular carcinoma it was shown that ENTPD2 converts extracellular ATP to AMP which prevents the differentiation of monocytic myeloid derived suppressor cells (MDSCs) to dendritic cells, therefore promoting the maintenance of MDSCs *in vitro* and *in vivo* (Chiu et al., *Nat Commun.* 8:517-28 (2017)).

[0007] ENTPD2 is expressed on cancer cells as described herein. New compositions and methods for regulating ENTPD2 activity and related therapeutic agents are highly desirable.

SUMMARY OF THE INVENTION

[0008] Provided herein are antibodies or antigen-binding fragments thereof, e.g., monoclonal antibodies or antigen-binding fragments thereof, that specifically bind to the ectoenzyme ectonucleoside triphosphate diphosphohydrolase 2 (ENTPD2). The ENTPD2 antibodies or antigen-binding fragments thereof are useful for treating ENTPD2-associated diseases, such as cancer.

[0009] In one aspect, provided herein are antibodies or antigen-binding fragments thereof that specifically bind to human ENTPD2 protein, wherein the antibody or antigen binding fragment thereof comprises a heavy chain complementarity determining region 1 (HCDR1), a heavy chain complementarity determining region 2 (HCDR2), a heavy chain complementarity determining region 3 (HCDR3), a light chain complementarity determining region 1 (LCDR1), a light chain complementarity determining region 2 (LCDR2), and a light chain complementarity determining region 3 (LCDR3) of any antibody or antigen binding fragment provided in Table 1. In some embodiments, the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 of such antibodies or antigen binding fragments are selected from the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 sequences provided in Table 1. In some embodiments, such antibodies or antigen binding fragments comprise a heavy chain variable region (VH) provided in Table 1. In some embodiments, such antibodies or antigen binding fragments comprise a light chain variable region (VL) provided in Table 1.

[0010] In another aspect, provided herein are antibodies or antigen binding fragments selected from any one of the following:

- 1) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 1,
an HCDR2 sequence comprising SEQ ID NO: 2,
an HCDR3 sequence comprising SEQ ID NO: 3,
an LCDR1 sequence comprising SEQ ID NO: 14,
an LCDR2 sequence comprising SEQ ID NO: 15, and
an LCDR3 sequence comprising SEQ ID NO: 16;
- 2) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 4,
an HCDR2 sequence comprising SEQ ID NO: 5,
an HCDR3 sequence comprising SEQ ID NO: 3,
an LCDR1 sequence comprising SEQ ID NO: 17,
an LCDR2 sequence comprising SEQ ID NO: 18, and
an LCDR3 sequence comprising SEQ ID NO: 19;
- 3) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 7,
an HCDR2 sequence comprising SEQ ID NO: 8,
an HCDR3 sequence comprising SEQ ID NO: 9,
an LCDR1 sequence comprising SEQ ID NO: 20,
an LCDR2 sequence comprising SEQ ID NO: 18, and
an LCDR3 sequence comprising SEQ ID NO: 16;
- 4) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 37,
an HCDR2 sequence comprising SEQ ID NO: 38,
an HCDR3 sequence comprising SEQ ID NO: 39,
an LCDR1 sequence comprising SEQ ID NO: 50,
an LCDR2 sequence comprising SEQ ID NO: 51, and
an LCDR3 sequence comprising SEQ ID NO: 52;

- 5) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 40,
an HCDR2 sequence comprising SEQ ID NO: 41,
an HCDR3 sequence comprising SEQ ID NO: 39,
an LCDR1 sequence comprising SEQ ID NO: 53,
an LCDR2 sequence comprising SEQ ID NO: 54, and
an LCDR3 sequence comprising SEQ ID NO: 55;
- 6) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 43,
an HCDR2 sequence comprising SEQ ID NO: 44,
an HCDR3 sequence comprising SEQ ID NO: 45,
an LCDR1 sequence comprising SEQ ID NO: 56,
an LCDR2 sequence comprising SEQ ID NO: 54, and
an LCDR3 sequence comprising SEQ ID NO: 52;
- 7) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 37,
an HCDR2 sequence comprising SEQ ID NO: 38,
an HCDR3 sequence comprising SEQ ID NO: 39,
an LCDR1 sequence comprising SEQ ID NO: 61,
an LCDR2 sequence comprising SEQ ID NO: 51, and
an LCDR3 sequence comprising SEQ ID NO: 52;
- 8) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 40,
an HCDR2 sequence comprising SEQ ID NO: 41,
an HCDR3 sequence comprising SEQ ID NO: 39,
an LCDR1 sequence comprising SEQ ID NO: 62,
an LCDR2 sequence comprising SEQ ID NO: 54, and
an LCDR3 sequence comprising SEQ ID NO: 55;
- 9) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 43,
an HCDR2 sequence comprising SEQ ID NO: 44,
an HCDR3 sequence comprising SEQ ID NO: 45,
an LCDR1 sequence comprising SEQ ID NO: 63,
an LCDR2 sequence comprising SEQ ID NO: 54, and
an LCDR3 sequence comprising SEQ ID NO: 52;

10) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 37,
an HCDR2 sequence comprising SEQ ID NO: 38,
an HCDR3 sequence comprising SEQ ID NO: 68,
an LCDR1 sequence comprising SEQ ID NO: 50,
an LCDR2 sequence comprising SEQ ID NO: 51, and
an LCDR3 sequence comprising SEQ ID NO: 52;

11) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 40,
an HCDR2 sequence comprising SEQ ID NO: 41,
an HCDR3 sequence comprising SEQ ID NO: 68,
an LCDR1 sequence comprising SEQ ID NO: 53,
an LCDR2 sequence comprising SEQ ID NO: 54, and
an LCDR3 sequence comprising SEQ ID NO: 55;

12) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 43,
an HCDR2 sequence comprising SEQ ID NO: 44,
an HCDR3 sequence comprising SEQ ID NO: 69,
an LCDR1 sequence comprising SEQ ID NO: 56,
an LCDR2 sequence comprising SEQ ID NO: 54, and
an LCDR3 sequence comprising SEQ ID NO: 52;

13) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 82,
an HCDR2 sequence comprising SEQ ID NO: 83,

an HCDR3 sequence comprising SEQ ID NO: 84,
an LCDR1 sequence comprising SEQ ID NO: 95,
an LCDR2 sequence comprising SEQ ID NO: 96, and
an LCDR3 sequence comprising SEQ ID NO: 97;

14) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 85,
an HCDR2 sequence comprising SEQ ID NO: 86,
an HCDR3 sequence comprising SEQ ID NO: 84,
an LCDR1 sequence comprising SEQ ID NO: 98,
an LCDR2 sequence comprising SEQ ID NO: 99, and
an LCDR3 sequence comprising SEQ ID NO: 100;

15) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 88,
an HCDR2 sequence comprising SEQ ID NO: 89,
an HCDR3 sequence comprising SEQ ID NO: 90,
an LCDR1 sequence comprising SEQ ID NO: 101,
an LCDR2 sequence comprising SEQ ID NO: 99, and
an LCDR3 sequence comprising SEQ ID NO: 97;

16) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 106,
an HCDR2 sequence comprising SEQ ID NO: 107,
an HCDR3 sequence comprising SEQ ID NO: 108,
an LCDR1 sequence comprising SEQ ID NO: 119,
an LCDR2 sequence comprising SEQ ID NO: 120, and
an LCDR3 sequence comprising SEQ ID NO: 121;

17) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 109,
an HCDR2 sequence comprising SEQ ID NO: 110,
an HCDR3 sequence comprising SEQ ID NO: 108,
an LCDR1 sequence comprising SEQ ID NO: 122,

an LCDR2 sequence comprising SEQ ID NO: 99, and
an LCDR3 sequence comprising SEQ ID NO: 123;

18) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 112,
an HCDR2 sequence comprising SEQ ID NO: 113,
an HCDR3 sequence comprising SEQ ID NO: 114,
an LCDR1 sequence comprising SEQ ID NO: 124,
an LCDR2 sequence comprising SEQ ID NO: 99, and
an LCDR3 sequence comprising SEQ ID NO: 121;

19) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 106,
an HCDR2 sequence comprising SEQ ID NO: 129,
an HCDR3 sequence comprising SEQ ID NO: 108,
an LCDR1 sequence comprising SEQ ID NO: 119,
an LCDR2 sequence comprising SEQ ID NO: 120, and
an LCDR3 sequence comprising SEQ ID NO: 121;

20) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 109,
an HCDR2 sequence comprising SEQ ID NO: 130,
an HCDR3 sequence comprising SEQ ID NO: 108,
an LCDR1 sequence comprising SEQ ID NO: 122,
an LCDR2 sequence comprising SEQ ID NO: 99, and
an LCDR3 sequence comprising SEQ ID NO: 123;

21) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 112,
an HCDR2 sequence comprising SEQ ID NO: 131,
an HCDR3 sequence comprising SEQ ID NO: 114,
an LCDR1 sequence comprising SEQ ID NO: 124,
an LCDR2 sequence comprising SEQ ID NO: 99, and
an LCDR3 sequence comprising SEQ ID NO: 121;

22) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 136,
an HCDR2 sequence comprising SEQ ID NO: 137,
an HCDR3 sequence comprising SEQ ID NO: 138,
an LCDR1 sequence comprising SEQ ID NO: 149,
an LCDR2 sequence comprising SEQ ID NO: 150, and
an LCDR3 sequence comprising SEQ ID NO: 151;

23) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 139,
an HCDR2 sequence comprising SEQ ID NO: 140,
an HCDR3 sequence comprising SEQ ID NO: 138,
an LCDR1 sequence comprising SEQ ID NO: 152,
an LCDR2 sequence comprising SEQ ID NO: 153, and
an LCDR3 sequence comprising SEQ ID NO: 154;

24) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 142,
an HCDR2 sequence comprising SEQ ID NO: 143,
an HCDR3 sequence comprising SEQ ID NO: 144,
an LCDR1 sequence comprising SEQ ID NO: 155,
an LCDR2 sequence comprising SEQ ID NO: 153, and
an LCDR3 sequence comprising SEQ ID NO: 151;

25) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 160,
an HCDR2 sequence comprising SEQ ID NO: 161,
an HCDR3 sequence comprising SEQ ID NO: 162,
an LCDR1 sequence comprising SEQ ID NO: 173,
an LCDR2 sequence comprising SEQ ID NO: 150, and
an LCDR3 sequence comprising SEQ ID NO: 174;

26) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 163,
an HCDR2 sequence comprising SEQ ID NO: 164,
an HCDR3 sequence comprising SEQ ID NO: 162,
an LCDR1 sequence comprising SEQ ID NO: 175,
an LCDR2 sequence comprising SEQ ID NO: 153, and
an LCDR3 sequence comprising SEQ ID NO: 176;

27) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 166,
an HCDR2 sequence comprising SEQ ID NO: 167,
an HCDR3 sequence comprising SEQ ID NO: 168,
an LCDR1 sequence comprising SEQ ID NO: 177,
an LCDR2 sequence comprising SEQ ID NO: 153, and
an LCDR3 sequence comprising SEQ ID NO: 174;

28) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 37,
an HCDR2 sequence comprising SEQ ID NO: 220,
an HCDR3 sequence comprising SEQ ID NO: 221,
an LCDR1 sequence comprising SEQ ID NO: 61,
an LCDR2 sequence comprising SEQ ID NO: 51, and
an LCDR3 sequence comprising SEQ ID NO: 52;

29) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 40,
an HCDR2 sequence comprising SEQ ID NO: 222,
an HCDR3 sequence comprising SEQ ID NO: 221,
an LCDR1 sequence comprising SEQ ID NO: 62,
an LCDR2 sequence comprising SEQ ID NO: 54, and
an LCDR3 sequence comprising SEQ ID NO: 55;

30) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 43,
an HCDR2 sequence comprising SEQ ID NO: 223,

an HCDR3 sequence comprising SEQ ID NO: 224,
an LCDR1 sequence comprising SEQ ID NO: 63,
an LCDR2 sequence comprising SEQ ID NO: 54, and
an LCDR3 sequence comprising SEQ ID NO: 52;

31) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 37,
an HCDR2 sequence comprising SEQ ID NO: 220,
an HCDR3 sequence comprising SEQ ID NO: 68,
an LCDR1 sequence comprising SEQ ID NO: 61,
an LCDR2 sequence comprising SEQ ID NO: 51, and
an LCDR3 sequence comprising SEQ ID NO: 52;

32) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 40,
an HCDR2 sequence comprising SEQ ID NO: 222,
an HCDR3 sequence comprising SEQ ID NO: 68,
an LCDR1 sequence comprising SEQ ID NO: 62,
an LCDR2 sequence comprising SEQ ID NO: 54, and
an LCDR3 sequence comprising SEQ ID NO: 55;

33) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 43,
an HCDR2 sequence comprising SEQ ID NO: 223,
an HCDR3 sequence comprising SEQ ID NO: 69,
an LCDR1 sequence comprising SEQ ID NO: 63,
an LCDR2 sequence comprising SEQ ID NO: 54, and
an LCDR3 sequence comprising SEQ ID NO: 52;

34) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 1,
an HCDR2 sequence comprising SEQ ID NO: 245,
an HCDR3 sequence comprising SEQ ID NO: 246,
an LCDR1 sequence comprising SEQ ID NO: 254,

an LCDR2 sequence comprising SEQ ID NO: 15, and
an LCDR3 sequence comprising SEQ ID NO: 255;

35) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 4,
an HCDR2 sequence comprising SEQ ID NO: 247,
an HCDR3 sequence comprising SEQ ID NO: 246,
an LCDR1 sequence comprising SEQ ID NO: 17,
an LCDR2 sequence comprising SEQ ID NO: 18, and
an LCDR3 sequence comprising SEQ ID NO: 256;

36) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 7,
an HCDR2 sequence comprising SEQ ID NO: 248,
an HCDR3 sequence comprising SEQ ID NO: 249,
an LCDR1 sequence comprising SEQ ID NO: 20,
an LCDR2 sequence comprising SEQ ID NO: 18, and
an LCDR3 sequence comprising SEQ ID NO: 255;

37) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 1,
an HCDR2 sequence comprising SEQ ID NO: 261,
an HCDR3 sequence comprising SEQ ID NO: 262,
an LCDR1 sequence comprising SEQ ID NO: 254,
an LCDR2 sequence comprising SEQ ID NO: 15, and
an LCDR3 sequence comprising SEQ ID NO: 16;

38) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 4,
an HCDR2 sequence comprising SEQ ID NO: 247,
an HCDR3 sequence comprising SEQ ID NO: 262,
an LCDR1 sequence comprising SEQ ID NO: 17,
an LCDR2 sequence comprising SEQ ID NO: 18, and
an LCDR3 sequence comprising SEQ ID NO: 19;

39) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 7,
an HCDR2 sequence comprising SEQ ID NO: 248,
an HCDR3 sequence comprising SEQ ID NO: 263,
an LCDR1 sequence comprising SEQ ID NO: 20,
an LCDR2 sequence comprising SEQ ID NO: 18, and
an LCDR3 sequence comprising SEQ ID NO: 16;

40) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 272,
an HCDR2 sequence comprising SEQ ID NO: 273,
an HCDR3 sequence comprising SEQ ID NO: 274,
an LCDR1 sequence comprising SEQ ID NO: 254,
an LCDR2 sequence comprising SEQ ID NO: 285, and
an LCDR3 sequence comprising SEQ ID NO: 16;

41) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 275,
an HCDR2 sequence comprising SEQ ID NO: 276,
an HCDR3 sequence comprising SEQ ID NO: 274,
an LCDR1 sequence comprising SEQ ID NO: 17,
an LCDR2 sequence comprising SEQ ID NO: 286, and
an LCDR3 sequence comprising SEQ ID NO: 19;

42) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 278,
an HCDR2 sequence comprising SEQ ID NO: 279,
an HCDR3 sequence comprising SEQ ID NO: 280,
an LCDR1 sequence comprising SEQ ID NO: 20,
an LCDR2 sequence comprising SEQ ID NO: 286, and
an LCDR3 sequence comprising SEQ ID NO: 16.

[0011] In another aspect, provided herein are antibodies or antigen binding fragments selected from any one of the following:

1) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 10 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 21 or a sequence at least about 95% or more identical thereto;

2) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 25 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 29 or a sequence at least about 95% or more identical thereto;

3) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 33 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 29 or a sequence at least about 95% or more identical thereto;

4) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 46 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 57 or a sequence at least about 95% or more identical thereto;

5) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 46 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 64 or a sequence at least about 95% or more identical thereto;

6) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 70 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 74 or a sequence at least about 95% or more identical thereto;

7) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 25 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 78 or a sequence at least about 95% or more identical thereto;

8) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 91 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 102 or a sequence at least about 95% or more identical thereto;

9) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 115 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 125 or a sequence at least about 95% or more identical thereto;

10) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 132 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 125 or a sequence at least about 95% or more identical thereto;

11) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 145 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 156 or a sequence at least about 95% or more identical thereto;

12) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 169 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 178 or a sequence at least about 95% or more identical thereto;

13) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 225 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 229 or a sequence at least about 95% or more identical thereto;

14) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 233 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 237 or a sequence at least about 95% or more identical thereto;

15) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 241 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 229 or a sequence at least about 95% or more identical thereto;

16) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 250 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 257 or a sequence at least about 95% or more identical thereto;

17) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 264 or a sequence at least about 95% or more

identical thereto, and a VL comprising SEQ ID NO: 268 or a sequence at least about 95% or more identical thereto; or

18) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 281 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 287 or a sequence at least about 95% or more identical thereto.

[0012] In another aspect, provided herein are antibodies or antigen binding fragments selected from any one of the following:

1) an antibody comprising a heavy chain comprising SEQ ID NO: 12 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 23 or a sequence at least about 95% or more identical thereto;

2) an antibody comprising a heavy chain comprising SEQ ID NO: 27 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 31 or a sequence at least about 95% or more identical thereto;

3) an antibody comprising a heavy chain comprising SEQ ID NO: 35 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 31 or a sequence at least about 95% or more identical thereto;

4) an antibody comprising a heavy chain comprising SEQ ID NO: 48 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 59 or a sequence at least about 95% or more identical thereto;

5) an antibody comprising a heavy chain comprising SEQ ID NO: 48 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 66 or a sequence at least about 95% or more identical thereto;

6) an antibody comprising a heavy chain comprising SEQ ID NO: 72 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 76 or a sequence at least about 95% or more identical thereto;

7) an antibody comprising a heavy chain comprising SEQ ID NO: 27 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 80 or a sequence at least about 95% or more identical thereto;

8) an antibody comprising a heavy chain comprising SEQ ID NO: 93 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 104 or a sequence at least about 95% or more identical thereto;

9) an antibody comprising a heavy chain comprising SEQ ID NO: 117 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 127 or a sequence at least about 95% or more identical thereto;

10) an antibody comprising a heavy chain comprising SEQ ID NO: 134 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 127 or a sequence at least about 95% or more identical thereto;

11) an antibody comprising a heavy chain comprising SEQ ID NO: 147 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 158 or a sequence at least about 95% or more identical thereto;

12) an antibody comprising a heavy chain comprising SEQ ID NO: 171 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 180 or a sequence at least about 95% or more identical thereto;

13) an antibody comprising a heavy chain comprising SEQ ID NO: 227 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 231 or a sequence at least about 95% or more identical thereto;

14) an antibody comprising a heavy chain comprising SEQ ID NO: 235 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 239 or a sequence at least about 95% or more identical thereto;

15) an antibody comprising a heavy chain comprising SEQ ID NO: 243 or a sequence at least about 95% or more identical thereto, and a light chain

comprising SEQ ID NO: 231 or a sequence at least about 95% or more identical thereto;

16) an antibody comprising a heavy chain comprising SEQ ID NO: 252 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 259 or a sequence at least about 95% or more identical thereto;

17) an antibody comprising a heavy chain comprising SEQ ID NO: 266 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 270 or a sequence at least about 95% or more identical thereto; or

18) an antibody comprising a heavy chain comprising SEQ ID NO: 283 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 289 or a sequence at least about 95% or more identical thereto.

[0013] Provided herein are also antibodies or antigen binding fragments thereof that specifically bind to an epitope in human ENTPD2, wherein the epitope comprises at least one (e.g., at least two, at least three, at least four, at least five, at least six, at least seven, at least eight, at least nine, at least ten, at least eleven, at least twelve, at least thirteen, at least fourteen, at least fifteen, at least twenty) of the following residues: His50, Asp76, Pro78, Gly79, Gly80, Tyr85, Asp87, Asn88, Gly91, Gln94, Ser95, Gly98, Glu101, Gln102, Gln105, Asp106, Arg245, Thr272, Gln273, Leu275, Asp278, Arg298, Ala347, Ala350, Thr351, Arg392, Ala393, Arg394, or Tyr398.

[0014] Provided herein are also antibodies or antigen binding fragments thereof that specifically bind to an epitope in human ENTPD2, wherein the epitope comprises at least one (e.g., at least two, at least three, at least four, at least five, at least six, at least seven, at least eight, at least nine, at least ten, at least eleven, at least twelve, at least thirteen, at least fourteen, at least fifteen, at least twenty) of the following residues: Gly79, Gln250, Leu253, Trp266, Arg268, Gly269, Phe270, Ser271, Thr272, Gln273, Val274, Leu275, Asp278, Arg298, Ser300, Ser302, Gly303, Thr380, Trp381, Ala382, Gly390, Gln391, Arg392, Ala393, Arg394, or Asp397.

[0015] In some embodiments, the antibodies or antigen binding fragments thereof described herein have an IgG1, IgG2, IgG3 or IgG4 isotype. In some embodiments, the antibodies or antigen binding fragments thereof described herein have an IgG1 isotype. In some embodiments, the antibodies or antigen binding fragments thereof described herein

comprise an Fc region selected from an IgG1 Fc region, an IgG2 Fc region, an IgG4 Fc region, or an IgG2/IgG4 hybrid Fc region. . In some embodiments, the antibodies or antigen binding fragments thereof described herein comprise an Fc region selected from an IgG1 Fc region. In some embodiments, the antibodies or antigen binding fragments thereof described herein comprise a modified Fc region. In some embodiments, the antibodies or antigen binding fragments thereof described herein comprise a modified Fc region having reduced antibody-dependent cellular cytotoxicity (ADCC) or complement-dependent cytotoxicity (CDC) activity compared to the parent antibody.

[0016] In another aspect, provided herein are antibodies or antigen binding fragments thereof that compete with any antibody or antigen binding fragment provided in Table 1 for binding to human ENTPD2 protein.

[0017] In another aspect, provided herein are antibodies or antigen binding fragments thereof that bind essentially the same ENTPD2 epitope as any antibody or antigen binding fragment provided in Table 1.

[0018] In some embodiments, the antibodies or antigen binding fragments thereof described herein bind to human ENTPD2 protein with a dissociation constant (KD) of less than 10nM, e.g., with a KD of less than 5nM, or with a KD of less than 3nM, e.g., as measured by Biacore. In some embodiments, the dissociation constant of the antibodies or antigen binding fragments thereof described herein to human ENTPD2 is measured by Biacore at 25 °C.

[0019] In some embodiments, the antibodies or antigen binding fragments thereof described herein inhibit human ENTPD2 enzymatic activity by at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, or at least 90%. In some embodiments, the enzymatic activity of human ENTPD2 is measured using an in vitro FRET assay which measures the hydrolysis of ATP to ADP by either recombinant ENTPD2 or ENTPD2 expressed on the surface of cells.

[0020] In some embodiments, the anti-human ENTPD2 antibodies or antigen binding fragments thereof described herein inhibit ENTPD2's ability of hydrolysis of adenosine triphosphate (ATP). In some embodiments, ENTPD2's ability of hydrolysis of ATP is measured using an in vitro FRET assay which measures the hydrolysis of ATP to ADP by either recombinant ENTPD2 or ENTPD2 expressed on the surface of cells.

[0021] In some embodiments, the anti-human ENTPD2 antibodies or antigen binding fragments thereof described herein interfere with ATP binding to ENTPD2 or trap ATP within the catalytic domain of ENTPD2. In some embodiments, ENTPD2's ability of

hydrolysis of ATP is measured using an in vitro FRET assay which measures the hydrolysis of ATP to ADP by either recombinant ENTPD2 or ENTPD2 expressed on the surface of cells.

[0022] In some embodiments, the antibodies or antigen binding fragments thereof described herein are human or humanized antibodies or fragments thereof.

[0023] In another aspect, provided herein are nucleic acids encoding an anti-human ENTPD2 antibody or antigen binding fragment thereof described herein. Such nucleic acids can encode polypeptides comprising segments or domains of the ENTPD2 antibodies or antigen binding fragments thereof described herein.

[0024] Also provided are vectors comprising such nucleic acids encoding an anti-human ENTPD2 antibody or antigen binding fragment thereof described herein. In some embodiments, the vector is selected from a DNA vector, a RNA vector, a plasmid, a cosmid, or a viral vector. In some embodiments, the vector is a viral vector based on any one of the following viruses: lentivirus, adenovirus, adeno-associated virus (AAV), Herpes Simplex Virus (HSV), parvovirus, retrovirus, vaccinia virus, Sinbis virus, influenza virus, reovirus, Newcastle disease virus (NDV), measles virus, vesicular stomatitis virus (VSV), poliovirus, poxvirus, Seneca Valley virus, coxsackievirus, enterovirus, myxoma virus, or maraba virus. In some embodiments, the vector is an AAV vector. In some embodiments, the vector is a lentiviral vector. In some embodiments, the vector further comprises a promoter, e.g., a tissue-specific promoter. In some embodiments, the vector further comprises a detectable marker.

[0025] Also provided herein are cells comprising a nucleic acid or set of nucleic acids encoding an anti-human ENTPD2 antibody or antigen binding fragment thereof described herein or a vector comprising such a nucleic acid or set of nucleic acids.

[0026] In another aspect, provided herein are pharmaceutical compositions comprising an anti-human ENTPD2 antibody or antigen binding fragment thereof described herein, a nucleic acid encoding such an antibody or antigen binding fragment, a vector comprising such a nucleic acid or set of nucleic acids, or a cell comprising a nucleic acid or sets of nucleic acids or vector described herein, and a pharmaceutically acceptable carrier.

[0027] In another aspect, provided herein are methods of producing an anti-human ENTPD2 antibody or antigen binding fragment thereof by culturing a cell comprising a nucleic acid or sets of nucleic acids encoding an anti-human ENTPD2 antibody or antigen binding fragment thereof or a vector comprising such a nucleic acid or sets of nucleic acids, and collecting the antibody or antigen binding fragment thereof from the culture medium.

[0028] In another aspect, provided herein are methods of treating a cancer in a subject in need thereof by administering to the subject a therapeutically effective amount of an anti-human ENTPD2 antibody or antigen binding fragment described herein, a nucleic acid or sets of nucleic acids encoding such an antibody or antigen binding fragment, a vector comprising a nucleic acid encoding such an antibody or antigen binding fragment, a cell comprising such a nucleic acid or sets of nucleic acids or vector, or a pharmaceutical composition comprising such an antibody or antigen binding fragment, nucleic acid or sets of nucleic acids, vector or cell. In some embodiments, the antibody or antigen binding fragment thereof, the nucleic acid or sets of nucleic acids, the vector, the cell, or the pharmaceutical composition, is administered to the subject through an intravenous, intratumoral or subcutaneous route.

[0029] In another aspect, provided herein are methods of stimulating an immune response in a subject by administering to the subject an anti-human ENTPD2 antibody or antigen binding fragment described herein, a nucleic acid or sets of nucleic acids encoding such an antibody or antigen binding fragment, a vector comprising a nucleic acid encoding such an antibody or antigen binding fragment, a cell comprising such a nucleic acid or sets of nucleic acids or vector, or a pharmaceutical composition comprising such an antibody or antigen binding fragment, nucleic acid or sets of nucleic acids, vector or cell, in an amount effective to stimulate the immune response.

[0030] In some embodiments, such methods can further include administration of at least one additional therapeutic agent to the subject.

[0031] In some embodiments, such methods can further include administration of at least two additional therapeutic agents to the subject.

[0032] In another aspect, provided herein is an antibody or antigen binding fragment thereof described herein, the nucleic acid or set of nucleic acids encoding such an antibody or antigen binding fragment thereof, a vector or a cell comprising such a nucleic acid or set of nucleic acids, or a pharmaceutical composition comprising such an antibody or antigen binding fragment thereof, nucleic acid or set of nucleic acids, vector, or cell, for use as a medicament.

[0033] In another aspect, provided herein is an antibody or antigen binding fragment thereof described herein, the nucleic acid encoding such an antibody or antigen binding fragment thereof, a vector or a cell comprising such a nucleic acid or set of nucleic acids, or a pharmaceutical composition comprising such an antibody or antigen binding fragment thereof, nucleic acid or set of nucleic acids, vector, or cell, for use in treatment of a cancer.

[0034] In another aspect, provided herein is a pharmaceutical composition comprising an antibody or antigen binding fragment thereof described herein, and at least one additional therapeutic agent or procedure.

[0035] In some embodiments, the at least one additional therapeutic agent or procedure is selected from one or more of chemotherapy, a targeted anti-cancer therapy, an oncolytic drug, a cytotoxic agent, an immune-based therapy, a cytokine, surgical procedure, a radiation procedure, an activator of a costimulatory molecule, an inhibitor of an inhibitory molecule, a vaccine, or a cell therapy.

[0036] In some embodiments, the at least one additional therapeutic agent is a PD-1 inhibitor, e.g., a PD-1 antibody. In some embodiments, the PD-1 inhibitor is selected from PDR001, Nivolumab, Pembrolizumab, Pidilizumab, MEDI0680, REGN2810, TSR-042, PF-06801591, or AMP-224.

[0037] In some embodiments, the at least one additional therapeutic agent is a PD-L1 inhibitor, e.g., a PD-L1 antibody. In some embodiments, the PD-L1 inhibitor is selected from FAZ053, Atezolizumab, Avelumab, Durvalumab, or BMS-936559.

[0038] In some embodiments, the at least one additional therapeutic agent is an A2AR antagonist. In some embodiments, the A2AR antagonist is selected from:

- i. an anti-CD73 antibody molecule, or antigen-binding fragment thereof, optionally wherein the anti-CD73 antibody is selected from:
 - a. an anti-CD73 antibody molecule comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 295 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 296, or an amino acid sequence at least 85%, 90%, 95% identical or higher to SEQ ID NO: 295 or 296;
 - b. an anti-CD73 antibody molecule comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 299 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 300, or an amino acid sequence at least 85%, 90%, 95% identical or higher to SEQ ID NO: 299 or 300;
 - c. an anti-CD73 antibody molecule comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 302 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 303, or an amino acid sequence at least 85%, 90%, 95% identical or higher to SEQ ID NO: 302 or 303;
 - d. an anti-CD73 antibody molecule comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 304 and a light chain

variable region comprising the amino acid sequence of SEQ ID NO: 305, or an amino acid sequence at least 85%, 90%, 95% identical or higher to SEQ ID NO: 304 or 305;

e. an anti-CD73 antibody molecule comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 306 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 307, or an amino acid sequence at least 85%, 90%, 95% identical or higher to SEQ ID NO: 306 or 307; or

f. an anti-CD73 antibody molecule comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 308 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 309, or an amino acid sequence at least 85%, 90%, 95% identical or higher to SEQ ID NO: 308 or 309; or

ii. PBF509/NIR178, CPI444/V81444, AZD4635/HTL-1071, Vipadenant, GBV-2034, AB928, Theophylline, Istradefylline, Tozadenant/SYN-115, KW-6356, ST-4206, and Preladenant/SCH 420814; or

iii. 5-bromo-2,6-di-(1H-pyrazol-1-yl)pyrimidine-4-amine, or a pharmaceutically acceptable salt thereof; (S)-7-(5-methylfuran-2-yl)-3-((6-(((tetrahydrofuran-3-yl)oxy)methyl)pyridin-2-yl)methyl)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-5-amine, or a pharmaceutically acceptable salt thereof; (R)-7-(5-methylfuran-2-yl)-3-((6-(((tetrahydrofuran-3-yl)oxy)methyl)pyridin-2-yl)methyl)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-5-amine, or racemate thereof, or a pharmaceutically acceptable salt thereof; 7-(5-methylfuran-2-yl)-3-((6-(((tetrahydrofuran-3-yl)oxy)methyl)pyridin-2-yl)methyl)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-5-amine, or a pharmaceutically acceptable salt thereof; and 6-(2-chloro-6-methylpyridin-4-yl)-5-(4-fluorophenyl)-1,2,4-triazin-3-amine, or a pharmaceutically acceptable salt thereof.

[0039] In some embodiments, the at least one additional therapeutic agent is selected from:

i. a CTLA-4 inhibitor, optionally wherein the CTLA-4 inhibitor is selected from Ipilimumab or Tremelimumab;

ii. a TIM-3 inhibitor, optionally wherein the TIM-3 inhibitor is selected from MBG453, TSR-022, or LY3321367;

iii. a LAG-3 inhibitor, optionally wherein the LAG-3 inhibitor is selected from LAG525, BMS-986016, TSR-033, MK-4280 or REGN3767;

- iv. a GITR agonist, optionally wherein the GITR agonist is selected from GWN323, BMS-986156, MK-4166, MK-1248, TRX518, INCAGN1876, AMG 228, or INBRX-110;
- v. an anti-CD3 multispecific antibody molecule, optionally wherein the anti-CD3 multispecific antibody molecule is an anti-CD3 x anti-CD123 bispecific antibody molecule (e.g., XENP14045), or an anti-CD3 x anti-CD20 bispecific antibody molecule (e.g., XENP13676);
- vi. a cytokine molecule, optionally wherein the cytokine molecule is IL-15 complexed with a soluble form of IL-15 receptor alpha (IL-15Ra);
- vii. a macrophage colony-stimulating factor (M-CSF) inhibitor, optionally wherein the M-CSF inhibitor is MCS110;
- viii. a CSF-1R inhibitor, optionally wherein the CSF-1R inhibitor is BLZ945;
- ix. an inhibitor of indoleamine 2,3-dioxygenase (IDO) and/or tryptophan 2,3-dioxygenase (TDO);
- x. a TGF- β inhibitor;
- xi. an oncolytic virus;
- xii. a chimeric antigen receptor (CAR) T-cell therapy.

[0040] In some embodiments, the at least one additional therapeutic agent is selected from: 1) a protein kinase C (PKC) inhibitor; 2) a heat shock protein 90 (HSP90) inhibitor; 3) an inhibitor of a phosphoinositide 3-kinase (PI3K) and/or target of rapamycin (mTOR); 4) an inhibitor of cytochrome P450 (e.g., a CYP17 inhibitor or a 17 α -Hydroxylase/C17-20 Lyase inhibitor); 5) an iron chelating agent; 6) an aromatase inhibitor; 7) an inhibitor of p53, e.g., an inhibitor of a p53/Mdm2 interaction; 8) an apoptosis inducer; 9) an angiogenesis inhibitor; 10) an aldosterone synthase inhibitor; 11) a smoothened (SMO) receptor inhibitor; 12) a prolactin receptor (PRLR) inhibitor; 13) a Wnt signaling inhibitor; 14) a CDK4/6 inhibitor; 15) a fibroblast growth factor receptor 2 (FGFR2)/fibroblast growth factor receptor 4 (FGFR4) inhibitor; 16) an inhibitor of macrophage colony-stimulating factor (M-CSF); 17) an inhibitor of one or more of c-KIT, histamine release, Flt3 (e.g., FLK2/STK1) or PKC; 18) an inhibitor of one or more of VEGFR-2 (e.g., FLK-1/KDR), PDGFRbeta, c-KIT or Raf kinase C; 19) a somatostatin agonist and/or a growth hormone release inhibitor; 20) an anaplastic lymphoma kinase (ALK) inhibitor; 21) an insulin-like growth factor 1 receptor (IGF-1R) inhibitor; 22) a P-Glycoprotein 1 inhibitor; 23) a vascular endothelial growth factor receptor (VEGFR) inhibitor; 24) a BCR-ABL kinase inhibitor; 25) an FGFR inhibitor; 26) an

inhibitor of CYP11B2; 27) a HDM2 inhibitor, e.g., an inhibitor of the HDM2-p53 interaction; 28) an inhibitor of a tyrosine kinase; 29) an inhibitor of c-MET; 30) an inhibitor of JAK; 31) an inhibitor of DAC; 32) an inhibitor of 11 β -hydroxylase; 33) an inhibitor of IAP; 34) an inhibitor of PIM kinase; 35) an inhibitor of Porcupine; 36) an inhibitor of BRAF, e.g., BRAF V600E or wild-type BRAF; 37) an inhibitor of HER3; 38) an inhibitor of MEK; 39) an inhibitor of a lipid kinase; or one or more agents as provided in Table 16.

[0041] In some embodiments, the antibody or antigen binding fragment, the nucleic acid or set of nucleic acids, the vector, the cell, or the pharmaceutical composition is administered concurrently with, prior to, or subsequent to, the at least one additional therapeutic agent.

[0042] In some embodiments, administering the antibody or antigen binding fragment of, the nucleic acid or set of nucleic acids, the vector, the cell, or the pharmaceutical composition has one or more of the following effects:

- (a) increased number of CD45+ CD4- CD8+ CD69+ CD25+ cells in a tumor or lesion site in the subject;
- (b) increased number of CD45+ CD8- CD4+ FOXP3- CD69+ CD25+ cells in a tumor or lesion site in the subject;
- (c) decreased plasma MCP1 or IL-1 β level in the subject; or
- (d) increased MCP1 level in a tumor or lesion site in the subject.

[0043] In another aspect, provided herein are use of an antibody or antigen binding fragment thereof described herein, the nucleic acid encoding such an antibody or antigen binding fragment thereof, a vector or a cell comprising such a nucleic acid, or a pharmaceutical composition comprising such an antibody or antigen binding fragment thereof, nucleic acid, vector, or cell, in the manufacture of a medicament for treatment of a cancer.

[0044] In another aspect, provided herein are methods of treating cancer in a subject in need thereof, such method comprising administering to the subject a therapeutically effective amount of an anti-human ENTPD2 antibody or antigen binding fragment described herein, in combination with a second therapeutic agent selected from a PD-1 inhibitor or a PD-L1 inhibitor.

[0045] In another aspect, provided herein are methods of stimulating an immune response in a subject, such method comprising administering to the subject a therapeutically effective amount of an anti-human ENTPD2 antibody or antigen binding fragment described

herein, in combination with a second therapeutic agent selected from a PD-1 inhibitor or a PD-L1 inhibitor.

[0046] In another aspect, provided herein are compositions comprising an anti-human ENTPD2 antibody or antigen binding fragment described herein for use, in combination with a second therapeutic agent selected from a PD-1 inhibitor or a PD-L1 inhibitor, in the treatment of cancer in a subject.

[0047] In another aspect, provided herein are compositions comprising an anti-human ENTPD2 antibody or antigen binding fragment described herein, in combination with a second therapeutic agent selected from a PD-1 inhibitor or a PD-L1 inhibitor, for use in the treatment of cancer in a subject.

[0048] In some embodiments, the PD-1 inhibitor is a PD-1 antibody. In some embodiments, the PD-1 inhibitor is selected from PDR001, Nivolumab, Pembrolizumab, Pidilizumab, MEDI0680, REGN2810, TSR-042, PF-06801591, or AMP-224.

[0049] In some embodiments, the PD-L1 inhibitor is a PD-L1 antibody. In some embodiments, the PD-L1 inhibitor is selected from FAZ053, Atezolizumab, Avelumab, Durvalumab, or BMS-936559.

[0050] In some embodiments, the cancer is an ENTPD2+ cancer. In some embodiments, the cancer is colorectal cancer (CRC), gastric cancer (e.g., stomach adenocarcinoma, gastric carcinoma), esophageal cancer (e.g. esophageal squamous cell carcinoma (ESCC)), pancreatic cancer, cholangiocarcinoma, lung cancer (e.g., small cell lung cancer), breast cancer (e.g., breast adenocarcinoma), or ovarian cancer.

[0051] All publications, patents, and accession numbers mentioned herein are hereby incorporated by reference in their entirety as if each individual publication or patent was specifically and individually indicated to be incorporated by reference.

BRIEF DESCRIPTION OF THE DRAWINGS

[0052] **FIG. 1A** depicts ENTPD2 expression across representative cancer cell lines as determined by flow cytometry. **FIG. 1B** is table (Table 20) showing ENTPD2 receptor density across representative cancer cell lines.

[0053] **FIG. 2** depicts representative IHC staining images of ENTPD2 in formalin-fixed paraffin-embedded primary colorectal, esophageal and ovarian tumor tissues.

[0054] **FIG. 3A** shows the amino acid sequence of anti-human ENTPD2 FAb22 heavy chain (SEQ ID NO: 330) and light chain (SEQ ID NO: 334) with the CDRs underlined

(as defined by Kabat), and residues located at the antibody-antigen interface labeled for each Fab as (*). **FIG. 3B** shows the amino acid sequence of anti-human ENTPD2 FAb23 heavy chain (SEQ ID NO: 336) and light chains (SEQ ID NO: 239) with the CDRs underlined (as defined by Kabat), and residues located at the antibody-antigen interface labeled with (*). **FIG. 3C** shows the amino acid sequence of the anti-mouse ENTPD2 FAb24 heavy chain (SEQ ID NO: 338) and light chains (SEQ ID NO: 340) with the CDRs underlined (as defined by Kabat), and residues located at the antibody-antigen interface labeled with (*).

[0055] **FIG. 4A** shows the amino acid sequence of recombinant human ENTPD2 (residues 29-462, Y350A mutant) used in crystallographic studies (SEQ ID NO: 1014), with the secondary structure elements shown below the amino acid sequence. Bars represent α -helices and arrows represent β -strands. Unlabeled arrows and bars from sequence formatting breaks are contiguous to preceding structural elements labeled. Unstructured regions are unmarked. Soluble extracellular domain of human ENTPD2 spans residues 29-462. The construct utilizes an N-terminal GP67 secretion signal peptide (first 38 residues highlighted in gray) with the signal peptide cleavage site after last residue, and a C-terminal hexahistidine (SEQ ID NO: 1010) metal affinity tag to facilitate purification. Asn129, Asn294, Asn378 and Asn443 are predicted N-linked glycosylation sites for which glycosylation is observed in crystal structures and shown in italics. Asn64 is also a predicted N-linked glycosylation site not observed in these crystal structures. Residues located at the antigen-Fab interface for the FAb22 and FAb23 complexes are indicated by (*) and (:) symbols, respectively, below the amino acid sequence. **FIG. 4B** shows the amino acid sequence of recombinant murine ENTPD2 (residues 29-462) used in crystallography studies (SEQ ID NO: 1015), with the secondary structure elements shown below the amino acid sequence. The bars represent α -helices and arrows represent β -strands. Unlabeled arrows and bars from line breaks are contiguous to preceding structural elements labeled. Unstructured regions are unmarked. Mature murine ENTPD2 starts from Thr29. The construct utilizes an N-terminal GP67 secretion signal peptide (residues 1-38), with the signal peptide cleavage site after residue 38, and a C-terminal hexahistidine (SEQ ID NO: 1010) metal affinity tag to facilitate purification. Asn129, Asn294, Asn378 and Asn443 are potential N-linked glycosylation sites shown in italics. Residues positioned at the antigen-FAb24 interface are indicated by (#) symbol beneath the amino acid sequence.

[0056] **FIG. 5A** shows a cartoon depiction of the human ENTPD2 ectodomain apo crystal structure with residues 33-453 shown. Two views are rotated by 90 degrees.

Consecutive secondary structural elements are labeled. Disulfides are shown as sticks. The amino- and carboxy- termini are labeled NT and CT, respectively. The membrane proximal lobe contains both N- and C-termini (subdomain 1: Pro36-Ser161 and Lys427-Phe461) and is shaded darker than the membrane distal lobe (subdomain 2: Gly162-Gln426). Substrate ATP binds deep within the interlobe cleft. The location of the ATP binding site is illustrated in **FIG. 5B**. Shown is the ATP analog AMP-PNP superposed in the human ENTPD2 active site from the rat ENTPD2 co-structure (PDB 3CJA).

[0057] **FIG. 6** illustrates an overview of anti-human ENTPD2 FAb22 in complex with human ENTPD2. Two views are shown 90 degrees apart. AMP-PNP is modeled in the ENTPD2 active site based upon superposition with the rat ENTPD2 co-structure PDB 3CJA. The heavy chain of the Fab is shaded darker.

[0058] **FIG. 7** illustrates an overview of anti-human ENTPD2 FAb23 in complex with human ENTPD2. Two views are shown 90 degrees apart. AMP-PNP is modeled in the ENTPD2 active site based upon superposition with the rat ENTPD2 co-structure PDB 3CJA. The heavy chain of the Fab is shaded darker.

[0059] **FIG. 8** illustrates an overview of anti-murine ENTPD2 FAb24 in complex with mouse ENTPD2. AMP-PNP is modeled in the ENTPD2 active site based upon superposition with the rat ENTPD2 co-structure PDB 3CJA. The heavy chain of the Fab is shaded darker.

[0060] **FIG. 9** is a plot illustrating long-term efficacy with anti-mouse ENTPD2 mAb13 in combination with anti-PD-1 Ab in the syngeneic B16LM3 tumor model.

[0061] **FIGs. 10A-10C** are graphs illustrating efficacy with anti-mouse ENTPD2 mAb13 in combination with anti-PD-1 Ab in the syngeneic B16F10 tumor model, associated with increased influx of activated CD8 and CD4 T helper cells at the tumor site on day 8 post treatment.

[0062] **FIGs. 11A-11B** depict characterization of the human ENTPD2 engineered model B16LM3 clone B5, illustrating expression of human ENTPD2 by FACS *in vitro* and sustainability of human ENTPD2 expression in tumors *in vivo* by IHC with the Novus anti-human CD39L1 Ab (1:40 dilution).

[0063] **FIGs. 12A-12B** are graphs illustrating dose response efficacy of anti-human ENTPD2 mAb1 and mAb6 in combination with anti-PD-1 Ab in the human ENTPD2 engineered B16LM3 clone B5 model.

[0064] **FIGs. 13A-13B** are dot plots showing plasma IL-1b (FIG. 13A) and MCP-1 (FIG. 13B) levels after treatment with anti-human ENTPD2 mAb1 or an isotype control in the human ENTPD2 engineered B16LM3 clone B5 xenograft model in C57BL/6 mice. **FIGs. 13C-13D** are dot plots showing IL-1 β (FIG. 13C) and MCP-1 (FIG. 13D) levels in tumor after treatment with anti-human ENTPD2 mAb1 or an isotype control in the human ENTPD2 engineered B16LM3 clone B5 xenograft model in C57BL/6 mice.

[0065] **FIG. 14** is a graph showing *in vivo* efficacy of anti-ENTPD2 mAb1 in combination with A2AR antagonist NIR178 in the human ENTPD2 engineered B16LM3 xenograft model in C57BL/6 mice.

[0066] **FIG. 15** is a graph showing representative activity of anti-ENTPD2 Abs in the biochemical human ENTPD2 functional assay. Anti-human ENTPD2 mAb1, mAb17, mAb19, and mAb21 potentially inhibit the catalytic activity of the recombinant human ENTPD2.

[0067] **FIGs. 16A-16B** depicts representative activity of anti-human ENTPD2 Abs in the human or cyno ENTPD2 NIH/3T3 or RKO cell-based functional assay.

[0068] **FIG. 17** depicts graph illustrating *in vitro* functional activity of anti-mouse ENTPD2 mAb13, mAb14, mAb15 in the mouse ENTPD2 NIH/3T3 cell-based functional assay.

DETAILED DESCRIPTION

[0069] Provided herein are antibodies or antigen binding fragments thereof, e.g., monoclonal antibodies or antigen binding fragments thereof, that specifically bind to the ectoenzyme ectonucleoside triphosphate diphosphohydrolase 2 (e.g., human ENTPD2 protein). The ENTPD2 antibodies or antigen binding fragments thereof are useful for treating ENTPD2-associated diseases, such as a cancer.

Definitions

[0070] As used in the specification and claims, the singular form “a”, “an” and “the” include plural references unless the context clearly dictates otherwise. For example, the term “a cell” includes a plurality of cells, including mixtures thereof.

[0071] Throughout this specification and the claims which follow, unless the context requires otherwise, the word “comprise”, and variations such as “comprises” and

"comprising", are used herein in their open-ended and non-limiting sense unless otherwise noted.

[0072] When used herein "consisting of" excludes any element, step, or ingredient not specified in the aspect, embodiment and/or claim element. When used herein, "consisting essentially of" does not exclude materials or steps that do not materially affect the basic and novel characteristics of the aspect, embodiment and/or claim.

[0073] In each instance herein any of the terms "comprising", "consisting essentially of" and "consisting of" may be replaced with either of the other two terms.

[0074] All numerical designations, e.g., pH, temperature, time, concentration, and molecular weight, including ranges, are approximations which are varied (+) or (-) by increments of 0.1. It is to be understood, although not always explicitly stated that all numerical designations are preceded by the term "about". It also is to be understood, although not always explicitly stated, that the reagents described herein are merely examples and that equivalents of such are known in the art.

[0075] As used herein, ectonucleoside triphosphate diphosphohydrolase 2 (ENTPD2) (also known as CD39 Antigen-Like 1, CD39-like-1, CD39L1, Ecto-ATP Diphosphohydrolase 2, ecto-ATPase, Ecto-ATPase 2, Ecto-ATPDase 2, NTPDase-2, NTPDase 2) refers to the type 2 enzyme of the ecto-nucleoside triphosphate diphosphohydrolase family (E-NTPDase), which are a family of ecto-nucleosidases that hydrolyze 5'-triphosphates. The ENTPD2 enzyme is encoded by the gene *ENTPD2*. The human *ENTPD2* gene is mapped to chromosomal location 9q34.3, and the genomic sequence of human *ENTPD2* gene can be found in GenBank at NC_000009.12. The mRNA and protein sequences of the *ENTPD2* human transcript variants can be found in GenBank with the following Accession Nos:

Isoform1: NM_203468.2 (mRNA) → NP_982293.1 (protein with 495 aa);

Isoform2: NM_001246.3 (mRNA) → NP_001237.1 (protein with 472 aa);

Ectonucleoside triphosphate diphosphohydrolase 2 isoform 1 [Homo sapiens, NP_982293.1]

MAGKVRSLPPLLLAAAGLAGLLLLCVPTRDVREPPALKYGIVLDAGSSH
TSMFIYKWPADKENDTGIVGQHSSCDVPGGGISSYADNPSGASQSLVGCL
EQALQDVPKERHAGTPLYLGATAGMRLNLTNPEASTSVLMAVTHTLTQY
PFD FRGARILSGQEEGVFGWVTANYLLENFIKYGWVGRWFRPRKGT LGAM
DLGGASTQITFETTSPAEDRASEVQLHLYGQHYRVYTHSFLCYGRDQVLQ
RLLASALQTHGFHPCWPRGFSTQVLLGDVYQSPCTMAQRPQNFNSSARVS

LSGSSDPHLCRDLVSGLFSFSSCPFSRCSFNGVFQPPVAGNFVAFSAFFY
 TVDFLRTSMGLPVATLQQLEAAAVNVCNQTWAQLQARVPGQRARLADYCA
 GAMFVQQLSRGYGFDERAFGGVIFQKKAADTAVGWALGYMLNLTNLIPA
 DPPGLRKGTDFSSWVLLLLFASALLAALVLLLRQVHSAKLPSTI (SEQ ID NO: 291)

**Homo sapiens ectonucleoside triphosphate diphosphohydrolase 2 (ENTPD2),
 transcript variant 1, mRNA [NM_203468.2]**

1 ggctccccgc actctccggg tccacgcac gtctctccgc gcgccccccc gcccatggcc
 61 gggaaggtgc ggtcactgt gcccgcgtg ctgctggccg ccgaggccct cccggcctc
 121 ctactctgt gcgtccccc ccgcgacgtc cgggagccgc ccgccctcaa gtatggcac
 181 gtctggacg ctggttctt acacacgtcc atgtttatc acaagtggcc ggcagacaag
 241 gagaacgaca caggcattgt ggccagcac agctcctgt atgtccagg tgggggcatc
 301 tccagctatg cagacaacct ttctggggcc agccagagtc ttgttgatg cctcgaacg
 361 gcgcttcagg atgtgccc aaagagacac gcgggcacac cctctacct gggagccaca
 421 gcgggtatgc gcctgctaa cctgaccaat ccagaggcct cgaccagtgt gctcatggca
 481 gtgactcaca cactgacca gtacccctt gacttccggg gtgcacgat cctctcgggc
 541 caggaagagg ggggttttg ctgggtgact gccaactacc tgcaggagaa ctcatcaag
 601 tacggctggg tgggcccgtg gtccggcca cggaggggga cactgggggc catggacctg
 661 ggggggtgct ctaccagat cacttttag acaaccagtc cagctagga cagagccagc
 721 gaggtccagc tgcattcta cggccagcac taccagctt acaccacag ctctctgc
 781 tatggccgtg accaggtct ccagaggctg ctggccagcg cctccagac ccagggttc
 841 caccctgct gcccagggg ctttccacc caagtgtgc tcgggatgt gtaccagta
 901 ccatgcacca tggccagcg gcccagaac ttaacagca gtccagggt cagcctgtca
 961 gggagcagt accccacct ctgccagat ctggtttct ggctcttcag ctctctcc
 1021 tgcccttct cccgatgct ttcaatgg gtctccagc cccagtgcc tgggaactt
 1081 gtggccttct ctgcttct ctactgtg gacttttgc ggacttcga tgggctgcc
 1141 gtggccacc tgcagcagc ggaggcagc gcagtgaat tctgaacca gacctgggt
 1201 cagctgaag ctgggtgcc agggcaacgg gcccgcctg ccgactactg cccggggcc
 1261 atgttcgtg agcagctgt gagtcgggc tacggctcg acgagcgcg ctccggcgc
 1321 gtgatcttc agaagaagg cgcggacac gcagtgggt gggcgctcg ctacatgctg
 1381 aacctgacca acctgatcc cgcgaccgc cgggggtgc gcaaggcac agacttcagc
 1441 tctgggtcg tctctgct gtcttcgcc tccgcgtcc tggctgcgt tctctgctg
 1501 ctgcgtcagg tgcactccg caagtgcca agcaccattt aggggcccac gggggcagc
 1561 gcccaccc tccccaacc cctgtatcc caccctgac tccaccctt cccacaacc
 1621 ctgtacctc caccctgta tcccaccc tccaccacc cctctccaa cctctctcc
 1681 cggcctgta tctgcattc ctccaccac cctctatcc ccaccgtcc accccacc
 1741 tgtttctcc atcttcac cccacctca ggtctctg ccctaaggca gccagga
 1801 taggaactga gactctgga cccacaggc cctgggtggg caaagagcg tcaatccagc
 1861 tcttgaacc cctccagcc gctcagcct ggcatcact gcaggcccc tgcctctct
 1921 cctctctc agggctgggt ctccagagc tggggcctg gtctgagaa tcagccctta
 1981 gaggtcctt ctgttagtc tgggtctga ctgggaggg tcacagcca cgggctggca
 2041 gccagccag cacctactg taaaaattt gtaataaaa gttttctta gagacgtgaa

2101 aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaa (SEQ ID NO: 292)

Ectonucleoside triphosphate diphosphohydrolase 2 isoform 2 [Homo sapiens, NP_001237.1]

MAGKVRSLPPLLLAAAGLAGLLLLCVPTRDVREPPALKYGIVLDAGSSH
TSMFIYKWPADKENDTGIVGQHSSCDVPGGGISSYADNPSGASQSLVGCL
EQALQDVPKERHAGTPLYLGATAGMRLNLNPEASTSVLMAVTHTLTQY
PFD FRGARILSGQEEGVFGWVTANYLLENFIKYGWVGRWFRPRKGT LGAM
DLGGASTQITFETTSPAEDRASEVQLHLYGQHYRVYTHSFLCYGRDQVLQ
RLLASALQTHGFHPCWPRGFSTQVLLGDVYQSPCTMAQRPQNFNSSARVS
LSGSSDPHLCDLVSGLFSFSSCPFSRCSFNGVFQPPVAGNFVAFSAFFY
TVDFLRTSMGLPVATLQQLAEEAVNVCNQTWAQQLSRGYGFDERAFGGV
IFQKKAADTAVGWALGYMLNLNLIPADPPGLRKGTDFSSWVVL LLLFAS
ALLAALVLLLRQVHSAKLPSTI (SEQ ID NO: 293)

Homo sapiens ectonucleoside triphosphate diphosphohydrolase 2 (ENTPD2), transcript variant 2, mRNA [NM_001246.3]

1 ggctccccgc actctccggg tccacgcatc gtctccccgc gcgccccccc gcccatggcc
61 gggagaggtgc ggtcactgct gccgccgctg ctgctggccg ccgcgggcct cgcgggcctc
121 ctactgctgt ggtccccac ccgcgacgtc cgggagccgc ccgcctcaa gtagtgcac
181 gtctggacg ctggttctc acacagctcc atgttatct acaagtggcc ggcagacaag
241 gagaacgaca caggcattgt gggccagcac agctcctgtg atgtccagg tgggggcatc
301 tccagctatg cagacaaccc ttctggggcc agccagagtc ttgttgatg cctcgaacag
361 gcgcttcagg atgtgcccc aaagagacac gcgggcacac ccctctacct gggagccaca
421 gcgggtatgc gcctgtcaa cctgaccaat ccagaggcct cgaccagtgt gctcatggca
481 gtgactcaca cactgacca gtaccccttt gactccggg gtgcacgcat cctctcggc
541 caggaagagg ggggtgttg ctgggtgact gccactacc tgctggagaa cttcatcaag
601 tacggctggg tgggcccgtg gtccggcca cggagggga cactgggggc catggacctg
661 gggggtgcct ctaccagat cacttttgag acaaccagtc cagctgagga cagagccagc
721 gaggtccagc tgcattcta cggccagcac taccagctc acaccacag cttcctctgc
781 tatggcgtg accaggtcct ccagaggctg ctggccagcg ccctccagac ccacggcttc
841 caccctgct ggcgagggg ctttccacc caagtgtgc tcgggatgt gtaccagtc
901 ccatgcacca tggccagcg gcccagaac ttcaacagca gtgccagggt cagcctgtca
961 gggagcagt accccacct ctgccagat ctggtttctg ggctctcag cttctctcc
1021 tgccctctc cccgatgtc ttcaatggg gtctccagc cccagtggc tgggaacttt
1081 gtggccttct ctgccttct ctacactgtg gacttttgc ggacttcgat ggggctgccc
1141 gtggccacc tgcagcagct ggagcgagc gcagtgaatg tctgcaacca gacctgggt
1201 cagcagctgc tgagtcgcg ctacggcttc gacgagcgcg ccttcggcgg cgtgatctc
1261 cagaagaagg ccgcgacac tgcagtggg tggcgctcg gctacatgt gaacctgacc
1321 aacctgatc ccgccgacc gccggggctg cgcaaggga cagacttcag ctctgggtc
1381 gtctctctg tctctctc ctccgcgtc ctggtcgcg ttgtctctg gctgcgtcag
1441 gtgactccg ccaagtgcc aagcaccatt taggggccga cgggggcagc tgcccatcc


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1501 ctcccccaac cctgtatcc ccaccccgta ctcccccccc tcccacaacc cctgtacctc
1561 ccacccctgt atccccaccc ctccaccac ccctctccca acctctctcc ccgcccctgt
1621 atctgcatt cctccacca cccttatcc ccacccgctc cccccacca ctgtttctc
1681 catcttcca cccaccctc agcgtctctg ccctaaggc agcccaggaa ataggaaactg
1741 agactctgtg acccacagga gcctgggtgg gcaaagagcg ctcaatccag ctcttgaac
1801 cctccagcc cgcttcagcc tgggcatcac tgcaggcccc gtgctctcc tctctctct
1861 cagggctggg tctccagaga gtggggcctt ggtcctgaga atcagccctt agaggctct
1921 tctgttagt ctgggtctgt actggggagg gtcacagccc acgggctggc agccagccca
1981 gcacctactt gtaaaaattt tgtaataaaa agttttctct agagacgtga aaaaaaaaaa
2041 aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaaaaa aaaaaaa (SEQ ID NO: 294)

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[0076] As used herein, human ENTPD2 protein also encompasses proteins that have over its full length at least about 70%, 71%, 72%, 73%, 74%, 75%, 76%, 77%, 78%, 79%, 80%, 81%, 82%, 83%, 84%, 85%, 86%, 87%, 88%, 89%, 90%, 91%, 92%, 93%, 94%, 95%, 96%, 97%, 98%, 99% or 100% sequence identity with any one of the ENTPD2 isoforms. The sequences of murine, Cynomolgus monkey, and other animal ENTPD2 proteins are known in the art.

[0077] The term “antibody”, as used herein, refers to a protein, or polypeptide sequence derived from an immunoglobulin molecule that specifically binds to an antigen. Antibodies can be polyclonal or monoclonal, multiple or single chain, or intact immunoglobulins, and may be derived from natural sources or from recombinant sources. For example, a naturally occurring IgG antibody can be a glycoprotein comprising at least two heavy (H) chains and two light (L) chains inter-connected by disulfide bonds. Each heavy chain is comprised of a heavy chain variable region (abbreviated herein as VH) and a heavy chain constant region. The heavy chain constant region is comprised of three domains, CH1, CH2 and CH3. Each light chain is comprised of a light chain variable region (abbreviated herein as VL) and a light chain constant region. The light chain constant region is comprised of one domain, CL. The VH and VL regions can be further subdivided into regions of hypervariability, termed complementarity determining regions (CDR), interspersed with regions that are more conserved, termed framework regions (FR). Each VH and VL is composed of three CDRs and four FRs arranged from amino-terminus to carboxyl-terminus in the following order: FR1, CDR1, FR2, CDR2, FR3, CDR3, FR4. The variable regions of the heavy and light chains contain a binding domain that interacts with an antigen. The constant regions of the antibodies may mediate the binding of the immunoglobulin to host tissues or factors, including various cells of the immune system (e.g., effector cells) and the

first component (C1q) of the classical complement system. An antibody can be a monoclonal antibody, human antibody, humanized antibody, camelised antibody, or chimeric antibody. The antibodies can be of any isotype (e.g., IgG, IgE, IgM, IgD, IgA and IgY), class (e.g., IgG1, IgG2, IgG3, IgG4, IgA1 and IgA2) or subclass.

[0078] The term “antibody fragment” or “antigen-binding fragment” refers to at least one portion of an antibody, that retains the ability to specifically interact with (e.g., by binding, steric hinderance, stabilizing/destabilizing, spatial distribution) an epitope of an antigen. Examples of antibody fragments include, but are not limited to, Fab, Fab', F(ab')₂, Fv fragments, scFv antibody fragments, disulfide-linked Fvs (sdFv), a Fd fragment consisting of the VH and CH1 domains, linear antibodies, single domain antibodies such as sdAb (either VL or VH), camelid VHH domains, multi-specific antibodies formed from antibody fragments such as a bivalent fragment comprising two Fab fragments linked by a disulfide bridge at the hinge region, and an isolated CDR or other epitope binding fragments of an antibody. An antigen binding fragment can also be incorporated into single domain antibodies, maxibodies, minibodies, nanobodies, intrabodies, diabodies, triabodies, tetrabodies, v-NAR and bis-scFv (see, e.g., Hollinger and Hudson, *Nature Biotechnology* 23:1126-1136, 2005). Antigen binding fragments can also be grafted into scaffolds based on polypeptides such as a fibronectin type III (Fn3) (see U.S. Patent No.: 6,703,199, which describes fibronectin polypeptide minibodies). The term “scFv” refers to a fusion protein comprising at least one antibody fragment comprising a variable region of a light chain and at least one antibody fragment comprising a variable region of a heavy chain, wherein the light and heavy chain variable regions are contiguously linked, e.g., via a synthetic linker, e.g., a short flexible polypeptide linker, and capable of being expressed as a single chain polypeptide, and wherein the scFv retains the specificity of the intact antibody from which it is derived. Unless specified, as used herein an scFv may have the VL and VH variable regions in either order, e.g., with respect to the N-terminal and C-terminal ends of the polypeptide, the scFv may comprise VL-linker-VH or may comprise VH-linker-VL.

[0079] The terms “complementarity determining region” or “CDR”, as used herein, refer to the sequences of amino acids within antibody variable regions which confer antigen specificity and binding affinity. For example, in general, there are three CDRs in each heavy chain variable region (e.g., HCDR1, HCDR2, and HCDR3) and three CDRs in each light chain variable region (e.g., LCDR1, LCDR2, and LCDR3). The precise amino acid sequence boundaries of a given CDR can be determined using any one of a number of well-known

schemes, including those described by Kabat et al. (1991), “Sequences of Proteins of Immunological Interest,” 5th Ed. Public Health Service, National Institutes of Health, Bethesda, MD (“Kabat” numbering scheme), Al-Lazikani et al., (1997) JMB 273,927-948 (“Chothia” numbering scheme), or a combination thereof, and ImMunoGenTics (IMGT) numbering (Lefranc, M.-P., The Immunologist, 7, 132-136 (1999); Lefranc, M.-P. et al., Dev. Comp. Immunol., 27, 55-77 (2003) (“IMGT” numbering scheme). In a combined Kabat and Chothia numbering scheme for a given CDR region (for example, HC CDR1, HC CDR2, HC CDR3, LC CDR1, LC CDR2 or LC CDR3), in some embodiments, the CDRs correspond to the amino acid residues that are defined as part of the Kabat CDR, together with the amino acid residues that are defined as part of the Chothia CDR. As used herein, the CDRs defined according to the “Chothia” number scheme are also sometimes referred to as “hypervariable loops.”

[0080] For example, under Kabat, the CDR amino acid residues in the heavy chain variable domain (VH) are numbered 31-35 (HCDR1) (e.g., insertion(s) after position 35), 50-65 (HCDR2), and 95-102 (HCDR3); and the CDR amino acid residues in the light chain variable domain (VL) are numbered 24-34 (LCDR1) (e.g., insertion(s) after position 27), 50-56 (LCDR2), and 89-97 (LCDR3). As another example, under Chothia, the CDR amino acids in the VH are numbered 26-32 (HCDR1) (e.g., insertion(s) after position 31), 52-56 (HCDR2), and 95-102 (HCDR3); and the amino acid residues in VL are numbered 26-32 (LCDR1) (e.g., insertion(s) after position 30), 50-52 (LCDR2), and 91-96 (LCDR3). By combining the CDR definitions of both Kabat and Chothia, the CDRs comprise or consist of, e.g., amino acid residues 26-35 (HCDR1), 50-65 (HCDR2), and 95-102 (HCDR3) in human VH and amino acid residues 24-34 (LCDR1), 50-56 (LCDR2), and 89-97 (LCDR3) in human VL. Under IMGT, the CDR amino acid residues in the VH are numbered approximately 26-35 (CDR1), 51-57 (CDR2) and 93-102 (CDR3), and the CDR amino acid residues in the VL are numbered approximately 27-32 (CDR1), 50-52 (CDR2), and 89-97 (CDR3) (numbering according to “Kabat”). Under IMGT, the CDR regions of an antibody can be determined using the program IMGT/DomainGap Align. Generally, unless specifically indicated, the antibody molecules can include any combination of one or more Kabat CDRs and/or Chothia CDRs.

[0081] The term “epitope” includes any protein determinant capable of specific binding to an immunoglobulin or otherwise interacting with a molecule. Epitopic determinants generally consist of chemically active surface groupings of molecules such as

amino acids or carbohydrate or sugar side chains and can have specific three-dimensional structural characteristics, as well as specific charge characteristics. An epitope may be “linear” or “conformational.” Conformational and linear epitopes are distinguished in that the binding to the former but not the latter is lost in the presence of denaturing solvents.

[0082] The term “monovalent antibody” as used herein, refers to an antibody that binds to a single epitope on a target molecule.

[0083] The term “bivalent antibody” as used herein, refers to an antibody that binds to two epitopes on at least two identical target molecules. The bivalent antibody may also crosslink the target molecules to one another. A “bivalent antibody” also refers to an antibody that binds to two different epitopes on at least two identical target molecules.

[0084] The term “multivalent antibody” refers to a single binding molecule with more than one valency, where “valency” is described as the number of antigen-binding moieties present per molecule of an antibody construct. As such, the single binding molecule can bind to more than one binding site on a target molecule. Examples of multivalent antibodies include, but are not limited to, bivalent antibodies, trivalent antibodies, tetravalent antibodies, pentavalent antibodies, and the like, as well as bispecific antibodies and biparatopic antibodies. For example, for ENTPD2, the multivalent antibody (e.g., a ENTPD2 biparatopic antibody) has a binding moiety for two domains of ENTPD2, respectively.

[0085] The term “multivalent antibody” also refers to a single binding molecule that has more than one antigen-binding moiety for two separate target molecules. For example, an antibody that binds to ENTPD2 (e.g., human ENTPD2 protein) and a second target molecule that is not ENTPD2. In one embodiment, a multivalent antibody is a tetravalent antibody that has four epitope binding domains. A tetravalent molecule may be bispecific and bivalent for each binding site on that target molecule.

[0086] The term “bispecific antibody” as used herein, refers to an antibody that binds to two or more different epitopes. In some embodiments, a bispecific antibody binds to two different targets. In some embodiments, a bispecific antibody binds to two different epitopes on a single target molecule. An antibody that binds to two different epitopes on a single target molecule is also known as a “biparatopic antibody.”

[0087] The phrases “monoclonal antibody” or “monoclonal antibody composition” as used herein refers to polypeptides, including antibodies, bispecific antibodies, etc., that have substantially identical amino acid sequence or are derived from the same genetic source. This

term also includes preparations of antibody molecules of single molecular composition. A monoclonal antibody composition displays a single binding specificity and affinity for a particular epitope.

[0088] The phrase “human antibody,” as used herein, includes antibodies having variable regions in which both the framework and CDR regions are derived from sequences of human origin. Furthermore, if the antibody contains a constant region, the constant region is also derived from such human sequences, e.g., human germline sequences, or mutated versions of human germline sequences or antibody containing consensus framework sequences derived from human framework sequences analysis, for example, as described in Knappik, et al. (2000. J Mol Biol 296, 57-86). The structures and locations of immunoglobulin variable domains, e.g., CDRs, may be defined using well known numbering schemes, e.g., the Kabat numbering scheme, the Chothia numbering scheme, or a combination of Kabat and Chothia, and ImMunoGenTics (IMGT) numbering (see, e.g., Sequences of Proteins of Immunological Interest, U.S. Department of Health and Human Services (1991), eds. Kabat et al.; Al Lazikani et al., (1997) J. Mol. Bio. 273:927-948); Kabat et al., (1991) Sequences of Proteins of Immunological Interest, 5th edit., NIH Publication no. 91-3242 U.S. Department of Health and Human Services; Chothia et al., (1987) J. Mol. Biol. 196:901-917; Chothia et al., (1989) Nature 342:877-883; Al-Lazikani et al., (1997) J. Mol. Biol. 273:927-948 and Lefranc, M.-P., The Immunologist, 7, 132-136 (1999); Lefranc, M.-P. et al., Dev. Comp. Immunol., 27, 55-77 (2003)).

[0089] The human antibodies of the invention may include amino acid residues not encoded by human sequences (e.g., mutations introduced by random or site-specific mutagenesis *in vitro* or by somatic mutation *in vivo*, or a conservative substitution to promote stability or manufacturing). However, the term “human antibody” as used herein, is not intended to include antibodies in which CDR sequences derived from the germline of another mammalian species, such as a mouse, have been grafted onto human framework sequences.

[0090] The phrase “recombinant human antibody” as used herein, includes all human antibodies that are prepared, expressed, created or isolated by recombinant means, such as antibodies isolated from an animal (e.g., a mouse) that is transgenic or transchromosomal for human immunoglobulin genes or a hybridoma prepared therefrom, antibodies isolated from a host cell transformed to express the human antibody, e.g., from a transfectoma, antibodies isolated from a recombinant, combinatorial human antibody library, and antibodies prepared, expressed, created or isolated by any other means that involve splicing of all or a portion of a

human immunoglobulin gene, sequences to other DNA sequences. Such recombinant human antibodies have variable regions in which the framework and CDR regions are derived from human germline immunoglobulin sequences. In certain embodiments, however, such recombinant human antibodies can be subjected to *in vitro* mutagenesis (or, when an animal transgenic for human Ig sequences is used, *in vivo* somatic mutagenesis) and thus the amino acid sequences of the VH and VL regions of the recombinant antibodies are sequences that, while derived from and related to human germline VH and VL sequences, may not naturally exist within the human antibody germline repertoire *in vivo*.

[0091] The term “Fc region” as used herein refers to a polypeptide comprising the CH3, CH2 and at least a portion of the hinge region of a constant domain of an antibody. Optionally, an Fc region may include a CH4 domain, present in some antibody classes. An Fc region, may comprise the entire hinge region of a constant domain of an antibody. In one embodiment, the invention comprises an Fc region and a CH1 region of an antibody. In one embodiment, the invention comprises an Fc region CH3 region of an antibody. In another embodiment, the invention comprises an Fc region, a CH1 region and a Ckappa/lambda region from the constant domain of an antibody. In one embodiment, a binding molecule of the invention comprises a constant region, e.g., a heavy chain constant region. In one embodiment, such a constant region is modified compared to a wild-type constant region. That is, the polypeptides of the invention disclosed herein may comprise alterations or modifications to one or more of the three heavy chain constant domains (CH1, CH2 or CH3) and/or to the light chain constant region domain (CL). Example modifications include additions, deletions or substitutions of one or more amino acids in one or more domains. Such changes may be included to optimize effector function, half-life, etc.

[0092] As used herein, the term “affinity” refers to the strength of interaction between antibody and antigen at single antigenic sites. Within each antigenic site, the variable region of the antibody “arm” interacts through weak non-covalent forces with the antigen at numerous sites; the more interactions, the stronger the affinity. As used herein, the term “high affinity” for an IgG antibody or fragment thereof (e.g., a Fab fragment) refers to an antibody having a knock down of 10^{-8} M or less, 10^{-9} M or less, or 10^{-10} M, or 10^{-11} M or less, or 10^{-12} M or less, or 10^{-13} M or less for a target antigen. However, high affinity binding can vary for other antibody isotypes. For example, high affinity binding for an IgM isotype refers to an antibody having a knock down of 10^{-7} M or less, or 10^{-8} M or less.

[0093] As used herein, the term “avidity” refers to an informative measure of the overall stability or strength of the antibody-antigen complex. It is controlled by three major factors: antibody epitope affinity; the valency of both the antigen and antibody; and the structural arrangement of the interacting parts. Ultimately these factors define the specificity of the antibody, that is, the likelihood that the particular antibody is binding to a precise antigen epitope.

[0094] The term “binding specificity” as used herein refers to the ability of an individual antibody combining site to react with one antigenic determinant and not with a different antigenic determinant. The combining site of the antibody is located in the Fab portion of the molecule and is constructed from the hypervariable regions of the heavy and light chains. Binding affinity of an antibody is the strength of the reaction between a single antigenic determinant and a single combining site on the antibody. It is the sum of the attractive and repulsive forces operating between the antigenic determinant and the combining site of the antibody.

[0095] The term “treat” and “treatment” refer to both therapeutic treatment and prophylactic or preventive measures, wherein the object is to prevent or slow down an undesired physiological change or disorder. For purpose of this invention, beneficial or desired clinical results include, but are not limited to, alleviation of symptoms, diminishment of extent of disease, stabilized (i.e., not worsening) state of disease, delay or slowing of disease progression, amelioration or palliation of the disease state, and remission (whether partial or total), whether detectable or undetectable. “Treatment” can also mean prolonging survival as compared to expected survival if not receiving treatment. In other embodiments the terms “treat”, “treatment” and “treating” refer to the inhibition of the progression of a proliferative disorder, either physically by, *e.g.*, stabilization of a discernible symptom, physiologically by, *e.g.*, stabilization of a physical parameter, or both. In other embodiments the terms “treat”, “treatment” and “treating” refer to the reduction or stabilization of tumor size or cancerous cell count.

[0096] The term “subject” refers to an animal, human or non-human, to whom treatment according to the methods of the present invention is provided. Veterinary and non-veterinary applications are contemplated. The term includes, but is not limited to, mammals, *e.g.*, humans, other primates, pigs, rodents such as mice and rats, rabbits, guinea pigs, hamsters, cows, horses, cats, dogs, sheep and goats. Typical subjects include humans, farm

animals, and domestic pets such as cats and dogs. In some embodiments, the subject is a human.

[0097] An “effective amount” refers to an amount sufficient to effect beneficial or desired results. For example, a therapeutic amount is one that achieves the desired therapeutic effect. This amount can be the same or different from a prophylactically effective amount, which is an amount necessary to prevent onset of disease or disease symptoms. An effective amount can be administered in one or more administrations, applications or dosages. A “therapeutically effective amount” of a therapeutic compound (i.e., an effective dosage) depends on the therapeutic compounds selected. The compositions can be administered from one or more times per day to one or more times per week. The skilled artisan will appreciate that certain factors may influence the dosage and timing required to effectively treat a subject, including but not limited to the severity of the disease or disorder, previous treatments, the general health and/or age of the subject, and other diseases present. Moreover, treatment of a subject with a therapeutically effective amount of the therapeutic compounds described herein can include a single treatment or a series of treatments.

[0098] The term “nucleic acid” or “polynucleotide” refers to deoxyribonucleic acids (DNA) or ribonucleic acids (RNA) and polymers thereof in either single- or double-stranded form. The term “set of nucleic acids” may, for example, include separate isolated nucleic acids encoding a light chain and a heavy chain of an antibody or domains of a bi-specific or multispecific antibody. Unless specifically limited, the term encompasses nucleic acids containing known analogues of natural nucleotides that have similar binding properties as the reference nucleic acid and are metabolized in a manner similar to naturally occurring nucleotides. Unless otherwise indicated, a particular nucleic acid sequence also implicitly encompasses conservatively modified variants thereof (e.g., degenerate codon substitutions), alleles, orthologs, SNPs, and complementary sequences as well as the sequence explicitly indicated. Specifically, degenerate codon substitutions may be achieved by generating sequences in which the third position of one or more selected (or all) codons is substituted with mixed-base and/or deoxyinosine residues (Batzner et al., *Nucleic Acid Res.* 19:5081 (1991); Ohtsuka et al., *J. Biol. Chem.* 260:2605-2608 (1985); and Rossolini et al., *Mol. Cell. Probes* 8:91-98 (1994)).

[0099] The terms “peptide”, “polypeptide”, and “protein” are used interchangeably, and refer to a compound comprised of amino acid residues covalently linked by peptide bonds. A protein or peptide must contain at least two amino acids, and no limitation is placed

on the maximum number of amino acids that can comprise a protein's or peptide's sequence. Polypeptides include any peptide or protein comprising two or more amino acids joined to each other by peptide bonds. As used herein, the term refers to both short chains, which also commonly are referred to in the art as peptides, oligopeptides and oligomers, for example, and to longer chains, which generally are referred to in the art as proteins, of which there are many types. "Polypeptides" include, for example, biologically active fragments, substantially homologous polypeptides, oligopeptides, homodimers, heterodimers, variants of polypeptides, modified polypeptides, derivatives, analogs, fusion proteins, among others. A polypeptide includes a natural peptide, a recombinant peptide, or a combination thereof.

[0100] The term "conservative sequence modifications" refers to amino acid modifications that do not significantly affect or alter the binding characteristics of the antibody or antibody fragment containing the amino acid sequence. Such conservative modifications include amino acid substitutions, additions and deletions. Modifications can be introduced into an antibody or antibody fragment of the invention by standard techniques known in the art, such as site-directed mutagenesis and PCR-mediated mutagenesis. Conservative amino acid substitutions are ones in which the amino acid residue is replaced with an amino acid residue having a similar side chain. Families of amino acid residues having similar side chains have been defined in the art. These families include amino acids with basic side chains (e.g., lysine, arginine, histidine), acidic side chains (e.g., aspartic acid, glutamic acid), uncharged polar side chains (e.g., glycine, asparagine, glutamine, serine, threonine, tyrosine, cysteine, tryptophan), nonpolar side chains (e.g., alanine, valine, leucine, isoleucine, proline, phenylalanine, methionine), beta-branched side chains (e.g., threonine, valine, isoleucine) and aromatic side chains (e.g., tyrosine, phenylalanine, tryptophan, histidine).

[0101] The term "homologous" or "identity" refers to the subunit sequence identity between two polymeric molecules, e.g., between two nucleic acid molecules, such as, two DNA molecules or two RNA molecules, or between two polypeptide molecules. When a subunit position in both of the two molecules is occupied by the same monomeric subunit; e.g., if a position in each of two DNA molecules is occupied by adenine, then they are homologous or identical at that position. The homology between two sequences is a direct function of the number of matching or homologous positions; e.g., if half (e.g., five positions in a polymer ten subunits in length) of the positions in two sequences are homologous, the two sequences are 50% homologous; if 90% of the positions (e.g., 9 of 10), are matched or

homologous, the two sequences are 90% homologous. Percentage of “sequence identity” can be determined by comparing two optimally aligned sequences over a comparison window, where the fragment of the amino acid sequence in the comparison window may comprise additions or deletions (e.g., gaps or overhangs) as compared to the reference sequence (which does not comprise additions or deletions) for optimal alignment of the two sequences. The percentage can be calculated by determining the number of positions at which the identical amino acid residue occurs in both sequences to yield the number of matched positions, dividing the number of matched positions by the total number of positions in the window of comparison, and multiplying the result by 100 to yield the percentage of sequence identity. The output is the percent identity of the subject sequence with respect to the query sequence.

[0102] The term “isolated” means altered or removed from the natural state. For example, a nucleic acid or a peptide naturally present in a living animal is not “isolated,” but the same nucleic acid or peptide partially or completely separated from the coexisting materials of its natural state is “isolated.” An isolated nucleic acid or protein can exist in substantially purified form, or can exist in a non-native environment such as, for example, a host cell. An isolated antibody is substantially free of other antibodies having different antigenic specificities (e.g., an isolated antibody that specifically binds ENTPD2 is substantially free of antibodies that specifically bind antigens other than ENTPD2). An isolated antibody that specifically binds a target molecule may, however, have cross-reactivity to the same antigens from other species, e.g., an isolated antibody that specifically binds ENTPD2 may bind ENTPD2 molecules from other species. Moreover, an isolated antibody may be substantially free of other cellular material and/or chemicals.

[0103] Unless otherwise defined, all technical and scientific terms used herein have the same meaning as commonly understood by one of ordinary skill in the art to which this invention pertains. Although methods and materials similar or equivalent to those described herein can be used to practice the invention, suitable methods and materials are described below. All publications, patent applications, patents, and other references mentioned herein are incorporated by reference in their entirety. In case of conflict, the present specification, including definitions, will control. In addition, the materials, methods, and examples are illustrative only and not intended to be limiting.

[0104] The details of one or more embodiments of the invention are set forth in the accompanying drawings and the description below. Other features, objects, and advantages of the invention will be apparent from the description and drawings, and from the claims.

Antibodies and Antigen-Binding Fragments Thereof That Specifically Bind To Human ENTPD2

[0105] In one aspect, provided herein are antibodies or antigen binding fragments thereof, e.g., monoclonal antibodies or antigen binding fragments thereof, that specifically bind to ENTPD2 protein (“ENTPD2 antibodies or antigen binding fragments” or “anti-ENTPD2 antibodies or antigen binding fragments”). In some embodiments, provided herein are antibodies or antigen binding fragments thereof, e.g., monoclonal antibodies or antigen binding fragments thereof, that specifically bind to human ENTPD2 protein (“human ENTPD2 antibodies or antigen binding fragments” or “anti-human ENTPD2 antibodies or antigen binding fragments”).

[0106] In some embodiments, the anti-ENTPD2 antibodies or antigen-binding fragments thereof (e.g., anti-human ENTPD2 antibodies or antigen binding fragments) provided herein include a heavy chain CDR1 (HCDR1), a heavy chain CDR2 (HCDR2), a heavy chain CDR3 (HCDR3), and a light chain CDR1 (LCDR1), a light chain CDR2 (LCDR2), and a light chain CDR3 (LCDR3). In some embodiments, the anti-ENTPD2 antibodies or antigen binding fragments (e.g., anti-human ENTPD2 antibodies or antigen binding fragments) provided herein include a heavy chain variable region (VH) comprising CDR1, CDR2, and CDR3 and a light chain variable region (VL) comprising CDR1, CDR2, and CDR3. In some embodiments, the anti-ENTPD2 antibodies or antigen-binding fragments (e.g., anti-human ENTPD2 antibodies or antigen binding fragments) provided herein include a full length heavy chain sequence (HC) and a full length light chain sequence (LC).

[0107] Table 1 lists the sequences of exemplary the ENTPD2 antibodies or antigen-binding fragments that specifically bind to human ENTPD2 protein.

Table 1. Sequences of Exemplary Monoclonal Antibodies (MABs) and Antibody Fragments (FABs) That Bind Human ENTPD2

ANTI-HUMAN ENTPD2 MAB1		
SEQ ID NO: 1	HCDR1 (KABAT)	DYNMD
SEQ ID NO: 2	HCDR2 (KABAT)	DINPKYDISTYNQQFKG
SEQ ID NO: 3	HCDR3 (KABAT)	RGFFLYYGINYYYFDV
SEQ ID NO: 4	HCDR1 (CHOTHIA)	GYTFTDY
SEQ ID NO: 5	HCDR2 (CHOTHIA)	NPKYDI

SEQ ID NO: 3	HCDR3 (CHOTHIA)	RGFFLYYGINYYYFDV
SEQ ID NO: 6	HCDR1 (COMBINED)	GYTFTDYNMD
SEQ ID NO: 2	HCDR2 (COMBINED)	DINPKYDISTYNQQFKG
SEQ ID NO: 3	HCDR3 (COMBINED)	RGFFLYYGINYYYFDV
SEQ ID NO: 7	HCDR1 (IMGT)	GYTFTDYN
SEQ ID NO: 8	HCDR2 (IMGT)	INPKYDIS
SEQ ID NO: 9	HCDR3 (IMGT)	ARRGFFLYYGINYYYFDV
SEQ ID NO: 10	VH	EVQLVQSGAEVKKPGESLKISCKASGYTFTDYNMD WVRQMPGKGLEWMGDINPKYDISTYNQQFKGQVTI SADKSIRTAYLQWSSLKASDTAMYVCARRGFFLYYG INYYYFDVWGQGLTVSS
SEQ ID NO: 11	VH DNA	GAAGTGCAGCTGGTGCAGTCTGGCGCCGAAGTGA AGAAGCCTGGCGAGTCCCTGAAGATCTCCTGCAAG GCCTCCGGCTACACCTTCACCGACTACAACATGGA CTGGGTGCGACAGATGCCCCGCAAGGGCCTGGAA TGGATGGGCGACATCAACCCTAAGTACGACATCTC CACCTACAACCAGCAGTTCAAGGGCCAAGTGACC ATCTCCGCCGACAAGTCCATCCGGACCGCCTACCT GCAGTGGTCTCCTGAAGGCCTCTGACACCGCCA TGTAATACTGCGCCAGACGGGGCTTCTTCTGTAC TACGGCATCACTACTACTTTCGACGTGTGGGG CCAGGGCACCCCTCGTGACAGTGTCTATCT
SEQ ID NO: 12	HC	EVQLVQSGAEVKKPGESLKISCKASGYTFTDYNMD WVRQMPGKGLEWMGDINPKYDISTYNQQFKGQVTI SADKSIRTAYLQWSSLKASDTAMYVCARRGFFLYYG INYYYFDVWGQGLTVSSASTKGPSVFPLAPSSKST SGGTAALGCLVKDYFPEPVTVSWNSGALTSVHTFP AVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSN TKVDKRVPEPKSCDKTHCTCPPELGGPSVFLFPP KPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDG VEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPP SREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPEN NYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFC SVMHEALHNHYTQKLSLSLSPGK
SEQ ID NO: 13	HC DNA	GAAGTGCAGCTGGTGCAGTCTGGCGCCGAAGTGA AGAAGCCTGGCGAGTCCCTGAAGATCTCCTGCAAG GCCTCCGGCTACACCTTCACCGACTACAACATGGA CTGGGTGCGACAGATGCCCCGCAAGGGCCTGGAA TGGATGGGCGACATCAACCCTAAGTACGACATCTC CACCTACAACCAGCAGTTCAAGGGCCAAGTGACC ATCTCCGCCGACAAGTCCATCCGGACCGCCTACCT GCAGTGGTCTCCTGAAGGCCTCTGACACCGCCA TGTAATACTGCGCCAGACGGGGCTTCTTCTGTAC TACGGCATCACTACTACTTTCGACGTGTGGGG CCAGGGCACCCCTCGTGACAGTGTCTATCTGCTAGCA CCAAGGGCCCAAGTGTGTTTCCCCTGGCCCCCAGC AGCAAGTCTACTTCCGGCGGAAGTCTGCCCTGGG TTGCCTGGTGAAGGACTACTTCCCCGAGCCCGTGA CAGTGTCTGGAAGTCTGGGGCTCTGACTTCCGGC GTGCACACCTTCCCCGCCGTGCTGCAGAGCAGCGG CCTGTACAGCCTGAGCAGCGTGGTGACAGTGCCT

		CCAGCTCTCTGGGAACCCAGACCTATATCTGCAAC GTGAACCACAAGCCCAGCAACACCAAGGTGGACA AGAGAGTGGAGCCCAAGAGCTGCGACAAGACCCA CACCTGCCCCCCTGCCAGCTCCAGAACTGCTGG GAGGGCCTTCCGTGTTCTGTTCCCCCACAAGCCC AAGGACACCCTGATGATCAGCAGGACCCCCGAGG TGACCTGCGTGGTGGTGGACGTGTCCCACGAGGAC CCAGAGGTGAAGTTCAACTGGTACGTGGACGGCGT GGAGGTGCACAACGCCAAGACCAAGCCCAGAGAG GAGCAGTACAACAGCACCTACAGGGTGGTGTCCGT GCTGACCGTGCTGCACCAGGACTGGCTGAACGGCA AAGAATACAAGTGCAAAGTCTCCAACAAGGCCCT GCCAGCCCCAATCGAAAAGACAATCAGCAAGGCC AAGGGCCAGCCACGGGAGCCCCAGGTGTACACCC TGCCCCCAGCCGGGAGGAGATGACCAAGAACCA GGTGTCCCTGACCTGTCTGGTGAAGGGCTTCTACC CCAGCGATATCGCCGTGGAGTGGGAGAGCAACGG CCAGCCCGAGAACAACCTACAAGACCACCCCCCA GTGCTGGACAGCGACGGCAGCTTCTTCTGTACAG CAAGCTGACCGTGGACAAGTCCAGGTGGCAGCAG GGCAACGTGTTTCAGCTGCAGCGTGATGCACGAGGC CCTGCACAACCACTACACCCAGAAGTCCCTGAGCC TGAGCCCCGGCAAG
SEQ ID NO: 14	LCDR1 (KABAT)	SASSSVSYIH
SEQ ID NO: 15	LCDR2 (KABAT)	STSNLAS
SEQ ID NO: 16	LCDR3 (KABAT)	HQWSSYPWT
SEQ ID NO: 17	LCDR1 (CHOTHIA)	SSSVSY
SEQ ID NO: 18	LCDR2 (CHOTHIA)	STS
SEQ ID NO: 19	LCDR3 (CHOTHIA)	WSSYPW
SEQ ID NO: 14	LCDR1 (COMBINED)	SASSSVSYIH
SEQ ID NO: 15	LCDR2 (COMBINED)	STSNLAS
SEQ ID NO: 16	LCDR3 (COMBINED)	HQWSSYPWT
SEQ ID NO: 20	LCDR1 (IMGT)	SSVS
SEQ ID NO: 18	LCDR2 (IMGT)	STS
SEQ ID NO: 16	LCDR3 (IMGT)	HQWSSYPWT
SEQ ID NO: 21	VL	DIQLTQSPSSLASVGDRTITCSASSSVSYIHWFOQK PGKAPKLLIYSTSNLASGVPSRFSGSGSGTFFTLTISSL QPEDFATYFCHQWSSYPWTFGQGTKVEIK
SEQ ID NO: 22	VL DNA	GATATCCAGCTGACCCAGTCCCCTTCCAGCCTGTC TGCCTCTGTGGGCGACAGAGTGACAATTACCTGCT CCGCCTCCTCCTCCGTGTCCTACATCCACTGGTTCC AGCAGAAGCCCGGCAAGGCCCCCAAGCTGCTGAT CTACTCCACCTCCAACCTGGCCTCCGGCGTGCCCT CTAGATTCTCCGGCTCTGGCTCTGGCACCTTTTTTA CCCTGACCATCTCCAGCCTGCAGCCCGAGGACTTC GCCACCTACTTTTGCCACCAAGTGGTCCAGCTACCC CTGGACCTTTGGCCAGGGCACCAAGGTGGAAATCA AG

SEQ ID NO: 23	LC	DIQLTQSPSSLSASVGDRTVITCSASSSVSYIHWFOQK PGKAPKLLIYSTSNLASGVPSRFSGSGSGTFFTLTISSL QPEDFATYFCHQWSSYPWTFGQGTKVEIKRTVAAPS VFIFPPSDEQLKSGTASVVCLLNFPYPREAKVQWKV DNALQSGNSQESVTEQDSKDYSLSTLTLKADYE KHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 24	LC DNA	GATATCCAGCTGACCCAGTCCCCTTCCAGCCTGTC TGCCTCTGTGGGCGACAGAGTGACAATTACCTGCT CCGCCTCCTCCTCCGTGTCCTACATCCACTGGTTCC AGCAGAAGCCCGGCAAGGCCCAAGCTGTGAT CTACTCCACCTCCAACCTGGCCTCCGGCGTGCCCT CTAGATTCTCCGGCTCTGGCTCTGGCACCTTTTTTA CCCTGACCATCTCCAGCCTGCAGCCCGAGGACTTC GCCACCTACTTTTGCCACCAAGTGGTCCAGCTACCC CTGGACCTTTGGCCAGGGCACCAAGGTGGAAATCA AGCGTACGGTGGCCGCTCCCAGCGTGTTTCATCTTC CCCCCAGCGACGAGCAGCTGAAGAGTGGCACCCG CCAGCGTGGTGTGCCTGCTGAACAACCTTCTACCCC CGGGAGGCCAAGGTGCAGTGGAAGGTGGACAACG CCCTGCAGAGCGGCAACAGCCAGGAGAGCGTCAC CGAGCAGGACAGCAAGGACTCCACCTACAGCCTG AGCAGCACCTGACCCTGAGCAAGGCCGACTACG AGAAGCATAAGGTGTACGCCTGCGAGGTGACCCA CCAGGGCCTGTCCAGCCCCGTGACCAAGAGCTTCA ACAGGGGCGAGTGC
ANTI-HUMAN ENTPD2 MAB2		
SEQ ID NO: 1	HCDR1 (KABAT)	DYNMD
SEQ ID NO: 2	HCDR2 (KABAT)	DINPKYDISTYNQQFKG
SEQ ID NO: 3	HCDR3 (KABAT)	RGFFLYYGINYYYFDV
SEQ ID NO: 4	HCDR1 (CHOTHIA)	GYTFTDY
SEQ ID NO: 5	HCDR2 (CHOTHIA)	NPKYDI
SEQ ID NO: 3	HCDR3 (CHOTHIA)	RGFFLYYGINYYYFDV
SEQ ID NO: 6	HCDR1 (COMBINED)	GYTFTDYNMD
SEQ ID NO: 2	HCDR2 (COMBINED)	DINPKYDISTYNQQFKG
SEQ ID NO: 3	HCDR3 (COMBINED)	RGFFLYYGINYYYFDV
SEQ ID NO: 7	HCDR1 (IMGT)	GYTFTDYN
SEQ ID NO: 8	HCDR2 (IMGT)	INPKYDIS
SEQ ID NO: 9	HCDR3 (IMGT)	ARRGFFLYYGINYYYFDV
SEQ ID NO: 25	VH	QVQLVQSGAEVVKPGASVKISCKASGYTFTDYNMD WVKQAPGQRLEWIGDINPKYDISTYNQQFKGKATIT VDKSASTAYMELSSLRSEDTAVYYCARRGFFLYYGI NYYYFDVWGQGLVTVSS
SEQ ID NO: 26	VH DNA	CAGGTGCAGCTGGTGCAGTCTGGCGCCGAGGTGGT GAAACCTGGCGCCTCCGTGAAGATCTCCTGCAAGG CCTCCGGCTACACCTTCACCGACTACAACATGGAC TGGGTGAAACAGGCCCTGGCCAGCGGCTGGAAT GGATCGGCGACATCAACCCTAAGTACGACATCTCC ACCTACAACCAGCAGTTCAAGGGCAAGGCCACCA TCACCGTGGACAAGTCCGCCTCCACCGCCTACATG GAAGTGTCTCTCCCTGCGGAGCGAGGACACCGCGT GTACTACTGCGCCAGACGGGGCTTCTTCTGTACT ACGGCATCACTACTACTACTTTCGACGTGTGGGGC CAGGGCACCTGGTGACAGTGTCTCTCC

SEQ ID NO: 27	HC	QVQLVQSGAEVVKPGASVKISCKASGYTFTDYNMD WVKQAPGQRLEWIGDINPKYDISTYNQQFKGKATIT VDKSASTAYMELSSLRSEDTAVYYCARRGFFLYYGI NYYYFDVWGQGLVTVSSASTKGPSVFPLAPSSKSTS GGTAALGCLVKDYFPEPTVSWNSGALTSGVHTFPA VLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNT KVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPK PKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGV EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGK EYKCKVSNKALPAPIEKTISKAKGQPREPVYTLPPS REEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSKS VMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 28	HC DNA	CAGGTGCAGCTGGTGCAGTCTGGCGCCGAGGTGGT GAAACCTGGCGCCTCCGTGAAGATCTCCTGCAAGG CCTCCGGCTACACCTTCACCGACTACAACATGGAC TGGGTGAAACAGGCCCCTGGCCAGCGGCTGGAAT GGATCGGCGACATCAACCCTAAGTACGACATCTCC ACCTACAACCAGCAGTTCAAGGGCAAGGCCACCA TCACCGTGGACAAGTCCGCCTCCACCGCTACATG GAACTGTCTCCTGCGGAGCGAGGACACCGCCGT GTACTACTGCGCCAGACGGGGCTTCTTCTGTACT ACGGCATCAACTACTACTACTTCGACGTGTGGGGC CAGGGCACCCTGGTGACAGTGTCTCCGCTAGCAC CAAGGGCCCAAGTGTGTTTCCCCTGGCCCCCAGCA GCAAGTCTACTTCCGGCGGAAGTGTGCTGCTGGGT TGCCTGGTGAAGGACTACTTCCCCGAGCCCGTGAC AGTGTCTGGAAGTCTGGGGCTCTGACTTCCGGCG TGCACACCTTCCCCGCCGTGCTGCAGAGCAGCGGC CTGTACAGCCTGAGCAGCGTGGTGACAGTGCCTC CAGCTCTCTGGGAACCCAGACCTATATCTGCAACG TGAACCACAAGCCCAGCAACACCAAGGTGGACAA GAGAGTGGAGCCCAAGAGCTGCGACAAGACCCAC ACCTGCCCCCCTGCCAGCTCCAGAAGTGTGGG AGGGCCTTCCGTGTTCTGTCCCCCACAAGCCCA AGGACACCCTGATGATCAGCAGGACCCCCGAGGT GACCTGCGTGGTGGTGGACGTGTCCACGAGGACC CAGAGGTGAAGTTCAACTGGTACGTGGACGGCGT GGAGGTGCACAACGCCAAGACCAAGCCCAGAGAG GAGCAGTACAACAGCACCTACAGGGTGGTGTCCGT GCTGACCGTGCTGCACCAGGACTGGCTGAACGGCA AAGAATACAAGTGCAAAGTCTCCAACAAGGCCCT GCCAGCCCCAATCGAAAAGACAATCAGCAAGGCC AAGGGCCAGCCACGGGAGCCCCAGGTGTACACCC TGCCCCCAGCCGGGAGGAGATGACCAAGAACCA GGTGTCCCTGACCTGTCTGGTGAAGGGCTTCTACC CCAGCGATATCGCCGTGGAGTGGGAGAGCAACGG CCAGCCCGAGAACAATACTACAAGACCACCCCCCA GTGCTGGACAGCGACGGCAGCTTCTTCTGTACAG CAAGCTGACCGTGGACAAGTCCAGGTGGCAGCAG GGCAACGTGTTCAAGCTGCAGCGTGATGCACGAGGC CCTGCACAACCACTACACCCAGAAGTCCCTGAGCC TGAGCCCCGCAAG
SEQ ID NO: 14	LCDR1 (KABAT)	SASSSVSYIH
SEQ ID NO: 15	LCDR2 (KABAT)	STSNLAS
SEQ ID NO: 16	LCDR3 (KABAT)	HQWSSYPWT
SEQ ID NO: 17	LCDR1 (CHOTHIA)	SSSVSY
SEQ ID NO: 18	LCDR2 (CHOTHIA)	STS

SEQ ID NO: 19	LCDR3 (CHOTHIA)	WSSYPW
SEQ ID NO: 14	LCDR1 (COMBINED)	SASSSVSYIH
SEQ ID NO: 15	LCDR2 (COMBINED)	STSNLAS
SEQ ID NO: 16	LCDR3 (COMBINED)	HQWSSYPWT
SEQ ID NO: 20	LCDR1 (IMGT)	SSVSY
SEQ ID NO: 18	LCDR2 (IMGT)	STS
SEQ ID NO: 16	LCDR3 (IMGT)	HQWSSYPWT
SEQ ID NO: 29	VL	EIVLTQSPATLSASPGERITLSCSASSSVSYIHWYQOK PGQAPRLLIYSTSNLASGIPARFSGSGSGTFYTLTISSV EPEDAAYYYCHQWSSYPWTFGGGKLEIK
SEQ ID NO: 30	VL DNA	GAGATCGTGTGACCCAGTCCCCTGCCACCCTGTC TGCCAGCCCTGGCGAGCGGATCACCTGTCTGTCT CCGCCTCCTCCTCCGTGTCTACATCCACTGGTATC AGCAGAAGCCCGGCCAGGCCCTCGGCTGTGTATC TACTCCACCTCCAACCTGGCCTCCGGCATCCCTGC CAGATTCTCCGGCTCTGGCTCCGGCACCTTTTACAC CCTGACCATCTCCAGCGTGGAACCCGAGGACGCCG CCGTGTACTACTGCCACCAGTGGTCCAGCTACCCC TGGACCTTCGGCGGAGGCACCAAGCTGGAATCA AG
SEQ ID NO: 31	LC	EIVLTQSPATLSASPGERITLSCSASSSVSYIHWYQOK PGQAPRLLIYSTSNLASGIPARFSGSGSGTFYTLTISSV EPEDAAYYYCHQWSSYPWTFGGGKLEIKRTVAAPS VFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKV DNALQSGNSQESVTEQDSKSTYSLSSTLTLKADYE KHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 32	LC DNA	GAGATCGTGTGACCCAGTCCCCTGCCACCCTGTC TGCCAGCCCTGGCGAGCGGATCACCTGTCTGTCT CCGCCTCCTCCTCCGTGTCTACATCCACTGGTATC AGCAGAAGCCCGGCCAGGCCCTCGGCTGTGTATC TACTCCACCTCCAACCTGGCCTCCGGCATCCCTGC CAGATTCTCCGGCTCTGGCTCCGGCACCTTTTACAC CCTGACCATCTCCAGCGTGGAACCCGAGGACGCCG CCGTGTACTACTGCCACCAGTGGTCCAGCTACCCC TGGACCTTCGGCGGAGGCACCAAGCTGGAATCA AGCGTACGGTGGCCGCTCCCAGCGTGTTCATCTTC CCCCCAGCGACGAGCAGCTGAAGAGTGGCACCG CCAGCGTGGTGTGCCTGTCTGAACAACCTTCTACCCC CGGGAGGCCAAGGTGCAGTGGAAGGTGGACAACG CCCTGCAGAGCGGCAACAGCCAGGAGAGCGTCAC CGAGCAGGACAGCAAGGACTCCACCTACAGCCTG AGCAGCACCCCTGACCCTGAGCAAGGCCGACTACG AGAAGCATAAGGTGTACGCCTGCGAGGTGACCCA CCAGGGCCTGTCCAGCCCCGTGACCAAGAGCTTCA ACAGGGGCGAGTGC
ANTI-HUMAN ENTPD2 MAB3		
SEQ ID NO: 1	HCDR1 (KABAT)	DYNMD
SEQ ID NO: 2	HCDR2 (KABAT)	DINPKYDISTYNQQFKG
SEQ ID NO: 3	HCDR3 (KABAT)	RGFFLYYGINYYYFDV
SEQ ID NO: 4	HCDR1 (CHOTHIA)	GYTFTDY
SEQ ID NO: 5	HCDR2 (CHOTHIA)	NPKYDI
SEQ ID NO: 3	HCDR3 (CHOTHIA)	RGFFLYYGINYYYFDV

SEQ ID NO: 6	HCDR1 (COMBINED)	GYTFTDYNMD
SEQ ID NO: 2	HCDR2 (COMBINED)	DINPKYDISTYNQQFKG
SEQ ID NO: 3	HCDR3 (COMBINED)	RGFFLYYGINYYYFDV
SEQ ID NO: 7	HCDR1 (IMGT)	GYTFTDYN
SEQ ID NO: 8	HCDR2 (IMGT)	INPKYDIS
SEQ ID NO: 9	HCDR3 (IMGT)	ARRGFFLYYGINYYYFDV
SEQ ID NO: 33	VH	QVQLVQSGAEVVKPGASVKISCKASGYTFTDYNMD WVKQAPGQRLEWIGDINPKYDISTYNQQFKGKATIT VDTASTAYMELSSLRSEDTAVYYCARRGFFLYYGI NYYYFDVWGQGLVTVSS
SEQ ID NO: 34	VH DNA	CAGGTGCAGCTGGTGCAGTCTGGCGCCGAGGTGGT GAAACCTGGCGCCTCCGTGAAGATCTCCTGCAAGG CCTCCGGCTACACCTTCACCGACTACAACATGGAC TGGGTGAAACAGGCCCCTGGCCAGCGGCTGGAAT GGATCGGCGACATCAACCCTAAGTACGACATCTCC ACCTACAACCAGCAGTTCAAGGGCAAGGCCACCA TCACCGTGGACACCTCCGCCTCCACCGCCTACATG GAACTGTCCTCCCTGCGGAGCGAGGACACCGCCGT GTACTACTGCGCCAGACGGGGCTTCTTCTGTACT ACGGCATCACTACTACTACTTCGACGTGTGGGGC CAGGGCACCTGGTGACAGTGTCTCTCC
SEQ ID NO: 35	HC	QVQLVQSGAEVVKPGASVKISCKASGYTFTDYNMD WVKQAPGQRLEWIGDINPKYDISTYNQQFKGKATIT VDTASTAYMELSSLRSEDTAVYYCARRGFFLYYGI NYYYFDVWGQGLVTVSSASTKGPSVFPLAPSSKSTS GGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPA VLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNT KVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPK PKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGV EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGK EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPS REEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSS VMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 36	HC DNA	CAGGTGCAGCTGGTGCAGTCTGGCGCCGAGGTGGT GAAACCTGGCGCCTCCGTGAAGATCTCCTGCAAGG CCTCCGGCTACACCTTCACCGACTACAACATGGAC TGGGTGAAACAGGCCCCTGGCCAGCGGCTGGAAT GGATCGGCGACATCAACCCTAAGTACGACATCTCC ACCTACAACCAGCAGTTCAAGGGCAAGGCCACCA TCACCGTGGACACCTCCGCCTCCACCGCCTACATG GAACTGTCCTCCCTGCGGAGCGAGGACACCGCCGT GTACTACTGCGCCAGACGGGGCTTCTTCTGTACT ACGGCATCACTACTACTACTTCGACGTGTGGGGC CAGGGCACCTGGTGACAGTGTCTCTCCGCTAGCAC CAAGGGCCCAAGTGTGTTTCCCCTGGCCCCCAGCA GCAAGTCTACTTCCGGCGGAACTGCTGCCCTGGGT TGCCTGGTGAAGGACTACTTCCCCGAGCCCGTGAC AGTGTCTGGAAGTCTGGGGCTCTGACTTCCGGCG TGCACACCTTCCCCGCCGTGCTGCAGAGCAGCGGC CTGTACAGCCTGAGCAGCGTGGTGACAGTGCCTC CAGCTCTCTGGGAACCCAGACCTATATCTGCAACG TGAACCACAAGCCCAGCAACACCAAGGTGGACAA GAGAGTGGAGCCCAAGAGCTGCGACAAGACCCAC ACCTGCCCCCCTGCCCAGCTCCAGAACTGCTGGG AGGGCCTTCCGTGTTCTCTGTTCCCCCCCCAAGCCCA

		AGGACACCCTGATGATCAGCAGGACCCCCGAGGT GACCTGCGTGGTGGTGGACGTGTCCACGAGGACC CAGAGGTGAAGTTCAACTGGTACGTGGACGGCGT GGAGGTGCACAACGCCAAGACCAAGCCCAGAGAG GAGCAGTACAACAGCACCTACAGGGTGGTGTCCGT GCTGACCGTGCTGCACCAGGACTGGCTGAACGGCA AAGAATACAAGTGCAAAGTCTCCAACAAGGCCCT GCCAGCCCCAATCGAAAAGACAATCAGCAAGGCC AAGGGCCAGCCACGGGAGCCCCAGGTGTACACCC TGCCCCCAGCCGGGAGGAGATGACCAAGAACCA GGTGTCCCTGACCTGTCTGGTGAAGGGCTTCTACC CCAGCGATATCGCCGTGGAGTGGGAGAGCAACGG CCAGCCCGAGAACAATACTACAAGACCACCCCCCA GTGCTGGACAGCGACGGCAGCTTCTTCTGTACAG CAAGCTGACCGTGGACAAGTCCAGGTGGCAGCAG GGCAACGTGTTTCAGCTGCAGCGTGATGCACGAGGC CCTGCACAACCACTACACCCAGAAGTCCCTGAGCC TGAGCCCCGGCAAG
SEQ ID NO: 14	LCDR1 (KABAT)	SASSSVSYIH
SEQ ID NO: 15	LCDR2 (KABAT)	STSNLAS
SEQ ID NO: 16	LCDR3 (KABAT)	HQWSSYPWT
SEQ ID NO: 17	LCDR1 (CHOTHIA)	SSSVSY
SEQ ID NO: 18	LCDR2 (CHOTHIA)	STS
SEQ ID NO: 19	LCDR3 (CHOTHIA)	WSSYPW
SEQ ID NO: 14	LCDR1 (COMBINED)	SASSSVSYIH
SEQ ID NO: 15	LCDR2 (COMBINED)	STSNLAS
SEQ ID NO: 16	LCDR3 (COMBINED)	HQWSSYPWT
SEQ ID NO: 20	LCDR1 (IMGT)	SSSVSY
SEQ ID NO: 18	LCDR2 (IMGT)	STS
SEQ ID NO: 16	LCDR3 (IMGT)	HQWSSYPWT
SEQ ID NO: 29	VL	EIVLTQSPATLSASPGERITLSCSASSSVSYIHWYQQK PGQAPRLLIYSTSNLASGIPARFSGSGSGTFYTLTISSV EPEDAAYYYCHQWSSYPWTFGGGTKLEIK
SEQ ID NO: 30	VL DNA	GAGATCGTGCTGACCCAGTCCCCTGCCACCCTGTC TGCCAGCCCTGGCGAGCGGATCACCTGTCTGCT CCGCCTCCTCCTCCGTGTCTACATCCACTGGTATC AGCAGAAGCCCGGCCAGGCCCTCGGCTGCTGATC TACTCCACCTCCAACCTGGCCTCCGGCATCCCTGC CAGATTCTCCGGCTCTGGCTCCGGCACCTTTTACAC CCTGACCATCTCCAGCGTGGAACCCGAGGACGCCG CCGTGTACTACTGCCACCAGTGGTCCAGTACCCC TGGACCTTCGGCGGAGGCACCAAGCTGGAATCA AG
SEQ ID NO: 31	LC	EIVLTQSPATLSASPGERITLSCSASSSVSYIHWYQQK PGQAPRLLIYSTSNLASGIPARFSGSGSGTFYTLTISSV EPEDAAYYYCHQWSSYPWTFGGGTKLEIKRTVAAPS VFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKV DNALQSGNSQESVTEQDSKSTYSLSSTLTLSKADYE KHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 32	LC DNA	GAGATCGTGCTGACCCAGTCCCCTGCCACCCTGTC TGCCAGCCCTGGCGAGCGGATCACCTGTCTGCT CCGCCTCCTCCTCCGTGTCTACATCCACTGGTATC AGCAGAAGCCCGGCCAGGCCCTCGGCTGCTGATC TACTCCACCTCCAACCTGGCCTCCGGCATCCCTGC

		CAGATTCTCCGGCTCTGGCTCCGGCACCTTTTACAC CCTGACCATCTCCAGCGTGGAACCCGAGGACGCCG CCGTGTACTACTGCCACCAGTGGTCCAGTACCCC TGGACCTTCGGCGGAGGCACCAAGCTGGAATCA AGCGTACGGTGGCCGCTCCAGCGTGTTTCATCTTC CCCCCAGCGACGAGCAGCTGAAGAGTGGCACCG CCAGCGTGGTGTGCCTGCTGAACAACCTTCTACCCC CGGGAGGCCAAGGTGCAGTGGAAAGGTGGACAACG CCCTGCAGAGCGGCAACAGCCAGGAGAGCGTCAC CGAGCAGGACAGCAAGGACTCCACCTACAGCCTG AGCAGCACCCCTGACCCTGAGCAAGGCCGACTACG AGAAGCATAAGGTGTACGCTGCGAGGTGACCCA CCAGGGCCTGTCCAGCCCCGTGACCAAGAGCTTCA ACAGGGGCGAGTGC
ANTI-HUMAN ENTPD2 MAB4		
SEQ ID NO: 37	HCDR1 (KABAT)	SGYYWN
SEQ ID NO: 38	HCDR2 (KABAT)	YISYDADNNYNPSLKN
SEQ ID NO: 39	HCDR3 (KABAT)	GYRYRGLGSYRGSYYYVMDY
SEQ ID NO: 40	HCDR1 (CHOTHIA)	GYSITSGY
SEQ ID NO: 41	HCDR2 (CHOTHIA)	SYDAD
SEQ ID NO: 39	HCDR3 (CHOTHIA)	GYRYRGLGSYRGSYYYVMDY
SEQ ID NO: 42	HCDR1 (COMBINED)	GYSITSGYYWN
SEQ ID NO: 38	HCDR2 (COMBINED)	YISYDADNNYNPSLKN
SEQ ID NO: 39	HCDR3 (COMBINED)	GYRYRGLGSYRGSYYYVMDY
SEQ ID NO: 43	HCDR1 (IMGT)	GYSITSGYY
SEQ ID NO: 44	HCDR2 (IMGT)	ISYDADN
SEQ ID NO: 45	HCDR3 (IMGT)	AGGYRYRGLGSYRGSYYYVMDY
SEQ ID NO: 46	VH	QIQLQESGPGLVKPSQTLSTCTVSGYSITSGYYWNW IRQHPGKGLEWIGYISYDADNNYNPSLKNRVTISRDT SKNQFSLKLSSVTAADTAVYYCAGGYRYRGLGSYR GSYYYVMDYWGQGTITVTVSS
SEQ ID NO: 47	VH DNA	CAGATCCAGCTGCAGGAATCTGGCCCTGGCCTGGT GAAACCCCTCCAGACCCTGTCCCTGACCTGCACCG TGTCGGGCTACTCCATCACCTCCGGCTACTACTGG AACTGGATCCGGCAGCACCCCGGCAAGGGCCTGG AATGGATCGGCTACATCTCCTACGACGCTGACAAC AACTACAACCCAGCCTGAAGAACAGAGTGACCA TCTCCCGGGACACCTCCAAGAACCAGTTCTCCCTG AAGCTGTCTCCGTGACCGCCGCTGACACCGCCGT GTACTACTGCGCTGGCGGCTACTACAGATACGGCC TGGGCTCCTACCGGGGCTCCTACTACTACGTGATG GACTACTGGGGCCAGGGCACCACCGTGACCGTGTC CTCT
SEQ ID NO: 48	HC	QIQLQESGPGLVKPSQTLSTCTVSGYSITSGYYWNW IRQHPGKGLEWIGYISYDADNNYNPSLKNRVTISRDT SKNQFSLKLSSVTAADTAVYYCAGGYRYRGLGSYR GSYYYVMDYWGQGTITVTVSSASTKGPSVFPLAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT FPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPS NTKVDKRVPEPKSCDKTHTCPPCPAPELLGGPSVFLFP PKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVD GVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL

		PSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NNYKTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFS CSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 49	HC DNA	CAGATCCAGCTGCAGGAATCTGGCCCTGGCCTGGT GAAACCCTCCCAGACCCTGTCCCTGACCTGCACCG TGTCCGGCTACTCCATCACCTCCGGCTACTACTGG AACTGGATCCGGCAGCACCCCGGCAAGGGCCTGG AATGGATCGGCTACATCTCCTACGACGCTGACAAC AACTACAACCCAGCCTGAAGAACAGAGTGACCA TCTCCCGGGACACCTCCAAGAACCAGTTCTCCCTG AAGCTGTCTCCGTGACCGCCGCTGACACCGCCGT GTACTACTGCGCTGGCGGCTACTACAGATACGGCC TGGGCTCCTACCGGGGCTCCTACTACTACGTGATG GACTACTGGGGCCAGGGCACCACCGTGACCGTGTC CTCTGCTAGCACCAAGGGCCCAAGTGTGTTTCCCC TGGCCCCCAGCAGCAAGTCTACTTCCGGCGGAACT GCTGCCCTGGGTTGCCTGGTGAAGGACTACTTCCC CGAGCCCGTGACAGTGTCTGGAACCTTGGGGCTC TGACTTCCGGCGTGACACCTTCCCGCCGTGCTG CAGAGCAGCGGCCTGTACAGCCTGAGCAGCGTGG TGACAGTGCCCTCCAGCTCTCTGGGAACCCAGACC TATATCTGCAACGTGAACCACAAGCCCAGCAACAC CAAGGTGGACAAGAGAGTGGAGCCCAAGAGCTGC GACAAGACCCACACCTGCCCCCCTGCCAGCTCC AGAACTGCTGGGAGGGCCTTCCGTGTTCTGTTCC CCCCAAGCCCAAGGACACCTGATGATCAGCAG GACCCCGAGGTGACCTGCGTGGTGGTGGACGTGT CCCACGAGGACCCAGAGGTGAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCACAACGCCAAGACC AAGCCCAGAGAGGAGCAGTACAACAGCACCTACA GGGTGGTGTCCGTGCTGACCGTGCTGCACCAGGAC TGGCTGAACGGCAAAGAATACAAGTGCAAAGTCT CCAACAAGGCCCTGCCAGCCCCAATCGAAAAGAC AATCAGCAAGGCCAAGGGCCAGCCACGGGAGCCC CAGGTGTACACCCTGCCCCCAGCCGGGAGGAGAT GACCAAGAACCAGGTGTCCCTGACCTGTCTGGTGA AGGGCTTCTACCCAGCGATATCGCCGTGGAGTGG GAGAGCAACGGCCAGCCGAGAACAACACTACAAGA CCACCCCCCAGTGCTGGACAGCGACGGCAGCTTC TTCCTGTACAGCAAGCTGACCGTGGACAAGTCCAG GTGGCAGCAGGGCAACGTGTTCACTGCAGCGTG ATGCACGAGGCCCTGCACAACCACTACACCCAGA AGTCCCTGAGCCTGAGCCCCGGCAAG
SEQ ID NO: 50	LCDR1 (KABAT)	KASQSVDYEGHSYMN
SEQ ID NO: 51	LCDR2 (KABAT)	AASNLES
SEQ ID NO: 52	LCDR3 (KABAT)	QQSNEPPT
SEQ ID NO: 53	LCDR1 (CHOTHIA)	SQSVDYEGHSY
SEQ ID NO: 54	LCDR2 (CHOTHIA)	AAS
SEQ ID NO: 55	LCDR3 (CHOTHIA)	SNEDPP
SEQ ID NO: 50	LCDR1 (COMBINED)	KASQSVDYEGHSYMN
SEQ ID NO: 51	LCDR2 (COMBINED)	AASNLES
SEQ ID NO: 52	LCDR3 (COMBINED)	QQSNEPPT
SEQ ID NO: 56	LCDR1 (IMGT)	QSVDYEGHSY
SEQ ID NO: 54	LCDR2 (IMGT)	AAS

SEQ ID NO: 52	LCDR3 (IMGT)	QQSNEDPPT
SEQ ID NO: 57	VL	ETVLTQSPATLSVSPGERATISCKASQSVDYEGHSYM NWYQQKPGQAPRLLIYAASNLESGIPARFSGSGSGTD FTLTISVVEPEDAATYYCQQSNEDPPTFGGGTKLEIK
SEQ ID NO: 58	VL DNA	GAGACAGTGCTGACCCAGTCCCCTGCCACCTGTC CGTGTCTCCCGGCGAGAGAGCCACCATCAGCTGCA AGGCCTCCAGTCCGTGGACTACGAAGGCCATTCC TACATGAACTGGTATCAGCAGAAGCCCGGCCAGG CCCCTCGGCTGCTGATCTACGCCGCCTCCAACCTG GAATCCGGCATCCCCTGCCCGGTTCTCCGGCTCTGG CTCTGGCACCAGCTTACCCTGACCATCTCCAGCG TGGAACCCGAGGACGCCGCCACCTACTACTGCCAG CAGTCCAACGAGGACCCCCACCTTCGGCGGAGG CACCAAGCTGGAAATCAAG
SEQ ID NO: 59	LC	ETVLTQSPATLSVSPGERATISCKASQSVDYEGHSYM NWYQQKPGQAPRLLIYAASNLESGIPARFSGSGSGTD FTLTISVVEPEDAATYYCQQSNEDPPTFGGGTKLEIKR TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAK VQWKVDNALQSGNSQESVTEQDSKSTYSLSTLTL SKADYEHKHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 60	LC DNA	GAGACAGTGCTGACCCAGTCCCCTGCCACCTGTC CGTGTCTCCCGGCGAGAGAGCCACCATCAGCTGCA AGGCCTCCAGTCCGTGGACTACGAAGGCCATTCC TACATGAACTGGTATCAGCAGAAGCCCGGCCAGG CCCCTCGGCTGCTGATCTACGCCGCCTCCAACCTG GAATCCGGCATCCCCTGCCCGGTTCTCCGGCTCTGG CTCTGGCACCAGCTTACCCTGACCATCTCCAGCG TGGAACCCGAGGACGCCGCCACCTACTACTGCCAG CAGTCCAACGAGGACCCCCACCTTCGGCGGAGG CACCAAGCTGGAAATCAAGCGTACGGTGGCCGCTC CCAGCGTGTTTCATCTTCCCCCCCAGCGACGAGCAG CTGAAGAGTGGCACC GCCAGCGTGGTGTGCCTGCT GAACAACCTTCTACCCCGGGAGGCCAAGGTGCAGT GGAAGGTGGACAACGCCCTGCAGAGCGGCAACAG CCAGGAGAGCGTCACCGAGCAGGACAGCAAGGAC TCCACCTACAGCCTGAGCAGCACCCTGACCCTGAG CAAGGCCGACTACGAGAAGCATAAGGTGTACGCC TGCGAGGTGACCCACCAGGGCCTGTCCAGCCCCGT GACCAAGAGCTTCAACAGGGGCGAGTGC
ANTI-HUMAN ENTPD2 MAB5		
SEQ ID NO: 37	HCDR1 (KABAT)	SGYYWN
SEQ ID NO: 38	HCDR2 (KABAT)	YISYDADNNYNPSLKN
SEQ ID NO: 39	HCDR3 (KABAT)	GYRYRYGLGSYRGSYYYVMDY
SEQ ID NO: 40	HCDR1 (CHOTHIA)	GYSITSGY
SEQ ID NO: 41	HCDR2 (CHOTHIA)	SYDAD
SEQ ID NO: 39	HCDR3 (CHOTHIA)	GYRYRYGLGSYRGSYYYVMDY
SEQ ID NO: 42	HCDR1 (COMBINED)	GYSITSGYYWN
SEQ ID NO: 38	HCDR2 (COMBINED)	YISYDADNNYNPSLKN
SEQ ID NO: 39	HCDR3 (COMBINED)	GYRYRYGLGSYRGSYYYVMDY
SEQ ID NO: 43	HCDR1 (IMGT)	GYSITSGYY
SEQ ID NO: 44	HCDR2 (IMGT)	ISYDADN
SEQ ID NO: 45	HCDR3 (IMGT)	AGGYRYRYGLGSYRGSYYYVMDY

SEQ ID NO: 46	VH	QIQLQESGPGLVKPSQTLSTCTVSGYSITSYGYWNW IRQHPGKGLEWIGYISYDADNNYNPSLKNRVTISRDT SKNQFSLKLSSVTAADTAVYYCAGGYRYGLGSYR GSYYYVMDYWGQGTTVTVSS
SEQ ID NO: 47	VH DNA	CAGATCCAGCTGCAGGAATCTGGCCCTGGCCTGGT GAAACCTCCCAGACCCTGTCCCTGACCTGCACCG TGTCCGGCTACTCCATCACCTCCGGCTACTACTGG AACTGGATCCGGCAGCACCCCGGCAAGGGCCTGG AATGGATCGGCTACATCTCCTACGACGCTGACAAC AACTACAACCCAGCCTGAAGAACAGAGTGACCA TCTCCCGGGACACCTCCAAGAACCAGTTCTCCCTG AAGCTGTCCTCCGTGACCGCCGCTGACACCGCCGT GTACTACTGCGCTGGCGGCTACTACAGATACGGCC TGGGCTCCTACCGGGGCTCCTACTACTACGTGATG GACTACTGGGGCCAGGGCACCACCGTGACCGTGTC CTCT
SEQ ID NO: 48	HC	QIQLQESGPGLVKPSQTLSTCTVSGYSITSYGYWNW IRQHPGKGLEWIGYISYDADNNYNPSLKNRVTISRDT SKNQFSLKLSSVTAADTAVYYCAGGYRYGLGSYR GSYYYVMDYWGQGTTVTVSSASTKGPSVFPLAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHT FPAVLQSSGLYSLSSVTVTPSSSLGTQTYICNVNHKPS NTKVDKRVPEPKSCDKTHTCPPAPPELLGGPSVFLFP PKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVD GVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL PSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFS CSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 49	HC DNA	CAGATCCAGCTGCAGGAATCTGGCCCTGGCCTGGT GAAACCTCCCAGACCCTGTCCCTGACCTGCACCG TGTCCGGCTACTCCATCACCTCCGGCTACTACTGG AACTGGATCCGGCAGCACCCCGGCAAGGGCCTGG AATGGATCGGCTACATCTCCTACGACGCTGACAAC AACTACAACCCAGCCTGAAGAACAGAGTGACCA TCTCCCGGGACACCTCCAAGAACCAGTTCTCCCTG AAGCTGTCCTCCGTGACCGCCGCTGACACCGCCGT GTACTACTGCGCTGGCGGCTACTACAGATACGGCC TGGGCTCCTACCGGGGCTCCTACTACTACGTGATG GACTACTGGGGCCAGGGCACCACCGTGACCGTGTC CTCTGCTAGCACCAAGGGCCCAAGTGTGTTTCCCC TGGCCCCCAGCAGCAAGTCTACTTCCGGCGGAAC GCTGCCCTGGGTTGCCTGGTGAAGGACTACTTCCC CGAGCCCGTGACAGTGTCTGGAACCTGCGGGCTC TGACTTCCGGCGTGACACCTTCCCCGCCGTGCTG CAGAGCAGCGGCCTGTACAGCCTGAGCAGCGTGG TGACAGTGCCCTCCAGCTCTCTGGGAACCCAGACC TATATCTGCAACGTGAACCACAAGCCCAGCAACAC CAAGGTGGACAAGAGAGTGGAGCCCAAGAGCTGC GACAAGACCCACACCTGCCCCCCTGCCAGCTCC AGAACTGCTGGGAGGGCCTTCCGTGTTCTGTTC CCCCCAAGCCCAAGGACACCCTGATGATCAGCAG GACCCCGAGGTGACCTGCGTGGTGGTGGACGTGT CCCACGAGGACCCAGAGGTGAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCACAACGCCAAGACC AAGCCCAGAGAGGAGCAGTACAACAGCACCTACA GGGTGGTGTCCGTGCTGACCGTGCTGCACCAGGAC TGGCTGAACGGCAAAGAATACAAGTGCAAAGTCT CCAACAAGGCCCTGCCAGCCCCAATCGAAAAGAC AATCAGCAAGGCCAAGGGCCAGCCACGGGAGCCC

		CAGGTGTACACCCTGCCCCCAGCCGGGAGGAGAT GACCAAGAACCAAGGTGTCCCTGACCTGTCTGGTGA AGGGCTTCTACCCAGCGATATCGCCGTGGAGTGG GAGAGCAACGGCCAGCCGAGAACAACACTACAAGA CCACCCCCCAGTGCTGGACAGCGACGGCAGCTTC TTCCTGTACAGCAAGCTGACCGTGGACAAGTCCAG GTGGCAGCAGGGCAACGTGTTCACTGTCAGCGTG ATGCACGAGGCCCTGCACAACCACTACACCCAGA AGTCCCTGAGCCTGAGCCCCGGCAAG
SEQ ID NO: 61	LCDR1 (KABAT)	KASQSVDDYDGN SYMN
SEQ ID NO: 51	LCDR2 (KABAT)	AASNLES
SEQ ID NO: 52	LCDR3 (KABAT)	QSNEDPPT
SEQ ID NO: 62	LCDR1 (CHOTHIA)	QSVDDYDGN SY
SEQ ID NO: 54	LCDR2 (CHOTHIA)	AAS
SEQ ID NO: 55	LCDR3 (CHOTHIA)	SNEDPP
SEQ ID NO: 61	LCDR1 (COMBINED)	KASQSVDDYDGN SYMN
SEQ ID NO: 51	LCDR2 (COMBINED)	AASNLES
SEQ ID NO: 52	LCDR3 (COMBINED)	QSNEDPPT
SEQ ID NO: 63	LCDR1 (IMGT)	QSVDDYDGN SY
SEQ ID NO: 54	LCDR2 (IMGT)	AAS
SEQ ID NO: 52	LCDR3 (IMGT)	QSNEDPPT
SEQ ID NO: 64	VL	ETVLTQSPATLSVSPGERATISCKASQSVDDYDGN SYMN NWYQQKPGQAPRLLIYAASNLES GIPARFSGSGSGTD FTLTISSEVEDAATYYCQSNEDPPTFGGGTKLEIK
SEQ ID NO: 65	VL DNA	GAGACAGTGTGACCCAGTCCCCTGCCACCCTGTC CGTGTCTCCCGGCGAGAGAGCCACCATCAGCTGCA AGGCCTCCCAAGTCCGTGGACTACGACGGCAACTCC TACATGAACTGGTATCAGCAGAAGCCCCGGCCAGG CCCCTCGGCTGCTGATCTACGCCGCCTCCAACCTG GAATCCGGCATCCCTGCCCGGTTCTCCGGCTCTGG CTCTGGCACCGACTTCACCCTGACCATCTCCAGCG TGGAACCCGAGGACGCCGCCACCTACTACTGCCAG CAGTCCAACGAGGACCCCCCACCTTCGGCGGAGG CACCAAGCTGGAAATCAAG
SEQ ID NO: 66	LC	ETVLTQSPATLSVSPGERATISCKASQSVDDYDGN SYMN NWYQQKPGQAPRLLIYAASNLES GIPARFSGSGSGTD FTLTISSEVEDAATYYCQSNEDPPTFGGGTKLEIKR TVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAK VQWKVDNALQSGNSQESVTEQDSKSTYSLSSITLTL SKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 67	LC DNA	GAGACAGTGTGACCCAGTCCCCTGCCACCCTGTC CGTGTCTCCCGGCGAGAGAGCCACCATCAGCTGCA AGGCCTCCCAAGTCCGTGGACTACGACGGCAACTCC TACATGAACTGGTATCAGCAGAAGCCCCGGCCAGG CCCCTCGGCTGCTGATCTACGCCGCCTCCAACCTG GAATCCGGCATCCCTGCCCGGTTCTCCGGCTCTGG CTCTGGCACCGACTTCACCCTGACCATCTCCAGCG TGGAACCCGAGGACGCCGCCACCTACTACTGCCAG CAGTCCAACGAGGACCCCCCACCTTCGGCGGAGG CACCAAGCTGGAAATCAAGCGTACGGTGGCCGCTC CCAGCGTGTTCATCTTCCCCCCCCAGCGACGACGAG CTGAAGAGTGGCACCGCCAGCGTGGTGTGCCTGCT GAACAACCTTCTACCCCCGGGAGGCCAAGGTGCAGT GGAAGGTGGACAACGCCCTGCAGAGCGGCAACAG

		CCAGGAGAGCGTCACCGAGCAGGACAGCAAGGAC TCCACCTACAGCCTGAGCAGCACCTGACCTGAG CAAGGCCGACTACGAGAAGCATAAGGTGTACGCC TGCGAGGTGACCCACCAGGGCCTGTCCAGCCCCGT GACCAAGAGCTTCAACAGGGGCGAGTGC
ANTI-HUMAN ENTPD2 MAB6		
SEQ ID NO: 37	HCDR1 (KABAT)	SGYYWN
SEQ ID NO: 38	HCDR2 (KABAT)	YISYDADNNYNPSLKN
SEQ ID NO: 68	HCDR3 (KABAT)	GYRYRGLGSYSGSYYYVMDY
SEQ ID NO: 40	HCDR1 (CHOTHIA)	GYSITSGY
SEQ ID NO: 41	HCDR2 (CHOTHIA)	SYDAD
SEQ ID NO: 68	HCDR3 (CHOTHIA)	GYRYRGLGSYSGSYYYVMDY
SEQ ID NO: 42	HCDR1 (COMBINED)	GYSITSGYYWN
SEQ ID NO: 38	HCDR2 (COMBINED)	YISYDADNNYNPSLKN
SEQ ID NO: 68	HCDR3 (COMBINED)	GYRYRGLGSYSGSYYYVMDY
SEQ ID NO: 43	HCDR1 (IMGT)	GYSITSGYY
SEQ ID NO: 44	HCDR2 (IMGT)	ISYDADN
SEQ ID NO: 69	HCDR3 (IMGT)	AGGYRYRGLGSYSGSYYYVMDY
SEQ ID NO: 70	VH	QVQLQESGPGLVKPSQTLSTCTVSGYSITSGYYWN WIRQHPGKGLEWMGYISYDADNNYNPSLKNRITISR DTSKNQFSLKLSSVTAADTAVYYCAGGYRYRGLGS YSGSYYYVMDYWGQGTITVTVSS
SEQ ID NO: 71	VH DNA	CAGGTGCAGCTGCAGGAATCTGGCCCTGGCCTGGT GAAACCTCCAGACCCTGTCCCTGACCTGCACCG TGTCCGGCTACTCCATCACCTCCGGCTACTACTGG AACTGGATCCGGCAGCACCCCGCAAGGGCCTGG AATGGATGGGCTACATCTCCTACGACGCTGACAAC AACTACAACCCAGCCTGAAGAACAGAATCACCA TCTCCCGGACACCTCCAAGAACCAGTTCTCCCTG AAGCTGTCTCCGTGACCGCCGCTGACACCGCCGT GTACTACTGCGCTGGCGGCTACTACAGATACGGCC TGGGCTCCTACTCCGGCTCCTACTACTACGTGATG GACTACTGGGGCCAGGGCACCACCGTGACCGTGTC CTCT
SEQ ID NO: 72	HC	QVQLQESGPGLVKPSQTLSTCTVSGYSITSGYYWN WIRQHPGKGLEWMGYISYDADNNYNPSLKNRITISR DTSKNQFSLKLSSVTAADTAVYYCAGGYRYRGLGS YSGSYYYVMDYWGQGTITVTVSSASTKGPSVFPLAPS SKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGV HTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNH KPSNTKVDKRVKPKSCDKTHTCPPCPAPPELLGGPSVF LFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNW YVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQD WLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQV YTLPPSREEMTKNQVSLTCLVKGFYPSDIAVEWESN GQPENNYKTPPVLDSDGSFFLYSKLTVDKSRWQQG NVFSCSVMHREALHNHYTQKSLSLSPGK
SEQ ID NO: 73	HC DNA	CAGGTGCAGCTGCAGGAATCTGGCCCTGGCCTGGT GAAACCTCCAGACCCTGTCCCTGACCTGCACCG TGTCCGGCTACTCCATCACCTCCGGCTACTACTGG AACTGGATCCGGCAGCACCCCGCAAGGGCCTGG AATGGATGGGCTACATCTCCTACGACGCTGACAAC AACTACAACCCAGCCTGAAGAACAGAATCACCA

		TCTCCCGGGACACCTCCAAGAACCAGTTCTCCCTG AAGCTGTCCTCCGTGACCGCCGCTGACACCGCCGT GTACTACTGCGCTGGCGGCTACTACAGATACGGCC TGGGCTCCTACTCCGGCTCCTACTACTACGTGATG GACTACTGGGGCCAGGGCACCACCGTGACCGTGTC CTCTGCTAGCACC AAGGGCCCAAGTGTGTTTCCCC TGGCCCCCAGCAGCAAGTCTACTTCCGGCGGAACT GCTGCCCTGGGTTGCCTGGTGAAGGACTACTTCCC CGAGCCCGTGACAGTGTCTGGAAGTCTGGGGCTC TGACTTCCGGCGTGACACCTTCCCGCCGTGCTG CAGAGCAGCGGCCTGTACAGCCTGAGCAGCGTGG TGACAGTGCCTCCAGCTCTCTGGGAACCCAGACC TATATCTGCAACGTGAACCACAAGCCCAGCAACAC CAAGGTGGACAAGAGAGTGGAGCCCAAGAGCTGC GACAAGACCCACACCTGCCCCCCTGCCAGCTCC AGAACTGCTGGGAGGGCCTTCCGTGTTCTGTTCC CCCCCAAGCCCAAGGACACCCTGATGATCAGCAG GACCCCGAGGTGACCTGCGTGGTGGTGGACGTGT CCCACGAGGACCCAGAGGTGAAGTTCAACTGGTA CGTGGACGGCGTGGAGGTGCACAACGCCAAGACC AAGCCCAGAGAGGAGCAGTACAACAGCACCTACA GGGTGGTGTCCGTGCTGACCGTGCTGCACAGGAC TGGCTGAACGGCAAAGAATACAAGTGCAAAGTCT CCAACAAGGCCCTGCCAGCCCCAATCGAAAAGAC AATCAGCAAGGCCAAGGGCCAGCCACGGGAGCCC CAGGTGTACACCCTGCCCCCAGCCGGGAGGAGAT GACCAAGAACCAGGTGTCCCTGACCTGTCTGGTGA AGGGCTTCTACCCAGCGATATCGCCGTGGAGTGG GAGAGCAACGGCCAGCCGAGAACAATACTACAAGA CCACCCCCCAGTGCTGGACAGCGACGGCAGCTTC TTCCTGTACAGCAAGCTGACCGTGGACAAGTCCAG GTGGCAGCAGGGCAACGTGTTCACTGCAGCGTG ATGCACGAGGCCCTGCACAACCACTACCCAGA AGTCCCTGAGCCTGAGCCCCGGAAG
SEQ ID NO: 50	LCDR1 (KABAT)	KASQSVDYEGHSYMN
SEQ ID NO: 51	LCDR2 (KABAT)	AASNLES
SEQ ID NO: 52	LCDR3 (KABAT)	QQSNEDPPT
SEQ ID NO: 53	LCDR1 (CHOTHIA)	SQSVDYEGHSY
SEQ ID NO: 54	LCDR2 (CHOTHIA)	AAS
SEQ ID NO: 55	LCDR3 (CHOTHIA)	SNEDPP
SEQ ID NO: 50	LCDR1 (COMBINED)	KASQSVDYEGHSYMN
SEQ ID NO: 51	LCDR2 (COMBINED)	AASNLES
SEQ ID NO: 52	LCDR3 (COMBINED)	QQSNEDPPT
SEQ ID NO: 56	LCDR1 (IMGT)	QSVDYEGHSY
SEQ ID NO: 54	LCDR2 (IMGT)	AAS
SEQ ID NO: 52	LCDR3 (IMGT)	QQSNEDPPT
SEQ ID NO: 74	VL	DTQMTQSPSSLSVSVGDRATITCKASQSVDYEGHSY MNWYQKPGKAPKLLIYAASNLESGVPSRFSGSGS GTDFTLTISVQPEDFATYYCQQSNEDPPTFGGGTKLEI K
SEQ ID NO: 75	VL DNA	GACACCCAGATGACCCAGTCCCCCTCCTCCCTGTC CGTGTCCGTGGGCGACAGAGCCACCATCACATGCA AGGCCTCCAGTCCGTGGACTACGAAGGCCATTCC TACATGAACTGGTATCAGCAGAAGCCCGGAAGG

		CCCCCAAGCTGCTGATCTACGCCGCCTCCAACCTG GAATCCGGCGTGCCCTCCAGATTCTCCGGCTCCGG CTCTGGCACCAGCTTCACCCCTGACCATCTCCAGCG TGCAGCCCGAGGACTTCGCCACCTACTACTGCCAG CAGTCCAACGAGGACCCCCCACCTTCGGCGGAGG CACCAAGCTGGAAATCAAG
SEQ ID NO: 76	LC	DTQMTQSPSSLVSVDRAITTCASQSVDYEGHSY MNWYQKPGKAPKLLIYAASNLESGVPSRFSGSGSG TDFTLTISVQPEDFATYYCQSNEDPPTFGGGTKLEI KRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPRE AKVQWKVDNALQSGNSQESVTEQDSKSTYLSSTL TLISKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 77	LC DNA	GACACCCAGATGACCCAGTCCCCCTCCTCCCTGTC CGTGTCCTGGGCGACAGAGCCACCATCACATGCA AGGCCTCCAGTCCGTGGACTACGAAGGCCATTCC TACATGAACTGGTATCAGCAGAAGCCCGGCAAGG CCCCCAAGCTGCTGATCTACGCCGCCTCCAACCTG GAATCCGGCGTGCCCTCCAGATTCTCCGGCTCCGG CTCTGGCACCAGCTTCACCCCTGACCATCTCCAGCG TGCAGCCCGAGGACTTCGCCACCTACTACTGCCAG CAGTCCAACGAGGACCCCCCACCTTCGGCGGAGG CACCAAGCTGGAAATCAAGCGTACGGTGGCCGCTC CCAGCGTGTTTCATCTTCCCCCCCAGCGACGAGCAG CTGAAGAGTGGCACCCGCCAGCGTGTTGTGCCTGCT GAACAACCTTCTACCCCCGGGAGGCCAAGGTGCAGT GGAAGGTGGACAACGCCCTGCAGAGCGGCAACAG CCAGGAGAGCGTCAACGAGCAGGACAGCAAGGAC TCCACCTACAGCCTGAGCAGCACCCTGACCCTGAG CAAGGCCGACTACGAGAAGCATAAGGTGTACGCC TGCGAGGTGACCCACCAGGGCCTGTCCAGCCCCGT GACCAAGAGCTTCAACAGGGGCGAGTGC
ANTI-HUMAN ENTPD2 MAB7		
SEQ ID NO: 1	HCDR1 (KABAT)	DYNMD
SEQ ID NO: 2	HCDR2 (KABAT)	DINPKYDISTYNQQFKG
SEQ ID NO: 3	HCDR3 (KABAT)	RGFFLYYGINYYYFDV
SEQ ID NO: 4	HCDR1 (CHOTHIA)	GYTFTDY
SEQ ID NO: 5	HCDR2 (CHOTHIA)	NPKYDI
SEQ ID NO: 3	HCDR3 (CHOTHIA)	RGFFLYYGINYYYFDV
SEQ ID NO: 6	HCDR1 (COMBINED)	GYTFTDYNMD
SEQ ID NO: 2	HCDR2 (COMBINED)	DINPKYDISTYNQQFKG
SEQ ID NO: 3	HCDR3 (COMBINED)	RGFFLYYGINYYYFDV
SEQ ID NO: 7	HCDR1 (IMGT)	GYTFTDYN
SEQ ID NO: 8	HCDR2 (IMGT)	INPKYDIS
SEQ ID NO: 9	HCDR3 (IMGT)	ARRGFFLYYGINYYYFDV
SEQ ID NO: 25	VH	QVQLVQSGAEVVKPGASVKISCKASGYTFTDYNMD WVKQAPGQRLEWIGDINPKYDISTYNQQFKGKATIT VDKSASTAYMELSSLRSEDTAVYYCARRGFFLYYGI NYYYFDVWGQGLVTVSS
SEQ ID NO: 26	VH DNA	CAGGTGCAGCTGGTGCAGTCTGGCGCCGAGGTGGT GAAACCTGGCGCCTCCGTGAAGATCTCCTGCAAGG CCTCCGGCTACACCTTCACCGACTACAACATGGAC TGGGTGAAACAGGCCCTGGCCAGCGGCTGGAAT GGATCGGCGACATCAACCCTAAGTACGACATCTCC

		ACCTACAACCAGCAGTTCAAGGGCAAGGCCACCA TCACCGTGGACAAGTCCGCCTCCACCGCTACATG GAACTGTCTCCTGCGGAGCGAGGACACCGCCGT GTACTACTGCGCCAGACGGGGCTTCTTCTGTACT ACGGCATCAACTACTACTACTTCGACGTGTGGGGC CAGGGCACCCCTGGTGACAGTGTCTCTCC
SEQ ID NO: 27	HC	QVQLVQSGAEVVKPGASVKISCKASGYTFTDYNMD WVKQAPGQRLEWIGDINPKYDISTYNQFKGKATIT VDKSASTAYMELSSLRSEDTAVYYCARRGFFLYYGI NYYYFDVWGQGLVTVSSASTKGPSVFPLAPSSKSTS GGTAALGCLVKDYFPEPVTWSNSGALTSGVHTFPA VLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNT KVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPK PKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGV EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGK EYKCKVSNKALPAPIEKISKAKGQPREPQVYTLPPS REEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSS VMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 28	HC DNA	CAGGTGCAGCTGGTGCAGTCTGGCGCCGAGGTGGT GAAACCTGGCGCCTCCGTGAAGATCTCCTGCAAGG CCTCCGGCTACACCTTCACCGACTACAACATGGAC TGGGTGAAACAGGCCCTGGCCAGCGGCTGGAAT GGATCGGCGACATCAACCCTAAGTACGACATCTCC ACCTACAACCAGCAGTTCAAGGGCAAGGCCACCA TCACCGTGGACAAGTCCGCCTCCACCGCTACATG GAACTGTCTCCTGCGGAGCGAGGACACCGCCGT GTACTACTGCGCCAGACGGGGCTTCTTCTGTACT ACGGCATCAACTACTACTACTTCGACGTGTGGGGC CAGGGCACCCCTGGTGACAGTGTCTCCGCTAGCAC CAAGGGCCCAAGTGTGTTTCCCCTGGCCCCCAGCA GCAAGTCTACTTCCGGCGGAAGTGTGCCCTGGGT TGCCTGGTGAAGGACTACTTCCCCGAGCCCGTGAC AGTGTCTGGAAGTCTGGGGCTCTGACTTCCGGCG TGACACCTTCCCCGCCGTGCTGCAGAGCAGCGGC CTGTACAGCCTGAGCAGCGTGGTGACAGTGGCCTC CAGCTCTCTGGGAACCCAGACCTATATCTGCAACG TGAACCACAAGCCCAGCAACACCAAGGTGGACAA GAGAGTGGAGCCCAAGAGCTGCGACAAGACCCAC ACCTGCCCCCCTGCCAGCTCCAGAACTGTGGG AGGGCCTTCCGTGTTCTGTTCCTGTTCCCCCAAGCCA AGGACACCCTGATGATCAGCAGGACCCCGAGGT GACCTGCGTGGTGGTGGACGTGTCCCACGAGACC CAGAGGTGAAGTTCAACTGGTACGTGGACGGCGT GGAGGTGCACAACGCCAAGACCAAGCCCAGAGAG GAGCAGTACAACAGCACCTACAGGGTGGTGTCCGT GCTGACCGTGCTGCACCAGGACTGGCTGAACGGCA AAGAATACAAGTGCAAGTCTCCAACAAGGCCCT GCCAGCCCCAATCGAAAAGACAATCAGCAAGGCC AAGGGCCAGCCACGGGAGCCCCAGGTGTACACCC TGCCCCCAGCCGGGAGGAGATGACCAAGAACCA GGTGTCCCTGACCTGTCTGGTGAAGGGCTTCTACC CCAGCGATATCGCCGTGGAGTGGGAGAGCAACGG CCAGCCCGAGAACAACTACAAGACCACCCCCCA GTGCTGGACAGCGACGGCAGCTTCTTCTGTACAG CAAGCTGACCGTGGACAAGTCCAGGTGGCAGCAG GGCAACGTGTTTCTGCTGCAGCGTGATGCACGAGGC CCTGCACAACCACTACACCCAGAAGTCCCTGAGCC TGAGCCCCGCAAG
SEQ ID NO: 14	LCDR1 (KABAT)	SASSSVSYIH

SEQ ID NO: 15	LCDR2 (KABAT)	STSNLAS
SEQ ID NO: 16	LCDR3 (KABAT)	HQWSSYPWT
SEQ ID NO: 17	LCDR1 (CHOTHIA)	SSSVSY
SEQ ID NO: 18	LCDR2 (CHOTHIA)	STS
SEQ ID NO: 19	LCDR3 (CHOTHIA)	WSSYPW
SEQ ID NO: 14	LCDR1 (COMBINED)	SASSSVSYIH
SEQ ID NO: 15	LCDR2 (COMBINED)	STSNLAS
SEQ ID NO: 16	LCDR3 (COMBINED)	HQWSSYPWT
SEQ ID NO: 20	LCDR1 (IMGT)	SSSVSY
SEQ ID NO: 18	LCDR2 (IMGT)	STS
SEQ ID NO: 16	LCDR3 (IMGT)	HQWSSYPWT
SEQ ID NO: 78	VL	EIVLTQSPATLSASPGEEITLSCSASSSVSYIHWYQQK PGQAPRLLIYSTSNLASGIPARFSGSGSGTFYTLTISSV EPEDAAYVYCHQWSSYPWTFGGGTKLEIK
SEQ ID NO: 79	VL DNA	GAGATCGTGTGACCCAGTCCCCTGCCACCCTGTC TGCCAGCCCTGGCGAGGAGATCACCTGTCTGCT CCGCCTCCTCCTCCGTGTCTACATCCACTGGTATC AGCAGAAGCCCGGCCAGGCCCTCGGCTGCTGATC TACTCCACCTCCAACCTGGCCTCCGGCATCCCTGC CAGATTCTCCGGCTCTGGCTCCGGCACCTTTTACAC CCTGACCATCTCCAGCGTGGAACCCGAGGACGCCG CCGTGTACTACTGCCACCAGTGGTCCAGTACCCC TGGACCTTCGGCGGAGGCACCAAGCTGGAATCA AG
SEQ ID NO: 80	LC	EIVLTQSPATLSASPGEEITLSCSASSSVSYIHWYQQK PGQAPRLLIYSTSNLASGIPARFSGSGSGTFYTLTISSV EPEDAAYVYCHQWSSYPWTFGGGTKLEIKRTVAAPS VFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKV DNALQSGNSQESVTEQDSKSTYSLSTLTLSKADYE KHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 81	LC DNA	GAGATCGTGTGACCCAGTCCCCTGCCACCCTGTC TGCCAGCCCTGGCGAGGAGATCACCTGTCTGCT CCGCCTCCTCCTCCGTGTCTACATCCACTGGTATC AGCAGAAGCCCGGCCAGGCCCTCGGCTGCTGATC TACTCCACCTCCAACCTGGCCTCCGGCATCCCTGC CAGATTCTCCGGCTCTGGCTCCGGCACCTTTTACAC CCTGACCATCTCCAGCGTGGAACCCGAGGACGCCG CCGTGTACTACTGCCACCAGTGGTCCAGTACCCC TGGACCTTCGGCGGAGGCACCAAGCTGGAATCA AGCGTACGGTGGCCGCTCCCAGCGTGTTTCATCTTC CCCCCAGCGACGAGCAGCTGAAGAGTGGCACCG CCAGCGTGGTGTGCCTGCTGAACAACCTTCTACCCC CGGGAGGCCAAGGTGCAGTGGAAGGTGGACAACG CCCTGCAGAGCGGCAACAGCCAGGAGAGCGTCAC CGAGCAGGACAGCAAGGACTCCACCTACAGCCTG AGCAGCACCTGACCCTGAGCAAGGCCGACTACG AGAAGCATAAGGTGTACGCCTGCGAGGTGACCCA CCAGGGCCTGTCCAGCCCCGTGACCAAGAGCTTCA ACAGGGGCGAGTGC
ANTI-HUMAN ENTPD2 MAB8		
SEQ ID NO: 82	HCDR1 (KABAT)	SSSAAWN
SEQ ID NO: 83	HCDR2 (KABAT)	RIYYRSKWYNDYAVSVKS
SEQ ID NO: 84	HCDR3 (KABAT)	GSYVTSSYEGFDY

SEQ ID NO: 85	HCDR1 (CHOTHIA)	GDSVSSSSA
SEQ ID NO: 86	HCDR2 (CHOTHIA)	YYRSKWY
SEQ ID NO: 84	HCDR3 (CHOTHIA)	GSYVTSSYEGFDY
SEQ ID NO: 87	HCDR1 (COMBINED)	GDSVSSSSAAWN
SEQ ID NO: 83	HCDR2 (COMBINED)	RIYYRSKWYNDYAVSVKS
SEQ ID NO: 84	HCDR3 (COMBINED)	GSYVTSSYEGFDY
SEQ ID NO: 88	HCDR1 (IMGT)	GDSVSSSSAA
SEQ ID NO: 89	HCDR2 (IMGT)	IYYRSKWYN
SEQ ID NO: 90	HCDR3 (IMGT)	ARGSYVTSSYEGFDY
SEQ ID NO: 91	VH	QVQLQQSGPGLVKPSQTLSTCAISGDSVSSSSAAWN WIRQSPSRGLEWLGRIYYRSKWYNDYAVSVKSRITIN PDTSKNQFSLQLNSVTPEDTAVYYCARGSYVTSSYE GFDYWGQGTLVTVSS
SEQ ID NO: 92	VH DNA	CAGGTGCAATTGCAGCAGAGCGGTCCGGGCCTGGT GAAACCGAGCCAGACCCTGAGCCTGACCTGCGCG ATTTCCGGAGATAGCGTGAGCTCTAGCTCTGCTGC TTGGAAGTGGATTTCGTCAGAGCCCGAGCCGTGGCC TCGAGTGGCTGGGCCGTATCTACTACCGTAGCAAA TGGTACAACGACTATGCCGTGAGCGTGAAAAGCC GCATTACCATTAAACCCGATACTTCGAAAAACAG TTTAGCCTGCAACTGAACAGCGTGACCCCGGAAGA TACGGCCGTGTATTATTGCGCGCGTGGTTCTTACGT TACTTCTTCTTACGAAGGTTTCGATTACTGGGGCCA AGGCACCCTGGTGACTGTTAGCTCA
SEQ ID NO: 93	HC	QVQLQQSGPGLVKPSQTLSTCAISGDSVSSSSAAWN WIRQSPSRGLEWLGRIYYRSKWYNDYAVSVKSRITIN PDTSKNQFSLQLNSVTPEDTAVYYCARGSYVTSSYE GFDYWGQGTLVTVSSASTKGPSVFPLAPSSKSTSGGT AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQ SSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVD KRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKD TLMISRTPETVTCVVDVSHEDPEVKFNWYVDGVEV HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKISKAKGQPREPQVYTLPPSREE MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKT TPPVLDSGSFFLYSKLTVDKSRWQQGNVFCFSVMH EALHNHYTQKLSLSLSPGK
SEQ ID NO: 94	HC DNA	CAGGTGCAATTGCAGCAGAGCGGTCCGGGCCTGGT GAAACCGAGCCAGACCCTGAGCCTGACCTGCGCG ATTTCCGGAGATAGCGTGAGCTCTAGCTCTGCTGC TTGGAAGTGGATTTCGTCAGAGCCCGAGCCGTGGCC TCGAGTGGCTGGGCCGTATCTACTACCGTAGCAAA TGGTACAACGACTATGCCGTGAGCGTGAAAAGCC GCATTACCATTAAACCCGATACTTCGAAAAACAG TTTAGCCTGCAACTGAACAGCGTGACCCCGGAAGA TACGGCCGTGTATTATTGCGCGCGTGGTTCTTACGT TACTTCTTCTTACGAAGGTTTCGATTACTGGGGCCA AGGCACCCTGGTGACTGTTAGCTCAGCCTCCACCA AGGGTCCATCGGTCTTCCCCCTGGCACCCCTCCTCC AAGAGCACCTCTGGGGGCACAGCGGCCCTGGGCT GCCTGGTCAAGGACTACTTCCCCGAACCGGTGACG GTGTCGTGGAACCTCAGGCGCCCTGACCAGCGGCGT GCACACCTTCCCGGCTGTCTTACAGTCCTCAGGAC TCTACTCCCTCAGCAGCGTGGTGACCGTGCCCTCC AGCAGCTTGGGCACCCAGACCTACATCTGCAACGT

		GAATCACAAAGCCCAGCAACACCAAGGTGGACAAG AGAGTTGAGCCCAAATCTTGTGACAAAACCTCACAC ATGCCCACCGTGCCCAGCACCTGAACTCCTGGGGG GACCGTCAGTCTTCCTCTTCCCCCAAAACCCAAG GACACCCTCATGATCTCCCGGACCCCTGAGGTCAC ATGCGTGGTGGTGGACGTGAGCCACGAAGACCCT GAGGTCAAGTTCAACTGGTACGTGGACGGCGTGG AGGTGCATAATGCCAAGACAAAGCCGCGGGAGGA GCAGTACAACAGCACGTACCGGGTGGTCAGCGTCC TCACCGTCTGCACCAGGACTGGCTGAATGGCAAG GAGTACAAGTGCAAGGTCTCCAACAAAGCCCTCCC AGCCCCATCGAGAAAACCATCTCCAAAGCCAAA GGGCAGCCCCGAGAACCACAGGTGTACACCCTGC CCCCATCCCGGGAGGAGATGACCAAGAACCAGGT CAGCCTGACCTGCCTGGTCAAAGGCTTCTATCCCA GCGACATCGCCGTGGAGTGGGAGAGCAATGGGCA GCCGGAGAACAACACTACAAGACCACGCCTCCCGTG CTGGACTCCGACGGCTCCTTCTTCTCTACAGCAA GCTCACCGTGGACAAGAGCAGGTGGCAGCAGGGG AACGTCTTCTCATGCTCCGTGATGCATGAGGCTCT GCACAACCACTACACGCAGAAGAGCCTCTCCCTGT CTCCGGGTAAA
SEQ ID NO: 95	LCDR1 (KABAT)	SGDNLPEKYAY
SEQ ID NO: 96	LCDR2 (KABAT)	DDNKRPS
SEQ ID NO: 97	LCDR3 (KABAT)	QSYGKWGWWTWV
SEQ ID NO: 98	LCDR1 (CHOTHIA)	DNLPEKY
SEQ ID NO: 99	LCDR2 (CHOTHIA)	DDN
SEQ ID NO: 100	LCDR3 (CHOTHIA)	YGKWGWWTW
SEQ ID NO: 95	LCDR1 (COMBINED)	SGDNLPEKYAY
SEQ ID NO: 96	LCDR2 (COMBINED)	DDNKRPS
SEQ ID NO: 97	LCDR3 (COMBINED)	QSYGKWGWWTWV
SEQ ID NO: 101	LCDR1 (IMGT)	NLPEKY
SEQ ID NO: 99	LCDR2 (IMGT)	DDN
SEQ ID NO: 97	LCDR3 (IMGT)	QSYGKWGWWTWV
SEQ ID NO: 102	VL	SYELTQPLSVSVALGQTARITCSGDNLPEKYAYWYQ QKPGQAPVLVIYDDNKRPSGIPERFSGSNSGNTATLTI SRAQAGDEADYYCQSYGKWGWWTWVFGGGTKLTVL
SEQ ID NO: 103	VL DNA	AGCTACGAACTGACCCAGCCGCTGTCCGTGAGCGT GGCTCTGGGCCAGACCGCGCGGATTACCTGTAGCG GCGATAACCTGCCGGAATAACGCTTACTGGTAC CAGCAGAAACCGGGCCAGGCGCCGGTGTGTTGA TCTACGACGACAACAACGTCAGCGCGGATCCCG GAACGTTTTAGCGGATCCAACAGCGCAACACCGC GACCCTGACCATTAGCCGCGCCAGGCGGGAGAC GAAGCGGATTATTACTGCCAGTCTTACGGTAAATG GGGTTGGACTTGGGTGTTTGGCGGCGGCACGAAGT TAACCGTCCTA
SEQ ID NO: 104	LC	SYELTQPLSVSVALGQTARITCSGDNLPEKYAYWYQ QKPGQAPVLVIYDDNKRPSGIPERFSGSNSGNTATLTI SRAQAGDEADYYCQSYGKWGWWTWVFGGGTKLTVL GQPKAAPSVTLFPPSSEELQANKATLVCLISDFYPGA VTVAWKADSSPVKAGVETTTPSKQSNKYAASSYLS LTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS

SEQ ID NO: 105	LC DNA	AGCTACGAACTGACCCAGCCGCTGTCCGTGAGCGT GGCTCTGGGCCAGACCGCGCGGATTACCTGTAGCG GCGATAACCTGCCGGAATAACGCTTACTGGTAC CAGCAGAAACCGGGCCAGGCGCCGGTGTGGTGA TCTACGACGACAACAAACGTCCGAGCGGCATCCCC GAACGTTTTAGCGGATCCAACAGCGGCAACACCGC GACCCTGACCATTAGCCGCGCCCAGGCGGGAGAC GAAGCGGATTATTACTGCCAGTCTTACGGTAAATG GGGTTGGACTTGGGTGTTTGGCGGCGGCACGAAGT TAACCGTCTTAGGTACAGCCCAAGGCTGCCCCCTCG GTCACTCTGTTCCCCGCCCTCTCTGAGGAGCTTCAA GCCAACAAGGCCACACTGGTGTGTCTCATAAGTGA CTTCTACCCGGGAGCCGTGACAGTGGCCTGGAAGG CAGATAGCAGCCCCGTCAAGGCGGGAGTGGAGAC CACCACACCCTCCAAACAAGCAACAACAAGTAC GCGGCCAGCAGCTATCTGAGCCTGACGCTGAGCA GTGGAAGTCCACAGAAGCTACAGCTGCCAGGTC ACGCATGAAGGGAGCACCGTGGAGAAGACAGTGG CCCCTACAGAATGTTC
ANTI-HUMAN ENTPD2 MAB9		
SEQ ID NO: 106	HCDR1 (KABAT)	SYAVS
SEQ ID NO: 107	HCDR2 (KABAT)	RIVPWLGHQTQYAQKFQG
SEQ ID NO: 108	HCDR3 (KABAT)	ESPGYRYSFDV
SEQ ID NO: 109	HCDR1 (CHOTHIA)	GGTFDSY
SEQ ID NO: 110	HCDR2 (CHOTHIA)	VPWLGH
SEQ ID NO: 108	HCDR3 (CHOTHIA)	ESPGYRYSFDV
SEQ ID NO: 111	HCDR1 (COMBINED)	GGTFDSYAVS
SEQ ID NO: 107	HCDR2 (COMBINED)	RIVPWLGHQTQYAQKFQG
SEQ ID NO: 108	HCDR3 (COMBINED)	ESPGYRYSFDV
SEQ ID NO: 112	HCDR1 (IMGT)	GGTFDSYA
SEQ ID NO: 113	HCDR2 (IMGT)	IVPWLGH
SEQ ID NO: 114	HCDR3 (IMGT)	ARESPGYRYSFDV
SEQ ID NO: 115	VH	QVQLVQSGAEVKKPGSSVKVSKASGGTFDSYAVS WVRQAPGQGLEWMGRIVPWLGHQTQYAQKFQGRVTI TADSTSTAYMELSSLRSEDTAVYYCARESPGYRYSF DVWDQGTLLTVSS
SEQ ID NO: 116	VH DNA	CAGGTGCAATTGGTGCAGAGCGGTGCCGAAGTGA AAAAACCGGGCAGCAGCGTGAAAGTTAGCTGCAA AGCATCCGGAGGGACGTTTACTCTTACGCTGTTT CTTGGGTGCGCCAGGCCCCGGGCCAGGGCCTCGAG TGGATGGGCCGTATCGTTCCGTGGCTGGGCCATAC TCAGTACGCCCAGAAATTTAGGGCCGGGTGACCA TTACCGCCGATGAAAGCACCAGCACCAGCCTATATG GAACTGAGCAGCCTGCGCAGCGAAGATACGGCCG TGTATTATTGCGCGCGTGAATCTCCGGGTTACCGTT ACTCTTTCGATGTTTGGGACCAAGGCACCCTGGTG ACTGTTAGCTCA
SEQ ID NO: 117	HC	QVQLVQSGAEVKKPGSSVKVSKASGGTFDSYAVS WVRQAPGQGLEWMGRIVPWLGHQTQYAQKFQGRVTI TADSTSTAYMELSSLRSEDTAVYYCARESPGYRYSF DVWDQGTLLTVSSASTKGPSVFPLAPSSKSTSGGTA ALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQS SGLYSLSVTVPSSSLGTQTYICNVNHKPSNTKVDK

		RVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTL MISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHN AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKC KVSNAKALPAPIEKTISKAKGQPREPVYTLPPSREEM TKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTT PPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHE ALHNHYTQKSLSLSPGK
SEQ ID NO: 118	HC DNA	CAGGTGCAATTGGTGCAGAGCGGTGCCGAAGTGA AAAAACCGGGCAGCAGCGTGAAAGTTAGCTGCAA AGCATCCGGAGGGACGTTTGACTCTTACGCTGTTT CTTGGGTGCGCCAGGCCCGGGCCAGGGCCCTCGAG TGGATGGGCCGTATCGTTCCGTGGCTGGGCCATAC TCAGTACGCCCAGAAATTTAGGGCCGGGTGACCA TTACCGCCGATGAAAGCACCAGCACCAGCCTATATG GAACTGAGCAGCCTGCGCAGCGAAGATACGGCCG TGTATTATTGCGCGCGTGAATCTCCGGGTACCGTT ACTCTTTTCGATGTTTGGGACCAAGGCACCCTGGTG ACTGTTAGCTCAGCCTCCACCAAGGGTCCATCGGT CTTCCCCCTGGCACCCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGA CTACTTCCCCGAACCGGTGACGGTGTCTGTGAACT CAGGCGCCCTGACCAGCGGCGTGACACACCTTCCCC GCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAG CAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCA CCCAGACCTACATCTGCAACGTGAATCACAAGCCC AGCAACACCAAGGTGGACAAGAGAGTTGAGCCCA AATCTTGTGACAAAACCTCACACATGCCCACCGTGC CCAGCACCTGAACTCCTGGGGGGACCGTCAGTCTT CCTCTTCCCCCAAAACCCAAGGACACCCTCATGA TCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTG GACGTGAGCCACGAAGACCCTGAGGTCAAGTTCA ACTGGTACGTGGACGGCGTGGAGGTGCATAATGCC AAGACAAAGCCGCGGGAGGAGCAGTACAACAGCA CGTACCGGGTGGTCAGCGTCCTCACCCTCCTGCAC CAGGACTGGCTGAATGGCAAGGAGTACAAGTGCA AGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAG AAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAG AACCACAGGTGTACACCCTGCCCCCATCCCGGGAG GAGATGACCAAGAACCAGGTGAGCCTGACCTGCCT GGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGG AGTGGGAGAGCAATGGGCAGCCGGAGAACAACTA CAAGACCACGCCTCCCGTGCTGGACTCCGACGGCT CCTTCTCCTCTACAGCAAGCTCACCCTGGACAAG AGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTC CGTGATGCATGAGGCTCTGCACAACCACTACACGC AGAAGAGCCTCTCCCTGTCTCCGGGTAAA
SEQ ID NO: 119	LCDR1 (KABAT)	SGDAIGEKYVY
SEQ ID NO: 120	LCDR2 (KABAT)	DDNNRPS
SEQ ID NO: 121	LCDR3 (KABAT)	ASYDLQQRWV
SEQ ID NO: 122	LCDR1 (CHOTHIA)	DAIGEKY
SEQ ID NO: 99	LCDR2 (CHOTHIA)	DDN
SEQ ID NO: 123	LCDR3 (CHOTHIA)	YDLQQRW
SEQ ID NO: 119	LCDR1 (COMBINED)	SGDAIGEKYVY
SEQ ID NO: 120	LCDR2 (COMBINED)	DDNNRPS
SEQ ID NO: 121	LCDR3 (COMBINED)	ASYDLQQRWV

SEQ ID NO: 124	LCDR1 (IMGT)	AIGEKY
SEQ ID NO: 99	LCDR2 (IMGT)	DDN
SEQ ID NO: 121	LCDR3 (IMGT)	ASYDLQQARWV
SEQ ID NO: 125	VL	SYELTQPLSVSVVALGQTARITCSGDAIGEKYVYWYQ QKPGQAPVLVIYDDNNRPSGIPERFSGSNSGNTATLTI SRAQAGDEADYYCASYDLQQARWVFGGGTKLTVL
SEQ ID NO: 126	VL DNA	AGCTACGAACTGACCCAGCCGCTGTCCGTGAGCGT GGCTCTGGGCCAGACCGCGCGGATTACCTGTAGCG GCGATGCTATCGGTGAAAAATACGTTTACTGGTAC CAGCAGAAACCGGGCCAGGCGCCGGTGCTGGTGA TCTACGACGACAACAACCGTCCGAGCGGCATCCCCG GAACGTTTTAGCGGATCCAACAGCGGCAACACCGC GACCCTGACCATTAGCCGCGCCCAGGCGGGAGAC GAAGCGGATTATTACTGCGCTTCTTACGACCTGCA GCAGGCTCGTTGGGTGTTTGGCGGCGGCACGAAGT TAACCGTCCTA
SEQ ID NO: 127	LC	SYELTQPLSVSVVALGQTARITCSGDAIGEKYVYWYQ QKPGQAPVLVIYDDNNRPSGIPERFSGSNSGNTATLTI SRAQAGDEADYYCASYDLQQARWVFGGGTKLTVL GQPKAAPSVTLFPPSSEELQANKATLVCLISDFYPGA VTVAWKADSSPVKAGVETTTTPSKQSNKYAASSYLS LTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS
SEQ ID NO: 128	LC DNA	AGCTACGAACTGACCCAGCCGCTGTCCGTGAGCGT GGCTCTGGGCCAGACCGCGCGGATTACCTGTAGCG GCGATGCTATCGGTGAAAAATACGTTTACTGGTAC CAGCAGAAACCGGGCCAGGCGCCGGTGCTGGTGA TCTACGACGACAACAACCGTCCGAGCGGCATCCCCG GAACGTTTTAGCGGATCCAACAGCGGCAACACCGC GACCCTGACCATTAGCCGCGCCCAGGCGGGAGAC GAAGCGGATTATTACTGCGCTTCTTACGACCTGCA GCAGGCTCGTTGGGTGTTTGGCGGCGGCACGAAGT TAACCGTCCTAGGTCAGCCCAAGGCTGCCCCCTCG GTCACCTGTGTTCCCGCCCTCCTCTGAGGAGCTTCAA GCCAACAAGGCCACACTGGTGTGTCTCATAAGTGA CTTCTACCCGGGAGCCGTGACAGTGGCCTGGAAGG CAGATAGCAGCCCCGTCAAGGCGGGAGTGGAGAC CACCACACCTCCAAACAAAGCAACAACAAGTAC GCGGCCAGCAGCTATCTGAGCCTGACGCTGAGCA GTGGAAGTCCACAGAAGCTACAGCTGCCAGGTC ACGCATGAAGGGAGCACCGTGGAGAAGACAGTGG CCCCTACAGAATGTTCA
ANTI-HUMAN ENTPD2 MAB10		
SEQ ID NO: 106	HCDR1 (KABAT)	SYAVS
SEQ ID NO: 129	HCDR2 (KABAT)	RIVPWLGFTRYAQKFQG
SEQ ID NO: 108	HCDR3 (KABAT)	ESPGYRYSFDV
SEQ ID NO: 109	HCDR1 (CHOTHIA)	GGTFDSY
SEQ ID NO: 130	HCDR2 (CHOTHIA)	VPWLGF
SEQ ID NO: 108	HCDR3 (CHOTHIA)	ESPGYRYSFDV
SEQ ID NO: 111	HCDR1 (COMBINED)	GGTFDSYAVS
SEQ ID NO: 129	HCDR2 (COMBINED)	RIVPWLGFTRYAQKFQG
SEQ ID NO: 108	HCDR3 (COMBINED)	ESPGYRYSFDV
SEQ ID NO: 112	HCDR1 (IMGT)	GGTFDSYA
SEQ ID NO: 131	HCDR2 (IMGT)	IVPWLGFT

SEQ ID NO: 114	HCDR3 (IMGT)	ARESPGYRYSFDV
SEQ ID NO: 132	VH	QVQLVQSGAEVKKPGSSVKVSKASGGTFDSYAVS WVRQAPGQGLEWMGRIVPWLGFTRYAQKFQGRVTI TADESTSTAYMELSSLRSEDTAVYYCARESPGYRYSF DVWDQGTLLTVSS
SEQ ID NO: 133	VH DNA	CAGGTGCAATTGGTGCAGAGCGGTGCCGAAGTGA AAAAACCGGGCAGCAGCGTGAAAGTTAGCTGCAA AGCATCCGGAGGGACGTTTGACTCTTACGCTGTTT CTTGGGTGCGCCAGGCCCGGGCCAGGGCCTCGAG TGGATGGGCGGTATCGTTCCGTGGCTGGGCTTCAC TCGTTACGCCCAGAAATTCAGGGCCGGGTGACCA TTACCGCCGATGAAAGCACCAGCACCAGCCTATATG GAACTGAGCAGCCTGCGCAGCGAAGATACGGCCG TGTATTATTGCGCGCGTGAATCTCCGGGTTACCGTT ACTCTTTTCGATGTTTGGGACCAAGGCACCCTGGTG ACTGTTAGCTCA
SEQ ID NO: 134	HC	QVQLVQSGAEVKKPGSSVKVSKASGGTFDSYAVS WVRQAPGQGLEWMGRIVPWLGFTRYAQKFQGRVTI TADESTSTAYMELSSLRSEDTAVYYCARESPGYRYSF DVWDQGTLLTVSSASTKGPSVFPLAPSSKSTSGGTA ALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQS SGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDK RVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTL MISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHN AKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKC KVSNAKALPAPIEKTISKAKGQPREPQVYTLPPSREEM TKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTT PPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHE ALHNHYTQKLSLSPGK
SEQ ID NO: 135	HC DNA	CAGGTGCAATTGGTGCAGAGCGGTGCCGAAGTGA AAAAACCGGGCAGCAGCGTGAAAGTTAGCTGCAA AGCATCCGGAGGGACGTTTGACTCTTACGCTGTTT CTTGGGTGCGCCAGGCCCGGGCCAGGGCCTCGAG TGGATGGGCGGTATCGTTCCGTGGCTGGGCTTCAC TCGTTACGCCCAGAAATTCAGGGCCGGGTGACCA TTACCGCCGATGAAAGCACCAGCACCAGCCTATATG GAACTGAGCAGCCTGCGCAGCGAAGATACGGCCG TGTATTATTGCGCGCGTGAATCTCCGGGTTACCGTT ACTCTTTTCGATGTTTGGGACCAAGGCACCCTGGTG ACTGTTAGCTCAGCCTCCACCAAGGGTCCATCGGT CTTCCCCCTGGCACCTCCTCCAAGAGCACCTCTG GGGGCACAGCGGCCCTGGGCTGCCTGGTCAAGGA CTACTTCCCCGAACCGGTGACGGTGTCTGTGGAAC CAGGCGCCCTGACCAGCGGCGTGACACCTTCCCG GCTGTCCTACAGTCCTCAGGACTCTACTCCCTCAG CAGCGTGGTGACCGTGCCCTCCAGCAGCTTGGGCA CCCAGACCTACATCTGCAACGTGAATCACAAGCCC AGCAACACCAAGGTGGACAAGAGAGTTGAGCCCA AATCTTGTGACAAAACCTCACACATGCCACCGTGC CCAGCACCTGAACTCCTGGGGGGACCGTCAGTCTT CCTCTTCCCCCAAAACCAAGGACACCCTCATGA TCTCCCGGACCCCTGAGGTCACATGCGTGGTGGTG GACGTGAGCCACGAAGACCCTGAGGTCAAGTTCA ACTGGTACGTGGACGGCGTGGAGGTGCATAATGCC AAGACAAAGCCGCGGGAGGAGCAGTACAACAGCA CGTACCGGGTGGTCAGCGTCCTCACCCTCCTGCAC CAGGACTGGCTGAATGGCAAGGAGTACAAGTGCA AGGTCTCCAACAAAGCCCTCCCAGCCCCCATCGAG AAAACCATCTCCAAAGCCAAAGGGCAGCCCCGAG AACCACAGGTGTACACCCTGCCCCCATCCCGGGAG

		GAGATGACCAAGAACCAGGTCAGCCTGACCTGCCT GGTCAAAGGCTTCTATCCCAGCGACATCGCCGTGG AGTGGGAGAGCAATGGGCAGCCGGAGAACAATA CAAGACCACGCCTCCCGTGCTGGACTCCGACGGCT CCTTCTTCTCTACAGCAAGCTCACCGTGGACAAG AGCAGGTGGCAGCAGGGGAACGTCTTCTCATGCTC CGTGATGCATGAGGCTCTGCACAACCACTACACGC AGAAGAGCCTCTCCCTGTCTCCGGGTAAA
SEQ ID NO: 119	LCDR1 (KABAT)	SGDAIGEKYVY
SEQ ID NO: 120	LCDR2 (KABAT)	DDNNRPS
SEQ ID NO: 121	LCDR3 (KABAT)	ASYDLQQARWV
SEQ ID NO: 122	LCDR1 (CHOTHIA)	DAIGEKY
SEQ ID NO: 99	LCDR2 (CHOTHIA)	DDN
SEQ ID NO: 123	LCDR3 (CHOTHIA)	YDLQQARW
SEQ ID NO: 119	LCDR1 (COMBINED)	SGDAIGEKYVY
SEQ ID NO: 120	LCDR2 (COMBINED)	DDNNRPS
SEQ ID NO: 121	LCDR3 (COMBINED)	ASYDLQQARWV
SEQ ID NO: 124	LCDR1 (IMGT)	AIGEKY
SEQ ID NO: 99	LCDR2 (IMGT)	DDN
SEQ ID NO: 121	LCDR3 (IMGT)	ASYDLQQARWV
SEQ ID NO: 125	VL	SYELTQPLSVSVALGQTARITCSGDAIGEKYVYWYQ QKPGQAPVLVIYDDNNRPSGIPERFSGSNSGNTATLTI SRAQAGDEADYYCASYDLQQARWVFGGGTKLTVL
SEQ ID NO: 126	VL DNA	AGCTACGAACTGACCCAGCCGCTGTCCGTGAGCGT GGCTCTGGGCCAGACCGCGCGGATTACCTGTAGCG GCGATGCTATCGGTGAAAAATACGTTTACTGGTAC CAGCAGAAACCGGGCCAGGCGCCGGTGCTGGTGA TCTACGACGACAACAACCGTCCGAGCGGCATCCCCG GAACGTTTTAGCGGATCCAACAGCGGCAACACCGC GACCCTGACCATTAGCCGCGCCCAGGCGGGAGAC GAAGCGGATTATTACTGCGCTTCTTACGACCTGCA GCAGGCTCGTTGGGTGTTTGGCGGGCGGCACGAAGT TAACCGTCCTA
SEQ ID NO: 127	LC	SYELTQPLSVSVALGQTARITCSGDAIGEKYVYWYQ QKPGQAPVLVIYDDNNRPSGIPERFSGSNSGNTATLTI SRAQAGDEADYYCASYDLQQARWVFGGGTKLTVL GQPKAAPSVTLFPPSSEELQANKATLVCLISDFYPGA VTVAWKADSSPVKAGVETTTTPSKQSNNKYAASSYLS LTPEQWKSHRSYSCQVTHEGSTVEKTVAPTECS
SEQ ID NO: 128	LC DNA	AGCTACGAACTGACCCAGCCGCTGTCCGTGAGCGT GGCTCTGGGCCAGACCGCGCGGATTACCTGTAGCG GCGATGCTATCGGTGAAAAATACGTTTACTGGTAC CAGCAGAAACCGGGCCAGGCGCCGGTGCTGGTGA TCTACGACGACAACAACCGTCCGAGCGGCATCCCCG GAACGTTTTAGCGGATCCAACAGCGGCAACACCGC GACCCTGACCATTAGCCGCGCCCAGGCGGGAGAC GAAGCGGATTATTACTGCGCTTCTTACGACCTGCA GCAGGCTCGTTGGGTGTTTGGCGGGCGGCACGAAGT TAACCGTCCTAGGTCAGCCCAAGGCTGCCCCCTCG GTCACCTCTGTTCCCGCCCTCCTCTGAGGAGCTTCAA GCCAACAAGGCCACACTGGTGTGTCTCATAGTTGA CTTCTACCCGGGAGCCGTGACAGTGGCCTGGAAGG CAGATAGCAGCCCCGTCAAGGCGGGAGTGGAGAC CACCACACCTCCAAACAAGCAACAACAAGTAC

		GCGGCCAGCAGCTATCTGAGCCTGACGCCTGAGCA GTGGAAGTCCCACAGAAGCTACAGCTGCCAGGTC ACGCATGAAGGGAGCACCGTGGAGAAGACAGTGG CCCCTACAGAATGTTCA
ANTI-HUMAN ENTPD2 MAB11		
SEQ ID NO: 136	HCDR1 (KABAT)	SYAMS
SEQ ID NO: 137	HCDR2 (KABAT)	VISGSGGSTYYADSVKG
SEQ ID NO: 138	HCDR3 (KABAT)	GDDYGDDYYYYGMDV
SEQ ID NO: 139	HCDR1 (CHOTHIA)	GFTFSSY
SEQ ID NO: 140	HCDR2 (CHOTHIA)	SGSGGS
SEQ ID NO: 138	HCDR3 (CHOTHIA)	GDDYGDDYYYYGMDV
SEQ ID NO: 141	HCDR1 (COMBINED)	GFTFSSYAMS
SEQ ID NO: 137	HCDR2 (COMBINED)	VISGSGGSTYYADSVKG
SEQ ID NO: 138	HCDR3 (COMBINED)	GDDYGDDYYYYGMDV
SEQ ID NO: 142	HCDR1 (IMGT)	GFTFSSYA
SEQ ID NO: 143	HCDR2 (IMGT)	ISGSGGST
SEQ ID NO: 144	HCDR3 (IMGT)	ARGDDYGDDYYYYGMDV
SEQ ID NO: 145	VH	EVQLLESGGGLVQSGGSLRLSCAASGFTFSSYAMSW VRQAPGKGLEWVSVISGSGGSTYYADSVKGRFTISR DNSKNTLYLQMNSLRAEDTAVYYCARGDDYGDDY YYYGMDVWGQGTITVTVSS
SEQ ID NO: 146	VH DNA	GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGT ACAGTCTGGGGGGTCCCTGAGACTCTCCTGTGCAG CCTCTGGATTACCTTTAGCAGCTATGCCATGAGC TGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGT GGGTCTCAGTTATTAGTGGTAGTGGTGGTAGCACA TACTACGCAGACTCCGTGAAGGGCCGGTTCACCAT CTCCAGAGACAATTCCAAGAACACGCTGTATCTGC AAATGAACAGCCTGAGAGCCGAGGACACGGCCGT ATATTACTGTGCGAGAGGGGATGACTACGGTGACG ACTACTACTACTACGGTATGGACGTCTGGGGCCAA GGGACCACGGTCACCGTCTCCTCA
SEQ ID NO: 147	HC	EVQLLESGGGLVQSGGSLRLSCAASGFTFSSYAMSW VRQAPGKGLEWVSVISGSGGSTYYADSVKGRFTISR DNSKNTLYLQMNSLRAEDTAVYYCARGDDYGDDY YYYGMDVWGQGTITVTVSSASTKGPSVFPLAPSSKST SGGTAALGCLVKDYFPEPTVSWNSGALTSGVHTFP AVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSN TKVDKRVKPKSCDKTHCTPPCPAPPELLGGPSVFLFPP KPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDG VEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTIKAKGQPREPQVYTLPP SREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPN NYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFC SVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 148	HC DNA	GAGGTGCAGCTGTTGGAGTCTGGGGGAGGCTTGGT ACAGTCTGGGGGGTCCCTGAGACTCTCCTGTGCAG CCTCTGGATTACCTTTAGCAGCTATGCCATGAGC TGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGT GGGTCTCAGTTATTAGTGGTAGTGGTGGTAGCACA TACTACGCAGACTCCGTGAAGGGCCGGTTCACCAT CTCCAGAGACAATTCCAAGAACACGCTGTATCTGC

		AAATGAACAGCCTGAGAGCCGAGGACACGGCCGT ATATTACTGTGCGAGAGGGGATGACTACGGTGACG ACTACTACTACTACGGTATGGACGTCTGGGGCCAA GGGACCACGGTCACCGTCTCCTCAGCTAGCACCAA GGGCCCCAAGTGTGTTTCCCCTGGCCCCCAGCAGCA AGTCTACTTCCGGCGGAAGTCTGCCCTGGGTTGC CTGGTGAAGGACTACTTCCCCGAGCCCCGTGACAGT GTCCTGGAAGTCTGGGGCTCTGACTTCCGGCGTGC ACACCTTCCCCGCCGTGCTGCAGAGCAGCGGCCCTG TACAGCCTGAGCAGCGTGGTGACAGTGCCCTCCAG CTCTCTGGGAACCCAGACCTATATCTGCAACGTGA ACCACAAGCCCAGCAACACCAAGGTGGACAAGAG AGTGGAGCCCAAGAGCTGCGACAAGACCCACACC TGCCCCCCTGCCAGCTCCAGAACTGCTGGGAGG GCCTTCCGTGTTCTGTTCCCCCCCCAAGCCCAAGG ACACCCTGATGATCAGCAGGACCCCCGAGGTGACC TGCCTGGTGGTGGACGTGTCCACGAGGACCCAGA GGTGAAGTTCAACTGGTACGTGGACGGCGTGGAG GTGCACAACGCCAAGACCAAGCCCAGAGAGGAGC AGTACAACAGCACCTACAGGGTGGTGTCCGTGCTG ACCGTGCTGCACCAGGACTGGCTGAACGGCAAAG AATACAAGTGCAAAGTCTCCAACAAGGCCCTGCCA GCCCCAATCGAAAAGACAATCAGCAAGGCCAAGG GCCAGCCACGGGAGCCCCAGGTGTACACCCTGCCC CCCAGCCGGGAGGAGATGACCAAGAACCAGGTGT CCCTGACCTGTCTGGTGAAGGGCTTCTACCCCAGC GATATCGCCGTGGAGTGGGAGAGCAACGGCCAGC CCGAGAACAACCTACAAGACCACCCCCCAGTGCTG GACAGCGACGGCAGCTTCTTCTGTACAGCAAGCT GACCGTGGACAAGTCCAGGTGGCAGCAGGGCAAC GTGTTTCAGCTGCAGCGTGATGCACGAGGCCCTGCA CAACCACTACACCCAGAAGTCCCTGAGCCTGAGCC CCGGCAAG
SEQ ID NO: 149	LCDR1 (KABAT)	RSSQSLLHGNRYNYLD
SEQ ID NO: 150	LCDR2 (KABAT)	LGSNRAS
SEQ ID NO: 151	LCDR3 (KABAT)	MQALQTPPT
SEQ ID NO: 152	LCDR1 (CHOTHIA)	SQSLLHGNRYNY
SEQ ID NO: 153	LCDR2 (CHOTHIA)	LGS
SEQ ID NO: 154	LCDR3 (CHOTHIA)	ALQTPP
SEQ ID NO: 149	LCDR1 (COMBINED)	RSSQSLLHGNRYNYLD
SEQ ID NO: 150	LCDR2 (COMBINED)	LGSNRAS
SEQ ID NO: 151	LCDR3 (COMBINED)	MQALQTPPT
SEQ ID NO: 155	LCDR1 (IMGT)	QSLLHGNRYNY
SEQ ID NO: 153	LCDR2 (IMGT)	LGS
SEQ ID NO: 151	LCDR3 (IMGT)	MQALQTPPT
SEQ ID NO: 156	VL	DIVMTQSPLSLPVTGPGEPAISCRSSQSLLHGNRYNYL DWYLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGT DFTLKISRVEAEDVGVYYCMQALQTPPTFGQGKVE IK
SEQ ID NO: 157	VL DNA	GATATTGTGATGACTCAGTCTCCACTCTCCCTGCCC GTCACCCCTGGAGAGCCGGCCTCCATCTCCTGCAG GTCTAGTCAGAGCCTCCTGCATGGTAATCGATACA ACTATTTGGATTGGTACCTGCAGAAGCCAGGGCAG TCTCCACAGCTCCTGATCTATTGGGTTCTAATCGG

		GCCTCCGGGGTCCCTGACAGGTTTCAGTGGCAGTGG ATCAGGCACAGATTTTACACTGAAAATCAGCAGAG TGGAGGCTGAGGATGTTGGGGTTTATTACTGCATG CAAGCTCTACAACTCCTCCGACGTTTCGGCCAAGG GACCAAGGTGGAAATCAAA
SEQ ID NO: 158	LC	DIVMTQSPLSLPVTGPASISCRSSQSLHGNRYNYL DWYLQKPGQSPQLLIYLGSRASGVPDRFSGSGSGT DFTLKISRVEAEDVGVYYCMQALQTPPTFGQGKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPRE AKVQWKVDNALQSGNSQESVTEQDSKDYSLSTL TLKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 159	LC DNA	GATATTGTGATGACTCAGTCTCCACTCTCCCTGCC GTCACCCCTGGAGAGCCGGCCTCCATCTCCTGCAG GTCTAGTCAGAGCCTCCTGCATGGTAATCGATACA ACTATTTGGATTGGTACCTGCAGAAGCCAGGGCAG TCTCCACAGCTCCTGATCTATTTGGGTTCTAATCGG GCCTCCGGGGTCCCTGACAGGTTTCAGTGGCAGTGG ATCAGGCACAGATTTTACACTGAAAATCAGCAGAG TGGAGGCTGAGGATGTTGGGGTTTATTACTGCATG CAAGCTCTACAACTCCTCCGACGTTTCGGCCAAGG GACCAAGGTGGAAATCAAACGAACTGTGGCTGCA CCAAGCGTGTTCATCTTCCCCCCCAGCGACGAGCA GCTGAAGAGTGGCACCAGCCAGCGTGGTGTGCCTGC TGAACAACCTTCTACCCCCGGGAGGCCAAGGTGCAG TGGAAGGTGGACAACGCCCTGCAGAGCGGCAACA GCCAGGAGAGCGTCACCGAGCAGGACAGCAAGGA CTCCACCTACAGCCTGAGCAGCACCTGACCCCTGA GCAAGGCCGACTACGAGAAGCATAAGGTGTACGC CTGCGAGGTGACCCACCAGGGCCTGTCCAGCCCCG TGACCAAGAGCTTCAACAGGGGCGAGTGC
ANTI-HUMAN ENTPD2 MAB12		
SEQ ID NO: 160	HCDR1 (KABAT)	SCSMN
SEQ ID NO: 161	HCDR2 (KABAT)	YISSSSTIYYADSVKG
SEQ ID NO: 162	HCDR3 (KABAT)	DQGNWNYDDYYNGLDV
SEQ ID NO: 163	HCDR1 (CHOTHIA)	GFTFNCS
SEQ ID NO: 164	HCDR2 (CHOTHIA)	SSSSST
SEQ ID NO: 162	HCDR3 (CHOTHIA)	DQGNWNYDDYYNGLDV
SEQ ID NO: 165	HCDR1 (COMBINED)	GFTFNCSMN
SEQ ID NO: 161	HCDR2 (COMBINED)	YISSSSTIYYADSVKG
SEQ ID NO: 162	HCDR3 (COMBINED)	DQGNWNYDDYYNGLDV
SEQ ID NO: 166	HCDR1 (IMGT)	GFTFNCS
SEQ ID NO: 167	HCDR2 (IMGT)	ISSSSTI
SEQ ID NO: 168	HCDR3 (IMGT)	ARDQGNWNYDDYYNGLDV
SEQ ID NO: 169	VH	EVLLVESGGGLVQPGGSLRLSCAASGFTFNCSMNW VRQAPGKGLEWVSYISSSSTIYYADSVKGRFTISR NAKNSLYLQMNSLKDEDTAVYYCARDQGNWNYDD YYNGLDVWGQGTITVTVSS
SEQ ID NO: 170	VH DNA	GAGGTGCTGCTGGTGGAGTCTGGGGGAGGCTTGGT ACAGCCTGGGGGGTCCCTGAGACTCTCCTGTGCAG CCTCTGGGTTACCTTCAATAGCTGTAGCATGAAC TGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGT GGGTTTCATACATTAGTAGTAGTAGTAGTACCATT TACTACGCAGACTCTGTGAAGGGCCGATTCACCAT

		CTCCAGAGACAATGCCAAGAACTCACTGTATCTGC AAATGAACAGCCTGAAAGACGAGGACACGGCTGT GTATTACTGTGCGAGAGATCAGGGTAACTGGAAC ACGACGACTACTACAACGGTTTGGACGTCTGGGGC CAAGGGACCACGGTCACCGTCTCCTCA
SEQ ID NO: 171	HC	EVLLVESGGGLVQPGGSLRLSCAASGFTFNSSCMNW VRQAPGKGLEWVSYISSSSTIYYADSVKGRFTISRD NAKNSLYLQMNSLKDEDTAVYYCARDQGNWNYDD YYNGLDVWGQGTITVTVSSASTKGPSVFPLAPSSKST SGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP AVLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSN TKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPP KPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDG VEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPP SREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPEN NYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFSC SVMHEALHNHYTQKLSLSLSPGK
SEQ ID NO: 172	HC DNA	GAGGTGCTGCTGGTGGAGTCTGGGGAGGCTTGGT ACAGCCTGGGGGGTCCCTGAGACTCTCCTGTGCAG CCTCTGGGTTCACCTTCAATAGCTGTAGCATGAAC TGGGTCCGCCAGGCTCCAGGGAAGGGGCTGGAGT GGGTTTCATACATTAGTAGTAGTAGTAGTACCATT TACTACGCAGACTCTGTGAAGGGCCGATTCACCAT CTCCAGAGACAATGCCAAGAACTCACTGTATCTGC AAATGAACAGCCTGAAAGACGAGGACACGGCTGT GTATTACTGTGCGAGAGATCAGGGTAACTGGAAC ACGACGACTACTACAACGGTTTGGACGTCTGGGGC CAAGGGACCACGGTCACCGTCTCCTCAGCTAGCAC CAAGGGCCCAAGTGTGTTTCCCCTGGCCCCCAGCA GCAAGTCTACTTCCGGCGGAACTGCTGCCCTGGGT TGCCTGGTGAAGGACTACTTCCCCGAGCCCGTGAC AGTGTCTGGAACCTCTGGGGCTCTGACTTCCGGCG TGCACACCTTCCCCGCCGTGCTGCAGAGCAGCGGC CTGTACAGCCTGAGCAGCGTGGTGACAGTGCCCTC CAGCTCTCTGGGAACCCAGACCTATATCTGCAACG TGAACCACAAGCCCAGCAACACCAAGGTGGACAA GAGAGTGGAGCCCAAGAGCTGCGACAAGACCCAC ACCTGCCCCCCTGCCAGCTCCAGAACTGCTGGG AGGGCCTTCCGTGTTCTGTTCCCCCCCCAAGCCCA AGGACACCCTGATGATCAGCAGGACCCCCGAGGT GACCTGCGTGGTGGTGGACGTGTCCACGAGGACC CAGAGGTGAAGTTCAACTGGTACGTGGACGGCGT GGAGGTGCACAACGCCAAGACCAAGCCCAGAGAG GAGCAGTACAACAGCACCTACAGGGTGGTGTCCGT GCTGACCGTGCTGCACCAGGACTGGCTGAACGGCA AAGAATACAAGTGCAAAGTCTCCAACAAGGCCCT GCCAGCCCCAATCGAAAAGACAATCAGCAAGGCC AAGGGCCAGCCACGGGAGCCCCAGGTGTACCCC TGCCCCCAGCCGGGAGGAGATGACCAAGAACCA GGTGTCCTGACCTGTCTGGTGAAGGGCTTCTACC CCAGCGATATCGCCGTGGAGTGGGAGAGCAACGG CCAGCCCGAGAACAATACTACAAGACCACCCCCCA GTGCTGGACAGCGACGGCAGCTTCTTCTGTACAG CAAGCTGACCGTGGACAAGTCCAGGTGGCAGCAG GGCAACGTGTTTCACTGTCAGCGTGATGCACGAGGC CCTGCACAACCACTACACCCAGAAGTCCCTGAGCC TGAGCCCCGGCAAG
SEQ ID NO: 173	LCDR1 (KABAT)	RSSQSLHNSNGYNYLD

SEQ ID NO: 150	LCDR2 (KABAT)	LGSNRAS
SEQ ID NO: 174	LCDR3 (KABAT)	MQALQTPLT
SEQ ID NO: 175	LCDR1 (CHOTHIA)	SQSLHNSGYN
SEQ ID NO: 153	LCDR2 (CHOTHIA)	LGS
SEQ ID NO: 176	LCDR3 (CHOTHIA)	ALQTPL
SEQ ID NO: 173	LCDR1 (COMBINED)	RSSQSLHNSGYNLD
SEQ ID NO: 150	LCDR2 (COMBINED)	LGSNRAS
SEQ ID NO: 174	LCDR3 (COMBINED)	MQALQTPLT
SEQ ID NO: 177	LCDR1 (IMGT)	QSLHNSGYN
SEQ ID NO: 153	LCDR2 (IMGT)	LGS
SEQ ID NO: 174	LCDR3 (IMGT)	MQALQTPLT
SEQ ID NO: 178	VL	DIVMTQSPLSLPVTGPGEPAISCRSSQSLHNSGYNLD DWYLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGT DFTLKISRVEAEDVGVYYCMQALQTPLTFGGGKVE IK
SEQ ID NO: 179	VL DNA	GATATTGTGATGACTCAGTCTCCACTCTCCCTGCCC GTCACCTCTGGAGAGCCGGCCTCCATCTCCTGCAG GTCTAGTCAGAGCCTCCTGCATAGTAATGGATACA ACTATTTGGATTGGTACCTGCAGAAGCCAGGGCAG TCTCCACAGCTCCTGATCTATTTGGGTTCTAATCGG GCCTCCGGGGTCCCTGACAGGTTCACTGGCAGTGG ATCAGGCACAGATTTTACACTGAAAATCAGCAGAG TGGAGGCTGAGGATGTTGGGGTTTATTACTGCATG CAAGCTCTACAACTCCTCTCACTTTCGGCGGAGG GACCAAGGTGGAGATCAAAA
SEQ ID NO: 180	LC	DIVMTQSPLSLPVTGPGEPAISCRSSQSLHNSGYNLD DWYLQKPGQSPQLLIYLGSNRASGVPDRFSGSGSGT DFTLKISRVEAEDVGVYYCMQALQTPLTFGGGKVE IKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPRE AKVQWKVDNALQSGNSQESVTEQDSKSTYSLSSTL TLSKADYEHKHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 181	LC DNA	GATATTGTGATGACTCAGTCTCCACTCTCCCTGCCC GTCACCTCTGGAGAGCCGGCCTCCATCTCCTGCAG GTCTAGTCAGAGCCTCCTGCATAGTAATGGATACA ACTATTTGGATTGGTACCTGCAGAAGCCAGGGCAG TCTCCACAGCTCCTGATCTATTTGGGTTCTAATCGG GCCTCCGGGGTCCCTGACAGGTTCACTGGCAGTGG ATCAGGCACAGATTTTACACTGAAAATCAGCAGAG TGGAGGCTGAGGATGTTGGGGTTTATTACTGCATG CAAGCTCTACAACTCCTCTCACTTTCGGCGGAGG GACCAAGGTGGAGATCAAACTACGGTGGCCGCT CCCAGCGTGTTTCATCTTCCCCCCCCAGCGACGAGCA GCTGAAGAGTGGCACCAGCCAGCGTGGTGTGCCTGC TGAACAACCTTCTACCCCCGGGAGGCCAAGGTGCAG TGGAAGGTGGACAACGCCCTGCAGAGCGGCAACA GCCAGGAGAGCGTCACCGAGCAGGACAGCAAGGA CTCCACCTACAGCCTGAGCAGCACCTGACCCTGA GCAAGGCCGACTACGAGAAGCATAAGGTGTACGC CTGCGAGGTGACCCACCAGGGCCTGTCCAGCCCCG TGACCAAGAGCTTCAACAGGGGCGAGTGC
ANTI-HUMAN ENTPD2 MAB16		
SEQ ID NO: 37	HCDR1 (KABAT)	SGYYWN
SEQ ID NO: 220	HCDR2 (KABAT)	YISYDGDNNYNPSLKN

SEQ ID NO: 221	HCDR3 (KABAT)	GYRYGLSYYYVMDY
SEQ ID NO: 40	HCDR1 (CHOTHIA)	GYSITSGY
SEQ ID NO: 222	HCDR2 (CHOTHIA)	SYDGD
SEQ ID NO: 221	HCDR3 (CHOTHIA)	GYRYGLSYYYVMDY
SEQ ID NO: 42	HCDR1 (COMBINED)	GYSITSGYYWN
SEQ ID NO: 220	HCDR2 (COMBINED)	YISYDGDNNYNPSLKN
SEQ ID NO: 221	HCDR3 (COMBINED)	GYRYGLSYYYVMDY
SEQ ID NO: 43	HCDR1 (IMGT)	GYSITSGYY
SEQ ID NO: 223	HCDR2 (IMGT)	ISYDGDN
SEQ ID NO: 224	HCDR3 (IMGT)	AGGYRYGLSYYYVMDY
SEQ ID NO: 225	VH	DIQLQESGPGLVKPSQSLTCSVTGYSITSGYYWNW IRQFPGNKLEWMGYISYDGDNNYNPSLKNRISITRDT SKNQFFLKLSSVTEDTATYYCAGGYRYGLSYYYV MDYWQGQTSVTVSS
SEQ ID NO: 226	VH DNA	GATATACAGCTTCAGGAGTCAGGACCTGGCCTCGT GAAACCTTCTCAGTCTCTGTCTCTCACCTGCTCTGT CACTGGCTACTCCATCACCAGTGGTTATTACTGGA ACTGGATCCGGCAGTTTCCAGGAAACAACTGGA ATGGATGGGCTACATAAGCTACGACGGTGACAAT AACTACAACCCATCTCTCAAAAATCGAATCTCCAT CACTCGTGACACATCTAAGAACCAGTTTTCTCTGA AGTTGAGTTCTGTGACTACTGAGGACACAGCTACA TATTACTGTGCAGGAGGCTACTATAGGTACGGCCT GTCGTATTACTATGTTATGGACTACTGGGGTCAAG GAACCTCAGTCACCGTCTCCTCA
SEQ ID NO: 227	HC	DIQLQESGPGLVKPSQSLTCSVTGYSITSGYYWNW IRQFPGNKLEWMGYISYDGDNNYNPSLKNRISITRDT SKNQFFLKLSSVTEDTATYYCAGGYRYGLSYYYV MDYWQGQTSVTVSSASTKGPSVFLAPSSKSTSGGT AALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQ SSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVD KRVEPKSCDKTHTCPPCPAPELGGPSVFLFPPKPKD TLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEV HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEY KCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREE MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKT TPPVLDSDGSFFLYSKLTVDKSRWQQGNVFSCSVMH EALHNHYTQKSLSLSPGK
SEQ ID NO: 228	HC DNA	GATATACAGCTTCAGGAGTCAGGACCTGGCCTCGT GAAACCTTCTCAGTCTCTGTCTCTCACCTGCTCTGT CACTGGCTACTCCATCACCAGTGGTTATTACTGGA ACTGGATCCGGCAGTTTCCAGGAAACAACTGGA ATGGATGGGCTACATAAGCTACGACGGTGACAAT AACTACAACCCATCTCTCAAAAATCGAATCTCCAT CACTCGTGACACATCTAAGAACCAGTTTTCTCTGA AGTTGAGTTCTGTGACTACTGAGGACACAGCTACA TATTACTGTGCAGGAGGCTACTATAGGTACGGCCT GTCGTATTACTATGTTATGGACTACTGGGGTCAAG GAACCTCAGTCACCGTCTCCTCAGCTAGCACCAAG GGCCCAAGTGTGTTTCCCCTGGCCCCCAGCAGCAA GTCTACTTCCGGCGGAAGTCTGCCCCTGGGTTGCC TGGTGAAGGACTACTTCCCCGAGCCCGTGACAGTG TCCTGGAAGTCTGGGGCTCTGACTTCCGGCGTGCA CACCTTCCCCGCCGTGCTGCAGAGCAGCGGCCTGT ACAGCCTGAGCAGCGTGGTGACAGTGCCCTCCAGC

		TCTCTGGGAACCCAGACCTATATCTGCAACGTGAA CCACAAGCCCAGCAACACCAAGGTGGACAAGAGA GTGGAGCCCAAGAGCTGCGACAAGACCCACACCT GCCCCCCTGCCAGCTCCAGAACTGCTGGGAGGG CCTTCCGTGTTCTGTTCCCCCCCCAAGCCCAAGGA CACCTGATGATCAGCAGGACCCCCGAGGTGACCT GCGTGGTGGTGGACGTGTCCCACGAGGACCCAGA GGTGAAGTTCAACTGGTACGTGGACGGCGTGGAG GTGCACAACGCCAAGACCAAGCCAGAGAGGAGC AGTACAACAGCACCTACAGGGTGGTGTCCGTGCTG ACCGTGCTGCACCAGGACTGGCTGAACGGCAAAG AATACAAGTGCAAAGTCTCCAACAAGGCCCTGCCA GCCCCAATCGAAAAGACAATCAGCAAGGCCAAGG GCCAGCCACGGGAGCCCCAGGTGTACACCTGCCC CCCAGCCGGGAGGAGATGACCAAGAACCAGGTGT CCCTGACCTGTCTGGTGAAGGGCTTCTACCCAGC GATATCGCCGTGGAGTGGGAGAGCAACGGCCAGC CCGAGAACAACCTACAAGACCACCCCCCAGTGCTG GACAGCGACGGCAGCTTCTTCCTGTACAGCAAGCT GACCGTGGACAAGTCCAGGTGGCAGCAGGGCAAC GTGTTCACTGTCAGCGTGATGCACGAGGCCCTGCA CAACCACTACACCCAGAAGTCCCTGAGCCTGAGCC CCGGCAAG
SEQ ID NO: 61	LCDR1 (KABAT)	KASQSVDDYDGN SYMN
SEQ ID NO: 51	LCDR2 (KABAT)	AASNLES
SEQ ID NO: 52	LCDR3 (KABAT)	QQSNEPPT
SEQ ID NO: 62	LCDR1 (CHOTHIA)	SQSVDDYDGN SY
SEQ ID NO: 54	LCDR2 (CHOTHIA)	AAS
SEQ ID NO: 55	LCDR3 (CHOTHIA)	SNEDPP
SEQ ID NO: 61	LCDR1 (COMBINED)	KASQSVDDYDGN SYMN
SEQ ID NO: 51	LCDR2 (COMBINED)	AASNLES
SEQ ID NO: 52	LCDR3 (COMBINED)	QQSNEPPT
SEQ ID NO: 63	LCDR1 (IMGT)	QSVDDYDGN SY
SEQ ID NO: 54	LCDR2 (IMGT)	AAS
SEQ ID NO: 52	LCDR3 (IMGT)	QQSNEPPT
SEQ ID NO: 229	VL	DTVLTSQSPASLAVSLGQRATISCKASQSVDDYDGN SY MNWYQQKPGQPPKLLIYAASNLESGIPARFSGSGGT DFTLNHPVEEEDAATYYCQQSNEPPTFGGGTKLEI K
SEQ ID NO: 230	VL DNA	GACACTGTGCTGACCCAATCTCCAGCCTCTTTGGC TGTGTCTCTAGGGCAGAGGGCCACCATCTCCTGCA AGGCCAGCCAAAGTGTGATTATGATGTTAATGAT TATATGAACTGGTACCAACAGAAACAGGACAGC CACCCAACTCCTCATCTATGCTGCATCCAATCTA GAATCTGGGATCCCAGCCAGGTTTAGTGGCAGTGG GTCTGGGACAGACTTCACCCTCAACATCCATCCTG TGGAGGAGGAGGATGCTGCAACCTATTACTGTCAG CAAAGTAATGAGGATCCTCCGACGTTTCGGTGGAGG CACCAAGCTGGAAATCAA
SEQ ID NO: 231	LC	DTVLTSQSPASLAVSLGQRATISCKASQSVDDYDGN SY MNWYQQKPGQPPKLLIYAASNLESGIPARFSGSGGT DFTLNHPVEEEDAATYYCQQSNEPPTFGGGTKLEI KRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPRE

		AKVQWKVDNALQSGNSQESVTEQDSKDSYSLSTL TLISKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 232	LC DNA	GACACTGTGCTGACCCAATCTCCAGCCTCTTTGGC TGTGTCTCTAGGGCAGAGGGCCACCATCTCCTGCA AGGCCAGCCAAAGTGTTGATTATGATGGTAATAGT TATATGAACTGGTACCAACAGAAACCAGGACAGC CACCCAAACTCCTCATCTATGCTGCATCCAATCTA GAATCTGGGATCCCAGCCAGGTTTAGTGGCAGTGG GTCTGGGACAGACTTCACCCTCAACATCCATCCTG TGGAGGAGGAGGATGCTGCAACCTATTACTGTCAG CAAAGTAATGAGGATCCTCCGACGTTCGGTGGAGG CACCAAGCTGGAAATCAAACGTACGGTGGCCGCTC CCAGCGTGTTCATCTTCCCCCCCAGCGACGAGCAG CTGAAGAGTGGCACC GCCAGCGTGGTGTGCCTGCT GAACAACCTTCTACCCCCGGGAGGCCAAGGTGCAGT GGAAGGTGGACAACGCCCTGCAGAGCGGCAACAG CCAGGAGAGCGTCACCGAGCAGGACAGCAAGGAG TCCACCTACAGCCTGAGCAGCACCCTGACCCTGAG CAAGGCCGACTACGAGAAGCATAAGGTGTACGCC TGCGAGGTGACCCACCAGGGCCTGTCCAGCCCCGT GACCAAGAGCTTCAACAGGGGCGAGTGC
ANTI-HUMAN ENTPD2 MAB17		
SEQ ID NO: 1	HCDR1 (KABAT)	DYNMD
SEQ ID NO: 2	HCDR2 (KABAT)	DINPKYDISTYNQQFKG
SEQ ID NO: 3	HCDR3 (KABAT)	RGFFLYYGINYYYFDV
SEQ ID NO: 4	HCDR1 (CHOTHIA)	GYTFTDY
SEQ ID NO: 5	HCDR2 (CHOTHIA)	NPKYDI
SEQ ID NO: 3	HCDR3 (CHOTHIA)	RGFFLYYGINYYYFDV
SEQ ID NO: 6	HCDR1 (COMBINED)	GYTFTDYNMD
SEQ ID NO: 2	HCDR2 (COMBINED)	DINPKYDISTYNQQFKG
SEQ ID NO: 3	HCDR3 (COMBINED)	RGFFLYYGINYYYFDV
SEQ ID NO: 7	HCDR1 (IMGT)	GYTFTDYN
SEQ ID NO: 8	HCDR2 (IMGT)	INPKYDIS
SEQ ID NO: 9	HCDR3 (IMGT)	ARRGFFLYYGINYYYFDV
SEQ ID NO: 233	VH	EVQLQQFGAELVKPGASVKISKASGYTFTDYNMD WVKQSHGKSLEWIGDINPKYDISTYNQQFKGKATLT VDKSSSTAYMELRSLTSEDVAVYYCARRGFFLYYGI NYYYFDVWGAGTTVTVSS
SEQ ID NO: 234	VH DNA	GAGGTCCAACCTGCAACAGTTTGGAGCTGAACTGGT GAAGCCTGGGGCTTCAGTGAAGATATCCTGCAAGG CTTCTGGCTACACATTCAGTGACTACAACATGGAC TGGGTGAAGCAGAGCCATGGAAAGAGCCTTGAGT GGATTGGAGATATTAATCCTAAGTATGATATTTCT ACCTACAATCAGCAATTCAAGGGAAAGGCCACATT GACTGTAGACAAGTCCTCCAGCACAGCCTACATGG AGCTCCGCAGCCTGACATCTGAGGACACTGCAGTC TATTATTGTGCAAGAAGAGGCTTTTTTCTTTACTAC GGTATTAATACTACTATTACTTCGATGTCTGGGGCGC AGGGACCACGGTCACCGTCTCCTCA
SEQ ID NO: 235	HC	EVQLQQFGAELVKPGASVKISKASGYTFTDYNMD WVKQSHGKSLEWIGDINPKYDISTYNQQFKGKATLT VDKSSSTAYMELRSLTSEDVAVYYCARRGFFLYYGI NYYYFDVWGAGTTVTVSSASTKGPSVFPLAPSSKSTS

		GGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPA VLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNT KVDKRVKPKSCDKTHTCPPCPAPELLGGPSVFLFPPK PKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGV EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGK EYKCKVSNKALPAPIEKTISKAKGQPREPVYTLPPS REEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSS VMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 236	HC DNA	GAGGTCCAAGTCAACAGTTTGGAGCTGAAGTGGT GAAGCCTGGGGCTTCAGTGAAGATATCCTGCAAGG CTTCTGGCTACACATTCAGTACTACAACATGGAC TGGGTGAAGCAGAGCCATGGAAAGAGCCTTGAGT GGATTGGAGATATTAATCCTAAGTATGATATTTCT ACCTACAATCAGCAATTCAGGGGAAAGGCCACATT GACTGTAGACAAGTCTCCAGCACAGCCTACATGG AGCTCCGCAGCCTGACATCTGAGGACACTGCAGTC TATTATTGTGCAAGAAGAGGCTTTTTTCTTTACTAC GGTATTAAGTACTATTACTTCGATGTCTGGGGCGC AGGGACCACGGTCACCGTCTCCTCAGCTAGCACCA AGGGCCCAAGTGTGTTTCCCCTGGCCCCCAGCAGC AAGTCTACTTCCGGCGGAAGTCTGCTGCCCTGGGTG CCTGGTGAAGGACTACTTCCCCGAGCCCGTGACAG TGTCCTGGAAGTCTGGGGCTCTGACTTCCGGCGTG CACACCTTCCCCGCGTGCTGCAGAGCAGCGGCCT GTACAGCCTGAGCAGCGTGGTGACAGTGCCTCCA GCTCTCTGGGAACCCAGACCTATATCTGCAACGTG AACCACAAGCCAGCAACACCAAGGTGGACAAGA GAGTGGAGCCCAAGAGCTGCGACAAGACCCACAC CTGCCCCCCTGCCAGCTCCAGAACTGCTGGGAG GGCCTTCCGTGTTCTGTTCCCCCCCCAAGCCCAAG GACACCCTGATGATCAGCAGGACCCCCGAGGTGA CCTGCGTGGTGGTGGACGTGTCCACGAGGACCCCA GAGGTGAAGTTCAACTGGTACGTGGACGGCGTGG AGGTGCACAACGCCAAGACCAAGCCAGAGAGGA GCAGTACAACAGCACCTACAGGGTGGTGTCCGTGC TGACCGTGCTGCACCAGGACTGGCTGAACGGCAA AGAATACAAGTGCAAAGTCTCCAACAAGGCCCTG CCAGCCCCAATCGAAAAGACAATCAGCAAGGCCA AGGGCCAGCCACGGGAGCCCCAGGTGTACACCCT GCCCCCAGCCGGGAGGAGATGACCAAGAACCAG GTGTCCCTGACCTGTCTGGTGAAGGGCTTCTACCC CAGCGATATCGCCGTGGAGTGGGAGAGCAACGGC CAGCCCGAGAACAACACTACAAGACCACCCCCCAG TGCTGGACAGCGACGGCAGCTTCTTCTGTACAGC AAGCTGACCGTGGACAAGTCCAGGTGGCAGCAGG GCAACGTGTTTCACTGACGCGTGTGACGAGGCC CTGCACAACCACTACACCCAGAAGTCCCTGAGCCT GAGCCCCGCAAG
SEQ ID NO: 14	LCDR1 (KABAT)	SASSSVSYIH
SEQ ID NO: 15	LCDR2 (KABAT)	STSNLAS
SEQ ID NO: 16	LCDR3 (KABAT)	HQWSSYPWT
SEQ ID NO: 17	LCDR1 (CHOTHIA)	SSSVSY
SEQ ID NO: 18	LCDR2 (CHOTHIA)	STS
SEQ ID NO: 19	LCDR3 (CHOTHIA)	WSSYPW
SEQ ID NO: 14	LCDR1 (COMBINED)	SASSSVSYIH

SEQ ID NO: 15	LCDR2 (COMBINED)	STSNLAS
SEQ ID NO: 16	LCDR3 (COMBINED)	HQWSSYPWT
SEQ ID NO: 20	LCDR1 (IMGT)	SSVS
SEQ ID NO: 18	LCDR2 (IMGT)	STS
SEQ ID NO: 16	LCDR3 (IMGT)	HQWSSYPWT
SEQ ID NO: 237	VL	QIVLTQSPAIMASASLGEEITLTCSASSSVSYIHWYQQK SGTSPITLLIYSTSNLASGVPSRFSGSGSGTFYSLTISSV EAEDAADYYCHQWSSYPWTFGGGKLEIK
SEQ ID NO: 238	VL DNA	CAAATTGTTCTCACCCAGTCTCCAGCAATCATGTCT GCATCTCTAGGGGAGGAGATCACCTAACCTGCAG TGCCAGCTCGAGTGTAAGTTACATACACTGGTACC AGCAGAAGTCAGGCACTTCTCCCACTCTTGATT TATAGCACATCCAATCTGGCTTCTGGAGTCCCTTCT CGCTTCAGTGGCAGTGGGTCTGGGACCTTTTATTCT CTCACAATCAGCAGTGTGGAGGCTGAAGATGCTGC CGATTATTACTGCCATCAGTGGAGTAGTTATCCAT GGACGTTTCGGTGGAGGCACCAAGCTGGAAATCAA A
SEQ ID NO: 239	LC	QIVLTQSPAIMASASLGEEITLTCSASSSVSYIHWYQQK SGTSPITLLIYSTSNLASGVPSRFSGSGSGTFYSLTISSV EAEDAADYYCHQWSSYPWTFGGGKLEIKRTVAAP SVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKV DNALQSGNSQESVTEQDSKSTYSLSSTLTLSKADYE KHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 240	LC DNA	CAAATTGTTCTCACCCAGTCTCCAGCAATCATGTCT GCATCTCTAGGGGAGGAGATCACCTAACCTGCAG TGCCAGCTCGAGTGTAAGTTACATACACTGGTACC AGCAGAAGTCAGGCACTTCTCCCACTCTTGATT TATAGCACATCCAATCTGGCTTCTGGAGTCCCTTCT CGCTTCAGTGGCAGTGGGTCTGGGACCTTTTATTCT CTCACAATCAGCAGTGTGGAGGCTGAAGATGCTGC CGATTATTACTGCCATCAGTGGAGTAGTTATCCAT GGACGTTTCGGTGGAGGCACCAAGCTGGAAATCAA ACGTACGGTGGCCGCTCCAGCGTGTTCATCTTCC CCCCCAGCGACGAGCAGCTGAAGAGTGGCACCGC CAGCGTGGTGTGCCTGCTGAACAATTCTACCCCC GGGAGGCCAAGGTGCAGTGGAAGGTGGACAACGC CCTGCAGAGCGGCAACAGCCAGGAGAGCGTCACC GAGCAGGACAGCAAGGACTCCACCTACAGCCTGA GCAGCACCTGACCTGAGCAAGGCCGACTACGA GAAGCATAAGGTGTACGCCTGCGAGGTGACCCAC CAGGGCCTGTCCAGCCCCGTGACCAAGAGCTTCAA CAGGGGCGAGTGC
ANTI-HUMAN ENTPD2 MAB18		
SEQ ID NO: 37	HCDR1 (KABAT)	SGYYWN
SEQ ID NO: 220	HCDR2 (KABAT)	YISYDGDNNYNPSLKN
SEQ ID NO: 68	HCDR3 (KABAT)	GYRYRLGSYSGSYYYVMDY
SEQ ID NO: 40	HCDR1 (CHOTHIA)	GYSITSGY
SEQ ID NO: 222	HCDR2 (CHOTHIA)	SYDGD
SEQ ID NO: 68	HCDR3 (CHOTHIA)	GYRYRLGSYSGSYYYVMDY
SEQ ID NO: 42	HCDR1 (COMBINED)	GYSITSGYYWN
SEQ ID NO: 220	HCDR2 (COMBINED)	YISYDGDNNYNPSLKN

SEQ ID NO: 68	HCDR3 (COMBINED)	GYRYRYGLGSYSGSYYYVMDY
SEQ ID NO: 43	HCDR1 (IMGT)	GYSITSGYY
SEQ ID NO: 223	HCDR2 (IMGT)	ISYDGDN
SEQ ID NO: 69	HCDR3 (IMGT)	AGGYRYRYGLGSYSGSYYYVMDY
SEQ ID NO: 241	VH	DIQLQESGPGLVKPSQSLSLTCSVTGYSITSGYYYWNW IRQFPGNKLEWMGYISYDGDNNYNPSLKNRISITRDT SKNQFFLKLSSVTEDTATYYCAGGYRYRYGLGSYSG SYYYVMDYWQGQTSVTVSS
SEQ ID NO: 242	VH DNA	GATATACAGCTTCAGGAGTCAGGACCTGGCCTCGT GAAACCTTCTCAGTCTCTGTCTCTCACCTGCTCTGT CACTGGCTACTCCATCACCAGTGGTTATTACTGGA ACTGGATCCGGCAGTTTCCAGGAAACAACTGGA ATGGATGGGCTACATAAGCTACGACGGTGACAAT AACTACAACCCATCTCTCAAAAATCGAATCTCCAT CACTCGTGACACATCTAAGAACCAGTTTTCTCTGA AGTTGAGTTCTGTGACTACTGAGGACACAGCTACA TATTACTGTGCAGGAGGCTACTATAGGTACGGCCT GGGCTCCTACTCCGGCTCGTATTACTATGTTATGG ACTACTGGGGTCAAGGAACCTCAGTCACCGTCTCC TCA
SEQ ID NO: 243	HC	DIQLQESGPGLVKPSQSLSLTCSVTGYSITSGYYYWNW IRQFPGNKLEWMGYISYDGDNNYNPSLKNRISITRDT SKNQFFLKLSSVTEDTATYYCAGGYRYRYGLGSYSG SYYYVMDYWQGQTSVTVSSASTKGPSVFLAPSSKS TSGGTAALGCLVKDYFPEPVTVSWNSGALTSVHTF PAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHNKPS NTKVDKRVKPKSCDKTHTCPPCPAPPELLGGPSVFLFP PKPKDTLMISRTPVTCVVVDVSHEDPEVKFNWYVD GVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLN GKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTL PSREEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPE NNYKTTTPVLDSGDSFFLYSKLTVDKSRWQQGNVFS CSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 244	HC DNA	GATATACAGCTTCAGGAGTCAGGACCTGGCCTCGT GAAACCTTCTCAGTCTCTGTCTCTCACCTGCTCTGT CACTGGCTACTCCATCACCAGTGGTTATTACTGGA ACTGGATCCGGCAGTTTCCAGGAAACAACTGGA ATGGATGGGCTACATAAGCTACGACGGTGACAAT AACTACAACCCATCTCTCAAAAATCGAATCTCCAT CACTCGTGACACATCTAAGAACCAGTTTTCTCTGA AGTTGAGTTCTGTGACTACTGAGGACACAGCTACA TATTACTGTGCAGGAGGCTACTATAGGTACGGCCT GGGCTCCTACTCCGGCTCGTATTACTATGTTATGG ACTACTGGGGTCAAGGAACCTCAGTCACCGTCTCC TCAGCTAGCACCAAGGGCCCAAGTGTTTCCCCT GGCCCCCAGCAGCAAGTCTACTTCCGGCGGAACCTG CTGCCCTGGGTTGCCTGGTGAAGGACTACTTCCCC GAGCCCCGTGACAGTGTCTGGAACCTCTGGGGCTCT GACTTCCGGCGTGACACCTTCCCCGCCGTGCTGC AGAGCAGCGGCCTGTACAGCCTGAGCAGCGTGGT GACAGTGCCCTCCAGCTCTCTGGGAACCCAGACCT ATATCTGCAACGTGAACCACAAGCCAGCAACACC AAGGTGGACAAGAGAGTGGAGCCCAAGAGCTGCG ACAAGACCCACACCTGCCCCCCTGCCAGCTCCA GAACTGCTGGGAGGGCCTTCCGTGTTCTCTGTTCCC CCCAAGCCCAAGGACACCCTGATGATCAGAGG ACCCCCGAGGTGACCTGCGTGGTGGTGACGTGTC CCACGAGGACCCAGAGGTGAAGTTCAACTGGTAC

		GTGGACGGCGTGGAGGTGCACAACGCCAAGACCA AGCCCAGAGAGGAGCAGTACAACAGCACCTACAG GGTGGTGTCCGTGCTGACCGTGTGCACCAGGACT GGCTGAACGGCAAAGAATACAAGTGCAAAGTCTC CAACAAGGCCCTGCCAGCCCCAATCGAAAAGACA ATCAGCAAGGCCAAGGGCCAGCCACGGGAGCCCC AGGTGTACACCCCTGCCCCCAGCCGGGAGGAGAT GACCAAGAACCAGGTGTCCCTGACCTGTCTGGTGA AGGGCTTCTACCCCAGCGATATCGCCGTGGAGTGG GAGAGCAACGGCCAGCCCGAGAACAACACTACAAGA CCACCCCCCAGTGCTGGACAGCGACGGCAGCTTC TTCCTGTACAGCAAGCTGACCGTGGACAAGTCCAG GTGGCAGCAGGGCAACGTGTTCAGCTGCAGCGTG ATGCACGAGGCCCTGCACAACCACTACACCCAGA AGTCCCTGAGCCTGAGCCCCGGCAAG
SEQ ID NO: 61	LCDR1 (KABAT)	KASQSVDDYDGN SYMN
SEQ ID NO: 51	LCDR2 (KABAT)	AASNLES
SEQ ID NO: 52	LCDR3 (KABAT)	QQSNE DPPT
SEQ ID NO: 62	LCDR1 (CHOTHIA)	SQSVDDYDGN SY
SEQ ID NO: 54	LCDR2 (CHOTHIA)	AAS
SEQ ID NO: 55	LCDR3 (CHOTHIA)	SNEDPP
SEQ ID NO: 61	LCDR1 (COMBINED)	KASQSVDDYDGN SYMN
SEQ ID NO: 51	LCDR2 (COMBINED)	AASNLES
SEQ ID NO: 52	LCDR3 (COMBINED)	QQSNE DPPT
SEQ ID NO: 63	LCDR1 (IMGT)	QSVDDYDGN SY
SEQ ID NO: 54	LCDR2 (IMGT)	AAS
SEQ ID NO: 52	LCDR3 (IMGT)	QQSNE DPPT
SEQ ID NO: 229	VL	DTVLTQSPASLAVSLGQRATISCKASQSVDDYDGN SY MNWYQQKPGQPPKLLIYAASNLESGIPARFSGSGGT DFTLNHPVEEEDAATYYCQQSNE DPPTFGGGTKLEI K
SEQ ID NO: 230	VL DNA	GACACTGTGCTGACCCAATCTCCAGCCTCTTTGGC TGTGTCTCTAGGGCAGAGGGCCACCATCTCCTGCA AGGCCAGCCAAAGTGTTGATTATGATGGTAATAGT TATATGAACTGGTACCAACAGAAACCAGGACAGC CACCCAAACTCCTCATCTATGCTGCATCCAATCTA GAATCTGGGATCCCAGCCAGGTTTAGTGGCAGTGG GTCTGGGACAGACTTCACCCTCAACATCCATCCTG TGGAGGAGGAGGATGCTGCAACCTATTACTGTCAG CAAAGTAATGAGGATCCTCCGACGTTCCGTGGAGG CACCAAGCTGGAAATCAAA
SEQ ID NO: 231	LC	DTVLTQSPASLAVSLGQRATISCKASQSVDDYDGN SY MNWYQQKPGQPPKLLIYAASNLESGIPARFSGSGGT DFTLNHPVEEEDAATYYCQQSNE DPPTFGGGTKLEI KRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPRE AKVQWKVDNALQSGNSQESVTEQDSKDSYSTLSSTL TLISKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 232	LC DNA	GACACTGTGCTGACCCAATCTCCAGCCTCTTTGGC TGTGTCTCTAGGGCAGAGGGCCACCATCTCCTGCA AGGCCAGCCAAAGTGTTGATTATGATGGTAATAGT TATATGAACTGGTACCAACAGAAACCAGGACAGC CACCCAAACTCCTCATCTATGCTGCATCCAATCTA GAATCTGGGATCCCAGCCAGGTTTAGTGGCAGTGG GTCTGGGACAGACTTCACCCTCAACATCCATCCTG

		TGGAGGAGGAGGATGCTGCAACCTATTACTGTCTAG CAAAGTAATGAGGATCCTCCGACGTTCGGTGGAGG CACCAAGCTGGAAATCAAACGTACGGTGGCCGCTC CCAGCGTGTTCATCTTCCCCCAGCGACGAGCAG CTGAAGAGTGGCACC GCCAGCGTGGTGTGCCTGCT GAACAACCTTCTACCCCGGGAGGCCAAGGTGCAGT GGAAGGTGGACAACGCCCTGCAGAGCGGCAACAG CCAGGAGAGCGTCACCGAGCAGGACAGCAAGGAC TCCACCTACAGCCTGAGCAGCACCTGACCCTGAG CAAGGCCGACTACGAGAAGCATAAGGTGTACGCC TGCGAGGTGACCCACCAGGGCCTGTCCAGCCCCGT GACCAAGAGCTTCAACAGGGGCGAGTGC
ANTI-HUMAN ENTPD2 MAB19		
SEQ ID NO: 1	HCDR1 (KABAT)	DYNMD
SEQ ID NO: 245	HCDR2 (KABAT)	DINPNYDITYNQRFKG
SEQ ID NO: 246	HCDR3 (KABAT)	RGFFPYGNSYYYFDV
SEQ ID NO: 4	HCDR1 (CHOTHIA)	GYTFTDY
SEQ ID NO: 247	HCDR2 (CHOTHIA)	NPNYDI
SEQ ID NO: 246	HCDR3 (CHOTHIA)	RGFFPYGNSYYYFDV
SEQ ID NO: 6	HCDR1 (COMBINED)	GYTFTDYNMD
SEQ ID NO: 245	HCDR2 (COMBINED)	DINPNYDITYNQRFKG
SEQ ID NO: 246	HCDR3 (COMBINED)	RGFFPYGNSYYYFDV
SEQ ID NO: 7	HCDR1 (IMGT)	GYTFTDYN
SEQ ID NO: 248	HCDR2 (IMGT)	INPNYDIT
SEQ ID NO: 249	HCDR3 (IMGT)	ARRGFFPYGNSYYYFDV
SEQ ID NO: 250	VH	EVQLQQFGAELVKPGTSVKISCKASGYTFTDYNMD WVKQSHGKSLEWIGDINPNYDITYNQRFKGKATLT VDKSSSTAYMELRSLTSEDVAVYYCARRGFFPYGN SYYYFDVWGAGTTVTVSS
SEQ ID NO: 251	VH DNA	GAGGTCCAGCTGCAACAGTTTGGAGCTGAGCTGGT GAAGCCTGGGACTTCAGTGAAGATATCCTGCAAGG CTTCTGGCTACACATTCAGTACTACAACATGGAC TGGGTGAAGCAGAGCCATGGAAAGAGCCTTGAGT GGATTGGAGATATTAATCCTAACTATGATATTACT ACCTACAACCAGAGGTTCAAGGGAAAGGCCACAT TGACTGTAGACAAGTCCTCCAGCACAGCCTACATG GAGCTCCGCAGCCTGACATCTGAGGACACTGCAGT CTATTACTGTGCAAGAAGAGGATTTTTTCCTTATTA CGGTAATAGCTACTATTACTTCGATGTCTGGGGCG CAGGGACCACGGTCACCGTCTCCTCA
SEQ ID NO: 252	HC	EVQLQQFGAELVKPGTSVKISCKASGYTFTDYNMD WVKQSHGKSLEWIGDINPNYDITYNQRFKGKATLT VDKSSSTAYMELRSLTSEDVAVYYCARRGFFPYGN SYYYFDVWGAGTTVTVSSASTKGPSVFPLAPSSKSTS GGTAALGCLVKDYFPEPTVSWNSGALTSGVHTFPA VLQSSGLYSLSSVTPSSSLGTQTYICNVNHKPSNT KVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPK PKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGV EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGK EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPS REEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSS VMHEALHNHYTQKSLSPGK

SEQ ID NO: 253	HC DNA	GAGGTCCAGCTGCAACAGTTTGGAGCTGAGCTGGT GAAGCCTGGGACTTCAGTGAAGATATCCTGCAAGG CTTCTGGCTACACATTCACTGACTACAACATGGAC TGGGTGAAGCAGAGCCATGGAAAGAGCCTTGAGT GGATTGGAGATATTAATCCTAACTATGATATTACT ACCTACAACCAGAGGTTCAAGGGAAAGGCCACAT TGACTGTAGACAAGTCCTCCAGCACAGCCTACATG GAGCTCCGAGCCTGACATCTGAGGACACTGCAGT CTATTACTGTGCAAGAAGAGGATTTTTTCCTTATTA CGGTAATAGCTACTATTACTTCGATGTCTGGGGCG CAGGGACCACGGTCACCGTCTCCTCAGCTAGCACC AAGGGCCCAAGTGTGTTTCCCCTGGCCCCCAGCAG CAAGTCTACTTCCGGCGGAAGTGTGCCCTGGGTT GCCTGGTGAAGGACTACTTCCCCGAGCCCCGTGACA GTGTCCTGGAAGTCTGGGGCTCTGACTTCCGGCGT GCACACCTTCCCCGCCGTGCTGCAGAGCAGCGGCC TGTACAGCCTGAGCAGCGTGGTGACAGTGCCCTCC AGCTCTCTGGGAACCCAGACCTATATCTGCAACGT GAACCACAAGCCCAGCAACACCAAGGTGGACAAG AGAGTGGAGCCCAAGAGCTGCGACAAGACCCACA CCTGCCCCCCTGCCAGCTCCAGAACTGCTGGGA GGGCCTTCCGTGTTCTGTTCCTGTTCCCCCAGCCAA GGACACCTGATGATCAGCAGGACCCCCGAGGTG ACCTGCGTGGTGGTGGACGTGTCCACGAGGACCC AGAGGTGAAGTTCAACTGGTACGTGGACGGCGTG GAGGTGCACAACGCCAAGACCAAGCCCAGAGAGG AGCAGTACAACAGCACCTACAGGGTGGTGTCCGTG CTGACCGTGTGTCACCAGGACTGGCTGAACGGCAA AGAATACAAGTGCAAAGTCTCCAACAAGGCCCTG CCAGCCCCAATCGAAAAGACAATCAGCAAGGCCA AGGGCCAGCCACGGGAGCCCCAGGTGTACACCT GCCCCCAGCCGGGAGGAGATGACCAAGAACCAG GTGTCCCTGACCTGTCTGGTGAAGGGCTTCTACCC CAGCGATATCGCCGTGGAGTGGGAGAGCAACGGC CAGCCCGAGAACAACACTACAAGACCACCCCCCAG TGCTGGACAGCGACGGCAGCTTCTTCTGTACAGC AAGCTGACCGTGGACAAGTCCAGGTGGCAGCAGG GCAACGTGTTAGCTGCAGCGTGATGCACGAGGCC CTGCACAACCACTACACCCAGAAGTCCCTGAGCCT GAGCCCCGGCAAG
SEQ ID NO: 254	LCDR1 (KABAT)	SASSSVSYMH
SEQ ID NO: 15	LCDR2 (KABAT)	STSNLAS
SEQ ID NO: 255	LCDR3 (KABAT)	HQWSNYPWT
SEQ ID NO: 17	LCDR1 (CHOTHIA)	SSSVSY
SEQ ID NO: 18	LCDR2 (CHOTHIA)	STS
SEQ ID NO: 256	LCDR3 (CHOTHIA)	WSNYPW
SEQ ID NO: 254	LCDR1 (COMBINED)	SASSSVSYMH
SEQ ID NO: 15	LCDR2 (COMBINED)	STSNLAS
SEQ ID NO: 255	LCDR3 (COMBINED)	HQWSNYPWT
SEQ ID NO: 20	LCDR1 (IMGT)	SSSVSY
SEQ ID NO: 18	LCDR2 (IMGT)	STS
SEQ ID NO: 255	LCDR3 (IMGT)	HQWSNYPWT

SEQ ID NO: 257	VL	QIVLTQSPTIMSASLGEEITLTCSASSSVSYMHWYQQ KSGTSPKLLIYSTSNLASGVPSRFSGSGSGTFYSLTISS VEAEDAADYYCHQWSNYPWTFGGGKLEIK
SEQ ID NO: 258	VL DNA	CAAATTGTTCTCACCCAGTCTCCAACAATCATGTCT GCATCTCTAGGGGAGGAGATCACCTTACCTGCAG TGCCAGCTCGAGTGTAAGTTACATGCACTGGTACC AGCAGAAGTCAGGCACTTCTCCCAAACCTTGATT TATAGCACATCCAACCTGGCTTCTGGAGTCCCTTCT CGCTTCAGTGGCAGTGGGTCTGGGACCTTTTATTCT CTCACAATCAGCAGTGTGGAGGCTGAAGATGCTGC CGATTATTACTGCCATCAGTGGAGTAATTATCCAT GGACGTTTCGGTGGAGGCACCAAGCTGGAAATCAA A
SEQ ID NO: 259	LC	QIVLTQSPTIMSASLGEEITLTCSASSSVSYMHWYQQ KSGTSPKLLIYSTSNLASGVPSRFSGSGSGTFYSLTISS VEAEDAADYYCHQWSNYPWTFGGGKLEIKRTVAA PSVFIFPPSDEQLKSGTASVVCLNNFYPREAKVQWK VDNALQSGNSQESVTEQDSKDYSLSTLTLSKADY EKHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 260	LC DNA	CAAATTGTTCTCACCCAGTCTCCAACAATCATGTCT GCATCTCTAGGGGAGGAGATCACCTTACCTGCAG TGCCAGCTCGAGTGTAAGTTACATGCACTGGTACC AGCAGAAGTCAGGCACTTCTCCCAAACCTTGATT TATAGCACATCCAACCTGGCTTCTGGAGTCCCTTCT CGCTTCAGTGGCAGTGGGTCTGGGACCTTTTATTCT CTCACAATCAGCAGTGTGGAGGCTGAAGATGCTGC CGATTATTACTGCCATCAGTGGAGTAATTATCCAT GGACGTTTCGGTGGAGGCACCAAGCTGGAAATCAA ACGTACGGTGGCCGCTCCCAGCGTGTTCATCTTCC CCCCCAGCGACGAGCAGCTGAAGAGTGGCACCGC CAGCGTGGTGTGCCTGCTGAACAACCTTCTACCCCC GGGAGGCCAAGGTGCAGTGGAAGGTGGACAACGC CCTGCAGAGCGGCAACAGCCAGGAGAGCGTCACC GAGCAGGACAGCAAGGACTCCACCTACAGCCTGA GCAGCACCTGACCCTGAGCAAGGCCGACTACGA GAAGCATAAGGTGTACGCCTGCGAGGTGACCCAC CAGGGCCTGTCCAGCCCCGTGACCAAGAGCTTCAA CAGGGGCGAGTGC
ANTI-HUMAN ENTPD2 MAB20		
SEQ ID NO: 1	HCDR1 (KABAT)	DYNMD
SEQ ID NO: 261	HCDR2 (KABAT)	DINPNYDITSYNQKFKG
SEQ ID NO: 262	HCDR3 (KABAT)	RGFFLYYGSSYYYFDV
SEQ ID NO: 4	HCDR1 (CHOTHIA)	GYTFTDY
SEQ ID NO: 247	HCDR2 (CHOTHIA)	NPNYDI
SEQ ID NO: 262	HCDR3 (CHOTHIA)	RGFFLYYGSSYYYFDV
SEQ ID NO: 6	HCDR1 (COMBINED)	GYTFTDYNMD
SEQ ID NO: 261	HCDR2 (COMBINED)	DINPNYDITSYNQKFKG
SEQ ID NO: 262	HCDR3 (COMBINED)	RGFFLYYGSSYYYFDV
SEQ ID NO: 7	HCDR1 (IMGT)	GYTFTDYN
SEQ ID NO: 248	HCDR2 (IMGT)	INPNYDIT
SEQ ID NO: 263	HCDR3 (IMGT)	ARRGFFLYYGSSYYYFDV
SEQ ID NO: 264	VH	EVQLQQFGAELVKPGASVKISCKASGYTFTDYNMD WVKQSHGKSLEWIGDINPNYDITSYNQKFKGKATLT

		VDKSSSTAYMELRSLTSEDVAVYYCARRGFFLYYGS SYYYFDVWGAGTTVTVSS
SEQ ID NO: 265	VH DNA	GAGGTCCAGCTGCAACAGTTTGGAGCTGAGCTGGT GAAGCCTGGGGCTTCAGTGAAGATATCCTGCAAGG CTTCTGGCTACACATTCAGTACTACAACATGGAC TGGGTGAAGCAGAGCCATGGAAAGAGCCTTGAGT GGATTGGAGATATTAATCCTAACTATGATATTACT AGCTACAACCAGAAAGTTCAAGGGAAAGGCCACAT TGACTGTAGACAAGTCCTCCAGCACAGCCTACATG GAGCTCCGCAGCCTGACATCTGAGGACACTGCAGT CTATTACTGTGCAAGAAGAGGGTTTTTCTTTACTA CGGTAGTAGCTACTATTACTTCGATGTCTGGGGCG CAGGGACCACGGTCACCGTCTCCTCA
SEQ ID NO: 266	HC	EVQLQQFGAELVKPGASVKISCKASGYTFTDYNMD WVKQSHGKSLEWIGDINPNYDITSYNQKFKGKATLT VDKSSSTAYMELRSLTSEDVAVYYCARRGFFLYYGS SYYYFDVWGAGTTVTVSSASTKGPSVFPLAPSSKSTS GGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPA VLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNT KVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPK PKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGV EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGK EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPS REEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN YKTTTPVLDSGFSFLYSKLTVDKSRWQQGNVFCSS VMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 267	HC DNA	GAGGTCCAGCTGCAACAGTTTGGAGCTGAGCTGGT GAAGCCTGGGGCTTCAGTGAAGATATCCTGCAAGG CTTCTGGCTACACATTCAGTACTACAACATGGAC TGGGTGAAGCAGAGCCATGGAAAGAGCCTTGAGT GGATTGGAGATATTAATCCTAACTATGATATTACT AGCTACAACCAGAAAGTTCAAGGGAAAGGCCACAT TGACTGTAGACAAGTCCTCCAGCACAGCCTACATG GAGCTCCGCAGCCTGACATCTGAGGACACTGCAGT CTATTACTGTGCAAGAAGAGGGTTTTTCTTTACTA CGGTAGTAGCTACTATTACTTCGATGTCTGGGGCG CAGGGACCACGGTCACCGTCTCCTCAGCTAGCACC AAGGGCCCAAGTGTGTTTCCCCTGGCCCCCAGCAG CAAGTCTACTTCCGGCGGAAGTCTGCCCTGGGTT GCCTGGTGAAGGACTACTTCCCCGAGCCCCGTGACA GTGTCCTGGAAGTCTGGGGCTCTGACTTCCGGCGT GCACACCTTCCCCGCCGTGCTGCAGAGCAGCGCC TGACAGCCTGAGCAGCGTGGTGACAGTGCCCTCC AGCTCTCTGGGAACCCAGACCTATATCTGCAACGT GAACCACAAGCCCAGCAACACCAAGGTGGACAAG AGAGTGGAGCCCAAGAGCTGCGACAAGACCCACA CCTGCCCCCCTGCCAGCTCCAGAACTGCTGGGA GGGCCTTCCGTGTTCTGTTCCTGTTCCCCCAGGCCAA GGACACCCTGATGATCAGCAGGACCCCCGAGGTG ACCTGCGTGGTGGTGGACGTGTCCACGAGGACCC AGAGGTGAAGTTCAACTGGTACGTGGACGGCGTG GAGGTGCACAACGCCAAGACCAAGCCAGAGAGG AGCAGTACAACAGCACCTACAGGGTGGTGTCCGTG CTGACCGTGCTGCACCAGGACTGGCTGAACGGCAA AGAATACAAGTGCAAAGTCTCCAACAAGGCCCTG CCAGCCCCAATCGAAAAGACAATCAGCAAGGCCA AGGGCCAGCCACGGGAGCCCCAGGTGTACACCCT GCCCCCAGCCGGGAGGAGATGACCAAGAACCAG GTGTCCCTGACCTGTCTGGTGAAGGGCTTCTACCC CAGCGATATCGCCGTGGAGTGGGAGAGCAACGGC

		CAGCCCGAGAACAACACTACAAGACCACCCCCCAG TGCTGGACAGCGACGGCAGCTTCTTCTGTACAGC AAGCTGACCGTGGACAAGTCCAGGTGGCAGCAGG GCAACGTGTTTCAGCTGCAGCGTGATGCACGAGGCC CTGCACAACCACTACACCCAGAAGTCCCTGAGCCT GAGCCCCGGCAAG
SEQ ID NO: 254	LCDR1 (KABAT)	SASSSVSYMH
SEQ ID NO: 15	LCDR2 (KABAT)	STSNLAS
SEQ ID NO: 16	LCDR3 (KABAT)	HQWSSYPWT
SEQ ID NO: 17	LCDR1 (CHOTHIA)	SSSVSY
SEQ ID NO: 18	LCDR2 (CHOTHIA)	STS
SEQ ID NO: 19	LCDR3 (CHOTHIA)	WSSYPW
SEQ ID NO: 254	LCDR1 (COMBINED)	SASSSVSYMH
SEQ ID NO: 15	LCDR2 (COMBINED)	STSNLAS
SEQ ID NO: 16	LCDR3 (COMBINED)	HQWSSYPWT
SEQ ID NO: 20	LCDR1 (IMGT)	SSSVSY
SEQ ID NO: 18	LCDR2 (IMGT)	STS
SEQ ID NO: 16	LCDR3 (IMGT)	HQWSSYPWT
SEQ ID NO: 268	VL	QIVLTQSPAISASLGEIITLCSASSSVSYMHWYQQ KSGTSPKLLIYSTSNLASGVPSRFSGSGSGTFYSLTISS VEAEDAADYYCHQWSSYPWTFGGGKLEIK
SEQ ID NO: 269	VL DNA	CAAATTGTTCTCACCCAGTCTCCAGCAATCATGTCT GCATCTCTAGGGGAGGAGATCACCTAACCTGCAG TGCCAGCTCGAGTGTAAGTTACATGCACTGGTACC AGCAGAAGTCAGGCACTTCTCCAAACTCTTGATT TATAGCACATCCAACCTGGCTTCTGGAGTCCCTTCT CGCTTCAGTGGCAGTGGGTCTGGGACCTTTTATTCT CTCACAATCAGCAGTGTGGAGGCTGAAGATGCTGC CGATTATTACTGCCATCAGTGGAGTAGTTATCCAT GGACGTTTCGGTGGAGGCACCAAGCTGGAAATCAA A
SEQ ID NO: 270	LC	QIVLTQSPAISASLGEIITLCSASSSVSYMHWYQQ KSGTSPKLLIYSTSNLASGVPSRFSGSGSGTFYSLTISS VEAEDAADYYCHQWSSYPWTFGGGKLEIKRTVAA PSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWK VDNALQSGNSQESVTEQDSKSTYLSSTLTLKADY EKHKVYACEVTHQGLSPVTKSFNRGEC
SEQ ID NO: 271	LC DNA	CAAATTGTTCTCACCCAGTCTCCAGCAATCATGTCT GCATCTCTAGGGGAGGAGATCACCTAACCTGCAG TGCCAGCTCGAGTGTAAGTTACATGCACTGGTACC AGCAGAAGTCAGGCACTTCTCCAAACTCTTGATT TATAGCACATCCAACCTGGCTTCTGGAGTCCCTTCT CGCTTCAGTGGCAGTGGGTCTGGGACCTTTTATTCT CTCACAATCAGCAGTGTGGAGGCTGAAGATGCTGC CGATTATTACTGCCATCAGTGGAGTAGTTATCCAT GGACGTTTCGGTGGAGGCACCAAGCTGGAAATCAA ACGTACGGTGGCCGCTCCCAGCGTGTTTCATCTTCC CCCCCAGCGACGAGCAGCTGAAGAGTGGCACCGC CAGCGTGGTGTGCCTGCTGAACAACCTTCTACCCCC GGGAGGCCAAGGTGCAGTGGAAGGTGGACAACGC CCTGCAGAGCGGCAACAGCCAGGAGAGCGTCACC GAGCAGGACAGCAAGGACTCCACCTACAGCCTGA GCAGCACCTGACCCTGAGCAAGGCCGACTACGA GAAGCATAAGGTGTACGCCTGCGAGGTGACCCAC

		CAGGGCCTGTCCAGCCCCGTGACCAAGAGCTTCAA CAGGGGCGAGTGC
ANTI-HUMAN ENTPD2 MAB21		
SEQ ID NO: 272	HCDR1 (KABAT)	EYTMH
SEQ ID NO: 273	HCDR2 (KABAT)	GINPNNGITYNQKFKG
SEQ ID NO: 274	HCDR3 (KABAT)	RGFPYYGYGTSLYYFDY
SEQ ID NO: 275	HCDR1 (CHOTHIA)	GYTFTEY
SEQ ID NO: 276	HCDR2 (CHOTHIA)	NPNNGI
SEQ ID NO: 274	HCDR3 (CHOTHIA)	RGFPYYGYGTSLYYFDY
SEQ ID NO: 277	HCDR1 (COMBINED)	GYTFTEYTMH
SEQ ID NO: 273	HCDR2 (COMBINED)	GINPNNGITYNQKFKG
SEQ ID NO: 274	HCDR3 (COMBINED)	RGFPYYGYGTSLYYFDY
SEQ ID NO: 278	HCDR1 (IMGT)	GYTFTEYT
SEQ ID NO: 279	HCDR2 (IMGT)	INPNNGIT
SEQ ID NO: 280	HCDR3 (IMGT)	ARRGFPYYGYGTSLYYFDY
SEQ ID NO: 281	VH	EVQLQQSGPELVKPGASVKISCKTSGYTFTEYTMHW VKQSHGKSLEWIGGINPNNGITYNQKFKGKATLTV DKSSSTAYMDLRSLTSEGSAVYYCARRGFPYYGYGTS LYYFDYWGQGTTLTVSS
SEQ ID NO: 282	VH DNA	GAGGTCCAGCTGCAACAGTCTGGACCTGAGCTGGT GAAGCCTGGGGCTTCAGTGAAGATATCCTGCAAGA CTTCTGGATACACATTCAGTGAATACACCATGCAC TGGGTGAAGCAGAGCCATGGAAAGAGCCTTGAGT GGATTGGAGGTATTAATCCTAACAAATGGTATTACT ACTTACAACCAGAAAGTTCAAGGGCAAGGCCACATT GACTGTAGACAAGTCCTCCAGCACAGCCTACATGG ACCTCCGACGCTGACATCTGAGGGTTCTGCAGTC TATTACTGTGCAAGAAGGGGATTCCCTATTTATTA CTACGGTACTAGCCTCTACTACTTTGACTACTGGG GCCAAGGCACCACTCTCACAGTCTCCTCA
SEQ ID NO: 283	HC	EVQLQQSGPELVKPGASVKISCKTSGYTFTEYTMHW VKQSHGKSLEWIGGINPNNGITYNQKFKGKATLTV DKSSSTAYMDLRSLTSEGSAVYYCARRGFPYYGYGTS LYYFDYWGQGTTLTVSSASTKGPSVFPLAPSSKSTSG GTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV LQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKP KDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGV EVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGK EYKCKVSNKALPAPIEKISKAKGQPREPQVYTLPPS REEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENN YKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVFCSS VMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 284	HC DNA	GAGGTCCAGCTGCAACAGTCTGGACCTGAGCTGGT GAAGCCTGGGGCTTCAGTGAAGATATCCTGCAAGA CTTCTGGATACACATTCAGTGAATACACCATGCAC TGGGTGAAGCAGAGCCATGGAAAGAGCCTTGAGT GGATTGGAGGTATTAATCCTAACAAATGGTATTACT ACTTACAACCAGAAAGTTCAAGGGCAAGGCCACATT GACTGTAGACAAGTCCTCCAGCACAGCCTACATGG ACCTCCGACGCTGACATCTGAGGGTTCTGCAGTC TATTACTGTGCAAGAAGGGGATTCCCTATTTATTA CTACGGTACTAGCCTCTACTACTTTGACTACTGGG

		GCCAAGGCACCACTCTCACAGTCTCCTCAGCTAGC ACCAAGGGCCCAAGTGTGTTTCCCCTGGCCCCCAG CAGCAAGTCTACTTCCGGCGGAAGTGTGCCCTGG GTTGCCTGGTGAAGGACTACTTCCCCGAGCCCGTG ACAGTGTCTTGAAGTCTGGGGCTCTGACTTCCGG CGTGACACCTTCCCCGCCGTGCTGCAGAGCAGCG GCCTGTACAGCCTGAGCAGCGTGGTGACAGTGCCC TCCAGCTCTCTGGGAACCCAGACCTATATCTGCAA CGTGAACCACAAGCCCAGCAACACCAAGGTGGAC AAGAGAGTGGAGCCCAAGAGCTGCGACAAGACCC ACACCTGCCCCCCTGCCAGCTCCAGAAGTGTG GGAGGGCCTTCCGTGTTCTGTTCCCCCCCCAAGCC CAAGGACACCCTGATGATCAGCAGGACCCCCGAG GTGACCTGCGTGGTGGTGGACGTGTCCACGAGGA CCCAGAGGTGAAGTTCAACTGGTACGTGGACGGC GTGGAGGTGCACAACGCCAAGACCAAGCCCAGAG AGGAGCAGTACAACAGCACCTACAGGGTGGTGTG CGTGCTGACCGTGCTGCACCAGGACTGGCTGAACG GCAAAGAATACAAGTGCAAAGTCTCCAACAAGGC CCTGCCAGCCCCAATCGAAAAGACAATCAGCAAG GCCAAGGGCCAGCCACGGGAGCCCCAGGTGTACA CCCTGCCCCCAGCCGGGAGGAGATGACCAAGAA CCAGGTGTCCCTGACCTGTCTGGTGAAGGGCTTCT ACCCCAGCGATATCGCCGTGGAGTGGGAGAGCAA CGGCCAGCCCCGAGAACAATAAGACCACCCCC CCAGTGCTGGACAGCGACGGCAGCTTCTTCCTGTA CAGCAAGCTGACCGTGGACAAGTCCAGGTGGCAG CAGGGCAACGTGTTTCTGCTGCAGCGTGATGCACGA GGCCCTGCACAACCACTACACCCAGAAGTCCCTGA GCCTGAGCCCCGGCAAG
SEQ ID NO: 254	LCDR1 (KABAT)	SASSSVSYMH
SEQ ID NO: 285	LCDR2 (KABAT)	TTSNLAS
SEQ ID NO: 16	LCDR3 (KABAT)	HQWSSYPWT
SEQ ID NO: 17	LCDR1 (CHOTHIA)	SSSVSY
SEQ ID NO: 286	LCDR2 (CHOTHIA)	TTS
SEQ ID NO: 19	LCDR3 (CHOTHIA)	WSSYPW
SEQ ID NO: 254	LCDR1 (COMBINED)	SASSSVSYMH
SEQ ID NO: 285	LCDR2 (COMBINED)	TTSNLAS
SEQ ID NO: 16	LCDR3 (COMBINED)	HQWSSYPWT
SEQ ID NO: 20	LCDR1 (IMGT)	SSVS
SEQ ID NO: 286	LCDR2 (IMGT)	TTS
SEQ ID NO: 16	LCDR3 (IMGT)	HQWSSYPWT
SEQ ID NO: 287	VL	QIVLTQSPAIMSASLGEEITLTCSSASSSVSYMHYQQ RSGTSPKLLIYTTSNLASGVPSRFGSGSGTFYSLTSS VEAEDAADYYCHQWSSYPWTFGGGKLEIK
SEQ ID NO: 288	VL DNA	CAAATTGTTCTCACCCAGTCTCCAGCAATCATGTCT GCATCTCTAGGGGAGGAGATCACCTAACCTGCAG TGCCAGCTCGAGTGTAAGTTACATGCACTGGTACC AGCAGAGGTCAGGCATTCTCCCAAACCTCTGATT TATACCACATCCAACCTGGCTTCTGGAGTCCCTTCT CGCTTCAGTGGCAGTGGGTCTGGGACCTTTTATTCT CTCACAATCAGCAGTGTGGAGGCTGAAGATGCTGC CGATTATTACTGCCATCAGTGGAGTAGTTATCCGT

		GGACGTTTCGGTGGAGGCACCAAGCTGGAAATCAA A
SEQ ID NO: 289	LC	QIVLTQSPAIMSASLGEEITLTCSSSSVSYMHWYQQ RSGTSPKLLIYTTSNLASGVPSRFSGSGSTFYSLTISS VEAEDAADYYCHQWSSYPWTFGGGKLEIKRTVAA PSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWK VDNALQSGNSQESVTEQDSKDSYLSSTLTLKADY EKHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 290	LC DNA	CAAATTGTTCTCACCCAGTCTCCAGCAATCATGTCT GCATCTCTAGGGGAGGAGATCACCTAACCTGCAG TGCCAGCTCGAGTGTAAGTTACATGCACTGGTACC AGCAGAGGTCAGGCACTTCTCCAAACTCTTGATT TATACCACATCCAACCTGGCTTCTGGAGTCCCTTCT CGCTTCAGTGGCAGTGGGTCTGGGACCTTTTATTCT CTCACAATCAGCAGTGTGGAGGCTGAAGATGCTGC CGATTATTACTGCCATCAGTGGAGTAGTTATCCGT GGACGTTTCGGTGGAGGCACCAAGCTGGAAATCAA ACGTACGGTGGCCGCTCCCAGCGTGTTCATCTTCC CCCCAGCGACGAGCAGCTGAAGAGTGGCACC GC CAGCGTGGTGTGCCTGCTGAACAACCTTCTACCCCC GGGAGGCCAAGGTGCAGTGGAAGGTGGACAACGC CCTGCAGAGCGGCAACAGCCAGGAGAGCGTCAAC GAGCAGGACAGCAAGGACTCCACCTACAGCCTGA GCAGCACCTTGACCCTGAGCAAGGCCGACTACGA GAAGCATAAGGTGTACGCCTGCGAGGTGACCCAC CAGGGCCTGTCCAGCCCCGTGACCAAGAGCTTCAA CAGGGGCGAGTGC
ANTI-HUMAN ENTPD2 FAB22		
SEQ ID NO: 37	HCDR1 (Kabat)	SGYYWN
SEQ ID NO: 220	HCDR2 (Kabat)	YISYDGDNNYNPSLKN
SEQ ID NO: 221	HCDR3 (Kabat)	GYRYGLSYYYVMDY
SEQ ID NO: 40	HCDR1 (Chothia)	GYSITSGY
SEQ ID NO: 222	HCDR2 (Chothia)	SYDGD
SEQ ID NO: 221	HCDR3 (Chothia)	GYRYGLSYYYVMDY
SEQ ID NO: 42	HCDR1 (Combined)	GYSITSGYYWN
SEQ ID NO: 220	HCDR2 (Combined)	YISYDGDNNYNPSLKN
SEQ ID NO: 221	HCDR3 (Combined)	GYRYGLSYYYVMDY
SEQ ID NO: 43	HCDR1 (IMGT)	GYSITSGYY
SEQ ID NO: 223	HCDR2 (IMGT)	ISYDGDN
SEQ ID NO: 224	HCDR3 (IMGT)	AGGYRYGLSYYYVMDY
SEQ ID NO: 328	VH	EVKLEQSGPGLVKPSQSLTCSVTGYSITSGYYWN WIRQFPGNKLEWMSYISYDGDNNYNPSLKNRISITRD TSKNQFFLKLSSVTEDTATYYCAGGYRYGLSYYY VMDYWGQGSVTVSA
SEQ ID NO: 329	VH DNA	GAAGTGAAGCTGGAGCAGTCAGGACCTGGCCTCG TGAAACCTTCTCAGTCTCTGTCTCTCACCTGCTCTG TCACTGGCTACTCCATCACCAAGTGGTTATTACTGG AACTGGATCCGGCAGTTTCCAGGAAACAACTGG AATGGATGAGCTACATAAGCTACGACGGTGACAA TAATAACAACCATCTCTCAAAAATCGAATCCCA TCACTCGTGACACATCTAAGAACCAGTTTTCTCTG AAGTTGAGTTCTGTGACTACTGAGGACACAGCTAC ATATTACTGTGCAGGAGGCTACTATAGGTACGGCC TGTCGTATTACTATGTTATGGACTACTGGGGTCAA GGAACCTCAGTCACAGTCTCCGCA

SEQ ID NO: 330	HC	EVKLEQSGPGLVKPSQSLTCSVTGYSITSGYYWN WIRQFPGNKLEWMSYISYDGDNNYNPSLKNRISITRD TSKNQFFLLKSSVTTEDTATYYCAGGYRYGLSYYY VMDYWGQGTSVTVSAASTKGPSVFPLAPSSKSTSGG TAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVL QSSGLYSLSSVVPSSSLGTQTYICNVNHKPSNTKV DKRVEPKSC
SEQ ID NO: 331	HC DNA	GAAGTGAAGCTGGAGCAGTCAGGACCTGGCCTCG TGAAACCTTCTCAGTCTCTGTCTCTCACCTGCTCTG TCACTGGCTACTCCATCACCAGTGGTTATTACTGG AACTGGATCCGGCAGTTTCCAGGAAACAACTGG AATGGATGAGCTACATAAGCTACGACGGTGACAA TAACTACAACCCATCTCTCAAAAATCGAATCTCCA TCACTCGTGACACATCTAAGAACCAGTTTTTCCTG AAGTTGAGTTCTGTGACTACTGAGGACACAGCTAC ATATTACTGTGCAGGAGGCTACTATAGGTACGGCC TGTCGTATTACTATGTTATGGACTACTGGGGTCAA GGAACCTCAGTCACAGTCTCCGCAgctagcaccagggcc aagtgtgttccctggccccagcagcaagtctactccggcggaactgtgccct gggttgccctgggaaggactacttccccgagccgtgacagtgtcctggaactctg gggtctgacttccggcgtgcacacctccccgccgtgctgcagagcagcgccct gtacagcctgagcagcgtgggtgacagtgcctccagctctctgggaaccagacct atatctgaacgtgaaccacaagcccagcaacaccaaggtggacaagagagtgga agcccaagagctgc
SEQ ID NO: 61	LCDR1 (Kabat)	KASQSVDDYDGN SYMN
SEQ ID NO: 51	LCDR2 (Kabat)	AASNLES
SEQ ID NO: 52	LCDR3 (Kabat)	QQSNE DPPT
SEQ ID NO: 62	LCDR1 (Chothia)	SQSVDDYDGN SY
SEQ ID NO: 54	LCDR2 (Chothia)	AAS
SEQ ID NO: 55	LCDR3 (Chothia)	SNEDPP
SEQ ID NO: 61	LCDR1 (Combined)	KASQSVDDYDGN SYMN
SEQ ID NO: 51	LCDR2 (Combined)	AASNLES
SEQ ID NO: 52	LCDR3 (Combined)	QQSNE DPPT
SEQ ID NO: 63	LCDR1 (IMGT)	QSVDDYDGN SY
SEQ ID NO: 54	LCDR2 (IMGT)	AAS
SEQ ID NO: 52	LCDR3 (IMGT)	QQSNE DPPT
SEQ ID NO: 332	VL	DIKMTQSPASLAVSLGQRATISCKASQSVDDYDGN SY MNWYQQKPGQPPLLIYAASNLESGIPARFSGSGSGT DFTLNHPVEEEDAATYYCQQSNE DPPTFGGGTKLEL K
SEQ ID NO: 333	VL DNA	GATATTAAGATGACCCAATCTCCAGCCTCTTTGGC TGTGTCTCTAGGGCAGAGGGCCACCATCTCCTGCA AGGCCAGCCAAAGTGTTGATTATGATGGTAATAGT TATATGAACTGGTACCAACAGAAACCAGGACAGC CACCCAAACTCCTCATCTATGCTGCATCCAATCTA GAATCTGGGATCCCAGCCAGGTTTAGTGGCAGTGG GTCTGGGACAGACTTCACCCTCAACATCCATCCTG TGGAGGAGGAGGATGCTGCAACCTATTACTGTGAG CAAAGTAATGAGGATCCTCCGACGTTCCGTGGAGG CACCAGCTGGAACCTCAA
SEQ ID NO: 334	LC	DIKMTQSPASLAVSLGQRATISCKASQSVDDYDGN SY MNWYQQKPGQPPLLIYAASNLESGIPARFSGSGSGT DFTLNHPVEEEDAATYYCQQSNE DPPTFGGGTKLEL KRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPRE AKVQWKVDNALQSGNSQESVTEQDSKDSYSTLSSTL TLISKADYEHKHKVYACEVTHQGLSSPVTKSFNRGEC

SEQ ID NO: 335	LC DNA	GATATTAAGATGACCCAATCTCCAGCCTCTTTGGC TGTGTCTCTAGGGCAGAGGGCCACCATCTCCTGCA AGGCCAGCCAAAGTGTTGATTATGATGGTAATAGT TATATGAACTGGTACCAACAGAAACCAGGACAGC CACCCAAACTCCTCATCTATGCTGCATCCAATCTA GAATCTGGGATCCCAGCCAGGTTTAGTGGCAGTGG GTCTGGGACAGACTTCACCCCTCAACATCCATCCTG TGGAGGAGGAGGATGCTGCAACCTATTACTGTCTAG CAAAGTAATGAGGATCCTCCGACGTTCCGTGGAGG CACCAAGCTGGAACCTCAAACgtacgggtggccgctccagcgtgt tcatttccccccagcgagcagcgtgaagagtgccaccgagcgtggtgtg cctgctgaacaacttctacccccgggagggccaaggtgcagtggaaggtggacaac gacctgcagagcggaacagccaggagagcgtcaccgagcaggacagcaagg actccacctacgcctgagcagcaccctgacctgagcaaggccgactacgagaa gcataaggtgtacgcctgcgaggtgacccaccaggcgctgtccagccccgtgacc aagagcttcaacaggggagtgctgc
ANTI-HUMAN ENTPD2 FAB23		
SEQ ID NO: 1	HCDR1 (KABAT)	DYNMD
SEQ ID NO: 2	HCDR2 (KABAT)	DINPKYDISTYNQQFKG
SEQ ID NO: 3	HCDR3 (KABAT)	RGFFLYYGINYYYFDV
SEQ ID NO: 4	HCDR1 (CHOTHIA)	GYTFTDY
SEQ ID NO: 5	HCDR2 (CHOTHIA)	NPKYDI
SEQ ID NO: 3	HCDR3 (CHOTHIA)	RGFFLYYGINYYYFDV
SEQ ID NO: 6	HCDR1 (COMBINED)	GYTFTDYNMD
SEQ ID NO: 2	HCDR2 (COMBINED)	DINPKYDISTYNQQFKG
SEQ ID NO: 3	HCDR3 (COMBINED)	RGFFLYYGINYYYFDV
SEQ ID NO: 7	HCDR1 (IMGT)	GYTFTDYN
SEQ ID NO: 8	HCDR2 (IMGT)	INPKYDIS
SEQ ID NO: 9	HCDR3 (IMGT)	ARRGFFLYYGINYYYFDV
SEQ ID NO: 233	VH	EVQLQQFGAELVKPGASVKISCKASGYTFTDYNMD WVKQSHGKSLEWIGDINPKYDISTYNQQFKGKATLT VDKSSSTAYMELRSLTSEDVAVYYCARRGFFLYYGI NYYYFDVWGAGTTVTVSS
SEQ ID NO: 234	VH DNA	GAGGTCCAAGTCAACAGTTTGGAGCTGAACTGGT GAAGCCTGGGGCTTCAGTGAAGATATCCTGCAAGG CTTCTGGCTACACATTCAGTACTACAACATGGAC TGGGTGAAGCAGAGCCATGGAAAGAGCCTTGAGT GGATTGGAGATATTAATCCTAAGTATGATATTTCT ACCTACAATCAGCAATTCAAGGGAAAGGCCACATT GACTGTAGACAAGTCCTCCAGCACAGCCTACATGG AGCTCCGCAGCCTGACATCTGAGGACACTGCAGTCT TATTATTGTGCAAGAAGAGGCTTTTTTCTTTACTAC GGTATTAATACTACTATTACTTCGATGTCTGGGGCGC AGGGACCACGGTCACCGTCTCCTCA
SEQ ID NO: 336	HC	EVQLQQFGAELVKPGASVKISCKASGYTFTDYNMD WVKQSHGKSLEWIGDINPKYDISTYNQQFKGKATLT VDKSSSTAYMELRSLTSEDVAVYYCARRGFFLYYGI NYYYFDVWGAGTTVTVSSASTKGPSVFPLAPSSKSTS GGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPA VLQSSGLYSLSSVVTVPSSSLGTQTYICNVNHKPSNT KVDKRVEPKSC
SEQ ID NO: 337	HC DNA	GAGGTCCAAGTCAACAGTTTGGAGCTGAACTGGT GAAGCCTGGGGCTTCAGTGAAGATATCCTGCAAGG

		CTTCTGGCTACACATTCACTGACTACAACATGGAC TGGGTGAAGCAGAGCCATGGAAAGAGCCTTGAGT GGATTGGAGATATTAATCCTAAGTATGATATTTCT ACCTACAATCAGCAATTCAAGGGAAAGGCCACATT GACTGTAGACAAGTCCTCCAGCACAGCCTACATGG AGCTCCGCAGCCTGACATCTGAGGACACTGCAGTC TATTATTGTGCAAGAAGAGGCTTTTTTCTTTACTAC GGTATTAATACTACTATTACTTCGATGTCTGGGGCGC AGGGACCACGGTCACCGTCTCCTCAgctagcaccaaggc ccaagtgtgttccccctggccccagcagcaagtctacttccggcggaactgctgcc ctgggttgctggtgaaggactacttccccgagcccgtagcagtgctggaactct ggggctctgacttccggcgtgcacaccttccccgccgtgctgcagagcagcgcc tgtacagcctgagcagcgtggtgacagtgcctccagctctctgggaaccagacc tatatctgcaacgtgaaccacaagccagcaacaccaaggtggacaagagagtgg agcccaagagctgc
SEQ ID NO: 14	LCDR1 (KABAT)	SASSSVSYIH
SEQ ID NO: 15	LCDR2 (KABAT)	STSNLAS
SEQ ID NO: 16	LCDR3 (KABAT)	HQWSSYPWT
SEQ ID NO: 17	LCDR1 (CHOTHIA)	SSSVSY
SEQ ID NO: 18	LCDR2 (CHOTHIA)	STS
SEQ ID NO: 19	LCDR3 (CHOTHIA)	WSSYPW
SEQ ID NO: 14	LCDR1 (COMBINED)	SASSSVSYIH
SEQ ID NO: 15	LCDR2 (COMBINED)	STSNLAS
SEQ ID NO: 16	LCDR3 (COMBINED)	HQWSSYPWT
SEQ ID NO: 20	LCDR1 (IMGT)	SSVS
SEQ ID NO: 18	LCDR2 (IMGT)	STS
SEQ ID NO: 16	LCDR3 (IMGT)	HQWSSYPWT
SEQ ID NO: 237	VL	QIVLTQSPAIMASASLGEEITLTCSASSSVSYIHWYQQK SGTSPDLLIYSTSNLASGVPSRFSGSGSGTFYSLTISSV EAEDAADYYCHQWSSYPWTFGGGTKLEIK
SEQ ID NO: 238	VL DNA	CAAATTGTTCTCACCCAGTCTCCAGCAATCATGTCT GCATCTCTAGGGGAGGAGATCACCTAACCTGCAG TGCCAGCTCGAGTGTAAGTTACATACTGGTACC AGCAGAAGTCAGGCACTTCTCCACACTCTTGATT TATAGCACATCCAATCTGGCTTCTGGAGTCCCTTCT CGCTTCAGTGGCAGTGGGTCTGGGACCTTTTATTCT CTCACAATCAGCAGTGTGGAGGCTGAAGATGCTGC CGATTATTACTGCCATCAGTGGAGTAGTTATCCAT GGACGTTTCGGTGGAGGCACCAAGCTGGAAATCAA A
SEQ ID NO: 239	LC	QIVLTQSPAIMASASLGEEITLTCSASSSVSYIHWYQQK SGTSPDLLIYSTSNLASGVPSRFSGSGSGTFYSLTISSV EAEDAADYYCHQWSSYPWTFGGGTKLEIKRTVAAP SVFIFPPSDEQLKSGTASVVCLLNMFYPREKVKQWKV DNALQSGNSQESVTEQDSKDYSLSTLTLSKADYE KHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 240	LC DNA	CAAATTGTTCTCACCCAGTCTCCAGCAATCATGTCT GCATCTCTAGGGGAGGAGATCACCTAACCTGCAG TGCCAGCTCGAGTGTAAGTTACATACTGGTACC AGCAGAAGTCAGGCACTTCTCCACACTCTTGATT TATAGCACATCCAATCTGGCTTCTGGAGTCCCTTCT CGCTTCAGTGGCAGTGGGTCTGGGACCTTTTATTCT CTCACAATCAGCAGTGTGGAGGCTGAAGATGCTGC CGATTATTACTGCCATCAGTGGAGTAGTTATCCAT

		GGACGTTCGGTGGAGGCACCAAGCTGGAAATCAA ACGTACGGTGGCCGCTCCCAGCGTGTTTCATCTTCC CCCCCAGCGACGAGCAGCTGAAGAGTGGCACCGC CAGCGTGGTGTGCCTGCTGAACAACCTTCTACCCCC GGGAGGCCAAGGTGCAGTGGAAAGGTGGACAACGC CCTGCAGAGCGGCAACAGCCAGGAGAGCGTCACC GAGCAGGACAGCAAGGACTCCACCTACAGCCTGA GCAGCACCTTGACCCTGAGCAAGGCCGACTACGA GAAGCATAAGGTGTACGCCTGCGAGGTGACCCAC CAGGGCCTGTCCAGCCCCGTGACCAAGAGCTTCAA CAGGGGCGAGTGC

[0108] In some embodiments, the anti-human ENTPD2 antibody or antibody fragment (e.g., an antigen binding fragment) comprises a VH domain having an amino acid sequence of any VH domain described in Table 1. Other suitable anti-human ENTPD2 antibodies or antibody fragments (e.g., antigen binding fragments) can include amino acids that have been mutated, yet have at least 80, 85, 90, 95, 96, 97, 98, or 99 percent identity in the VH domain with the VH regions depicted in the sequences described in Table 1. The present disclosure in certain embodiments also provides antibodies or antibody fragments (e.g., antigen binding fragments) that specifically bind to human ENTPD2, wherein the antibodies or antibody fragments (e.g., antigen binding fragments) comprise a VH CDR having an amino acid sequence of any one of the VH CDRs listed in Table 1. In particular embodiments, the invention provides antibodies or antibody fragments (e.g., antigen binding fragments) that specifically bind to human ENTPD2, comprising (or alternatively, consist of) one, two, three, four, five or more VH CDRs having an amino acid sequence of any one of the VH CDRs listed in Table 1.

[0109] In some embodiments, the anti-human ENTPD2 antibody or antibody fragment (e.g., antigen binding fragment) comprises a VL domain having an amino acid sequence of any VL domain described in Table 1. Other suitable anti-human ENTPD2 antibodies or antibody fragments (e.g., antigen binding fragments) can include amino acids that have been mutated, yet have at least 80, 85, 90, 95, 96, 97, 98, or 99 percent identity in the VL domain with the VL regions depicted in the sequences described in Table 1. The present disclosure also provides antibodies or antibody fragments (e.g., antigen binding fragments) that specifically bind to human ENTPD2, the antibodies or antibody fragments (e.g., antigen binding fragments) comprise a VL CDR having an amino acid sequence of any one of the VL CDRs listed in Table 1. In particular, the invention provides antibodies or antibody fragments (e.g., antigen binding fragments) that specifically bind to human

ENTPD2, which comprise (or alternatively, consist of) one, two, three or more VL CDRs having an amino acid sequence of any one of the VL CDRs listed in Table 1.

[0110] Other anti-human ENTPD2 antibodies or antibody fragments (*e.g.*, antigen binding fragment) disclosed herein include amino acids that have been mutated, yet have at least 80, 85, 90, 95, 96, 97, 98, or 99 percent identity in the CDR regions with the CDR regions depicted in the sequences described in Table 1. In some embodiments, it includes mutant amino acid sequences wherein no more than 1, 2, 3, 4 or 5 amino acids have been mutated in the CDR regions when compared with the CDR regions depicted in the sequence described in Table 1.

[0111] Also provided herein are nucleic acid sequences that encode VH, VL, full length heavy chain, and full length light chain of antibodies and antigen binding fragments thereof that specifically bind to human ENTPD2, *e.g.*, the nucleic acid sequences in Table 1. Such nucleic acid sequences can be optimized for expression in mammalian cells.

[0112] Other anti-human ENTPD2 antibodies disclosed herein include those where the amino acids or nucleic acids encoding the amino acids have been mutated, yet have at least 80, 85, 90, 95, 96, 97, 98, or 99 percent identity to the sequences described in Table 1. In some embodiments, antibodies or antigen binding fragments thereof include mutant amino acid sequences wherein no more than 1, 2, 3, 4 or 5 amino acids have been mutated in the variable regions when compared with the variable regions depicted in the sequence described in Table 1, while retaining substantially the same therapeutic activity.

[0113] Since each provided antibody binds to human ENTPD2, the VH, VL, full length light chain, and full length heavy chain sequences (amino acid sequences and the nucleotide sequences encoding the amino acid sequences) can be “mixed and matched” to create other ENTPD2-binding antibodies disclosed herein. Such “mixed and matched” ENTPD2-binding antibodies can be tested using binding assays known in the art (*e.g.*, ELISAs, assays described in the Exemplification). When chains are mixed and matched, a VH sequence from a particular VH/VL pairing should be replaced with a structurally similar VH sequence. A full length heavy chain sequence from a particular full length heavy chain / full length light chain pairing should be replaced with a structurally similar full length heavy chain sequence. A VL sequence from a particular VH/VL pairing should be replaced with a structurally similar VL sequence. A full length light chain sequence from a particular full length heavy chain / full length light chain pairing should be replaced with a structurally similar full length light chain sequence.

[0114] Accordingly, in one embodiment, the invention provides an isolated monoclonal antibody or antigen binding fragment thereof having: a heavy chain variable region (VH) comprising an amino acid sequence selected from any one of SEQ ID NOs: 10, 25, 33, 46, 70, 91, 115, 132, 145, 169, 225, 233, 241, 250, 264, 281, 328; and a light chain variable region (VL) comprising an amino acid sequence selected from any one of SEQ ID NOs: 21, 29, 57, 64, 74, 78, 102, 125, 156, 178, 229, 237, 257, 268, 287, 332; wherein the antibody specifically binds to human ENTPD2.

[0115] In another embodiment, the invention provides (i) an isolated monoclonal antibody having: a full length heavy chain (HC) comprising an amino acid sequence selected from any one of SEQ ID NOs: 12, 27, 35, 48, 72, 93, 117, 134, 147, 171, 227, 235, 243, 252, 266, 283, 330; and a full length light chain (LC) comprising an amino acid sequence selected from any one of SEQ ID NOs: 23, 31, 59, 66, 76, 80, 104, 127, 158, 180, 231, 239, 259, 270, 289, 334; or (ii) a functional protein comprising an antigen binding portion thereof.

[0116] In another embodiment, the present disclosure provides human ENTPD2-binding antibodies or antibody fragments thereof that comprise the heavy chain CDR1, CDR2 and CDR3 and light chain CDR1, CDR2 and CDR3 as described in Table 1, or combinations thereof. The amino acid sequences of the VH CDR1s of the antibodies are shown in SEQ ID NOs: 1, 4, 6, 7, 37, 40, 42, 43, 82, 85, 87, 88, 106, 109, 111, 112, 136, 139, 141, 142, 160, 163, 165, 166, 185, 187, 188, 206, 207, 208, 213, 214, 215, 272, 275, 277. The amino acid sequences of the VH CDR2s of the antibodies and are shown in SEQ ID NOs: 2, 5, 8, 38, 41, 44, 83, 86, 89, 107, 110, 113, 129, 130, 131, 137, 140, 143, 161, 164, 167, 186, 189, 220, 222, 223, 245, 247, 248, 261, 273, 276, 279. The amino acid sequences of the VH CDR3s of the antibodies are shown in SEQ ID NO: 3, 39, 68, 84, 108, 138, 162, 221, 246, 262, 277, 274, 9, 45, 69, 90, 114, 144, 168, 190, 224, 249, 263, 274, 280. The amino acid sequences of the VL CDR1s of the antibodies are shown in SEQ ID NOs: 14, 17, 20, 50, 53, 56, 61, 62, 63, 95, 98, 101, 119, 122, 124, 149, 152, 155, 173, 175, 177, 198, 201, 254. The amino acid sequences of the VL CDR2s of the antibodies are shown in SEQ ID NOs: 15, 18, 51, 54, 96, 99, 120, 150, 153, 199, 285, 286. The amino acid sequences of the VL CDR3s of the antibodies are shown in SEQ ID NOs: 16, 19, 52, 55, 97, 100, 121, 123, 151, 154, 174, 176, 200, 255, 256.

[0117] Given that each of the antibodies binds human ENTPD2 and that antigen-binding specificity is provided primarily by the CDR1, CDR2 and CDR3 regions, the VH CDR1, CDR2 and CDR3 sequences and VL CDR1, CDR2 and CDR3 sequences can be “mixed and matched” (i.e., CDRs from different antibodies can be mixed and matched),

although each antibody must contain a VH CDR1, CDR2 and CDR3 and a VL CDR1, CDR2 and CDR3 to create other human ENTPD2-binding antibodies disclosed herein. Such “mixed and matched” ENTPD2-binding antibodies can be tested using the binding assays known in the art and those described in the Examples (*e.g.*, ELISAs). When VH CDR sequences are mixed and matched, the CDR1, CDR2 and/or CDR3 sequence from a particular VH sequence should be replaced with a structurally similar CDR sequence(s). Likewise, when VL CDR sequences are mixed and matched, the CDR1, CDR2 and/or CDR3 sequence from a particular VL sequence should be replaced with a structurally similar CDR sequence(s). It will be readily apparent to the ordinarily skilled artisan that novel VH and VL sequences can be created by substituting one or more VH and/or VL CDR region sequences with structurally similar sequences from CDR sequences shown herein for monoclonal antibodies of the present disclosure.

[0118] Accordingly, the present disclosure provides an isolated monoclonal antibody or antigen binding region thereof comprising a heavy chain CDR1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 1, 4, 6, 7, 37, 40, 42, 43, 82, 85, 87, 88, 106, 109, 111, 112, 136, 139, 141, 142, 160, 163, 165, 166, 182, 187, 188, 206, 207, 208, 213, 214, 215, 272, 275, 277; a heavy chain CDR2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 2, 5, 8, 38, 41, 44, 83, 86, 89, 107, 110, 113, 129, 130, 131, 137, 140, 143, 161, 164, 167, 183, 189, 220, 222, 223, 245, 247, 248, 261, 273, 276; a heavy chain CDR3 comprising an amino acid sequence selected from the group consisting of SEQ ID NO: 3, 39, 68, 84, 108, 138, 162, 221, 246, 262, 277, 274, 9, 45, 69, 90, 114, 144, 168, 190, 224, 249, 263, 274, 280; a light chain CDR1 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 14, 17, 20, 50, 53, 56, 61, 62, 63, 95, 98, 101, 119, 122, 124, 149, 152, 155, 173, 175, 177, 195, 201, 254; a light chain CDR2 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 15, 18, 51, 54, 96, 99, 120, 150, 153, 196, 285, 286; and a light chain CDR3 comprising an amino acid sequence selected from the group consisting of SEQ ID NOs: 16, 19, 52, 55, 97, 100, 121, 123, 151, 154, 174, 176, 197, 255, 256; wherein the antibody specifically binds human ENTPD2.

[0119] In certain embodiments, an antibody that specifically binds to human ENTPD2 is an antibody or antibody fragment (*e.g.*, antigen binding fragment) that is described in Table 1.

[0120] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a heavy chain complementarity determining

region 1 (HCDR1) comprising the amino acid sequence of SEQ ID NO: 1, 4, 6 or 7; a heavy chain complementarity determining region 2 (HCDR2) comprising the amino acid sequence of SEQ ID NO: 2, 5 or 8; a heavy chain complementarity determining region 3 (HCDR3) comprising the amino acid sequence of SEQ ID NO: 3 or 9; a light chain complementarity determining region 1 (LCDR1) comprising the amino acid sequence of SEQ ID NO: 14, 17, or 20; a light chain complementarity determining region 2 (LCDR2) comprising the amino acid sequence of SEQ ID NO: 15 or 18; and a light chain complementarity determining region 3 (LCDR3) comprising the amino acid sequence of SEQ ID NO: 16 or 19.

[0121] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 1; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 2; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 3; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 14; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 15; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16.

[0122] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 4; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 5; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 3; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 18; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 19.

[0123] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 6; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 2; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 3; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 14; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 15; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16.

[0124] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 7; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 8; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 9; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 20; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 18; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16.

[0125] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a HCDR1 comprising the amino acid

sequence of SEQ ID NO: 37, 40, 42 or 43; a HCDR2 comprising the amino acid sequence of SEQ ID NO: 38, 41, or 44; a HCDR3 comprising the amino acid sequence of SEQ ID NO: 39 or 45; a LCDR1 comprising the amino acid sequence of SEQ ID NO: 50, 53 or 56; a LCDR2 comprising the amino acid sequence of SEQ ID NO: 51 or 54; and a LCDR3 comprising the amino acid sequence of SEQ ID NO: 52 or 55.

[0126] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 37; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 38; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 39; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 50; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 51; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 52.

[0127] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 40; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 41; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 39; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 53; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 54; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 55.

[0128] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 42; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 38; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 39; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 50; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 51; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 52.

[0129] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 43; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 44; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 45; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 56; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 54; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 52.

[0130] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a HCDR1 comprising the amino acid sequence of SEQ ID NO: 37, 40, 42 or 43; a HCDR2 comprising the amino acid sequence of SEQ ID NO: 38, 41, or 44; a HCDR3 comprising the amino acid sequence of SEQ ID NO: 39 or 45; a LCDR1 comprising the amino acid sequence of SEQ ID NO: 61, 62, or 63; a LCDR2 comprising the amino acid sequence of SEQ ID NO: 51 or 54; and a LCDR3 comprising the amino acid sequence of SEQ ID NO: 52 or 55.

[0131] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 37; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 38; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 39; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 61; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 51; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 52.

[0132] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 40; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 41; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 39; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 62; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 54; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 55.

[0133] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 42; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 38; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 39; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 61; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 51; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 52.

[0134] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 43; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 44; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 45; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 63; an LCDR2 comprising the amino

acid sequence of SEQ ID NO: 54; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 52.

[0135] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a HCDR1 comprising the amino acid sequence of SEQ ID NO: 37, 40, 42 or 43; a HCDR2 comprising the amino acid sequence of SEQ ID NO: 38, 41, or 44; a HCDR3 comprising the amino acid sequence of SEQ ID NO: 68 or 69; a LCDR1 comprising the amino acid sequence of SEQ ID NO: 50, 53 or 56; a LCDR2 comprising the amino acid sequence of SEQ ID NO: 51 or 54; and a LCDR3 comprising the amino acid sequence of SEQ ID NO: 52 or 55.

[0136] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 37; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 38; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 68; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 50; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 51; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 52.

[0137] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 40; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 41; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 68; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 53; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 54; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 55.

[0138] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 42; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 38; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 68; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 50; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 51; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 52.

[0139] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 43; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 44; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 69; an LCDR1

comprising the amino acid sequence of SEQ ID NO: 56; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 54; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 52.

[0140] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a HCDR1 comprising the amino acid sequence of SEQ ID NO: 82, 85, 87, or 88; a HCDR2 comprising the amino acid sequence of SEQ ID NO: 83, 86, or 89; a HCDR3 comprising the amino acid sequence of SEQ ID NO: 84 or 90; a LCDR1 comprising the amino acid sequence of SEQ ID NO: 95, 98, or 101; a LCDR2 comprising the amino acid sequence of SEQ ID NO: 96 or 99; and a LCDR3 comprising the amino acid sequence of SEQ ID NO: 97 or 100.

[0141] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 82; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 83; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 84; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 95; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 96; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 97.

[0142] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 85; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 86; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 84; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 98; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 99; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 100.

[0143] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 87; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 83; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 84; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 95; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 96; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 97.

[0144] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 88; an HCDR2 comprising the amino acid sequence of SEQ ID

NO: 89; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 90; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 101; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 99; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 97.

[0145] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a HCDR1 comprising the amino acid sequence of SEQ ID NO: 106, 109, 111, or 112; a HCDR2 comprising the amino acid sequence of SEQ ID NO: 107, 110, or 113; a HCDR3 comprising the amino acid sequence of SEQ ID NO: 108 or 114; a LCDR1 comprising the amino acid sequence of SEQ ID NO: 119, 122, or 124; a LCDR2 comprising the amino acid sequence of SEQ ID NO: 99 or 120; and a LCDR3 comprising the amino acid sequence of SEQ ID NO: 121 or 123.

[0146] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 106; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 107; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 108; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 119; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 120; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 121.

[0147] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 109; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 110; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 108; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 122; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 99; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 123.

[0148] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 111; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 107; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 119; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 120; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 121; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 108.

[0149] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid

sequence of SEQ ID NO: 112; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 113; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 114; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 124; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 99; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 121.

[0150] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a HCDR1 comprising the amino acid sequence of SEQ ID NO: 106, 109, 111, or 112; a HCDR2 comprising the amino acid sequence of SEQ ID NO: 129, 130, or 131; a HCDR3 comprising the amino acid sequence of SEQ ID NO: 108 or 114; a LCDR1 comprising the amino acid sequence of SEQ ID NO: 119, 122, or 124; a LCDR2 comprising the amino acid sequence of SEQ ID NO: 99 or 120; and a LCDR3 comprising the amino acid sequence of SEQ ID NO: 121 or 123.

[0151] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 106; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 129; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 108; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 119; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 120; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 121.

[0152] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 109; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 130; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 108; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 122; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 99; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 123.

[0153] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 111; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 129; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 108; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 119; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 120; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 121.

[0154] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 112; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 131; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 114; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 124; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 99; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 121.

[0155] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a HCDR1 comprising the amino acid sequence of SEQ ID NO: 136, 139, 141, or 142; a HCDR2 comprising the amino acid sequence of SEQ ID NO: 137, 140, or 143; a HCDR3 comprising the amino acid sequence of SEQ ID NO: 138 or 144; a LCDR1 comprising the amino acid sequence of SEQ ID NO: 149, 152, or 155; a LCDR2 comprising the amino acid sequence of SEQ ID NO: 150 or 153; and a LCDR3 comprising the amino acid sequence of SEQ ID NO: 151 or 154.

[0156] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 136; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 137; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 138; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 149; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 150; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 151.

[0157] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 139; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 140; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 138; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 152; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 153; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 154.

[0158] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 141; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 137; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 138; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 149; an LCDR2 comprising the amino

acid sequence of SEQ ID NO: 150; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 151.

[0159] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 142; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 143; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 144; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 155; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 153; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 151.

[0160] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a HCDR1 comprising the amino acid sequence of SEQ ID NO: 160, 163, 165, or 166; a HCDR2 comprising the amino acid sequence of SEQ ID NO: 161, 164, or 167; a HCDR3 comprising the amino acid sequence of SEQ ID NO: 162 or 168; a LCDR1 comprising the amino acid sequence of SEQ ID NO: 173, 175, or 177; a LCDR2 comprising the amino acid sequence of SEQ ID NO: 150 or 153; and a LCDR3 comprising the amino acid sequence of SEQ ID NO: 174 or 176.

[0161] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 160; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 161; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 162; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 173; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 150; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 174.

[0162] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 163; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 164; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 162; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 175; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 153; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 176.

[0163] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 165; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 161; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 162; an LCDR1

comprising the amino acid sequence of SEQ ID NO: 173; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 150; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 174.

[0164] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 166; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 167; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 168; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 177; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 153; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 174.

[0165] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a HCDR1 comprising the amino acid sequence of SEQ ID NO: 37, 40, 42, or 43; a HCDR2 comprising the amino acid sequence of SEQ ID NO: 220, 222, or 223; a HCDR3 comprising the amino acid sequence of SEQ ID NO: 221 or 224; a LCDR1 comprising the amino acid sequence of SEQ ID NO: 61, 62, or 63; a LCDR2 comprising the amino acid sequence of SEQ ID NO: 51 or 54; and a LCDR3 comprising the amino acid sequence of SEQ ID NO: 52 or 55.

[0166] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 37; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 220; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 221; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 61; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 51; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 52.

[0167] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 40; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 222; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 221; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 62; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 54; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 55.

[0168] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 42; an HCDR2 comprising the amino acid sequence of SEQ ID

NO: 220; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 221; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 61; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 51; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 52.

[0169] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 43; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 223; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 224; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 63; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 54; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 52.

[0170] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a HCDR1 comprising the amino acid sequence of SEQ ID NO: 37, 40, 42 or 43; a HCDR2 comprising the amino acid sequence of SEQ ID NO: 220, 222, or 223; a HCDR3 comprising the amino acid sequence of SEQ ID NO: 68 or 69; a LCDR1 comprising the amino acid sequence of SEQ ID NO: 61, 62, or 63; a LCDR2 comprising the amino acid sequence of SEQ ID NO: 51 or 54; and a LCDR3 comprising the amino acid sequence of SEQ ID NO: 52 or 55.

[0171] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 37; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 220; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 68; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 61; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 51; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 52.

[0172] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 40; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 222; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 68; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 62; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 54; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 55.

[0173] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid

sequence of SEQ ID NO: 42; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 220; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 68; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 61; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 51; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 52.

[0174] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 43; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 223; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 69; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 63; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 54; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 52.

[0175] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a HCDR1 comprising the amino acid sequence of SEQ ID NO: 1, 4, 6, or 7; a HCDR2 comprising the amino acid sequence of SEQ ID NO: 245, 247, or 248; a HCDR3 comprising the amino acid sequence of SEQ ID NO: 246 or 249; a LCDR1 comprising the amino acid sequence of SEQ ID NO: 17, 20, or 254; a LCDR2 comprising the amino acid sequence of SEQ ID NO: 15 or 18; and a LCDR3 comprising the amino acid sequence of SEQ ID NO: 255 or 256.

[0176] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 1; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 245; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 246; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 254; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 15; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 255.

[0177] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 4; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 247; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 246; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 18; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 256.

[0178] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 6; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 254; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 246; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 254; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 15; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 255.

[0179] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 7; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 248; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 249; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 20; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 18; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 255.

[0180] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a HCDR1 comprising the amino acid sequence of SEQ ID NO: 1, 4, 6, or 7; a HCDR2 comprising the amino acid sequence of SEQ ID NO: 247, 248, or 261; a HCDR3 comprising the amino acid sequence of SEQ ID NO: 262 or 263; a LCDR1 comprising the amino acid sequence of SEQ ID NO: 17, 20, or 254; a LCDR2 comprising the amino acid sequence of SEQ ID NO: 15 or 18; and a LCDR3 comprising the amino acid sequence of SEQ ID NO: 16 or 19.

[0181] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 1; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 261; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 262; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 254; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 15; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16.

[0182] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 4; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 247; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 262; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 17; an LCDR2 comprising the amino

acid sequence of SEQ ID NO: 18; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 19.

[0183] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 6; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 261; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 262; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 254; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 15; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16.

[0184] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 7; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 248; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 263; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 20; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 18; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16.

[0185] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a HCDR1 comprising the amino acid sequence of SEQ ID NO: 272, 275, or 278; a HCDR2 comprising the amino acid sequence of SEQ ID NO: 273, 276, or 279; a HCDR3 comprising the amino acid sequence of SEQ ID NO: 274, 277, or 280; a LCDR1 comprising the amino acid sequence of SEQ ID NO: 17, 20, or 254; a LCDR2 comprising the amino acid sequence of SEQ ID NO: 285 or 286; and a LCDR3 comprising the amino acid sequence of SEQ ID NO: 16 or 19.

[0186] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 272; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 273; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 274; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 254; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16.

[0187] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 275; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 276; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 274; an LCDR1

comprising the amino acid sequence of SEQ ID NO: 17; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 286; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 19.

[0188] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 277; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 273; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 274; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 254; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 285; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16.

[0189] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises an HCDR1 comprising the amino acid sequence of SEQ ID NO: 278; an HCDR2 comprising the amino acid sequence of SEQ ID NO: 279; an HCDR3 comprising the amino acid sequence of SEQ ID NO: 280; an LCDR1 comprising the amino acid sequence of SEQ ID NO: 20; an LCDR2 comprising the amino acid sequence of SEQ ID NO: 286; and an LCDR3 comprising the amino acid sequence of SEQ ID NO: 16.

[0190] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 10 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 21 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0191] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 25 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 29 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0192] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 33 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 29 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0193] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 46 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 57 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0194] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 46 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 64 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0195] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 70 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 74 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0196] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a heavy chain variable region (VH)

comprising the amino acid sequence of SEQ ID NO: 25 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 78 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0197] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 91 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 102 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0198] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 115 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 125 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0199] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 132 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 125 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0200] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 145 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions,

insertions, deletions, or modifications), and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 156 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0201] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 169 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 178 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0202] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 225 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 229 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0203] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 233 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 237 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0204] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 241 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 229 (or a sequence at least about 90%, 95%, 99% or

more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0205] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 250 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 257 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0206] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 264 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 268 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0207] In some embodiments, the antibody or antigen binding region thereof that specifically binds to human ENTPD2 comprises a heavy chain variable region (VH) comprising the amino acid sequence of SEQ ID NO: 281 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain variable region (VL) comprising the amino acid sequence of SEQ ID NO: 287 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0208] In some embodiments, the antibody that specifically binds to human ENTPD2 comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 12 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain comprising the amino acid sequence of SEQ ID NO: 23 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0209] In some embodiments, the antibody that specifically binds to human ENTPD2 comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 27 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain comprising the amino acid sequence of SEQ ID NO: 31 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0210] In some embodiments, the antibody that specifically binds to human ENTPD2 comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 35 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain comprising the amino acid sequence of SEQ ID NO: 31 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0211] In some embodiments, the antibody that specifically binds to human ENTPD2 comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 48 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain comprising the amino acid sequence of SEQ ID NO: 59 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0212] In some embodiments, the antibody that specifically binds to human ENTPD2 comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 48 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain comprising the amino acid sequence of SEQ ID NO: 66 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0213] In some embodiments, the antibody that specifically binds to human ENTPD2 comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 72 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain comprising the amino acid sequence of SEQ ID NO: 76 (or a sequence at least about 90%,

95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0214] In some embodiments, the antibody that specifically binds to human ENTPD2 comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 27 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain comprising the amino acid sequence of SEQ ID NO: 80 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0215] In some embodiments, the antibody that specifically binds to human ENTPD2 comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 93 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain comprising the amino acid sequence of SEQ ID NO: 104 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0216] In some embodiments, the antibody that specifically binds to human ENTPD2 comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 117 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain comprising the amino acid sequence of SEQ ID NO: 127 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0217] In some embodiments, the antibody that specifically binds to human ENTPD2 comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 134 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain comprising the amino acid sequence of SEQ ID NO: 127 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0218] In some embodiments, the antibody that specifically binds to human ENTPD2 comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 147 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain

comprising the amino acid sequence of SEQ ID NO: 158 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0219] In some embodiments, the antibody that specifically binds to human ENTPD2 comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 171 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain comprising SEQ ID NO: 180 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0220] In some embodiments, the antibody that specifically binds to human ENTPD2 comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 227 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain comprising the amino acid sequence of SEQ ID NO: 231 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0221] In some embodiments, the antibody that specifically binds to human ENTPD2 comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 235 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain comprising the amino acid sequence of SEQ ID NO: 239 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0222] In some embodiments, the antibody that specifically binds to human ENTPD2 comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 243 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain comprising the amino acid sequence of SEQ ID NO: 231 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0223] In some embodiments, the antibody that specifically binds to human ENTPD2 comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 252 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two,

three or more substitutions, insertions, deletions, or modifications), and a light chain comprising the amino acid sequence of SEQ ID NO: 259 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0224] In some embodiments, the antibody that specifically binds to human ENTPD2 comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 266 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain comprising the amino acid sequence of SEQ ID NO: 270 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0225] In some embodiments, the antibody that specifically binds to human ENTPD2 comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 283 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications), and a light chain comprising the amino acid sequence of SEQ ID NO: 289 (or a sequence at least about 90%, 95%, 99% or more identical thereto, and/or having one, two, three or more substitutions, insertions, deletions, or modifications).

[0226] In some embodiments, the present invention provides an antibody or antigen-binding fragment thereof, which bind to human ENTPD2 protein with a dissociation constant (K_D) of less than 10nM, e.g., a K_D of less than 9nM, less than 8nM, less than 7nM, less than 6nM, less than 5nM, less than 4nM, less than 3nM, less than 2nM, less than 1nM, e.g., as measured by Biacore. In some embodiments, the antibodies or antigen-binding fragments provided herein bind to human ENTPD2 protein with a dissociation constant (K_D) of less than 5nM, e.g., as measured by Biacore. In some embodiments, the antibodies or antigen-binding fragments provided herein bind to human ENTPD2 protein with a dissociation constant (K_D) of less than 3nM, e.g., as measured by Biacore. In some embodiments, the antibodies or antigen-binding fragments provided herein bind to human ENTPD2 protein with a dissociation constant (K_D) of less than 1nM, e.g., as measured by Biacore. In some embodiments, the dissociation constant of the antibodies or antigen binding fragments thereof described herein to human ENTPD2 is measured by Biacore at 25 °C.

[0227] Provided herein are also antibodies or antigen binding fragments thereof that specifically bind to an epitope in human ENTPD2, wherein the epitope comprises at least one

(e.g., at least two, at least three, at least four, at least five, at least six, at least seven, at least eight, at least nine, at least ten, at least eleven, at least twelve, at least thirteen, at least fourteen, at least fifteen, at least twenty) of the following residues: His50, Asp76, Pro78, Gly79, Gly80, Tyr85, Asp87, Asn88, Gly91, Gln94, Ser95, Gly98, Glu101, Gln102, Gln105, Asp106, Arg245, Thr272, Gln273, Leu275, Asp278, Arg298, Ala347, Ala350, Thr351, Arg392, Ala393, Arg394, or Tyr398. In some embodiments, such antibodies or antigen binding fragments include, but are not limited to, MAb1, MAb2, MAb3, MAb7, MAb17, MAb19, MAb20, MAb21, and Fab23 as disclosed in Table 1.

[0228] Provided herein are also antibodies or antigen binding fragments thereof that specifically bind to an epitope in human ENTPD2, wherein the epitope comprises at least one (e.g., at least two, at least three, at least four, at least five, at least six, at least seven, at least eight, at least nine, at least ten, at least eleven, at least twelve, at least thirteen, at least fourteen, at least fifteen, at least twenty) of the following residues: Gly79, Gln250, Leu253, Trp266, Arg268, Gly269, Phe270, Ser271, Thr272, Gln273, Val274, Leu275, Asp278, Arg298, Ser300, Ser302, Gly303, Thr380, Trp381, Ala382, Gly390, Gln391, Arg392, Ala393, Arg394, or Asp397. In some embodiments, such antibodies or antigen binding fragments include, but are not limited to, MAb4, MAb5, MAb6, MAb16, MAb18, and Fab22 as disclosed in Table 1.

[0229] Once a desired epitope on an antigen is determined, it is possible to generate antibodies to that epitope, e.g., using the techniques described in the present invention. Alternatively, during the discovery process, the generation and characterization of antibodies may elucidate information about desirable epitopes. From this information, it is then possible to competitively screen antibodies for binding to the same epitope. An approach to achieve this is to conduct cross-competition studies to find antibodies that competitively bind with one another, e.g., the antibodies compete for binding to the antigen. A high throughput process for “binning” antibodies based upon their cross-competition is described in International Patent Application No. WO 2003/48731. As will be appreciated by one of skill in the art, practically anything to which an antibody can specifically bind could be an epitope. An epitope can comprises those residues to which the antibody binds.

[0230] Generally, antibodies specific for a particular target antigen will preferentially recognize an epitope on the target antigen in a complex mixture of proteins and/or macromolecules.

[0231] Regions of a given polypeptide that include an epitope can be identified using any number of epitope mapping techniques, well known in the art. See, e.g., Epitope Mapping Protocols in *Methods in Molecular Biology*, Vol. 66 (Glenn E. Morris, Ed., 1996, Humana Press, Totowa, N.J). For example, linear epitopes may be determined by e.g., concurrently synthesizing large numbers of peptides on solid supports, the peptides corresponding to portions of the protein molecule, and reacting the peptides with antibodies while the peptides are still attached to the supports. Such techniques are known in the art and described in, e.g., U.S. Pat. No. 4,708,871; Geysen et al., (1984) *Proc. Natl. Acad. Sci. USA* 81:3998-4002; Geysen et al., (1985) *Proc. Natl. Acad. Sci. USA* 82:78-182; Geysen et al., (1986) *Mol. Immunol.* 23:709-715. Similarly, conformational epitopes are readily identified by determining spatial conformation of amino acids such as by, e.g., x-ray crystallography and two-dimensional nuclear magnetic resonance. See, e.g., Epitope Mapping Protocols, supra. Antigenic regions of proteins can also be identified using standard antigenicity and hydrophathy plots, such as those calculated using, e.g., the Omega version 1.0 software program available from the Oxford Molecular Group. This computer program employs the Hopp/Woods method, Hopp et al., (1981) *Proc. Natl. Acad. Sci. USA* 78:3824-3828; for determining antigenicity profiles, and the Kyte-Doolittle technique, Kyte et al., (1982) *J. Mol. Biol.* 157:105-132; for hydrophathy plots.

[0232] The antibody molecule can be a polyclonal or a monoclonal antibody. A monoclonal antibody can be made by hybridoma technology or by methods that do not use hybridoma technology (e.g., recombinant methods). In some embodiments, the antibody can be recombinantly produced, e.g., produced by phage display or by combinatorial methods.

[0233] Phage display and combinatorial methods for generating antibodies are known in the art (as described in, e.g., Ladner et al. U.S. Patent No. 5,223,409; Kang et al. International Publication No. WO 92/18619; Dower et al. International Publication No. WO 91/17271; Winter et al. International Publication WO 92/20791; Markland et al. International Publication No. WO 92/15679; Breitling et al. International Publication WO 93/01288; McCafferty et al. International Publication No. WO 92/01047; Garrard et al. International Publication No. WO 92/09690; Ladner et al. International Publication No. WO 90/02809; Fuchs et al. (1991) *Bio/Technology* 9:1370-1372; Hay et al. (1992) *Hum Antibod Hybridomas* 3:81-85; Huse et al. (1989) *Science* 246:1275-1281; Griffiths et al. (1993) *EMBO J* 12:725-734; Hawkins et al. (1992) *J Mol Biol* 226:889-896; Clackson et al. (1991) *Nature* 352:624-628; Gram et al. (1992) *PNAS* 89:3576-3580; Garrad et al. (1991)

Bio/Technology 9:1373-1377; Hoogenboom et al. (1991) Nuc Acid Res 19:4133-4137; and Barbas et al. (1991) PNAS 88:7978-7982).

[0234] In one embodiment, the antibody is a fully human antibody (e.g., an antibody made in a mouse which has been genetically engineered to produce an antibody from a human immunoglobulin sequence), or a non-human antibody, e.g., a rodent (mouse or rat), goat, primate (e.g., monkey), camel antibody.

[0235] An antibody can be one in which the variable region, or a portion thereof, e.g., the CDRs, are generated in a non-human organism, e.g., a rat or mouse. Chimeric, CDR-grafted, and humanized antibodies are within the invention. Antibodies generated in a non-human organism, e.g., a rat or mouse, and then modified, e.g., in the variable framework or constant region, to decrease antigenicity in a human are within the invention.

[0236] Chimeric and/or humanized antibodies, can be engineered to minimize the immune response by a human patient to antibodies produced in non-human subjects or derived from the expression of non-human antibody genes. Chimeric antibodies comprise a non-human animal antibody variable region and a human antibody constant region. Such antibodies retain the epitope binding specificity of the original monoclonal antibody, but may be less immunogenic when administered to humans, and therefore more likely to be tolerated by the patient. For example, one or all (e.g., one, two, or three) of the variable regions of the light chain(s) and/or one or all (e.g., one, two, or three) of the variable regions the heavy chain(s) of a mouse antibody (e.g., a mouse monoclonal antibody) can each be joined to a human constant region, such as, without limitation an IgG1 human constant region. Chimeric monoclonal antibodies can be produced by recombinant DNA techniques known in the art. For example, a gene encoding the constant region of a non-human antibody molecule can be substituted with a gene encoding a human constant region (see Robinson et al., PCT Patent Publication PCT/US86/02269; Akira, et al., European Patent Application 184,187; or Taniguchi, M., European Patent Application 171,496). In addition, other suitable techniques that can be used to generate chimeric antibodies are described, for example, in U.S. Patent Nos. 4,816,567; 4,978,775; 4,975,369; and 4,816,397.

[0237] A chimeric antibody can be further “humanized” by replacing portions of the variable region not involved in antigen binding with equivalent portions from human variable regions. Humanized antibodies comprise one or more human framework regions in the variable region together with non-human (e.g., mouse, rat, or hamster) complementarity-determining regions (CDRs) of the heavy and/or light chain. In some embodiments, a

humanized antibody comprises sequences that are entirely human except for the CDR regions. Humanized antibodies are typically less immunogenic to humans, relative to non-humanized antibodies, and thus offer therapeutic benefits in certain situations. Humanized ENTPD2 antibodies can be generated using methods known in the art. See for example, Hwang et al., *Methods* 36:35, 2005; Queen et al., *Proc. Natl. Acad. Sci. U.S.A.* 86:10029-10033, 1989; Jones et al., *Nature* 321:522-25, 1986; Riechmann et al., *Nature* 332:323-27, 1988; Verhoeven et al., *Science* 239:1534-36, 1988; Orlandi et al., *Proc. Natl. Acad. Sci. U.S.A.* 86:3833-3837, 1989; U.S. Patent Nos. 5,225,539; 5,530,101; 5,585,089; 5,693,761; 5,693,762; and 6,180,370; and WO 90/07861.

[0238] Human ENTPD2 antibodies can be generated using methods that are known in the art. For example, the humaneering technology used to converting non-human antibodies into engineered human antibodies. U.S. Patent Publication No. 20050008625 describes an *in vivo* method for replacing a nonhuman antibody variable region with a human variable region in an antibody while maintaining the same or providing better binding characteristics relative to that of the nonhuman antibody. The method relies on epitope guided replacement of variable regions of a non-human reference antibody with a fully human antibody. The resulting human antibody is generally structurally unrelated to the reference nonhuman antibody, but binds to the same epitope on the same antigen as the reference antibody. Briefly, the serial epitope-guided complementarity replacement approach is enabled by setting up a competition in cells between a “competitor” and a library of diverse hybrids of the reference antibody (“test antibodies”) for binding to limiting amounts of antigen in the presence of a reporter system which responds to the binding of test antibody to antigen. The competitor can be the reference antibody or derivative thereof such as a single-chain Fv fragment. The competitor can also be a natural or artificial ligand of the antigen which binds to the same epitope as the reference antibody. The only requirements of the competitor are that it binds to the same epitope as the reference antibody, and that it competes with the reference antibody for antigen binding. The test antibodies have one antigen-binding V-region in common from the nonhuman reference antibody, and the other V-region selected at random from a diverse source such as a repertoire library of human antibodies. The common V-region from the reference antibody serves as a guide, positioning the test antibodies on the same epitope on the antigen, and in the same orientation, so that selection is biased toward the highest antigen-binding fidelity to the reference antibody.

[0239] Many types of reporter system can be used to detect desired interactions between test antibodies and antigen. For example, complementing reporter fragments may be linked to antigen and test antibody, respectively, so that reporter activation by fragment complementation only occurs when the test antibody binds to the antigen. When the test antibody- and antigen-reporter fragment fusions are co-expressed with a competitor, reporter activation becomes dependent on the ability of the test antibody to compete with the competitor, which is proportional to the affinity of the test antibody for the antigen. Other reporter systems that can be used include the reactivator of an auto-inhibited reporter reactivation system (RAIR) as disclosed in U.S. patent application Ser. No. 10/208,730 (Publication No. 20030198971), or competitive activation system disclosed in U.S. patent application Ser. No. 10/076,845 (Publication No. 20030157579).

[0240] With the serial epitope-guided complementarity replacement system, selection is made to identify cells expresses a single test antibody along with the competitor, antigen, and reporter components. In these cells, each test antibody competes one-on-one with the competitor for binding to a limiting amount of antigen. Activity of the reporter is proportional to the amount of antigen bound to the test antibody, which in turn is proportional to the affinity of the test antibody for the antigen and the stability of the test antibody. Test antibodies are initially selected on the basis of their activity relative to that of the reference antibody when expressed as the test antibody. The result of the first round of selection is a set of “hybrid” antibodies, each of which is comprised of the same non-human V-region from the reference antibody and a human V-region from the library, and each of which binds to the same epitope on the antigen as the reference antibody. One of more of the hybrid antibodies selected in the first round will have an affinity for the antigen comparable to or higher than that of the reference antibody.

[0241] In the second V-region replacement step, the human V-regions selected in the first step are used as guide for the selection of human replacements for the remaining non-human reference antibody V-region with a diverse library of cognate human V-regions. The hybrid antibodies selected in the first round may also be used as competitors for the second round of selection. The result of the second round of selection is a set of fully human antibodies which differ structurally from the reference antibody, but which compete with the reference antibody for binding to the same antigen. Some of the selected human antibodies bind to the same epitope on the same antigen as the reference antibody. Among these selected

human antibodies, one or more binds to the same epitope with an affinity which is comparable to or higher than that of the reference antibody.

[0242] Using a mouse or chimeric ENTPD2 antibody, human antibodies that bind to human ENTPD2 with the same binding specificity and the same or better binding affinity can be generated. In addition, such human ENTPD2 antibodies can also be commercially obtained from companies which customarily produce human antibodies, e.g., KaloBios, Inc. (Mountain View, Calif.).

[0243] In some embodiments, the present invention provides an antibody or antigen-binding fragment thereof that bind to human ENTPD2 protein and modulates one or more ENTPD2 activities/functions, e.g., inhibiting the enzymatic activities of human ENTPD2, e.g., by at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, or at least 90%. In some embodiments, the enzymatic activity of human ENTPD2 is measured using an in vitro FRET assay which measures the hydrolysis of ATP to ADP by either recombinant ENTPD2 or ENTPD2 expressed on the surface of cells.

[0244] In some embodiments, the anti-human ENTPD2 antibodies or antigen binding fragments thereof described herein inhibit ENTPD2's ability of hydrolysis of adenosine triphosphate (ATP). In some embodiments, ENTPD2's ability of hydrolysis of ATP is measured using an in vitro FRET assay which measures the hydrolysis of ATP to ADP by either recombinant ENTPD2 or ENTPD2 expressed on the surface of cells.

[0245] In some embodiments, the anti-human ENTPD2 antibodies or antigen binding fragments thereof described herein interfere with ATP binding to ENTPD2 or trap ATP within the catalytic domain of ENTPD2. In some embodiments, interference with ATP binding to ENTPD2 or trapping ATP within the catalytic domain of ENTPD2 is measured using an in vitro FRET assay which measures the hydrolysis of ATP to ADP by either recombinant ENTPD2 or ENTPD2 expressed on the surface of cells.

Antibodies and Antigen-Binding Fragments Thereof That Specifically Bind To Mouse ENTPD2

[0246] Also provided herein are antibodies or antigen binding fragments thereof, e.g., monoclonal antibodies or antigen binding fragments thereof, that specifically bind to mouse ENTPD2 protein. Table 26 lists the sequences of exemplary the ENTPD2 antibodies or antigen-binding fragments that specifically bind to mouse ENTPD2 protein.

Table 26. Sequences of Exemplary Monoclonal Antibodies (MABs) and Antibody Fragments (FABs) That Bind Mouse ENTPD2

ANTI-mouse ENTPD2 MAB13		
SEQ ID NO: 182	HCDR1 (KABAT)	HYGMN
SEQ ID NO: 183	HCDR2 (KABAT)	WINTDTGNPTYADDFKG
SEQ ID NO: 184	HCDR3 (KABAT)	YGTLYSGYGFFDS
SEQ ID NO: 185	HCDR1 (CHOTHIA)	GYTFTHY
SEQ ID NO: 186	HCDR2 (CHOTHIA)	NTDTGN
SEQ ID NO: 184	HCDR3 (CHOTHIA)	YGTLYSGYGFFDS
SEQ ID NO: 187	HCDR1 (COMBINED)	GYTFTHYGMN
SEQ ID NO: 183	HCDR2 (COMBINED)	WINTDTGNPTYADDFKG
SEQ ID NO: 184	HCDR3 (COMBINED)	YGTLYSGYGFFDS
SEQ ID NO: 188	HCDR1 (IMGT)	GYTFTHYG
SEQ ID NO: 189	HCDR2 (IMGT)	INTDTGNP
SEQ ID NO: 190	HCDR3 (IMGT)	VRYGTLVSGYGFFDS
SEQ ID NO: 191	VH	QVQLVQSGAELKQPGQSVKISKASGYTFTHYGMN WVKQAPGQGLKWMGWINTDTGNPTYADDFKGRFV FSLDTSVSTAYLQISNLKNEDTATYYCVRYGTLVSGY GFFDSWGGQGLVTVSS
SEQ ID NO: 192	VH DNA	CAGGTCCAGCTGGTGCAGTCAGGAGCTGAGCTGA AGCAGCCTGGACAGTCGGTGAAGATCTCCTGCAAG GCTTCAGGGTACACCTTCACACACTATGGGATGAA CTGGGTGAAGCAGGCACAGGACAGGGTCTAAAG TGGATGGGCTGGATCAACACTGACACTGGGAATCC AACATATGCTGATGACTTCAAAGGACGGTTTGTCT TCTCCTGGACACCTCTGTCAGCACTGCATATCTGC AGATCAGCAACCTCAAGAATGAAGACACGGCCAC GTATTACTGTGTGAGATATGGAACCCTATATAGCG GATATGGGTTTTTTTTTGATTCTGGGGCCAAGGG ACCCTGGTCACCGTCTCTCA
SEQ ID NO: 193	HC	QVQLVQSGAELKQPGQSVKISKASGYTFTHYGMN WVKQAPGQGLKWMGWINTDTGNPTYADDFKGRFV FSLDTSVSTAYLQISNLKNEDTATYYCVRYGTLVSGY GFFDSWGGQGLVTVSSAKTTAPSVYPLAPVCGDTT GSSVTLGCLVKGYFPEPVTLTWNSGSLSSGVHTFPAV

		LQSDLYTLSSSVTVTSSTWPSQSITCNVAHPASSTKV DKKIEPRGPTIKPCPPCKCPAPNLLGGPSVFIFPPKIKD VLMISLSPIVTCVVVDVSEDDPDVQISWFVNNVEVHT AQTQTHREDYNSTLRVVSALPIQHQDWMMSGKEFKC KVNNKDLPAPIERTISKPKGSVRAPQVYVLPPEEEM TKKQVTLTCMVTDFMPEDIYVEWTNNGKTELNYKN TEPVLDSDGSYFMYSKLRVEKKNWVERNSYSCSVV HEGLHNHHTTKSFSRTPGK
SEQ ID NO: 194	HC DNA	CAGGTCCAGCTGGTGCAGTCAGGAGCTGAGCTGA AGCAGCCTGGACAGTCGGTGAAGATCTCCTGCAAG GCTTCAGGGTACACCTTCACACACTATGGGATGAA CTGGGTGAAGCAGGCACCAGGACAGGGTCTAAAG TGGATGGGCTGGATCAACACTGACACTGGGAATCC AACATATGCTGATGACTTCAAAGGACGGTTTGTCT TCTCCTGGACACCTCTGTCAGCACTGCATATCTGC AGATCAGCAACCTCAAGAATGAAGACACGGCCAC GTATTACTGTGTGAGATATGGAACCTATATAGCG GATATGGGTTTTTTTTTGGATTCTGGGGCCAAGGG ACCCTGGTCACCGTCTCCTCAGCCAAGACCACCGC CCCCAGCGGTACCCCCCTGGCCCCCGTGTGCGGCG ATACCACCGGCAGCAGCGTGACCCTGGGCTGCCTG GTGAAGGGCTACTTCCCCGAGCCCGTGACCCTGAC CTGGAACAGCGGCTCCCTGAGCAGCGGCGTGCAC ACCTTCCCCGCGGTGCTGCAGAGCGACCTGTACAC CCTGTCCAGCTCCGTGACCGTGACAAGCAGCACCT GGCCCAGCCAGAGCATCACCTGCAACGTGGCCAC CCCCGCCAGCAGCACCAGGTGGACAAGAAGATCG AGCCCAGGGGCCCCACCATCAAGCCCTGCCCCCCC TGCAAGTGCCAGCCCCCAACCTGCTGGGCGGACC CAGCGTGTTTCATCTTCCCCCCCCAAGATCAAGGACG TGCTGATGATCAGCCTGAGCCCCATCGTGACCTGC GTGGTGGTGGACGTGAGCGAGGACGACCCGACG TGCAGATCAGCTGGTTCGTGAACAACGTGGAGGTG CACACCGCCCAGACCCAGACCCACCGGGAGGACT ACAACAGCACCCCTGCGCGTCTGTGCCCTGCCC ATCCAGCACCCAGGACTGGATGAGCGGCAAGAAT TCAAGTGCAAGGTGAACAACAAGGACCTGCCTGC CCCCATCGAGCGGACCATCAGCAAGCCCAAGGGC AGCGTGAGAGCCCCCAGGTGTACGTGCTGCCCCC TCCCAGGAAGAGATGACCAAGAAACAGGTGACA CTGACCTGCATGGTGACCGACTTCATGCCCAGGA CATCTACGTGGAGTGGACCAACAACGGCAAGACC GAGCTGAACTACAAGAACACCGAGCCTGTGCTGG ACAGCGACGGCAGCTACTTCATGTACAGCAAGCTG CGGGTGGAGAAGAAAACTGGGTGGAGCGGAACA GCTACAGCTGCAGCGTGGTGCACGAGGGCCTGCAC AACCACCACACCACCAAGAGCTTCAGCCGGACCCC CGGCAAG
SEQ ID NO: 195	LCDR1 (KABAT)	KSSQSLFNSNTNKNYLN

SEQ ID NO: 196	LCDR2 (KABAT)	YASTRHT
SEQ ID NO: 197	LCDR3 (KABAT)	QQWYSYPWT
SEQ ID NO: 198	LCDR1 (CHOTHIA)	SQSLFNSNTNKNY
SEQ ID NO: 199	LCDR2 (CHOTHIA)	YAS
SEQ ID NO: 200	LCDR3 (CHOTHIA)	WYSYPW
SEQ ID NO: 195	LCDR1 (COMBINED)	KSSQSLFNSNTNKNYLN
SEQ ID NO: 196	LCDR2 (COMBINED)	YASTRHT
SEQ ID NO: 197	LCDR3 (COMBINED)	QQWYSYPWT
SEQ ID NO: 201	LCDR1 (IMGT)	QSLFNSNTNKNY
SEQ ID NO: 199	LCDR2 (IMGT)	YAS
SEQ ID NO: 197	LCDR3 (IMGT)	QQWYSYPWT
SEQ ID NO: 202	VL	DIMMTQSPSSLSVSAGEKATITCKSSQSLFNSNTNKN YLNWYLQKPGQSPKLLFYYASTRHTGVPDRFIGSGS GTDFTLTITSVQDEDLADYYCQQWYSYPWTFGPGTK LEIK
SEQ ID NO: 203	VL DNA	GACATCATGATGACCCAGTCTCCATCATCCCTGAG TGTGTCAGCAGGAGAGAAAGCCACTATCACCTGCA AGTCCAGTCAGAGTCTTTTCAACAGTAACACCAAC AAGAACTACTTGAAGTGGTACCTGCAGAAACCAG GGCAGTCTCCTAAACTGCTGTTCTATTATGCATCCA CTAGGCATACTGGGGTCCCTGATCGCTTCATAGGC AGTGGATCTGGGACAGATTTCACTCTCACCATCAC CAGTGTCCAGGATGAAGACCTGGCAGATTATTACT GTCAGCAGTGGTATAGCTACCCGTGGACGTTTCGGA CCTGGCACCAAGCTGGAAATCAAA
SEQ ID NO: 204	LC	DIMMTQSPSSLSVSAGEKATITCKSSQSLFNSNTNKN YLNWYLQKPGQSPKLLFYYASTRHTGVPDRFIGSGS GTDFTLTITSVQDEDLADYYCQQWYSYPWTFGPGTK LEIKRADAAPTVSIFPPSSEQLTSGGASVVCFLNNFYP KDINVKWKIDGSRQNGVLNSWTDQDSKDSTYSMS STLTTLTKDEYERHNSYTCEATHKTSTSPIVKSFNENE C
SEQ ID NO: 205	LC DNA	GACATCATGATGACCCAGTCTCCATCATCCCTGAG TGTGTCAGCAGGAGAGAAAGCCACTATCACCTGCA AGTCCAGTCAGAGTCTTTTCAACAGTAACACCAAC AAGAACTACTTGAAGTGGTACCTGCAGAAACCAG GGCAGTCTCCTAAACTGCTGTTCTATTATGCATCCA CTAGGCATACTGGGGTCCCTGATCGCTTCATAGGC

		AGTGGATCTGGGACAGATTTCACTCTCACCATCAC CAGTGTCCAGGATGAAGACCTGGCAGATTATTACT GTCAGCAGTGGTATAGCTACCCGTGGACGTTTCGGA CCTGGCACCAAGCTGGAAATCAAACGCGCTGATGC CGCCCCCTACCGTGAGCATCTTCCCCCCCAGCAGCG AGCAGCTGACCAGCGGCGGAGCCAGCGTGGTGTG CTTCCTGAACAACCTTCTACCCCAAGGACATCAACG TGAAGTGGAAGATCGACGGCAGCGAGCGGCAGAA CGGCGTGCTGAACAGCTGGACCGACCAGGACAGC AAGGACTCCACCTACAGCATGAGCAGCACCTGAC CCTGACCAAGGACGAGTACGAGCGGCACAACAGC TACACCTGCGAGGCCACCCACAAGACCAGCACCA GCCCCATCGTGAAGAGCTTCAACCGGAACGAGTGC
ANTI-mouse ENTPD2 MAB14		
SEQ ID NO: 182	HCDR1 (KABAT)	HYGMN
SEQ ID NO: 183	HCDR2 (KABAT)	WINTDTGNPTYADDFKG
SEQ ID NO: 184	HCDR3 (KABAT)	YGTLYSGYGFFDS
SEQ ID NO: 206	HCDR1 (CHOTHIA)	GYTFWHY
SEQ ID NO: 186	HCDR2 (CHOTHIA)	NTDTGN
SEQ ID NO: 184	HCDR3 (CHOTHIA)	YGTLYSGYGFFDS
SEQ ID NO: 207	HCDR1 (COMBINED)	GYTFWHYGMN
SEQ ID NO: 183	HCDR2 (COMBINED)	WINTDTGNPTYADDFKG
SEQ ID NO: 184	HCDR3 (COMBINED)	YGTLYSGYGFFDS
SEQ ID NO: 208	HCDR1 (IMGT)	GYTFWHYG
SEQ ID NO: 189	HCDR2 (IMGT)	INTDTGNP
SEQ ID NO: 190	HCDR3 (IMGT)	VRYGTLYSGYGFFDS
SEQ ID NO: 209	VH	QVQLVQSGAELKQPGQSVKISKASGYTFWHYGMN WVKQAPGQGLKWMGWINTDTGNPTYADDFKGRFV FSLDTSVSTAYLQISNLKNEDTATYYCVRYGTLYSGY GFFDSWGQGTLVTVSS
SEQ ID NO: 210	VH DNA	CAGGTCCAGCTGGTGCAGTCAGGAGCTGAGCTGA AGCAGCCTGGACAGTCGGTGAAGATCTCCTGCAAG GCTTCAGGGTACACCTTCTGGCACTATGGGATGAA CTGGGTGAAGCAGGCACAGGACAGGGTCTAAAG TGGATGGGCTGGATCAACACTGACACTGGGAATCC AACATATGCTGATGACTTCAAAGGACGGTTTGTCT

		TCTCCTTGGACACCTCTGTCAGCACTGCATATCTGC AGATCAGCAACCTCAAGAATGAAGACACGGCCAC GTATTACTGTGTGAGATATGGAACCTATATAGCG GATATGGGTTTTTTTTTGATTCTGGGGCCAAGGG ACCCTGGTCACCGTCTCCTCA
SEQ ID NO: 211	HC	QVQLVQSGAELKQPGQSVKISKASGYTFWHYGMN WVKQAPGQGLKWMGWINTDTGNPTYADDFKGRFV FSLDTSVSTAYLQISNLKNEDTATYYCVRYGTLVSGY GFFDTSWGQGLVTVSSAKTTAPSVYPLAPVCGDIT GSSVTLGCLVKGYFPEPVLTWNSGSLSSGVHTFPAV LQSDLYTLSSSVTVTSSTWPSQSITCNVAHPASSTKV DKKIEPRGPTIKPCPKCPAPNLLGGPSVFIFPPKIKD VLMISLSPVTCVVVDVSEDDPDVQISWFWNNVEVHT AQTQTHREDYNSTLRVVSALPIQHWDWMSGKEFKC KVNNDLPAPIERTISKPKGSVRAPQVYVLPPEEEM TKKQVTLTCMVTDFMPEDIYVEWTNNGKTELNYKN TEPVLDSGSYFMYSKLRVEKKNWVERNSYSCSVV HEGLHNHHTTKSFSRTPGK
SEQ ID NO: 212	HC DNA	CAGGTCCAGCTGGTGCAGTCAGGAGCTGAGCTGA AGCAGCCTGGACAGTCGGTGAAGATCTCCTGCAAG GCTTCAGGGTACACCTTCTGGCACTATGGGATGAA CTGGGTGAAGCAGGCACAGGACAGGGTCTAAAG TGGATGGGCTGGATCAACACTGACACTGGGAATCC AACATATGCTGATGACTTCAAAGGACGGTTTGTCT TCTCCTTGGACACCTCTGTCAGCACTGCATATCTGC AGATCAGCAACCTCAAGAATGAAGACACGGCCAC GTATTACTGTGTGAGATATGGAACCTATATAGCG GATATGGGTTTTTTTTTGATTCTGGGGCCAAGGG ACCCTGGTCACCGTCTCCTCAGCCAAGACCACCGC CCCCAGCGTGTACCCCTGGCCCCCGTGTGCGGCG ATACCACCGGCAGCAGCGTGACCCTGGGCTGCCTG GTGAAGGGCTACTTCCCCGAGCCCGTGACCCTGAC CTGGAACAGCGGCTCCCTGAGCAGCGGCGTGAC ACCTTCCCCGCGGTGCTGCAGAGCGACCTGTACAC CCTGTCCAGCTCCGTGACCCTGACAAGCAGCACCT GGCCAGCCAGAGCATCACCTGCAACGTGGCCAC CCCGCCAGCAGCACCAGGTGGACAAGAAGATCG AGCCAGGGGCCCCACCATCAAGCCCTGCCCCCCC TGCAAGTGCCCAGCCCCAACCTGCTGGGCGGACC CAGCGTGTTCATCTTCCCCCAAGATCAAGGACG TGCTGATGATCAGCCTGAGCCCCATCGTGACCTGC GTGGTGGTGGACGTGAGCGAGGACGACCCGACG TGCAGATCAGCTGGTTCGTGAACAACGTGGAGGTG CACACCGCCAGACCCAGACCCACCGGGAGGACT ACAACAGCACCTGCGCGTCGTGTCCGCCCTGCC ATCCAGCACCAAGGACTGGATGAGCGGCAAGAAT TCAAGTGCAAGGTGAACAACAAGGACCTGCCTGC CCCCATCGAGCGGACCATCAGCAAGCCCAAGGGC AGCGTGAGAGCCCCCAGGTGTACGTGCTGCCCC TCCCGAGGAAGAGATGACCAAGAAACAGGTGACA CTGACCTGCATGGTGACCGACTTCATGCCCGAGGA

		CATCTACGTGGAGTGGACCAACAACGGCAAGACC GAGCTGAACTACAAGAACACCGAGCCTGTGCTGG ACAGCGACGGCAGCTACTTCATGTACAGCAAGCTG CGGGTGGAGAAGAAAACTGGGTGGAGCGGAACA GCTACAGCTGCAGCGTGGTGCACGAGGGCCTGCAC AACCACCACACCACCAAGAGCTTCAGCCGGACCCC CGGCAAG
SEQ ID NO: 195	LCDR1 (KABAT)	KSSQSLFNSNTNKNYLN
SEQ ID NO: 196	LCDR2 (KABAT)	YASTRHT
SEQ ID NO: 197	LCDR3 (KABAT)	QQWYSYPWT
SEQ ID NO: 198	LCDR1 (CHOTHIA)	SQSLFNSNTNKNY
SEQ ID NO: 199	LCDR2 (CHOTHIA)	YAS
SEQ ID NO: 200	LCDR3 (CHOTHIA)	WYSYPW
SEQ ID NO: 195	LCDR1 (COMBINED)	KSSQSLFNSNTNKNYLN
SEQ ID NO: 196	LCDR2 (COMBINED)	YASTRHT
SEQ ID NO: 197	LCDR3 (COMBINED)	QQWYSYPWT
SEQ ID NO: 201	LCDR1 (IMGT)	QSLFNSNTNKNY
SEQ ID NO: 199	LCDR2 (IMGT)	YAS
SEQ ID NO: 197	LCDR3 (IMGT)	QQWYSYPWT
SEQ ID NO: 202	VL	DIMMTQSPSSLSVSAGEKATITCKSSQSLFNSNTNKN YLNWYLQKPGQSPKLLFYYASTRHTGVPDRFIGSGS GTDFTLTITSVQDEDLADYYCQQWYSYPWTFGPGTK LEIK
SEQ ID NO: 203	VL DNA	GACATCATGATGACCCAGTCTCCATCATCCCTGAG TGTGTCAGCAGGAGAGAAAGCCACTATCACCTGCA AGTCCAGTCAGAGTCTTTTCAACAGTAACACCAAC AAGAACTACTTGAACCTGGTACCTGCAGAAACCAG GGCAGTCTCCTAAACTGCTGTTCTATTATGCATCCA CTAGGCATACTGGGGTCCCTGATCGCTTCATAGGC AGTGGATCTGGGACAGATTTCACTCTCACCATCAC CAGTGTCCAGGATGAAGACCTGGCAGATTATTACT GTCAGCAGTGGTATAGCTACCCGTGGACGTTTCGGA CCTGGCACCAAGCTGGAAATCAAA
SEQ ID NO: 204	LC	DIMMTQSPSSLSVSAGEKATITCKSSQSLFNSNTNKN YLNWYLQKPGQSPKLLFYYASTRHTGVPDRFIGSGS GTDFTLTITSVQDEDLADYYCQQWYSYPWTFGPGTK LEIKRADAAPTVSIFPPSSEQLTSGGASVVCFLNNFYP

		KDINVKWKIDGSRQNGVLNSWTDQDSKSTYSMS STLTLTKDEYERHNSYTCEATHKTSTSPIVKSFNRC
SEQ ID NO: 205	LC DNA	GACATCATGATGACCCAGTCTCCATCATCCCTGAG TGTGTCAGCAGGAGAGAAAGCCACTATCACCTGCA AGTCCAGTCAGAGTCTTTTCAACAGTAACACCAAC AAGAACTACTTGAAGTGGTACCTGCAGAAACCAG GGCAGTCTCCTAAACTGCTGTTCTATTATGCATCCA CTAGGCATACTGGGGTCCCTGATCGCTTCATAGGC AGTGGATCTGGGACAGATTTCACTCTCACCATCAC CAGTGTCCAGGATGAAGACCTGGCAGATTATTACT GTCAGCAGTGGTATAGCTACCCGTGGACGTTTCGGA CCTGGCACCAAGCTGGAAATCAAACGCGCTGATGC CGCCCCCTACCGTGAGCATCTTCCCCCCCAGCAGCG AGCAGCTGACCAGCGGCGGAGCCAGCGTGGTGTG CTTCCTGAACAACCTTCTACCCCAAGGACATCAACG TGAAGTGGAAGATCGACGGCAGCGAGCGGCAGAA CGGCGTGCTGAACAGCTGGACCGACCAGGACAGC AAGGACTCCACCTACAGCATGAGCAGCACCTGAC CCTGACCAAGGACGAGTACGAGCGGCACAACAGC TACACCTGCGAGGCCACCCACAAGACCAGCACCA GCCCCATCGTGAAGAGCTTCAACCGGAACGAGTGC
ANTI-mouse ENTPD2 MAB15		
SEQ ID NO: 182	HCDR1 (KABAT)	HYGMN
SEQ ID NO: 183	HCDR2 (KABAT)	WINTDTGNPTYADDFKG
SEQ ID NO: 184	HCDR3 (KABAT)	YGTLYSGYGFFDS
SEQ ID NO: 213	HCDR1 (CHOTHIA)	GYTFHHY
SEQ ID NO: 186	HCDR2 (CHOTHIA)	NTDTGN
SEQ ID NO: 184	HCDR3 (CHOTHIA)	YGTLYSGYGFFDS
SEQ ID NO: 214	HCDR1 (COMBINED)	GYTFHHYGMN
SEQ ID NO: 183	HCDR2 (COMBINED)	WINTDTGNPTYADDFKG
SEQ ID NO: 184	HCDR3 (COMBINED)	YGTLYSGYGFFDS
SEQ ID NO: 215	HCDR1 (IMGT)	GYTFHHYG
SEQ ID NO: 189	HCDR2 (IMGT)	INTDTGNP
SEQ ID NO: 190	HCDR3 (IMGT)	VRYGTLYSGYGFFDS

SEQ ID NO: 216	VH	QVQLVQSGAELKQPGQSVKISCKASGYTFHHYGMN WVKQAPGQGLKWMGWINTDTGNPTYADDFKGRFV FSLDTSVSTAYLQISNLKNEDTATYYCVRYGTLVSGY GFFFDSWGQGLVTVSS
SEQ ID NO: 217	VH DNA	CAGGTCCAGCTGGTGCAGTCAGGAGCTGAGCTGA AGCAGCCTGGACAGTCGGTGAAGATCTCCTGCAAG GCTTCAGGGTACACCTTCCACCACTATGGGATGAA CTGGGTGAAGCAGGCACCAAGGACAGGGTCTAAAG TGGATGGGCTGGATCAACACTGACACTGGGAATCC AACATATGCTGATGACTTCAAAGGACGGTTTGTCT TCTCCTTGGACACCTCTGTCAGCACTGCATATCTGC AGATCAGCAACCTCAAGAATGAAGACACGGCCAC GTATTACTGTGTGAGATATGGAACCTATATAGCG GATATGGGTTTTTTTTTGATTCTGGGGCCAAGGG ACCCTGGTCACCGTCTCCTCA
SEQ ID NO: 218	HC	QVQLVQSGAELKQPGQSVKISCKASGYTFHHYGMN WVKQAPGQGLKWMGWINTDTGNPTYADDFKGRFV FSLDTSVSTAYLQISNLKNEDTATYYCVRYGTLVSGY GFFFDSWGQGLVTVSSAKTTAPSVYPLAPVCGDTT GSSVTLGCLVKGYFPEPVLTWNSGSLSSGVHTFPAV LQSDLYTLSSSVTVTSSTWPSQSITCNVAHPASSTKV DKKIEPRGPTIKPCPPCKCPAPNLLGGPSVFIFPPKIKD VLMISLSPIVTCVVVDVSEDDPDVQISWVFNNEVHT AQTQTHREDYNSTLRVVSALPIQHQDWMGKEFKC KVNNKDLPAPIERTISKPKGSVRAPQVYVLPPEEEM TKKQVTLTCMVTDFMPEDIYVEWTNNGKTELNYKN TEPVLSDGSYFMYSKLRVEKKNWVERNSYSCSVV HEGLHNHHTTKSFSRTPGK
SEQ ID NO: 219	HC DNA	CAGGTCCAGCTGGTGCAGTCAGGAGCTGAGCTGA AGCAGCCTGGACAGTCGGTGAAGATCTCCTGCAAG GCTTCAGGGTACACCTTCCACCACTATGGGATGAA CTGGGTGAAGCAGGCACCAAGGACAGGGTCTAAAG TGGATGGGCTGGATCAACACTGACACTGGGAATCC AACATATGCTGATGACTTCAAAGGACGGTTTGTCT TCTCCTTGGACACCTCTGTCAGCACTGCATATCTGC AGATCAGCAACCTCAAGAATGAAGACACGGCCAC GTATTACTGTGTGAGATATGGAACCTATATAGCG GATATGGGTTTTTTTTTGATTCTGGGGCCAAGGG ACCCTGGTCACCGTCTCCTCAGCCAAGACCACCGC CCCCAGCGTGTACCCCTGGCCCCCGTGTGCGGCG ATACCACCGGCAGCAGCGTGACCCTGGGCTGCCTG GTGAAGGGCTACTTCCCCGAGCCCGTGACCCTGAC CTGGAACAGCGGCTCCCTGAGCAGCGGCGTGAC ACCTTCCCCGCCGTGCTGCAGAGCGACCTGTACAC CCTGTCCAGCTCCGTGACCGTGACAAGCAGCACCT GGCCAGCCAGAGCATCACCTGCAACGTGGCCAC CCCGCCAGCAGCACCAAGGTGGACAAGAAGATCG AGCCAGGGGCCCCACCATCAAGCCCTGCCCCCCC TGCAAGTGCCAGCCCCCAACCTGCTGGGCGGACC CAGCGTGTTTCATCTTCCCCCCCCAAGATCAAGGACG

		TGCTGATGATCAGCCTGAGCCCCATCGTGACCTGC GTGGTGGTGGACGTGAGCGAGGACGACCCCGACG TGCAGATCAGCTGGTTCGTGAACAACGTGGAGGTG CACACCGCCCAGACCCAGACCCACCGGGAGGACT ACAACAGCACCCCTGCGCGTCGTGTCCGCCCTGCCC ATCCAGCACCCAGGACTGGATGAGCGGCAAAGAAT TCAAGTGCAAGGTGAACAACAAGGACCTGCCTGC CCCCATCGAGCGGACCATCAGCAAGCCCAAGGGC AGCGTGAGAGCCCCCAGGTGTACGTGCTGCCCCC TCCCGAGGAAGAGATGACCAAGAAACAGGTGACA CTGACCTGCATGGTGACCGACTTCATGCCCAGGA CATCTACGTGGAGTGGACCAACAACGGCAAGACC GAGCTGAACTACAAGAACACCGAGCCTGTGCTGG ACAGCGACGGCAGCTACTTCATGTACAGCAAGCTG CGGGTGGAGAAGAAAACTGGGTGGAGCGGAACA GCTACAGCTGCAGCGTGGTGCACGAGGGCCTGCAC AACCACCACACCACCAAGAGCTTCAGCCGGACCCC CGGCAAG
SEQ ID NO: 195	LCDR1 (KABAT)	KSSQSLFNSNTNKNYLN
SEQ ID NO: 196	LCDR2 (KABAT)	YASTRHT
SEQ ID NO: 197	LCDR3 (KABAT)	QQWYSPWT
SEQ ID NO: 198	LCDR1 (CHOTHIA)	SQSLFNSNTNKNY
SEQ ID NO: 199	LCDR2 (CHOTHIA)	YAS
SEQ ID NO: 200	LCDR3 (CHOTHIA)	WYSPW
SEQ ID NO: 195	LCDR1 (COMBINED)	KSSQSLFNSNTNKNYLN
SEQ ID NO: 196	LCDR2 (COMBINED)	YASTRHT
SEQ ID NO: 197	LCDR3 (COMBINED)	QQWYSPWT
SEQ ID NO: 201	LCDR1 (IMGT)	QSLFNSNTNKNY
SEQ ID NO: 199	LCDR2 (IMGT)	YAS
SEQ ID NO: 197	LCDR3 (IMGT)	QQWYSPWT
SEQ ID NO: 202	VL	DIMMTQSPSSLVSAGEKATITCKSSQSLFNSNTNKN YLNWYLQKPGQSPKLLFYYASTRHTGVPDRFIGSGS GTDFTLTITSVQDEDLADYYCQQWYSPWTFGPGTK LEIK
SEQ ID NO: 203	VL DNA	GACATCATGATGACCCAGTCTCCATCATCCCTGAG TGTGTGACGAGGAGAGAAAGCCACTATCACCTGCA AGTCCAGTCAGAGTCTTTTCAACAGTAACACCAAC AAGAACTACTTGAAGTGGTACCTGCAGAAACCAG

		GGCAGTCTCCTAAACTGCTGTTCTATTATGCATCCA CTAGGCATACTGGGGTCCCTGATCGCTTCATAGGC AGTGGATCTGGGACAGATTTCACTCTCACCATCAC CAGTGTCCAGGATGAAGACCTGGCAGATTATTACT GTCAGCAGTGGTATAGCTACCCGTGGACGTTTCGGA CCTGGCACCAAGCTGGAAATCAAA
SEQ ID NO: 204	LC	DIMMTQSPSSLVSAGEKATITCKSSQSLFNSNTNKN YLNWYLQKPGQSPKLLFYYASTRHTGVPDRFIGSGS GTDFTLTITSVQDEDLADYYCQWYSYPWTFGPGTK LEIKRADAAPTVSIFPPSSEQLTSGGASVVCFLNNFYP KDINVKWKIDGSRQNGVLNSWTDQDSKDYSTYSMS STLTLTKDEYERHNSYTCEATHKTTSTSPIVKSFNENE C
SEQ ID NO: 205	LC DNA	GACATCATGATGACCCAGTCTCCATCATCCCTGAG TGTGTGACAGGAGAGAAAGCCACTATCACCTGCA AGTCCAGTCAGAGTCTTTTCAACAGTAACACCAAC AAGAACTACTTGAAGTGGTACCTGCAGAAACCAG GGCAGTCTCCTAAACTGCTGTTCTATTATGCATCCA CTAGGCATACTGGGGTCCCTGATCGCTTCATAGGC AGTGGATCTGGGACAGATTTCACTCTCACCATCAC CAGTGTCCAGGATGAAGACCTGGCAGATTATTACT GTCAGCAGTGGTATAGCTACCCGTGGACGTTTCGGA CCTGGCACCAAGCTGGAAATCAAAACGCGCTGATGC CGCCCCCTACCGTGAGCATCTTCCCCCCCAGCAGCG AGCAGCTGACCAGCGGCGGAGCCAGCGTGGTGTG CTTCCTGAACAACCTTCTACCCCAAGGACATCAACG TGAAGTGGAAAGATCGACGGCAGCGAGCGGCAGAA CGGCGTGCTGAACAGCTGGACCGACCAGGACAGC AAGGACTCCACCTACAGCATGAGCAGCACCCCTGAC CCTGACCAAGGACGAGTACGAGCGGCACAACAGC TACACCTGCGAGGCCACCCACAAGACCAGCACCA GCCCCATCGTGAAGAGCTTCAACCGGAACGAGTGC
ANTI-mouse ENTPD2 FAB24		
SEQ ID NO: 182	HCDR1 (KABAT)	HYGMN
SEQ ID NO: 183	HCDR2 (KABAT)	WINTDTGNPTYADDFKG
SEQ ID NO: 184	HCDR3 (KABAT)	YGTLYSGYGFFDS
SEQ ID NO: 185	HCDR1 (CHOTHIA)	GYTFTHY
SEQ ID NO: 186	HCDR2 (CHOTHIA)	NTDTGN
SEQ ID NO: 184	HCDR3 (CHOTHIA)	YGTLYSGYGFFDS
SEQ ID NO: 187	HCDR1 (COMBINED)	GYTFTHYGMN

SEQ ID NO: 183	HCDR2 (COMBINED)	WINTDTGNPTYADDFKG
SEQ ID NO: 184	HCDR3 (COMBINED)	YGTLYSGYGFFDS
SEQ ID NO: 188	HCDR1 (IMGT)	GYTFTHYG
SEQ ID NO: 189	HCDR2 (IMGT)	INTDTGNP
SEQ ID NO: 190	HCDR3 (IMGT)	VRYGTLYSGYGFFDS
SEQ ID NO: 191	VH	QVQLVQSGAELKQPGQSVKISCKASGYTFTHYGMN WVKQAPGQGLKWMGWINTDTGNPTYADDFKGRFV FSLDTSVSTAYLQISNLKNEDTATYYCVRYGTLYSGY GFFDSWGQGLVTVSS
SEQ ID NO: 192	VH DNA	CAGGTCCAGCTGGTGCAGTCAGGAGCTGAGCTGA AGCAGCCTGGACAGTCGGTGAAGATCTCCTGCAAG GCTTCAGGGTACACCTTCACACACTATGGGATGAA CTGGGTGAAGCAGGCACAGGACAGGGTCTAAAG TGGATGGGCTGGATCAACACTGACACTGGGAATCC AACATATGCTGATGACTTCAAAGGACGGTTTGTCT TCTCCTTGGACACCTCTGTCAGCACTGCATATCTGC AGATCAGCAACCTCAAGAATGAAGACACGGCCAC GTATTACTGTGTGAGATATGGAACCCTATATAGCG GATATGGGTTTTTTTTTGATTCTGGGGCCAAGGG ACCCTGGTCACCGTCTCCTCA
SEQ ID NO: 338	HC	QVQLVQSGAELKQPGQSVKISCKASGYTFTHYGMN WVKQAPGQGLKWMGWINTDTGNPTYADDFKGRFV FSLDTSVSTAYLQISNLKNEDTATYYCVRYGTLYSGY GFFDSWGQGLVTVSSASTKGPSVFPLAPSSKSTSG GTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV LQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTK VDKRVEPKSC
SEQ ID NO: 339	HC DNA	CAGGTCCAGCTGGTGCAGTCAGGAGCTGAGCTGA AGCAGCCTGGACAGTCGGTGAAGATCTCCTGCAAG GCTTCAGGGTACACCTTCACACACTATGGGATGAA CTGGGTGAAGCAGGCACAGGACAGGGTCTAAAG TGGATGGGCTGGATCAACACTGACACTGGGAATCC AACATATGCTGATGACTTCAAAGGACGGTTTGTCT TCTCCTTGGACACCTCTGTCAGCACTGCATATCTGC AGATCAGCAACCTCAAGAATGAAGACACGGCCAC GTATTACTGTGTGAGATATGGAACCCTATATAGCG GATATGGGTTTTTTTTTGATTCTGGGGCCAAGGG ACCCTGGTCACCGTCTCCTCAgctagcaccaggcccaagt tggttccctggccccagcagcaagtctactccggcggaactgtgcctgggt gcctggtgaaggactactccccgagccgtgacagtgtcctggaactgtgggct ctgactccggcgtgcacacctccccgccgtgctgcagagcagcgccgtgtacag cctgagcagcgtggtgacagtgcctccagctctctgggaaccagacatatct

		gcaacgtgaaccacaagcccagcaacaccaaggtggacaagagagtgagagccc aagagctgc
SEQ ID NO: 195	LCDR1 (KABAT)	KSSQSLFNSNTNKNYLN
SEQ ID NO: 196	LCDR2 (KABAT)	YASTRHT
SEQ ID NO: 197	LCDR3 (KABAT)	QQWYSYPWT
SEQ ID NO: 198	LCDR1 (CHOTHIA)	SQSLFNSNTNKNY
SEQ ID NO: 199	LCDR2 (CHOTHIA)	YAS
SEQ ID NO: 200	LCDR3 (CHOTHIA)	WYSYPW
SEQ ID NO: 195	LCDR1 (COMBINED)	KSSQSLFNSNTNKNYLN
SEQ ID NO: 196	LCDR2 (COMBINED)	YASTRHT
SEQ ID NO: 197	LCDR3 (COMBINED)	QQWYSYPWT
SEQ ID NO: 201	LCDR1 (IMGT)	QSLFNSNTNKNY
SEQ ID NO: 199	LCDR2 (IMGT)	YAS
SEQ ID NO: 197	LCDR3 (IMGT)	QQWYSYPWT
SEQ ID NO: 202	VL	DIMMTQSPSSLSVSAGEKATITCKSSQSLFNSNTNKN YLNWYLQKPGQSPKLLFYYASTRHTGVPDRFIGSGS GTDFTLTITSVQDEDLADYYCQQWYSYPWTFGPGTK LEIK
SEQ ID NO: 203	VL DNA	GACATCATGATGACCCAGTCTCCATCATCCCTGAG TGTGTCAGCAGGAGAGAAAGCCACTATCACCTGCA AGTCCAGTCAGAGTCTTTTCAACAGTAACACCAAC AAGAACTACTTGAAGTGGTACCTGCAGAAACCAG GGCAGTCTCCTAAACTGCTGTTCTATTATGCATCCA CTAGGCATACTGGGGTCCCTGATCGTTTCATAGGC AGTGGATCTGGGACAGATTTCACTCTCACCATCAC CAGTGTCCAGGATGAAGACCTGGCAGATTATTACT GTCAGCAGTGGTATAGCTACCCGTGGACGTTTCGGA CCTGGCACCAAGCTGGAAATCAAA
SEQ ID NO: 340	LC	DIMMTQSPSSLSVSAGEKATITCKSSQSLFNSNTNKN YLNWYLQKPGQSPKLLFYYASTRHTGVPDRFIGSGS GTDFTLTITSVQDEDLADYYCQQWYSYPWTFGPGTK LEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYP REAKVQWKVDNALQSGNSQESVTEQDSKSTYSLSS TLTLKADYEHKVVYACEVTHQGLSSPVTKSFNERGE C
SEQ ID NO: 341	LC DNA	GACATCATGATGACCCAGTCTCCATCATCCCTGAG TGTGTCAGCAGGAGAGAAAGCCACTATCACCTGCA

		AGTCCAGTCAGAGTCTTTTCAACAGTAACACCAAC AAGAACTACTTGAAGTGGTACCTGCAGAAACCAG GGCAGTCTCCTAAACTGCTGTTCTATTATGCATCCA CTAGGCATACTGGGGTCCCTGATCGCTTCATAGGC AGTGGATCTGGGACAGATTTCACTCTCACCATCAC CAGTGTCCAGGATGAAGACCTGGCAGATTATTACT GTCAGCAGTGGTATAGCTACCCGTGGACGTTCCGA CCTGGCACCAAGCTGGAAATCAA Acgtacgggtggccgctcc cagcgtgtcatcttccccccagcgacgagcagctgaagagtggcaccgccagc gtggtgtgcctgctgaacaacttctacccccgggagggccaaggtgcagtgggaagg tggacaacgccctgcagagcggcaacagccaggagagcgtcaccgagcaggac agcaaggactccacctacgcctgagcagcacctgaccctgagcaaggccgac tacgagaagcataaggtgtacgcctgcaggtgacccaccagggcctgtccagcc ccgtgaccaagagcttcaacaggggcgagtgc

[0247] In some embodiments, the anti-mouse ENTPD2 antibody or antibody fragment (e.g., an antigen binding fragment) comprises a VH domain having an amino acid sequence of any VH domain described in Table 26. Other suitable anti-mouse ENTPD2 antibodies or antibody fragments (e.g., antigen binding fragments) can include amino acids that have been mutated, yet have at least 80, 85, 90, 95, 96, 97, 98, or 99 percent identity in the VH domain with the VH regions depicted in the sequences described in Table 26. The present disclosure in certain embodiments also provides antibodies or antibody fragments (e.g., antigen binding fragments) that specifically bind to mouse ENTPD2, wherein the antibodies or antibody fragments (e.g., antigen binding fragments) comprise a VH CDR having an amino acid sequence of any one of the VH CDRs listed in Table 26. In particular embodiments, the invention provides antibodies or antibody fragments (e.g., antigen binding fragments) that specifically bind to mouse ENTPD2, comprising (or alternatively, consist of) one, two, three, four, five or more VH CDRs having an amino acid sequence of any one of the VH CDRs listed in Table 26.

[0248] In some embodiments, the anti-mouse ENTPD2 antibody or antibody fragment (e.g., antigen binding fragment) comprises a VL domain having an amino acid sequence of any VL domain described in Table 26. Other suitable anti-mouse ENTPD2 antibodies or antibody fragments (e.g., antigen binding fragments) can include amino acids that have been mutated, yet have at least 80, 85, 90, 95, 96, 97, 98, or 99 percent identity in the VL domain with the VL regions depicted in the sequences described in Table 26. The present disclosure also provides antibodies or antibody fragments (e.g., antigen binding fragments) that specifically bind to mouse ENTPD2, the antibodies or antibody fragments (e.g., antigen binding fragments) comprise a VL CDR having an amino acid sequence of any

one of the VL CDRs listed in Table 26. In particular, the invention provides antibodies or antibody fragments (e.g., antigen binding fragments) that specifically bind to mouse ENTPD2, which comprise (or alternatively, consist of) one, two, three or more VL CDRs having an amino acid sequence of any one of the VL CDRs listed in Table 26.

[0249] Other anti-mouse ENTPD2 antibodies or antibody fragments (e.g., antigen binding fragment) disclosed herein include amino acids that have been mutated, yet have at least 80, 85, 90, 95, 96, 97, 98, or 99 percent identity in the CDR regions with the CDR regions depicted in the sequences described in Table 26. In some embodiments, it includes mutant amino acid sequences wherein no more than 1, 2, 3, 4 or 5 amino acids have been mutated in the CDR regions when compared with the CDR regions depicted in the sequence described in Table 26.

[0250] Also provided herein are nucleic acid sequences that encode VH, VL, full length heavy chain, and full length light chain of antibodies and antigen binding fragments thereof that specifically bind to mouse ENTPD2, e.g., the nucleic acid sequences in Table 26. Such nucleic acid sequences can be optimized for expression in mammalian cells.

[0251] Provided herein are also antibodies or antigen binding fragments thereof that specifically bind to an epitope in mouse ENTPD2, wherein the epitope comprises at least one (e.g., at least two, at least three, at least four, at least five, at least six, at least seven, at least eight, at least nine, at least ten, at least eleven, at least twelve, at least thirteen, at least fourteen, at least fifteen, at least twenty) of the following residues: Ser74, Cys75, Asp76, Tyr349, Tyr350, Asp353, Phe354, Thr357, Val358, Gly360, Gln385, Ala386, Arg387, Val388, Pro389, Gly390, Gln391, Thr393, Arg394, or Tyr398.

Framework and Engineered or Modified Antibodies

[0252] An antibody of the invention further can be prepared using an antibody having one or more of the VH and/or VL sequences as starting material to engineer a modified antibody, which modified antibody may have altered properties from the starting antibody. An antibody can be engineered by modifying one or more residues within one or both variable regions (i.e., VH and/or VL), for example within one or more CDR regions and/or within one or more framework regions. Additionally or alternatively, an antibody can be engineered by modifying residues within the constant region(s), for example to alter the effector function(s) of the antibody.

[0253] One type of variable region engineering that can be performed is CDR grafting. Antibodies interact with target antigens predominantly through amino acid residues

that are located in the six heavy and light chain complementarity determining regions (CDRs). For this reason, the amino acid sequences within CDRs are more diverse between individual antibodies than sequences outside of CDRs. Because CDR sequences are responsible for most antibody-antigen interactions, it is possible to express recombinant antibodies that mimic the properties of specific naturally occurring antibodies by constructing expression vectors that include CDR sequences from the specific naturally occurring antibody grafted onto framework sequences from a different antibody with different properties (see, e.g., Riechmann, L. et al., 1998 *Nature* 332:323-327; Jones, P. et al., 1986 *Nature* 321:522-525; Queen, C. et al., 1989 *Proc. Natl. Acad., U.S.A.* 86:10029-10033; U.S. Pat. No. 5,225,539 to Winter, and U.S. Pat. Nos. 5,530,101; 5,585,089; 5,693,762 and 6,180,370 to Queen et al.)

[0254] Such framework sequences can be obtained from public DNA databases or published references that include germline antibody gene sequences or rearranged antibody sequences. For example, germline DNA sequences for human heavy and light chain variable region genes can be found in the “VBase” human germline sequence database (available on the Internet at www.mrc-cpe.cam.ac.uk/vbase), as well as in Kabat, E. A., et al., 1991 *Sequences of Proteins of Immunological Interest*, Fifth Edition, U.S. Department of Health and Human Services, NIH Publication No. 91-3242; Tomlinson, I. M., et al., 1992 *J. Mol. Biol.* 227:776-798; and Cox, J. P. L. et al., 1994 *Eur. J Immunol.* 24:827-836). ; For example, germline DNA sequences for human heavy and light chain variable region genes and rearranged antibody sequences can be found in “IMGT” database (available on the Internet at www.imgt.org; see Lefranc, M.P. et al., 1999 *Nucleic Acids Res.* 27:209-212).

[0255] An example of framework sequences for use in the antibodies and antigen binding fragments thereof of the invention are those that are structurally similar to the framework sequences used by selected antibodies and antigen binding fragments thereof of the invention, e.g., consensus sequences and/or framework sequences used by monoclonal antibodies of the invention. The VH CDR1, 2 and 3 sequences, and the VL CDR1, 2 and 3 sequences, can be grafted onto framework regions that have the identical sequence as that found in the germline immunoglobulin gene from which the framework sequence derive, or the CDR sequences can be grafted onto framework regions that contain one or more mutations as compared to the germline sequences. For example, it has been found that in certain instances it is beneficial to mutate residues within the framework regions to maintain or enhance the antigen binding ability of the antibody (see e.g., U.S. Pat. Nos. 5,530,101; 5,585,089; 5,693,762 and 6,180,370 to Queen et al).

[0256] Another type of variable region modification is to mutate amino acid residues within the VH and/or VL CDR1, CDR2 and/or CDR3 regions to thereby improve one or more binding properties (e.g., affinity) of the antibody of interest, known as “affinity maturation”. Site-directed mutagenesis or PCR-mediated mutagenesis can be performed to introduce the mutation(s) and the effect on antibody binding, or other functional property of interest, can be evaluated in *in vitro* or *in vivo* assays as described herein and provided in the Examples. Conservative modifications (as discussed above) can be introduced. The mutations may be amino acid substitutions, additions or deletions. Moreover, typically no more than one, two, three, four or five residues within a CDR region are altered.

[0257] A wide variety of antibody/immunoglobulin frameworks or scaffolds can be employed so long as the resulting polypeptide includes at least one binding region which specifically binds to ENTPD2 (e.g., human ENTPD2 protein). Such frameworks or scaffolds include the 5 main idiotypes of human immunoglobulins, antigen-binding fragments thereof, and include immunoglobulins of other animal species, preferably having humanized aspects. Single heavy-chain antibodies such as those identified in camelids are of particular interest in this regard. Novel frameworks, scaffolds and fragments continue to be discovered and developed by those skilled in the art.

[0258] In one aspect, the invention pertains to a method of generating non-immunoglobulin based antibodies using non-immunoglobulin scaffolds onto which CDRs of the invention can be grafted. Known or future non-immunoglobulin frameworks and scaffolds may be employed, as long as they comprise a binding region specific for the target ENTPD2 protein. Known non-immunoglobulin frameworks or scaffolds include, but are not limited to, fibronectin (Compound Therapeutics, Inc., Waltham, Mass.), ankyrin (Molecular Partners AG, Zurich, Switzerland), domain antibodies (Domantis, Ltd., Cambridge, Mass., and Ablynx nv, Zwijnaarde, Belgium), lipocalin (Pieris Proteolab AG, Freising, Germany), small modular immuno-pharmaceuticals (Trubion Pharmaceuticals Inc., Seattle, Wash.), maxybodies (Avidia, Inc., Mountain View, Calif.), Protein A (Affibody AG, Sweden), and affilin (gamma-crystallin or ubiquitin) (SciI Proteins GmbH, Halle, Germany).

[0259] The fibronectin scaffolds are based on fibronectin type III domain (e.g., the tenth module of the fibronectin type III (10 Fn3 domain)). The fibronectin type III domain has 7 or 8 beta strands which are distributed between two beta sheets, which themselves pack against each other to form the core of the protein, and further containing loops (analogous to CDRs) which connect the beta strands to each other and are solvent exposed. There are at least three such loops at each edge of the beta sheet sandwich, where the edge is the boundary

of the protein perpendicular to the direction of the beta strands (see U.S. Pat. No. 6,818,418). These fibronectin-based scaffolds are not an immunoglobulin, although the overall fold is closely related to that of the smallest functional antibody fragment, the variable region of the heavy chain, which comprises the entire antigen recognition unit in camel and llama IgG. Because of this structure, the non-immunoglobulin antibody mimics antigen binding properties that are similar in nature and affinity for those of antibodies. These scaffolds can be used in a loop randomization and shuffling strategy *in vitro* that is similar to the process of affinity maturation of antibodies *in vivo*. These fibronectin-based molecules can be used as scaffolds where the loop regions of the molecule can be replaced with CDRs of the invention using standard cloning techniques.

[0260] The ankyrin technology is based on using proteins with ankyrin derived repeat modules as scaffolds for bearing variable regions which can be used for binding to different targets. The ankyrin repeat module is a 33 amino acid polypeptide consisting of two anti-parallel alpha-helices and a beta-turn. Binding of the variable regions is mostly optimized by using ribosome display.

[0261] Avimers are derived from natural A-domain containing protein such as LRP-1. These domains are used by nature for protein-protein interactions and in human over 250 proteins are structurally based on A-domains. Avimers consist of a number of different “A-domain” monomers (2-10) linked via amino acid linkers. Avimers can be created that can bind to the target antigen using the methodology described in, for example, U.S. Patent Application Publication Nos. 20040175756; 20050053973; 20050048512; and 20060008844.

[0262] Affibody affinity ligands are small, simple proteins composed of a three-helix bundle based on the scaffold of one of the IgG-binding domains of Protein A. Protein A is a surface protein from the bacterium *Staphylococcus aureus*. This scaffold domain consists of 58 amino acids, 13 of which are randomized to generate affibody libraries with a large number of ligand variants (See e.g., U.S. Pat. No. 5,831,012). Affibody molecules mimic antibodies, they have a molecular weight of 6 kDa, compared to the molecular weight of antibodies, which is 150 kDa. In spite of its small size, the binding site of affibody molecules is similar to that of an antibody.

[0263] Anticalins are products developed by the company Pieris ProteoLab AG. They are derived from lipocalins, a widespread group of small and robust proteins that are usually involved in the physiological transport or storage of chemically sensitive or insoluble compounds. Several natural lipocalins occur in human tissues or body liquids. The protein architecture is reminiscent of immunoglobulins, with hypervariable loops on top of a rigid

framework. However, in contrast with antibodies or their recombinant fragments, lipocalins are composed of a single polypeptide chain with 160 to 180 amino acid residues, being just marginally bigger than a single immunoglobulin domain. The set of four loops, which makes up the binding pocket, shows pronounced structural plasticity and tolerates a variety of side chains. The binding site can thus be reshaped in a proprietary process in order to recognize prescribed target molecules of different shape with high affinity and specificity. One protein of lipocalin family, the bilin-binding protein (BBP) of *Pieris Brassicae* has been used to develop anticalins by mutagenizing the set of four loops. One example of a patent application describing anticalins is in PCT Publication No. WO 199916873.

[0264] Affilin molecules are small non-immunoglobulin proteins which are designed for specific affinities towards proteins and small molecules. New affilin molecules can be very quickly selected from two libraries, each of which is based on a different human derived scaffold protein. Affilin molecules do not show any structural homology to immunoglobulin proteins. Currently, two affilin scaffolds are employed, one of which is gamma crystalline, a human structural eye lens protein and the other is "ubiquitin" superfamily proteins. Both human scaffolds are very small, show high temperature stability and are almost resistant to pH changes and denaturing agents. This high stability is mainly due to the expanded beta sheet structure of the proteins. Examples of gamma crystalline derived proteins are described in WO200104144 and examples of "ubiquitin-like" proteins are described in WO2004106368.

[0265] Protein epitope mimetics (PEM) are medium-sized, cyclic, peptide-like molecules (MW 1-2 kDa) mimicking beta-hairpin secondary structures of proteins, the major secondary structure involved in protein-protein interactions.

[0266] Engineered antibodies and antigen-binding fragments thereof of the invention include those in which modifications have been made to framework residues within VH and/or VL, e.g. to improve the properties of the antibody. Typically such framework modifications are made to decrease the immunogenicity of the antibody. For example, one approach is to "backmutate" one or more framework residues to the corresponding germline sequence. More specifically, an antibody that has undergone somatic mutation may contain framework residues that differ from the germline sequence from which the antibody is derived. Such residues can be identified by comparing the antibody framework sequences to the germline sequences from which the antibody is derived. To return the framework region sequences to their germline configuration, the somatic mutations can be "backmutated" to the germline sequence by, for example, site-directed mutagenesis. Such "backmutated"

antibodies are also intended to be encompassed by the invention.

[0267] Another type of framework modification involves mutating one or more residues within the framework region, or even within one or more CDR regions, to remove T cell-epitopes to thereby reduce the potential immunogenicity of the antibody. This approach is also referred to as “deimmunization” and is described in further detail in U.S. Patent Publication No. 20030153043 by Carr et al.

[0268] In addition or alternative to modifications made within the framework or CDR regions, antibodies of the invention may be engineered to include modifications within the Fc region, typically to alter one or more functional properties of the antibody, such as serum half-life, complement fixation, Fc receptor binding, and/or antigen-dependent cellular cytotoxicity. Furthermore, an antibody of the invention may be chemically modified (e.g., one or more chemical moieties can be attached to the antibody) or be modified to alter its glycosylation, again to alter one or more functional properties of the antibody. Each of these embodiments is described in further detail below. The numbering of residues in the Fc region is that of the EU index of Kabat.

[0269] In one embodiment, the hinge region of CH1 is modified such that the number of cysteine residues in the hinge region is altered, e.g., increased or decreased. This approach is described further in U.S. Pat. No. 5,677,425 by Bodmer et al. The number of cysteine residues in the hinge region of CH1 is altered to, for example, facilitate assembly of the light and heavy chains or to increase or decrease the stability of the antibody.

[0270] In another embodiment, the Fc hinge region of an antibody is mutated to decrease the biological half-life of the antibody. More specifically, one or more amino acid mutations are introduced into the CH2-CH3 domain interface region of the Fc-hinge fragment such that the antibody has impaired Staphylococcal protein A (SpA) binding relative to native Fc-hinge domain SpA binding. This approach is described in further detail in U.S. Pat. No. 6,165,745 by Ward et al.

[0271] In another embodiment, the antibody is modified to increase its biological half-life. Various approaches are possible. For example, one or more of the following mutations can be introduced: T252L, T254S, T256F, as described in U.S. Pat. No. 6,277,375 to Ward. Alternatively, to increase the biological half life, the antibody can be altered within the CH1 or CL region to contain a salvage receptor binding epitope taken from two loops of a CH2 domain of an Fc region of an IgG, as described in U.S. Pat. Nos. 5,869,046 and 6,121,022 by Presta et al.

[0272] In one embodiment, the Fc region is altered by replacing at least one amino

acid residue with a different amino acid residue to alter the effector functions of the antibody. For example, one or more amino acids can be replaced with a different amino acid residue such that the antibody has an altered affinity for an effector ligand but retains the antigen-binding ability of the parent antibody. The effector ligand to which affinity is altered can be, for example, an Fc receptor or the C1 component of complement. This approach is described in further detail in U.S. Pat. Nos. 5,624,821 and 5,648,260, both by Winter et al.

[0273] In another embodiment, one or more amino acids selected from amino acid residues can be replaced with a different amino acid residue such that the antibody has altered C1q binding and/or reduced or abolished complement dependent cytotoxicity (CDC). This approach is described in further detail in U.S. Pat. No. 6,194,551 by Idusogie et al.

[0274] In another embodiment, one or more amino acid residues are altered to thereby alter the ability of the antibody to fix complement. This approach is described further in PCT Publication WO 94/29351 by Bodmer et al.

[0275] In some embodiments, the ENTPD2-binding antibodies or antigen binding fragments thereof contain a human IgG1 constant region. In some embodiments, the human IgG1 constant region includes an Fc region.

[0276] In some embodiments, the Fc region of the ENTPD2-binding antibodies or antigen binding fragments thereof includes one or more mutations mediating reduced or no antibody-dependent cellular cytotoxicity (ADCC) or complement-dependent cytotoxicity (CDC). In some embodiments, amino acid residues L234 and L235 of the IgG1 constant region are substituted to A234 and A235. In some embodiments, amino acid residue N267 of the IgG1 constant region is substituted to A267. In some embodiments, amino acid residues D265 and P329 of the IgG1 constant region are substituted to A265 and A329. In certain embodiments, the Fc region optionally comprises a mutation or combination of mutations conferring reduced effector function selected from any one of D265A, P329A, P329G, N297A, D265A/P329A, D265A/N297A, L234/L235A, P329A/L234A/L235A, and P329G/L234A/L235A. In some embodiments, the Fc region comprises a mutation or combination of mutations conferring reduced effector function selected from any one of D265A, P329A, P329G, N297A, D265A/P329A, D265A/N297A, L234/L235A, P329A/L234A/L235A, and P329G/L234A/L235A (all positions by EU numbering).

[0277] In yet another embodiment, the Fc region is modified to increase the ability of the antibody to mediate antibody dependent cellular cytotoxicity (ADCC) and/or to increase the affinity of the antibody for an Fc-gamma receptor by modifying one or more amino acids. This approach is described further in PCT Publication WO 00/42072 by Presta. Moreover,

the binding sites on human IgG1 for Fc-gamma RI, Fc-gamma RII, Fc-gamma RIII and FcRn have been mapped and variants with improved binding have been described (see Shields, R. L. et al., 2001 J. Biol. Chem. 276:6591-6604). For example, the Fc region can comprise a mutation or combination of mutations conferring increased effector function selected from any one of S239D, I332E, A330L, S298A, E333A, E333S, K334A, K236A, K236W, F243L, P247I, D280H, K290S, R292P, S298D, S298V, Y300L, V305I, A339D, A339Q, A339T, P396L (all positions by EU numbering).

[0278] In still another embodiment, the glycosylation of an antibody is modified. For example, an aglycosylated antibody can be made (i.e., the antibody lacks glycosylation). Glycosylation can be altered to, for example, increase the affinity of the antibody for antigen. Such carbohydrate modifications can be accomplished by, for example, altering one or more sites of glycosylation within the antibody sequence. For example, one or more amino acid substitutions can be made that result in elimination of one or more variable region framework glycosylation sites to thereby eliminate glycosylation at that site. Such aglycosylation may increase the affinity of the antibody for antigen. Such an approach is described in further detail in U.S. Pat. Nos. 5,714,350 and 6,350,861 by Co et al.

[0279] Additionally or alternatively, an antibody can be made that has an altered type of glycosylation, such as a hypofucosylated antibody having reduced amounts of fucosyl residues or an antibody having increased bisecting GlcNAc structures. Such altered glycosylation patterns have been demonstrated to increase the ADCC ability of antibodies. Such carbohydrate modifications can be accomplished by, for example, expressing the antibody in a host cell with altered glycosylation machinery. Cells with altered glycosylation machinery have been described in the art and can be used as host cells in which to express recombinant antibodies of the invention to thereby produce an antibody with altered glycosylation. For example, EP 1,176,195 by Hang et al. describes a cell line with a functionally disrupted FUT8 gene, which encodes a fucosyl transferase, such that antibodies expressed in such a cell line exhibit hypofucosylation. PCT Publication WO 03/035835 by Presta describes a variant CHO cell line, LecI3 cells, with reduced ability to attach fucose to Asn (297)-linked carbohydrates, also resulting in hypofucosylation of antibodies expressed in that host cell (see also Shields, R. L. et al., 2002 J. Biol. Chem. 277:26733-26740). PCT Publication WO 99/54342 by Umana et al. describes cell lines engineered to express glycoprotein-modifying glycosyl transferases (e.g., beta (1,4)--N acetylglucosaminyltransferase III (GnTIII)) such that antibodies expressed in the engineered cell lines exhibit increased bisecting GlcNAc structures which results in increased ADCC

activity of the antibodies (see also Umana et al., 1999 Nat. Biotech. 17:176-180).

[0280] In some embodiments, the ENTPD2 antibody has an IgG1 isotype with one or more mutations (*e.g.*, relative to a wild-type Fc region of the same isotype). In some embodiments, the one or more mutations are selected from N297A, N297Q (BoltS et al. (1993) *Eur J Immunol* 23:403-411), D265A, L234A, L235A (McEarchern et al., (2007) *Blood*, 109:1185-1192), C226S, C229S (McEarchern et al., (2007) *Blood*, 109:1185-1192), P238S (Davis et al., (2007) *J Rheumatol*, 34:2204-2210), E233P, L234V (McEarchern et al., (2007) *Blood*, 109:1185-1192), P238A, A327Q, A327G, P329A (Shields RL. et al., (2001) *J Bioi Chern.* 276(9):6591-604), K322A, L234F, L235E (Hezareh, et al., (2001) *J Viral* 75, 12161-12168; Oganessian et al., (2008). *Acta Crystallographica* 64, 700-704), P331S (Oganessian et al., (2008) *Acta Crystallographica* 64, 700-704), T394D (Wilkinson et al. (2013) *MAbs* 5(3): 406-417), A330L, M252Y, S254T, and/or T256E, where the amino acid position is according to the EU or Kabat numbering convention. In certain embodiments, the Fc region further includes an amino acid deletion at a position corresponding to glycine 236 according to the EU or Kabat numbering convention.

[0281] In some embodiments, the antibody has an IgG1 isotype with a heavy chain constant region that contains a C220S mutation according to the EU or Kabat numbering convention.

[0282] In some embodiments, the Fc region contains one or more mutations selected from L234F, L235E, P331S, D265A, and/or N297Q, according to EU or Kabat numbering convention. In some embodiments, the Fc region contains one or more mutations selected from L234A, L235A, D265A, P329A, N297A, N297Q according to EU or Kabat numbering convention.

[0283] In certain embodiments, the antibody has an IgG2 isotype. In some embodiments, the antibody contains a human IgG2 constant region. In some embodiments, the human IgG2 constant region includes an Fc region. In some embodiments, the Fc region contains one or more modifications. For example, in some embodiments, the Fc region contains one or more mutations (*e.g.*, relative to a wild-type Fc region of the same isotype). In some embodiments, the one or more mutations are selected from V234A, G237A, P238S, H268A, H268E, H268Q, V309L, N297A, N297Q, V309L, A330S, P331S, C232S, C233S, M252Y, S254T, and/or T256E, where the amino acid position is according to the EU or Kabat numbering convention.

[0284] In certain embodiments, the antibody has an IgG4 isotype. In some embodiments, the antibody contains a human IgG4 constant region. In some embodiments,

the human IgG4 constant region includes an Fc region. In some embodiments, the Fc region contains one or more modifications. For example, in some embodiments, the Fc region contains one or more mutations (*e.g.*, relative to a wild-type Fc region of the same isotype). In some embodiments, the one or more mutations are selected from E233P, F234V, L234A, L235A, G237A, E318A (Hutchins et al. (1995) Proc Natl Acad Sci USA, 92:11980-11984), S228P, L236E, S241P, L248E (Reddy et al., (2000) J Immunol, 164:1925-1933; Angal et al., (1993) Mol Immunol. 30(1):105-8; US 8614299 B2), T394D, M252Y, S254T, T256E, N297A, and/or N297Q, where the amino acid position is according to the EU or Kabat numbering convention.

[0285] In some embodiments, the Fc region further contains one or more additional mutations selected from a M252Y, S254T, and/or T256E, where the amino acid position is according to the EU or Kabat numbering convention.

[0286] In some embodiments, one or more of the IgG1 variants described herein may be combined with an A330L mutation (Lazaret al., (2006) Proc Natl Acad Sci USA, 103:4005-4010), or one or more of L234F, L235E, and/or P331S mutations (Sazinsky et al., (2008) Proc Natl Acad Sci USA, 105:20167-20172), where the amino acid position is according to the EU or Kabat numbering convention, to eliminate complement activation. In some embodiments, the IgG variants described herein may be combined with one or more mutations to enhance the antibody half-life in human serum (*e.g.* M252Y, S254T, T256E mutations according to the EU or Kabat numbering convention) (Dall'Acqua et al., (2006) J Biol Chem, 281:23514-23524; and Strohl et al., (2009) Current Opinion in Biotechnology, 20:685-691).

[0287] In some embodiments, an IgG4 variant of the present disclosure may be combined with an S228P mutation according to the EU or Kabat numbering convention (Angal et al., (1993) Mol Immunol, 30:105-108) and/or with one or more mutations described in Peters et al., (2012) J Biol Chem. 13;287(29):24525-33) to enhance antibody stabilization.

[0288] In some embodiments, the antibody has an Fc region selected from an IgG2 Fc region, an IgG4 Fc region, or an IgG2/IgG4 hybrid Fc region.

Camelid Antibodies

[0289] Antibody proteins obtained from members of the camel and dromedary (*Camelus bactrianus* and *Camelus dromedarius*) family including new world members such as llama species (*Lama pacos*, *Lama glama* and *Lama vicugna*) have been characterized with respect to size, structural complexity and antigenicity for human subjects. Certain IgG

antibodies from this family of mammals as found in nature lack light chains, and are thus structurally distinct from the typical four chain quaternary structure having two heavy and two light chains, for antibodies from other animals. See PCT/EP93/02214 (WO 94/04678 published 3 Mar. 1994).

[0290] A region of the camelid antibody which is the small single variable domain identified as VHH can be obtained by genetic engineering to yield a small protein having high affinity for a target, resulting in a low molecular weight antibody-derived protein known as a “camelid nanobody.” See U.S. Pat. No. 5,759,808 issued Jun. 2, 1998; see also Stijlemans, B. et al., 2004 J Biol Chem 279: 1256-1261; Dumoulin, M. et al., 2003 Nature 424: 783-788; Pleschberger, M. et al. 2003 Bioconjugate Chem 14: 440-448; Cortez-Retamozo, V. et al. 2002 Int J Cancer 89: 456-62; and Lauwereys, M. et al. 1998 EMBO J 17: 3512-3520. Engineered libraries of camelid antibodies and antibody fragments are commercially available, for example, from Ablynx, Ghent, Belgium. As with other antibodies and antigen-binding fragments thereof of non-human origin, an amino acid sequence of a camelid antibody can be altered recombinantly to obtain a sequence that more closely resembles a human sequence, i.e., the nanobody can be “humanized.” Thus the natural low antigenicity of camelid antibodies to humans can be further reduced.

[0291] The camelid nanobody has a molecular weight approximately one-tenth that of a human IgG molecule, and the protein has a physical diameter of only a few nanometers. One consequence of the small size is the ability of camelid nanobodies to bind to antigenic sites that are functionally invisible to larger antibody proteins, i.e., camelid nanobodies are useful as reagents detect antigens that are otherwise cryptic using classical immunological techniques, and as possible therapeutic agents. Thus yet another consequence of small size is that a camelid nanobody can inhibit as a result of binding to a specific site in a groove or narrow cleft of a target protein, and hence can serve in a capacity that more closely resembles the function of a classical low molecular weight drug than that of a classical antibody.

[0292] The low molecular weight and compact size further result in camelid nanobodies being extremely thermostable, stable to extreme pH and to proteolytic digestion, and poorly antigenic. Another consequence is that camelid nanobodies readily move from the circulatory system into tissues, and even cross the blood-brain barrier and can treat disorders that affect nervous tissue. Nanobodies can further facilitated drug transport across the blood brain barrier. See U.S. patent application 20040161738 published Aug. 19, 2004. These features combined with the low antigenicity to humans indicate great therapeutic potential. Further, these molecules can be fully expressed in prokaryotic cells such as *E. coli* and are

expressed as fusion proteins with bacteriophage and are functional.

[0293] Accordingly, a feature of the present invention is a camelid antibody or nanobody having high affinity for ENTPD2. In one embodiment herein, the camelid antibody or nanobody is naturally produced in the camelid animal, i.e., is produced by the camelid following immunization with ENTPD2 or a peptide fragment thereof, using techniques described herein for other antibodies. Alternatively, the ENTPD2-binding camelid nanobody is engineered, i.e., produced by selection for example from a library of phage displaying appropriately mutagenized camelid nanobody proteins using panning procedures with ENTPD2 as a target as described in the examples herein. Engineered nanobodies can further be customized by genetic engineering to have a half life in a recipient subject of from 45 minutes to two weeks. In a specific embodiment, the camelid antibody or nanobody is obtained by grafting the CDRs sequences of the heavy or light chain of the human antibodies of the invention into nanobody or single domain antibody framework sequences, as described for example in PCT/EP93/02214.

Bispecific Molecules and Multivalent Antibodies

[0294] In another aspect, the present invention features bispecific or multispecific molecules comprising a ENTPD2-binding antibody, or a fragment thereof, of the invention. An antibody of the invention, or antigen-binding regions thereof, can be derivatized or linked to another functional molecule, e.g., another peptide or protein (e.g., another antibody or ligand for a receptor) to generate a bispecific molecule that binds to at least two different binding sites or target molecules. The antibody of the invention may in fact be derivatized or linked to more than one other functional molecule to generate multi-specific molecules that bind to more than two different binding sites and/or target molecules; such multi-specific molecules are also intended to be encompassed by the term "bispecific molecule" as used herein. To create a bispecific molecule of the invention, an antibody of the invention can be functionally linked (e.g., by chemical coupling, genetic fusion, noncovalent association or otherwise) to one or more other binding molecules, such as another antibody, antibody fragment, peptide or binding mimetic, such that a bispecific molecule results.

[0295] Accordingly, the present invention includes bispecific molecules comprising at least one first binding specificity for ENTPD2 and a second binding specificity for a second target epitope. For example, the second target epitope is another epitope of ENTPD2 different from the first target epitope.

[0296] Additionally, for the invention in which the bispecific molecule is multi-

specific, the molecule can further include a third binding specificity, in addition to the first and second target epitope.

[0297] In one embodiment, the bispecific molecules of the invention comprise as a binding specificity at least one antibody, or an antibody fragment thereof, including, e.g., a Fab, Fab', F(ab')₂, Fv, or a single chain Fv. The antibody may also be a light chain or heavy chain dimer, or any minimal fragment thereof such as a Fv or a single chain construct as described in Ladner et al. U.S. Pat. No. 4,946,778.

[0298] Diabodies are bivalent, bispecific molecules in which VH and VL domains are expressed on a single polypeptide chain, connected by a linker that is too short to allow for pairing between the two domains on the same chain. The VH and VL domains pair with complementary domains of another chain, thereby creating two antigen binding sites (see e.g., Holliger et al., 1993 Proc. Natl. Acad. Sci. USA 90:6444-6448; Poijak et al., 1994 Structure 2:1121-1123). Diabodies can be produced by expressing two polypeptide chains with either the structure VHA-VLB and VHB-VLA (VH-VL configuration), or VLA-VHB and VLB-VHA (VL-VH configuration) within the same cell. Most of them can be expressed in soluble form in bacteria. Single chain diabodies (scDb) are produced by connecting the two diabody-forming polypeptide chains with linker of approximately 15 amino acid residues (see Holliger and Winter, 1997 Cancer Immunol. Immunother., 45 (3-4):128-30; Wu et al., 1996 Immunotechnology, 2 (1):21-36). scDb can be expressed in bacteria in soluble, active monomeric form (see Holliger and Winter, 1997 Cancer Immunol. Immunother., 45 (34): 128-30; Wu et al., 1996 Immunotechnology, 2 (1):21-36; Pluckthun and Pack, 1997 Immunotechnology, 3 (2): 83-105; Ridgway et al., 1996 Protein Eng., 9 (7):617-21). A diabody can be fused to Fc to generate a "di-diabody" (see Lu et al., 2004 J. Biol. Chem., 279 (4):2856-65).

[0299] Other antibodies which can be employed in the bispecific molecules of the invention are murine, chimeric and humanized monoclonal antibodies.

[0300] The bispecific molecules of the present invention can be prepared by conjugating the constituent binding specificities, using methods known in the art. For example, each binding specificity of the bispecific molecule can be generated separately and then conjugated to one another. When the binding specificities are proteins or peptides, a variety of coupling or cross-linking agents can be used for covalent conjugation. Examples of cross-linking agents include protein A, carbodiimide, N-succinimidyl-5-acetylthioacetate (SATA), 5,5'-dithiobis (2-nitrobenzoic acid) (DTNB), o-phenylenedimaleimide (oPDM), N-succinimidyl-3-(2-pyridyldithio)propionate (SPDP), and sulfosuccinimidyl 4-(N-

maleimidomethyl)cyclohexane-1-carboxylate (sulfo-SMCC) (see e.g., Karpovsky et al., 1984 J. Exp. Med. 160:1686; Liu, M A et al., 1985 Proc. Natl. Acad. Sci. USA 82:8648). Other methods include those described in Paulus, 1985 Behring Ins. Mitt. No. 78, 118-132; Brennan et al., 1985 Science 229:81-83), and Glennie et al., 1987 J. Immunol. 139: 2367-2375). Conjugating agents are SATA and sulfo-SMCC, both available from Pierce Chemical Co. (Rockford, Ill.).

[0301] When the binding specificities are antibodies, they can be conjugated by sulfhydryl bonding of the C-terminus hinge regions of the two heavy chains. In a particularly embodiment, the hinge region is modified to contain an odd number of sulfhydryl residues, for example one, prior to conjugation.

[0302] Alternatively, both binding specificities can be encoded in the same vector and expressed and assembled in the same host cell. This method is particularly useful where the bispecific molecule is a mAb X mAb, mAb X Fab, Fab X F(ab')₂ or ligand X Fab fusion protein. A bispecific molecule of the invention can be a single chain molecule comprising one single chain antibody and a binding determinant, or a single chain bispecific molecule comprising two binding determinants. Bispecific molecules may comprise at least two single chain molecules. Methods for preparing bispecific molecules are described for example in U.S. Pat. No. 5,260,203; U.S. Pat. No. 5,455,030; U.S. Pat. No. 4,881,175; U.S. Pat. No. 5,132,405; U.S. Pat. No. 5,091,513; U.S. Pat. No. 5,476,786; U.S. Pat. No. 5,013,653; U.S. Pat. No. 5,258,498; and U.S. Pat. No. 5,482,858.

[0303] Binding of the bispecific molecules to their specific targets can be confirmed by, for example, enzyme-linked immunosorbent assay (ELISA), radioimmunoassay (REA), FACS analysis, bioassay (e.g., growth inhibition), or Western Blot assay. Each of these assays generally detects the presence of protein-antibody complexes of particular interest by employing a labeled reagent (e.g., an antibody) specific for the complex of interest.

[0304] In another aspect, the present invention provides multivalent compounds comprising at least two identical or different antigen-binding portions of the antibodies and antigen-binding fragments thereof of the invention binding to ENTPD2. The antigen-binding portions can be linked together via protein fusion or covalent or noncovalent linkage. Alternatively, methods of linkage has been described for the bispecific molecules. Tetravalent compounds can be obtained for example by cross-linking antibodies and antigen-binding fragments thereof of the invention with an antibody or antigen-binding fragment that binds to the constant regions of the antibodies and antigen-binding fragments thereof of the invention, for example the Fc or hinge region.

[0305] Trimerizing domain are described for example in Borean patent EP 1 012 280B1. Pentamerizing modules are described for example in PCT/EP97/05897.

[0306] In some embodiments, the ENTPD2-binding antibodies or antigen binding fragments thereof are bispecific antibodies that recognize a first antigen and a second antigen. In some embodiments, the first antigen is human ENTPD2 or a naturally occurring variant thereof. In some embodiments, the second antigen may be a protein, lipid, polysaccharide, or glycolipid expressed on one or more tumor cells.

Antibodies with Extended Half Life

[0307] The present invention provides for antibodies that specifically bind to ENTPD2 (e.g., human ENTPD2 protein) and have an extended half-life *in vivo*.

[0308] Many factors may affect a protein's half life *in vivo*. For examples, kidney filtration, metabolism in the liver, degradation by proteolytic enzymes (proteases), and immunogenic responses (e.g., protein neutralization by antibodies and uptake by macrophages and dendritic cells). A variety of strategies can be used to extend the half life of the antibodies and antigen-binding fragments thereof of the present invention. For example, by chemical linkage to polyethylene glycol (PEG), reCODE PEG, antibody scaffold, polysialic acid (PSA), hydroxyethyl starch (HES), albumin-binding ligands, and carbohydrate shields; by genetic fusion to proteins binding to serum proteins, such as albumin, IgG, FcRn, and transferrin; by coupling (genetically or chemically) to other binding moieties that bind to serum proteins, such as nanobodies, Fabs, DARPins, avimers, affibodies, and anticalins; by genetic fusion to rPEG, albumin, domain of albumin, albumin-binding proteins, and Fc; or by incorporation into nanocarriers, slow release formulations, or medical devices.

[0309] To prolong the serum circulation of antibodies *in vivo*, inert polymer molecules such as high molecular weight PEG can be attached to the antibodies or a fragment thereof with or without a multifunctional linker either through site-specific conjugation of the PEG to the N- or C-terminus of the antibodies or via epsilon-amino groups present on lysine residues. To pegylate an antibody, the antibody, antigen-binding fragment thereof, typically is reacted with polyethylene glycol (PEG), such as a reactive ester or aldehyde derivative of PEG, under conditions in which one or more PEG groups become attached to the antibody or antibody fragment. The pegylation can be carried out by an acylation reaction or an alkylation reaction with a reactive PEG molecule (or an analogous reactive water-soluble polymer). As used herein, the term "polyethylene glycol" is intended to encompass any one of the forms of PEG that have been used to derivatize other proteins, such as mono (C1-

C10)alkoxy- or aryloxy-polyethylene glycol or polyethylene glycol-maleimide. In one embodiment, the antibody to be pegylated is an aglycosylated antibody. Linear or branched polymer derivatization that results in minimal loss of biological activity will be used. The degree of conjugation can be closely monitored by SDS-PAGE and mass spectrometry to ensure proper conjugation of PEG molecules to the antibodies. Unreacted PEG can be separated from antibody-PEG conjugates by size-exclusion or by ion-exchange chromatography. PEG-derivatized antibodies can be tested for binding activity as well as for *in vivo* efficacy using methods well-known to those of skill in the art, for example, by immunoassays described herein. Methods for pegylating proteins are known in the art and can be applied to the antibodies and antigen-binding fragments thereof of the invention. See for example, EP 0154316 by Nishimura et al. and EP 0401384 by Ishikawa et al.

[0310] Other modified pegylation technologies include reconstituting chemically orthogonal directed engineering technology (ReCODE PEG), which incorporates chemically specified side chains into biosynthetic proteins via a reconstituted system that includes tRNA synthetase and tRNA. This technology enables incorporation of more than 30 new amino acids into biosynthetic proteins in *E. coli*, yeast, and mammalian cells. The tRNA incorporates a normative amino acid any place an amber codon is positioned, converting the amber from a stop codon to one that signals incorporation of the chemically specified amino acid.

[0311] Recombinant pegylation technology (rPEG) can also be used for serum half-life extension. This technology involves genetically fusing a 300-600 amino acid unstructured protein tail to an existing pharmaceutical protein. Because the apparent molecular weight of such an unstructured protein chain is about 15-fold larger than its actual molecular weight, the serum half-life of the protein is greatly increased. In contrast to traditional PEGylation, which requires chemical conjugation and repurification, the manufacturing process is greatly simplified and the product is homogeneous.

[0312] Polysialylation is another technology, which uses the natural polymer polysialic acid (PSA) to prolong the active life and improve the stability of therapeutic peptides and proteins. PSA is a polymer of sialic acid (a sugar). When used for protein and therapeutic peptide drug delivery, polysialic acid provides a protective microenvironment on conjugation. This increases the active life of the therapeutic protein in the circulation and prevents it from being recognized by the immune system. The PSA polymer is naturally found in the human body. It was adopted by certain bacteria which evolved over millions of years to coat their walls with it. These naturally polysialylated bacteria were then able, by virtue of molecular

mimicry, to foil the body's defense system. PSA can be easily produced from such bacteria in large quantities and with predetermined physical characteristics. Bacterial PSA is completely non-immunogenic, even when coupled to proteins, as it is chemically identical to PSA in the human body.

[0313] Another technology include the use of hydroxyethyl starch ("HES") derivatives linked to antibodies. HES is a modified natural polymer derived from waxy maize starch and can be metabolized by the body's enzymes. HES solutions are usually administered to substitute deficient blood volume and to improve the rheological properties of the blood. Hesylation of an antibody enables the prolongation of the circulation half-life by increasing the stability of the molecule, as well as by reducing renal clearance, resulting in an increased biological activity. By varying different parameters, such as the molecular weight of HES, a wide range of HES antibody conjugates can be customized.

[0314] Antibodies having an increased half-life *in vivo* can also be generated introducing one or more amino acid modifications (i.e., substitutions, insertions or deletions) into an IgG constant domain, or FcRn binding fragment thereof (preferably a Fc or hinge Fc domain fragment). See, e.g., International Publication No. WO 98/23289; International Publication No. WO 97/34631; and U.S. Pat. No. 6,277,375.

[0315] Further, antibodies can be conjugated to albumin in order to make the antibody or antibody fragment more stable *in vivo* or have a longer half life *in vivo*. The techniques are well-known in the art, see, e.g., International Publication Nos. WO 93/15199, WO 93/15200, and WO 01/77137; and European Patent No. EP 413,622.

[0316] The strategies for increasing half life is especially useful in nanobodies, fibronectin-based binders, and other antibodies or proteins for which increased *in vivo* half life is desired.

Antibody Conjugates

[0317] The present invention provides antibodies or antigen-binding fragments thereof that specifically bind to the extracellular domain of ENTPD2 (e.g., human ENTPD2 protein) recombinantly fused or chemically conjugated (including both covalent and non-covalent conjugations) to a heterologous protein or polypeptide (or antigen-binding fragment thereof, preferably to a polypeptide of at least 10, at least 20, at least 30, at least 40, at least 50, at least 60, at least 70, at least 80, at least 90 or at least 100 amino acids) to generate fusion proteins. In particular, the invention provides fusion proteins comprising an antigen-binding fragment of an antibody described herein (e.g., a Fab fragment, Fd fragment, Fv

fragment, F (ab)₂ fragment, a VH domain, a VH CDR, a VL domain or a VL CDR) and a heterologous protein, polypeptide, or peptide. Methods for fusing or conjugating proteins, polypeptides, or peptides to an antibody or an antibody fragment are known in the art. See, e.g., U.S. Pat. Nos. 5,336,603, 5,622,929, 5,359,046, 5,349,053, 5,447,851, and 5,112,946; European Patent Nos. EP 307,434 and EP 367,166; International Publication Nos. WO 96/04388 and WO 91/06570; Ashkenazi et al., 1991, Proc. Natl. Acad. Sci. USA 88: 10535-10539; Zheng et al., 1995, J. Immunol. 154:5590-5600; and Vil et al., 1992, Proc. Natl. Acad. Sci. USA 89:11337-11341.

[0318] Additional fusion proteins may be generated through the techniques of gene-shuffling, motif-shuffling, exon-shuffling, and/or codon-shuffling (collectively referred to as “DNA shuffling”). DNA shuffling may be employed to alter the activities of antibodies and antigen-binding fragments thereof of the invention (e.g., antibodies and antigen-binding fragments thereof with higher affinities and lower dissociation rates). See, generally, U.S. Pat. Nos. 5,605,793, 5,811,238, 5,830,721, 5,834,252, and 5,837,458; Patten et al., 1997, Curr. Opin. Biotechnol. 8:724-33; Harayama, 1998, Trends Biotechnol. 16 (2):76-82; Hansson, et al., 1999, J. Mol. Biol. 287:265-76; and Lorenzo and Blasco, 1998, Biotechniques 24 (2):308-313). Antibodies and antigen-binding fragments thereof, or the encoded antibodies and antigen-binding fragments thereof, may be altered by being subjected to random mutagenesis by error-prone PCR, random nucleotide insertion or other methods prior to recombination. A polynucleotide encoding an antibody antigen-binding fragment thereof that specifically binds to ENTPD2 (e.g., human ENTPD2 protein) may be recombined with one or more components, motifs, sections, parts, domains, fragments, etc. of one or more heterologous molecules.

[0319] Moreover, the antibodies and antigen-binding fragments thereof can be fused to marker sequences, such as a peptide to facilitate purification. In one embodiment, the marker amino acid sequence is a hexa-histidine peptide (SEQ ID NO: 1010), such as the tag provided in a pQE vector (QIAGEN, Inc., 9259 Eton Avenue, Chatsworth, Calif., 91311), among others, many one of which are commercially available. As described in Gentz et al., 1989, Proc. Natl. Acad. Sci. USA 86:821-824, for instance, hexa-histidine (SEQ ID NO: 1010) provides for convenient purification of the fusion protein. Other peptide tags useful for purification include, but are not limited to, the hemagglutinin (“HA”) tag, which corresponds to an epitope derived from the influenza hemagglutinin protein (Wilson et al., 1984, Cell 37:767), and the “FLAG” tag.

[0320] In one embodiment, antibodies and antigen-binding fragments thereof of the

present invention antigen-binding fragments thereof conjugated to a diagnostic or detectable agent. Such antibodies can be useful for monitoring or prognosing the onset, development, progression and/or severity of a disease or disorder as part of a clinical testing procedure, such as determining the efficacy of a particular therapy. Such diagnosis and detection can be accomplished by coupling the antibody to detectable substances including, but not limited to, various enzymes, such as, but not limited to, horseradish peroxidase, alkaline phosphatase, beta-galactosidase, or acetylcholinesterase; prosthetic groups, such as, but not limited to, streptavidin/biotin and avidin/biotin; fluorescent materials, such as, but not limited to, umbelliferone, fluorescein, fluorescein isothiocyanate, rhodamine, dichlorotriazinylamine fluorescein, dansyl chloride or phycoerythrin; luminescent materials, such as, but not limited to, luminol; bioluminescent materials, such as but not limited to, luciferase, luciferin, and aequorin; radioactive materials, such as, but not limited to, iodine (^{131}I , ^{125}I , ^{123}I , and ^{121}I), carbon (^{14}C), sulfur (^{35}S), tritium (^3H), indium (^{115}In , ^{113}In , ^{112}In , and ^{111}In), technetium (^{99}Tc), thallium (^{201}Tl), gallium (^{68}Ga , ^{67}Ga), palladium (^{103}Pd), molybdenum (^{99}Mo), xenon (^{133}Xe), fluorine (^{18}F), ^{153}Sm , ^{177}Lu , ^{159}Gd , ^{149}Pm , ^{140}La , ^{175}Yb , ^{166}Ho , ^{90}Y , ^{47}Sc , ^{186}Re , ^{188}Re , ^{142}Pr , ^{105}Rh , ^{97}Ru , ^{68}Ge , ^{57}Co , ^{65}Zn , ^{85}Sr , ^{32}P , ^{153}Gd , ^{169}Yb , ^{51}Cr , ^{54}Mn , ^{75}Se , ^{113}Sn , and ^{117}Tm ; and positron emitting metals using various positron emission tomographies, and nonradioactive paramagnetic metal ions.

[0321] Further, an antibody antigen-binding fragment thereof may be conjugated to a therapeutic moiety or drug moiety. Therapeutic moieties or drug moieties are not to be construed as limited to classical chemical therapeutic agents. For example, the drug moiety may be a protein, peptide, or polypeptide possessing a desired biological activity. Such proteins may include, for example, a toxin such as abrin, ricin A, pseudomonas exotoxin, cholera toxin, or diphtheria toxin; a protein such as tumor necrosis factor, alpha-interferon, beta-interferon, nerve growth factor, platelet derived growth factor, tissue plasminogen activator, an apoptotic agent, an anti-angiogenic agent; or, a biological response modifier such as, for example, a lymphokine.

[0322] Moreover, an antibody can be conjugated to therapeutic moieties such as a radioactive metal ion, such as alpha-emitters such as ^{213}Bi or macrocyclic chelators useful for conjugating radiometal ions, including but not limited to, ^{131}In , ^{131}Lu , ^{131}Y , ^{131}Ho , ^{131}Sm , to polypeptides. In one embodiment, the macrocyclic chelator is 1,4,7,10-tetraazacyclododecane- $\text{N,N',N'',N'''}\text{-tetraacetic acid (DOTA)}$ which can be attached to the antibody via a linker molecule. Such linker molecules are commonly known in the art and described in Denardo et al., 1998, Clin Cancer Res. 4 (10):2483-90; Peterson et al., 1999,

Bioconjug. Chem. 10 (4):553-7; and Zimmerman et al., 1999, Nucl. Med. Biol. 26 (8):943-50, each incorporated by reference in their entireties.

[0323] Techniques for conjugating therapeutic moieties to antibodies are well known, see, e.g., Amon et al., "Monoclonal Antibodies For Immunotargeting Of Drugs In Cancer Therapy," in Monoclonal Antibodies And Cancer Therapy, Reisfeld et al. (eds.), pp. 243-56 (Alan R. Liss, Inc. 1985); Hellstrom et al., "Antibodies For Drug Delivery", in Controlled Drug Delivery (2nd Ed.), Robinson et al. (eds.), pp. 623-53 (Marcel Dekker, Inc. 1987); Thorpe, "Antibody Carriers Of Cytotoxic Agents In Cancer Therapy: A Review", in Monoclonal Antibodies 84: Biological And Clinical Applications, Pinchera et al. (eds.), pp. 475-506 (1985); "Analysis, Results, And Future Prospective Of The Therapeutic Use Of Radiolabeled Antibody In Cancer Therapy", in Monoclonal Antibodies For Cancer Detection And Therapy, Baldwin et al. (eds.), pp. 303-16 (Academic Press 1985), and Thorpe et al., 1982, Immunol. Rev. 62:119-58.

[0324] Antibodies may also be attached to solid supports, which are particularly useful for immunoassays or purification of the target antigen. Such solid supports include, but are not limited to, glass, cellulose, polyacrylamide, nylon, polystyrene, polyvinyl chloride or polypropylene.

Nucleic Acids Encoding the Antibodies, Vectors and Host Cells

[0325] Also provided herein are nucleic acids encoding an antibody or antigen binding fragment thereof described herein. Such nucleic acids can encode polypeptides comprising segments or domains of the ENTPD2 antibodies or antigen-binding fragments thereof described above. Such nucleic acids or polynucleotides can encode at least one CDR region and usually all three CDR regions from the heavy or light chain of the ENTPD2 antibodies described herein. Such nucleic acids or polynucleotides can also encode all or substantially all of the variable region sequence of the heavy chain and/or the light chain of the ENTPD2 antibodies described herein. Such nucleic acids or polynucleotides can also encode both a variable region and a constant region of the antibody. Because of the degeneracy of the code, a variety of nucleic acid sequences will encode each of the immunoglobulin amino acid sequences. For example, the invention features a first and second nucleic acid encoding heavy and light chain variable regions, respectively, of an anti-human ENTPD2 antibody molecule chosen from one or more of the antibody molecules disclosed herein. The nucleic acid can comprise a nucleotide sequence as set forth in Table 1, or a sequence substantially identical thereto (e.g., a sequence having at least about 85%, 90%,

95%, or 99% sequence identity thereto, or which differs by no more than 3, 6, 15, 30, or 45 nucleotides from the sequences shown in Table 1).

[0326] In certain embodiments, the nucleic acid can comprise a nucleotide sequence encoding at least one, two, or three CDRs or hypervariable loops from a heavy chain variable region having an amino acid sequence as set forth in Table 1, or a sequence substantially homologous thereto (*e.g.*, a sequence having at least about 85%, 90%, 95%, or 99% sequence identity thereto, and/or having one or more substitutions, *e.g.*, conserved substitutions). In other embodiments, the nucleic acid can comprise a nucleotide sequence encoding at least one, two, or three CDRs or hypervariable loops from a light chain variable region having an amino acid sequence as set forth in Table 1, or a sequence substantially homologous thereto (*e.g.*, a sequence having at least about 85%, 90%, 95%, or 99% sequence identity thereto, and/or having one or more substitutions, *e.g.*, conserved substitutions). In yet another embodiment, the nucleic acid can comprise a nucleotide sequence encoding at least one, two, three, four, five, or six CDRs or hypervariable loops from heavy and light chain variable regions having an amino acid sequence as set forth in Table 1, or a sequence substantially homologous thereto (*e.g.*, a sequence having at least about 85%, 90%, 95%, or 99% sequence identity thereto, and/or having one or more substitutions, *e.g.*, conserved substitutions).

[0327] In certain embodiments, the nucleic acid can comprise a nucleotide sequence encoding at least one, two, or three CDRs or hypervariable loops from a heavy chain variable region having the nucleotide sequence as set forth in Table 1, a sequence substantially homologous thereto (*e.g.*, a sequence having at least about 85%, 90%, 95%, or 99% sequence identity thereto). In another embodiment, the nucleic acid can comprise a nucleotide sequence encoding at least one, two, or three CDRs or hypervariable loops from a light chain variable region having the nucleotide sequence as set forth in Table 1, or a sequence substantially homologous thereto (*e.g.*, a sequence having at least about 85%, 90%, 95%, or 99% sequence identity thereto). In yet another embodiment, the nucleic acid can comprise a nucleotide sequence encoding at least one, two, three, four, five, or six CDRs or hypervariable loops from heavy and light chain variable regions having the nucleotide sequence as set forth in Table 1, or a sequence substantially homologous thereto (*e.g.*, a sequence having at least about 85%, 90%, 95%, or 99% sequence identity thereto).

[0328] The polynucleotide sequences can be produced by *de novo* solid-phase DNA synthesis or by PCR mutagenesis of an existing sequence encoding an ENTPD2-binding antibody or its binding fragment. Direct chemical synthesis of nucleic acids can be accomplished by methods known in the art, such as the phosphotriester method of Narang et

al., 1979, *Meth. Enzymol.* 68:90; the phosphodiester method of Brown et al., *Meth. Enzymol.* 68:109, 1979; the diethylphosphoramidite method of Beaucage et al., *Tetra. Lett.*, 22:1859, 1981; and the solid support method of U.S. Pat. No. 4,458,066. Introducing mutations to a polynucleotide sequence by PCR can be performed as described in, e.g., *PCR Technology: Principles and Applications for DNA Amplification*, H. A. Erlich (Ed.), Freeman Press, NY, N.Y., 1992; *PCR Protocols: A Guide to Methods and Applications*, Innis et al. (Ed.), Academic Press, San Diego, Calif., 1990; Mattila et al., *Nucleic Acids Res.* 19:967, 1991; and Eckert et al., *PCR Methods and Applications* 1:17, 1991.

[0329] Also provided herein are vectors (e.g., expression vectors) comprising a nucleic acid encoding a polypeptide comprising a segment or domain of the ENTPD2 antibodies or antigen-binding fragments thereof described herein. Such vectors can be employed to express and/or produce the ENTPD2-binding antibodies or antigen-binding fragments thereof. The term “expression vector” refers to a carrier nucleic acid molecule into which a desired coding sequence can be inserted for introduction into a cell where it can be expressed. The vector can be a DNA vector, a RNA vector, a plasmid, a cosmid, or a viral vector, or artificial chromosomes (see, e.g., Harrington et al., *Nat Genet* 15:345, 1997). For example, nonviral vectors useful for expression of the ENTPD2-binding antibodies or antigen-binding fragments thereof in mammalian (e.g., human) cells include pThioHis A, B & C, pcDNA3.1/His, pEBVHis A, B & C, (Invitrogen, San Diego, Calif.), MPSV vectors, and numerous other vectors known in the art for expressing proteins. For example, one class of vectors utilizes DNA elements which are derived from animal viruses such as, for example, bovine papilloma virus, polyoma virus, adenovirus, vaccinia virus, baculovirus, retroviruses (Rous Sarcoma Virus, MMTV or MOMLV) or SV40 virus. Another class of vectors utilizes RNA elements derived from RNA viruses such as Semliki Forest virus, Eastern Equine Encephalitis virus and Flaviviruses.

[0330] Useful viral vectors include vectors based on any one of the following viruses: retroviruses, lentiviruses, adenoviruses, adeno-associated viruses, herpes viruses (e.g., Herpes Simplex Virus (HSV)), vectors based on SV40, papilloma virus, HBP Epstein Barr virus, vaccinia virus, Sinbis virus, influenza virus, reovirus, Newcastle disease virus (NDV), measles virus, vesicular stomatitis virus (VSV), parvovirus, poliovirus, poxvirus, Seneca Valley virus, coxsackievirus, enterovirus, myxoma virus, maraba virus, or Semliki Forest virus (SFV). See, Brent et al., *supra*; Smith, *Annu. Rev. Microbiol.* 49:807, 1995; and Rosenfeld et al., *Cell* 68:143, 1992.

[0331] In some embodiments, the vector is a lentiviral vector. Vectors derived from retroviruses such as the lentivirus are suitable tools to achieve long-term gene transfer since they allow long-term, stable integration of a transgene and its propagation in daughter cells. Lentiviral vectors have the added advantage over vectors derived from onco-retroviruses such as murine leukemia viruses in that they can transduce non-proliferating cells, such as hepatocytes. They also have the added advantage of low immunogenicity. A retroviral vector may also be, e.g., a gammaretroviral vector. A gammaretroviral vector may include, e.g., a promoter, a packaging signal (ψ), a primer binding site (PBS), one or more (e.g., two) long terminal repeats (LTR), and a transgene of interest, e.g., a gene encoding a CAR. A gammaretroviral vector may lack viral structural genes such as gag, pol, and env. Exemplary gammaretroviral vectors include Murine Leukemia Virus (MLV), Spleen-Focus Forming Virus (SFFV), and Myeloproliferative Sarcoma Virus (MPSV), and vectors derived therefrom. Other gammaretroviral vectors are described, e.g., in Tobias Maetzig et al., “Gammaretroviral Vectors: Biology, Technology and Application” *Viruses*. 2011 Jun; 3(6): 677–713.

[0332] In some embodiments, the vector is an adeno-associated virus (AAV) vector, e.g., a recombinant AAV (rAAV) vector. “AAV” is an abbreviation for adeno-associated virus, and may be used to refer to the virus itself or derivatives thereof. The term covers all subtypes and both naturally occurring and recombinant forms, except where required otherwise. The abbreviation “rAAV” refers to recombinant adeno-associated virus, also referred to as a recombinant AAV vector (or “rAAV vector”). The term “AAV” includes, for example, AAV type 1 (AAV1), AAV type 2 (AAV2), AAV type 3 (AAV3), AAV type 4 (AAV4), AAV type 5 (AAV5), AAV type 6 (AAV6), AAV type 7 (AAV7), AAV type 8 (AAV8), AAV type 9 (AAV9), AAV type 10 (AAV10, including AAVrh10), AAV type 12 (AAV12), avian AAV, bovine AAV, canine AAV, equine AAV, primate AAV, non-primate AAV, and ovine AAV. “Primate AAV” refers to AAV that infect primates, “non-primate AAV” refers to AAV that infect non-primate mammals, “bovine AAV” refers to AAV that infect bovine mammals, and so on.

[0333] The genomic sequences of various serotypes of AAV, as well as the sequences of the native inverted terminal repeats (ITRs), Rep proteins, and capsid subunits are known in the art. Such sequences may be found in the literature or in public databases such as GenBank. See, e.g., GenBank Accession NOs. NC-002077 (AAV1), AF063497 (AAV1), NC-001401 (AAV2), AF043303 (AAV2), NC-001729 (AAV3), NC-001829 (AAV4), U89790 (AAV4), NC-006152 (AAV5), AF513851 (AAV7), AF513852 (AAV8), and NC-

006261 (AAV8); or in publications such as WO2005033321 (AAV1-9), the disclosures of which are incorporated by reference herein. See also, e.g., Srivistava et al. (1983) J. Virology 45:555; Chiorini et al. (1998) J. Virology 71 :6823; Chiorini et al. (1999) J. Virology 73: 1309; Bantel-Schaal et al. (1999) J. Virology 73:939; Xiao et al. (1999) J. Virology 73:3994; Muramatsu et al. (1996) Virology 221 :208; Shade et al.,(1986) J. Virol. 58:921; Gao et al. (2002) Proc. Nat. Acad. Sci. USA 99: 11854; Moris et al. (2004) Virology 33:375-383; international patent publications WO 00/28061, WO 99/61601, WO 98/11244; and U. S. Pat. No. 6,156,303.

[0334] An “rAAV vector” as used herein refers to an AAV vector comprising a polynucleotide sequence not of AAV origin (i.e., a polynucleotide heterologous to AAV), typically a sequence of interest for the genetic transformation of a cell. In some embodiments, the heterologous polynucleotide may be flanked by at least one, and sometimes by two, AAV inverted terminal repeat (ITR) sequences. The term rAAV vector encompasses both rAAV vector particles and rAAV vector plasmids. An rAAV vector may either be single-stranded (ssAAV) or self-complementary (scAAV). An “AAV virus” or “AAV viral particle” or “rAAV vector particle” refers to a viral particle composed of at least one AAV capsid protein (typically by all of the capsid proteins of a wild-type AAV) and an encapsidated polynucleotide rAAV vector. If the particle comprises a heterologous polynucleotide (i.e., a polynucleotide other than a wild-type AAV genome such as a transgene to be delivered to a mammalian cell), it is typically referred to as an “rAAV vector particle” or simply an “rAAV vector.” Thus, production of rAAV particle necessarily includes production of rAAV vector, as such a vector is contained within an rAAV particle.

[0335] In some embodiments, the vector can be a recombinant DNA molecule containing a nucleic acid encoding an antibody that binds to human ENTPD2 protein. “Recombinant” as used herein means that the vector, polynucleotide, polypeptide or cell is the product of various combinations of cloning, restriction or ligation steps (e.g. relating to a polynucleotide or polypeptide comprised therein), and/or other procedures that result in a construct that is distinct from a product found in nature. A recombinant virus or vector is a viral particle comprising a recombinant polynucleotide. The terms respectively include replicates of the original polynucleotide construct and progeny of the original virus construct.

[0336] The recombinant vector typically includes one or more regulatory sequences operatively linked to the nucleic acid sequence to be expressed. The term “regulatory sequence” includes promoters, enhancers, and other expression control elements (e.g., polyadenylation signals). Regulatory sequences include those which direct constitutive

expression of a nucleotide sequence, as well as tissue-specific regulatory and/or inducible sequences. Expression vectors can also include elements designed to optimize messenger RNA stability and translatability in host cells, and/or drug selection markers for establishing permanent, stable cell clones expressing an antibody that binds to human ENTPD2 protein. The design of the expression vector can depend on such factors as the choice of the host cell to be transformed, the level of expression of protein desired, and the like. General methods for generating such recombinant expression vectors can be found in Sambrook and Russell eds. (2001) *Molecular Cloning: A Laboratory Manual*, 3rd edition; the series Ausubel et al. eds. (2007 with updated through 2010) *Current Protocols in Molecular Biology*, among others known in the art.

[0337] A “promoter” is a control sequence that is a region of a nucleic acid sequence at which initiation and rate of transcription are controlled. It may contain genetic elements at which regulatory proteins and molecules may bind such as RNA polymerase and other transcription factors. The phrases “operatively positioned”, “operatively linked”, “under control”, and “under transcriptional control” mean that a promoter is in a correct functional location and/or orientation in relation to a nucleic acid sequence to control transcriptional initiation and/or expression of that sequence. A promoter may or may not be used in conjunction with an “enhancer”, which refers to a cis-acting regulatory sequence involved in the transcriptional activation of a nucleic acid sequence.

[0338] A promoter may be one naturally-associated with a gene or sequence, as may be obtained by isolating the 5' non-coding sequences located upstream of the coding segment and/or exon. Such a promoter can be referred to as “endogenous”. Similarly, an enhancer may be one naturally associated with a nucleic acid sequence, located either downstream or upstream of that sequence. Alternatively, certain advantages will be gained by positioning the coding nucleic acid segment under the control of a recombinant or heterologous promoter, which refers to a promoter that is not normally associated with a nucleic acid sequence in its natural environment. A recombinant or heterologous enhancer refers also to an enhancer not normally associated with a nucleic acid sequence in its natural environment. Such promoters or enhancers may include promoters or enhancers of other genes, and promoters or enhancers isolated from any other prokaryotic, viral, or eukaryotic cell, and promoters or enhancers not “naturally-occurring”, i.e., containing different elements of different transcriptional regulatory regions and/or mutations that alter expression. In addition to producing nucleic acid sequences of promoters and enhancers synthetically, sequences may be produced using recombinant cloning and/or nucleic acid amplification technology, for example PCR, in

connection with the compositions disclosed herein (see US 4683202, US 5928906). Furthermore, it is contemplated the control sequences that direct transcription and/or expression of sequences within non-nuclear organelles such as mitochondria, chloroplasts, and the like, can be employed as well.

[0339] The promoters employed can be constitutive, inducible, synthetic, tissue- or cell-specific, and/or useful under the appropriate conditions to direct high level expression of the introduced DNA segment, such as is advantageous in the large-scale production of recombinant proteins and/or peptides. In addition, other regulatory elements may also be incorporated to improve expression of a nucleic acid encoding an antibody that binds to human ENTPD2 protein, *e.g.*, enhancers, ribosomal binding site, transcription termination sequences, and the like.

[0340] In some embodiments, a constitutive promoter is employed to provide constant expression of an anti-human ENTPD2 antibody. Examples of a constitutive promoter include, but not limited to, the immediate early cytomegalovirus (CMV) promoter, the simian virus 40 (SV40) early promoter, mouse mammary tumor virus (MMTV) promoter, human immunodeficiency virus (HIV) long terminal repeat (LTR) promoter, MoMuLV promoter, an avian leukemia virus promoter, an Epstein-Barr virus immediate early promoter, a Rous sarcoma virus promoter, as well as human gene promoters such as, but not limited to, the actin promoter, the myosin promoter, the elongation factor-1 α promoter, the hemoglobin promoter, and the creatine kinase promoter.

[0341] Inducible promoters are also contemplated as part of the present disclosure. The use of an inducible promoter provides a molecular switch capable of turning on expression of the polynucleotide sequence which it is operatively linked when such expression is desired, or turning off the expression when expression is not desired. Examples of inducible promoters include, but are not limited to a metallothionein promoter, a glucocorticoid promoter, a progesterone promoter, and a tetracycline promoter.

[0342] In some embodiments, a tissue- or cell-specific promoter is employed to provide expression of an anti-human ENTPD2 antibody only in specific tissues or cells. The identity of tissue- or cell-specific promoters or elements, as well as assays to characterize their activities, is well known to those of skill in the art. Examples include the human LIMK2 gene (Nomoto *et al.* 1999, *Gene*, 236(2):259-271), the somatostatin receptor 2 gene (Kraus *et al.*, 1998, *FEBS Lett.*, 428(3): 165-170), murine epididymal retinoic acid-binding gene (Lareyre *et al.*, 1999, *J. Biol. Chem.*, 274(12):8282-8290), human CD4 (Zhao-Emonet *et al.*,

1998, *Biochim. Biophys. Acta*, 1442(2-3): 109-119), mouse alpha2 (XI) collagen (Tsumaki, *et al.*, 1998, *J. Biol. Chem.*, 273(36):22861-22864), D1A dopamine receptor gene (Lee, *et al.*, 1997, *J. Auton. Nerv. Syst.*, 74(2-3):86-90), insulin-like growth factor II (Wu *et al.*, 1997, *Biochem. Biophys. Res. Commun.*, 233(1):221-226), human platelet endothelial cell adhesion molecule-1 (Almendo *et al.*, 1996, *J. Immunol.*, 157(12):5411-5421), muscle creatine kinase (MCK) promoter (Wang *et al.*, *Gene Ther.* 2008 Nov;15(22):1489-99).

[0343] In some embodiments, a synthetic promoter is employed to provide expression of an anti-human ENTPD2 antibody. Synthetic promoters can greatly exceed the transcriptional potencies of natural promoters. For example, the synthetic promoters that do not get shut off or reduced in activity by the endogenous cellular machinery or factors can be selected. Other elements, including trans-acting factor binding sites and enhancers may be inserted into the synthetic promoter to improve transcriptional efficiency. Synthetic promoters can be rationally designed and chemically synthesized to combine the best features of both synthetic and biological promoters. Synthetic oligos are annealed and ligated through several processes to generate the full-length chemically synthesized promoter. Synthetic promoters can be inducible or cell-type specific promoters.

[0344] A specific initiation signal also may be required for efficient translation of coding sequences. These signals include the ATG initiation codon or adjacent sequences. Exogenous translational control signals, including the ATG initiation codon, may need to be provided. One of ordinary skill in the art would readily be capable of determining this and providing the necessary signals. It is well known that the initiation codon must be “in-frame” with the reading frame of the desired coding sequence to ensure translation of the entire insert. The exogenous translational control signals and initiation codons can be either natural or synthetic. The efficiency of expression may be enhanced by the inclusion of appropriate transcription enhancer elements.

[0345] Expression can employ any appropriate host cells known in the art, for example, mammalian host cells, bacterial host cells, yeast host cells, insect host cells, etc. Both prokaryotic and eukaryotic expression systems are widely available. In some embodiments, the expression system is a mammalian cell expression, such as a CHO cell expression system. In some embodiments, a nucleic acid may be codon-optimized to facilitate expression in a desired host cell. It will be important to employ a promoter and/or enhancer that effectively directs the expression of the DNA segment in the cell type, organelle, and organism chosen for expression. Those of skill in the art of molecular biology

generally know the use of promoters, enhancers, and cell type combinations for protein expression, for example, see Sambrook *et al.* (2001).

[0346] Most transcribed eukaryotic RNA molecules will undergo RNA splicing to remove introns from the primary transcripts. Vectors containing genomic eukaryotic sequences may require donor and/or acceptor splicing sites to ensure proper processing of the transcript for protein expression (see Chandler *et al.*, 1997, Proc. Natl. Acad. Sci. USA, 94(8):3596-601).

[0347] The vectors or constructs of the present disclosure will generally comprise at least one termination signal. A “termination signal” or “terminator” is comprised of the DNA sequences involved in specific termination of a RNA transcript by a RNA polymerase. Thus, in certain embodiments a termination signal that ends the production of a RNA transcript is contemplated. A terminator may be necessary *in vivo* to achieve desirable message levels. In eukaryotic systems, the terminator region may also comprise specific DNA sequences that permit site-specific cleavage of the new transcript so as to expose a polyadenylation site. This signals a specialized endogenous polymerase to add a stretch of about 200 A residues (poly A) to the 3' end of the transcript. RNA molecules modified with this polyA tail appear to more stable and are translated more efficiently. Thus, in other embodiments involving eukaryotes, it is preferred that the terminator comprises a signal for the cleavage of the RNA, and it is more preferred that the terminator signal promotes polyadenylation of the message. The terminator and/or polyadenylation site elements can serve to enhance message levels and/or to minimize read through from the cassette into other sequences. Terminators contemplated for use in the disclosure include any known terminator of transcription described herein or known to one of ordinary skill in the art, including but not limited to, for example, the termination sequences of genes, such as for example the bovine growth hormone terminator or viral termination sequences, such as for example the SV40 terminator. In certain embodiments, the termination signal may be a lack of transcribable or translatable sequence, such as due to a sequence truncation.

[0348] In expression, particularly eukaryotic expression, one will typically include a polyadenylation signal to effect proper polyadenylation of the transcript. The nature of the polyadenylation signal is not believed to be crucial to the successful practice of the disclosure, and/or any such sequence may be employed. Preferred embodiments include the SV40 polyadenylation signal and/or the bovine growth hormone polyadenylation signal, convenient and/or known to function well in various target cells. Polyadenylation may increase the stability of the transcript or may facilitate cytoplasmic transport.

[0349] To propagate a vector in a host cell, it may contain one or more origins of replication sites (often termed “ori”), which is a specific nucleic acid sequence at which replication is initiated. Alternatively an autonomously replicating sequence (ARS) can be employed if the host cell is yeast.

[0350] In certain embodiments of the disclosure, cells containing a nucleic acid construct of the present disclosure may be identified *in vitro* or *in vivo* by including a marker in the expression vector. Such markers would confer an identifiable change to the cell permitting easy identification of cells containing the expression vector. Generally, a selectable marker is one that confers a property that allows for selection. A positive selectable marker is one in which the presence of the marker allows for its selection, while a negative selectable marker is one in which its presence prevents its selection. An example of a positive selectable marker is a drug resistance marker.

[0351] Usually the inclusion of a drug selection marker aids in the cloning and identification of transformants, for example, genes that confer resistance to neomycin, puromycin, hygromycin, DHFR, GPT, zeocin and histidinol are useful selectable markers. In addition to markers conferring a phenotype that allows for the discrimination of transformants based on the implementation of conditions, other types of markers including screenable markers such as GFP, whose basis is colorimetric analysis, are also contemplated. Alternatively, screenable enzymes such as herpes simplex virus thymidine kinase (HSV-tk) or chloramphenicol acetyltransferase (CAT) may be utilized. One of skill in the art would also know how to employ immunologic markers, possibly in conjunction with FACS analysis. The marker used is not believed to be important, so long as it is capable of being expressed simultaneously with the nucleic acid encoding a gene product. Further examples of selectable and screenable markers are well known to one of skill in the art.

[0352] The expression vectors may also provide a secretion signal sequence position to form a fusion protein with polypeptides encoded by inserted ENTPD2-binding antibody sequences. More often, the inserted ENTPD2-binding antibody sequences are linked to a signal sequences before inclusion in the vector. Vectors to be used to receive sequences encoding ENTPD2-binding antibody light and heavy chain variable domains sometimes also encode constant regions or parts thereof. Such vectors allow expression of the variable regions as fusion proteins with the constant regions thereby leading to production of intact antibodies and antigen-binding fragments thereof. Typically, such constant regions are human.

[0353] Generation of an expression vector can utilize a vector that includes a multiple cloning site (MCS), which is a nucleic acid region that contains multiple restriction enzyme sites, any one of which can be used in conjunction with standard recombinant technology to digest the vector. See Carbonelli *et al.*, 1999, Levenson *et al.*, 1998, and Cocea, 1997. “Restriction enzyme digestion” refers to catalytic cleavage of a nucleic acid molecule with an enzyme that functions only at specific locations in a nucleic acid molecule. Many one of these restriction enzymes are commercially available. Use of such enzymes is widely understood by those of skill in the art. Frequently, a vector is linearized or fragmented using a restriction enzyme that cuts within the MCS to enable exogenous sequences to be ligated to the vector. “Ligation” refers to the process of forming phosphodiester bonds between two nucleic acid fragments, which may or may not be contiguous with each other. Techniques involving restriction enzymes and ligation reactions are well known to those of skill in the art of recombinant technology.

[0354] Methods for introducing expression vectors containing the polynucleotide sequences of interest vary depending on the type of cellular host. For example, calcium chloride transfection is commonly utilized for prokaryotic cells, whereas calcium phosphate treatment or electroporation may be used for other cellular hosts (see generally Sambrook *et al.*, *supra*). Other methods include, e.g., electroporation, calcium phosphate treatment, liposome-mediated transformation, injection and microinjection, ballistic methods/gene gun, virosomes, immunoliposomes, polycation:nucleic acid conjugates, naked DNA, artificial virions, fusion to the herpes virus structural protein VP22, agent-enhanced uptake of DNA, *ex vivo* transduction, protoplast fusion, retroviral transduction, viral transfection, lipid based transfection or other conventional techniques. In the case of protoplast fusion, the cells are grown in media and screened for the appropriate activity. For long-term, high-yield production of recombinant proteins, stable expression will often be desired. For example, cell lines which stably express polypeptides can be prepared using expression vectors which contain viral origins of replication or endogenous expression elements and a selectable marker gene. Following the introduction of the vector, cells may be allowed to grow for 1-2 days in an enriched media before they are switched to selective media. The purpose of the selectable marker is to confer resistance to selection, and its presence allows growth of cells which successfully express the introduced sequences in selective media. Resistant, stably transfected cells can be proliferated using tissue culture techniques appropriate to the cell type. Methods and conditions for culturing the resulting transfected cells and for recovering the antibody molecule produced are known to those skilled in the art, and may be varied or

optimized depending upon the specific expression vector and mammalian host cell employed, based upon the present description.

[0355] Also provided herein are cells that include any one of the expression vectors described herein. In some embodiments, the disclosure features a host cell that includes a nucleic acid molecule described herein. Such cells can be a host cell or a therapeutic cell. The terms “host cell” and “recombinant host cell” are used interchangeably herein, which refer to not only to the particular subject cell but to the progeny or potential progeny of such a cell. Because certain modifications may occur in succeeding generations due to either mutation or environmental influences, such progeny may not, in fact, be identical to the parent cell, but are still included within the scope of the term as used herein.

[0356] In one embodiment, the host cells are genetically engineered to comprise nucleic acids encoding the antibody molecule. In one embodiment, the host cells are genetically engineered by using an expression cassette. The phrase “expression cassette” refers to nucleotide sequences, which are capable of effecting expression of a gene in hosts compatible with such sequences. Such cassettes may include a promoter, an open reading frame with or without introns, and a termination signal. Additional factors necessary or helpful in effecting expression may also be used, such as, for example, an inducible promoter.

[0357] The host cells for harboring and expressing the ENTPD2-binding antibody chains can be, but is not limited to, a eukaryotic cell or a prokaryotic cell, such as a bacterial cell, an insect cell, or a human cell. *E. coli* is one prokaryotic host useful for cloning and expressing the polynucleotides of the present invention. Other microbial hosts suitable for use include bacilli, such as *Bacillus subtilis*, and other enterobacteriaceae, such as *Salmonella*, *Serratia*, and various *Pseudomonas* species. In these prokaryotic hosts, one can also make expression vectors, which typically contain expression control sequences compatible with the host cell (e.g., an origin of replication). In addition, any number of a variety of well-known promoters will be present, such as the lactose promoter system, a tryptophan (trp) promoter system, a beta-lactamase promoter system, or a promoter system from phage lambda. The promoters typically control expression, optionally with an operator sequence, and have ribosome binding site sequences and the like, for initiating and completing transcription and translation. Other microbes, such as yeast, can also be employed to express ENTPD2-binding polypeptides of the invention. Insect cells in combination with baculovirus vectors can also be used. Suitable insect cells include, but are not limited to, Sf9 cells.

[0358] In one embodiment, mammalian host cells are used to express and produce the

ENTPD2-binding antibodies of the present invention. For example, they can be either a hybridoma cell line expressing endogenous immunoglobulin genes (e.g., the 1D6.C9 myeloma hybridoma cell) or a mammalian cell line harboring an exogenous expression vector (e.g., the SP2/0 myeloma cell). These include any normal mortal or normal or abnormal immortal animal or human cell. For example, a number of suitable host cell lines capable of secreting intact immunoglobulins have been developed including the CHO cell lines, various Cos cell lines, HeLa cells, myeloma cell lines, transformed B-cells and hybridomas. The use of mammalian tissue cell culture to express polypeptides is discussed generally in, e.g., Winnacker, *From Genes to Clones*, VCH Publishers, N.Y., N.Y., 1987. Expression vectors for mammalian host cells can include expression control sequences, such as an origin of replication, a promoter, and an enhancer (see, e.g., Queen, et al., *Immunol. Rev.* 89:49-68, 1986), and necessary processing information sites, such as ribosome binding sites, RNA splice sites, polyadenylation sites, and transcriptional terminator sequences. These expression vectors usually contain promoters derived from mammalian genes or from mammalian viruses. Suitable promoters may be constitutive, cell type-specific, stage-specific, and/or modulatable or regulatable. Useful promoters include, but are not limited to, the metallothionein promoter, the constitutive adenovirus major late promoter, the dexamethasone-inducible MMTV promoter, the SV40 promoter, the MRP pol III promoter, the constitutive MPSV promoter, the tetracycline-inducible CMV promoter (such as the human immediate-early CMV promoter), the constitutive CMV promoter, and promoter-enhancer combinations known in the art.

[0359] A host cell can be used to produce or express an antibody that binds to human ENTPD2 protein. Accordingly, the disclosure also features methods for producing an antibody that binds to human ENTPD2 protein using a host cell. In one embodiment, the method includes culturing the host cell (into which a recombinant expression vector encoding the antibody has been introduced) in a suitable medium, such that the antibody that binds to human ENTPD2 protein is produced. In another embodiment, the method further includes isolating the antibody from the medium or the host cell. Suitable eukaryotic cells include, but are not limited to, Vero cells, HeLa cells, COS cells, CHO cells, HEK293 cells, BHK cells and MDCKII cells.

Producing Monoclonal Antibodies

[0360] Monoclonal antibodies (mAbs) can be produced by a variety of techniques, including conventional monoclonal antibody methodology, e.g., the standard somatic cell

hybridization technique of Kohler and Milstein, 1975 Nature 256: 495. Many techniques for producing monoclonal antibody can be employed e.g., viral or oncogenic transformation of B lymphocytes.

[0361] An animal system for preparing hybridomas is the murine system. Hybridoma production in the mouse is a well established procedure. Immunization protocols and techniques for isolation of immunized splenocytes for fusion are known in the art. Fusion partners (e.g., murine myeloma cells) and fusion procedures are also known.

[0362] In some embodiments, the antibodies of the invention are humanized monoclonal antibodies. Chimeric or humanized antibodies and antigen-binding fragments thereof of the present invention can be prepared based on the sequence of a murine monoclonal antibody prepared as described above. DNA encoding the heavy and light chain immunoglobulins can be obtained from the murine hybridoma of interest and engineered to contain non-murine (e.g., human) immunoglobulin sequences using standard molecular biology techniques. For example, to create a chimeric antibody, the murine variable regions can be linked to human constant regions using methods known in the art (see e.g., U.S. Pat. No. 4,816,567 to Cabilly et al.). To create a humanized antibody, the murine CDR regions can be inserted into a human framework using methods known in the art. See e.g., U.S. Pat. No. 5,225,539 to Winter, and U.S. Pat. Nos. 5,530,101; 5,585,089; 5,693,762 and 6,180,370 to Queen et al.

[0363] In some embodiments, the antibodies of the invention are human monoclonal antibodies. Such human monoclonal antibodies directed against ENTPD2 can be generated using transgenic or transchromosomic mice carrying parts of the human immune system rather than the mouse system. These transgenic and transchromosomic mice include mice referred to herein as HuMAb mice and KM mice, respectively, and are collectively referred to herein as “human Ig mice”.

[0364] The HuMAb Mouse® (Medarex, Inc.) contains human immunoglobulin gene miniloci that encode un-rearranged human heavy (mu and gamma) and kappa light chain immunoglobulin sequences, together with targeted mutations that inactivate the endogenous mu and kappa chain loci (see e.g., Lonberg, et al., 1994 Nature 368 (6474): 856-859). Accordingly, the mice exhibit reduced expression of mouse IgM or K, and in response to immunization, the introduced human heavy and light chain transgenes undergo class switching and somatic mutation to generate high affinity human IgG-kappa monoclonal (Lonberg, N. et al., 1994 supra; reviewed in Lonberg, N., 1994 Handbook of Experimental Pharmacology 113:49-101; Lonberg, N. and Huszar, D., 1995 Intern. Rev. Immunol. 13: 65-

93, and Harding, F. and Lonberg, N., 1995 *Ann. N.Y. Acad. Sci.* 764:536-546). The preparation and use of HuMAb mice, and the genomic modifications carried by such mice, is further described in Taylor, L. et al., 1992 *Nucleic Acids Research* 20:6287-6295; Chen, J. et al., 1993 *International Immunology* 5: 647-656; Tuaillon et al., 1993 *Proc. Natl. Acad. Sci. USA* 94:3720-3724; Choi et al., 1993 *Nature Genetics* 4:117-123; Chen, J. et al., 1993 *EMBO J.* 12: 821-830; Tuaillon et al., 1994 *J. Immunol.* 152:2912-2920; Taylor, L. et al., 1994 *International Immunology* 579-591; and Fishwild, D. et al., 1996 *Nature Biotechnology* 14: 845-851. See further, U.S. Pat. Nos. 5,545,806; 5,569,825; 5,625,126; 5,633,425; 5,789,650; 5,877,397; 5,661,016; 5,814,318; 5,874,299; and 5,770,429; all to Lonberg and Kay; U.S. Pat. No. 5,545,807 to Surani et al.; PCT Publication Nos. WO 92103918, WO 93/12227, WO 94/25585, WO 97113852, WO 98/24884 and WO 99/45962, all to Lonberg and Kay; and PCT Publication No. WO 01/14424 to Korman et al.

[0365] In some embodiments, human antibodies can be raised using a mouse that carries human immunoglobulin sequences on transgenes and transchromosomes such as a mouse that carries a human heavy chain transgene and a human light chain transchromosome. Such mice, referred to herein as “KM mice,” are described in detail in PCT Publication WO 02/43478 to Ishida et al.

[0366] Still further, alternative transgenic animal systems expressing human immunoglobulin genes are available in the art and can be used to raise ENTPD2-binding antibodies and antigen-binding fragments thereof. For example, an alternative transgenic system referred to as the Xenomouse (Abgenix, Inc.) can be used. Such mice are described in, e.g., U.S. Pat. Nos. 5,939,598; 6,075,181; 6,114,598; 6,150,584 and 6,162,963 to Kucherlapati et al.

[0367] Moreover, alternative transchromosomal animal systems expressing human immunoglobulin genes are available in the art and can be used to raise ENTPD2-binding antibodies of the invention. For example, mice carrying both a human heavy chain transchromosome and a human light chain transchromosome, referred to as “TC mice” can be used; such mice are described in Tomizuka et al., 2000 *Proc. Natl. Acad. Sci. USA* 97:722-727. Furthermore, cows carrying human heavy and light chain transchromosomes have been described in the art (Kuroiwa et al., 2002 *Nature Biotechnology* 20:889-894) and can be used to raise ENTPD2 binding antibodies of the invention.

[0368] Human monoclonal antibodies can also be prepared using phage display methods for screening libraries of human immunoglobulin genes. Such phage display methods for isolating human antibodies are established in the art or described in the examples

below. See for example: U.S. Pat. Nos. 5,223,409; 5,403,484; and 5,571,698 to Ladner et al; U.S. Pat. Nos. 5,427,908 and 5,580,717 to Dower et al; U.S. Pat. Nos. 5,969,108 and 6,172,197 to McCafferty et al; and U.S. Pat. Nos. 5,885,793; 6,521,404; 6,544,731; 6,555,313; 6,582,915 and 6,593,081 to Griffiths et al.

[0369] Human monoclonal antibodies of the invention can also be prepared using SCID mice into which human immune cells have been reconstituted such that a human antibody response can be generated upon immunization. Such mice are described in, for example, U.S. Pat. Nos. 5,476,996 and 5,698,767 to Wilson et al.

Methods of Engineering Modified Antibodies

[0370] As discussed above, the ENTPD2-binding antibodies having VH and VL sequences or full length heavy and light chain sequences shown herein can be used to create new ENTPD2-binding antibodies by modifying full length heavy chain and/or light chain sequences, VH and/or VL sequences, or the constant region(s) attached thereto. Thus, in another aspect of the invention, the structural features of ENTPD2-binding antibody of the invention are used to create structurally related ENTPD2-binding antibodies that retain at least one functional property of the antibodies and antigen-binding fragments thereof of the invention, such as binding to and inhibit human ENTPD2.

[0371] For example, one or more CDR regions of the antibodies and antigen-binding fragments thereof of the present invention, or mutations thereof, can be combined recombinantly with known framework regions and/or other CDRs to create additional, recombinantly-engineered, ENTPD2-binding antibodies and antigen-binding fragments thereof of the invention, as discussed above. Other types of modifications include those described in the previous section. The starting material for the engineering method is one or more of the VH and/or VL sequences provided herein, or one or more CDR regions thereof. To create the engineered antibody, it is not necessary to actually prepare (i.e., express as a protein) an antibody having one or more of the VH and/or VL sequences provided herein, or one or more CDR regions thereof. Rather, the information contained in the sequence (s) is used as the starting material to create a “second generation” sequence(s) derived from the original sequence(s) and then the “second generation” sequence(s) is prepared and expressed as a protein.

[0372] The altered antibody sequence can also be prepared by screening antibody libraries having fixed CDR3 sequences or minimal essential binding determinants as described in US20050255552 and diversity on CDR1 and CDR2 sequences. The screening

can be performed according to any screening technology appropriate for screening antibodies from antibody libraries, such as phage display technology.

[0373] Standard molecular biology techniques can be used to prepare and express the altered antibody sequence. The antibody encoded by the altered antibody sequence (s) is one that retains one, some or all of the functional properties of the ENTPD2-binding antibodies described herein, which functional properties include, but are not limited to, specifically binding to and stabilize human ENTPD2 protein.

[0374] The functional properties of the altered antibodies can be assessed using standard assays available in the art and/or described herein, such as those set forth in the Examples (e.g., ELISAs).

[0375] In some embodiments, the methods of engineering antibodies and antigen-binding fragments thereof of the invention, mutations can be introduced randomly or selectively along all or part of an ENTPD2-binding antibody coding sequence and the resulting modified ENTPD2-binding antibodies can be screened for binding activity and/or other functional properties as described herein. Mutational methods have been described in the art. For example, PCT Publication WO 02/092780 describes methods for creating and screening antibody mutations using saturation mutagenesis, synthetic ligation assembly, or a combination thereof. Alternatively, PCT Publication WO 03/074679 describes methods of using computational screening methods to optimize physiochemical properties of antibodies.

Characterization of the Antibodies

[0376] The antibodies and antigen-binding fragments thereof of the invention can be characterized by various functional assays. For example, they can be characterized by their ability to bind to the ENTPD2 protein (e.g., human ENTPD2 protein).

[0377] The ability of an antibody to bind to ENTPD2 (e.g., human ENTPD2 protein) can be detected by labelling the antibody of interest directly, or the antibody may be unlabeled and binding detected indirectly using various sandwich assay formats known in the art.

[0378] In some embodiments, the ENTPD2-binding antibodies and antigen-binding fragments thereof of the invention block or compete with binding of a reference ENTPD2-binding antibody to ENTPD2 protein (e.g., human ENTPD2 protein). These can be fully human or humanized ENTPD2-binding antibodies described above. They can also be other human, mouse, chimeric or humanized ENTPD2-binding antibodies which bind to the same epitope as the reference antibody. The capacity to block or compete with the reference

antibody binding indicates that ENTPD2-binding antibody under test binds to the same or similar epitope as that defined by the reference antibody, or to an epitope which is sufficiently proximal to the epitope bound by the reference ENTPD2-binding antibody. Such antibodies are especially likely to share the advantageous properties identified for the reference antibody. The capacity to block or compete with the reference antibody may be determined by, e.g., a competition binding assay. With a competition binding assay, the antibody under test is examined for ability to inhibit specific binding of the reference antibody to a common antigen, such as ENTPD2 protein (e.g., human ENTPD2 protein). A test antibody competes with the reference antibody for specific binding to the antigen if an excess of the test antibody substantially inhibits binding of the reference antibody. Substantial inhibition means that the test antibody reduces specific binding of the reference antibody usually by at least 10%, 25%, 50%, 75%, or 90%.

[0379] There are a number of known competition binding assays that can be used to assess competition of an antibody with a reference antibody for binding to a particular protein, in this case, ENTPD2 (e.g., human ENTPD2 protein). These include, e.g., solid phase direct or indirect radioimmunoassay (RIA), solid phase direct or indirect enzyme immunoassay (EIA), sandwich competition assay (see Stahli et al., *Methods in Enzymology* 9:242-253, 1983); solid phase direct biotin-avidin EIA (see Kirkland et al., *J. Immunol.* 137:3614-3619, 1986); solid phase direct labeled assay, solid phase direct labeled sandwich assay (see Harlow & Lane, *supra*); solid phase direct label RIA using I-125 label (see Morel et al., *Molec. Immunol.* 25:7-15, 1988); solid phase direct biotin-avidin EIA (Cheung et al., *Virology* 176:546-552, 1990); and direct labeled RIA (Moldenhauer et al., *Scand. J. Immunol.* 32:77-82, 1990). Typically, such an assay involves the use of purified antigen bound to a solid surface or cells bearing either of these, an unlabelled test ENTPD2-binding antibody and a labelled reference antibody. Competitive inhibition is measured by determining the amount of label bound to the solid surface or cells in the presence of the test antibody. Usually the test antibody is present in excess. Antibodies identified by competition assay (competing antibodies) include antibodies binding to the same epitope as the reference antibody and antibodies binding to an adjacent epitope sufficiently proximal to the epitope bound by the reference antibody for steric hindrance to occur.

[0380] To determine if the selected ENTPD2-binding monoclonal antibodies bind to unique epitopes, each antibody can be biotinylated using commercially available reagents (e.g., reagents from Pierce, Rockford, Ill.). Competition studies using unlabeled monoclonal antibodies and biotinylated monoclonal antibodies can be performed using ENTPD2 protein

coated-ELISA plates. Biotinylated MAb binding can be detected with a streptavidin-alkaline phosphatase probe. To determine the isotype of a purified ENTPD2-binding antibody, isotype ELISA can be performed. For example, wells of microtiter plates can be coated with 1 µg/ml of anti-human IgG overnight at 4°C. After blocking with 1% BSA, the plates are reacted with 1 µg/ml or less of the monoclonal ENTPD2-binding antibody or purified isotype controls, at ambient temperature for one to two hours. The wells can then be reacted with either human IgG1 or human IgM-specific alkaline phosphatase-conjugated probes. Plates are then developed and analyzed so that the isotype of the purified antibody can be determined.

[0381] To demonstrate binding of monoclonal ENTPD2-binding antibodies to live cells expressing ENTPD2 protein (e.g., human ENTPD2 protein), flow cytometry can be used. Briefly, cell lines expressing ENTPD2 (grown under standard growth conditions) can be mixed with various concentrations of ENTPD2-binding antibody in PBS containing 0.1% BSA and 10% fetal calf serum, and incubated at 37°C for 1 hour. After washing, the cells are reacted with fluorescein-labeled anti-human IgG antibody under the same conditions as the primary antibody staining. The samples can be analyzed by FACScan instrument using light and side scatter properties to gate on single cells. An alternative assay using fluorescence microscopy may be used (in addition to or instead of) the flow cytometry assay. Cells can be stained exactly as described above and examined by fluorescence microscopy. This method allows visualization of individual cells, but may have diminished sensitivity depending on the density of the antigen.

[0382] ENTPD2-binding antibodies and antigen-binding fragments thereof of the invention can be further tested for reactivity with ENTPD2 protein (e.g., human ENTPD2 protein) or antigenic fragment by Western blotting. Briefly, purified ENTPD2 protein (e.g., human ENTPD2 protein) or fusion proteins, or cell extracts from cells expressing ENTPD2 can be prepared and subjected to sodium dodecyl sulfate polyacrylamide gel electrophoresis. After electrophoresis, the separated antigens are transferred to nitrocellulose membranes, blocked with 10% fetal calf serum, and probed with the monoclonal antibodies to be tested. Human IgG binding can be detected using anti-human IgG alkaline phosphatase and developed with BCIP/NBT substrate tablets (Sigma Chem. Co., St. Louis, Mo.).

[0383] ENTPD2-binding antibodies and antigen-binding fragments thereof of the invention can be further tested for their abilities to modulate one or more ENTPD2 activities/functions.

[0384] ENTPD2-binding antibodies and antigen-binding fragments thereof of the

invention can also be tested using any of the methods or assays described in the Examples.

Methods of Treatment and Therapeutic Use

[0385] The antibodies of the present invention have numerous *in vitro* and *in vivo* diagnostic and therapeutic utilities involving the diagnosis and treatment of disorders with ENTPD2-dependent pathophysiology. For example, these molecules can be administered to cells in culture, *in vitro* or *ex vivo*, or to human subjects, e.g., *in vivo*, to treat, prevent and to diagnose a variety disorders with ENTPD2-dependent pathophysiology. Accordingly, in one aspect provided herein are methods of treating a cancer in a subject in need thereof by administering to the subject a therapeutically effective amount of an antibody or antigen binding fragment thereof described herein, a nucleic acid encoding such an antibody or antigen binding fragment, a vector comprising a nucleic acid encoding such an antibody or antigen binding fragment, a cell comprising such a nucleic acid or vector, or a pharmaceutical composition comprising such an antibody or antigen binding fragment, nucleic acid, vector or cell. In one aspect, the invention provides a method of inhibiting or reducing growth of tumor cells in a subject comprising administering to the subject a therapeutically effective amount of an anti-human ENTPD2 antibody as disclosed herein.

[0386] In another aspect, a method of treating a subject, e.g., reducing or ameliorating, a hyperproliferative condition or disorder (e.g., a cancer), e.g., solid tumor, a hematological cancer, soft tissue tumor, or a metastatic lesion, in a subject is provided.

[0387] Accordingly, in one embodiment, the invention provides a method of inhibiting growth of tumor cells in a subject, comprising administering to the subject a therapeutically effective amount of one or more anti-human ENTPD2 antibody molecule or functional fragment thereof as described herein alone or in combination with other agents, e.g., therapeutic agents, or therapeutic modalities.

[0388] In some embodiments, such methods can further comprise a step of assaying expression levels of ENTPD2 in a sample obtained from a subject, e.g., tissue biopsy of the subject.

[0389] The term cancer is meant to include all types of cancerous growths or oncogenic processes, metastatic tissues or malignantly transformed cells, tissues, or organs, irrespective of histopathologic type or stage of invasiveness. Examples of cancerous disorders include, but are not limited to, solid tumors, soft tissue tumors, and metastatic lesions. Examples of solid tumors include malignancies, e.g., sarcomas, adenocarcinomas,

and carcinomas, of the various organ systems, such as those affecting liver, lung, breast, lymphoid, gastrointestinal (e.g., colon), genitourinary tract (e.g., renal, urothelial cells), prostate and pharynx. Adenocarcinomas include malignancies such as most colon cancers, rectal cancer, renal-cell carcinoma, liver cancer (hepatocarcinoma, e.g., an advanced hepatocarcinoma, with or without a viral infection, e.g., a chronic viral hepatitis), non-small cell carcinoma of the lung, cancer of the small intestine and cancer of the esophagus. Squamous cell carcinomas include malignancies, e.g., in the lung, esophagus, skin, head and neck region, oral cavity, anus, and cervix.

[0390] Metastatic lesions of the aforementioned cancers can also be treated or prevented using the methods and compositions of the invention.

[0391] Exemplary cancers whose growth can be inhibited using the antibodies molecules disclosed herein include cancers typically responsive to immunotherapy. Non-limiting examples of preferred cancers for treatment include gastrointestinal cancer (e.g. gastric (stomach) cancer, colorectal cancer (CRC)), cancer of the esophagus (e.g. esophageal squamous cell carcinoma (ESCC)), pancreatic cancer, and cholangiocarcinoma. Additionally, refractory or recurrent malignancies can be treated using the antibody molecules described herein.

[0392] Examples of other cancers that can be treated include lung cancer (e.g., a non-small cell lung cancer (NSCLC) (e.g., a NSCLC with squamous and/or non-squamous histology, or a NSCLC adenocarcinoma)), a melanoma (e.g., an advanced melanoma), a renal cancer (e.g., a renal cell carcinoma, e.g., clear cell renal cell carcinoma), a liver cancer, a myeloma (e.g., a multiple myeloma), a prostate cancer, a breast cancer (e.g., a breast cancer that does not express one, two or all of estrogen receptor, progesterone receptor, or Her2/neu, e.g., a triple negative breast cancer), a pancreatic cancer, a head and neck cancer (e.g., head and neck squamous cell carcinoma (HNSCC), anal cancer, gastro-esophageal cancer, thyroid cancer, cervical cancer, a lymphoproliferative disease (e.g., a post-transplant lymphoproliferative disease) or a hematological cancer, T-cell lymphoma, a non-Hodgkin's lymphoma, or a leukemia (e.g., a myeloid leukemia), bone cancer, pancreatic cancer, skin cancer, cancer of the head or neck, cutaneous or intraocular malignant melanoma, uterine cancer, ovarian cancer, rectal cancer, anal cancer, gastro-esophageal cancer, stomach cancer, testicular cancer, uterine cancer, carcinoma of the fallopian tubes, carcinoma of the endometrium, carcinoma of the cervix, carcinoma of the vagina, carcinoma of the vulva, Hodgkin Disease, non-Hodgkin lymphoma, myeloma (e.g., multiple myeloma) cancer of the

esophagus, cancer of the small intestine, cancer of the endocrine system, cancer of the thyroid gland, cancer of the parathyroid gland, cancer of the adrenal gland, sarcoma of soft tissue, cancer of the urethra, cancer of the penis, chronic or acute leukemias including acute myeloid leukemia, chronic myeloid leukemia, acute lymphoblastic leukemia, chronic lymphocytic leukemia, solid tumors of childhood, lymphocytic lymphoma, cancer of the bladder, cancer of the kidney (e.g. renal cancer, e.g., a renal cell carcinoma (RCC) (e.g., a metastatic RCC or clear cell renal cell carcinoma)), cancer of the ureter, carcinoma of the renal pelvis, neoplasm of the central nervous system (CNS), primary CNS lymphoma, tumor angiogenesis, spinal axis tumor, brain stem glioma, pituitary adenoma, Kaposi's sarcoma, epidermoid cancer, squamous cell cancer, T-cell lymphoma, environmentally induced cancers including those induced by asbestos, and combinations of said cancers.

[0393] In some embodiments, the therapies here can be used to treat a patient that has (or is identified as having) a cancer associated with an infection, e.g., a viral or bacterial infection. Exemplary cancers include cervical cancer, anal cancer, HPV-associated head and neck squamous cell cancer, HPV-associated esophageal papillomas, HHV6-associated lymphomas, EBV-associated lymphomas (including Burkitt lymphoma), Gastric MALT lymphoma, other infection-associated MALT lymphomas, HCC, and Kaposi's sarcoma.

[0394] In other embodiments, the cancer is a hematological malignancy or cancer including but is not limited to a leukemia or a lymphoma. For example, the anti-human ENTPD2 antibody molecule or a antigen-binding fragment thereof alone or in combination with other agents, e.g., therapeutic agents, can be used to treat cancers and malignancies including, but not limited to, e.g., acute leukemias including but not limited to, e.g., B-cell acute lymphoid leukemia ("BALL"), T-cell acute lymphoid leukemia ("TALL"), acute lymphoid leukemia (ALL); one or more chronic leukemias including but not limited to, e.g., chronic myelogenous leukemia (CML), chronic lymphocytic leukemia (CLL); additional hematologic cancers or hematologic conditions including, but not limited to, e.g., B cell prolymphocytic leukemia, blastic plasmacytoid dendritic cell neoplasm, Burkitt's lymphoma, diffuse large B cell lymphoma, Follicular lymphoma, Hairy cell leukemia, small cell- or a large cell-follicular lymphoma, malignant lymphoproliferative conditions, MALT lymphoma, mantle cell lymphoma, Marginal zone lymphoma, multiple myeloma, myelodysplasia and myelodysplastic syndrome, non-Hodgkin lymphoma, plasmablastic lymphoma, plasmacytoid dendritic cell neoplasm, Waldenstrom macroglobulinemia, and "preleukemia" which are a

diverse collection of hematological conditions united by ineffective production (or dysplasia) of myeloid blood cells, and the like.

[0395] In one embodiment, the cancer is chosen from a colon cancer (e.g., colorectal cancer (CRC) or colorectal adenocarcinoma), gastric cancer (e.g., stomach adenocarcinoma, gastric carcinoma), esophageal cancer (e.g. esophageal squamous cell carcinoma (ESCC)), pancreatic cancer, cholangiocarcinoma, lung cancer (e.g., small cell lung cancer), breast cancer (e.g., breast adenocarcinoma) or ovarian cancer.

[0396] In one embodiment, the cancer is colorectal cancer (CRC) or colorectal adenocarcinoma.

[0397] In another embodiment, the cancer is gastric cancer.

[0398] In yet another embodiment, the cancer is esophageal squamous cell carcinoma (ESCC).

[0399] In yet another embodiment, the cancer is overexpressing ENTPD2 (ENTPD2 positive/ENTPD2+) such as ENTPD2+ CRC, ENTPD2+ stomach cancer (e.g. ENTPD2 gastric cancer), ENTPD2+ esophageal squamous cell carcinoma (ENTPD2+ ESCC).

[0400] The antibody or antigen binding fragment thereof described herein, the nucleic acid encoding such an antibody or antigen binding fragment, or the vector or cell comprising a nucleic acid encoding such an antibody or antigen binding fragment, or the pharmaceutical composition comprising such an antibody or antigen binding fragment, nucleic acid, vector, or cell, can be administered to the subject through an intravenous, intratumoral or subcutaneous route. In some embodiments, such an antibody or or fragment thereof, nucleic acid, vector, cell, or pharmaceutical composition, is administered intravenously.

[0401] Also provided is an antibody or antigen binding fragment thereof described herein, a pharmaceutical composition comprising such an antibody or antigen binding fragment, a nucleic acid encoding such an antibody or antigen binding fragment, or a vector comprising a nucleic acid encoding such an antibody or antigen binding fragment, for use in the treatment of a cancer.

[0402] The present disclosure also includes uses of an antibody or antigen binding fragment thereof described herein, a pharmaceutical composition comprising such an antibody or antigen binding fragment, a nucleic acid encoding such an antibody or antigen

binding fragment, or a vector comprising a nucleic acid encoding such an antibody or antigen binding fragment, in the manufacture of a medicament for treatment of a cancer.

Combination Therapies

[0403] The various treatments described above can be combined with another treatment. The present disclosure also relates to a pharmaceutical composition comprising a combination according to the disclosure described herein, in particular together with instructions for simultaneous, separate or sequential use (especially for being jointly active) thereof in the treatment of a cancer. For example, the ENTPD2 antibodies or antigen-binding fragments thereof described herein can be combined with one or more of standard of care treatment (e.g., for a cancer), another antibody molecule, an immunomodulator (e.g., an activator of a costimulatory molecule or an inhibitor of a coinhibitory molecule); a vaccine, e.g., a therapeutic cancer vaccine; or other forms of cell therapy, as described below.

[0404] Accordingly, the methods of treating a cancer described herein can further include administering at least one additional therapeutic agent to the subject in need of treatment. Also provided herein are methods of treating a cancer comprising administering at least two additional therapeutic agents to the subject in need of treatment.

[0405] The term “combination” refers to either a fixed combination in one dosage unit form, or a combined administration where a compound of the present invention and at least one combination partner (e.g. at least one other drug as explained below, also referred to as “therapeutic agent(s)” or “co-agent(s)”) may be administered independently at the same time or separately within time intervals, especially where these time intervals allow that the combination partners show a cooperative, e.g. synergistic effect. The single components may be packaged in a kit or separately. One or both of the components (e.g., powders or liquids) may be reconstituted or diluted to a desired dose prior to administration. The terms “co-administration” or “combined administration” or the like as utilized herein are meant to encompass administration of the selected combination partner to a single subject in need thereof (e.g. a patient), and are intended to include treatment regimens in which the agents are not necessarily administered by the same route of administration or at the same time. The term “pharmaceutical combination” as used herein means a product that results from the mixing or combining of more than one therapeutic agent and includes both fixed and non-fixed combinations of the therapeutic agents. The term “fixed combination” means that the therapeutic agents, e.g. a compound of the present invention and a combination partner, are

both administered to a patient simultaneously in the form of a single entity or dosage. The term “non-fixed combination” means that the therapeutic agents, e.g., a compound of the present invention and at least one combination partner, are administered to a patient as separate entities either simultaneously, concurrently or sequentially with no specific time limits, wherein such administration provides therapeutically effective levels of the at least two compounds in the body of the patient. The latter also applies to cocktail therapy, e.g. the administration of three or more therapeutic agents.

[0406] The term “pharmaceutical combination” as used herein refers to either a fixed combination in one dosage unit form, or non-fixed combination or a kit of parts for the combined administration where two or more therapeutic agents may be administered independently at the same time or separately within time intervals, especially where these time intervals allow that the combination partners show a cooperative, e.g. synergistic effect.

[0407] The term “combination therapy” refers to the administration of two or more therapeutic agents to treat a therapeutic condition or disorder described in the present disclosure. Such administration encompasses co-administration of these therapeutic agents in a substantially simultaneous manner, such as in a single capsule having a fixed ratio of active ingredients. Alternatively, such administration encompasses co-administration in multiple, or in separate containers (e.g., tablets, capsules, powders, and liquids) for each active ingredient. Powders and/or liquids may be reconstituted or diluted to a desired dose prior to administration. In addition, such administration also encompasses use of each type of therapeutic agent in a sequential manner, either at approximately the same time or at different times. In either case, the treatment regimen will provide beneficial effects of the drug combination in treating the conditions or disorders described herein.

[0408] The anti-human ENTPD2 antibody molecules can be used in combination with other therapies. For example, the combination therapy can include a composition of the present invention co-formulated with, and/or co-administered with, one or more additional therapeutic agents, e.g., one or more anti-cancer agents, cytotoxic or cytostatic agents, hormone treatment, vaccines, and/or other immunotherapies. In other embodiments, the antibody molecules are administered in combination with other therapeutic treatment modalities, including surgery, radiation, cryosurgery, and/or thermotherapy. Such combination therapies may advantageously utilize lower dosages of the administered therapeutic agents, thus avoiding possible toxicities or complications associated with the various monotherapies.

[0409] By “in combination with”, it is not intended to imply that the therapy or the therapeutic agents must be administered at the same time and/or formulated for delivery together, although these methods of delivery are within the scope described herein.

[0410] The anti-human ENTPD2 antibody molecules can be administered concurrently with, prior to, or subsequent to, at least one or more other additional therapies or therapeutic agents. The anti-human ENTPD2 antibody molecule and the other at least one agent or therapeutic protocol can be administered in any order. In general, each agent will be administered at a dose and/or on a time schedule determined for that agent. It will further be appreciated that the at least one additional therapeutic agent utilized in this combination may be administered together in a single composition or administered separately in different compositions. In general, it is expected that additional therapeutic agents utilized in combination be utilized at levels that do not exceed the levels at which they are utilized individually. In some embodiments, the levels utilized in combination will be lower than those utilized individually.

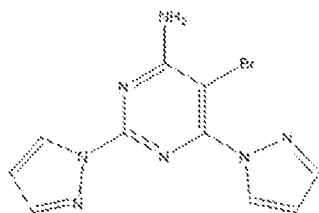
[0411] The present disclosure thus inter alia pertains to a combination product for simultaneous, separate or sequential use, such as a combined preparation or a pharmaceutical fixed combination, or a combination of such preparation and combination.

Exemplary Adenosine A2A Receptor Antagonists

[0412] In certain embodiments, the anti-human ENTPD2 molecules described herein are administered in combination with at least one adenosine A2A receptor (A2AR) antagonist. In certain embodiments, the anti-human ENTPD2 molecules described herein are administered in combination with at least two adenosine A2A receptor (A2AR) antagonists. Exemplary A2AR antagonists include, but are not limited to, e.g., PBF509/NIR178 (Palobiofarma/Novartis), CPI444/V81444 (Corvus/Genentech), AZD4635/HTL-1071 (AstraZeneca/Heptares), Vipadenant (Redox/Juno), GBV-2034 (Globavir), AB928 (Arcus Biosciences), Theophylline, Istradefylline (Kyowa Hakko Kogyo), Tozadenant/SYN-115 (Acorda), KW-6356 (Kyowa Hakko Kogyo), ST-4206 (Leadiant Biosciences), and Preladenant/SCH 420814 (Merck/Schering).

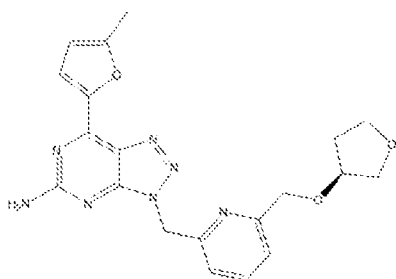
[0413] In certain embodiments, the A2AR antagonist is PBF509/NIR178. PBF509/NIR178 and other A2AR antagonists are disclosed in US 8,796,284 and WO 2017/025918, herein incorporated by reference in their entirety. In certain embodiments, the A2AR antagonist is 5-bromo-2,6-di-(1H-pyrazol-1-yl)pyrimidine-4-amine, or a

pharmaceutically acceptable salt thereof. In certain embodiments, the A2AR antagonist has the following structure:



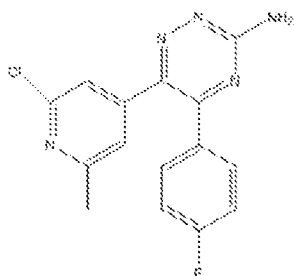
, or a pharmaceutically acceptable salt thereof.

[0414] In certain embodiments, the A2AR antagonist is CPI444/V81444. CPI-444 and other A2AR antagonists are disclosed in WO 2009/156737, herein incorporated by reference in its entirety. In certain embodiments, the A2AR antagonist is (*S*)-7-(5-methylfuran-2-yl)-3-((6-(((tetrahydrofuran-3-yl)oxy)methyl)pyridin-2-yl)methyl)-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-5-amine, or a pharmaceutically acceptable salt thereof. In certain embodiments, the A2AR antagonist is (*R*)-7-(5-methylfuran-2-yl)-3-((6-(((tetrahydrofuran-3-yl)oxy)methyl)pyridin-2-yl)methyl)-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-5-amine, or racemate thereof, or a pharmaceutically acceptable salt thereof. In certain embodiments, the A2AR antagonist is 7-(5-methylfuran-2-yl)-3-((6-(((tetrahydrofuran-3-yl)oxy)methyl)pyridin-2-yl)methyl)-3*H*-[1,2,3]triazolo[4,5-*d*]pyrimidin-5-amine, or a pharmaceutically acceptable salt thereof. In certain embodiments, the A2AR antagonist has the following structure:



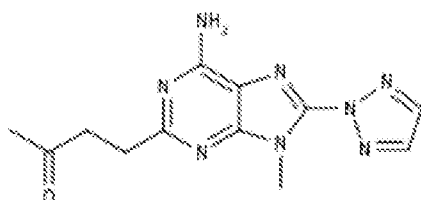
, or a pharmaceutically acceptable salt thereof.

[0415] In certain embodiments, the A2AR antagonist is AZD4635/HTL-1071. A2AR antagonists are disclosed in WO 2011/095625, herein incorporated by reference in its entirety. In certain embodiments, the A2AR antagonist is 6-(2-chloro-6-methylpyridin-4-yl)-5-(4-fluorophenyl)-1,2,4-triazin-3-amine, or a pharmaceutically acceptable salt thereof. In certain embodiments, the A2AR antagonist has the following structure:



, or a pharmaceutically acceptable salt thereof.

[0416] In certain embodiments, the A2AR antagonist is ST-4206 (Leadiant Biosciences). In certain embodiments, the A2AR antagonist is an A2AR antagonist described in US 9,133,197, herein incorporated by reference in its entirety. In certain embodiments, the A2AR antagonist has the following structure:



, or a pharmaceutically acceptable salt

thereof.

[0417] In certain embodiments, the A2AR antagonist is an A2AR antagonist described in US8114845, US9029393, US20170015758, or US20160129108, herein incorporated by reference in their entirety.

[0418] In certain embodiments, the A2AR antagonist is istradefylline (CAS Registry Number: 155270-99-8). Istradefylline is also known as KW-6002 or 8-[(E)-2-(3,4-dimethoxyphenyl)vinyl]-1,3-diethyl-7-methyl-3,7-dihydro-1H-purine-2,6-dione. Istradefylline is disclosed, *e.g.*, in LeWitt *et al.* (2008) *Annals of Neurology* 63 (3): 295–302).

[0419] In certain embodiments, the A2aR antagonist is tozadenant (Biotie). Tozadenant is also known as SYN115 or 4-hydroxy-N-(4-methoxy-7-morpholin-4-yl)-1,3-benzothiazol-2-yl)-4-methylpiperidine-1-carboxamide. Tozadenant blocks the effect of endogenous adenosine at the A2a receptors, resulting in the potentiation of the effect of dopamine at the D2 receptor and inhibition of the effect of glutamate at the mGluR5 receptor. In some embodiments, the A2aR antagonist is preladenant (CAS Registry Number: 377727-87-2). Preladenant is also known as SCH 420814 or 2-(2-Furanyl)-7-[2-[4-[4-(2-

methoxyethoxy)phenyl]-1-piperazinyl]ethyl]7H-pyrazolo[4,3-e][1,2,4]triazolo[1,5-c]pyrimidine-5-amine. Preladenant was developed as a drug that acted as a potent and selective antagonist at the adenosine A2A receptor.

[0420] In certain embodiments, the A2aR antagonist is vipadenant. Vipadenant is also known as BIIB014, V2006, or 3-[(4-amino-3-methylphenyl)methyl]-7-(furan-2-yl)triazolo[4,5-d]pyrimidin-5-amine.

[0421] Other exemplary A2aR antagonists include, *e.g.*, ATL-444, MSX-3, SCH-58261, SCH-412,348, SCH-442,416, VER-6623, VER-6947, VER-7835, CGS-15943, or ZM-241,385.

[0422] In some embodiments, the A2aR antagonist is an A2aR pathway antagonist, *e.g.*, a CD-73 inhibitor, *e.g.*, an anti-CD73 antibody. Targeting the extracellular production of adenosine by CD73 may reduce the immunosuppressive effects of adenosine. Anti-CD73 antibodies have a range of activities, *e.g.*, inhibition of CD73 ectonucleotidase activity, relief from AMP-mediated lymphocyte suppression, and inhibition of syngeneic tumor growth. Anti-CD73 antibodies can drive changes in both myeloid and lymphoid infiltrating leukocyte populations within the tumor microenvironment. These changes include, *e.g.*, increases in CD8 effector cells and activated macrophages, as well as a reduction in the proportions of myeloid-derived suppressor cells (MDSC) and regulatory T lymphocytes. In one embodiment, an anti-CD73 antibody molecule is a full antibody molecule or an antigen-binding fragment thereof. In some embodiments, the anti-CD73 antibody molecule is chosen from any of the antibody molecules listed in Table 2. In other embodiments, the anti-CD73 antibody molecule comprises a heavy chain variable domain sequence, a light chain variable domain sequence, or both, as disclosed in Table 2. In certain embodiments, the anti-CD73 antibody molecule binds to a CD73 protein and reduces, *e.g.*, inhibits or antagonizes, an activity of CD73, *e.g.*, human CD73.

[0423] In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in WO2016/075099, herein incorporated by reference in its entirety. In one embodiment, the anti-CD73 antibody molecule is MEDI 9447, *e.g.*, as disclosed in WO2016/075099. Alternative names for MEDI 9447 include clone 10.3 or 73combo3. MEDI 9447 is an IgG1 antibody that inhibits, *e.g.*, antagonizes, an activity of CD73. MEDI 9447 and other anti-CD73 antibody molecules are also disclosed in WO2016/075176 and US2016/0129108, the entire contents of which are herein incorporated by reference in their entirety.

[0424] In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of MEDI 9477. The amino acid sequence of the heavy chain variable domain of MEDI 9477 is disclosed as SEQ ID NO: 295 (see Table 2). The amino acid sequence of the light chain variable domain of MEDI 9477 is disclosed as SEQ ID NO: 296 (see Table 2).

[0425] In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in WO2016/081748, herein incorporated by reference in its entirety. In one embodiment, the anti-CD73 antibody molecule is 11F11, e.g., as disclosed in WO2016/081748. 11F11 is an IgG2 antibody that inhibits, e.g., antagonizes, an activity of CD73. Antibodies derived from 11F11, e.g., CD73.4, and CD73.10; clones of 11F11, e.g., 11F11-1 and 11F11-2; and other anti-CD73 antibody molecules are disclosed in WO2016/081748 and US 9,605,080, the entire contents of which are herein incorporated by reference in their entirety.

[0426] In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of 11F11-1 or 11F11-2. The amino acid sequence of the heavy chain variable domain of 11F11-1 is disclosed as SEQ ID NO: 302 (see Table 2). The amino acid sequence of the light chain variable domain of 11F11-1 is disclosed as SEQ ID NO: 303 (see Table 2). The amino acid sequence of the heavy chain variable domain of 11F11-2 is disclosed as SEQ ID NO: 299 (see Table 2). The amino acid sequence of the light chain variable domain of 11F11-2 is disclosed as SEQ ID NO: 300 (see Table 2). In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain, a light chain, or both, of 11F11-1 or 11F11-2. The heavy and light chain amino acid sequences of 11F11-1 are disclosed as SEQ ID NO: 297 and SEQ ID NO: 301, respectively (see Table 2). The heavy and light chain amino acid sequences of 11F11-2 are disclosed as SEQ ID NO: 294 and SEQ ID NO: 298, respectively (see Table 2).

[0427] In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in e.g., US 9,605,080, herein incorporated by reference in its entirety.

[0428] In one embodiment, the anti-CD73 antibody molecule is CD73.4, e.g., as disclosed in US 9,605,080. In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of CD73.4. The amino acid sequence of the heavy chain variable domain of CD73.4 is disclosed as SEQ ID NO: 304 (see Table 2). The amino acid sequence of the light chain variable domain of 11F11-2 is disclosed as SEQ ID NO: 305 (see Table 2).

[0429] In one embodiment, the anti-CD73 antibody molecule is CD73.10, e.g., as disclosed in US 9,605,080. In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of CD73.10. The amino acid sequence of the heavy chain variable domain of CD73.10 is disclosed as SEQ ID NO: 306 (see Table 2). The amino acid sequence of the light chain variable domain of CD73.10 is disclosed as SEQ ID NO: 307 (see Table 2).

[0430] In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in WO2009/0203538, herein incorporated by reference in its entirety. In one embodiment, the anti-CD73 antibody molecule is 067-213, e.g., as disclosed in WO2009/0203538.

[0431] In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of 067-213. The amino acid sequence of the heavy chain variable domain of 067-213 is disclosed as SEQ ID NO: 308 (see Table 2). The amino acid sequence of the light chain variable domain of 067-213 is disclosed as SEQ ID NO: 309 (see Table 2).

[0432] In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in US 9,090,697, herein incorporated by reference in its entirety. In one embodiment, the anti-CD73 antibody molecule is TY/23, e.g., as disclosed in US 9,090,697. In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of TY/23.

[0433] In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in WO2016/055609, herein incorporated by reference in its entirety. In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of an anti-CD73 antibody disclosed in WO2016/055609.

[0434] In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in WO2016/146818, herein incorporated by reference in its entirety. In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of an anti-CD73 antibody disclosed in WO2016/146818.

[0435] In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in WO2004/079013, herein incorporated by reference in its entirety. In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain,

a light chain variable domain, or both, of an anti-CD73 antibody disclosed in WO2004/079013.

[0436] In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in WO2012/125850, herein incorporated by reference in its entirety. In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of an anti-CD73 antibody disclosed in WO2012/125850.

[0437] In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in WO2015/004400, herein incorporated by reference in its entirety. In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of an anti-CD73 antibody disclosed in WO2015/004400.

[0438] In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in WO2007/146968, herein incorporated by reference in its entirety. In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of an anti-CD73 antibody disclosed in WO2007/146968.

[0439] In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in US2007/0042392, herein incorporated by reference in its entirety. In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of an anti-CD73 antibody disclosed in US2007/0042392.

[0440] In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in US2009/0138977, herein incorporated by reference in its entirety. In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of an anti-CD73 antibody disclosed in US2009/0138977.

[0441] In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in Flocke *et al.*, Eur J Cell Biol. 1992 Jun;58(1):62-70, herein incorporated by reference in its entirety. In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of an anti-CD73 antibody disclosed in Flocke *et al.*, Eur J Cell Biol. 1992 Jun;58(1):62-70.

[0442] In one embodiment, the anti-CD73 antibody molecule is an anti-CD73 antibody disclosed in Stagg *et al.*, PNAS. 2010 Jan 107(4): 1547-1552, herein incorporated

by reference in its entirety. In some embodiments, the anti-CD73 antibody molecule is TY/23 or TY11.8, as disclosed in Stagg *et al.* In one embodiment, the anti-CD73 antibody molecule comprises a heavy chain variable domain, a light chain variable domain, or both, of an anti-CD73 antibody disclosed in Stagg *et al.*

[0443] In one embodiment, the anti-human ENTPD2 antibody as described herein is administered in combination with an anti-CD73 antibody molecule, for example as described herein, and an A2AR antagonist, optionally selected from the group comprising PBF509/NIR178, CPI444/V81444, AZD4635/HTL-1071, Vipadenant, GBV-2034, AB928, Theophylline, Istradefylline, Tozadenant/SYN-115, KW-6356, ST-4206, and Preladenant/SCH 420814.

Table 2. Sequences of exemplary anti-CD73 antibody molecules

<i>WO2016075099</i> MEDI 9447		
SEQ ID NO: 295	VH	EVQLLES GGG LVQP GGS LRLSCAASGFT FSSYAYS WV RQAPGK GLEWVSAISGSGGR TYYADSVKGRFTISR DNS KNTLYLQMN SLRAEDTAVYYCAR LGYGRVDEWGRG TLVTVSS
SEQ ID NO: 296	VL	QSVLTQPPSASGTPGQRVTISCSGSLSNIGRNPVNWYQ QLPGTAPKLLIYLDNLRLSGVPDRFSGSKSGTSASLAIS GLQSEDEADYYCATWDDSHPGWTFGGG TKLTVL
<i>WO2016/081748</i> 11F11-2		
SEQ ID NO: 297	HC	QVQLVESGGGVVQPGRSLRLSCATSGFTFSNYGMHW VRQAPGKGLEWVAVILYDGSNKYYPD SVKGRFTISR D NSKNTLYLQMN SLRAEDTAVYYCARGGSSWYPDSFDI WGQGTMTVTVSSASTKGPSVFPLAPCSRSTSESTAALGC LVKDYPPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSL SSVVTVPSSNFGTQTYTCNV DHKPSNTKVDKTV ERKC CVECPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCV VVDVSHEDPEVQFNWYVDGVEVHNA TKPREEQFNS TFRVVS VLT VVHQDWLNGKEYKCKVSNKGLPAPIEKT ISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY PSDIAVEWESNGQPENNYKTTPPMLDSDGSFFLYSKLT VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 298	LC	DIQMTQSPSSLSASVGDRVTITCRASQGISSWLAWYQQ KPEKAPKSLIYAASSLQSGVPSRFSGSGSGTDFTLTISL QPEDFATYYCQQYNSYPLTFGGG TKVEIKRTVAAPSVF IFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNA LQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHKV YACEVTHQGLSPVTKSFNRGEC
SEQ ID NO: 299	VH	QVQLVESGGGVVQPGRSLRLSCATSGFTFSNYGMHW VRQAPGKGLEWVAVILYDGSNKYYPD SVKGRFTISR D

		NSKNTLYLQMNSLRAEDTAVYYCARGGSSWYPDSFDI WGQGTMTVTVSS
SEQ ID NO: 300	VL kappa	DIQMTQSPSSLSASVGDRVITTCRASQGISSWLAWYQQ KPEKAPKSLIYAASSLQSGVPSRFSGSGSGTDFTLTISL QPEDFATYYCQQYNSYPLTFGGGGTKVEIK
WO2016/081748 11F11-1		
SEQ ID NO: 297	HC	QVQLVESGGGVVQPGRSLRLSCATSGFTFSNYGMHW VRQAPGKGLEWVAVILYDGSNKYYPD SVKGRFTISR NSKNTLYLQMNSLRAEDTAVYYCARGGSSWYPDSFDI WGQGTMTVTVSSASTKGPSVFPLAPCSRSTSESTAALGC LVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSL SSVVTVPSSNFGTQTYTCNV D HKPSNTKVDKTV ERKC CVECPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCV VVDVSHEDPEVQFNWYVDGVEVHNAKTKPREEQFNS TFRVSVSLTVVHQDWLNGKEYKCKVSNKGLPAPIEKT ISKTKGQPREPQVYTLPPSREEMTKNQVSLTCLVKGFY PSDIAVEWESNGQPENNYKTTPPMLDSDGSFFLYSKLT VDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 301	LC	EIVLTQSPATLSLSPGERATLSCRASQGVSSYLAWYQQ KPGQAPRLLIYDASN RATGIPARFSGSGPGTDFTLTISL EPEDFAVYYCQQRSNWHLTFGGGGTKVEIKRTVAAPSV FIFPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDN ALQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHK VYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 302	VH	QVQLVESGGGVVQPGRSLRLSCATSGFTFSNYGMHW VRQAPGKGLEWVAVILYDGSNKYYPD SVKGRFTISR NSKNTLYLQMNSLRAEDTAVYYCARGGSSWYPDSFDI WGQGTMTVTVSS
SEQ ID NO: 303	VL kappa	EIVLTQSPATLSLSPGERATLSCRASQGVSSYLAWYQQ KPGQAPRLLIYDASN RATGIPARFSGSGPGTDFTLTISL EPEDFAVYYCQQRSNWHLTFGGGGTKVEIK
US9605080 CD73.4		
SEQ ID NO: 304	VH	QVQLVESGGGVVQPGRSLRLSCAASGFTFSNYGMHW VRQAPGKGLEWVAVILYDGSNKYYPD SVKGRFTISR NSKNTLYLQMNSLRAEDTAVYYCARGGSSWYPDSFDI WGQGTMTVTVSS
SEQ ID NO: 305	VL kappa	DIQMTQSPSSLSASVGDRVITTCRASQGISSWLAWYQQ KPEKAPKSLIYAASSLQSGVPSRFSGSGSGTDFTLTISL QPEDFATYYCQQYNSYPLTFGGGGTKVEIK
US9605080 CD73.10		
SEQ ID NO: 306	VH	QVQLVESGGGVVQPGRSLRLSCAASGFTFSNYGMHW VRQAPGKGLEWVAVIWDENSKYYPD SVKGRFTISR NSKNTLYLQMNSLRAEDTAVYYCARGGSSWYPDSFDI WGQGTMTVTVSS
SEQ ID NO: 307	VL kappa	DIQMTQSPSSLSASVGDRVITTCRASQGISSWLAWYQQ KPEKAPKSLIYAASSLQSGVPSRFSGSGSGTDFTLTISL QPEDFATYYCQQYNSYPLTFGGGGTKVEIK

US9388249 067-213		
SEQ ID NO: 308	VH	EVQLVESGGGLVQPGRSLRLSCAASGFTFDDYAMHW VRQAPGKGLEWVSGISWNSGSIGYADSVKGRFTISRDN AKNSLYLQMNSLRAEDTALYYCVRSGSYNYYYGMD VWGQGTTVTVSR
SEQ ID NO: 309	VL	QSVLTQPPSASGTPGQRVTISCSGSSSNIGSNTVNWYQ QLPGTAPKLLIYSNNQRPSGVPDRFSGSKSGTSASLAIS GLQSEDEADYYCAAWDDSLNGWVFGGGTKLTVLG

[0444] The anti-CD73 antibody molecules used in the combination therapies disclosed herein can include any of the VH/VL sequences disclosed in Table 2, or an amino acid sequence substantially identical thereto (e.g., at least 80%, 85%, 90%, 95%, 99% or more identical thereto). Exemplary sequences for CD73 antibodies include:

(i) the VH and VL amino acid sequences for MEDI 9447, SEQ ID NOs: 295-296, respectively, or an amino acid sequence substantially identical thereto (e.g., at least 80%, 85%, 90%, 95%, 99% or more identical to SEQ ID NOs: 295-296);

(ii) the HC and LC amino acid sequences for 11F11-2, SEQ ID NOs: 297-298, respectively, or an amino acid sequence substantially identical thereto (e.g., at least 80%, 85%, 90%, 95%, 99% or more identical to SEQ ID NOs: 297-298);

(iii) the VH and VL amino acid sequences for 11F11-2, SEQ ID NOs: 299-300, respectively, or an amino acid sequence substantially identical thereto (e.g., at least 80%, 85%, 90%, 95%, 99% or more identical to SEQ ID NOs: 299-300);

(iv) the HC and LC amino acid sequences for 11F11-1, SEQ ID NOs: 297 and 301, respectively, or an amino acid sequence substantially identical thereto (e.g., at least 80%, 85%, 90%, 95%, 99% or more identical to SEQ ID NOs: 297 and 301);

(v) the VH and VL amino acid sequences for 11F11-1, SEQ ID NOs: 302-303, respectively, or an amino acid sequence substantially identical thereto (e.g., at least 80%, 85%, 90%, 95%, 99% or more identical to SEQ ID NOs: 302-303);

(vi) the VH and VL amino acid sequences for CD73.4, SEQ ID NOs: 304-305, respectively, or an amino acid sequence substantially identical thereto (e.g., at least 80%, 85%, 90%, 95%, 99% or more identical to SEQ ID NOs: 304-305);

(vii) the VH and VL amino acid sequences for CD73.10, SEQ ID NOs: 306-307, respectively, or an amino acid sequence substantially identical thereto (e.g., at least 80%, 85%, 90%, 95%, 99% or more identical to SEQ ID NOs: 306-307); or

(viii) the VH and VL amino acid sequences for 067-213, SEQ ID NOs: 308-309, respectively, or an amino acid sequence substantially identical thereto (e.g., at least 80%, 85%, 90%, 95%, 99% or more identical to SEQ ID NOs: 308-309).

[0445] The anti-human ENTPD2 antibody as described herein can be combined with an inhibitor of a co-inhibitory molecule (e.g., a PD-1 inhibitor (e.g., an anti-PD-1 antibody molecule), a PD-L1 inhibitor (e.g., an anti-PD-L1 antibody molecule), a PD-L2 inhibitor (e.g., an anti-PD-L2 antibody molecule), a LAG-3 inhibitor (e.g., an anti-LAG-3 antibody molecule), a TIM-3 inhibitor (e.g., an anti-TIM-3 antibody molecule)), an activator of a co-stimulatory molecule (e.g., a GITR agonist (e.g., an anti-GITR antibody molecule)), a cytokine (e.g., IL-15 complexed with a soluble form of IL-15 receptor alpha (IL-15Ra)), or any combination thereof.

PD-1 Inhibitors

[0446] In certain embodiments, the ENTPD2 antibody as described herein is administered in combination with a PD-1 inhibitor. In some embodiments, the PD-1 inhibitor is chosen from PDR001 (Novartis), Nivolumab (Bristol-Myers Squibb), Pembrolizumab (Merck & Co), Pidilizumab (CureTech), MEDI0680 (Medimmune), REGN2810 (Regeneron), TSR-042 (Tesaro), PF-06801591 (Pfizer), BGB-A317 (Beigene), BGB-108 (Beigene), INCSHR1210 (Incyte), or AMP-224 (Amplimmune).

Exemplary PD-1 Inhibitors

[0447] In one embodiment, the PD-1 inhibitor is an anti-PD-1 antibody molecule. In one embodiment, the PD-1 inhibitor is an anti-PD-1 antibody molecule as described in US 2015/0210769, published on July 30, 2015, entitled “Antibody Molecules to PD-1 and Uses Thereof,” incorporated by reference in its entirety.

[0448] In one embodiment, the anti-PD-1 antibody molecule comprises at least one, two, three, four, five or six complementarity determining regions (CDRs) (or collectively all of the CDRs) from a heavy and light chain variable region comprising an amino acid sequence shown in Table 3 (e.g., from the heavy and light chain variable region sequences of BAP049-Clone-E or BAP049-Clone-B disclosed in Table 3), or encoded by a nucleotide sequence shown in Table 3. In some embodiments, the CDRs are according to the Kabat

definition (*e.g.*, as set out in Table 3). In some embodiments, the CDRs are according to the Chothia definition (*e.g.*, as set out in Table 3). In some embodiments, the CDRs are according to the combined CDR definitions of both Kabat and Chothia (*e.g.*, as set out in Table 3). In one embodiment, the combination of Kabat and Chothia CDR of VH CDR1 comprises the amino acid sequence GYTFTTYWMH (SEQ ID NO: 541). In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions (*e.g.*, conservative amino acid substitutions) or deletions, relative to an amino acid sequence shown in Table 3, or encoded by a nucleotide sequence shown in Table 3.

[0449] In one embodiment, the anti-PD-1 antibody molecule comprises a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence of SEQ ID NO: 501, a VHCDR2 amino acid sequence of SEQ ID NO: 502, and a VHCDR3 amino acid sequence of SEQ ID NO: 503; and a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO: 510, a VLCDR2 amino acid sequence of SEQ ID NO: 511, and a VLCDR3 amino acid sequence of SEQ ID NO: 512, each disclosed in Table 3.

[0450] In one embodiment, the antibody molecule comprises a VH comprising a VHCDR1 encoded by the nucleotide sequence of SEQ ID NO: 524, a VHCDR2 encoded by the nucleotide sequence of SEQ ID NO: 525, and a VHCDR3 encoded by the nucleotide sequence of SEQ ID NO: 526; and a VL comprising a VLCDR1 encoded by the nucleotide sequence of SEQ ID NO: 529, a VLCDR2 encoded by the nucleotide sequence of SEQ ID NO: 530, and a VLCDR3 encoded by the nucleotide sequence of SEQ ID NO: 531, each disclosed in Table 3.

[0451] In one embodiment, the anti-PD-1 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 506, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 506. In one embodiment, the anti-PD-1 antibody molecule comprises a VL comprising the amino acid sequence of SEQ ID NO: 520, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 520. In one embodiment, the anti-PD-1 antibody molecule comprises a VL comprising the amino acid sequence of SEQ ID NO: 516, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 516. In one embodiment, the anti-PD-1 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 506 and a VL comprising the amino acid sequence of SEQ ID NO: 520. In one embodiment, the anti-PD-1 antibody molecule comprises a VH comprising the amino acid

sequence of SEQ ID NO: 506 and a VL comprising the amino acid sequence of SEQ ID NO: 516.

[0452] In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 507, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 507. In one embodiment, the antibody molecule comprises a VL encoded by the nucleotide sequence of SEQ ID NO: 521 or 517, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 521 or 517. In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 507 and a VL encoded by the nucleotide sequence of SEQ ID NO: 521 or 517.

[0453] In one embodiment, the anti-PD-1 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 508, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 508. In one embodiment, the anti-PD-1 antibody molecule comprises a light chain comprising the amino acid sequence of SEQ ID NO: 522, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 522. In one embodiment, the anti-PD-1 antibody molecule comprises a light chain comprising the amino acid sequence of SEQ ID NO: 518, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 518. In one embodiment, the anti-PD-1 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 508 and a light chain comprising the amino acid sequence of SEQ ID NO: 522. In one embodiment, the anti-PD-1 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 508 and a light chain comprising the amino acid sequence of SEQ ID NO: 518.

[0454] In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 509, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 509. In one embodiment, the antibody molecule comprises a light chain encoded by the nucleotide sequence of SEQ ID NO: 523 or 519, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 523 or 519. In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 509 and a light chain encoded by the nucleotide sequence of SEQ ID NO: 523 or 519.

[0455] The antibody molecules described herein can be made by vectors, host cells, and methods described in US 2015/0210769, incorporated by reference in its entirety.

Table 3. Amino acid and nucleotide sequences of exemplary anti-PD-1 antibody molecules

BAP049-Clone-B HC		
SEQ ID NO: 501 (Kabat)	HCDR1	TYWMH
SEQ ID NO: 502 (Kabat)	HCDR2	NIYPGTGGSNFDEKFKN
SEQ ID NO: 503 (Kabat)	HCDR3	WTTGTGAY
SEQ ID NO: 504 (Chothia)	HCDR1	GYTFTTY
SEQ ID NO: 505 (Chothia)	HCDR2	YPGTGG
SEQ ID NO: 503 (Chothia)	HCDR3	WTTGTGAY
SEQ ID NO: 506	VH	EVQLVQSGAEVKKPGESLRISCKGSGYTFTTYWMHWVRQATGQG LEWMGNIYPGTGGSNFDEKFKNRVTITADKSTSTAYMELSSLRSE DTAVYYCTRWTGTGAYWGQGTITVTVSS
SEQ ID NO: 507	DNA VH	GAGGTGCAGCTGGTGCAGTCAGGCGCCGAAGTGAAGAAGCCCG GCGAGTCACTGAGAATTAGCTGTAAAGGTTTCAGGCTACACCTT CACTACCTACTGGATGCACTGGGTCCGCCAGGCTACCGGTCAA GGCCTCGAGTGGATGGGTAATATCTACCCCGGCACCGGCGGCT CTAACTTCGACGAGAAGTTTAAGAATAGAGTGACTATCACCGC CGATAAGTCTACTAGCACCGCCTATATGGAAGTGTCTAGCCTGA GATCAGAGGACACCGCCGTCTACTACTGCACTAGGTGGACTAC CGGCACAGGCGCCTACTGGGGTCAAGGCACTACCGTGACCGTG TCTAGC
SEQ ID NO: 508	Heavy chain	EVQLVQSGAEVKKPGESLRISCKGSGYTFTTYWMHWVRQATGQG LEWMGNIYPGTGGSNFDEKFKNRVTITADKSTSTAYMELSSLRSE DTAVYYCTRWTGTGAYWGQGTITVTVSSASTKGPSVFPLAPCSRS TSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL YSLSSVTVTPSSSLGKITYTCNVDHKPSNTKVDKRVESKYGPCCPP CPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQF NWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKE YKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVS LTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSGDSFFLYSRL TVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLG
SEQ ID NO: 509	DNA heavy chain	GAGGTGCAGCTGGTGCAGTCAGGCGCCGAAGTGAAGAAGCCCG GCGAGTCACTGAGAATTAGCTGTAAAGGTTTCAGGCTACACCTT CACTACCTACTGGATGCACTGGGTCCGCCAGGCTACCGGTCAA GGCCTCGAGTGGATGGGTAATATCTACCCCGGCACCGGCGGCT CTAACTTCGACGAGAAGTTTAAGAATAGAGTGACTATCACCGC CGATAAGTCTACTAGCACCGCCTATATGGAAGTGTCTAGCCTGA GATCAGAGGACACCGCCGTCTACTACTGCACTAGGTGGACTAC CGGCACAGGCGCCTACTGGGGTCAAGGCACTACCGTGACCGTG TCTAGCGCTAGCACTAAGGGCCCGTCCGTGTTCCCCCTGGCACC TTGTAGCCGGAGCACTAGCGAATCCACCGCTGCCCTCGGCTGCC TGGTCAAGGATTACTTCCCGGAGCCCGTGACCGTGTCTCTGGAAC AGCGGAGCCCTGACCTCCGGAGTGCACACCTTCCCCGCTGTGCT GCAGAGCTCCGGGCTGTACTCGCTGTCTCGGTGGTCAAGGTGC CTTCATCTAGCCTGGGTACCAAGACCTACACTTGCAACGTGGAC CACAAGCCTTCCAACACTAAGGTGGACAAGCGCGTCAATCGA AGTACGGCCACCGTGCCCGCCTTGTCCTCCGCGCCGGAGTTCCTC

		GGCGGTCCCTCGGTCTTTCTGTTCCACCGAAGCCCAAGGACAC TTTGATGATTTCCTCGCACCCCTGAAGTGACATGCGTGGTCTGG ACGTGTCACAGGAAGATCCGGAGGTGCAGTTCAATTGGTACGT GGATGGCGTCGAGGTGCACAACGCCAAAACCAAGCCGAGGGA GGAGCAGTTCAACTCCACTTACCGCGTCGTGTCCGTGCTGACGG TGCTGCATCAGGACTGGCTGAACGGGAAGGAGTACAAGTGCAA AGTGTCCAACAAGGGACTTCCTAGCTCAATCGAAAAGACCATC TCGAAAGCCAAGGGACAGCCCCGGGAACCCCAAGTGTATACCC TGCCACCGAGCCAGGAAGAAATGACTAAGAACCAAGTCTCATT GACTTGCCTTGTGAAGGGCTTCTACCCATCGGATATCGCCGTGG AATGGGAGTCCAACGGCCAGCCGGAACAACACTACAAGACCA CCCCCTCCGGTGTGACTCAGACGGATCCTTCTTCTCTACTCG CGGCTGACCGTGGATAAGAGCAGATGGCAGGAGGGAAATGTGT TCAGCTGTTCTGTGATGCATGAAGCCCTGCACAACCACTACACT CAGAAGTCCCTGTCCCTCTCCCTGGGA
BAP049-Clone-B LC		
SEQ ID NO: 510 (Kabat)	LCDR1	KSSQSLDLSGNQKNFLT
SEQ ID NO: 511 (Kabat)	LCDR2	WASTRES
SEQ ID NO: 512 (Kabat)	LCDR3	QNDYSYPYT
SEQ ID NO: 513 (Chothia)	LCDR1	SQSLDLSGNQKNF
SEQ ID NO: 514 (Chothia)	LCDR2	WAS
SEQ ID NO: 515 (Chothia)	LCDR3	DYSYPY
SEQ ID NO: 516	VL	EIVLTQSPATLSLSPGERATLSCKSSQSLDLSGNQKNFLT WYQQKPGKAPKLLIYWASTRESGVPSRFSGSGSGTDFTFTIS SLQPEDVATYYCQNDYSYPYTFGQGTKEIK
SEQ ID NO: 517	DNA VL	GAGATCGTCCTGACTCAGTCACCCGCTACCCTGAGCCTGAGCCC TGGCGAGCGGGCTACACTGAGCTGTAAATCTAGTCAGTCACTG CTGGATAGCGGTAATCAGAAGAACTTCTGACCTGGTATCAGC AGAAGCCCGGTAAAGCCCCTAAGCTGCTGATCTACTGGGCCCTC TACTAGAGAATCAGGCGTGCCCTCTAGGTTTAGCGGTAGCGGT AGTGGCACCGACTTCACCTTCACTATCTCTAGCCTGCAGCCCGA GGATATCGCTACCTACTACTGTCAGAACGACTATAGCTACCCCT ACACCTTCGGTCAAGGCACTAAGGTCGAGATTAAG
SEQ ID NO: 518	Light chain	EIVLTQSPATLSLSPGERATLSCKSSQSLDLSGNQKNFLT WYQQKPGKAPKLLIYWASTRESGVPSRFSGSGSGTDFTFTIS SLQPEDVATYYCQNDYSYPYTFGQGTKEIKRTVAAPSVFIFPPS DEQLKSGTASVVCCLNNFYPREAKVQWKVDNALQSGNSQESVTEQ DSKDYSLSTLTLSKADYEEKHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 519	DNA light chain	GAGATCGTCCTGACTCAGTCACCCGCTACCCTGAGCCTGAGCCC TGGCGAGCGGGCTACACTGAGCTGTAAATCTAGTCAGTCACTG CTGGATAGCGGTAATCAGAAGAACTTCTGACCTGGTATCAGC AGAAGCCCGGTAAAGCCCCTAAGCTGCTGATCTACTGGGCCCTC TACTAGAGAATCAGGCGTGCCCTCTAGGTTTAGCGGTAGCGGT AGTGGCACCGACTTCACCTTCACTATCTCTAGCCTGCAGCCCGA GGATATCGCTACCTACTACTGTCAGAACGACTATAGCTACCCCT ACACCTTCGGTCAAGGCACTAAGGTCGAGATTAAGCGTACGGT GGCCGCTCCAGCGTGTTCATCTTCCCCCCCAGCGACGAGCAGC TGAAGAGCGGCACCGCCAGCGTGGTGTGCTGCTGAACAATT

		CTACCCCCGGGAGGCCAAGGTGCAGTGGAAGGTGGACAACGCC CTGCAGAGCGGCAACAGCCAGGAGAGCGTCACCGAGCAGGAC AGCAAGGACTCCACCTACAGCCTGAGCAGCACCCCTGACCCTGA GCAAGGCCGACTACGAGAAGCATAAGGTGTACGCCTGCGAGGT GACCCACCAGGGCCTGTCCAGCCCCGTGACCAAGAGCTTCAAC AGGGGCGAGTGC
BAP049-Clone-E HC		
SEQ ID NO: 501 (Kabat)	HCDR1	TYWMH
SEQ ID NO: 502 (Kabat)	HCDR2	NIYPGTGGSNFDEKFKN
SEQ ID NO: 503 (Kabat)	HCDR3	WTTGTGAY
SEQ ID NO: 504 (Chothia)	HCDR1	GYTFTTY
SEQ ID NO: 505 (Chothia)	HCDR2	YPGTGG
SEQ ID NO: 503 (Chothia)	HCDR3	WTTGTGAY
SEQ ID NO: 506	VH	EVQLVQSGAEVKKPGESLRISCKGSGYTFTTYWMHWVRQATGQG LEWMGNIYPGTGGSNFDEKFKNRVTITADKSTSTAYMELSSLRSE DTAVYYCTRWTGTGAYWGQGTITVTVSS
SEQ ID NO: 507	DNA VH	GAGGTGCAGCTGGTGCAGTCAGGCGCCGAAGTGAAGAAGCCCG GCGAGTCACTGAGAATTAGCTGTAAAGGTTCAAGCTACACCTT CACTACCTACTGGATGCACTGGGTCCGCCAGGCTACCGGTCAA GGCCTCGAGTGGATGGGTAATATCTACCCCGGCACCGGCGGCT CTAACTTCGACGAGAAGTTAAGAATAGAGTGACTATCACCGC CGATAAGTCTACTAGCACCGCCTATATGGAAGTGTCTAGCCTGA GATCAGAGGACACCGCCGTCTACTACTGCACTAGGTGGACTAC CGGCACAGGCGCCTACTGGGGTCAAGGCACTACCGTGACCGTG TCTAGC
SEQ ID NO: 508	Heavy chain	EVQLVQSGAEVKKPGESLRISCKGSGYTFTTYWMHWVRQATGQG LEWMGNIYPGTGGSNFDEKFKNRVTITADKSTSTAYMELSSLRSE DTAVYYCTRWTGTGAYWGQGTITVTVSSASTKGPSVFPLAPCSRS TSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL YSLSSVTVTPSSSLGKTYTCNVDPKPSNTKVDKRVESKYGPCCPP CPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVVSQEDPEVQF NWWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDWLNGKE YKCKVSNKGLPSSIEKTIKAKGPQPREPVYTLPPSQEEMTKNQVS LTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRL TVDKSRWQEGNVFSCSVMEALHNHYTQKSLSLSLG
SEQ ID NO: 509	DNA heavy chain	GAGGTGCAGCTGGTGCAGTCAGGCGCCGAAGTGAAGAAGCCCG GCGAGTCACTGAGAATTAGCTGTAAAGGTTCAAGCTACACCTT CACTACCTACTGGATGCACTGGGTCCGCCAGGCTACCGGTCAA GGCCTCGAGTGGATGGGTAATATCTACCCCGGCACCGGCGGCT CTAACTTCGACGAGAAGTTAAGAATAGAGTGACTATCACCGC CGATAAGTCTACTAGCACCGCCTATATGGAAGTGTCTAGCCTGA GATCAGAGGACACCGCCGTCTACTACTGCACTAGGTGGACTAC CGGCACAGGCGCCTACTGGGGTCAAGGCACTACCGTGACCGTG TCTAGCGCTAGCACTAAGGGCCCGTCCGTGTTCCCCCTGGCACC TTGTAGCCGGAGCACTAGCGAATCCACCGCTGCCCTCGGCTGCC TGGTCAAGGATTACTTCCCGGAGCCCGTGACCGTGTCTGGAAC AGCGGAGCCCTGACCTCCGGAGTGACACCTTCCCGCTGTGCT GCAGAGCTCCGGGCTGTACTCGCTGTCGTCGGTGGTCAACGGTGC

		CTTCATCTAGCCTGGGTACCAAGACCTACACTTGCAACGTGGAC CACAAGCCTTCCAACACTAAGGTGGACAAGCGCGTCGAATCGA AGTACGGCCACCGTGCCCGCCTTGTCGCGCGCCGAGTTCCTC GGCGGTCCCTCGGTCTTTCTGTTCCACCGAAGCCCAAGGACAC TTTGATGATTTCGCGCACCCCTGAAGTGACATGCGTGGTCTGG ACGTGTCACAGGAAGATCCGGAGGTGCAGTTCAATTGGTACGT GGATGGCGTCGAGGTGCACAACGCCAAAACCAAGCCGAGGGA GGAGCAGTTCAACTCCACTTACCGCGTCGTGTCCGTGCTGACGG TGCTGCATCAGGACTGGCTGAACGGGAAGGAGTACAAGTGCAA AGTGTCCAACAAGGGACTTCCTAGCTCAATCGAAAAGACCATC TCGAAAGCCAAGGGACAGCCCCGGGAACCCCAAGTGTATACCC TGCCACCGAGCCAGGAAGAAATGACTAAGAACCAAGTCTCATT GACTTGCCTTGTGAAGGGCTTCTACCCATCGGATATCGCCGTGG AATGGGAGTCCAACGGCCAGCCGGAACAACAATAAGACCA CCCCCTCCGGTGCTGGACTCAGACGGATCCTTCTTCTCTACTCG CGGCTGACCGTGGATAAGAGCAGATGGCAGGAGGGAAATGTGT TCAGCTGTTCTGTGATGCATGAAGCCCTGCACAACCACTACACT CAGAAGTCCCTGTCCCTCTCCCTGGGA
BAP049-Clone-E LC		
SEQ ID NO: 510 (Kabat)	LCDR1	KSSQSLDSDGNQKNFLT
SEQ ID NO: 511 (Kabat)	LCDR2	WASTRES
SEQ ID NO: 512 (Kabat)	LCDR3	QNDYSYPYT
SEQ ID NO: 513 (Chothia)	LCDR1	SQSLDSDGNQKNF
SEQ ID NO: 514 (Chothia)	LCDR2	WAS
SEQ ID NO: 515 (Chothia)	LCDR3	DYSYPY
SEQ ID NO: 520	VL	EIVLTQSPATLSLSPGERATLSCKSSQSLDSDGNQKNFLTWYQQKP GQAPRLLIYWASTRESGVPSRFSGSGSGTDFTFTISSLEAEDAATYY CQNDYSYPYTFGQGTKVEIK
SEQ ID NO: 521	DNA VL	GAGATCGTCCTGACTCAGTCACCCGCTACCCTGAGCCTGAGCCC TGGCGAGCGGGCTACACTGAGCTGTAAATCTAGTCAGTCACTG CTGGATAGCGGTAATCAGAAGAACTTCTGACCTGGTATCAGC AGAAGCCCGGTCAAGCCCCTAGACTGCTGATCTACTGGGCCTCT ACTAGAGAATCAGGCGTGCCCTCTAGGTTTACGCGTAGCGGTA GTGGCACCGACTTCACCTTCACTATCTCTAGCCTGGAAGCCGAG GACGCCGCTACCTACTACTGTGACAACGACTATAGCTACCCCTA CACCTTCGGTCAAGGCACTAAGGTCGAGATTAAG
SEQ ID NO: 522	Light chain	EIVLTQSPATLSLSPGERATLSCKSSQSLDSDGNQKNFLTWYQQKP GQAPRLLIYWASTRESGVPSRFSGSGSGTDFTFTISSLEAEDAATYY CQNDYSYPYTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVV CLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKSTYLSST LTLKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 523	DNA light chain	GAGATCGTCCTGACTCAGTCACCCGCTACCCTGAGCCTGAGCCC TGGCGAGCGGGCTACACTGAGCTGTAAATCTAGTCAGTCACTG CTGGATAGCGGTAATCAGAAGAACTTCTGACCTGGTATCAGC AGAAGCCCGGTCAAGCCCCTAGACTGCTGATCTACTGGGCCTCT ACTAGAGAATCAGGCGTGCCCTCTAGGTTTACGCGTAGCGGTA GTGGCACCGACTTCACCTTCACTATCTCTAGCCTGGAAGCCGAG GACGCCGCTACCTACTACTGTGACAACGACTATAGCTACCCCTA

		CACCTTCGGTCAAGGCACTAAGGTCGAGATTAAGCGTACGGTG GCCGCTCCCAGCGTGTTCATCTTCCCCCCCAGCGACGAGCAGCT GAAGAGCGGCACCGCCAGCGTGGTGTGCCTGCTGAACAACCTTC TACCCCCGGGAGGCCAAGGTGCAGTGGAAGGTGGACAACGCCC TGCAGAGCGGCAACAGCCAGGAGAGCGTCACCGAGCAGGACA GCAAGGACTCCACCTACAGCCTGAGCAGCACCTGACCCTGAG CAAGGCCGACTACGAGAAGCATAAGGTGTACGCCTGCGAGGTG ACCCACCAGGGCCTGTCCAGCCCCGTGACCAAGAGCTTCAACA GGGGCGAGTGC
BAP049-Clone-B HC		
SEQ ID NO: 524 (Kabat)	HCDR1	ACCTACTGGATGCAC
SEQ ID NO: 525 (Kabat)	HCDR2	AATATCTACCCCGGCACCGGCGGCTCTAACTTCGACGAGAAGT TTAAGAAT
SEQ ID NO: 526 (Kabat)	HCDR3	TGGACTACCGGCACAGGCGCCTAC
SEQ ID NO: 527 (Chothia)	HCDR1	GGCTACACCTTCACTACCTAC
SEQ ID NO: 528 (Chothia)	HCDR2	TACCCCGGCACCGGCGGC
SEQ ID NO: 526 (Chothia)	HCDR3	TGGACTACCGGCACAGGCGCCTAC
BAP049-Clone-B LC		
SEQ ID NO: 529 (Kabat)	LCDR1	AAATCTAGTCAGTCACTGCTGGATAGCGGTAATCAGAAGAACT TCCTGACC
SEQ ID NO: 530 (Kabat)	LCDR2	TGGGCCTCTACTAGAGAATCA
SEQ ID NO: 531 (Kabat)	LCDR3	CAGAACGACTATAGCTACCCCTACACC
SEQ ID NO: 532 (Chothia)	LCDR1	AGTCAGTCACTGCTGGATAGCGGTAATCAGAAGAACTTC
SEQ ID NO: 533 (Chothia)	LCDR2	TGGGCCTCT
SEQ ID NO: 534 (Chothia)	LCDR3	GACTATAGCTACCCCTAC
BAP049-Clone-E HC		
SEQ ID NO: 524 (Kabat)	HCDR1	ACCTACTGGATGCAC
SEQ ID NO: 525 (Kabat)	HCDR2	AATATCTACCCCGGCACCGGCGGCTCTAACTTCGACGAGAAGT TTAAGAAT
SEQ ID NO: 526 (Kabat)	HCDR3	TGGACTACCGGCACAGGCGCCTAC
SEQ ID NO: 527 (Chothia)	HCDR1	GGCTACACCTTCACTACCTAC
SEQ ID NO: 528 (Chothia)	HCDR2	TACCCCGGCACCGGCGGC
SEQ ID NO: 526 (Chothia)	HCDR3	TGGACTACCGGCACAGGCGCCTAC
BAP049-Clone-E LC		
SEQ ID NO: 529 (Kabat)	LCDR1	AAATCTAGTCAGTCACTGCTGGATAGCGGTAATCAGAAGAACT TCCTGACC
SEQ ID NO: 530 (Kabat)	LCDR2	TGGGCCTCTACTAGAGAATCA
SEQ ID NO: 531 (Kabat)	LCDR3	CAGAACGACTATAGCTACCCCTACACC
SEQ ID NO: 532 (Chothia)	LCDR1	AGTCAGTCACTGCTGGATAGCGGTAATCAGAAGAACTTC

SEQ ID NO: 533 (Chothia)	LCDR2	TGGGCCTCT
SEQ ID NO: 534 (Chothia)	LCDR3	GACTATAGCTACCCCTAC

Other Exemplary PD-1 Inhibitors

[0456] In one embodiment, the anti-PD-1 antibody molecule is Nivolumab (Bristol-Myers Squibb), also known as MDX-1106, MDX-1106-04, ONO-4538, BMS-936558, or OPDIVO®. Nivolumab (clone 5C4) and other anti-PD-1 antibodies are disclosed in US 8,008,449 and WO 2006/121168, incorporated by reference in their entirety. In one embodiment, the anti-PD-1 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of Nivolumab, *e.g.*, as disclosed in Table 4.

[0457] In one embodiment, the anti-PD-1 antibody molecule is Pembrolizumab (Merck & Co), also known as Lambrolizumab, MK-3475, MK03475, SCH-900475, or KEYTRUDA®. Pembrolizumab and other anti-PD-1 antibodies are disclosed in Hamid, O. *et al.* (2013) *New England Journal of Medicine* 369 (2): 134–44, US 8,354,509, and WO 2009/114335, incorporated by reference in their entirety. In one embodiment, the anti-PD-1 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of Pembrolizumab, *e.g.*, as disclosed in Table 4.

[0458] In one embodiment, the anti-PD-1 antibody molecule is Pidilizumab (CureTech), also known as CT-011. Pidilizumab and other anti-PD-1 antibodies are disclosed in Rosenblatt, J. *et al.* (2011) *J Immunotherapy* 34(5): 409-18, US 7,695,715, US 7,332,582, and US 8,686,119, incorporated by reference in their entirety. In one embodiment, the anti-PD-1 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of Pidilizumab, *e.g.*, as disclosed in Table 4.

[0459] In one embodiment, the anti-PD-1 antibody molecule is MEDI0680 (Medimmune), also known as AMP-514. MEDI0680 and other anti-PD-1 antibodies are disclosed in US 9,205,148 and WO 2012/145493, incorporated by reference in their entirety. In one embodiment, the anti-PD-1 antibody molecule comprises one or more of the CDR

sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of MEDI0680.

[0460] In one embodiment, the anti-PD-1 antibody molecule is REGN2810 (Regeneron). In one embodiment, the anti-PD-1 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of REGN2810.

[0461] In one embodiment, the anti-PD-1 antibody molecule is PF-06801591 (Pfizer). In one embodiment, the anti-PD-1 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of PF-06801591.

[0462] In one embodiment, the anti-PD-1 antibody molecule is BGB-A317 or BGB-108 (Beigene). In one embodiment, the anti-PD-1 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of BGB-A317 or BGB-108.

[0463] In one embodiment, the anti-PD-1 antibody molecule is INCSHR1210 (Incyte), also known as INCSHR01210 or SHR-1210. In one embodiment, the anti-PD-1 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of INCSHR1210.

[0464] In one embodiment, the anti-PD-1 antibody molecule is TSR-042 (Tesar), also known as ANB011. In one embodiment, the anti-PD-1 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of TSR-042.

[0465] Further known anti-PD-1 antibodies include those described, *e.g.*, in WO 2015/112800, WO 2016/092419, WO 2015/085847, WO 2014/179664, WO 2014/194302, WO 2014/209804, WO 2015/200119, US 8,735,553, US 7,488,802, US 8,927,697, US 8,993,731, and US 9,102,727, incorporated by reference in their entirety.

[0466] In one embodiment, the anti-PD-1 antibody is an antibody that competes for binding with, and/or binds to the same epitope on PD-1 as, one of the anti-PD-1 antibodies described herein.

[0467] In one embodiment, the PD-1 inhibitor is a peptide that inhibits the PD-1 signaling pathway, *e.g.*, as described in US 8,907,053, incorporated by reference in its

entirety. In one embodiment, the PD-1 inhibitor is an immunoadhesin (*e.g.*, an immunoadhesin comprising an extracellular or PD-1 binding portion of PD-L1 or PD-L2 fused to a constant region (*e.g.*, an Fc region of an immunoglobulin sequence). In one embodiment, the PD-1 inhibitor is AMP-224 (B7-DCIg (Amplimmune), *e.g.*, disclosed in WO 2010/027827 and WO 2011/066342, incorporated by reference in their entirety).

Table 4. Amino acid sequences of other exemplary anti-PD-1 antibody molecules

Nivolumab		
SEQ ID NO: 535	Heavy chain	QVQLVESGGGVVQPGRSLRLDCKASGITFSNSGMHWVRQAPGKGLEWVAV IWYDGSKRYADSVKGRFTISRDNKNTLFLQMNSLRAEDTAVYYCATND DYWGQGTLLTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPTV SWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNVDPKPSN TKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCV DVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLHQDW LNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEEMTKNQVSL TCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSRLTVDKSR WQEGNVFSCSVMEALHNHYTQKSLSLSLGK
SEQ ID NO: 536	Light chain	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASN RATGIPARFSGSGGTDFLTITISLEPEDFAVYYCQQSSNWPRFTGQGTKVEI KRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSG NSQESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSF NRGEC
Pembrolizumab		
SEQ ID NO: 537	Heavy chain	QVQLVQSGVEVKKPGASVKVSCASGYTFTNYYMYWVRQAPGQGLEWM GGINPSNGGTNFKNEKFNKRVTLTDSSTTTAYMELKSLQFDDTAVYYCARR DYRFDMGFDYWGQGTITVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVK DYFPEPTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYT CNVDHKPSNTKVDKRVESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMIS RTPETVCVVDVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSV LTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQEE MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYS RLTVDKSRWQEGNVFSCSVMEALHNHYTQKSLSLSLGK
SEQ ID NO: 538	Light chain	EIVLTQSPATLSLSPGERATLSCRASKGVSTSGYSYLHWYQQKPGQAPRLLI YLASYLESQVAPARFSGSGGTDFLTITISLEPEDFAVYYCQHSRDLPLTFGGG TKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNA LQSGNSQESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPV TKSFNRGEC
Pidilizumab		
SEQ ID NO: 539	Heavy chain	QVQLVQSGSELKKPGASVKISKASGYTFTNYGMNVWRQAPGQGLQWMG WINTDSGESTYAEFEKGRFVFLDTSVNTAYLQITSLTAEDTGMVFCVRVGY DALDYWGQGTLLTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEP VTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGKTKYTCNVNHNK PSNTKVDKRVESKCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPE VTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLT VLHQDWLNGKEYKCKVSNKALPAPIEKISKAKGQPREPQVYTLPPSREEM TKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKL TVDKSRWQEGNVFSCSVMEALHNHYTQKSLSLSPGK

SEQ ID NO: 540	Light chain	EIVLTQSPSSLSASVGDRVTITCSARSSVSVMHWFQKPGKAPKLWIYRTSN LASGVPSRFSGSGSGTSYCLTINSLQPEDFATYYCQQRSSFPLTFGGGTKLEIK RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGN SQESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFN RGEC

[0468] In one embodiment the anti-human ENTPD2 antibody as described herein is administered in combination with at least one PD1 inhibitor as described herein and at least one A2A receptor antagonist as described herein.

PD-L1 Inhibitors

[0469] In certain embodiments, the anti-human ENTPD2 antibody as described herein is administered in combination with a PD-L1 inhibitor. The PD-L1 inhibitor may be an antibody, an antigenbinding fragment thereof, an immunoadhesin, a fusion protein, or an oligopeptide. In some embodiments, the PD-L1 inhibitor is chosen from FAZ053 (Novartis), Atezolizumab, also known as Tecentriq® (Genentech/Roche), Avelumab, also known as Bavencio® (Merck Serono and Pfizer), Durvalumab, also known as Imfinzi® (MedImmune/AstraZeneca), or BMS-936559 (Bristol-Myers Squibb).

Exemplary PD-L1 Inhibitors

[0470] In one embodiment, the PD-L1 inhibitor is an anti-PD-L1 antibody molecule. In one embodiment, the PD-L1 inhibitor is an anti-PD-L1 antibody molecule as disclosed in US 2016/0108123, published on April 21, 2016, entitled “Antibody Molecules to PD-L1 and Uses Thereof,” incorporated by reference in its entirety.

[0471] In one embodiment, the anti-PD-L1 antibody molecule comprises at least one, two, three, four, five or six complementarity determining regions (CDRs) (or collectively all of the CDRs) from a heavy and light chain variable region comprising an amino acid sequence shown in Table 5 (*e.g.*, from the heavy and light chain variable region sequences of BAP058-Clone O or BAP058-Clone N disclosed in Table 5), or encoded by a nucleotide sequence shown in Table 5. In some embodiments, the CDRs are according to the Kabat definition (*e.g.*, as set out in Table 5). In some embodiments, the CDRs are according to the Chothia definition (*e.g.*, as set out in Table 5). In some embodiments, the CDRs are according to the combined CDR definitions of both Kabat and Chothia (*e.g.*, as set out in Table 5). In one embodiment, the combination of Kabat and Chothia CDR of VH CDR1 comprises the amino acid sequence GYTFTSYWMY (SEQ ID NO: 647). In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three,

four, five, six or more changes, *e.g.*, amino acid substitutions (*e.g.*, conservative amino acid substitutions) or deletions, relative to an amino acid sequence shown in Table 5, or encoded by a nucleotide sequence shown in Table 5.

[0472] In one embodiment, the anti-PD-L1 antibody molecule comprises a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence of SEQ ID NO: 601, a VHCDR2 amino acid sequence of SEQ ID NO: 602, and a VHCDR3 amino acid sequence of SEQ ID NO: 603; and a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO: 609, a VLCDR2 amino acid sequence of SEQ ID NO: 610, and a VLCDR3 amino acid sequence of SEQ ID NO: 611, each disclosed in Table 5.

[0473] In one embodiment, the anti-PD-L1 antibody molecule comprises a VH comprising a VHCDR1 encoded by the nucleotide sequence of SEQ ID NO: 628, a VHCDR2 encoded by the nucleotide sequence of SEQ ID NO: 629, and a VHCDR3 encoded by the nucleotide sequence of SEQ ID NO: 630; and a VL comprising a VLCDR1 encoded by the nucleotide sequence of SEQ ID NO: 633, a VLCDR2 encoded by the nucleotide sequence of SEQ ID NO: 634, and a VLCDR3 encoded by the nucleotide sequence of SEQ ID NO: 635, each disclosed in Table 5.

[0474] In one embodiment, the anti-PD-L1 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 606, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 606. In one embodiment, the anti-PD-L1 antibody molecule comprises a VL comprising the amino acid sequence of SEQ ID NO: 616, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 616. In one embodiment, the anti-PD-L1 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 620, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 620. In one embodiment, the anti-PD-L1 antibody molecule comprises a VL comprising the amino acid sequence of SEQ ID NO: 624, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 624. In one embodiment, the anti-PD-L1 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 606 and a VL comprising the amino acid sequence of SEQ ID NO: 616. In one embodiment, the anti-PD-L1 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 620 and a VL comprising the amino acid sequence of SEQ ID NO: 624.

[0475] In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 607, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 607. In one embodiment, the antibody molecule

comprises a VL encoded by the nucleotide sequence of SEQ ID NO: 617, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 617. In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 621, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 621. In one embodiment, the antibody molecule comprises a VL encoded by the nucleotide sequence of SEQ ID NO: 625, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 625. In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 607 and a VL encoded by the nucleotide sequence of SEQ ID NO: 617. In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 621 and a VL encoded by the nucleotide sequence of SEQ ID NO: 625.

[0476] In one embodiment, the anti-PD-L1 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 608, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 608. In one embodiment, the anti-PD-L1 antibody molecule comprises a light chain comprising the amino acid sequence of SEQ ID NO: 618, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 618. In one embodiment, the anti-PD-L1 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 622, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 622. In one embodiment, the anti-PD-L1 antibody molecule comprises a light chain comprising the amino acid sequence of SEQ ID NO: 626, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 626. In one embodiment, the anti-PD-L1 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 608 and a light chain comprising the amino acid sequence of SEQ ID NO: 618. In one embodiment, the anti-PD-L1 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 622 and a light chain comprising the amino acid sequence of SEQ ID NO: 626.

[0477] In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 615, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 615. In one embodiment, the antibody molecule comprises a light chain encoded by the nucleotide sequence of SEQ ID NO: 619, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 619. In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 623, or a nucleotide sequence at least 85%, 90%, 95%,

or 99% identical or higher to SEQ ID NO: 623. In one embodiment, the antibody molecule comprises a light chain encoded by the nucleotide sequence of SEQ ID NO: 627, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 627. In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 615 and a light chain encoded by the nucleotide sequence of SEQ ID NO: 619. In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 623 and a light chain encoded by the nucleotide sequence of SEQ ID NO: 627.

[0478] The antibody molecules described herein can be made by vectors, host cells, and methods described in US 2016/0108123, incorporated by reference in its entirety.

Table 5. Amino acid and nucleotide sequences of exemplary anti-PD-L1 antibody molecules

BAP058-Clone O HC		
SEQ ID NO: 601 (Kabat)	HCDR1	SYWMY
SEQ ID NO: 602 (Kabat)	HCDR2	RIDPNSGSTKYNEKFN
SEQ ID NO: 603 (Kabat)	HCDR3	DYRKGLYAMDY
SEQ ID NO: 604 (Chothia)	HCDR1	GYTFTSY
SEQ ID NO: 605 (Chothia)	HCDR2	DPNSGS
SEQ ID NO: 603 (Chothia)	HCDR3	DYRKGLYAMDY
SEQ ID NO: 606	VH	EVQLVQSGAEVKKPGATVKISCKVSGYTFTSYWMYWVRQARGQ RLEWIGRIDPNSGSTKYNEKFNRTISRDN SKNTLYLQMNSLRA EDTAVYYCARDYRKGLYAMDYWGQGTTVTVSS
SEQ ID NO: 607	DNA VH	GAAGTGCAGCTGGTGCAGTCAGGCGCCGAAGTGAAGAAACCC GGCGCTACCGTGAAGATTAGCTGTAAAGTCTCAGGCTACACCT TCACTAGCTACTGGATGTACTGGGTCCGACAGGCTAGAGGGCA AAGACTGGAGTGGATCGGTAGAATCGACCCTAATAGCGGCTC TACTAAGTATAACGAGAAAGTTTAAGAATAGGTTCACTATTAGT AGGGATAACTCTAAGAACACCCTGTACCTGCAGATGAATAGC CTGAGAGCCGAGGACACCGCCGTCTACTACTGCGCTAGAGACT ATAGAAAGGGCCTGTACGCTATGGACTACTGGGGTCAAGGCA CTACCGTGACCGTGTCTTCA
SEQ ID NO: 608	Heavy chain	EVQLVQSGAEVKKPGATVKISCKVSGYTFTSYWMYWVRQARGQ RLEWIGRIDPNSGSTKYNEKFNRTISRDN SKNTLYLQMNSLRA EDTAVYYCARDYRKGLYAMDYWGQGTTVTVSSASTKGPSVFPL APCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV LQSSGLYSLSSVTVPSSSLGKTYTCNVDPHKPSNTKVDKRVESK YGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVVS QEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPSQ EEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLD SDGSFFLYSRLTVDKSRWQEGNVFSCSVMEALHNHYTQKSLSL SLG

SEQ ID NO: 615	DNA heavy chain	GAAGTGCAGCTGGTGCAGTCAGGCGCCGAAGTGAAGAAACCC GGCGCTACCGTGAAGATTAGCTGTAAAGTCTCAGGCTACACCT TCACTAGCTACTGGATGTACTGGGTCCGACAGGCTAGAGGGCA AAGACTGGAGTGGATCGGTAGAATCGACCCTAATAGCGGCTC TACTAAGTATAACGAGAAGTTTAAGAATAGGTTCACTATTAGT AGGGATAACTCTAAGAACACCCTGTACCTGCAGATGAATAGC CTGAGAGCCGAGGACACCGCCGTCTACTACTGCGCTAGAGACT ATAGAAAGGGCCTGTACGCTATGGACTACTGGGGTCAAGGCA CTACCGTGACCGTGTCTTCAGCTAGCACTAAGGGCCCCGTCCGT GTTCCCCCTGGCACCTTGTAGCCGGAGCACTAGCGAATCCACC GCTGCCCTCGGCTGCCTGGTCAAGGATTACTTCCCGGAGCCCG TGACCGTGTCTGGAACAGCGGAGCCCTGACCTCCGGAGTGCA CACCTTCCCCGCTGTGCTGCAGAGCTCCGGGCTGTACTCGCTG TCGTCCGTGGTCACGGTGCCTTCATCTAGCCTGGGTACCAAGA CCTACACTTGAACGTGGACCACAAGCCTTCCAACACTAAGGT GGACAAGCGCGTCGAATCGAAGTACGGCCACCGTGCCCCGCC TTGTCCCGCGCCGGAGTTCCTCGGCGGTCCCTCGGTCTTTCTGT TCCCACCGAAGCCCAAGGACACTTGTATGATTTCCCGCACCCC TGAAGTGACATGCGTGGTTCGTGGACGTGTACAGGAAGATCC GGAGGTGCAGTTCAATTGGTACGTGGATGGCGTCGAGGTGCA CAACGCCAAAACCAAGCCGAGGGAGGAGCAGTTCAACTCCAC TTACCGCGTCTGTGTCGTGCTGACGGTGTGCATCAGGACTGG CTGAACGGGAAGGAGTACAAGTGCAAGTGTCCAACAAGGGA CTTCCTAGCTCAATCGAAAAGACCATCTCGAAAGCCAAGGGA CAGCCCCGGGAACCCCAAGTGTATACCCTGCCACCGAGCCAG GAAGAAATGACTAAGAACCAAGTCTCATTGACTTGCCTTGTGA AGGGCTTCTACCCATCGGATATCGCCGTGGAATGGGAGTCCAA CGGCCAGCCGGAACAACTACAAGACCACCCCTCCGGTGTGCT GGACTCAGACGGATCCTTCTTCTCTACTCGCGGCTGACCGTG GATAAGAGCAGATGGCAGGAGGGAAATGTGTTCAGCTGTTCT GTGATGCATGAAGCCCTGCACAACCACTACACTCAGAAAGTCCC TGTCCTCTCCCTGGGA
BAP058-Clone O LC		
SEQ ID NO: 609 (Kabat)	LCDR1	KASQDVGTAVA
SEQ ID NO: 610 (Kabat)	LCDR2	WASTRHT
SEQ ID NO: 611(Kabat)	LCDR3	QQYNSYPLT
SEQ ID NO: 612 (Chothia)	LCDR1	SQDVGT
SEQ ID NO: 613 (Chothia)	LCDR2	WAS
SEQ ID NO: 614 (Chothia)	LCDR3	YNSYPL
SEQ ID NO: 616	VL	AIQLTQSPSSLSASVGDRTITCKASQDVGTAVAWYLQKPGQSPQ LLIYWASTRHTGVPSTRFSGSGSGTDFTFTISSLEAEDAATYYCQQY NSYPLTFGQGTKVEIK
SEQ ID NO: 617	DNA VL	GCTATTAGCTGACTCAGTCACCTAGTAGCCTGAGCGCTAGTG TGGCGATAGAGTGACTATCACCTGTAAAGCCTCTCAGGACGT GGGCACCGCCGTGGCCTGGTATCTGCAGAAGCCTGGTCAATCA CCTCAGCTGCTGATCTACTGGGCCTCTACTAGACACACCGGCG TGCCCTCTAGGTTTAGCGGTAGCGGTAGTGGCACCAGCTTAC CTTCACTATCTTCTCACTGGAAGCCGAGGACGCCGCTACCTAC TACTGTCAGCAGTATAATAGCTACCCCTGACCTTCGGTCAAG GCACTAAGGTCGAGATTAAG
SEQ ID NO: 618	Light chain	AIQLTQSPSSLSASVGDRTITCKASQDVGTAVAWYLQKPGQSPQ LLIYWASTRHTGVPSTRFSGSGSGTDFTFTISSLEAEDAATYYCQQY NSYPLTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVCLLN NFYPREAKVQWKVDNALQSGNSQESVTEQDSKSTYSLSTLT SKADYEKHKVYACEVTHQGLSPVTKSFNRGEC

SEQ ID NO: 619	DNA light chain	GCTATTTCAGCTGACTCAGTCACCTAGTAGCCTGAGCGCTAGTG TGGGCGATAGAGTGACTATCACCTGTAAAGCCTCTCAGGACGT GGGCACCGCCGTGGCCTGGTATCTGCAGAAGCCTGGTCAATCA CCTCAGCTGCTGATCTACTGGGCCTCTACTAGACACACCGGCG TGCCCTCTAGGTTTAGCGGTAGCGGTAGTGGCACCGACTTCAC CTTCACTATCTCTTCACTGGAAGCCGAGGACGCCGCTACCTAC TACTGTCAGCAGTATAATAGCTACCCCTGACCTTCGGTCAAG GCACTAAGGTCGAGATTAAGCGTACGGTGGCCGCTCCAGCGT GTTTCATCTTCCCCCCCAGCGACGAGCAGCTGAAGAGCGGCACC GCCAGCGTGGTGTGCCTGCTGAACAACCTTACCCCCGGGAGG CCAAGGTGCAGTGAAGGTGGACAACGCCCTGCAGAGCGGCA ACAGCCAGGAGAGCGTCACCGAGCAGGACAGCAAGGACTCCA CCTACAGCCTGAGCAGCACCTGACCCTGAGCAAGGCCGACT ACGAGAAGCATAAGGTGTACGCCTGCGAGGTGACCCACCAGG GCCTGTCCAGCCCCGTGACCAAGAGCTTCAACAGGGGCGAGT GC
BAP058-Clone N HC		
SEQ ID NO: 601 (Kabat)	HCDR1	SYWMY
SEQ ID NO: 602 (Kabat)	HCDR2	RIDPNSGSTKYNEKFN
SEQ ID NO: 603 (Kabat)	HCDR3	DYRKGLYAMDY
SEQ ID NO: 604 (Chothia)	HCDR1	GYTFTSY
SEQ ID NO: 605 (Chothia)	HCDR2	DPNSGS
SEQ ID NO: 603 (Chothia)	HCDR3	DYRKGLYAMDY
SEQ ID NO: 620	VH	EVQLVQSGAEVKKPGATVKISCKVSGYTFTSYWMYWVRQATGQ GLEWMGRIDPNSGSTKYNEKFNKRVTTITADKSTSTAYMELSSLRS EDTAVYYCARDYRKGLYAMDYWGQGTITVTVSS
SEQ ID NO: 621	DNA VH	GAAGTGCAGCTGGTGCAGTCAGGCGCCGAAGTGAAGAAACCC GGCGTACCGTGAAGATTAGCTGTAAAGTCTCAGGCTACACCT TCACTAGCTACTGGATGTACTGGGTCCGACAGGCTACCGGTCA AGGCCTGGAGTGGATGGGTAGAATCGACCCTAATAGCGGCTC TACTAAGTATAACGAGAAGTTTAAGAATAGAGTGACTATCACC GCCGATAAGTCTACTAGCACCGCCTATATGGAAGTGTCTAGCC TGAGATCAGAGGACACCGCCGTCTACTACTGCGCTAGAGACTA TAGAAAGGGCCTGTACGCTATGGACTACTGGGGTCAAGGCAC TACCGTGACCGTGTCTTCA
SEQ ID NO: 622	Heavy chain	EVQLVQSGAEVKKPGATVKISCKVSGYTFTSYWMYWVRQATGQ GLEWMGRIDPNSGSTKYNEKFNKRVTTITADKSTSTAYMELSSLRS EDTAVYYCARDYRKGLYAMDYWGQGTITVTVSSASTKGPSVFPL APCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAV LQSSGLYSLSSVTVPSSSLGKTYTCNVDPKPSNTKVDKRVESK YGPCCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVS QEDPEVFQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKGLPSSIEKTIKAKGQPREPQVYTLPPSQ EEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLD SDGSFFLYSRLTVDKSRWQEGNVFSCSVMEALHNHYTQKLSLSL SLG
SEQ ID NO: 623	DNA heavy chain	GAAGTGCAGCTGGTGCAGTCAGGCGCCGAAGTGAAGAAACCC GGCGTACCGTGAAGATTAGCTGTAAAGTCTCAGGCTACACCT TCACTAGCTACTGGATGTACTGGGTCCGACAGGCTACCGGTCA AGGCCTGGAGTGGATGGGTAGAATCGACCCTAATAGCGGCTC TACTAAGTATAACGAGAAGTTTAAGAATAGAGTGACTATCACC GCCGATAAGTCTACTAGCACCGCCTATATGGAAGTGTCTAGCC TGAGATCAGAGGACACCGCCGTCTACTACTGCGCTAGAGACTA TAGAAAGGGCCTGTACGCTATGGACTACTGGGGTCAAGGCAC TACCGTGACCGTGTCTTCACTAGCTAGCTAAGGGCCCGTCCGTG

		TTCCCCCTGGCACCTTGTAGCCGGAGCACTAGCGAATCCACCG CTGCCCTCGGCTGCCTGGTCAAGGATTACTTCCCGGAGCCCGT GACCGTGTCTTGGAAACAGCGGAGCCCTGACCTCCGGAGTGCA CACCTTCCCCGCTGTGCTGCAGAGCTCCGGGCTGTACTCGCTG TCGTGGTGGTACGGTGCCTTCATCTAGCCTGGGTACCAAGA CCTACACTTGCAACGTGGACCACAAGCCTTCCAACACTAAGGT GGACAAGCGCGTCAATCGAAGTACGGCCACCGTGCCCGCC TTGTCCCGCGCCGGAGTTCCTCGGCGGTCCCTCGGTCTTTCTGT TCCCACCGAAGCCCAAGGACACTTTGATGATTTCCCGCACCCC TGAAGTGACATGCGTGGTGGTGGACGTGTCACAGGAAGATCC GGAGGTGCAGTTCAATTGGTACGTGGATGGCGTCGAGGTGCA CAACGCCAAAACCAAGCCGAGGGAGGAGCAGTTCAACTCCAC TTACCGCGTCGTGTCCGTGCTGACGGTGTGTCATCAGGACTGG CTGAACGGGAAGGAGTACAAGTGCAAAGTGTCCAACAAGGGA CTTCTAGCTCAATCGAAAAGACCATCTCGAAAGCCAAGGGA CAGCCCCGGGAACCCCAAGTGTATACCCTGCCACCGAGCCAG GAAGAAATGACTAAGAACCAAGTCTCATTGACTTGCCTTGTGA AGGGCTTCTACCCATCGGATATCGCCGTGGAATGGGAGTCCAA CGGCCAGCCGGAACCAACTACAAGACCACCCCTCCGGTGTCT GGACTCAGACGGATCCTTCTTCTCTACTCGCGGCTGACCGTG GATAAGAGCAGATGGCAGGAGGGAAATGTGTTCACTGTTCT GTGATGCATGAAGCCCTGCACAACCACTACACTCAGAAGTCCC TGTCCTCTCCCTGGGA
BAP058-Clone N LC		
SEQ ID NO: 609 (Kabat)	LCDR1	KASQDVGTAVA
SEQ ID NO: 610 (Kabat)	LCDR2	WASTRHT
SEQ ID NO: 611(Kabat)	LCDR3	QQYNSYPLT
SEQ ID NO: 612 (Chothia)	LCDR1	SQDVGT
SEQ ID NO: 613 (Chothia)	LCDR2	WAS
SEQ ID NO: 614 (Chothia)	LCDR3	YNSYPL
SEQ ID NO: 624	VL	DVVMTQSPLSLPVTLGQPASISCKASQDVGTAVAWYQQKPGQAP RLLIYWASTRHTGVPSRFSGSGSGTEFTLTISLQPDFFATYYCQQ YNSYPLTFGQGTKVEIK
SEQ ID NO: 625	DNA VL	GACGTCGTGATGACTCAGTCACCCCTGAGCCTGCCCCGTGACCC TGGGGCAGCCCGCCTCTATTAGCTGTAAAGCCTCTCAGGACGT GGGCACCGCCGTGGCCTGGTATCAGCAGAAGCCAGGGCAAGC CCCTAGACTGCTGATCTACTGGGCCTCTACTAGACACACCCGGC GTGCCCTCTAGGTTTAGCGGTAGCGGTAGTGGCACCGAGTTCA CCCTGACTATCTTCACTGCAGCCCGACGACTTCGCTACCTAC TACTGTCAGCAGTATAATAGCTACCCCTGACCTTCGGTCAAG GCACTAAGGTCGAGATTAAG
SEQ ID NO: 626	Light chain	DVVMTQSPLSLPVTLGQPASISCKASQDVGTAVAWYQQKPGQAP RLLIYWASTRHTGVPSRFSGSGSGTEFTLTISLQPDFFATYYCQQ YNSYPLTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLL NNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSYLSSTLT LSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 627	DNA light chain	GACGTCGTGATGACTCAGTCACCCCTGAGCCTGCCCCGTGACCC TGGGGCAGCCCGCCTCTATTAGCTGTAAAGCCTCTCAGGACGT GGGCACCGCCGTGGCCTGGTATCAGCAGAAGCCAGGGCAAGC CCCTAGACTGCTGATCTACTGGGCCTCTACTAGACACACCCGGC GTGCCCTCTAGGTTTAGCGGTAGCGGTAGTGGCACCGAGTTCA CCCTGACTATCTTCACTGCAGCCCGACGACTTCGCTACCTAC TACTGTCAGCAGTATAATAGCTACCCCTGACCTTCGGTCAAG GCACTAAGGTCGAGATTAAGCGTACGGTGGCCGCTCCAGCGT GTTCACTTCCCCCCCAGCGACGAGCAGCTGAAGAGCGGCACC

		GCCAGCGTGGTGTGCTGCTGAACAACCTTCTACCCCCGGGAGG CCAAGGTGCAGTGGAAGGTGGACAACGCCCTGCAGAGCGGCA ACAGCCAGGAGAGCGTCACCGAGCAGGACAGCAAGGACTCCA CCTACAGCCTGAGCAGCACCTGACCCTGAGCAAGGCCGACT ACGAGAAGCATAAGGTGTACGCCTGCGAGGTGACCCACCAGG GCCTGTCCAGCCCCGTGACCAAGAGCTTCAACAGGGGCGAGT GC
BAP058-Clone O HC		
SEQ ID NO: 628 (Kabat)	HCDR1	agctactggatgtac
SEQ ID NO: 629 (Kabat)	HCDR2	agaatcgaccctaataagcggctctactaagtataacgagaagttaagaat
SEQ ID NO: 630 (Kabat)	HCDR3	gactatagaaaggcctgtacgctatggactac
SEQ ID NO: 631 (Chothia)	HCDR1	ggctacaccttcactagctac
SEQ ID NO: 632 (Chothia)	HCDR2	gaccctaataagcggctct
SEQ ID NO: 630 (Chothia)	HCDR3	gactatagaaaggcctgtacgctatggactac
BAP058-Clone O LC		
SEQ ID NO: 633 (Kabat)	LCDR1	aaagcctctcaggacgtgggcaccgccgtggcc
SEQ ID NO: 634 (Kabat)	LCDR2	tgggcctctactagacacacc
SEQ ID NO: 635 (Kabat)	LCDR3	cagcagtataatagctacccctgacc
SEQ ID NO: 636 (Chothia)	LCDR1	tctcaggacgtgggcaccgcc
SEQ ID NO: 637 (Chothia)	LCDR2	tgggcctct
SEQ ID NO: 638 (Chothia)	LCDR3	tataatagctacccctg
BAP058-Clone N HC		
SEQ ID NO: 628 (Kabat)	HCDR1	agctactggatgtac
SEQ ID NO: 629 (Kabat)	HCDR2	agaatcgaccctaataagcggctctactaagtataacgagaagttaagaat
SEQ ID NO: 630 (Kabat)	HCDR3	gactatagaaaggcctgtacgctatggactac
SEQ ID NO: 631 (Chothia)	HCDR1	ggctacaccttcactagctac
SEQ ID NO: 632 (Chothia)	HCDR2	gaccctaataagcggctct
SEQ ID NO: 630 (Chothia)	HCDR3	gactatagaaaggcctgtacgctatggactac
BAP058-Clone N LC		
SEQ ID NO: 633 (Kabat)	LCDR1	aaagcctctcaggacgtgggcaccgccgtggcc
SEQ ID NO: 634 (Kabat)	LCDR2	tgggcctctactagacacacc
SEQ ID NO: 635 (Kabat)	LCDR3	cagcagtataatagctacccctgacc
SEQ ID NO: 636 (Chothia)	LCDR1	tctcaggacgtgggcaccgcc
SEQ ID NO: 637 (Chothia)	LCDR2	tgggcctct
SEQ ID NO: 638 (Chothia)	LCDR3	tataatagctacccctg

Other Exemplary PD-L1 Inhibitors

[0479] In one embodiment, the anti-PD-L1 antibody molecule is Atezolizumab (Genentech/Roche), also known as MPDL3280A, RG7446, RO5541267, YW243.55.S70, or TECENTRIQ™. Atezolizumab and other anti-PD-L1 antibodies are disclosed in US 8,217,149, incorporated by reference in its entirety. In one embodiment, the anti-PD-L1 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of Atezolizumab, *e.g.*, as disclosed in Table 6.

[0480] In one embodiment, the anti-PD-L1 antibody molecule is Avelumab (Merck Serono and Pfizer), also known as MSB0010718C or Bavencio®. Avelumab and other anti-PD-L1 antibodies are disclosed in WO 2013/079174, incorporated by reference in its entirety. In one embodiment, the anti-PD-L1 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of Avelumab, *e.g.*, as disclosed in Table 6.

[0481] In one embodiment, the anti-PD-L1 antibody molecule is Durvalumab (MedImmune/AstraZeneca), also known as MEDI4736 or Imfinzi®. Durvalumab and other anti-PD-L1 antibodies are disclosed in US 8,779,108, incorporated by reference in its entirety. In one embodiment, the anti-PD-L1 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of Durvalumab, *e.g.*, as disclosed in Table 6.

[0482] In one embodiment, the anti-PD-L1 antibody molecule is BMS-936559 (Bristol-Myers Squibb), also known as MDX-1105 or 12A4. BMS-936559 and other anti-PD-L1 antibodies are disclosed in US 7,943,743 and WO 2015/081158, incorporated by reference in their entirety. In one embodiment, the anti-PD-L1 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of BMS-936559, *e.g.*, as disclosed in Table 6.

[0483] Further known anti-PD-L1 antibodies include those described, *e.g.*, in WO 2015/181342, WO 2014/100079, WO 2016/000619, WO 2014/022758, WO 2014/055897, WO 2015/061668, WO 2013/079174, WO 2012/145493, WO 2015/112805, WO 2015/109124, WO 2015/195163, US 8,168,179, US 8,552,154, US 8,460,927, and US 9,175,082, incorporated by reference in their entirety.

[0484] In one embodiment, the anti-PD-L1 antibody is an antibody that competes for binding with, and/or binds to the same epitope on PD-L1 as, one of the anti-PD-L1 antibodies described herein.

Table 6. Amino acid sequences of other exemplary anti-PD-L1 antibody molecules

Atezolizumab		
SEQ ID NO: 639	Heavy chain	EVQLVESGGGLVQPGGSLRLSCAASGFTFSDSWIHVVRQAPGKGLEWVAWI SPYGGSTYYADSVKGRFTISADTSKNTAYLQMNSLRAEDTAVYYCARRHWP GGFDYWGGQGLTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEP VTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGTQTYICNVNHKP SNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVT CVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYASTYRVVSVLTVLH QDWLNGKEYKCKVSNKALPAPIEKISKAKGQPREPQVYTLPPSREEMTKNQ VSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKS RWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 640	Light chain	DIQMTQSPSSLSASVGDRTITCRASQDVSTAVAWYQQKPGKAPKLLIYSASF LYSGVPSRFSGSGSGTDFTLTISLQPEDFATYYCQQLYHPATFGQGTKVEIK RTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGNS QESVTEQDSKDYSLSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNR GEC
Avelumab		
SEQ ID NO: 641	Heavy chain	EVQLLESGGGLVQPGGSLRLSCAASGFTFSSYIMMWVRQAPGKGLEWVSSII PSGGITFYADTVKGRFTISRDNSKNTLYLQMNSLRAEDTAVYYCARIKLGT TTVDYWGGQGLTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEP VTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGTQTYICNVNHKP SNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVT CVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLH QDWLNGKEYKCKVSNKALPAPIEKISKAKGQPREPQVYTLPPSRDELTKNQ VSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKS RWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 642	Light chain	QSALTQPASVSGSPGQSITISCTGTSSDVGGYNYVSWYQQHPGKAPKLMYD VSNRPSGVSNRFSGSKSGNTASLTISGLQAEDADYYCYYTSSSTRVFGTGT KVTVLGQPKANPTVTLFPPSSEELQANKATLVCLISDFYPGAVTVAWKADGS PVKAGVETTKPSKQSNNKYAASSYLSLTPEQWKSHRSYSCQVTHEGSTVEKT VAPTECS
Durvalumab		
SEQ ID NO: 643	Heavy chain	EVQLVESGGGLVQPGGSLRLSCAASGFTFSRYWMSWVRQAPGKGLEWVANI KQDGSEKYYVDSVKGRFTISRDNAKNSLYLQMNSLRAEDTAVYYCAREGG WFGELAFDYWGQGLTVTVSSASTKGPSVFPLAPSSKSTSGGTAALGCLVKDY FPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGTQTYICNV NHKPSNTKVDKRVKPKSCDKTHTCPPCPAPEFEGGPSVFLFPPKPKDTLMISR TPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSV LTVLHQDWLNGKEYKCKVSNKALPASIEKISKAKGQPREPQVYTLPPSREE MTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSK LTVDKSRWQQGNVFSCSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 644	Light chain	EIVLTQSPGTLSPGERATLSCRASQRVSSSYLAWYQQKPGQAPRLIYDAS SRATGIPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQYGLPWTFGQGTKVEI KRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQSGN

		SQESVTEQDSKDSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNR GEC
BMS-936559		
SEQ ID NO: 645	VH	QVQLVQSGAEVKKPGSSVKVCKTSGDTFTSTYAIWVVRQAPGQGLEWMGGII PIFGKAHYAQKFQGRVTITADESTSTAYMELSSLRSEDTAVYFCARKFHFVSG SPFGMDVWGQGTTVTVSS
SEQ ID NO: 646	VL	EIVLTQSPATLSLSPGERATLSCRASQSVSSYLAWYQQKPGQAPRLLIYDASN RATGIPARFSGSGSGTDFTLTISLSEPEDFAVYYCQQRSNWPTFGQGTKVEIK

[0485] In one embodiment the anti-human ENTPD2 antibody as described herein is administered in combination with at least one PD-L1 inhibitor as described herein and at least one A2A receptor antagonist as described herein.

LAG-3 Inhibitors

[0486] In certain embodiments, the anti-human ENTPD2 antibody described herein is administered in combination with a LAG-3 inhibitor. The LAG-3 inhibitor may be an antibody, an antigen-binding fragment thereof, an immunoadhesin, a fusion protein, or oligopeptide. In some embodiments, the LAG-3 inhibitor is chosen from LAG525 (Novartis), BMS-986016 (Bristol-Myers Squibb), TSR-033 (Tesar), MK-4280 (Merck & Co), or REGN3767 (Regeneron).

Exemplary LAG-3 Inhibitors

[0487] In one embodiment, the LAG-3 inhibitor is an anti-LAG-3 antibody molecule. In one embodiment, the LAG-3 inhibitor is an anti-LAG-3 antibody molecule as disclosed in US 2015/0259420, published on September 17, 2015, entitled “Antibody Molecules to LAG-3 and Uses Thereof,” incorporated by reference in its entirety.

[0488] In one embodiment, the anti-LAG-3 antibody molecule comprises at least one, two, three, four, five or six complementarity determining regions (CDRs) (or collectively all of the CDRs) from a heavy and light chain variable region comprising an amino acid sequence shown in Table 7 (*e.g.*, from the heavy and light chain variable region sequences of BAP050-Clone I or BAP050-Clone J disclosed in Table 7), or encoded by a nucleotide sequence shown in Table 7. In some embodiments, the CDRs are according to the Kabat definition (*e.g.*, as set out in Table 7). In some embodiments, the CDRs are according to the Chothia definition (*e.g.*, as set out in Table 7). In some embodiments, the CDRs are according to the combined CDR definitions of both Kabat and Chothia (*e.g.*, as set out in Table 7). In one embodiment, the combination of Kabat and Chothia CDR of VH CDR1

comprises the amino acid sequence GFTLTNYGMN (SEQ ID NO: 766). In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions (*e.g.*, conservative amino acid substitutions) or deletions, relative to an amino acid sequence shown in Table 7, or encoded by a nucleotide sequence shown in Table 7.

[0489] In one embodiment, the anti-LAG-3 antibody molecule comprises a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence of SEQ ID NO: 701, a VHCDR2 amino acid sequence of SEQ ID NO: 702, and a VHCDR3 amino acid sequence of SEQ ID NO: 703; and a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO: 710, a VLCDR2 amino acid sequence of SEQ ID NO: 711, and a VLCDR3 amino acid sequence of SEQ ID NO: 712, each disclosed in Table 7.

[0490] In one embodiment, the anti-LAG-3 antibody molecule comprises a VH comprising a VHCDR1 encoded by the nucleotide sequence of SEQ ID NO: 736 or 737, a VHCDR2 encoded by the nucleotide sequence of SEQ ID NO: 738 or 739, and a VHCDR3 encoded by the nucleotide sequence of SEQ ID NO: 740 or 741; and a VL comprising a VLCDR1 encoded by the nucleotide sequence of SEQ ID NO: 746 or 747, a VLCDR2 encoded by the nucleotide sequence of SEQ ID NO: 748 or 749, and a VLCDR3 encoded by the nucleotide sequence of SEQ ID NO: 750 or 751, each disclosed in Table 7. In one embodiment, the anti-LAG-3 antibody molecule comprises a VH comprising a VHCDR1 encoded by the nucleotide sequence of SEQ ID NO: 758 or 737, a VHCDR2 encoded by the nucleotide sequence of SEQ ID NO: 759 or 739, and a VHCDR3 encoded by the nucleotide sequence of SEQ ID NO: 760 or 741; and a VL comprising a VLCDR1 encoded by the nucleotide sequence of SEQ ID NO: 746 or 747, a VLCDR2 encoded by the nucleotide sequence of SEQ ID NO: 748 or 749, and a VLCDR3 encoded by the nucleotide sequence of SEQ ID NO: 750 or 751, each disclosed in Table 7.

[0491] In one embodiment, the anti-LAG-3 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 706, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 706. In one embodiment, the anti-LAG-3 antibody molecule comprises a VL comprising the amino acid sequence of SEQ ID NO: 718, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 718. In one embodiment, the anti-LAG-3 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 724, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 724. In one embodiment, the anti-LAG-3 antibody molecule comprises a VL comprising the amino acid sequence of SEQ

ID NO: 730, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 730. In one embodiment, the anti-LAG-3 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 706 and a VL comprising the amino acid sequence of SEQ ID NO: 718. In one embodiment, the anti-LAG-3 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 724 and a VL comprising the amino acid sequence of SEQ ID NO: 730.

[0492] In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 707 or 708, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 707 or 708. In one embodiment, the antibody molecule comprises a VL encoded by the nucleotide sequence of SEQ ID NO: 719 or 720, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 719 or 720. In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 725 or 726, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 725 or 726. In one embodiment, the antibody molecule comprises a VL encoded by the nucleotide sequence of SEQ ID NO: 731 or 732, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 731 or 732. In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 707 or 708 and a VL encoded by the nucleotide sequence of SEQ ID NO: 719 or 720. In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 725 or 726 and a VL encoded by the nucleotide sequence of SEQ ID NO: 731 or 732.

[0493] In one embodiment, the anti-LAG-3 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 709, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 709. In one embodiment, the anti-LAG-3 antibody molecule comprises a light chain comprising the amino acid sequence of SEQ ID NO: 721, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 721. In one embodiment, the anti-LAG-3 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 727, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 727. In one embodiment, the anti-LAG-3 antibody molecule comprises a light chain comprising the amino acid sequence of SEQ ID NO: 733, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 733. In one embodiment, the anti-LAG-3 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 709 and a light chain comprising the amino acid sequence of SEQ ID NO:

721. In one embodiment, the anti-LAG-3 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 727 and a light chain comprising the amino acid sequence of SEQ ID NO: 733.

[0494] In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 716 or 717, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 716 or 717. In one embodiment, the antibody molecule comprises a light chain encoded by the nucleotide sequence of SEQ ID NO: 722 or 723, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 722 or 723. In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 728 or 729, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 728 or 729. In one embodiment, the antibody molecule comprises a light chain encoded by the nucleotide sequence of SEQ ID NO: 734 or 735, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 734 or 735. In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 716 or 717 and a light chain encoded by the nucleotide sequence of SEQ ID NO: 722 or 723. In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 728 or 729 and a light chain encoded by the nucleotide sequence of SEQ ID NO: 734 or 735.

[0495] The antibody molecules described herein can be made by vectors, host cells, and methods described in US 2015/0259420, incorporated by reference in its entirety.

Table 7. Amino acid and nucleotide sequences of exemplary anti-LAG-3 antibody molecules

BAP050-Clone I HC		
SEQ ID NO: 701 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 702 (Kabat)	HCDR2	WINTDTGEPTYADDFKG
SEQ ID NO: 703 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 704 (Chothia)	HCDR1	GFTLTNY
SEQ ID NO: 705 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 703 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 706	VH	QVQLVQSGAEVKKPGASVKVSCKASGFTLTNYGMNWVRQARGQ RLEWIGWINTDTGEPTYADDFKGRFVFSLDTSVSTAYLQISSLKAE DTAVYYCARNPPYYYGTNNAEAMDYWGQGTTVTVSS

SEQ ID NO: 707	DNA VH	CAAGTGCAGCTGGTGCAGTCGGGAGCCGAAGTGAAGAAGCCTG GAGCCTCGGTGAAGGTGTCGTGCAAGGCATCCGGATTACCCCT CACCAATTACGGGATGAACTGGGTGAGACAGGCCCGGGGTCAA CGGCTGGAGTGGATCGGATGGATTAACACCGACACCGGGGAGC CTACCTACGCGGACGATTTCAGGGACGGTTCGTGTTCTCCCTC GACACCTCCGTGTCCACCGCTACCTCCAAATCTCCTCACTGAA AGCGGAGGACACCGCCGTGTACTATTGCGCGAGGAACCCGCCC TACTACTACGGAACCAACAACGCCGAAGCCATGGACTACTGGG GCCAGGGCACCCTGTGACTGTGTCCAGC
SEQ ID NO: 708	DNA VH	CAGGTGCAGCTGGTGCAGTCTGGCGCCGAAGTGAAGAAACCTG GCGCCTCCGTGAAGGTGTCCTGCAAGGCCTCTGGCTTACCCCTG ACCAACTACGGCATGAACTGGGTGCGACAGGCCAGGGGCCAGC GGCTGGAATGGATCGGCTGGATCAACACCGACACCGGCGAGCC TACCTACGCCGACGACTTCAAGGGCAGATTCTGTGTTCTCCCTGG ACACCTCCGTGTCCACCGCTACCTGCAGATCTCCAGCCTGAAG GCCGAGGATACCGCCGTGTACTACTGCGCCCGGAACCCCCCTT ACTACTACGGCACCAACAACGCCGAGGCCATGGACTATTGGGG CCAGGGCACCACCGTGACCGTGTCTCT
SEQ ID NO: 709	Heavy chain	QVQLVQSGAEVKKPGASVKVSCKASGFTLTNYGMNWVRQARGQ RLEWIGWINTDTGEPTYADDFKGRFVFSLDTSVSTAYLQISSLKA DTAVYYCARNPPYYYGTNNAEAMDYWGQTTVTVSSASTKGPS VFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTF PAVLQSSGLYSLSSVTVPSSSLGKTYTCNVDHKPSNTKVDKRV ESKYGPPCPPPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVL HQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTLPPS QEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLD SDGSFFLYSRLTVDKSRWQEGNVFSCSVMHREALHNHYTQKSLSL LG
SEQ ID NO: 716	DNA heavy chain	CAAGTGCAGCTGGTGCAGTCGGGAGCCGAAGTGAAGAAGCCTG GAGCCTCGGTGAAGGTGTCGTGCAAGGCATCCGGATTACCCCT CACCAATTACGGGATGAACTGGGTGAGACAGGCCCGGGGTCAA CGGCTGGAGTGGATCGGATGGATTAACACCGACACCGGGGAGC CTACCTACGCGGACGATTTCAGGGACGGTTCGTGTTCTCCCTC GACACCTCCGTGTCCACCGCTACCTCCAAATCTCCTCACTGAA AGCGGAGGACACCGCCGTGTACTATTGCGCGAGGAACCCGCCC TACTACTACGGAACCAACAACGCCGAAGCCATGGACTACTGGG GCCAGGGCACCCTGTGACTGTGTCCAGCGCTCCACTAAGGG CCCGTCCGTGTTCCCCCTGGCACCTTGTAGCCGGAGCACTAGCG AATCCACCGCTGCCCTCGGCTGCCTGGTCAAGGATTACTTCCCG GAGCCCGTGACCGTGTCTGGAACAGCGGAGCCCTGACCTCCG GAGTGCACACCTTCCCCGCTGTGCTGCAGAGCTCCGGGCTGTAC TCGCTGTCGTGCGGTGGTCACGGTGCCTTCATCTAGCCTGGGTAC CAAGACCTACACTTGCAACGTGGACCACAAGCCTTCCAACACT AAGGTGGACAAGCGCGTCGAATCGAAGTACGGCCCAACCGTGCC CGCCTTGTCCCGCGCCGGAGTTCCTCGGCGGTCCCTCGGTCTTT CTGTTCCACCGAAGCCCAAGGACACTTTGATGATTTCCCGCAC CCCTGAAGTGACATGCGTGGTCTGTTGACGTGTACAGGAAGAT CCGGAGGTGCAGTTCAATTGGTACGTGGATGGCGTCGAGGTGC ACAACGCCAAAACCAAGCCGAGGGAGGAGCAGTTCAACTCCAC TTACCGCGTCGTGTCCGTGCTGACGGTGTGTCATCAGGACTGGC TGAACGGGAAGGAGTACAAGTGCAAAGTGTCCAACAAGGGAC

		TTCCTAGCTCAATCGAAAAGACCATCTCGAAAGCCAAGGGACA GCCCCGGGAACCCCAAGTGTATACCCTGCCACCGAGCCAGGAA GAAATGACTAAGAACCAAGTCTCATTGACTTGCCTTGTGAAGG GCTTCTACCCATCGGATATCGCCGTGGAATGGGAGTCCAACGG CCAGCCGGAAAAACAATAAGACCAACCCCTCCGGTGTGGAC TCAGACGGATCCTTCTTCTCTACTCGCGGTGACCGTGGATAA GAGCAGATGGCAGGAGGGAAATGTGTTTCAGCTGTTCTGTGATG CATGAAGCCCTGCACAACCACTACACTCAGAAGTCCCTGTCCCT CTCCCTGGGA
SEQ ID NO: 717	DNA heavy chain	CAGGTGCAGCTGGTGCAGTCTGGCGCCGAAGTGAAGAAACCTG GCGCCTCCGTGAAGGTGTCTGCAAGGCCTCTGGCTTACCCCTG ACCAACTACGGCATGAAGTGGGTGCGACAGGCCAGGGGCCAGC GGCTGGAATGGATCGGCTGGATCAACACCGACACCGGCGAGCC TACCTACGCCGACGACTTCAAGGGCAGATTCTGTGTTCTCCCTGG ACACCTCCGTGTCCACCGCCTACCTGCAGATCTCCAGCCTGAAG GCCGAGGATACCGCCGTGTACTACTGCGCCCGGAACCCCCCTT ACTACTACGGCACCAACAACGCCGAGGCCATGGACTATTGGGG CCAGGGCACCACCGTGACCGTGTCTCTGCTTCTACCAAGGGGC CCAGCGTGTTCCTCCCTGGCCCCCTGCTCCAGAAGCACCAGCGA GAGCACAGCCGCCCTGGGCTGCCTGGTGAAGGACTACTTCCCC GAGCCCGTGACCGTGTCTGGAACAGCGGAGCCCTGACCAGCG GCGTGACACCTTCCCCGCCGTGCTGCAGAGCAGCGGCCGTGA CAGCCTGAGCAGCGTGGTGACCGTGCCAGCAGCAGCCTGGGC ACCAAGACCTACACCTGTAACGTGGACCACAAGCCCAGCAACA CCAAGGTGGACAAGAGGGTGGAGAGCAAGTACGGCCCCACCCT GCCCCCCTGCCCAGCCCCGAGTTCCTGGGCGGACCCAGCGT GTTCTGTTCCTCCCAAGCCCAAGGACACCCTGATGATCAGCA GAACCCCCGAGGTGACCTGTGTGGTGGTGGACGTGTCCCAGGA GGACCCCCGAGGTCCAGTTCAACTGGTACGTGGACGGCGTGGAG GTGACAACGCCAAGACCAAGCCCAGAGAGGAGCAGTTTAACA GCACCTACCGGGTGGTGTCCGTGCTGACCGTGTGACCCAGGA CTGGCTGAACGGCAAAGAGTACAAGTGTAAGGTCTCCAACAAG GGCCTGCCAAGCAGCATCGAAAAGACCATCAGCAAGGCCAAG GGCCAGCCTAGAGAGCCCCAGGTCTACACCTGCCACCCAGCC AAGAGGAGATGACCAAGAACCAGGTGTCCCTGACCTGTCTGGT GAAGGGCTTCTACCCAAGCGACATCGCCGTGGAGTGGGAGAGC AACGGCCAGCCGAGAACAATAAGACCAACCCCCCAGTGC TGGACAGCGACGGCAGCTTCTTCTGTACAGCAGGCTGACCGT GGACAAGTCCAGATGGCAGGAGGGCAACGTCTTTAGCTGCTCC GTGATGCACGAGGCCCTGCACAACCACTACACCCAGAAGAGCC TGAGCCTGTCCCTGGGC
BAP050-Clone I LC		
SEQ ID NO: 710 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 711 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 712 (Kabat)	LCDR3	QQYYNLPWT
SEQ ID NO: 713 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 714 (Chothia)	LCDR2	YTS
SEQ ID NO: 715 (Chothia)	LCDR3	YYNLPW

SEQ ID NO: 718	VL	DIQMTQSPSSLSASVGDRVTITCSSSQDISNYLNWYLQKPGQSPQL LIYYTSTLHLGVPSRFSGSGSGTEFTLTISSLQPDDEFATYYCQYYN LPWTFGQGTKVEIK
SEQ ID NO: 719	DNA VL	GATATTCAGATGACTCAGTCACCTAGTAGCCTGAGCGCTAGTGT GGGCGATAGAGTGACTATCACCTGTAGCTCTAGTCAGGATATCT CTAACTACCTGAACTGGTATCTGCAGAAGCCCGGTCAATCACCT CAGCTGCTGATCTACTACACTAGCACCTGCACCTGGGCGTGCC CTCTAGGTTTAGCGGTAGCGGTAGTGGCACCGAGTTCACCTGA CTATCTCTAGCCTGCAGCCCGACGACTTCGCTACCTACTACTGT CAGCAGTACTATAACCTGCCCTGGACCTTCGGTCAAGGCACTA AGGTCGAGATTAAG
SEQ ID NO: 720	DNA VL	GACATCCAGATGACCCAGTCCCCCTCCAGCCTGTCTGCTTCCGT GGGCGACAGAGTGACCATCACCTGTTCTCCAGCCAGGACATC TCCAACTACCTGAACTGGTATCTGCAGAAGCCCGGCCAGTCCCC TCAGCTGCTGATCTACTACACTCCACCCTGCACCTGGGCGTGCC CCTCCAGATTTTCCGGCTCTGGCTCTGGCACCGAGTTTACCCTG ACCATCAGCTCCCTGCAGCCCGACGACTTCGCCACCTACTACTG CCAGCAGTACTACAACCTGCCCTGGACCTTCGGCCAGGGCACC AAGGTGGAATCAAG
SEQ ID NO: 721	Light chain	DIQMTQSPSSLSASVGDRVTITCSSSQDISNYLNWYLQKPGQSPQL LIYYTSTLHLGVPSRFSGSGSGTEFTLTISSLQPDDEFATYYCQYYN LPWTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNF YPREAKVQWKVDNALQSGNSQESVTEQDSKSTYLSSTLTLSKA DYEKHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 722	DNA light chain	GATATTCAGATGACTCAGTCACCTAGTAGCCTGAGCGCTAGTGT GGGCGATAGAGTGACTATCACCTGTAGCTCTAGTCAGGATATCT CTAACTACCTGAACTGGTATCTGCAGAAGCCCGGTCAATCACCT CAGCTGCTGATCTACTACACTAGCACCTGCACCTGGGCGTGCC CTCTAGGTTTAGCGGTAGCGGTAGTGGCACCGAGTTCACCTGA CTATCTCTAGCCTGCAGCCCGACGACTTCGCTACCTACTACTGT CAGCAGTACTATAACCTGCCCTGGACCTTCGGTCAAGGCACTA AGGTCGAGATTAAGCGTACGGTGGCCGCTCCCAGCGTGTTTCAT CTTCCCCCCCAGCGACGAGCAGCTGAAGAGCGGCACCGCCAGC GTGGTGTGCCTGCTGAACAACCTTCTACCCCGGGAGGCCAAGG TGCAGTGGAAGGTGGACAACGCCCTGCAGAGCGGCAACAGCCA GGAGAGCGTCACCGAGCAGGACAGCAAGGACTCCACCTACAGC CTGAGCAGCACCTGACCCTGAGCAAGGCCGACTACGAGAAGC ATAAGGTGTACGCCTGCGAGGTGACCCACCAGGGCCTGTCCAG CCCCGTGACCAAGAGCTTCAACAGGGGCGAGTGC
SEQ ID NO: 723	DNA light chain	GACATCCAGATGACCCAGTCCCCCTCCAGCCTGTCTGCTTCCGT GGGCGACAGAGTGACCATCACCTGTTCTCCAGCCAGGACATC TCCAACTACCTGAACTGGTATCTGCAGAAGCCCGGCCAGTCCCC TCAGCTGCTGATCTACTACACTCCACCCTGCACCTGGGCGTGCC CCTCCAGATTTTCCGGCTCTGGCTCTGGCACCGAGTTTACCCTG ACCATCAGCTCCCTGCAGCCCGACGACTTCGCCACCTACTACTG CCAGCAGTACTACAACCTGCCCTGGACCTTCGGCCAGGGCACC AAGGTGGAATCAAGCGTACGGTGGCCGCTCCCAGCGTGTTCA TCTTCCCCCAAGCGACGAGCAGCTGAAGAGCGGCACCGCCAG CGTGGTGTGTCTGCTGAACAACCTTCTACCCAGGGAGGCCAAG GTGCAGTGGAAGGTGGACAACGCCCTGCAGAGCGGCAACAGCC AGGAGAGCGTCACCGAGCAGGACAGCAAGGACTCCACCTACA GCCTGAGCAGCACCTGACCCTGAGCAAGGCCGACTACGAGAA

		GCACAAGGTGTACGCCTGTGAGGTGACCCACCAGGGCCTGTCC AGCCCCGTGACCAAGAGCTTCAACAGGGGCGAGTGC
BAP050-Clone J HC		
SEQ ID NO: 701 (Kabat)	HCDR1	NYGMN
SEQ ID NO: 702 (Kabat)	HCDR2	WINTDTGEPTYADDFKG
SEQ ID NO: 703 (Kabat)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 704 (Chothia)	HCDR1	GFTLTNY
SEQ ID NO: 705 (Chothia)	HCDR2	NTDTGE
SEQ ID NO: 703 (Chothia)	HCDR3	NPPYYYGTNNAEAMDY
SEQ ID NO: 724	VH	QVQLVQSGAEVKKPGASVKVSCKASGFTLTNYGMNWVRQAPGQ GLEWMGWINTDTGEPTYADDFKGRFVFSLDTSVSTAYLQISSLKA EDTAVYYCARNPPYYYGTNNAEAMDYWGQGTITVTVSS
SEQ ID NO: 725	DNA VH	CAGGTGCAGCTGGTGCAGTCAGGCGCCGAAGTGAAGAAACCCG GCGCTAGTGTGAAAGTCAGCTGTAAAGCTAGTGGCTTACCCT GACTAACTACGGGATGAACTGGGTCCGCCAGGCCCCAGGTCAA GGCCTCGAGTGGATGGGCTGGATTAACACCGACACCGGCGAGC CTACCTACGCCGACGACTTTAAGGGCAGATTCTGTGTTAGCCTG GACACTAGTGTGTCTACCGCTACCTGCAGATCTCTAGCCTGAA GGCCGAGGACACCGCCGTCTACTACTGCGCTAGAAACCCCCC TACTACTACGGCACTAACAACGCCGAGGCTATGGACTACTGGG GTCAAGGCACTACCGTGACCGTGTCTAGC
SEQ ID NO: 726	DNA VH	CAGGTGCAGCTGGTGCAGTCAGGCGCCGAAGTGAAGAAACCTG GCGCTCCGTGAAGGTGTCCTGCAAGGCCTCTGGCTTACCCTG ACCAACTACGGCATGAACTGGGTGCGACAGGCCCCCTGGACAGG GCCTGGAATGGATGGGCTGGATCAACACCGACACCGGCGAGCC TACCTACGCCGACGACTTCAAGGGCAGATTCTGTGTTCTCCCTGG ACACCTCCGTGTCCACCGCCTACCTGCAGATCTCCAGCCTGAAG GCCGAGGATACCGCCGTGTACTACTGCGCCCGGAACCCCCCTT ACTACTACGGCACCAACAACGCCGAGGCCATGGACTATTGGGG CCAGGGCACCAACCGTGACCGTGTCTCT
SEQ ID NO: 727	Heavy chain	QVQLVQSGAEVKKPGASVKVSCKASGFTLTNYGMNWVRQAPGQ GLEWMGWINTDTGEPTYADDFKGRFVFSLDTSVSTAYLQISSLKA EDTAVYYCARNPPYYYGTNNAEAMDYWGQGTITVTVSSASTKGP SVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHT FPAVLQSSGLYSLSSVVTVPSSSLGKTYTCNVDPKPSNTKVDKRV ESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVVD VSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVVSVLTVL HQDWLNGKEYKCKVSNKGLPSSIEKTIKAKGQPREPQVYTLPPS QEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTPPVLD SDGSFFLYSRLTVDKSRWQEGNVFSCSVMEALHNHYTQKLSLS LG
SEQ ID NO: 728	DNA heavy chain	CAGGTGCAGCTGGTGCAGTCAGGCGCCGAAGTGAAGAAACCCG GCGCTAGTGTGAAAGTCAGCTGTAAAGCTAGTGGCTTACCCT GACTAACTACGGGATGAACTGGGTCCGCCAGGCCCCAGGTCAA GGCCTCGAGTGGATGGGCTGGATTAACACCGACACCGGCGAGC CTACCTACGCCGACGACTTTAAGGGCAGATTCTGTGTTAGCCTG GACACTAGTGTGTCTACCGCTACCTGCAGATCTCTAGCCTGAA GGCCGAGGACACCGCCGTCTACTACTGCGCTAGAAACCCCCC

		TACTACTACGGCACTAACAACGCCGAGGCTATGGACTACTGGG GTCAAGGCACTACCGTGACCGTGTCTAGCGCTAGCACTAAGGG CCCGTCCGTGTTCCCCCTGGCACCTTGTAGCCGGAGCACTAGCG AATCCACCGCTGCCCTCGGCTGCCTGGTCAAGGATTACTTCCCG GAGCCCGTGACCGTGTCTGGAACAGCGGAGCCCTGACCTCCG GAGTGCACACCTTCCCCGCTGTGCTGCAGAGCTCCGGGCTGTAC TCGCTGTCTGTCGGTGGTCACGGTGCCTTCATCTAGCCTGGGTAC CAAGACCTACACTTGCAACGTGGACCACAAGCCTTCCAACACT AAGGTGGACAAGCGCGTCGAATCGAAGTACGGCCCAACCGTGCC CGCCTTGTCCCGCGCCGGAGTTCTCGGCGGTCCCTCGGTCTTT CTGTTCCACCGAAGCCCAAGGACACTTTGATGATTTCCCGCAC CCCTGAAGTGACATGCGTGGTCTGTTGGACGTGTACAGGAAGAT CCGGAGGTGCAGTTCAATTGGTACGTGGATGGCGTCGAGGTGC ACAACGCCAAAACCAAGCCGAGGGAGGAGCAGTTCAACTCCAC TTACCGCGTCTGTGTCCTGTGCTGACGGTGTGTCATCAGGACTGGC TGAACGGGAAGGAGTACAAGTGCAAAGTGTCCAACAAGGGAC TTCCTAGCTCAATCGAAAAGACCATCTCGAAAGCCAAGGGACA GCCCCGGGAACCCCAAGTGTATACCCTGCCACCGAGCCAGGAA GAAATGACTAAGAACCAAGTCTCATTGACTTGCCTTGTGAAGG GCTTCTACCCATCGGATATCGCCGTGGAATGGGAGTCCAACGG CCAGCCGGAACCAACTACAAGACCACCCCTCCGGTGTGTTGAC TCAGACGGATCCTTCTTCTCTACTCGCGGTGACCGTGGATAA GAGCAGATGGCAGGAGGGAAATGTGTTTCAGCTGTTCTGTGATG CATGAAGCCCTGCACAACCACTACACTCAGAAGTCCCTGTCCCT CTCCCTGGGA
SEQ ID NO: 729	DNA heavy chain	CAGGTGCAGCTGGTGCAGTCTGGCGCCGAAGTGAAGAAACCTG GCGCCTCCGTGAAGGTGTCTGCAAGGCCTCTGGCTTACCCCTG ACCAACTACGGCATGAACTGGGTGCGACAGGCCCCCTGGACAGG GCCTGGAATGGATGGGCTGGATCAACACCGACACCGGCGAGCC TACCTACGCCGACGACTTCAAGGGCAGATTCTGTGTTCTCCCTGG ACACCTCCGTGTCCACCGCCTACCTGCAGATCTCCAGCCTGAAG GCCGAGGATACCGCCGTGTACTACTGCGCCCGGAACCCCCCTT ACTACTACGGCACCAACAACGCCGAGGCCATGGACTATTGGGG CCAGGGCACCAACCGTGACCGTGTCTCTGCTTCTACCAAGGGGC CCAGCGTGTTCCTCTGGCCCCCTGCTCCAGAAGCACCAGCGA GAGCACAGCCGCCCTGGGCTGCCTGGTGAAGGACTACTTCCCC GAGCCCGTGACCGTGTCTGGAACAGCGGAGCCCTGACCAGCG GCGTGCACACCTTCCCCGCGGTGCTGCAGAGCAGCGGCCTGTA CAGCCTGAGCAGCGTGGTGACCGTGCCAGCAGCAGCCTGGGC ACCAAGACCTACACCTGTAACGTGGACCACAAGCCCAGCAACA CCAAGGTGGACAAGAGGGTGGAGAGCAAGTACGGCCCAACCT GCCCCCCTGCCAGCCCCCGAGTTCCTGGGCGGACCCAGCGT GTTCTGTTCCTCTCAAGCCCAAGGACACCCTGATGATCAGCA GAACCCCCGAGGTGACCTGTGTGGTGGTGGACGTGTCCCAGGA GGACCCCCGAGGTCCAGTTCAACTGGTACGTGGACGGCGTGGAG GTGCACAACGCCAAGACCAAGCCCAGAGAGGAGCAGTTTAACA GCACCTACCGGGTGGTGTCCGTGCTGACCGTGTGACCAAGGA CTGGCTGAACGGCAAAGAGTACAAGTGTAAAGTCTCCAACAAG GGCCTGCCAAGCAGCATCGAAAAGACCATCAGCAAGGCCAAG GGCCAGCCTAGAGAGCCCCAGGTCTACACCTGCCACCCAGCC AAGAGGAGATGACCAAGAACCAGGTGTCCCTGACCTGTCTGGT GAAGGGCTTCTACCAAGCGACATCGCCGTGGAGTGGGAGAGC

		AACGGCCAGCCCAGAGAACAACACTACAAGACCACCCCCCAGTGC TGGACAGCGACGGCAGCTTCTTCCTGTACAGCAGGCTGACCGT GGACAAGTCCAGATGGCAGGAGGGCAACGTCTTTAGCTGCTCC GTGATGCACGAGGCCCTGCACAACCACTACACCCAGAAGAGCC TGAGCCTGTCCCTGGGC
BAP050-Clone J LC		
SEQ ID NO: 710 (Kabat)	LCDR1	SSSQDISNYLN
SEQ ID NO: 711 (Kabat)	LCDR2	YTSTLHL
SEQ ID NO: 712 (Kabat)	LCDR3	QYYNLPWT
SEQ ID NO: 713 (Chothia)	LCDR1	SQDISNY
SEQ ID NO: 714 (Chothia)	LCDR2	YTS
SEQ ID NO: 715 (Chothia)	LCDR3	YYNLPW
SEQ ID NO: 730	VL	DIQMTQSPSSLASVGDRTITCSSSQDISNYLNWYQQKPGKAPKL LIYYTSTLHLGIPPRFSGSGYGTDFLTINNIESEDAAYYFCQYYN LPWTFGQGTKVEIK
SEQ ID NO: 731	DNA VL	GATATTCAGATGACTCAGTCACCTAGTAGCCTGAGCGCTAGTGT GGGCGATAGAGTGACTATCACCTGTAGCTCTAGTCAGGATATCT CTAACTACCTGAACTGGTATCAGCAGAAGCCCCGGTAAAGCCCC TAAGCTGCTGATCTACTACACTAGCACCTGCACCTGGGAATCC CCCCTAGGTTTAGCGGTAGCGGCTACGGCACCGACTTCACCCTG ACTATTAACAATATCGAGTCAGAGGACGCCGCTACTACTTCTG TCAGCAGTACTATAACCTGCCCTGGACCTTCGGTCAAGGCACTA AGGTCGAGATTAAG
SEQ ID NO: 732	DNA VL	GACATCCAGATGACCCAGTCCCCCTCCAGCCTGTCTGCTTCCGT GGGCGACAGAGTGACCATCACCTGTTCTCCAGCCAGGACATC TCCAACCTACCTGAACTGGTATCAGCAGAAGCCCCGGCAAGCCCC CCAAGCTGCTGATCTACTACACCTCCACCCTGCACCTGGGCATC CCCCCTAGATTCTCCGGCTCTGGCTACGGCACCGACTTCACCCT GACCATCAACAACATCGAGTCCGAGGACGCCGCTACTACTTC TGCCAGCAGTACTACAACCTGCCCTGGACCTTCGGCCAGGGCA CCAAGGTGGAAATCAAG
SEQ ID NO: 733	Light chain	DIQMTQSPSSLASVGDRTITCSSSQDISNYLNWYQQKPGKAPKL LIYYTSTLHLGIPPRFSGSGYGTDFLTINNIESEDAAYYFCQYYN LPWTFGQGTKVEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNMF YPREAKVQWKVDNALQSGNSQESVTEQDSKSTYSLSTLTL SKA DYEKHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 734	DNA light chain	GATATTCAGATGACTCAGTCACCTAGTAGCCTGAGCGCTAGTGT GGGCGATAGAGTGACTATCACCTGTAGCTCTAGTCAGGATATCT CTAACTACCTGAACTGGTATCAGCAGAAGCCCCGGTAAAGCCCC TAAGCTGCTGATCTACTACACTAGCACCTGCACCTGGGAATCC CCCCTAGGTTTAGCGGTAGCGGCTACGGCACCGACTTCACCCTG ACTATTAACAATATCGAGTCAGAGGACGCCGCTACTACTTCTG TCAGCAGTACTATAACCTGCCCTGGACCTTCGGTCAAGGCACTA AGGTCGAGATTAAGCGTACGGTGGCCGCTCCCAGCGTGTTTCAT CTCCCCCCCCAGCGACGAGCAGCTGAAGAGCGGCACCGCCAGC GTGGTGTGCCTGCTGAACAATTCTACCCCCGGGAGGCCAAGG TGCAGTGGAAGGTGGACAACGCCCTGCAGAGCGGCAACAGCCA GGAGAGCGTCACCGAGCAGGACAGCAAGGACTCCACCTACAGC

		CTGAGCAGCACCTGACCCTGAGCAAGGCCGACTACGAGAAGC ATAAGGTGTACGCCTGCGAGGTGACCCACCAGGGCCTGTCCAG CCCCGTGACCAAGAGCTTCAACAGGGGCGAGTGC
SEQ ID NO: 735	DNA light chain	GACATCCAGATGACCCAGTCCCCCTCCAGCCTGTCTGCTTCCGT GGGCGACAGAGTGACCATCACCTGTTCTCCAGCCAGGACATC TCCAACTACCTGAACTGGTATCAGCAGAAGCCCGCAAGGCC CCAAGCTGCTGATCTACTACACCTCCACCCTGCACCTGGGCATC CCCCCTAGATTCTCCGGCTCTGGCTACGGCACCAGCTTCACCCT GACCATCAACAACATCGAGTCCGAGGACGCCGCCTACTACTTC TGCCAGCAGTACTACAACCTGCCCTGGACCTTCGGCCAGGGCA CCAAGGTGGAAATCAAGCGTACGGTGGCCGCTCCCAGCGTGT CATCTTCCCCCAAGCGACGAGCAGCTGAAGAGCGGCACCGCC AGCGTGGTGTGTCTGCTGAACAACCTTCTACCCAGGGAGGCCA AGGTGCAGTGGAAGGTGGACAACGCCCTGCAGAGCGGCAACA GCCAGGAGAGCGTCACCGAGCAGGACAGCAAGGACTCCACCTA CAGCCTGAGCAGCACCTGACCCTGAGCAAGGCCGACTACGAG AAGCACAAGGTGTACGCCTGTGAGGTGACCCACCAGGGCCTGT CCAGCCCCGTGACCAAGAGCTTCAACAGGGGCGAGTGC
BAP050-Clone I HC		
SEQ ID NO: 736 (Kabat)	HCDR1	AATTACGGGATGAAC
SEQ ID NO: 737 (Kabat)	HCDR1	AACTACGGCATGAAC
SEQ ID NO: 738 (Kabat)	HCDR2	TGGATTAACACCGACACCGGGGAGCCTACCTACGCGGACGATT TCAAGGGA
SEQ ID NO: 739 (Kabat)	HCDR2	TGGATCAACACCGACACCGGCGAGCCTACCTACGCCGACGACT TCAAGGGC
SEQ ID NO: 740 (Kabat)	HCDR3	AACCCGCCCTACTACTACGGAACCAACAACGCCGAAGCCATGG ACTAC
SEQ ID NO: 741 (Kabat)	HCDR3	AACCCCCCTTACTACTACGGCACCAACAACGCCGAGGCCATGG ACTAT
SEQ ID NO: 742 (Chothia)	HCDR1	GGATTACCCCTCACCAATTAC
SEQ ID NO: 743 (Chothia)	HCDR1	GGCTTCACCCTGACCAACTAC
SEQ ID NO: 744 (Chothia)	HCDR2	AACACCGACACCGGGGAG
SEQ ID NO: 745 (Chothia)	HCDR2	AACACCGACACCGGCGAG
SEQ ID NO: 740 (Chothia)	HCDR3	AACCCGCCCTACTACTACGGAACCAACAACGCCGAAGCCATGG ACTAC
SEQ ID NO: 741 (Chothia)	HCDR3	AACCCCCCTTACTACTACGGCACCAACAACGCCGAGGCCATGG ACTAT
BAP050-Clone I LC		
SEQ ID NO: 746 (Kabat)	LCDR1	AGCTCTAGTCAGGATATCTCTAACTACCTGAAC
SEQ ID NO: 747 (Kabat)	LCDR1	TCCTCCAGCCAGGACATCTCCAACCTACCTGAAC
SEQ ID NO: 748 (Kabat)	LCDR2	TACACTAGCACCTGACCTG
SEQ ID NO: 749 (Kabat)	LCDR2	TACACCTCCACCCTGACCTG
SEQ ID NO: 750 (Kabat)	LCDR3	CAGCAGTACTATAACCTGCCCTGGACC
SEQ ID NO: 751 (Kabat)	LCDR3	CAGCAGTACTACAACCTGCCCTGGACC
SEQ ID NO: 752 (Chothia)	LCDR1	AGTCAGGATATCTCTAACTAC

SEQ ID NO: 753 (Chothia)	LCDR1	AGCCAGGACATCTCCAACACTAC
SEQ ID NO: 754 (Chothia)	LCDR2	TACACTAGC
SEQ ID NO: 755 (Chothia)	LCDR2	TACACCTCC
SEQ ID NO: 756 (Chothia)	LCDR3	TACTATAACCTGCCCTGG
SEQ ID NO: 757 (Chothia)	LCDR3	TACTACAACCTGCCCTGG
BAP050-Clone J HC		
SEQ ID NO: 758 (Kabat)	HCDR1	AACTACGGGATGAAC
SEQ ID NO: 737 (Kabat)	HCDR1	AACTACGGCATGAAC
SEQ ID NO: 759 (Kabat)	HCDR2	TGGATTAACACCGACACCGGCGAGCCTACCTACGCCGACGACT TTAAGGGC
SEQ ID NO: 739 (Kabat)	HCDR2	TGGATCAACACCGACACCGGCGAGCCTACCTACGCCGACGACT TCAAGGGC
SEQ ID NO: 760 (Kabat)	HCDR3	AACCCCCCTACTACTACGGCACTAACAACGCCGAGGCTATGG ACTAC
SEQ ID NO: 741 (Kabat)	HCDR3	AACCCCCCTTACTACTACGGCACCAACAACGCCGAGGCCATGG ACTAT
SEQ ID NO: 761 (Chothia)	HCDR1	GGCTTCACCCTGACTAACTAC
SEQ ID NO: 743 (Chothia)	HCDR1	GGCTTCACCCTGACCAACTAC
SEQ ID NO: 744 (Chothia)	HCDR2	AACACCGACACCGGGGAG
SEQ ID NO: 745 (Chothia)	HCDR2	AACACCGACACCGGCGAG
SEQ ID NO: 760 (Chothia)	HCDR3	AACCCCCCTACTACTACGGCACTAACAACGCCGAGGCTATGG ACTAC
SEQ ID NO: 741 (Chothia)	HCDR3	AACCCCCCTTACTACTACGGCACCAACAACGCCGAGGCCATGG ACTAT
BAP050-Clone J LC		
SEQ ID NO: 746 (Kabat)	LCDR1	AGCTCTAGTCAGGATATCTCTAACTACCTGAAC
SEQ ID NO: 747 (Kabat)	LCDR1	TCCTCCAGCCAGGACATCTCCAACACTACCTGAAC
SEQ ID NO: 748 (Kabat)	LCDR2	TACACTAGCACCTGCACCTG
SEQ ID NO: 749 (Kabat)	LCDR2	TACACCTCCACCCTGCACCTG
SEQ ID NO: 750 (Kabat)	LCDR3	CAGCAGTACTATAACCTGCCCTGGACC
SEQ ID NO: 751 (Kabat)	LCDR3	CAGCAGTACTACAACCTGCCCTGGACC
SEQ ID NO: 752 (Chothia)	LCDR1	AGTCAGGATATCTCTAACTAC
SEQ ID NO: 753 (Chothia)	LCDR1	AGCCAGGACATCTCCAACACTAC
SEQ ID NO: 754 (Chothia)	LCDR2	TACACTAGC
SEQ ID NO: 755 (Chothia)	LCDR2	TACACCTCC

SEQ ID NO: 756 (Chothia)	LCDR3	TACTATAACCTGCCCTGG
SEQ ID NO: 757 (Chothia)	LCDR3	TACTACAACCTGCCCTGG

Other Exemplary LAG-3 Inhibitors

[0496] In one embodiment, the anti-LAG-3 antibody molecule is BMS-986016 (Bristol-Myers Squibb), also known as BMS986016. BMS-986016 and other anti-LAG-3 antibodies are disclosed in WO 2015/116539 and US 9,505,839, incorporated by reference in their entirety. In one embodiment, the anti-LAG-3 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of BMS-986016, *e.g.*, as disclosed in Table 8.

[0497] In one embodiment, the anti-LAG-3 antibody molecule is TSR-033 (Tesaro). In one embodiment, the anti-LAG-3 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of TSR-033.

[0498] In one embodiment, the anti-LAG-3 antibody molecule is MK-4280 (Merck & Co). In one embodiment, the anti-LAG-3 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of MK-4280.

[0499] In one embodiment, the anti-LAG-3 antibody molecule is REGN3767 (Regeneron). In one embodiment, the anti-LAG-3 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of REGN3767.

[0500] In one embodiment, the anti-LAG-3 antibody molecule is IMP731 or GSK2831781 (GSK and Prima BioMed). IMP731 and other anti-LAG-3 antibodies are disclosed in WO 2008/132601 and US 9,244,059, incorporated by reference in their entirety. In one embodiment, the anti-LAG-3 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of IMP731, *e.g.*, as disclosed in Table 8. In one embodiment, the anti-LAG-3 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of GSK2831781.

[0501] In one embodiment, the anti-LAG-3 antibody molecule is IMP761 (Prima BioMed). In one embodiment, the anti-LAG-3 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of IMP761.

[0502] Further known anti-LAG-3 antibodies include those described, *e.g.*, in WO 2008/132601, WO 2010/019570, WO 2014/140180, WO 2015/116539, WO 2015/200119, WO 2016/028672, US 9,244,059, US 9,505,839, incorporated by reference in their entirety.

[0503] In one embodiment, the anti-LAG-3 antibody is an antibody that competes for binding with, and/or binds to the same epitope on LAG-3 as, one of the anti-LAG-3 antibodies described herein.

[0504] In one embodiment, the anti-LAG-3 inhibitor is a soluble LAG-3 protein, *e.g.*, IMP321 (Prima BioMed), *e.g.*, as disclosed in WO 2009/044273, incorporated by reference in its entirety.

Table 8. Amino acid sequences of other exemplary anti-LAG-3 antibody molecules

BMS-986016		
SEQ ID NO: 762	Heavy chain	QVQLQQWGAGLLKPSETLSLTCAVYGGSFSDYYWNWIRQPPGKGLE WIGEINHRGSTNSNPSLKSRLVTLSDTSKNQFSLKLSVTAADTAVYYC AFGYSDYEYNWFDPWGQGTLTVTSSASTKGPSVFPLAPCSRSTSESTA ALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTV PSSSLGKTYTCNVDPKPSNTKVDKRVESKYGPCCPPCPAPEFLGGPSV FLFPPKPKDTLMISRTPEVTCVVVDVSQEDPEVQFNWYVDGVEVHNA KTKPREEQFNSTYRVVSVLTVHLQDNLNGKEYKCKVSNKGLPSSIEKT ISKAKGQPREPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWES NGQPENNYKTTTPVLDSDGSFFLYSRLTVDKSRWQEGNVFSCSV MHE ALHNHYTQKSLSLSLGK
SEQ ID NO: 763	Light chain	EIVLTQSPATLSLSPGERATLSCRASQSISSYLAWYQQKPGQAPRLIYD ASNRATGIPARFSGSGSGTDFTLTISLEPEDFAVYYCQQRSNWPLTFG QGTNLEIKRTVAAPSVFIFPPSDEQLKSGTASVCLLNNFYPREAKVQW KVDNALQSGNSQESVTEQDSKSTYSLSSLTLSKADYEEKHKVYACE VTHQGLSSPVTKSFNRGEC
IMP731		
SEQ ID NO: 764	Heavy chain	QVQLKESGPGLVAPSQSLSTCTVSGFSLTAYGVNWRQPPGKGLEWL GMIWDDGSTDYNALSKSRLSISKDNSKSQVFLKMNSLQTDITARYYC AREGDVAFDYWGQGTTLTVSSASTKGPSVFPLAPSSKSTSGGTAALGC LVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPS GTQTYICNVNHKPSNTKVDKKVEPKSCDKTHTCPPCPAPELLGGPSV LFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAK TKPREEQYNSTYRVVSVLTVHLQDNLNGKEYKCKVSNKALPAPIEKTI SKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESN GQPENNYKTTTPVLDSDGSFFLYSKLTVDKSRWQQGNVSCSV MHEA LHNHYTQKSLSLSPGK

SEQ ID NO: 765	Light chain	DIVMTQSPSSLAIVSVGQKVTMSCKSSQSLNLSNQKNYLAWYQQKPG QSPKLLVYFASTRDSGVPDRFIGSGSGTDFTLTISSVQAEDLADYFCLQ HFGTPPTFGGGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFY PREAKVQWKVDNALQSGNSQESVTEQDSKDSSTYSSTLTLSKADYE KHKVYACEVTHQGLSSPVTKSFNRGEC

TIM-3 Inhibitors

[0505] In certain embodiments, the anti-human ENTPD2 antibody as described herein is administered in combination with a TIM-3 inhibitor. The TIM-3 inhibitor may be an antibody, an antigen-binding fragment thereof, an immunoadhesin, a fusion protein, or an oligopeptide. In some embodiments, the TIM-3 inhibitor is chosen from MBG453 (Novartis), TSR-022 (Tesaro) or LY3321367 (Eli Lilly).

Exemplary TIM-3 Inhibitors

[0506] In one embodiment, the TIM-3 inhibitor is an anti-TIM-3 antibody molecule. In one embodiment, the TIM-3 inhibitor is an anti-TIM-3 antibody molecule as disclosed in US 2015/0218274, published on August 6, 2015, entitled “Antibody Molecules to TIM-3 and Uses Thereof,” incorporated by reference in its entirety.

[0507] In one embodiment, the anti-TIM-3 antibody molecule comprises at least one, two, three, four, five or six complementarity determining regions (CDRs) (or collectively all of the CDRs) from a heavy and light chain variable region comprising an amino acid sequence shown in Table 9 (*e.g.*, from the heavy and light chain variable region sequences of ABTIM3-hum11 or ABTIM3-hum03 disclosed in Table 9), or encoded by a nucleotide sequence shown in Table 9. In some embodiments, the CDRs are according to the Kabat definition (*e.g.*, as set out in Table 9). In some embodiments, the CDRs are according to the Chothia definition (*e.g.*, as set out in Table 9). In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions (*e.g.*, conservative amino acid substitutions) or deletions, relative to an amino acid sequence shown in Table 9, or encoded by a nucleotide sequence shown in Table 9.

[0508] In one embodiment, the anti-TIM-3 antibody molecule comprises a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence of SEQ ID NO: 801, a VHCDR2 amino acid sequence of SEQ ID NO: 802, and a VHCDR3 amino acid sequence of SEQ ID NO: 803; and a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO: 810, a VLCDR2 amino acid sequence of SEQ ID NO: 811,

and a VLCDR3 amino acid sequence of SEQ ID NO: 812, each disclosed in Table 9. In one embodiment, the anti-TIM-3 antibody molecule comprises a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence of SEQ ID NO: 801, a VHCDR2 amino acid sequence of SEQ ID NO: 820, and a VHCDR3 amino acid sequence of SEQ ID NO: 803; and a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO: 810, a VLCDR2 amino acid sequence of SEQ ID NO: 811, and a VLCDR3 amino acid sequence of SEQ ID NO: 812, each disclosed in Table 9.

[0509] In one embodiment, the anti-TIM-3 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 806, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 806. In one embodiment, the anti-TIM-3 antibody molecule comprises a VL comprising the amino acid sequence of SEQ ID NO: 816, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 816. In one embodiment, the anti-TIM-3 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 822, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 822. In one embodiment, the anti-TIM-3 antibody molecule comprises a VL comprising the amino acid sequence of SEQ ID NO: 826, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 826. In one embodiment, the anti-TIM-3 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 806 and a VL comprising the amino acid sequence of SEQ ID NO: 816. In one embodiment, the anti-TIM-3 antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 822 and a VL comprising the amino acid sequence of SEQ ID NO: 826.

[0510] In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 807, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 807. In one embodiment, the antibody molecule comprises a VL encoded by the nucleotide sequence of SEQ ID NO: 817, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 817. In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 823, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 823. In one embodiment, the antibody molecule comprises a VL encoded by the nucleotide sequence of SEQ ID NO: 827, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 827. In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 807 and a VL encoded by the nucleotide sequence of SEQ ID NO: 817. In one embodiment, the

antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 823 and a VL encoded by the nucleotide sequence of SEQ ID NO: 827.

[0511] In one embodiment, the anti-TIM-3 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 808, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 808. In one embodiment, the anti-TIM-3 antibody molecule comprises a light chain comprising the amino acid sequence of SEQ ID NO: 818, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 818. In one embodiment, the anti-TIM-3 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 824, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 824. In one embodiment, the anti-TIM-3 antibody molecule comprises a light chain comprising the amino acid sequence of SEQ ID NO: 828, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 828. In one embodiment, the anti-TIM-3 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 808 and a light chain comprising the amino acid sequence of SEQ ID NO: 818. In one embodiment, the anti-TIM-3 antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 824 and a light chain comprising the amino acid sequence of SEQ ID NO: 828.

[0512] In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 809, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 809. In one embodiment, the antibody molecule comprises a light chain encoded by the nucleotide sequence of SEQ ID NO: 819, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 819. In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 825, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 825. In one embodiment, the antibody molecule comprises a light chain encoded by the nucleotide sequence of SEQ ID NO: 829, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 829. In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 809 and a light chain encoded by the nucleotide sequence of SEQ ID NO: 819. In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 825 and a light chain encoded by the nucleotide sequence of SEQ ID NO: 829.

[0513] The antibody molecules described herein can be made by vectors, host cells, and methods described in US 2015/0218274, incorporated by reference in its entirety.

Table 9. Amino acid and nucleotide sequences of exemplary anti-TIM-3 antibody molecules

ABTIM3-hum11		
SEQ ID NO: 801 (Kabat)	HCDR1	SYNMH
SEQ ID NO: 802 (Kabat)	HCDR2	DIYPGNGDTSYNQKFKG
SEQ ID NO: 803 (Kabat)	HCDR3	VGGAFPMDY
SEQ ID NO: 804 (Chothia)	HCDR1	GYTFTSY
SEQ ID NO: 805 (Chothia)	HCDR2	YPGNGD
SEQ ID NO: 803 (Chothia)	HCDR3	VGGAFPMDY
SEQ ID NO: 806	VH	QVQLVQSGAEVKKPGSSVKVSCKASGYTFTSYNMHWVRQAPG QGLEWMGDIYPGNGDTSYNQKFKGRVTITADKSTSTVYMELSS LRSEDTAVYYCARVGGAFPMDYWGQGTITVTVSS
SEQ ID NO: 807	DNA VH	CAGGTGCAGCTGGTGCAGTCAGGCGCCGAAGTGAAGAAACC CGGCTCTAGCGTGAAAGTTTCTTGTAAGCTAGTGGCTACAC CTTCACTAGCTATAATATGCACTGGGTTCGCCAGGCCCCAGG GCAAGGCCTCGAGTGGATGGGCGATATCTACCCCGGGAACGG CGACACTAGTTATAATCAGAAGTTTAAGGGTAGAGTCACTAT CACCGCCGATAAGTCTACTAGCACCGTCTATATGGAAGTGAAG TTCCCTGAGGTCTGAGGACACCGCCGTCTACTACTGCGCTAG AGTGGGCGGAGCCTTCCCTATGGACTACTGGGGTCAAGGCAC TACCGTGACCGTGTCTAGC
SEQ ID NO: 808	Heavy chain	QVQLVQSGAEVKKPGSSVKVSCKASGYTFTSYNMHWVRQAPG QGLEWMGDIYPGNGDTSYNQKFKGRVTITADKSTSTVYMELSS LRSEDTAVYYCARVGGAFPMDYWGQGTITVTVSSASTKGPSVFP LAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP AVLQSSGLYSLSVVTVPSSSLGKTYTCNVDPKPSNTKVDKRV ESKYGPPCPPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVV DVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYRVSFLT VLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTL PPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTP PVLDSDSGFFLYSRLTVDKSRWQEGNVFSCSVMHLEHNHYTQ KSLSLSLG
SEQ ID NO: 809	DNA heavy chain	CAGGTGCAGCTGGTGCAGTCAGGCGCCGAAGTGAAGAAACC CGGCTCTAGCGTGAAAGTTTCTTGTAAGCTAGTGGCTACAC CTTCACTAGCTATAATATGCACTGGGTTCGCCAGGCCCCAGG GCAAGGCCTCGAGTGGATGGGCGATATCTACCCCGGGAACGG CGACACTAGTTATAATCAGAAGTTTAAGGGTAGAGTCACTAT CACCGCCGATAAGTCTACTAGCACCGTCTATATGGAAGTGAAG TTCCCTGAGGTCTGAGGACACCGCCGTCTACTACTGCGCTAG AGTGGGCGGAGCCTTCCCTATGGACTACTGGGGTCAAGGCAC TACCGTGACCGTGTCTAGCGCTAGCACTAAGGGCCCCGTCCGT GTTCCCCCTGGCACCTTGTAGCCGGAGCACTAGCGAATCCAC CGCTGCCCTCGGCTGCCTGGTCAAGGATTACTTCCCGGAGCC CGTGACCGTGTCTGGAACAGCGGAGCCCTGACCTCCGGAGT GCACACCTTCCCCGCTGTGCTGCAGAGCTCCGGGTGTACTC GCTGTCTGTCGGTGGTCACGGTGCCTTCATCTAGCTGGGTACC AAGACCTACACTTGCAACGTGGACCACAAGCCTTCCAACACT AAGGTGGACAAGCGCGTCGAATCGAAGTACGGCCACCGTG CCCGCCTTGTCCCGCGCCGAGTTCCTCGGCGGTCCCTCGGTC TTTCTGTTCCCAACGAAGCCCAAGGACACTTTGATGATTTCCC GCACCCCTGAAGTGACATGCGTGGTTCGTGGACGTGTACAGG AAGATCCGGAGGTGCAGTTCAATTGGTACGTGGATGGCGTCG AGGTGCACAACGCCAAAACCAAGCCGAGGGAGGAGCAGTTC

		AACTCCACTTACCGCGTCGTGTCCGTGCTGACGGTGTCTGCATC AGGACTGGCTGAACGCGGAAGGAGTACAAGTGCAAAGTGTCC AACAAGGGACTTCCTAGCTCAATCGAAAAGACCATCTCGAAA GCCAAGGGACAGCCCCGGAACCCCAAGTGTATACCCTGCCA CCGAGCCAGGAAGAAATGACTAAGAACCAAGTCTCATTGACT TGCCTTGTGAAGGGCTTCTACCCATCGGATATCGCCGTGGAA TGGGAGTCCAACGCGCCAGCCGGAACCAACTACAAGACCAC CCCTCCGGTGCTGGACTCAGACGGATCCTTCTTCTCTACTCG CGGCTGACCGTGGATAAGAGCAGATGGCAGGAGGGAAATGT GTTTCAGCTGTTCTGTGATGCATGAAGCCCTGCACAACCACTA CACTCAGAAAGTCCCTGTCCCTCTCCCTGGGA
SEQ ID NO: 810 (Kabat)	LCDR1	RASESVEYYGTSLMQ
SEQ ID NO: 811 (Kabat)	LCDR2	AASNVES
SEQ ID NO: 812 (Kabat)	LCDR3	QQSRKDPST
SEQ ID NO: 813 (Chothia)	LCDR1	SESVEYYGTS
SEQ ID NO: 814 (Chothia)	LCDR2	AAS
SEQ ID NO: 815 (Chothia)	LCDR3	SRKDPS
SEQ ID NO: 816	VL	AIQLTQSPSSLSASVGDRTITCRASESVEYYGTSLMQWYQQKP GKAPKLLIYAASNVESGVPSRFSGSGSGTDFLTITSSLPEDFATY FCQQSRKDPSTFGGGTKVEIK
SEQ ID NO: 817	DNA VL	GCTATTCAGCTGACTCAGTCACCTAGTAGCCTGAGCGCTAGT GTGGGCGATAGAGTGACTATCACCTGTAGAGCTAGTGAATCA GTCGAGTACTACGGCACTAGCCTGATGCAGTGGTATCAGCAG AAGCCCCGGAAAGCCCCCTAAGCTGCTGATCTACGCCGCCTCT AACGTGGAATCAGGCGTGCCCTCTAGGTTTAGCGGTAGCGGT AGTGGCACCGACTTCACCCTGACTATCTCTAGCCTGCAGCCC GAGGACTTCGCTACCTACTTCTGTGTCAGCAGTCTAGGAAGGAC CCTAGCACCTTCGCGGAGGCACTAAGGTCGAGATTAAG
SEQ ID NO: 818	Light chain	AIQLTQSPSSLSASVGDRTITCRASESVEYYGTSLMQWYQQKP GKAPKLLIYAASNVESGVPSRFSGSGSGTDFLTITSSLPEDFATY FCQQSRKDPSTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTAS VVCLLNFPYPREAKVQWKVDNALQSGNSQESVTEQDSKSTYS LSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 819	DNA light chain	GCTATTCAGCTGACTCAGTCACCTAGTAGCCTGAGCGCTAGT GTGGGCGATAGAGTGACTATCACCTGTAGAGCTAGTGAATCA GTCGAGTACTACGGCACTAGCCTGATGCAGTGGTATCAGCAG AAGCCCCGGAAAGCCCCCTAAGCTGCTGATCTACGCCGCCTCT AACGTGGAATCAGGCGTGCCCTCTAGGTTTAGCGGTAGCGGT AGTGGCACCGACTTCACCCTGACTATCTCTAGCCTGCAGCCC GAGGACTTCGCTACCTACTTCTGTGTCAGCAGTCTAGGAAGGAC CCTAGCACCTTCGCGGAGGCACTAAGGTCGAGATTAAGCGT ACGGTGCCGCTCCCAGCGTGTTTCATCTTCCCCCCCAGCGAC GAGCAGCTGAAGAGCGGCACCGCCAGCGTGGTGTGCCTGCTG AACAACCTTCTACCCCCGGGAGGCCAAGGTGCAGTGGAAGGTG GACAACGCCCTGCAGAGCGGCAACAGCCAGGAGAGCGTCAC CGAGCAGGACAGCAAGGACTCCACCTACAGCCTGAGCAGCA CCCTGACCCTGAGCAAGGCCGACTACGAGAAGCATAAGGTGT ACGCCTGCGAGGTGACCCACCAGGGCCTGTCCAGCCCCGTGA CCAAGAGCTTCAACAGGGGCGAGTGC
ABTIM3-hum03		
SEQ ID NO: 801 (Kabat)	HCDR1	SYNMH
SEQ ID NO: 820 (Kabat)	HCDR2	DIYPGQGDTSYNQKFKG
SEQ ID NO: 803 (Kabat)	HCDR3	VGGAFPM DY
SEQ ID NO: 804 (Chothia)	HCDR1	GYTFTSY
SEQ ID NO: 821 (Chothia)	HCDR2	YPGQGD
SEQ ID NO: 803 (Chothia)	HCDR3	VGGAFPM DY
SEQ ID NO: 822	VH	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPG QGLEWIGDIYPGQGDTSYNQKFKGRATMTADKSTSTVYMELSS LRSEDTAVYYCARVGGAFPM DYWGQGLTVTVSS

SEQ ID NO: 823	DNA VH	CAGGTGCAGCTGGTGCAGTCAGGCGCCGAAGTGAAGAAACC CGGCGCTAGTGTGAAAGTTAGCTGTAAAGCTAGTGGCTATAC TTTCACTTCTTATAATATGCACTGGGTCCGCCAGGCCCCAGGT CAAGGCCTCGAGTGGATCGGCGATATCTACCCCGGTCAAGGC GACACTTCCTATAATCAGAAGTTTAAGGGTAGAGCTACTATG ACCGCCGATAAGTCTACTTCTACCGTCTATATGGAAGTGAAGT CCCTGAGGTCTGAGGACACCGCCGTCTACTACTGCGCTAGAG TGGGCGGAGCCTTCCCAATGGACTACTGGGGTCAAGGCACCC TGGTCACCGTGTCTAGC
SEQ ID NO: 824	Heavy chain	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPG QGLEWIGDIYPGQGDTSYNQKFKGRATMTADKSTSTVYMELSS LRSEDTAVYYCARVGGAFPMGYWGQGLTVTVSSASTKGPSVFP LAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFP AVLQSSGLYSLSVVTVPSSSLGTKYTCNVDHKPSNTKVDKRV ESKYGPPCPPCPAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVV DVSQEDPEVQFNWYVDGVEVHNAKTKPREEQFNSTYR VVSVLT VLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQPREPQVYTL PPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTP PVLDSGSEFLYSRLTVDKSRWQEGNVFSCSVMEALHNHYTQ KSLSLSLG
SEQ ID NO: 825	DNA heavy chain	CAGGTGCAGCTGGTGCAGTCAGGCGCCGAAGTGAAGAAACC CGGCGCTAGTGTGAAAGTTAGCTGTAAAGCTAGTGGCTATAC TTTCACTTCTTATAATATGCACTGGGTCCGCCAGGCCCCAGGT CAAGGCCTCGAGTGGATCGGCGATATCTACCCCGGTCAAGGC GACACTTCCTATAATCAGAAGTTTAAGGGTAGAGCTACTATG ACCGCCGATAAGTCTACTTCTACCGTCTATATGGAAGTGAAGT CCCTGAGGTCTGAGGACACCGCCGTCTACTACTGCGCTAGAG TGGGCGGAGCCTTCCCAATGGACTACTGGGGTCAAGGCACCC TGGTCACCGTGTCTAGCGCTAGCCTAAGGGCCCCGTCCGTGT TCCCCCTGGCACCTTGTAGCCGGAGCACTAGCGAATCCACCG CTGCCCTCGGCTGCCTGGTCAAGGATTACTTCCCGGAGCCCGT GACCGTGTCTGGAACAGCGGAGCCCTGACCTCCGGAGTGCA CACCTTCCCCGCTGTGCTGCAGAGCTCCGGGCTGTACTCGCTG TCGTCCGTGGTCACGGTGCCTTCATCTAGCCTGGGTACCAAG ACCTACACTTGCAACGTGGACCACAAGCCTTCCAACACTAAG GTGGACAAGCGCGTCGAATCGAAGTACGGCCCCACCGTGCCCG CCTTGTCCCGCGCCGGAGTTCCTCGGCGGTCCCTCGGTCTTTC TGTTCCCAACGAAGCCCAAGGACACTTTGATGATTTCGCA CCCCTGAAGTGACATGCGTGGTCTGTGGACGTGTACAGGAAG ATCCGGAGGTGCAGTTCAATTGGTACGTGGATGGCGTTCGAGG TGCACAACGCCAAAACCAAGCCGAGGGAGGAGCAGTTCAAC TCCACTTACCGCGTCTGTCCGTGCTGACGGTGTGTCATCAGG ACTGGCTGAACGGGAAGGAGTACAAGTGCAAAAGTGCCAAC AAGGGACTTCCTAGCTCAATCGAAAAGACCATCTCGAAAGCC AAGGGACAGCCCCGGGAACCCCAAGTGTATACCCTGCCACCG AGCCAGGAAGAAATGACTAAGAACCAAGTCTCATTGACTTGC CTTGTGAAGGGCTTCTACCCATCGGATATCGCCGTGGAATGG GAGTCCAACGGCCAGCCGGAACAACACTACAAGACCACCCC TCCGGTGTGGAAGTCAAGAGCAGATGGCAGGAGGAAATGTGTT CAGCTGTTCTGTGATGCATGAAGCCCTGCACAACCACTACAC TCAGAAGTCCCTGTCCCTCTCCCTGGGA
SEQ ID NO: 810 (Kabat)	LCDR1	RASESVEYYGTSLMQ
SEQ ID NO: 811 (Kabat)	LCDR2	AASNVES
SEQ ID NO: 812 (Kabat)	LCDR3	QOSRKDPST
SEQ ID NO: 813 (Chothia)	LCDR1	SESVEYYGTS
SEQ ID NO: 814 (Chothia)	LCDR2	AAS
SEQ ID NO: 815 (Chothia)	LCDR3	SRKDPS

SEQ ID NO: 826	VL	DIVLTQSPDSLAVSLGERATINCRASESVEYYGTSLMQWYQQKP GQPPKLLIYAASNVESGVPDRFSGSGSGTDFTLTISLQAEDVAV YYCQQSRKDPSTFGGGTKVEIK
SEQ ID NO: 827	DNA VL	GATATCGTCTGACTCAGTCACCCGATAGCCTGGCCGTCAGC CTGGGCGAGCGGGCTACTATTAAGTGTAGAGCTAGTGAATCA GTCGAGTACTACGGCACTAGCCTGATGCAGTGGTATCAGCAG AAGCCCGGTCAACCCCTAAGCTGCTGATCTACGCCGCCTCT AACGTGGAATCAGGCGTGCCCGATAGGTTTAGCGGTAGCGGT AGTGGCACCGACTTCACCCTGACTATTAGTAGCCTGCAGGCC GAGGACGTGGCCGTCTACTACTGTCAGCAGTCTAGGAAGGAC CCTAGCACCTTCGGCGGAGGCACTAAGGTGCGAGATTAAG
SEQ ID NO: 828	Light chain	DIVLTQSPDSLAVSLGERATINCRASESVEYYGTSLMQWYQQKP GQPPKLLIYAASNVESGVPDRFSGSGSGTDFTLTISLQAEDVAV YYCQQSRKDPSTFGGGTKVEIKRTVAAPSVFIFPPSDEQLKSGTA SVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSITY SLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC
SEQ ID NO: 829	DNA light chain	GATATCGTCTGACTCAGTCACCCGATAGCCTGGCCGTCAGC CTGGGCGAGCGGGCTACTATTAAGTGTAGAGCTAGTGAATCA GTCGAGTACTACGGCACTAGCCTGATGCAGTGGTATCAGCAG AAGCCCGGTCAACCCCTAAGCTGCTGATCTACGCCGCCTCT AACGTGGAATCAGGCGTGCCCGATAGGTTTAGCGGTAGCGGT AGTGGCACCGACTTCACCCTGACTATTAGTAGCCTGCAGGCC GAGGACGTGGCCGTCTACTACTGTCAGCAGTCTAGGAAGGAC CCTAGCACCTTCGGCGGAGGCACTAAGGTGCGAGATTAAGCGT ACGGTGGCCGCTCCCAGCGTGTTTCATCTTCCCCCCCAGCGAC GAGCAGCTGAAGAGCGGCACCGCCAGCGTGGTGTGCCTGCTG AACAACTTCTACCCCGGGAGGCCAAGGTGCAAGTGAAGGTG GACAACGCCCTGCAGAGCGGCAACAGCCAGGAGAGCGTCAC CGAGCAGGACAGCAAGGACTCCACCTACAGCCTGAGCAGCA CCCTGACCCTGAGCAAGGCCGACTACGAGAAGCATAAGGTGT ACGCCTGCGAGGTGACCCACCAGGGCCTGTCCAGCCCCGTGA CCAAGAGCTTCAACAGGGGCGAGTGC

Other Exemplary TIM-3 Inhibitors

[0514] In one embodiment, the anti-TIM-3 antibody molecule is TSR-022 (AnaptysBio/Tesaro). In one embodiment, the anti-TIM-3 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of TSR-022. In one embodiment, the anti-TIM-3 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of APE5137 or APE5121, *e.g.*, as disclosed in Table 10. APE5137, APE5121, and other anti-TIM-3 antibodies are disclosed in WO 2016/161270, incorporated by reference in its entirety.

[0515] In one embodiment, the anti-TIM-3 antibody molecule is LY3321367 (Eli Lilly). In one embodiment, the anti-TIM-3 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of LY3321367.

[0516] In one embodiment, the anti-TIM-3 antibody molecule is the antibody clone F38-2E2. In one embodiment, the anti-TIM-3 antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of F38-2E2.

[0517] Further known anti-TIM-3 antibodies include those described, *e.g.*, in WO 2016/111947, WO 2016/071448, WO 2016/144803, US 8,552,156, US 8,841,418, and US 9,163,087, incorporated by reference in their entirety.

[0518] In one embodiment, the anti-TIM-3 antibody is an antibody that competes for binding with, and/or binds to the same epitope on TIM-3 as, one of the anti-TIM-3 antibodies described herein.

Table 10. Amino acid sequences of other exemplary anti-TIM-3 antibody molecules

APE5137		
SEQ ID NO: 830	VH	EVQLLESGGGLVQPGGSLRLSCAAASGFTFSSYDMSWVRQAPGKGLDWVS TISGGGTYTYYQDSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCASMD YWGQGTITVTVSSA
SEQ ID NO: 831	VL	DIQMTQSPSSLASVSGDRVTITCRASQSIRRYLNWYHQKPGKAPKLLIYGAS TLQSGVPSRFSGSGSGTDFTLTISLQPEDFAVYYCQQSHSAPLTFGGGKVE IKR
APE5121		
SEQ ID NO: 832	VH	EVQVLES GGGLVQPGGSLRLYCVASGFTFSGSYAMSWVRQAPGKGLEWVS AISGSGGSTYYADSVKGRFTISRDN SKNTLYLQMNSLRAEDTAVYYCAKKY YVGADYWGQGLTVTVSSG
SEQ ID NO: 833	VL	DIVMTQSPDSLAVSLGERATINCKSSQSVLYSSNNKNYLA WYQHKPGQPPK LLIYWASTRESGV PDRFSGSGSGTDFTLTISLQAEDVAVYYCQQYYSSPLTF GGGTKIEVK

CTLA-4 Inhibitors

[0519] In certain embodiments, the anti-human ENTPD2 antibody molecule described herein is administered in combination with a CTLA-4 inhibitor. The CTLA-4 inhibitor may be an antibody, an antigen binding fragment thereof, an immunoadhesin, a fusion protein, or an oligopeptide. In some embodiments, the CTLA-4 inhibitor is Ipilimumab (Yervoy[®], Bristol-Myers Squibb) or Tremelimumab (Pfizer). The antibody Ipilimumab and other anti-CTLA-4 antibodies are disclosed in US 6,984,720, herein incorporated by reference. The antibody Tremelimumab and other anti-CTLA-4 antibodies are disclosed in US 7,411,057, herein incorporated by reference.

GITR Agonists

[0520] In certain embodiments, the anti-human ENTPD2 antibody as described herein is administered in combination with a GITR agonist. The GITR agonist may be an antibody, an antigen binding fragment thereof, an immunoadhesin, a fusion protein, or an oligopeptide. In some embodiments, the GITR agonist is GWN323 (Novartis), BMS-986156 (BMS), MK-4166 or MK-1248 (Merck), TRX518 (Leap Therapeutics), INCAGN1876 (Incyte/Agenus), AMG 228 (Amgen) or INBRX-110 (Inhibrx).

Exemplary Anti-GITR Antibody Molecules

[0521] In one embodiment, the GITR agonist is an anti-GITR antibody molecule. In one embodiment, the GITR agonist is an anti-GITR antibody molecule as described in WO 2016/057846, published on April 14, 2016, entitled “Compositions and Methods of Use for Augmented Immune Response and Cancer Therapy,” incorporated by reference in its entirety.

[0522] In one embodiment, the anti-GITR antibody molecule comprises at least one, two, three, four, five or six complementarity determining regions (CDRs) (or collectively all of the CDRs) from a heavy and light chain variable region comprising an amino acid sequence shown in Table 11 (*e.g.*, from the heavy and light chain variable region sequences of MAB7 disclosed in Table 11), or encoded by a nucleotide sequence shown in Table 11. In some embodiments, the CDRs are according to the Kabat definition (*e.g.*, as set out in Table 11). In some embodiments, the CDRs are according to the Chothia definition (*e.g.*, as set out in Table 11). In one embodiment, one or more of the CDRs (or collectively all of the CDRs) have one, two, three, four, five, six or more changes, *e.g.*, amino acid substitutions (*e.g.*, conservative amino acid substitutions) or deletions, relative to an amino acid sequence shown in Table 11, or encoded by a nucleotide sequence shown in Table 11.

[0523] In one embodiment, the anti-GITR antibody molecule comprises a heavy chain variable region (VH) comprising a VHCDR1 amino acid sequence of SEQ ID NO: 909, a VHCDR2 amino acid sequence of SEQ ID NO: 911, and a VHCDR3 amino acid sequence of SEQ ID NO: 913; and a light chain variable region (VL) comprising a VLCDR1 amino acid sequence of SEQ ID NO: 914, a VLCDR2 amino acid sequence of SEQ ID NO: 916, and a VLCDR3 amino acid sequence of SEQ ID NO: 918, each disclosed in Table 11.

[0524] In one embodiment, the anti-GITR antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 901, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 901. In one embodiment, the

anti-GITR antibody molecule comprises a VL comprising the amino acid sequence of SEQ ID NO: 902, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 902. In one embodiment, the anti-GITR antibody molecule comprises a VH comprising the amino acid sequence of SEQ ID NO: 901 and a VL comprising the amino acid sequence of SEQ ID NO: 902.

[0525] In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 905, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 905. In one embodiment, the antibody molecule comprises a VL encoded by the nucleotide sequence of SEQ ID NO: 906, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 906. In one embodiment, the antibody molecule comprises a VH encoded by the nucleotide sequence of SEQ ID NO: 905 and a VL encoded by the nucleotide sequence of SEQ ID NO: 906.

[0526] In one embodiment, the anti-GITR antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 903, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 903. In one embodiment, the anti-GITR antibody molecule comprises a light chain comprising the amino acid sequence of SEQ ID NO: 904, or an amino acid sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 904. In one embodiment, the anti-GITR antibody molecule comprises a heavy chain comprising the amino acid sequence of SEQ ID NO: 903 and a light chain comprising the amino acid sequence of SEQ ID NO: 904.

[0527] In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 907, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 907. In one embodiment, the antibody molecule comprises a light chain encoded by the nucleotide sequence of SEQ ID NO: 908, or a nucleotide sequence at least 85%, 90%, 95%, or 99% identical or higher to SEQ ID NO: 908. In one embodiment, the antibody molecule comprises a heavy chain encoded by the nucleotide sequence of SEQ ID NO: 907 and a light chain encoded by the nucleotide sequence of SEQ ID NO: 908.

[0528] The antibody molecules described herein can be made by vectors, host cells, and methods described in WO 2016/057846, incorporated by reference in its entirety.

Table 11. Amino acid and nucleotide sequences of exemplary anti-GITR antibody molecule

MAB7		

SEQ ID NO: 901	VH	EVQLVESGGGLVQSGGSLRLSCAASGFSLSYGVVDWVRQAP GKGLEWVGVIWGGGGTTYASSLMGRFTISRDNKNTLYLQ MNSLRAEDTAVYYCARHAYGHDGGFAMDYWGQGTLLTVS S
SEQ ID NO: 902	VL	EIVMTQSPATLSVSPGERATLSCRASESVSSNVAWYQQRPGQ APRLLIYGASNRATGIPARFSGSGSGTDFTLTISRLEPEDFAVY YCGQSYSPFTFGQGTKLEIK
SEQ ID NO: 903	Heavy Chain	EVQLVESGGGLVQSGGSLRLSCAASGFSLSYGVVDWVRQAP GKGLEWVGVIWGGGGTTYASSLMGRFTISRDNKNTLYLQ MNSLRAEDTAVYYCARHAYGHDGGFAMDYWGQGTLLTVS SASTKGPSVFPLAPSSKSTSGGTAALGCLVKDYFPEPVTVSW NSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGTQTYICN VNHKPSNTKVDKRVEPKSCDKTHTCPPCPAPELLGGPSVFLF PPKPKDTLMISRTPEVTCVVDVSHEDPEVKFNWYVDGVEV HNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV SKALPAPIEKTKAKGQPREPQVYTLPPSREEMTKNQVSLTCL LVKGFYPSDIAVEWESNGQPENNYKTTTPVLDSDGSFFLYSK LTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK
SEQ ID NO: 904	Light Chain	EIVMTQSPATLSVSPGERATLSCRASESVSSNVAWYQQRPGQ APRLLIYGASNRATGIPARFSGSGSGTDFTLTISRLEPEDFAVY YCGQSYSPFTFGQGTKLEIKRTVAAPSVFIFPPSDEQLKSGT ASVVCLLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSK DSTYLSSTLTLSKADYEEKHKVYACEVTHQGLSSPVTKSFNR GEC
SEQ ID NO: 905	DNA VH	GAGGTGCAGCTGGTGGAATCTGGCGGCGGACTGGTGCAG TCCGGCGGCTCTCTGAGACTGTCTTGCCTGCGCTCCGCTT CTCCCTGTCCTCTTACGGCGTGACTGGGTGCGACAGGCC CCTGGCAAGGGCCTGGAATGGGTGGGAGTGATCTGGGGC GGAGGCGGCACCTACTACGCCTCTTCCCTGATGGGCCGGT TCACCATCTCCCGGGACAACCTCCAAGAACACCCTGTACCT GCAGATGAACCTCCCTGCGGGCCGAGGACACCGCCGTGTAC TACTGCGCCAGACACGCCTACGGCCACGACGGCGGCTTCG CCATGGATTATTGGGGCCAGGGCACCTGGTGACAGTGTC CTCC
SEQ ID NO: 906	DNA VL	GAGATCGTGATGACCCAGTCCCCCGCCACCCTGTCTGTGT CTCCCGGCGAGAGAGCCACCCTGAGCTGCAGAGCCTCCGA GTCCGTGTCCTCCAACGTGGCCTGGTATCAGCAGAGACCT GGTCAGGCCCCCTCGGCTGCTGATCTACGGCGCCTCTAACC GGGCCACCGGCATCCCTGCCAGATTCTCCGGCTCCGGCAG CGGCACCGACTTCACCCTGACCATCTCCCGGCTGGAACCC GAGGACTTCGCCGTGTACTACTGCGGCCAGTCCTACTCAT ACCCCTTCACCTTCGGCCAGGGCACCAAGCTGGAAATCAA G

SEQ ID NO: 907	DNA Heavy Chain	GAGGTGCAGCTGGTGAATCTGGCGGCGGACTGGTGCAG TCCGGCGGCTCTCTGAGACTGTCTTGCCTGCCCTCCGGCTT CTCCCTGTCCTCTTACGGCGTGGACTGGGTGCGACAGGCC CCTGGCAAGGGCCTGGAATGGGTGGGAGTGATCTGGGGC GGAGGCGGCACCTACTACGCCTCTTCCCTGATGGGCCGGT TCACCATCTCCCGGGACAACCTCCAAGAACACCCTGTACCT GCAGATGAACTCCCTGCGGGCCGAGGACACCGCCGTGTAC TACTGCGCCAGACACGCCTACGGCCACGACGGCGGCTTCG CCATGGATTATTGGGGCCAGGGCACCCCTGGTGACAGTGTCT CTCCGCTAGCACCAAGGGCCCAAGTGTGTTTCCCTGGCC CCCAGCAGCAAGTCTACTTCCGGCGGAAGTGTGCCCTGG GTTGCCTGGTGAAGGACTACTTCCCCGAGCCCGTGACAGT GTCCTGGAAGTCTGGGGCTCTGACTTCCGGCGTGACACCC TCCCCGCGGTGCTGCAGAGCAGCGGCCTGTACAGCCTGA GCAGCGTGGTGACAGTGCCCTCCAGCTCTCTGGGAACCCA GACCTATATCTGCAACGTGAACCACAAGCCAGCAACACC AAGGTGGACAAGAGAGTGGAGCCCAAGAGCTGCGACAAG ACCCACACCTGCCCCCCTGCCAGCTCCAGAAGTGTGG GAGGGCCTTCCGTGTTCTGTTCCCCCACAAGCCCAAGGA CACCTGATGATCAGCAGGACCCCGAGGTGACCTGCGTG GTGGTGGACGTGTCCACGAGGACCCAGAGGTGAAGTTC AACTGGTACGTGGACGGCGTGGAGGTGCACAACGCCAAG ACCAAGCCCAGAGAGGAGCAGTACAACAGCACCTACAGG GTGGTGTCCGTGCTGACCGTGCTGCACCAGGACTGGCTGA ACGGCAAAGAATACAAGTGCAAAGTCTCCAACAAGGCC TGCCAGCCCCAATCGAAAAGACAATCAGCAAGGCCAAGG GCCAGCCACGGGAGCCCCAGGTGTACACCTGCCCCCAG CCGGGAGGAGATGACCAAGAACCAGGTGTCCCTGACCTG TCTGGTGAAGGGCTTCTACCCAGCGATATCGCCGTGGAG TGGGAGAGCAACGGCCAGCCCGAGAACAACTACAAGACC ACCCCCCAGTGCTGGACAGCGACGGCAGCTTCTTCCTGT ACAGCAAGCTGACCGTGGACAAGTCCAGGTGGCAGCAGG GCAACGTGTTTACGTGCAGCGTGATGCACGAGGCCCTGCA CAACCACTACACCCAGAAGTCCCTGAGCCTGAGCCCCGGC AAG
SEQ ID NO: 908	DNA Light Chain	GAGATCGTGATGACCCAGTCCCCCGCCACCCTGTCTGTGT CTCCCGGCGAGAGAGCCACCCTGAGCTGCAGAGCCTCCGA GTCCGTGTCCTCCAACGTGGCCTGGTATCAGCAGAGACCT GGTCAGGCCCCCTCGGCTGCTGATCTACGGCGCCTCTAAC GGGCCACCGGCATCCCTGCCAGATTCTCCGGCTCCGGCAG CGGCACCGACTTCACCCTGACCATCTCCCGGTGGAACCC GAGGACTTCGCGGTGTACTACTGCGGCCAGTCTACTCAT ACCCCTTCACCTTCGCGCCAGGGCACCAAGCTGGAAATCAA GCGTACGGTGGCCGCTCCAGCGTGTTTCATCTTCCCCC AGCGACGAGCAGCTGAAGAGCGGCACCGCCAGCGTGGTG TGCCTGCTGAACAATTCTACCCCGGGAGGCCAAGGTGC AGTGGAAGGTGGACAACGCCCTGCAGAGCGGCAACAGCC AGGAGAGCGTCACCGAGCAGGACAGCAAGGACTCCACCT ACAGCCTGAGCAGCACCCCTGACCCTGAGCAAGGCCGACT ACGAGAAGCATAAGGTGTACGCTGCGAGGTGACCCACC AGGGCCTGTCCAGCCCCGTGACCAAGAGCTTCAACAGGG GCGAGTGC
SEQ ID NO: 909 (KABAT)	HCDR1	SYGVD
SEQ ID NO: 910 (CHOTHIA)	HCDR1	GFSLSY
SEQ ID NO: 911 (KABAT)	HCDR2	VIWGGGGTYTASSLMG
SEQ ID NO: 912 (CHOTHIA)	HCDR2	WGGGG
SEQ ID NO: 913 (KABAT)	HCDR3	HAYGHDGGFAMDY
SEQ ID NO: 913 (CHOTHIA)	HCDR3	HAYGHDGGFAMDY
SEQ ID NO: 914 (KABAT)	LCDR1	RASESVSSNVA
SEQ ID NO: 915 (CHOTHIA)	LCDR1	SESVSSN

SEQ ID NO: 916 (KABAT)	LCDR2	GASNRAT
SEQ ID NO: 917 (CHOTHIA)	LCDR2	GAS
SEQ ID NO: 918 (KABAT)	LCDR3	GQSYSPFT
SEQ ID NO: 919 (CHOTHIA)	LCDR3	SYSYPF

Other Exemplary anti-GITR Antibodies and Agonists

[0529] In one embodiment, the anti-GITR antibody molecule is BMS-986156 (Bristol-Myers Squibb), also known as BMS 986156 or BMS986156. BMS-986156 and other anti-GITR antibodies are disclosed, *e.g.*, in US 9,228,016 and WO 2016/196792, incorporated by reference in their entirety. In one embodiment, the anti-GITR antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of BMS-986156, *e.g.*, as disclosed in ~~Table 12~~Table 12.

[0530] In one embodiment, the anti-GITR antibody molecule is MK-4166 or MK-1248 (Merck). MK-4166, MK-1248, and other anti-GITR antibodies are disclosed, *e.g.*, in US 8,709,424, WO 2011/028683, WO 2015/026684, and Mahne *et al. Cancer Res.* 2017; 77(5):1108-1118, incorporated by reference in their entirety. In one embodiment, the anti-GITR antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of MK-4166 or MK-1248.

[0531] In one embodiment, the anti-GITR antibody molecule is TRX518 (Leap Therapeutics). TRX518 and other anti-GITR antibodies are disclosed, *e.g.*, in US 7,812,135, US 8,388,967, US 9,028,823, WO 2006/105021, and Ponte J *et al. (2010) Clinical Immunology*; 135:S96, incorporated by reference in their entirety. In one embodiment, the anti-GITR antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of TRX518.

[0532] In one embodiment, the anti-GITR antibody molecule is INCAGN1876 (Incyte/Agenus). INCAGN1876 and other anti-GITR antibodies are disclosed, *e.g.*, in US 2015/0368349 and WO 2015/184099, incorporated by reference in their entirety. In one embodiment, the anti-GITR antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of INCAGN1876.

[0533] In one embodiment, the anti-GITR antibody molecule is AMG 228 (Amgen). AMG 228 and other anti-GITR antibodies are disclosed, *e.g.*, in US 9,464,139 and WO

2015/031667, incorporated by reference in their entirety. In one embodiment, the anti-GITR antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of AMG 228.

[0534] In one embodiment, the anti-GITR antibody molecule is INBRX-110 (Inhibrx). INBRX-110 and other anti-GITR antibodies are disclosed, *e.g.*, in US 2017/0022284 and WO 2017/015623, incorporated by reference in their entirety. In one embodiment, the GITR agonist comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of INBRX-110.

[0535] In one embodiment, the GITR agonist (*e.g.*, a fusion protein) is MEDI 1873 (MedImmune), also known as MEDI1873. MEDI 1873 and other GITR agonists are disclosed, *e.g.*, in US 2017/0073386, WO 2017/025610, and Ross *et al. Cancer Res* 2016; 76(14 Suppl): Abstract nr 561, incorporated by reference in their entirety. In one embodiment, the GITR agonist comprises one or more of an IgG Fc domain, a functional multimerization domain, and a receptor binding domain of a glucocorticoid-induced TNF receptor ligand (GITRL) of MEDI 1873.

[0536] Further known GITR agonists (*e.g.*, anti-GITR antibodies) include those described, *e.g.*, in WO 2016/054638, incorporated by reference in its entirety.

[0537] In one embodiment, the anti-GITR antibody is an antibody that competes for binding with, and/or binds to the same epitope on GITR as, one of the anti-GITR antibodies described herein.

[0538] In one embodiment, the GITR agonist is a peptide that activates the GITR signaling pathway. In one embodiment, the GITR agonist is an immunoadhesin binding fragment (*e.g.*, an immunoadhesin binding fragment comprising an extracellular or GITR binding portion of GITRL) fused to a constant region (*e.g.*, an Fc region of an immunoglobulin sequence).

Table 12. Amino acid sequences of other exemplary anti-GITR antibody molecules

BMS-986156		
SEQ ID NO: 920	VH	QVQLVESGGGVVQPGRSLRLSCAASGFTFSSYGMHWVRQAPGKGL EWVAVIWYEGSNKYYADSVKGRFTISRDN SKNTLYLQMNSLRAED TAVYYCARGGSMVRGDYYYGMDVWGQGTTVTVSS
SEQ ID NO: 921	VL	AIQLTQSPSSLASVSGDRVTITCRASQGISSALAWYQQKPGKAPKLLI YDASSLESQVPSRFSGSGSGTDFLTISLQPEDFATYYCQQFNSYPY TFGQGTKLEIK

Exemplary anti-CD3 multispecific antibody molecules

[0539] In certain embodiments, the anti-human ENTPD2 antibody molecule described herein is administered in combination with an anti-CD3 multispecific antibody molecule (e.g., an anti-CD3 bispecific antibody molecule). In one embodiment, the anti-CD3 multispecific antibody molecule binds to CD3 and a target tumor antigen (TTA). In one embodiment, the TTA is chosen from CD19, CD20, CD38, or CD123. In one embodiment, the anti-CD3 multispecific antibody molecule is in a format disclosed in FIGs 1A, 1B, 1C, and 125 of WO 2016/182751, herein incorporated by reference in its entirety.

[0540] In one embodiment, the anti-CD3 multispecific antibody molecule is an anti-CD3 x anti-CD123 bispecific antibody molecule, e.g., XENP14045 (e.g., as set out in Table 15) or an anti-CD3 x anti-CD123 bispecific antibody molecule disclosed in WO 2016/086189 or WO 2016/182751, herein incorporated by reference in their entirety. In one embodiment, the anti-CD3 x anti-CD123 bispecific antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of XENP14045, or an amino acid sequence substantially identical thereto (e.g., a sequence having at least about 85%, 90%, or 95% sequence identity thereto).

[0541] In one embodiment, the anti-CD3 multispecific antibody is an anti-CD3 x anti-CD20 bispecific antibody molecule, e.g., XENP13676 (e.g., as set out in Table 13) or an anti-CD3 x anti-CD20 bispecific antibody molecule disclosed in WO 2016/086189 or WO 2016/182751, herein incorporated by reference in their entirety. In one embodiment, the anti-CD3 x anti-CD20 bispecific antibody molecule comprises one or more of the CDR sequences (or collectively all of the CDR sequences), the heavy chain or light chain variable region sequence, or the heavy chain or light chain sequence of XENP13676, or an amino acid sequence substantially identical thereto (e.g., a sequence having at least about 85%, 90%, or 95% sequence identity thereto).

Table 13. Amino acid sequences of exemplary anti-CD3 bispecific antibody molecules

XENP14045 (anti-CD123 x anti-CD3 Fab-scFv-Fc)		
SEQ ID NO: 314	Heavy chain 1 (anti-CD123 Fab-Fc)	QVQLQQSGAEVKKPGASVKVSCKASGYTFTDYYMKWVKQSHGKS LEWMGDIIPSNNGATFYNQKFKGKATLTVD RSTSTAYMELSSLRSED TAVYYCARSHLLRASWFAYWGQGLTVTVSSASTKGPSVFPLAPSSK STSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSSGL YSLSSVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKTHT CPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEV KFNWYVDGVEVHNAKTKPREEEYNSTYRVVSVLTVLHQDWLNGK EYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKNQVS

		LTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYSKLT VDKSRWEQGDVFSCSVMEALHNHYTQKSLSLSPGK
SEQ ID NO: 315	Heavy chain 2 (anti-CD3 scFv-Fc)	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGL EWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRA EDTAVYYCVRHGNFGDSYVSWFAYWGQGLTVTVSSGKPGSGKPG SGKPGSGKPGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYA NWWQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQ PEDEADYYCALWYSNHWFVGGGKTLTVLEPKSSDKTHTCPPCPAP PVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV SNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVK GFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSR WQQGNVFSCSVMEALHNHYTQKSLSLSPGK
SEQ ID NO: 316	Light chain	DFVMTQSPDSLAVSLGERATINCKSSQSLNTGNQKNYLTWYQQKP GQPPKLLIYWASTRESGVPDRFTGSGSGTDFTLTISSLQAEDVAVYY CQNDYSYPYTFGGGTGLEIKRTVAAPSVFIFPPSDEQLKSGTASVVC LLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSYSTLSSTLT LSKADYEEKHKVYACEVTHQGLSSPVTKSFNRGEC
XENP13676 (anti- CD20 x anti-CD3 Fab-scFv-Fc)		
SEQ ID NO: 317	Heavy chain 1 (Fab-Fc)	QVQLVQSGAEVKKPGASVKVSCKASGYTFTSYNMHWVRQAPGQG LEWMGAIYPGNGDTSYNQKFQGRVTITADKSISTAYMELSSLRSED TAVYYCARSTYYGGDWYFNVWGAGTLTVTVSSASTKGPSVFPLAPS SKSTSGGTAALGCLVKDYFPEPVTVSWNSGALTSGVHTFPAVLQSS GLYSLSSVTVPSSSLGTQTYICNVNHKPSDTKVDKKVEPKSCDKT HTCPPCPAPPVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDP EVKFNWYVDGVEVHNAKTKPREEYNSTYRVVSVLTVLHQDWLNG KEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSREEMTKN QVSLTCDVSGFYPSDIAVEWESDGPENNYKTPPVLDSDGSFFLYS KLTVDKSRWEQGDVFSCSVMEALHNHYTQKSLSLSPGK
SEQ ID NO: 318	Heavy chain 2 (scFv-Fc)	EVQLVESGGGLVQPGGSLRLSCAASGFTFSTYAMNWVRQAPGKGL EWVGRIRSKYNNYATYYADSVKGRFTISRDDSKNTLYLQMNSLRA EDTAVYYCVRHGNFGDSYVSWFAYWGQGLTVTVSSGKPGSGKPG SGKPGSGKPGSQAVVTQEPSLTVSPGGTVTLTCGSSTGAVTTSNYA NWWQKPGKSPRGLIGGTNKRAPGVPARFSGSLLGGKAALTISGAQ PEDEADYYCALWYSNHWFVGGGKTLTVLEPKSSDKTHTCPPCPAP PVAGPSVFLFPPKPKDTLMISRTPEVTCVVVDVKHEDPEVKFNWYV DGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKV SNKALPAPIEKTISKAKGQPREPQVYTLPPSREQMTKNQVKLTCLVK GFYPSDIAVEWESNGQPENNYKTPPVLDSDGSFFLYSKLTVDKSR WQQGNVFSCSVMEALHNHYTQKSLSLSPGK
SEQ ID NO: 319	Light chain	QIVLTQSPSSLSASVGDRTITCRASSSVSYIHWFQKPGKSPKPLIY ATSNLASGVPVRFSGSGSDTYTLTISSLQPEDFATYYCQQWTSNPP TFGGGTKEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPRE AKVQWKVDNALQSGNSQESVTEQDSKDSYSTLSSTLTLSKADYEEK HKVYACEVTHQGLSSPVTKSFNRGEC

IL15/IL-15Ra complexes

[0542] In certain embodiments, the anti-human ENTPD2 antibody as described herein is administered in combination with an IL-15/IL-15Ra complex. In some embodiments, the IL-15/IL-15Ra complex is chosen from NIZ985 (Novartis), ATL-803 (Altor) or CYP0150 (Cytune).

Exemplary IL-15/IL-15Ra complexes

[0543] In one embodiment, the IL-15/IL-15Ra complex comprises human IL-15 complexed with a soluble form of human IL-15Ra. The complex may comprise IL-15 covalently or noncovalently bound to a soluble form of IL-15Ra. In a particular embodiment, the human IL-15 is noncovalently bonded to a soluble form of IL-15Ra. In a particular embodiment, the human IL-15 of the composition comprises an amino acid sequence of SEQ ID NO: 1001 in Table 14 and the soluble form of human IL-15Ra comprises an amino acid sequence of SEQ ID NO:1002 in Table 14, as described in WO 2014/066527, incorporated by reference in its entirety. The molecules described herein can be made by vectors, host cells, and methods described in WO 2007/084342, incorporated by reference in its entirety.

Table 14. Amino acid and nucleotide sequences of exemplary IL-15/IL-15Ra complexes

NIZ985		
SEQ ID NO: 1001	Human IL-15	NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCCKVTAMKCFLEL QVISLESGDASIHDTVENLIILANNSLSSNGNVTESGCKECEEEEEKNI KEFLQSFVHIVQMFINTS
SEQ ID NO: 1002	Human Soluble IL-15Ra	ITCPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLN KATNVAHWTTPSLKCIKDPALVHQRPAAPPSTVTTAGVTPQPESLSPSG KEPAASSPSSNNTAATTAAIVPGSQLMPSPKSPSTGTTEISSHESHGTPS QTTAKNWELTASASHQPPGVYPQG

Other exemplary IL-15/IL-15Ra complexes

[0544] In one embodiment, the IL-15/IL-15Ra complex is ALT-803, an IL-15/IL-15Ra Fc fusion protein (IL-15N72D:IL-15RaSu/Fc soluble complex). ALT-803 is disclosed in WO 2008/143794, incorporated by reference in its entirety. In one embodiment, the IL-15/IL-15Ra Fc fusion protein comprises the sequences as disclosed in Table 15.

[0545] In one embodiment, the IL-15/IL-15Ra complex comprises IL-15 fused to the sushi domain of IL-15Ra (CYP0150, Cytune). The sushi domain of IL-15Ra refers to a domain beginning at the first cysteine residue after the signal peptide of IL-15Ra, and ending at the fourth cysteine residue after said signal peptide. The complex of IL-15 fused to the sushi domain of IL-15Ra is disclosed in WO 2007/04606 and WO 2012/175222, incorporated by reference in their entirety. In one embodiment, the IL-15/IL-15Ra sushi domain fusion comprises the sequences as disclosed in Table 15.

[0546] In one embodiment, the IL-15/IL-15Ra complex comprises a fusion protein of IL-15 and IL-15Ra, which may further comprise a linker, particularly a glycine-serine linker,

connecting the IL-15 and IL-15Ra as disclosed in WO 2014/186469 (Board of Regents, the University of Texas System), incorporated by reference in its entirety. In one embodiment, the IL-15/IL-15Ra fusion protein comprises the sequence as disclosed in Table 15.

[0547] In one embodiment, the IL-15/IL-15Ra complex comprises a fusion protein of a sushi domain of IL-15Ra and IL-15, linked by a glycine-serine linker, as disclosed in WO 2015/109124 (Kadmon Corp.), incorporated by reference in its entirety. In one embodiment, the IL-15/IL-15Ra fusion protein comprises the sequence as disclosed in Table 15.

[0548] In one embodiment, the IL-15/IL-15Ra complex comprises a fusion protein of IL-15, IL-15Ra, a Fc domain and a RGD peptide, preferably configured as RGD polypeptide-Fc domain-IL-15 polypeptide-IL-15Ra polypeptide, as disclosed in WO 2017/000913 (Numab Biopharmaceuticals), incorporated by reference in its entirety. In one embodiment, the RGD -Fc-IL-15-IL-15Ra fusion protein comprises the sequence as disclosed in Table 15.

[0549] In one embodiment, the IL-15/IL-15Ra complex comprises a heterodimeric protein comprising IL-15 linked to a first Fc domain and IL-15Ra linked to a second Fc domain. The IL-15 is the mature form of human IL-15 and the IL-15Ra is the extracellular domain of human IL-15Ra or a truncated variant thereof such as IL-15Ra-sushi. The two Fc domains may comprise mutations to enable heterodimer formation via “Knob-into-Hole” interactions and exemplary constructs are disclosed in WO 2015/103928 (Jiangsu Hendrui Medicine Co), incorporated by reference in its entirety.

[0550] In one embodiment, the IL-15/IL-15Ra complex comprises a combination of IL-15 comprising a cys amino acid mutation and IL-15Ra (extracellular or sushi domain thereof) comprising a cys mutation to facilitate the formation of intramolecular disulfide bonds between the polypeptides. Sequences of IL-15 and IL-15Ra with mutation combinations are disclosed in WO 2016/095642 (Jiangsu Hendrui Medicine Co), incorporated by reference in its entirety.

[0551] In one embodiment, the IL-15/IL-15Ra complex comprises a heterodimeric protein comprising IL-15 linked to a first Fc domain and IL-15Ra linked to a second Fc domain. The first and second Fc domains may have a set of amino acid substitutions as listed: S267K/L368D/K370S; S267K/LS364K/E357Q; S364K/E357Q; L36HD/K370S; L36HD/K370S; S364K; L36HE/K370S; S364K; T411T/E360E/Q362E; D401K; L368D/K370S; S364K/E357L and K370S; S364K/E357Q, according to EU numbering, and in addition may comprise further amino acid substitutions and substitutions to ablate Fcγ receptor binding as disclosed in WO 2018/071919 (Xencor, Inc.), incorporated by reference in its entirety.

Table 15. Amino acid sequences of other exemplary IL-15/IL-15Ra complexes

ALT-803 (Altor)		
SEQ ID NO: 1003	IL-15N72D	NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLELQVISLESGDASIHTVENLIILANDSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS
SEQ ID NO: 1004	IL-15RaSu/ Fc	ITCPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIREPKSCDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGK
IL-15 / IL-15Ra sushi domain fusion (Cytune)		
SEQ ID NO: 1005	Human IL-15	NWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLELQVISLESGDASIHTVENLIILANNSLSSNGNVTESGCKECEELEEXKNIKEFLQSFVHIVQMFINTS Where X is E or K
SEQ ID NO: 1006	Human IL-15Ra sushi and hinge domains	ITCPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIRDPAHVHQRPAAPP
IL-15 / IL-15Ra fusion protein (University of Texas)		
SEQ ID NO: 1007	IL-15/IL-15Ra fusion protein with Gly-Ser linker	MDWTWILFLVAAATRVHSNWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLELQVISLESGDASIHTVENLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTSSGGGSGGGGSGGGGSGGGGSGGGSLQITCPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIRDPAHVHQRPAAPPSTVTAGVTPQPESLSPSGKEPAASSPSSNNTAATTAAIVPGSQLMPSKSPSTGTTEISSHESSHGTPSQTTAKNWELTASASHQPPGVYPQGHSDTTVAISTSTVLLCGLSAVSLACYLKSRQTPPLASVEMEAMEALPVTWGTSSRDEDLNCSHHLRMDYKDDDDKDYKDDDDKDYKDDDDK
IL-15Ra / IL-15 fusion protein (Kadmon Corp.)		
SEQ ID NO: 1008	Sushi-IL-15Ra/ IL-15 fusion protein with Gly-Ser linker	CPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIRDPAHVHQRPAAPPSSGGSGGGSGGGSGGGSLQNWVNVISDLKKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLELQVISLESGDASIHTVENLIILANNSLSSNGNVTESGCKECEELEEKNIKEFLQSFVHIVQMFINTS
RGD -Fc-IL-15-IL-15Ra fusion protein (Numab Biopharmaceuticals)		
SEQ ID NO: 1009	RGD-Fc-IL-15-IL-15Ra	ACDCRGDCFCGGGGGSDKTHTCPPCPAPELLGGPSVFLFPPKPKDTLMISRTPEVTCVVVDVSHEDPEVKFNWYVDGVEVHNAKTKPREEQYNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKALPAPIEKTISKAKGQPREPQVYTLPPSRDELTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPPVLDSDGSFFLYSKLTVDKSRWQQGNVFCFSVMHEALHNHYTQKSLSLSPGKGGGGSPPPMSVEHADIWVKSYSLYSRERYICNSGFKRKAGTSSLTECVLNKATNVAHWTTPSLKCIRDPAHVH

		QRPAPPSTVSGGSGGGSGGGSGGGGSLQNWVNVISDL KKIEDLIQSMHIDATLYTESDVHPSCKVTAMKCFLLQLV ISLESGDASIHTVENLIILANNSLSSNGNVTESGCKECEE LEEKNIKEFLQSFVHIVQMFINTS

Exemplary CSF-1/1R Binding Agents

[0552] In certain embodiments, the anti-human ENTPD2 antibody molecule described herein is administered in combination with a CSF-1/1R binding agent.

[0553] In some embodiments, the CSF-1/1R binding agent is an inhibitor of macrophage colony-stimulating factor (M-CSF). M-CSF is also sometimes known as CSF-1.

[0554] In another embodiment, the CSF-1/1R binding agent is a CSF-1R tyrosine kinase inhibitor, 4-((2-(((1R,2R)-2-hydroxycyclohexyl)amino)benzo[d]thiazol-6-yl)oxy)-N-methylpicolinamide (Compound A15), or a compound disclosed in PCT Publication No. WO 2005/073224. In some embodiments, the CSF-1/1R binding agent is an M-CSF inhibitor, Compound A33, or a binding agent to CSF-1 disclosed in PCT Publication No. WO 2004/045532 or PCT Publication No WO 2005/068503 including RX1 or 5H4 (*e.g.*, an antibody molecule or Fab fragment against M-CSF).

[0555] In some embodiments, the CSF-1/1R binding agent is a CSF1R inhibitor or 4-(2-(((1R, 2R)-2-hydroxycyclohexylamino)benzothiazol-6-yloxy)-N-methylpicolinamide. 4-(2-(((1R, 2R)-2-hydroxycyclohexylamino)benzothiazol-6-yloxy)-N-methylpicolinamide is disclosed as example 157 at page 117 of PCT Publication No. WO 2007/121484.

[0556] In some embodiments, the CSF-1/1R binding agent is pexidartinib (CAS Registry Number 1029044-16-3). Pexidartinib is also known as PLX3397 or 5-((5-chloro-1H-pyrrolo[2,3-b]pyridin-3-yl)methyl)-N-((6-(trifluoromethyl)pyridin-3-yl)methyl)pyridin-2-amine. Pexidartinib is a small-molecule receptor tyrosine kinase (RTK) inhibitor of KIT, CSF1R and FLT3.

[0557] In some embodiments, the CSF-1/1R binding agent is emactuzumab. Emactuzumab is also known as RG7155 or RO5509554. Emactuzumab is a humanized IgG1 mAb targeting CSF1R.

[0558] In some embodiments, the CSF-1/1R binding agent is FPA008. FPA008 is a humanized mAb that inhibits CSF1R.

Exemplary IDO/TDO Inhibitors

[0559] In certain embodiments, the anti-human ENTPD2 antibody molecule described herein is administered in combination with an inhibitor of indoleamine 2,3-dioxygenase (IDO) and/or tryptophan 2,3-dioxygenase (TDO).

[0560] In some embodiments, the IDO/TDO inhibitor is chosen from (4E)-4-[(3-chloro-4-fluoroanilino)-nitrosomethylidene]-1,2,5-oxadiazol-3-amine (also known as INCB24360 or Epacadostat; CAS Registry Number: 1204669-58-8 (Incyte)), Indoximod (1-methyl-D-tryptophan), α -cyclohexyl-5H-Imidazo[5,1-a]isoindole-5-ethanol (also known as NLG919) or BMS-986205 (also known as F001287 or ONO-7701).

[0561] In some embodiments, the IDO/TDO inhibitor is Epacadostat. It is a potent and selective indoleamine 2,3-dioxygenase (IDO1) inhibitor with an IC_{50} of 10 nM. Epacadostat is highly selective over other related enzymes such as IDO2 or tryptophan 2,3-dioxygenase (TDO).

[0562] In some embodiments, the IDO/TDO inhibitor is Indoximod (New Link Genetics). Indoximod, the D isomer of 1-methyl-tryptophan, is an orally administered small-molecule indoleamine 2,3-dioxygenase (IDO) pathway inhibitor that disrupts the mechanisms by which tumors evade immune-mediated destruction. NLG919 is a potent IDO pathway inhibitor with a K_i/EC_{50} of 7nM/75nM, respectively, in cell free assays.

[0563] In some embodiments, the IDO/TDO inhibitor is BMS-986205 (also known as F001287 or ONO-7701) (Flexus/BMS). BMS-986205 is a small molecule inhibitor of indoleamine 2,3-dioxygenase 1 (IDO1).

Exemplary TGF- β Inhibitors

[0564] In certain embodiments, the anti-human ENTPD2 antibody molecule described herein is administered in combination with a transforming growth factor beta (TGF- β) inhibitor. The TGF- β inhibitor may be an antibody, an antigen binding fragment thereof, an immunoadhesin, a fusion protein, or an oligopeptide. In some embodiments, the TGF- β inhibitor is chosen from fresolimumab and XOMA 089 (Xoma).

[0565] TGF- β belongs to a large family of structurally-related cytokines including, *e.g.*, bone morphogenetic proteins (BMPs), growth and differentiation factors, activins and inhibins. In some embodiments, the TGF- β inhibitors described herein can bind and/or inhibit one or more isoforms of TGF- β (*e.g.*, one, two, or all of TGF- β 1, TGF- β 2, or TGF- β 3).

[0566] In some embodiments, the TGF- β inhibitor is fresolimumab (CAS Registry Number: 948564-73-6). Fresolimumab is also known as GC1008. Fresolimumab is a human monoclonal antibody that binds to and inhibits TGF-beta isoforms 1, 2 and 3. Fresolimumab is disclosed, *e.g.*, in WO 2006/086469, US 8,383,780, and US 8,591,901.

[0567] The heavy chain of fresolimumab has the amino acid sequence of:
 QVQLVQSGAEVKKPGSSVKVSCASGYTFSSNVISWVRQAPGQGLEWMGGVPIVDI
 ANYAQRFKGRVTITADESTSTTYMELSSLRSEDNAVYYCASTLGLVLDAMDYWGQG
 TLVTVSSASTKGPSVFPLAPCSRSTSESTAALGCLVKDYFPEPVTVSWNSGALTSGVH
 TTPAVLQSSGLYSLSSVTVPSSSLGKTYTCNVDPKPSNTKVDKRVESKYGPPCPSC
 PAPEFLGGPSVFLFPPKPKDTLMISRTPEVTCVVDVVSQEDPEVQFNWYVDGVEVHN
 AKTKPREEQFNSTYRVVSVLTVLHQDWLNGKEYKCKVSNKGLPSSIEKTISKAKGQP
 REPQVYTLPPSQEEMTKNQVSLTCLVKGFYPSDIAVEWESNGQPENNYKTTTPVLDS
 DGSFFLYSRLTVDKSRWQEGNVFSCSVMHEALHNHYTQKSLSLSLGK (SEQ ID NO:
 1012).

[0568] The light chain of fresolimumab has the amino acid sequence of:
 ETVLTQSPGTLSSLSPGERATLSCRASQSLGSSYLAWYQQKPGQAPRLLIYGASSRAPG
 IPDRFSGSGSGTDFTLTISRLEPEDFAVYYCQQYADSPITFGQGTRLEIKRTVAAPSVFI
 FPPSDEQLKSGTASVVCCLNNFYPREAKVQWKVDNALQSGNSQESVTEQDSKDSTY
 SLSSITLTLKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC (SEQ ID NO: 1013).

[0569] In some embodiments, the TGF- β inhibitor is XOMA 089. XOMA 089 is also known as XPA.42.089. XOMA 089 is a fully human monoclonal antibody that binds and neutralizes TGF-beta 1 and 2 ligands while sparing TGF-beta 3.

[0570] The heavy chain variable region of XOMA 089 has the amino acid sequence of:
 QVQLVQSGAEVKKPGSSVKVSCASGGTFSSYAISWVRQAPGQGLEWMGGIPIFGT
 ANYAQKFQGRVTITADESTSTAYMELSSLRSEDNAVYYCARGLWEVRALPSVYWGQ
 GTLVTVSS (SEQ ID NO: 310) (disclosed as SEQ ID NO: 6 in WO2012/167143).

[0571] The light chain variable region of XOMA 089 has the amino acid sequence of:
 SYELTQPPSVSVAPGQTARITCGANDIGSKSVHWYQQKAGQAPVLVVSIEDIIRPSGIP
 ERISGSNSGNTATLTISRVEAGDEADYYCQVWDRDSDQYVFGTGTKVTVLG (SEQ ID
 NO: 311) (disclosed as SEQ ID NO: 8 in WO2012/167143).

Exemplary VEGFR Inhibitors

[0572] In certain embodiments, the anti-human ENTPD2 antibody molecule described herein is administered in combination with a vascular endothelial growth factor (VEGF) receptor inhibitor (*e.g.*, an inhibitor of one or more of VEGFR (*e.g.*, VEGFR-1, VEGFR-2, or VEGFR-3) or VEGF).

[0573] In some embodiments, the VEGFR inhibitor is vatalanib succinate (Compound A47) or a compound disclosed in EP 296122.

[0574] In some embodiment, the VEGFR inhibitor is an inhibitor of one or more of VEGFR-2, PDGFRbeta, KIT or Raf kinase C, 1-methyl-5-((2-(5-(trifluoromethyl)-1H-imidazol-2-yl)pyridin-4-yl)oxy)-N-(4-(trifluoromethyl)phenyl)-1H-benzo[d]imidazol-2-amine (Compound A37) or a compound disclosed in PCT Publication No. WO 2007/030377.

[0575] Other exemplary VEGFR pathway inhibitors that can be used in the combinations disclosed herein include, *e.g.*, bevacizumab (AVASTIN®), axitinib (INLYTA®); brivanib alaninate (BMS-582664, (S)-((R)-1-(4-(4-Fluoro-2-methyl-1H-indol-5-yloxy)-5-methylpyrrolo[2,1-f][1,2,4]triazin-6-yloxy)propan-2-yl)2-aminopropanoate); sorafenib (NEXAVAR®); pazopanib (VOTRIENT®); sunitinib malate (SUTENT®); cediranib (AZD2171, CAS 288383-20-1); vandetanib (CAPRELSA® or AZD6474); motesanib diphosphate (AMG706, CAS 857876-30-3, N-(2,3-dihydro-3,3-dimethyl-1H-indol-6-yl)-2-[(4-pyridinylmethyl)amino]-3-pyridinecarboxamide, described in PCT Publication No. WO 02/066470); linfanib (ABT869, CAS 796967-16-3); cabozantinib (XL184, CAS 849217-68-1); lestaurtinib (CAS 111358-88-4); N-[5-[[[5-(1,1-dimethylethyl)-2-oxazolyl]methyl]thio]-2-thiazolyl]-4-piperidinecarboxamide (BMS38703, CAS 345627-80-7); (3R,4R)-4-amino-1-((4-((3-methoxyphenyl)amino)pyrrolo[2,1-f][1,2,4]triazin-5-yl)methyl)piperidin-3-ol (BMS690514); N-(3,4-Dichloro-2-fluorophenyl)-6-methoxy-7-[[3 α ,5 β ,6 α]-octahydro-2-methylcyclopenta[c]pyrrol-5-yl]methoxy]-4-quinazolinamine (XL647, CAS 781613-23-8); 4-methyl-3-[[1-methyl-6-(3-pyridinyl)-1H-pyrazolo[3,4-d]pyrimidin-4-yl]amino]-N-[3-(trifluoromethyl)phenyl]-benzamide (BHG712, CAS 940310-85-0); aflibercept (EYLEA®), and endostatin (ENDOSTAR®).

[0576] Exemplary anti-VEGF antibodies that can be used in the combinations disclosed herein include, *e.g.*, a monoclonal antibody that binds to the same epitope as the monoclonal anti-VEGF antibody A4.6.1 produced by hybridoma ATCC HB 10709; a recombinant humanized anti-VEGF monoclonal antibody generated according to Presta *et al.* (1997) Cancer Res. 57:4593-4599. In one embodiment, the anti-VEGF antibody is Bevacizumab (BV), also known as rhuMAb VEGF or AVASTIN®. It comprises mutated

human IgG1 framework regions and antigen-binding complementarity- determining regions from the murine anti-hVEGF monoclonal antibody A.4.6.1 that blocks binding of human VEGF to its receptors. Bevacizumab and other humanized anti-VEGF antibodies are further described in U.S. Pat. No. 6,884,879 issued Feb. 26, 2005. Additional antibodies include the G6 or B20 series antibodies (*e.g.*, G6-31, B20-4.1), as described in PCT Publication No. WO2005/012359, PCT Publication No. WO2005/044853. For additional antibodies, *see* U.S. Pat. Nos. 7,060,269, 6,582,959, 6,703,020, 6,054,297, WO98/45332, WO 96/30046, WO94/10202, EP 0666868B1, U.S. Patent Application Publication Nos. 2006/009360, 2005/0186208, 2003/0206899, 2003/0190317, 2003/0203409, and 2005/0112126; and Popkov *et al*, *Journal of Immunological Methods* 288: 149-164 (2004). Other antibodies include those that bind to a functional epitope on human VEGF comprising of residues F17, M18, D19, Y21, Y25, Q89, 191, K101, E103, and C104 or, alternatively, comprising residues F17, Y21, Q22, Y25, D63, 183 and Q89.

Exemplary EGFR Inhibitors

[0577] In some embodiments, the anti-human ENTPD2 antibody molecule, *e.g.*, the anti- ENTPD2 antibody molecule described herein, is used, in combination with a tyrosine kinase inhibitor (*e.g.*, a receptor tyrosine kinase (RTK) inhibitor). Exemplary tyrosine kinase inhibitor include, but are not limited to, an epidermal growth factor (EGF) pathway inhibitor (*e.g.*, an epidermal growth factor receptor (EGFR) inhibitor), a vascular endothelial growth factor (VEGF) pathway inhibitor (*e.g.*, a vascular endothelial growth factor receptor (VEGFR) inhibitor (*e.g.*, a VEGFR-1 inhibitor, a VEGFR-2 inhibitor, a VEGFR-3 inhibitor)), a platelet derived growth factor (PDGF) pathway inhibitor (*e.g.*, a platelet derived growth factor receptor (PDGFR) inhibitor (*e.g.*, a PDGFR- β inhibitor)), a RAF-1 inhibitor, a KIT inhibitor and a RET inhibitor. In certain embodiments, the anti-human ENTPD2 antibody molecule described herein is administered in combination with an inhibitor of Epidermal Growth Factor Receptor (EGFR).

[0578] In some embodiments, the EGFR inhibitor is (R,E)-N-(7-chloro-1-(1-(4-(dimethylamino)but-2-enoyl)azepan-3-yl)-1H-benzo[d]imidazol-2-yl)-2-methylisonicotinamide (Compound A40) or a compound disclosed in PCT Publication No. WO 2013/184757.

[0579] In some embodiments, the EGFR inhibitor is chosen from one of more of erlotinib (Tarceva®), gefitinib (Iressa®), cetuximab (Erbix®), panitumumab (Vectibix®),

necitumumab (Portrazza®), dacomitinib, nimotuzumab, Imgatuzumab, afatinib, or osimertinib (Tagrisso).

[0580] Other anticancer agents, e.g., tyrosine kinase inhibitors pathway inhibitors, that can be used in the combinations disclosed herein include, but are not limited to, Selected tyrosine kinase inhibitors are chosen from sunitinib (Sutent®), or sorafenib (Nexavar®).

[0581] In some embodiments, the anti-cancer agent used in combination with the hedgehog inhibitor is selected from the group consisting of: axitinib (AG013736), bosutinib (SKI-606), cediranib (RECENTIN™, AZD2171), dasatinib (SPRYCEL®, BMS-354825), erlotinib (TARCEVA®), gefitinib (IRESSA®), imatinib (Gleevec®, CGP57148B, STI-571), lestaurtinib (CEP-701), neratinib (HKI-272), nilotinib (TASIGNA®), semaxanib (semaxinib, SU5416), sunitinib (SUTENT®, SU11248), toceranib (PALLADIA®), vandetanib (ZACTIMA®, ZD6474), vatalanib (PTK787, PTK/ZK), trastuzumab (HERCEPTIN®), bevacizumab (AVASTIN®), rituximab (RITUXAN®), cetuximab (ERBITUX®), panitumumab (VECTIBIX®), ranibizumab (Lucentis®), nilotinib (TASIGNA®), sorafenib (NEXAVAR®), alemtuzumab (CAMPATH®), gemtuzumab ozogamicin (MYLOTARG®), ENMD-2076, PCI-32765, AC220, BIBW 2992 (TOVOK™), SGX523, PF-04217903, PF-02341066, PF-299804, BMS-777607, ABT-869, MP470, BIBF 1120 (VARGATEF®), AP24534, JNJ-26483327, MGCD265, DCC-2036, BMS-690154, CEP-11981, tivozanib (AV-951), OSI-930, MM-121, XL-184, XL-647, XL228, AEE788, AG-490, AST-6, BMS-599626, CUDC-101, PD153035, pelitinib (EKB-569), vandetanib (zactima), WZ3146, WZ4002, WZ8040, ABT-869 (linifanib), AEE788, AP24534 (ponatinib), AV-951(tivozanib), axitinib, BAY 73-4506 (regorafenib), brivanib alaninate (BMS-582664), brivanib (BMS-540215), cediranib (AZD2171), CP 673451, CYC116, E7080, Ki8751, masitinib (AB1010), MGCD-265, motesanib diphosphate (AMG-706), MP-470, OSI-930, Pazopanib Hydrochloride, PD173074, Sorafenib Tosylate(Bay 43-9006), SU 5402SU 5402, TSU-68 (SU6668)., vatalanib, XL880 (GSK1363089, EXEL-2880).

Exemplary c-MET Inhibitors

[0582] In certain embodiments, the anti-human ENTPD2 antibody molecule described herein is administered in combination with an inhibitor of c-MET.

[0583] In some embodiments, the c-MET inhibitor is Compound A17 or a compound described in U.S. Patent Nos. 7,767,675 and 8,420,645).

[0584] In some embodiments, the c-MET inhibitor is JNJ-38877605. JNJ-38877605 is an orally available, small molecule inhibitor of c-Met. JNJ-38877605 selectively binds to

c-MET, thereby inhibiting c-MET phosphorylation and disrupting c-Met signal transduction pathways.

[0585] In some embodiments, the c-Met inhibitor is AMG 208. AMG 208 is a selective small-molecule inhibitor of c-MET. AMG 208 inhibits the ligand-dependent and ligand-independent activation of c-MET, inhibiting its tyrosine kinase activity, which may result in cell growth inhibition in tumors that overexpress c-Met.

[0586] In some embodiments, the c-Met inhibitor is AMG 337. AMG 337 is an orally bioavailable inhibitor of c-Met. AMG 337 selectively binds to c-MET, thereby disrupting c-MET signal transduction pathways.

[0587] In some embodiments, the c-Met inhibitor is LY2801653. LY2801653 is an orally available, small molecule inhibitor of c-Met. LY2801653 selectively binds to c-MET, thereby inhibiting c-MET phosphorylation and disrupting c-Met signal transduction pathways.

[0588] In some embodiments, c-Met inhibitor is MSC2156119J. MSC2156119J is an orally bioavailable inhibitor of c-Met. MSC2156119J selectively binds to c-MET, which inhibits c-MET phosphorylation and disrupts c-Met-mediated signal transduction pathways.

[0589] In some embodiments, the c-MET inhibitor is capmatinib. Capmatinib is also known as INCB028060. Capmatinib is an orally bioavailable inhibitor of c-MET. Capmatinib selectively binds to c-Met, thereby inhibiting c-Met phosphorylation and disrupting c-Met signal transduction pathways.

[0590] In some embodiments, the c-MET inhibitor is crizotinib. Crizotinib is also known as PF-02341066. Crizotinib is an orally available aminopyridine-based inhibitor of the receptor tyrosine kinase anaplastic lymphoma kinase (ALK) and the c-Met/hepatocyte growth factor receptor (HGFR). Crizotinib, in an ATP-competitive manner, binds to and inhibits ALK kinase and ALK fusion proteins. In addition, crizotinib inhibits c-Met kinase, and disrupts the c-Met signaling pathway. Altogether, this agent inhibits tumor cell growth.

[0591] In some embodiments, the c-MET inhibitor is golvatinib. Golvatinib is an orally bioavailable dual kinase inhibitor of c-MET and VEGFR-2 with potential antineoplastic activity. Golvatinib binds to and inhibits the activities of both c-MET and VEGFR-2, which may inhibit tumor cell growth and survival of tumor cells that overexpress these receptor tyrosine kinases.

[0592] In some embodiments, the c-MET inhibitor is tivantinib. Tivantinib is also known as ARQ 197. Tivantinib is an orally bioavailable small molecule inhibitor of c-MET. Tivantinib binds to the c-MET protein and disrupts c-Met signal transduction pathways,

which may induce cell death in tumor cells overexpressing c-MET protein or expressing constitutively activated c-Met protein.

Exemplary IAP Inhibitors

[0593] In certain embodiments, the anti-human ENTPD2 antibody molecule described herein is administered in combination with an inhibitor of Inhibitor of Apoptosis Protein (IAP).

[0594] In some embodiments, the IAP inhibitor is (S)-N-((S)-1-cyclohexyl-2-((S)-2-(4-(4-fluorobenzoyl)thiazol-2-yl)pyrrolidin-1-yl)-2-oxoethyl)-2-(methylamino)propanamide (Compound A21) or a compound disclosed in U.S. Patent No. 8,552,003.

Exemplary mTOR Inhibitors

[0595] In certain embodiments, the anti-human ENTPD2 antibody molecule described herein is administered in combination with an inhibitor of mammalian target of rapamycin (mTOR).

[0596] In some embodiments, the mTOR inhibitor is 8-(6-Methoxy-pyridin-3-yl)-3-methyl-1-(4-piperazin-1-yl-3-trifluoromethyl-phenyl)-1,3-dihydro-imidazo[4,5-c]quinolin-2-one (Compound A41).

[0597] In some embodiments, the mTOR inhibitor is everolimus (also known as RAD001 or AFINITOR®; Compound A36) or a compound first disclosed in PCT Publication No. WO 94/09010.

[0598] In some embodiments, the mTOR inhibitor is chosen from one or more of temsirolimus (TORISEL®), PF-4691502, GDC0980, OSI-027, GSK1059615, KU-0063794, WYE-354, Palomid 529 (P529), PF-04691502, gedatolisib (PF-05212384, PKI-587), ridaforolimus (formally known as deferolimus, (1R,2R,4S)-4-[(2R)-2-[(1R,9S,12S,15R,16E,18R,19R,21R, 23S,24E,26E,28Z,30S,32S,35R)-1,18-dihydroxy-19,30-dimethoxy-15,17,21,23, 29,35-hexamethyl-2,3,10,14,20-pentaoxo-11,36-dioxo-4-azatricyclo[30.3.1.0^{4,9}] hexatriaconta-16,24,26,28-tetraen-12-yl]propyl]-2-methoxycyclohexyl dimethylphosphinate, also known as AP23573 and MK8669, and described in PCT Publication No. WO 03/064383); rapamycin (AY22989, SIROLIMUS®); simapimod (CAS Registry Number: 164301-51-3); (5-{2,4-Bis[(3S)-3-methylmorpholin-4-yl]pyrido[2,3-d]pyrimidin-7-yl}-2-methoxyphenyl)methanol (AZD8055); 2-Amino-8-[trans-4-(2-hydroxyethoxy)cyclohexyl]-6-(6-methoxy-3-pyridinyl)-4-methyl-pyrido[2,3-d]pyrimidin-7(8H)-one (PF04691502, CAS Registry Number: 1013101-36-4); N2-[1,4-

dioxo-4-[[4-(4-oxo-8-phenyl-4H-1-benzopyran-2-yl)morpholinium-4-yl]methoxy]butyl]-L-arginylglycyl-L- α -aspartyl-L-serine inner salt (SF1126, CAS Registry Number: 936487-67-1) (SEQ ID NO: 1011), or XL765 (SAR245409).

Exemplary PI3K- γ , - δ Inhibitors

[0599] In certain embodiments, the anti-human ENTPD2 antibody molecule described herein is administered in combination with an inhibitor of phosphatidylinositol-4,5-bisphosphate 3-kinase (PI3K), *e.g.*, phosphatidylinositol-4,5-bisphosphate 3-kinase gamma and/or delta (PI3K- γ , δ).

[0600] In some embodiments, the PI3K inhibitor is an inhibitor of delta and gamma isoforms of PI3K. Exemplary PI3K inhibitors that can be used in combination are described in, *e.g.*, WO 2010/036380, WO 2010/006086, WO 09/114870, WO 05/113556. In some embodiments, the PI3K inhibitor is chosen from one or more of GSK 2126458, GDC-0980, GDC-0941, Sanofi XL147, XL756, XL147, PF-46915032, CAL-101, CAL 263, SF1126, PX-886, and a dual PI3K inhibitor.

[0601] In some embodiments, the PI3K- γ , δ inhibitor is idelalisib (CAS Registry Number: 870281-82-6). Idelalisib is also known as ZYDELIG®, GS-1101, CAL-101, or 5-Fluoro-3-phenyl-2-[(1S)-1-(7H-purin-6-ylamino)propyl]-4(3H)-quinazolinone. Idelalisib blocks P110 δ , the delta isoform of PI3K. Idelalisib is disclosed, *e.g.*, in Wu *et al. Journal of Hematology & Oncology* (2013) 6: 36.

[0602] In some embodiments, the PI3K- γ , δ inhibitor is 8-(6-Methoxy-pyridin-3-yl)-3-methyl-1-(4-piperazin-1-yl-3-trifluoromethyl-phenyl)-1,3-dihydro-imidazo[4,5-c]quinolin-2-one (Compound A41).

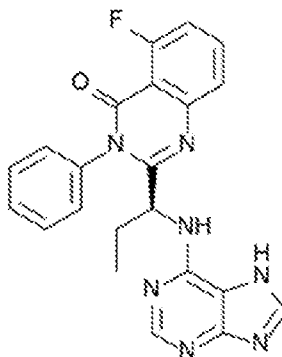
[0603] Other exemplary PI3K- γ , δ inhibitors that can be used in the combination include, *e.g.*, pictilisib (GDC-0941), LY294002, pilaralisib (XL147), PI-3065, PI-103, VS-5584 (SB2343), CZC24832, duvelisib (IPI-145, INK1197), TG100-115, CAY10505, GSK1059615, PF-04691502, AS-605240, voxtalisib (SAR245409, XL765), IC-87114, omipalisib (GSK2126458, GSK458), TG100713, gedatolisib (PF-05212384, PKI-587), PKI-402, XL147 analogue, PIK-90, PIK-293, PIK-294, 3-Methyladenine (3-MA), AS-252424, AS-604850, or apitolisib (GDC-0980, RG7422).

[0604] In some embodiments, the PI3K inhibitor is Compound A8 or a compound described in PCT Publication No. WO2010/029082.

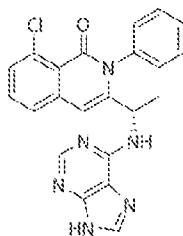
[0605] In some embodiments, the PI3K inhibitor is a pan-PI3K inhibitor, (4S,5R)-3-(2'-amino-2-morpholino-4'-(trifluoromethyl)-[4,5'-bipyrimidin]-6-yl)-4-(hydroxymethyl)-5-

methyloxazolidin-2-one (Compound A13) or a compound disclosed in PCT Publication No. WO2013/124826.

[0606] Exemplary PI3K- γ , - δ inhibitors include, but are not limited to, duvelisib and idelalisib. Idelalisib (also called GS-1101 or CAL-101; Gilead) is a small molecule that blocks the delta isoform of PI3K. The structure of idelalisib (5-Fluoro-3-phenyl-2-[(1*S*)-1-(7*H*-purin-6-ylamino)propyl]-4(3*H*)-quinazolinone) is shown below.



[0607] Duvelisib (also called IPI-145; Infinity Pharmaceuticals and Abbvie) is a small molecule that blocks PI3K- δ , γ . The structure of duvelisib (8-Chloro-2-phenyl-3-[(1*S*)-1-(9*H*-purin-6-ylamino)ethyl]-1(2*H*)-isoquinolinone) is shown below.



[0608] In one embodiment, the inhibitor is a dual phosphatidylinositol 3-kinase (PI3K) and mTOR inhibitor selected from 2-Amino-8-[*trans*-4-(2-hydroxyethoxy)cyclohexyl]-6-(6-methoxy-3-pyridinyl)-4-methyl-pyrido[2,3-*d*]pyrimidin-7(8*H*)-one (PF-04691502); *N*-[4-[[4-(Dimethylamino)-1-piperidinyl]carbonyl]phenyl]-*N'*-[4-(4,6-di-4-morpholinyl-1,3,5-triazin-2-yl)phenyl]urea (PF-05212384, PKI-587); apitolisib (GDC-0980, RG7422); 2,4-Difluoro-*N*-{2-(methoxy)-5-[4-(4-pyridazinyl)-6-quinolinyl]-3-pyridinyl}benzenesulfonamide (GSK2126458); 8-(6-methoxypyridin-3-yl)-3-methyl-1-(4-(piperazin-1-yl)-3-(trifluoromethyl)phenyl)-1*H*-imidazo[4,5-*c*]quinolin-2(3*H*)-one Maleic acid (NVP-BGT226); 3-[4-(4-Morpholinyl)pyrido[3',2':4,5]furo[3,2-*d*]pyrimidin-2-yl]phenol

(PI-103); 5-(9-isopropyl-8-methyl-2-morpholino-9H-purin-6-yl)pyrimidin-2-amine (VS-5584, SB2343); or N-[2-[(3,5-Dimethoxyphenyl)amino]quinoxalin-3-yl]-4-[(4-methyl-3-methoxyphenyl)carbonyl]aminophenylsulfonamide (XL765).

Exemplary JAK Inhibitors

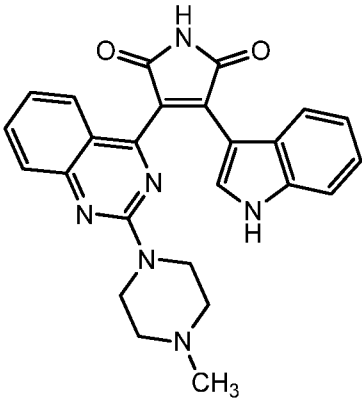
[0609] In certain embodiments, the anti-human ENTPD2 antibody molecule described herein is administered in combination with an inhibitor of Janus kinase (JAK).

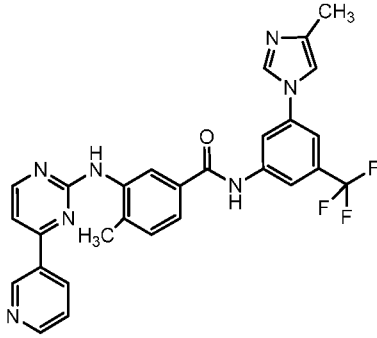
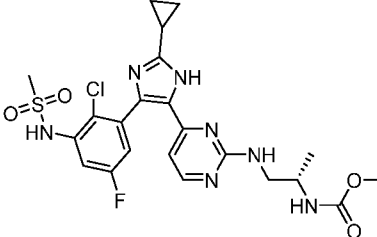
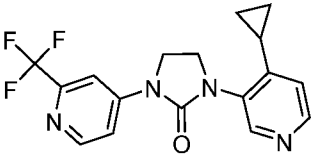
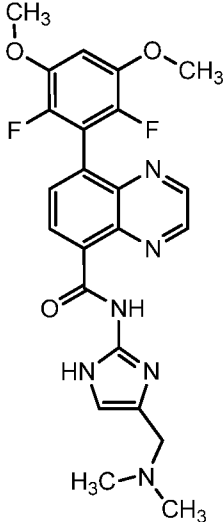
[0610] In some embodiments, the JAK inhibitor is 2-fluoro-N-methyl-4-(7-(quinolin-6-ylmethyl)imidazo[1,2-b][1,2,4]triazin-2-yl)benzamide (Compound A17), or a dihydrochloric salt thereof, or a compound disclosed in PCT Publication No. WO 2007/070514.

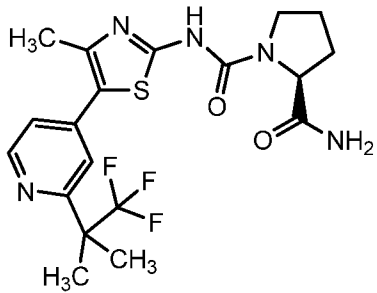
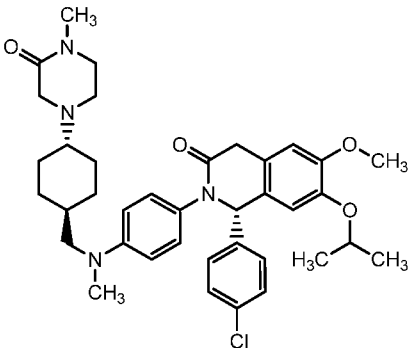
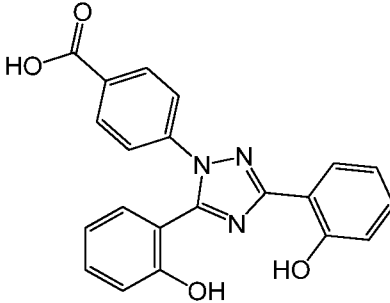
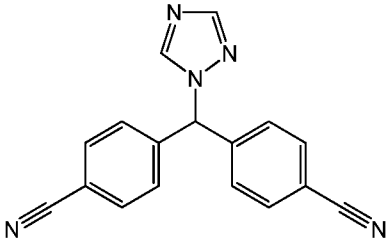
[0611] In some embodiment, the JAK inhibitor is ruxolitinib phosphate (also known as JAKAFI; Compound A18) or a compound disclosed in PCT Publication No. WO 2007/070514.

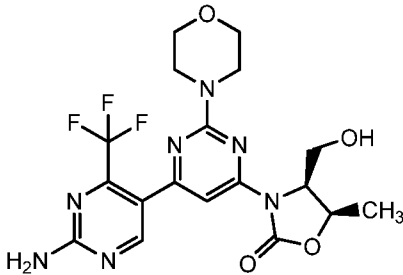
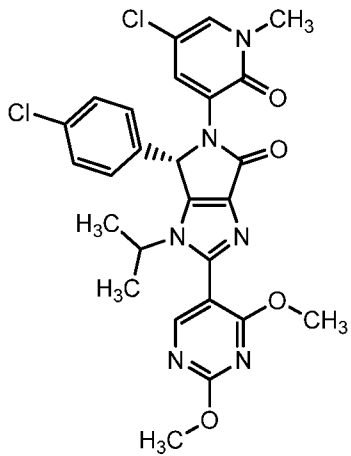
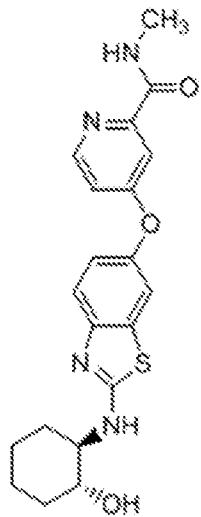
[0612] In certain embodiments, any of the combinations disclosed herein, alternatively or in combination, further includes one or more of the agents described in Table 16.

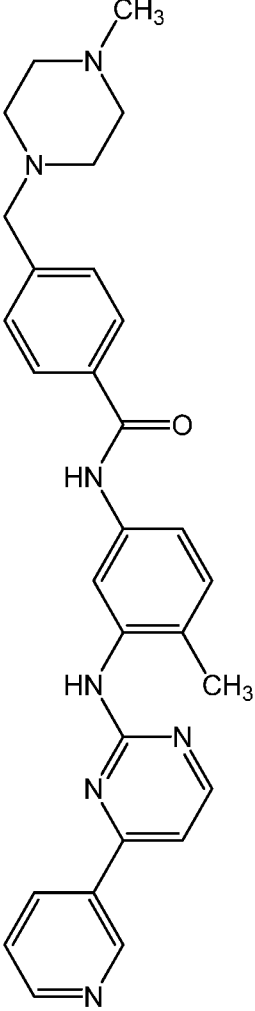
Table 16. Selected therapeutic agents that can be administered in combination with the anti-human ENTPD2 antibody molecules, e.g., as a single agent or in combination with other immunomodulators described herein. Each publication listed in this Table is herein incorporated by reference in its entirety, including all structural formulae therein.

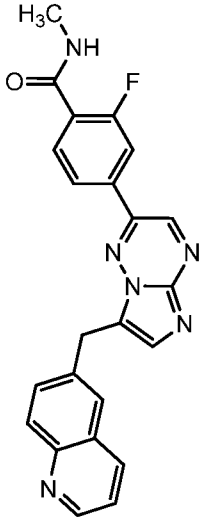
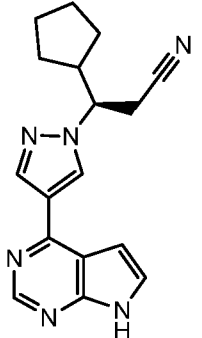
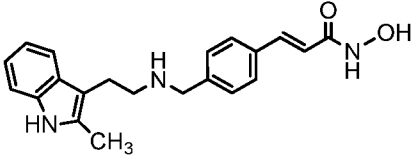
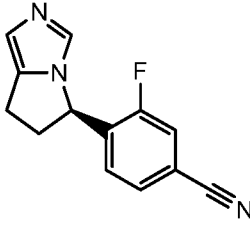
Compound Designation	Generic Name Tradename	Compound Structure	Patents / Patent Application Publications
A1	Sotrastaurin		EP 1682103 US 2007/142401 WO 2005/039549

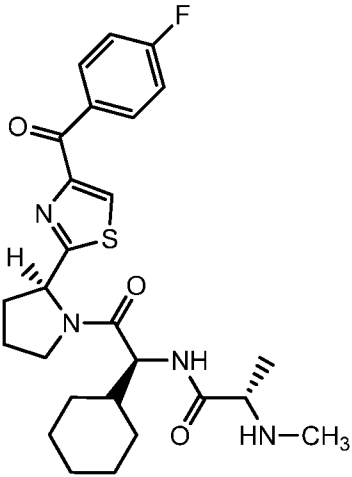
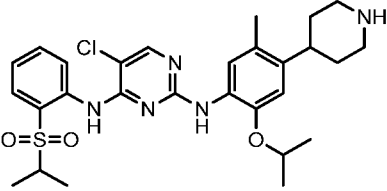
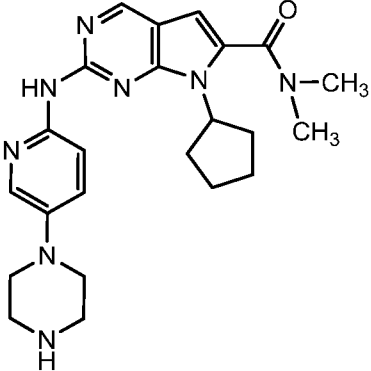
A2	Nilotinib HCl monohydrate TASIGNA®	 HCl • H ₂ O	WO 2004/005281 US 7,169,791
A3			WO2011/023773
A4			WO2012/149413
A7			WO 2009/141386 US 2010/0105667

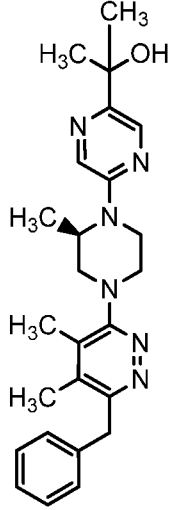
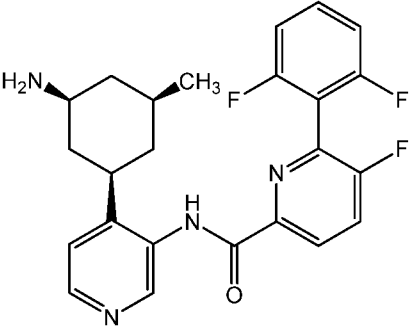
A8			WO 2010/029082
A10			WO 2011/076786
A11	Deferasirox EXJADE®		WO 1997/049395
A12	Letrozole FEMARA®		US 4,978,672

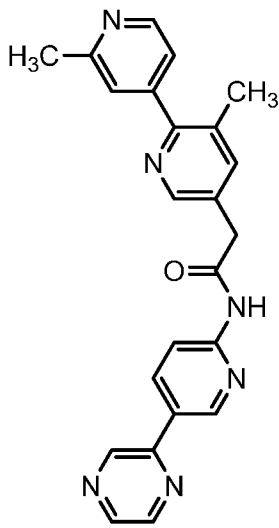
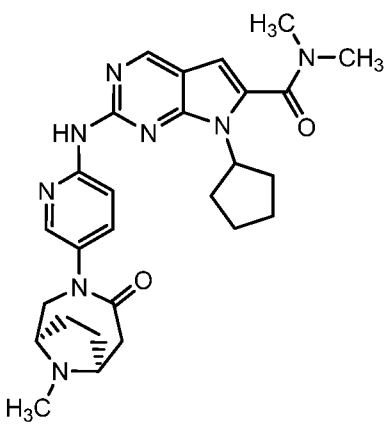
A13			WO 2013/124826 US 2013/0225574
A14			WO 2013/111105
A15			WO2007/121484

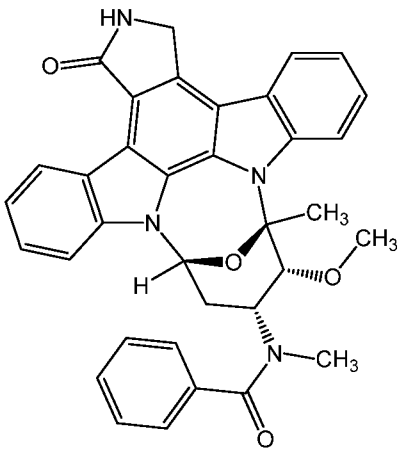
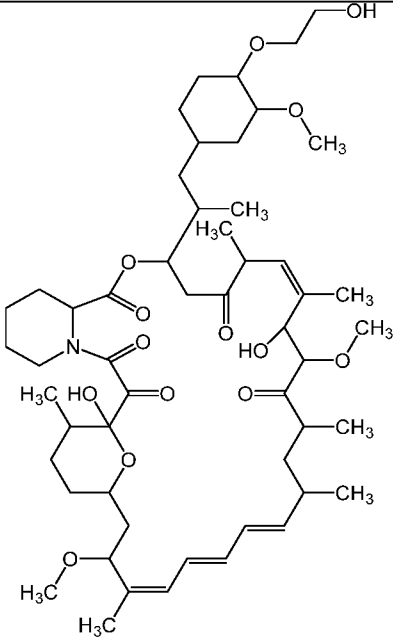
A16	Imatinib mesylate GLEEVEC®	 Mesylate	WO 1999/003854
A17			EP 2099447 US 7,767,675 US 8,420,645

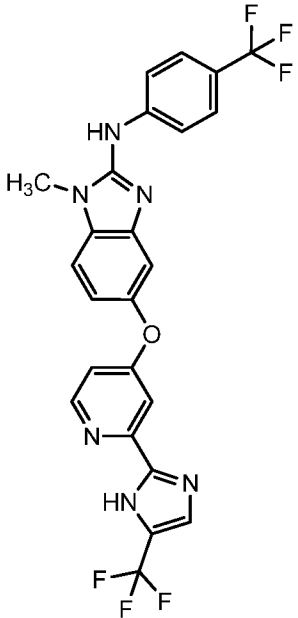
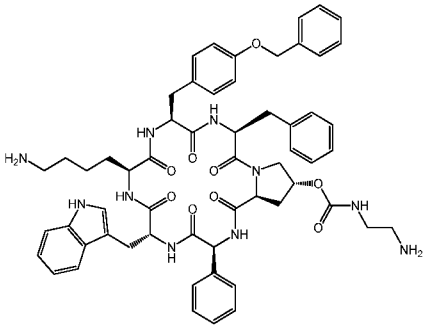
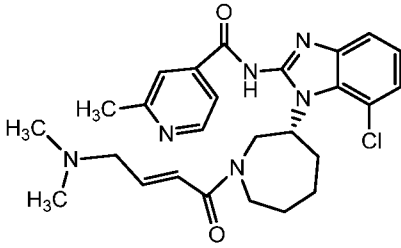
		 Dihydrochloric salt	
A18	Ruxolitinib Phosphate JAKAFI®	 H₃PO₄	WO 2007/070514 EP 2474545 US 7,598,257 WO 2014/018632
A19	Panobinostat		WO 2014/072493 WO 2002/022577 EP 1870399
A20	Osilodrostat		WO 2007/024945

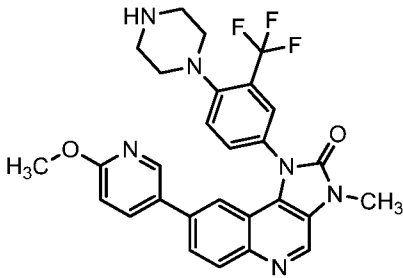
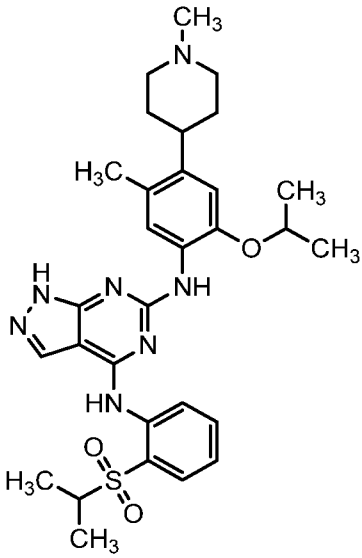
A21			WO 2008/016893 EP 2051990 US 8,546,336
A23	ceritinib ZYKADIA TM		WO 2008/073687 US 8,039,479
A24	Ribociclib KISQALI®		US 8,415,355 US 8,685,980

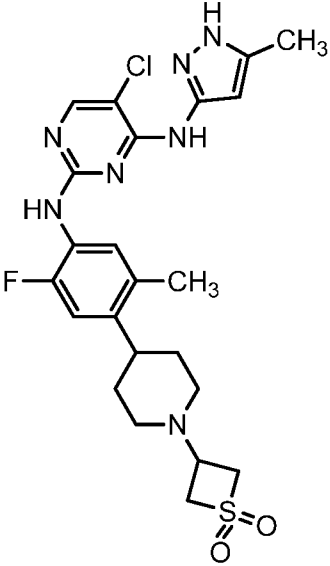
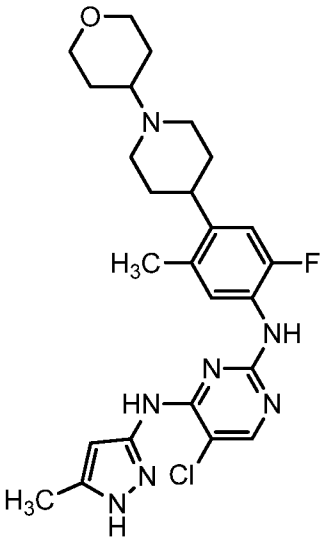
A25			WO 2010/007120
A26		Human monoclonal antibody to PRLR	US 7,867,493
A27			WO 2010/026124 EP 2344474 US 2010/0056576 WO2008/106692

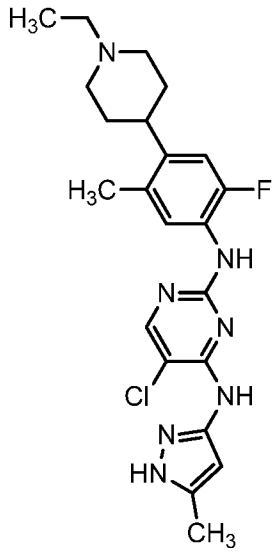
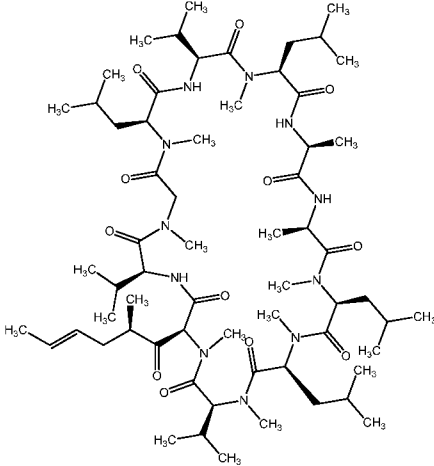
A28			WO 2010/101849
A30			WO 2011/101409
A31		Human monoclonal antibody to HER3	WO 2012/022814 EP 2606070 US 8,735,551
A32		Antibody Drug Conjugate (ADC)	WO 2014/160160 Ab: 12425 (<i>see</i> Table 1, paragraph [00191]) Linker: SMCC (<i>see</i> paragraph [00117]) Payload: DM1 (<i>see</i> paragraph [00117])

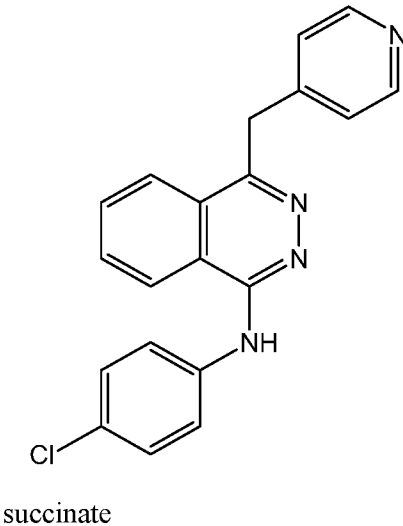
			[00111] See also Claim 29
A33		Monoclonal antibody or Fab to M-CSF	WO 2004/045532
A35	Midostaurin		WO 2003/037347 EP 1441737 US 2012/252785
A36	Everolimus AFINITOR [®]		WO 1994/009010 WO 2014/085318

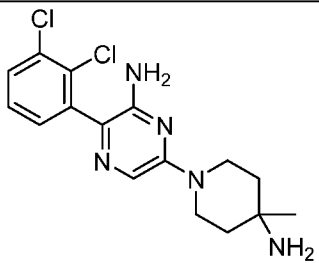
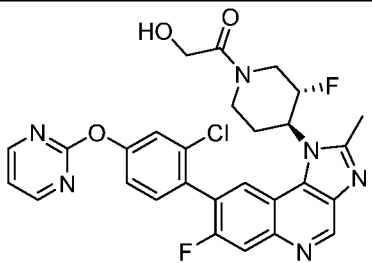
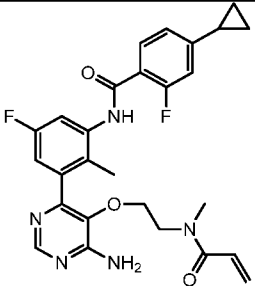
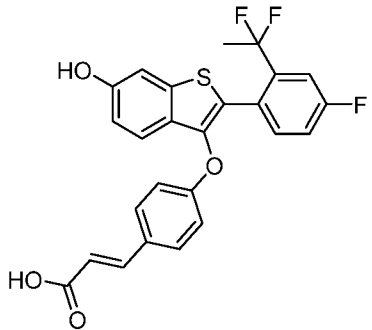
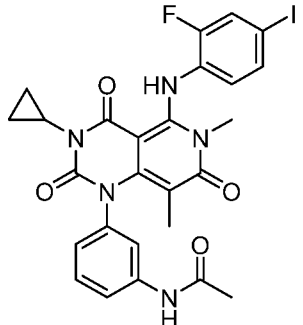
A37			WO 2007/030377 US 7,482,367
A38	Pasireotide diaspartate SIGNIFOR [®]		WO2002/010192 US 7,473,761
A40			WO 2013/184757

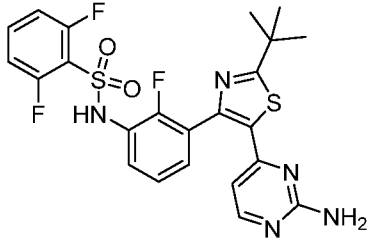
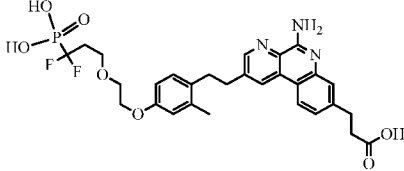
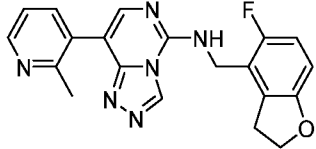
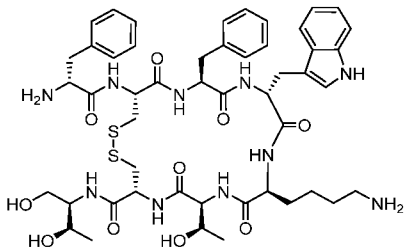
A41			WO 2006/122806
A42			WO 2008/073687 US 8,372,858

A43			WO 2010/002655 US 8,519,129
A44			WO 2010/002655 US 8,519,129

A45			WO 2010/002655
A46	Valspodar AMDRAY TM		EP 296122

A47	Vatalanib succinate	 succinate	WO 98/35958
A48		IDH inhibitor	WO2014/141104
A49	Asciminib	BCR-ABL inhibitor	WO2013/171639 WO2013/171640 WO2013/171641 WO2013/171642
A50		cRAF inhibitor	WO2014/151616
A51		ERK1/2 ATP competitive inhibitor	WO2015/066188
A52			WO2010/015613 WO2013030803 US 7,989,497
A53		or a choline salt thereof	WO2015/107493

			
A54			WO2015/022662
A55			US 9,512,084 WO/2015/079417
A56			WO2014/130310
A57	trametinib		WO2005/121142 US 7,378,423

A58	dabrafenib		WO 2009/137391 US 7,994,185
A59			WO2011/049677
A60			WO 2016/103155 US 9580437 EP 3237418
A61	octreotide		US 4,395,403 EP 0 029 579

[0613] The anti-human ENTPD2 antibody molecules as described herein can be administered in combination with an additional therapeutic agent. In some embodiments, the additional therapeutic agent is chosen from one or more of: 1) a protein kinase C (PKC) inhibitor; 2) a heat shock protein 90 (HSP90) inhibitor; 3) an inhibitor of a phosphoinositide 3-kinase (PI3K) and/or target of rapamycin (mTOR); 4) an inhibitor of cytochrome P450 (e.g., a CYP17 inhibitor or a 17 α -Hydroxylase/C17-20 Lyase inhibitor); 5) an iron chelating agent; 6) an aromatase inhibitor; 7) an inhibitor of p53, e.g., an inhibitor of a p53/Mdm2 interaction; 8) an apoptosis inducer; 9) an angiogenesis inhibitor; 10) an aldosterone synthase inhibitor; 11) a smoothened (SMO) receptor inhibitor; 12) a prolactin receptor (PRLR) inhibitor; 13) a Wnt signaling inhibitor; 14) a CDK4/6 inhibitor; 15) a fibroblast growth factor receptor 2 (FGFR2)/fibroblast growth factor receptor 4 (FGFR4) inhibitor; 16) an inhibitor of macrophage colony-stimulating factor (M-CSF); 17) an inhibitor of one or more of histamine release, Flt3 (e.g., FLK2/STK1) or PKC; 18) an inhibitor of one

or more of VEGFR-2 (e.g., FLK-1/KDR), PDGFRbeta, c-KIT or Raf kinase C; 19) a somatostatin agonist and/or a growth hormone release inhibitor; 20) an anaplastic lymphoma kinase (ALK) inhibitor; 21) an insulin-like growth factor 1 receptor (IGF-1R) inhibitor; 22) a P-Glycoprotein 1 inhibitor; 23) a vascular endothelial growth factor receptor (VEGFR) inhibitor; 24) a BCR-ABL kinase inhibitor; 25) an FGFR inhibitor; 26) an inhibitor of CYP11B2; 27) a HDM2 inhibitor, e.g., an inhibitor of the HDM2-p53 interaction; 28) an inhibitor of a tyrosine kinase; 29) an inhibitor of c-MET; 30) an inhibitor of JAK; 31) an inhibitor of DAC; 32) an inhibitor of 11 β -hydroxylase; 33) an inhibitor of IAP; 34) an inhibitor of PIM kinase; 35) an inhibitor of Porcupine; 36) an inhibitor of BRAF, e.g., BRAF V600E or wild-type BRAF; 37) an inhibitor of HER3; 38) an inhibitor of MEK; or 39) an inhibitor of a lipid kinase, e.g., as described herein and in Table 1.

[0614] In one embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with a PKC inhibitor, Sotrastaurin (Compound A1), or a compound disclosed in PCT Publication No. WO 2005/039549, to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the PKC inhibitor is Sotrastaurin (Compound A1) or a compound disclosed in PCT Publication No. WO 2005/039549.

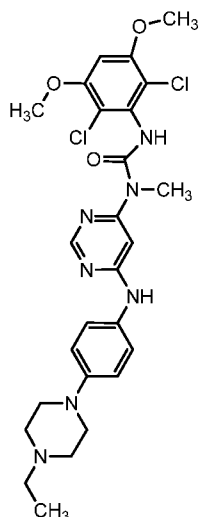
[0615] In one embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with a BCR-ABL inhibitor, nilotinib (Compound A2, Tasigna®), or a compound disclosed in PCT Publication No. WO 2004/005281, to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the BCR-ABL inhibitor is nilotinib, or a compound disclosed in PCT Publication No. WO 2004/005281.

[0616] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with an HSP90 inhibitor, to treat a disorder, *e.g.*, a disorder described herein, *e.g.*, a cancer.

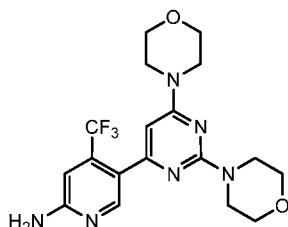
[0617] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, is used in combination with an inhibitor of PI3K and/or mTOR, 8-(6-Methoxy-pyridin-3-yl)-3-methyl-1-(4-piperazin-1-yl-3-trifluoromethyl-phenyl)-1,3-dihydro-imidazo[4,5-c]quinolin-2-one (Compound A41), to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the PI3K and/or mTOR

inhibitor is 8-(6-Methoxy-pyridin-3-yl)-3-methyl-1-(4-piperazin-1-yl-3-trifluoromethyl-phenyl)-1,3-dihydro-imidazo[4,5-c]quinolin-2-one (Compound A41).

[0618] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with an FGFR inhibitor, 3-(2,6-dichloro-3,5-dimethoxyphenyl)-1-(6-((4-(4-ethylpiperazin-1-yl)phenyl)amino)pyrimidin-4-yl)-1-methylurea (Compound A5) or a compound disclosed in US Patent 8,552,002, to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the FGFR inhibitor is 3-(2,6-dichloro-3,5-dimethoxyphenyl)-1-(6-((4-(4-ethylpiperazin-1-yl)phenyl)amino)pyrimidin-4-yl)-1-methylurea (Compound A5) or a compound disclosed in US Patent No. 8,552,002. Compound A5 has the following structure:



[0619] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with a PI3K inhibitor, Buparlisib (Compound A6), or a compound disclosed in PCT Publication No. WO 2007/084786, to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the PI3K inhibitor is Buparlisib (Compound A6) or a compound disclosed in PCT Publication No. WO 2007/084786. Compound A6 has the following structure:



a.

[0620] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with an FGFR inhibitor, 8-(2,6-difluoro-3,5-dimethoxyphenyl)-N-(4-((dimethylamino)methyl)-1H-imidazol-2-yl)quinoxaline-5-carboxamide (Compound A7) or a compound disclosed in PCT Publication No. WO 2009/141386 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the FGFR inhibitor is 8-(2,6-difluoro-3,5-dimethoxyphenyl)-N-(4-((dimethylamino)methyl)-1H-imidazol-2-yl)quinoxaline-5-carboxamide (Compound A7) or a compound disclosed in a PCT Publication No. WO 2009/141386.

[0621] In another embodiment the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with a PI3K inhibitor, (S)-N1-(4-methyl-5-(2-(1,1,1-trifluoro-2-methylpropan-2-yl)pyridin-4-yl)thiazol-2-yl)pyrrolidine-1,2-dicarboxamide (Compound A8) or a compound disclosed PCT Publication No. WO 2010/029082 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the PI3K inhibitor is (S)-N1-(4-methyl-5-(2-(1,1,1-trifluoro-2-methylpropan-2-yl)pyridin-4-yl)thiazol-2-yl)pyrrolidine-1,2-dicarboxamide (Compound A8) or a compound disclosed PCT Publication No. WO 2010/029082.

[0622] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with an inhibitor of cytochrome P450 (*e.g.*, a CYP17 inhibitor) or a compound disclosed in PCT Publication No. WO 2010/149755, to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the cytochrome P450 inhibitor (*e.g.*, the CYP17 inhibitor) is a compound disclosed in PCT Publication No. WO 2010/149755; US 8,263,635 B2; or EP 2445903 B1.

[0623] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with an HDM2 inhibitor, (S)-1-(4-chlorophenyl)-7-isopropoxy-6-methoxy-2-(4-(methyl(((1r,4S)-4-(4-methyl-3-oxopiperazin-1-yl)cyclohexyl)methyl)amino)phenyl)-1,2-

dihydroisoquinolin-3(4H)-one (Compound A10) or a compound disclosed in PCT Publication No. WO 2011/076786 to treat a disorder, *e.g.*, a disorder described herein). In one embodiment, the HDM2 inhibitor is (S)-1-(4-chlorophenyl)-7-isopropoxy-6-methoxy-2-(4-(methyl(((1r,4S)-4-(4-methyl-3-oxopiperazin-1-yl)cyclohexyl)methyl)amino)phenyl)-1,2-dihydroisoquinolin-3(4H)-one (Compound A10) or a compound disclosed in PCT Publication No. WO 2011/076786.

[0624] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with an iron chelating agent, Deferasirox (also known as EXJADE; Compound A11), or a compound disclosed in PCT Publication No. WO 1997/049395 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the iron chelating agent is Deferasirox or a compound disclosed in PCT Publication No. WO 1997/049395. In one embodiment, the iron chelating agent is Deferasirox (Compound A11).

[0625] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with an aromatase inhibitor, Letrozole (also known as FEMARA; Compound A12), or a compound disclosed in US 4,978,672 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the aromatase inhibitor is Letrozole (Compound A12) or a compound disclosed in US Patent 4,978,672.

[0626] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with a PI3K inhibitor, *e.g.*, a pan-PI3K inhibitor, (4S,5R)-3-(2'-amino-2-morpholino-4'-(trifluoromethyl)-[4,5'-bipyrimidin]-6-yl)-4-(hydroxymethyl)-5-methyloxazolidin-2-one (Compound A13) or a compound disclosed in PCT Publication No. WO2013/124826 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the PI3K inhibitor is (4S,5R)-3-(2'-amino-2-morpholino-4'-(trifluoromethyl)-[4,5'-bipyrimidin]-6-yl)-4-(hydroxymethyl)-5-methyloxazolidin-2-one (Compound A13) or a compound disclosed in PCT Publication No. WO2013/124826.

[0627] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with an inhibitor of p53 and/or a p53/Mdm2 interaction, (S)-5-(5-chloro-1-methyl-2-oxo-1,2-dihydropyridin-3-yl)-6-(4-chlorophenyl)-2-(2,4-dimethoxypyrimidin-5-yl)-1-isopropyl-5,6-dihydropyrrolo[3,4-d]imidazol-4(1H)-one (Compound A14), or a compound disclosed in PCT Publication No. WO2013/111105 to treat a disorder, *e.g.*, a disorder

described herein. In one embodiment, the p53 and/or a p53/Mdm2 interaction inhibitor is (S)-5-(5-chloro-1-methyl-2-oxo-1,2-dihydropyridin-3-yl)-6-(4-chlorophenyl)-2-(2,4-dimethoxypyrimidin-5-yl)-1-isopropyl-5,6-dihydropyrrolo[3,4-d]imidazol-4(1H)-one (Compound A14) or a compound disclosed in PCT Publication No. WO2013/111105.

[0628] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with a CSF-1R tyrosine kinase inhibitor, 4-((2-(((1R,2R)-2-hydroxycyclohexyl)amino)benzo[d]thiazol-6-yl)oxy)-N-methylpicolinamide (Compound A15), or a compound disclosed in PCT Publication No. WO 2005/073224 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the CSF-1R tyrosine kinase inhibitor is 4-((2-(((1R,2R)-2-hydroxycyclohexyl)amino)benzo[d]thiazol-6-yl)oxy)-N-methylpicolinamide (Compound A15) or a compound disclosed in PCT Publication No. WO 2005/073224.

[0629] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with an apoptosis inducer and/or an angiogenesis inhibitor, such as Imatinib mesylate (also known as GLEEVEC®; Compound A16) or a compound disclosed in PCT Publication No. WO1999/003854 to treat a disorder, *e.g.*, a disorder described. In one embodiment, the apoptosis inducer and/or an angiogenesis inhibitor is Imatinib mesylate (Compound A16) or a compound disclosed in PCT Publication No. WO1999/003854.

[0630] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with a JAK inhibitor, 2-fluoro-N-methyl-4-(7-(quinolin-6-ylmethyl)imidazo[1,2-b][1,2,4]triazin-2-yl)benzamide (Compound A17), or a dihydrochloric salt thereof, or a compound disclosed in PCT Publication No. WO 2007/070514, to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the JAK inhibitor is 2-fluoro-N-methyl-4-(7-(quinolin-6-ylmethyl)imidazo[1,2-b][1,2,4]triazin-2-yl)benzamide (Compound A17), or a dihydrochloric salt thereof, or a compound disclosed in PCT Publication No. WO 2007/070514.

[0631] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with a JAK inhibitor, Ruxolitinib Phosphate (also known as JAKAFI; Compound A18) or a compound disclosed in PCT Publication No. WO 2007/070514 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the JAK inhibitor is

Ruxolitinib Phosphate (Compound A18) or a compound disclosed in PCT Publication No. WO 2007/070514.

[0632] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with a deacetylase (DAC) inhibitor, Panobinostat (Compound A19), or a compound disclosed in PCT Publication No. WO 2014/072493 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the DAC inhibitor is Panobinostat (Compound A19) or a compound disclosed in PCT Publication No. WO 2014/072493.

[0633] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with an inhibitor of one or more of cytochrome P450 (*e.g.*, 11B2), aldosterone or angiogenesis, Osilodrostat (Compound A20), or a compound disclosed in PCT Publication No. WO2007/024945 to treat a disorder, *e.g.*, a disorder described herein.

[0634] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with a IAP inhibitor, (S)-N-((S)-1-cyclohexyl-2-((S)-2-(4-(4-fluorobenzoyl)thiazol-2-yl)pyrrolidin-1-yl)-2-oxoethyl)-2-(methylamino)propanamide (Compound A21) or a compound disclosed in US 8,552,003 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the IAP inhibitor is (S)-N-((S)-1-cyclohexyl-2-((S)-2-(4-(4-fluorobenzoyl)thiazol-2-yl)pyrrolidin-1-yl)-2-oxoethyl)-2-(methylamino)propanamide (Compound A21) or a compound disclosed in US Patent 8,552,003.

[0635] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination a Smoothened (SMO) inhibitor, (R)-2-(5-(4-(6-benzyl-4,5-dimethylpyridazin-3-yl)-2-methylpiperazin-1-yl)pyrazin-2-yl)propan-2-ol (Compound A25), or a compound disclosed in PCT Publication No. WO 2010/007120 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the SMO inhibitor is (R)-2-(5-(4-(6-benzyl-4,5-dimethylpyridazin-3-yl)-2-methylpiperazin-1-yl)pyrazin-2-yl)propan-2-ol (Compound A25), or a compound disclosed in PCT Publication No. WO 2010/007120.

[0636] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with an Alk inhibitor, ceritinib (also known as ZYKADIA; Compound A23) to treat a disorder, *e.g.*, a disorder described herein.

[0637] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with a JAK and/or CDK4/6 inhibitor, 7-cyclopentyl-N,N-dimethyl-2-((5-(piperazin-1-yl)pyridin-2-yl)amino)-7H-pyrrolo[2,3-d]pyrimidine-6-carboxamide (Compound A24), or a compound disclosed in US Patent 8,415,355 or US Patent 8,685,980 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the JAK and/or CDK4/6 inhibitor is 7-cyclopentyl-N,N-dimethyl-2-((5-(piperazin-1-yl)pyridin-2-yl)amino)-7H-pyrrolo[2,3-d]pyrimidine-6-carboxamide (Compound A24) or a compound disclosed in US Patent 8,415,355 or US Patent 8,685,980.

[0638] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination a prolactin receptor (PRLR) inhibitor, a human monoclonal antibody molecule (Compound A26) as disclosed in US Patent 7,867,493), to treat a disorder, *e.g.*, a disorder described herein.

[0639] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with a PIM Kinase inhibitor, N-(4-((1R,3S,5S)-3-amino-5-methylcyclohexyl)pyridin-3-yl)-6-(2,6-difluorophenyl)-5-fluoropicolinamide (Compound A27) or a compound disclosed in PCT Publication No. WO 2010/026124 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the PIM Kinase inhibitor is N-(4-((1R,3S,5S)-3-amino-5-methylcyclohexyl)pyridin-3-yl)-6-(2,6-difluorophenyl)-5-fluoropicolinamide (Compound A27) or a compound disclosed in PCT Publication No. WO 2010/026124.

[0640] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination a Wnt signaling inhibitor, 2-(2',3-dimethyl-[2,4'-bipyridin]-5-yl)-N-(5-(pyrazin-2-yl)pyridin-2-yl)acetamide (Compound A28) or a compound disclosed in PCT publication No. WO 2010/101849 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the Wnt signaling inhibitor is 2-(2',3-dimethyl-[2,4'-bipyridin]-5-yl)-N-(5-(pyrazin-2-yl)pyridin-2-yl)acetamide (Compound A28) or a compound disclosed in PCT publication No. WO 2010/101849. In one embodiment, the Wnt signaling inhibitor is 2-(2',3-dimethyl-[2,4'-bipyridin]-5-yl)-N-(5-(pyrazin-2-yl)pyridin-2-yl)acetamide (Compound A28).

[0641] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in

combination with a BRAF inhibitor, to treat a disorder, *e.g.*, a disorder described herein, *e.g.*, a cancer.

[0642] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination a CDK4/6 inhibitor, 7-cyclopentyl-N,N-dimethyl-2-((5-((1R,6S)-9-methyl-4-oxo-3,9-diazabicyclo[4.2.1]nonan-3-yl)pyridin-2-yl)amino)-7H-pyrrolo[2,3-d]pyrimidine-6-carboxamide (Compound A30), or a compound disclosed in PCT publication No. WO 2011/101409 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the CDK4/6 inhibitor is 7-cyclopentyl-N,N-dimethyl-2-((5-((1R,6S)-9-methyl-4-oxo-3,9-diazabicyclo[4.2.1]nonan-3-yl)pyridin-2-yl)amino)-7H-pyrrolo[2,3-d]pyrimidine-6-carboxamide (Compound A30) or a compound disclosed in PCT publication No. WO 2011/101409.

[0643] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with a HER3 inhibitor, Compound A31, or a compound disclosed in PCT Publication No. WO 2012/022814, to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the HER3 inhibitor is Compound A31 or a compound disclosed in PCT Publication WO 2012/022814.

[0644] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination an FGFR2 and/or FGFR4 inhibitor, Compound A32, or a compound disclosed in a publication PCT Publication No. WO 2014/160160 (*e.g.*, an antibody molecule drug conjugate against an FGFR2 and/or FGFR4, *e.g.*, mAb 12425), to treat a disorder, *e.g.*, a disorder described herein. In some embodiments, Compound A32 is an antibody molecule drug conjugate against an FGFR2 and/or FGFR4, *e.g.*, mAb 12425.

[0645] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination an M-CSF inhibitor, Compound A33, or a compound disclosed in PCT Publication No. WO 2004/045532 (*e.g.*, an antibody molecule or Fab fragment against M-CSF), to treat a disorder, *e.g.*, a disorder described herein.

[0646] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with a MEK inhibitor, to treat a disorder, *e.g.*, a cancer as described herein.

[0647] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination an inhibitor of one or more of c-KIT, histamine release, Flt3 (*e.g.*, FLK2/STK1) or PKC, Midostaurin (Compound A35) or a compound disclosed in PCT Publication No. WO 2003/037347 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the inhibitor is Midostaurin (Compound A35) or compound disclosed in PCT Publication No. WO 2003/037347.

[0648] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination an inhibitor of one or more of VEGFR-2, PDGFRbeta, KIT or Raf kinase C, 1-methyl-5-((2-(5-(trifluoromethyl)-1H-imidazol-2-yl)pyridin-4-yl)oxy)-N-(4-(trifluoromethyl)phenyl)-1H-benzo[d]imidazol-2-amine (Compound A37) or a compound disclosed in PCT Publication No. WO 2007/030377 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the inhibitor of one or more of VEGFR-2, PDGFRbeta, KIT or Raf kinase C is 1-methyl-5-((2-(5-(trifluoromethyl)-1H-imidazol-2-yl)pyridin-4-yl)oxy)-N-(4-(trifluoromethyl)phenyl)-1H-benzo[d]imidazol-2-amine (Compound A37) or a compound disclosed in PCT Publication No. WO 2007/030377.

[0649] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination a somatostatin agonist and/or growth hormone release inhibitor, Pasireotide diaspertate (also known as SIGNIFOR; Compound A38) or a compound disclosed in PCT Publication No. WO2002/010192 or US Patent No. 7,473,761 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the somatostatin agonist and/or growth hormone release inhibitor is Pasireotide diaspertate (Compound A38) or a compound disclosed in PCT Publication No. WO2002/010192 or US Patent No. 7,473,761.

[0650] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination a signal transduction modulator and/or angiogenesis inhibitor, *e.g.*, to treat a disorder such as a cancer as described herein.

[0651] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with an EGFR inhibitor, (R,E)-N-(7-chloro-1-(1-(4-(dimethylamino)but-2-enoyl)azepan-3-yl)-1H-benzo[d]imidazol-2-yl)-2-methylisonicotinamide (Compound A40) or a compound disclosed in PCT Publication No. WO 2013/184757 to treat a disorder, *e.g.*, a

disorder described herein. In one embodiment, the EGFR inhibitor is (R,E)-N-(7-chloro-1-(1-(4-(dimethylamino)but-2-enoyl)azepan-3-yl)-1H-benzo[d]imidazol-2-yl)-2-methylisonicotinamide (Compound A40) or a compound disclosed in PCT Publication No. WO 2013/184757. In one embodiment, an anti-human ENTPD2 antibody molecule is used in combination with (R,E)-N-(7-chloro-1-(1-(4-(dimethylamino)but-2-enoyl)azepan-3-yl)-1H-benzo[d]imidazol-2-yl)-2-methylisonicotinamide (Compound A40), or a compound disclosed in PCT Publication No. WO 2013/184757, to treat a disorder such as a cancer.

[0652] In some embodiments, the EGFR inhibitor, (R,E)-N-(7-chloro-1-(1-(4-(dimethylamino)but-2-enoyl)azepan-3-yl)-1H-benzo[d]imidazol-2-yl)-2-methylisonicotinamide (Compound A40), or a compound disclosed in PCT Publication No. WO 2013/184757, is administered in combination with an inhibitor of ENTPD2 (*e.g.*, an anti-human ENTPD2 antibody molecule) to treat a cancer.

[0653] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination an ALK inhibitor, N⁶-(2-isopropoxy-5-methyl-4-(1-methylpiperidin-4-yl)phenyl)-N⁴-(2-(isopropylsulfonyl)phenyl)-1H-pyrazolo[3,4-d]pyrimidine-4,6-diamine (Compound A42) or a compound disclosed in PCT Publication No. WO 2008/073687 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the ALK inhibitor is N⁶-(2-isopropoxy-5-methyl-4-(1-methylpiperidin-4-yl)phenyl)-N⁴-(2-(isopropylsulfonyl)phenyl)-1H-pyrazolo[3,4-d]pyrimidine-4,6-diamine (Compound A42) or a compound disclosed in PCT Publication No. WO 2008/073687.

[0654] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination an IGF-1R inhibitor, 3-(4-(4-((5-chloro-4-((5-methyl-1H-pyrazol-3-yl)amino)pyrimidin-2-yl)amino)-5-fluoro-2-methylphenyl)piperidin-1-yl)thietane 1,1-dioxide (Compound A43), 5-chloro-N²-(2-fluoro-5-methyl-4-(1-(tetrahydro-2H-pyran-4-yl)piperidin-4-yl)phenyl)-N⁴-(5-methyl-1H-pyrazol-3-yl)pyrimidine-2,4-diamine (Compound A44), or 5-chloro-N²-(4-(1-ethylpiperidin-4-yl)-2-fluoro-5-methylphenyl)-N⁴-(5-methyl-1H-pyrazol-3-yl)pyrimidine-2,4-diamine (Compound A45) or a compound disclosed in PCT Publication No. WO 2010/002655 to treat a disorder, *e.g.*, a disorder described. In one embodiment, the IGF-1R inhibitor is 3-(4-(4-((5-chloro-4-((5-methyl-1H-pyrazol-3-yl)amino)pyrimidin-2-yl)amino)-5-fluoro-2-methylphenyl)piperidin-1-yl)thietane 1,1-dioxide (Compound A43), 5-chloro-N²-(2-fluoro-5-methyl-4-(1-(tetrahydro-2H-pyran-4-yl)piperidin-4-yl)phenyl)-N⁴-(5-methyl-1H-pyrazol-3-yl)pyrimidine-2,4-diamine (Compound A44), 5-chloro-N²-(4-(1-

ethylpiperidin-4-yl)-2-fluoro-5-methylphenyl)-N⁴-(5-methyl-1H-pyrazol-3-yl)pyrimidine-2,4-diamine (Compound A45), or a compound disclosed in PCT Publication No. WO 2010/002655.

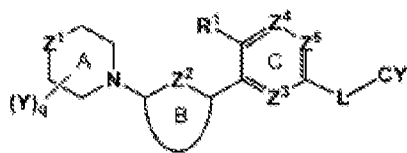
[0655] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination a P-Glycoprotein 1 inhibitor, Valspodar (also known as AMDRAY; Compound A46) or a compound disclosed in EP 296122 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the P-Glycoprotein 1 inhibitor is Valspodar (Compound A46) or a compound disclosed in EP 296122.

[0656] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination one or more of a VEGFR inhibitor, Vatalanib succinate (Compound A47) or a compound disclosed in EP 296122 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the VEGFR inhibitor is Vatalanib succinate (Compound A47) or a compound disclosed in EP 296122.

[0657] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with an IDH inhibitor or a compound disclosed in WO2014/141104 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the IDH inhibitor is a compound disclosed in PCT Publication No. WO2014/141104.

[0658] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with a BCL-ABL inhibitor or a compound disclosed in PCT Publication No. WO2013/171639, WO2013/171640, WO2013/171641, or WO2013/171642 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the BCL-ABL inhibitor is a compound disclosed in PCT Publication No. WO2013/171639, WO2013/171640, WO2013/171641, or WO2013/171642.

[0659] In another embodiment, the combination, *e.g.*, a combination comprising an anti-human ENTPD2 antibody molecule as described herein, includes or is used in combination with a c-RAF inhibitor or a compound disclosed in PCT Publication No. WO2014/151616 to treat a disorder, *e.g.*, a disorder described herein. In one embodiment, the c-RAF inhibitor is Compound A50 or a compound disclosed in PCT Publication No. WO2014/151616. In some embodiments, the c-RAF inhibitor or Compound A50 is a compound of formula (I):



- b. $\{f\}$
- c. or a pharmaceutically acceptable salt thereof, wherein:
- d. Z^1 is O, S, S(=O) or SO_2 ;
- e. Z^2 is N, S or CR^a , where R^a is H, halo, C_{1-4} alkyl or C_{1-4} haloalkyl;
- f. R^1 is CN, halo, OH, C_{1-4} alkoxy, or C_{1-4} alkyl that is optionally substituted with one to three groups selected from halo, C_{1-4} alkoxy, CN, and hydroxyl;
- g. Ring B is selected from phenyl, pyridine, pyrimidine, pyrazine, pyridazine, pyridone, pyrimidone, pyrazinone, pyridazinone, and thiazole, each of which is optionally substituted with up to two groups selected from halo, OH, CN, C_{1-4} alkyl, C_{2-4} alkenyl, -O- $(C_{1-4}$ alkyl), NH_2 , $NH-(C_{1-4}$ alkyl), $-N(C_{1-4}$ alkyl) $_2$, $-SO_2R^2$, $NHSO_2R^2$, $NHC(O)R^2$, $NHCO_2R^2$, C_{3-6} cycloalkyl, 5-6 membered heteroaryl, -O- C_{3-6} cycloalkyl, -O-(5-6-membered heteroaryl), C_{4-8} heterocycloalkyl, and -O-(4-8 membered heterocycloalkyl), where each heterocycloalkyl and heteroaryl contains up to three heteroatoms selected from N, O and S as ring members,
- i. where each C_{1-4} alkyl, C_{2-4} alkenyl, C_{3-6} cycloalkyl, 5-6 membered heteroaryl, and 4-8 membered heterocycloalkyl is each optionally substituted with up to three groups selected from oxo, hydroxyl, halo, C_{1-4} alkyl, C_{1-4} haloalkyl, C_{1-4} alkoxy, and $-(CH_2)_{1-2}Q$ where Q is OH, C_{1-4} alkoxy, -CN, NH_2 , $-NHR^3$, $-N(R^3)_2$, $-SO_2R^3$, $NHSO_2R^3$, $NHC(O)OR^3$, or $NHC(O)R^3$; each R^2 and R^3 is independently C_{1-4} alkyl; and
- ii. Ring B is optionally fused to a 5-6 membered aromatic or nonaromatic ring containing up to two heteroatoms selected from N, O and S, where the 5-6 membered ring can be substituted with halo, C_{1-4} alkyl, C_{1-4} haloalkyl, or C_{1-4} alkoxy, and if the fused ring is non-aromatic the substituent options can further include oxo;
- h. each Y is independently selected from C_{1-4} alkyl, C_{1-4} alkoxy, CN, halo, oxo, $-(CH_2)_pOR^4$, $-(CH_2)_pN(R^4)_2$, $-(CH_2)_pNHC(O)R^4$, $-(CH_2)_pNHCOO(C_{1-4}$ alkyl), and imidazole,
- i. or two Y groups on Ring A are optionally taken together to form a ring fused to or bridging Ring A, where said fused or bridging ring optionally contains a heteroatom selected from N, O and S as a ring member, and is optionally substituted with up to two groups selected from C_{1-4} alkyl, C_{1-4} alkoxy, CN, halo, oxo, $-(CH_2)_pOR^4$, $-(CH_2)_pN(R^4)_2$, $-(CH_2)_pNHC(O)R^4$, and $-(CH_2)_pNHCOO(C_{1-4}$ alkyl);
- j. each R^4 is independently H or C_{1-4} alkyl;

- k. each p is independently 0, 1, or 2;
- l. q is 0, 1 or 2;
- m. Z^3 , Z^4 , and Z^5 are independently selected from CH and N and optionally NO;
- n. L is -C(=O)-NR⁴-[CY] or -NR⁴-C(=O)-[CY], where [CY] indicates which atom of L is attached to CY; and
 - o. CY is an aromatic ring selected from phenyl, pyridine, pyrimidine, pyrazine, pyridazine, pyridone, thiazole, isothiazole, oxazole, pyrazole, and isoxazole, wherein the ring is optionally fused to a thiophene, imidazole, oxazolone, or pyrrole ring;
 - p. and CY is substituted with up to two groups selected from halo, CN, R⁵, OR⁵, SO₂R⁵, -S(=NH)(=O)R⁵, OH, NH₂, NHR⁵, and -N(R⁵)₂,
 - i. wherein each R⁵ is independently C₁₋₄ alkyl, C₂₋₄ alkenyl, C₂₋₆ heterocyclyl, 5-membered heteroaryl containing up to three heteroatoms selected from N, O and S as ring members, or C₃₋₈ cycloalkyl, and R⁵ is optionally substituted with up to four groups selected from oxo, halo, CN, R⁶, OH, OR⁶, SO₂R⁶, NH₂, NHR⁶, N(R⁶)₂, NHSO₂R⁶, NHCOOR⁶, NHC(=O)R⁶, -CH₂OR⁷, -CH₂N(R⁷)₂, wherein each
 - q. R⁶ is independently C₁₋₄ alkyl, and each R⁷ is independently H or C₁₋₄ alkyl;
 - r. and two R⁴, R⁵, R⁶, or R⁷ on the same nitrogen atom can be taken together to form a 5-6 membered heterocyclic ring optionally containing an additional N, O or S as a ring member and optionally substituted with up to two groups selected from C₁₋₄ alkyl, oxo, halo, OH, and C₁₋₄ alkoxy.

Exemplary Cell therapies

[0660] Anti-human ENTPD2 antibody molecules can also be combined with a cell therapy, e.g., a chimeric antigen receptor (CAR) therapy, a T cell therapy, a natural killer (NK) cell therapy, or a dendritic cell therapy.

Combinations with CAR therapies

[0661] The anti-human ENTPD2 antibody molecules described herein can be administered in combination with a second therapeutic, e.g., a cell comprising a chimeric antigen receptor (CAR). The CAR may comprise i) an extracellular antigen binding domain, ii) a transmembrane domain, and iii) an intracellular signaling domain (which may comprise one or both of a primary signaling domain and a costimulatory domain). The CAR may further comprise a leader sequence and/or a hinge sequence. In specific embodiments, the

CAR construct comprises a scFv domain, wherein the scFv may be preceded by an optional leader sequence, and followed by an optional hinge sequence, a transmembrane region, and an intracellular signaling domain, e.g., wherein the domains are contiguous with and in the same reading frame to form a single fusion protein.

[0662] In some embodiments, the CAR molecule comprises a CD19 CAR molecule described herein, e.g., a CD19 CAR molecule described in US 2015/0283178, e.g., CTL019. In embodiments, the CD19 CAR comprises an amino acid, or has a nucleotide sequence shown in US 2015/0283178, incorporated herein by reference in its entirety, or a sequence substantially identical thereto (e.g., a sequence having at least about 85%, 90%, or 95% sequence identity thereto).

[0663] In one embodiment, the CAR T cell that binds to CD19 has the USAN designation TISAGENLEUCCEL-T. CTL019 is made by a gene modification of T cells mediated by stable insertion via transduction with a self-inactivating, replication deficient lentiviral (LV) vector containing the CTL019 transgene under the control of the EF-1 alpha promoter. CTL019 can be a mixture of transgene positive and negative T cells that are delivered to the subject on the basis of percent transgene positive T cells.

[0664] In one embodiment, the CD19 CAR comprises an amino acid sequence provided as SEQ ID NO: 12 in PCT publication WO2012/079000. In embodiment, the amino acid sequence is:

MALPVTALLLPLALLLHAARPdiqmtqtsslsaslgdrvtiscrasqdiskylnwyqqkpdgtvkliiy
htsrhsgvpsrfsfgsgsgtdysltisnleqediptyfcqqntlpytfgggtkleitggsgggsggggsevkqlqesg
pglvapsqslsvtctvsgvslpdygvswirpprkglewlgviwgsettyynsalksrliikdnksqvflkmnslqtd
dtaiyycahyyyggsyamydwgqgtsvtvssttpaprpptaptiasqplsrpeacrpaaggavhtrgldfacdiyi
waplagtcgvllslvitlyckrgrklllyifkqpfmrpvqttqeedgcscrfeeeeeggcclrvkfsrsadapaykqgqn
qlynelnlgrreeydvldkrrgdpemggkprknppqeglynelqkdkmacayseigmkgerrrgkghdglyqglst
atkdtydalhmqlppr (SEQ ID NO: 312),

or a sequence substantially identical thereto (e.g., a sequence having at least about 85%, 90%, or 95% sequence identity thereto), with or without the signal peptide sequence indicated in capital letters.

[0665] In one embodiment, the amino acid sequence is:

diqmtqtsslsaslgdrvtiscrasqdiskylnwyqqkpdgtvkliiyhtsrhsgvpsrfsfgsgsgtdysltisnleqedi
ptyfcqqntlpytfgggtkleitggsgggsggggsevkqlqesgpglvapsqslsvtctvsgvslpdygvswirpp

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NOM DU FICHIER / FILE NAME :

NOTE POUR LE TOME / VOLUME NOTE:

CLAIMS

1. An antibody or antigen binding fragment thereof that specifically binds to human ENTPD2 protein, wherein the antibody or antigen binding fragment thereof comprises a heavy chain complementarity determining region 1 (HCDR1), a heavy chain complementarity determining region 2 (HCDR2), a heavy chain complementarity determining region 3 (HCDR3), a light chain complementarity determining region 1 (LCDR1), a light chain complementarity determining region 2 (LCDR2), and a light chain complementarity determining region 3 (LCDR3) of any antibody or antigen binding fragment provided in Table 1.

2. The antibody or antigen binding fragment thereof of claim 1, wherein the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 are selected from the HCDR1, HCDR2, HCDR3, LCDR1, LCDR2, and LCDR3 sequences provided in Table 1.

3. The antibody or antigen binding fragment thereof of claim 1 or claim 2, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable region provided in Table 1.

4. The antibody or antigen binding fragment thereof of any one of claims 1-3, wherein the antibody or antigen binding fragment thereof comprises a light chain variable region provided in Table 1.

5. The antibody or antigen binding fragment thereof of claim 1 or claim 2, wherein the antibody or antigen binding fragment thereof is selected from any one of the following:

- 1) an antibody or antigen binding fragment thereof comprising:
 - an HCDR1 sequence comprising SEQ ID NO: 1,
 - an HCDR2 sequence comprising SEQ ID NO: 2,
 - an HCDR3 sequence comprising SEQ ID NO: 3,
 - an LCDR1 sequence comprising SEQ ID NO: 14,
 - an LCDR2 sequence comprising SEQ ID NO: 15, and
 - an LCDR3 sequence comprising SEQ ID NO: 16;

- 2) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 4,
an HCDR2 sequence comprising SEQ ID NO: 5,
an HCDR3 sequence comprising SEQ ID NO: 3,
an LCDR1 sequence comprising SEQ ID NO: 17,
an LCDR2 sequence comprising SEQ ID NO: 18, and
an LCDR3 sequence comprising SEQ ID NO: 19;

3) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 7,
an HCDR2 sequence comprising SEQ ID NO: 8,
an HCDR3 sequence comprising SEQ ID NO: 9,
an LCDR1 sequence comprising SEQ ID NO: 20,
an LCDR2 sequence comprising SEQ ID NO: 18, and
an LCDR3 sequence comprising SEQ ID NO: 16;

4) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 37,
an HCDR2 sequence comprising SEQ ID NO: 38,
an HCDR3 sequence comprising SEQ ID NO: 39,
an LCDR1 sequence comprising SEQ ID NO: 50,
an LCDR2 sequence comprising SEQ ID NO: 51, and
an LCDR3 sequence comprising SEQ ID NO: 52;

5) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 40,
an HCDR2 sequence comprising SEQ ID NO: 41,
an HCDR3 sequence comprising SEQ ID NO: 39,
an LCDR1 sequence comprising SEQ ID NO: 53,
an LCDR2 sequence comprising SEQ ID NO: 54, and
an LCDR3 sequence comprising SEQ ID NO: 55;

6) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 43,
an HCDR2 sequence comprising SEQ ID NO: 44,

an HCDR3 sequence comprising SEQ ID NO: 45,
an LCDR1 sequence comprising SEQ ID NO: 56,
an LCDR2 sequence comprising SEQ ID NO: 54, and
an LCDR3 sequence comprising SEQ ID NO: 52;

7) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 37,
an HCDR2 sequence comprising SEQ ID NO: 38,
an HCDR3 sequence comprising SEQ ID NO: 39,
an LCDR1 sequence comprising SEQ ID NO: 61,
an LCDR2 sequence comprising SEQ ID NO: 51, and
an LCDR3 sequence comprising SEQ ID NO: 52;

8) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 40,
an HCDR2 sequence comprising SEQ ID NO: 41,
an HCDR3 sequence comprising SEQ ID NO: 39,
an LCDR1 sequence comprising SEQ ID NO: 62,
an LCDR2 sequence comprising SEQ ID NO: 54, and
an LCDR3 sequence comprising SEQ ID NO: 55;

9) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 43,
an HCDR2 sequence comprising SEQ ID NO: 44,
an HCDR3 sequence comprising SEQ ID NO: 45,
an LCDR1 sequence comprising SEQ ID NO: 63,
an LCDR2 sequence comprising SEQ ID NO: 54, and
an LCDR3 sequence comprising SEQ ID NO: 52;

10) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 37,
an HCDR2 sequence comprising SEQ ID NO: 38,
an HCDR3 sequence comprising SEQ ID NO: 68,
an LCDR1 sequence comprising SEQ ID NO: 50,

an LCDR2 sequence comprising SEQ ID NO: 51, and
an LCDR3 sequence comprising SEQ ID NO: 52;

11) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 40,
an HCDR2 sequence comprising SEQ ID NO: 41,
an HCDR3 sequence comprising SEQ ID NO: 68,
an LCDR1 sequence comprising SEQ ID NO: 53,
an LCDR2 sequence comprising SEQ ID NO: 54, and
an LCDR3 sequence comprising SEQ ID NO: 55;

12) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 43,
an HCDR2 sequence comprising SEQ ID NO: 44,
an HCDR3 sequence comprising SEQ ID NO: 69,
an LCDR1 sequence comprising SEQ ID NO: 56,
an LCDR2 sequence comprising SEQ ID NO: 54, and
an LCDR3 sequence comprising SEQ ID NO: 52;

13) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 82,
an HCDR2 sequence comprising SEQ ID NO: 83,
an HCDR3 sequence comprising SEQ ID NO: 84,
an LCDR1 sequence comprising SEQ ID NO: 95,
an LCDR2 sequence comprising SEQ ID NO: 96, and
an LCDR3 sequence comprising SEQ ID NO: 97;

14) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 85,
an HCDR2 sequence comprising SEQ ID NO: 86,
an HCDR3 sequence comprising SEQ ID NO: 84,
an LCDR1 sequence comprising SEQ ID NO: 98,
an LCDR2 sequence comprising SEQ ID NO: 99, and
an LCDR3 sequence comprising SEQ ID NO: 100;

- 15) an antibody or antigen binding fragment thereof comprising:
- an HCDR1 sequence comprising SEQ ID NO: 88,
 - an HCDR2 sequence comprising SEQ ID NO: 89,
 - an HCDR3 sequence comprising SEQ ID NO: 90,
 - an LCDR1 sequence comprising SEQ ID NO: 101,
 - an LCDR2 sequence comprising SEQ ID NO: 99, and
 - an LCDR3 sequence comprising SEQ ID NO: 97;
- 16) an antibody or antigen binding fragment thereof comprising:
- an HCDR1 sequence comprising SEQ ID NO: 106,
 - an HCDR2 sequence comprising SEQ ID NO: 107,
 - an HCDR3 sequence comprising SEQ ID NO: 108,
 - an LCDR1 sequence comprising SEQ ID NO: 119,
 - an LCDR2 sequence comprising SEQ ID NO: 120, and
 - an LCDR3 sequence comprising SEQ ID NO: 121;
- 17) an antibody or antigen binding fragment thereof comprising:
- an HCDR1 sequence comprising SEQ ID NO: 109,
 - an HCDR2 sequence comprising SEQ ID NO: 110,
 - an HCDR3 sequence comprising SEQ ID NO: 108,
 - an LCDR1 sequence comprising SEQ ID NO: 122,
 - an LCDR2 sequence comprising SEQ ID NO: 99, and
 - an LCDR3 sequence comprising SEQ ID NO: 123;
- 18) an antibody or antigen binding fragment thereof comprising:
- an HCDR1 sequence comprising SEQ ID NO: 112,
 - an HCDR2 sequence comprising SEQ ID NO: 113,
 - an HCDR3 sequence comprising SEQ ID NO: 114,
 - an LCDR1 sequence comprising SEQ ID NO: 124,
 - an LCDR2 sequence comprising SEQ ID NO: 99, and
 - an LCDR3 sequence comprising SEQ ID NO: 121;
- 19) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 106,
an HCDR2 sequence comprising SEQ ID NO: 129,
an HCDR3 sequence comprising SEQ ID NO: 108,
an LCDR1 sequence comprising SEQ ID NO: 119,
an LCDR2 sequence comprising SEQ ID NO: 120, and
an LCDR3 sequence comprising SEQ ID NO: 121;

20) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 109,
an HCDR2 sequence comprising SEQ ID NO: 130,
an HCDR3 sequence comprising SEQ ID NO: 108
an LCDR1 sequence comprising SEQ ID NO: 122,
an LCDR2 sequence comprising SEQ ID NO: 99, and
an LCDR3 sequence comprising SEQ ID NO: 123;

21) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 112,
an HCDR2 sequence comprising SEQ ID NO: 131,
an HCDR3 sequence comprising SEQ ID NO: 114,
an LCDR1 sequence comprising SEQ ID NO: 124,
an LCDR2 sequence comprising SEQ ID NO: 99, and
an LCDR3 sequence comprising SEQ ID NO: 121;

22) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 136,
an HCDR2 sequence comprising SEQ ID NO: 137,
an HCDR3 sequence comprising SEQ ID NO: 138,
an LCDR1 sequence comprising SEQ ID NO: 149,
an LCDR2 sequence comprising SEQ ID NO: 150, and
an LCDR3 sequence comprising SEQ ID NO: 151;

23) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 139,
an HCDR2 sequence comprising SEQ ID NO: 140,

an HCDR3 sequence comprising SEQ ID NO: 138,
an LCDR1 sequence comprising SEQ ID NO: 152,
an LCDR2 sequence comprising SEQ ID NO: 153, and
an LCDR3 sequence comprising SEQ ID NO: 154;

24) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 142,
an HCDR2 sequence comprising SEQ ID NO: 143,
an HCDR3 sequence comprising SEQ ID NO: 144,
an LCDR1 sequence comprising SEQ ID NO: 155,
an LCDR2 sequence comprising SEQ ID NO: 153, and
an LCDR3 sequence comprising SEQ ID NO: 151;

25) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 160,
an HCDR2 sequence comprising SEQ ID NO: 161,
an HCDR3 sequence comprising SEQ ID NO: 162,
an LCDR1 sequence comprising SEQ ID NO: 173,
an LCDR2 sequence comprising SEQ ID NO: 150, and
an LCDR3 sequence comprising SEQ ID NO: 174;

26) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 163,
an HCDR2 sequence comprising SEQ ID NO: 164,
an HCDR3 sequence comprising SEQ ID NO: 162,
an LCDR1 sequence comprising SEQ ID NO: 175,
an LCDR2 sequence comprising SEQ ID NO: 153, and
an LCDR3 sequence comprising SEQ ID NO: 176;

27) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 166,
an HCDR2 sequence comprising SEQ ID NO: 167,
an HCDR3 sequence comprising SEQ ID NO: 168,
an LCDR1 sequence comprising SEQ ID NO: 177,

an LCDR2 sequence comprising SEQ ID NO: 153, and
an LCDR3 sequence comprising SEQ ID NO: 174;

28) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 37,
an HCDR2 sequence comprising SEQ ID NO: 220,
an HCDR3 sequence comprising SEQ ID NO: 221,
an LCDR1 sequence comprising SEQ ID NO: 61,
an LCDR2 sequence comprising SEQ ID NO: 51, and
an LCDR3 sequence comprising SEQ ID NO: 52;

29) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 40,
an HCDR2 sequence comprising SEQ ID NO: 222,
an HCDR3 sequence comprising SEQ ID NO: 221,
an LCDR1 sequence comprising SEQ ID NO: 62,
an LCDR2 sequence comprising SEQ ID NO: 54, and
an LCDR3 sequence comprising SEQ ID NO: 55;

30) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 43,
an HCDR2 sequence comprising SEQ ID NO: 223,
an HCDR3 sequence comprising SEQ ID NO: 224,
an LCDR1 sequence comprising SEQ ID NO: 63,
an LCDR2 sequence comprising SEQ ID NO: 54, and
an LCDR3 sequence comprising SEQ ID NO: 52;

31) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 37,
an HCDR2 sequence comprising SEQ ID NO: 220,
an HCDR3 sequence comprising SEQ ID NO: 68,
an LCDR1 sequence comprising SEQ ID NO: 61,
an LCDR2 sequence comprising SEQ ID NO: 51, and
an LCDR3 sequence comprising SEQ ID NO: 52;

32) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 40,
an HCDR2 sequence comprising SEQ ID NO: 222,
an HCDR3 sequence comprising SEQ ID NO: 68,
an LCDR1 sequence comprising SEQ ID NO: 62,
an LCDR2 sequence comprising SEQ ID NO: 54, and
an LCDR3 sequence comprising SEQ ID NO: 55;

33) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 43,
an HCDR2 sequence comprising SEQ ID NO: 223,
an HCDR3 sequence comprising SEQ ID NO: 69,
an LCDR1 sequence comprising SEQ ID NO: 63,
an LCDR2 sequence comprising SEQ ID NO: 54, and
an LCDR3 sequence comprising SEQ ID NO: 52;

34) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 1,
an HCDR2 sequence comprising SEQ ID NO: 245,
an HCDR3 sequence comprising SEQ ID NO: 246,
an LCDR1 sequence comprising SEQ ID NO: 254,
an LCDR2 sequence comprising SEQ ID NO: 15, and
an LCDR3 sequence comprising SEQ ID NO: 255;

35) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 4,
an HCDR2 sequence comprising SEQ ID NO: 247,
an HCDR3 sequence comprising SEQ ID NO: 246,
an LCDR1 sequence comprising SEQ ID NO: 17,
an LCDR2 sequence comprising SEQ ID NO: 18, and
an LCDR3 sequence comprising SEQ ID NO: 256;

36) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 7,
an HCDR2 sequence comprising SEQ ID NO: 248,
an HCDR3 sequence comprising SEQ ID NO: 249,
an LCDR1 sequence comprising SEQ ID NO: 20,
an LCDR2 sequence comprising SEQ ID NO: 18, and
an LCDR3 sequence comprising SEQ ID NO: 255;

37) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 1,
an HCDR2 sequence comprising SEQ ID NO: 261,
an HCDR3 sequence comprising SEQ ID NO: 262,
an LCDR1 sequence comprising SEQ ID NO: 254,
an LCDR2 sequence comprising SEQ ID NO: 15, and
an LCDR3 sequence comprising SEQ ID NO: 16;

38) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 4,
an HCDR2 sequence comprising SEQ ID NO: 247,
an HCDR3 sequence comprising SEQ ID NO: 262,
an LCDR1 sequence comprising SEQ ID NO: 17,
an LCDR2 sequence comprising SEQ ID NO: 18, and
an LCDR3 sequence comprising SEQ ID NO: 19;

39) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 7,
an HCDR2 sequence comprising SEQ ID NO: 248,
an HCDR3 sequence comprising SEQ ID NO: 263,
an LCDR1 sequence comprising SEQ ID NO: 20,
an LCDR2 sequence comprising SEQ ID NO: 18, and
an LCDR3 sequence comprising SEQ ID NO: 16;

40) an antibody or antigen binding fragment thereof comprising:

an HCDR1 sequence comprising SEQ ID NO: 272,
an HCDR2 sequence comprising SEQ ID NO: 273,

an HCDR3 sequence comprising SEQ ID NO: 274,
an LCDR1 sequence comprising SEQ ID NO: 254,
an LCDR2 sequence comprising SEQ ID NO: 285, and
an LCDR3 sequence comprising SEQ ID NO: 16;

41) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 275,
an HCDR2 sequence comprising SEQ ID NO: 276,
an HCDR3 sequence comprising SEQ ID NO: 274,
an LCDR1 sequence comprising SEQ ID NO: 17,
an LCDR2 sequence comprising SEQ ID NO: 286, and
an LCDR3 sequence comprising SEQ ID NO: 19;

42) an antibody or antigen binding fragment thereof comprising:
an HCDR1 sequence comprising SEQ ID NO: 278,
an HCDR2 sequence comprising SEQ ID NO: 279,
an HCDR3 sequence comprising SEQ ID NO: 280,
an LCDR1 sequence comprising SEQ ID NO: 20,
an LCDR2 sequence comprising SEQ ID NO: 286, and
an LCDR3 sequence comprising SEQ ID NO: 16.

6. The antibody or antigen binding fragment thereof of any one of claims 1-5, wherein the antibody or antigen binding fragment thereof is selected from any one of the following:

1) an antibody or antigen binding fragment thereof comprising a heavy chain variable region (VH) comprising SEQ ID NO: 10 or a sequence at least about 95% or more identical thereto, and a light chain variable region (VL) comprising SEQ ID NO: 21 or a sequence at least about 95% or more identical thereto;

2) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 25 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 29 or a sequence at least about 95% or more identical thereto;

3) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 33 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 29 or a sequence at least about 95% or more identical thereto;

4) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 46 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 57 or a sequence at least about 95% or more identical thereto;

5) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 46 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 64 or a sequence at least about 95% or more identical thereto;

6) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 70 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 74 or a sequence at least about 95% or more identical thereto;

7) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 25 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 78 or a sequence at least about 95% or more identical thereto;

8) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 91 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 102 or a sequence at least about 95% or more identical thereto;

9) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 115 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 125 or a sequence at least about 95% or more identical thereto;

10) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 132 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 125 or a sequence at least about 95% or more identical thereto;

11) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 145 or a sequence at least about 95% or more

identical thereto, and a VL comprising SEQ ID NO: 156 or a sequence at least about 95% or more identical thereto;

12) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 169 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 178 or a sequence at least about 95% or more identical thereto;

13) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 225 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 229 or a sequence at least about 95% or more identical thereto;

14) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 233 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 237 or a sequence at least about 95% or more identical thereto;

15) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 241 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 229 or a sequence at least about 95% or more identical thereto;

16) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 250 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 257 or a sequence at least about 95% or more identical thereto;

17) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 264 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 268 or a sequence at least about 95% or more identical thereto; or

18) an antibody or antigen binding fragment thereof comprising a VH comprising SEQ ID NO: 281 or a sequence at least about 95% or more identical thereto, and a VL comprising SEQ ID NO: 287 or a sequence at least about 95% or more identical thereto.

7. The antibody or antigen binding fragment thereof of any one of claims 1-6, wherein the antibody or antigen binding fragment thereof is selected from any one of the following:

- 1) an antibody comprising a heavy chain comprising SEQ ID NO: 12 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 23 or a sequence at least about 95% or more identical thereto;
- 2) an antibody comprising a heavy chain comprising SEQ ID NO: 27 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 31 or a sequence at least about 95% or more identical thereto;
- 3) an antibody comprising a heavy chain comprising SEQ ID NO: 35 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 31 or a sequence at least about 95% or more identical thereto;
- 4) an antibody comprising a heavy chain comprising SEQ ID NO: 48 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 59 or a sequence at least about 95% or more identical thereto;
- 5) an antibody comprising a heavy chain comprising SEQ ID NO: 48 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 66 or a sequence at least about 95% or more identical thereto;
- 6) an antibody comprising a heavy chain comprising SEQ ID NO: 72 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 76 or a sequence at least about 95% or more identical thereto;
- 7) an antibody comprising a heavy chain comprising SEQ ID NO: 27 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 80 or a sequence at least about 95% or more identical thereto;
- 8) an antibody comprising a heavy chain comprising SEQ ID NO: 93 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 104 or a sequence at least about 95% or more identical thereto;
- 9) an antibody comprising a heavy chain comprising SEQ ID NO: 117 or a sequence at least about 95% or more identical thereto, and a light chain

comprising SEQ ID NO: 127 or a sequence at least about 95% or more identical thereto;

10) an antibody comprising a heavy chain comprising SEQ ID NO: 134 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 127 or a sequence at least about 95% or more identical thereto;

11) an antibody comprising a heavy chain comprising SEQ ID NO: 147 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 158 or a sequence at least about 95% or more identical thereto;

12) an antibody comprising a heavy chain comprising SEQ ID NO: 171 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 180 or a sequence at least about 95% or more identical thereto;

13) an antibody comprising a heavy chain comprising SEQ ID NO: 227 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 231 or a sequence at least about 95% or more identical thereto;

14) an antibody comprising a heavy chain comprising SEQ ID NO: 235 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 239 or a sequence at least about 95% or more identical thereto;

15) an antibody comprising a heavy chain comprising SEQ ID NO: 243 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 231 or a sequence at least about 95% or more identical thereto;

16) an antibody comprising a heavy chain comprising SEQ ID NO: 252 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 259 or a sequence at least about 95% or more identical thereto;

17) an antibody comprising a heavy chain comprising SEQ ID NO: 266 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 270 or a sequence at least about 95% or more identical thereto; or

18) an antibody comprising a heavy chain comprising SEQ ID NO: 283 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 289 or a sequence at least about 95% or more identical thereto.

8. The antibody or antigen binding fragment thereof of any one of claims 1-7, wherein the antibody or antigen binding fragment thereof comprises:

- an HCDR1 sequence comprising SEQ ID NO: 1,
- an HCDR2 sequence comprising SEQ ID NO: 2,
- an HCDR3 sequence comprising SEQ ID NO: 3,
- an LCDR1 sequence comprising SEQ ID NO: 14,
- an LCDR2 sequence comprising SEQ ID NO: 15, and
- an LCDR3 sequence comprising SEQ ID NO: 16.

9. The antibody or antigen binding fragment thereof of any one of claims 1-7, wherein the antibody or antigen binding fragment thereof comprises:

- an HCDR1 sequence comprising SEQ ID NO: 4,
- an HCDR2 sequence comprising SEQ ID NO: 5,
- an HCDR3 sequence comprising SEQ ID NO: 3,
- an LCDR1 sequence comprising SEQ ID NO: 17,
- an LCDR2 sequence comprising SEQ ID NO: 18, and
- an LCDR3 sequence comprising SEQ ID NO: 19.

10. The antibody or antigen binding fragment thereof of any one of claims 1-7, wherein the antibody or antigen binding fragment thereof comprises:

- an HCDR1 sequence comprising SEQ ID NO: 7,
- an HCDR2 sequence comprising SEQ ID NO: 8,
- an HCDR3 sequence comprising SEQ ID NO: 9,
- an LCDR1 sequence comprising SEQ ID NO: 20,
- an LCDR2 sequence comprising SEQ ID NO: 18, and
- an LCDR3 sequence comprising SEQ ID NO: 16.

11. The antibody or antigen binding fragment thereof of any one of claims 1-7, wherein the antibody or antigen binding fragment thereof comprises a heavy chain variable

region (VH) comprising SEQ ID NO: 10 or a sequence at least about 95% or more identical thereto, and a light chain variable region (VL) comprising SEQ ID NO: 21 or a sequence at least about 95% or more identical thereto.

12. The antibody or antigen binding fragment thereof of any one of claims 1-7, wherein the antibody or antigen binding fragment thereof comprises SEQ ID NO: 12 or a sequence at least about 95% or more identical thereto, and a light chain comprising SEQ ID NO: 23 or a sequence at least about 95% or more identical thereto.

13. The antibody or antigen binding fragment thereof of any one of claims 1-12, wherein the antibody or antigen binding fragment thereof binds to an epitope in human ENTPD2, wherein the epitope comprises at least one of the following residues: His50, Asp76, Pro78, Gly79, Gly80, Tyr85, Asp87, Asn88, Gly91, Gln94, Ser95, Gly98, Glu101, Gln102, Gln105, Asp106, Arg245, Thr272, Gln273, Leu275, Asp278, Arg298, Ala347, Ala350, Thr351, Arg392, Ala393, Arg394, or Tyr398.

14. The antibody or antigen binding fragment thereof of any one of claims 1-12, wherein the antibody or antigen binding fragment thereof binds to an epitope in human ENTPD2, wherein the epitope comprises at least one of the following residues: Gly79, Gln250, Leu253, Trp266, Arg268, Gly269, Phe270, Ser271, Thr272, Gln273, Val274, Leu275, Asp278, Arg298, Ser300, Ser302, Gly303, Thr380, Trp381, Ala382, Gly390, Gln391, Arg392, Ala393, Arg394, or Asp397.

15. An antibody or antigen binding fragment thereof that specifically binds to an epitope in human ENTPD2, wherein the epitope comprises at least one of the following residues: His50, Asp76, Pro78, Gly79, Gly80, Tyr85, Asp87, Asn88, Gly91, Gln94, Ser95, Gly98, Glu101, Gln102, Gln105, Asp106, Arg245, Thr272, Gln273, Leu275, Asp278, Arg298, Ala347, Ala350, Thr351, Arg392, Ala393, Arg394, or Tyr398.

16. An antibody or antigen binding fragment thereof that specifically binds to an epitope in human ENTPD2, wherein the epitope comprises at least one of the following residues: Gly79, Gln250, Leu253, Trp266, Arg268, Gly269, Phe270, Ser271, Thr272,

Gln273, Val274, Leu275, Asp278, Arg298, Ser300, Ser302, Gly303, Thr380, Trp381, Ala382, Gly390, Gln391, Arg392, Ala393, Arg394, or Asp397.

17. An antibody or antigen binding fragment thereof that competes with any antibody or antigen binding fragment provided in Table 1 for binding to human ENTPD2 protein.

18. An antibody or antigen binding fragment thereof that binds to the same epitope as, substantially the same epitope as, an epitope that overlaps with, or an epitope that substantially overlaps with, the epitope of any antibody or antigen binding fragment provided in Table 1.

19. The antibody or antigen binding fragment thereof of any one of claims 1-18, wherein the antibody or antigen-binding fragment thereof binds to human ENTPD2 protein with a dissociation constant (K_D) of less than 10nM, e.g., as measured by Biacore.

20. The antibody or antigen binding fragment thereof of any one of claims 1-18, wherein the antibody or antigen-binding fragment thereof binds to human ENTPD2 protein with a dissociation constant (K_D) of less than 5nM, e.g., as measured by Biacore.

21. The antibody or antigen binding fragment thereof of any one of claims 1-18, wherein the antibody or antigen-binding fragment thereof binds to human ENTPD2 protein with a dissociation constant (K_D) of less than 3nM, e.g., as measured by Biacore.

22. The antibody or antigen binding fragment thereof of any one of claims 1-21, wherein the antibody or antigen binding fragment thereof inhibits human ENTPD2 enzymatic activity by at least 40%, at least 50%, at least 60%, at least 70%, at least 80%, or at least 90%.

23. The antibody or antigen binding fragment thereof of any one of claims 1-22, wherein the antibody or antigen binding fragment thereof inhibits ENTPD2's ability of hydrolysis of adenosine triphosphate (ATP).

24. The antibody or antigen binding fragment thereof of any one of claims 1-23, wherein the antibody or antigen binding fragment thereof interferes with ATP binding to ENTPD2 or traps ATP within the catalytic domain of ENTPD2.

25. The antibody or antigen binding fragment thereof of any one of claims 1-24, wherein the antibody has an IgG1, IgG2, IgG3 or IgG4 isotype.
26. The antibody or antigen binding fragment thereof of any one of claims 1-25, wherein the antibody or antigen binding fragment thereof comprises an Fc region selected from an IgG1 Fc region, an IgG2 Fc region, an IgG4 Fc region, or an IgG2/IgG4 hybrid Fc region.
27. The antibody or antigen binding fragment thereof of any one of claims 1-26, wherein the antibody or antigen binding fragment thereof comprises a modified Fc region that has reduced antibody-dependent cellular cytotoxicity (ADCC) or complement-dependent cytotoxicity (CDC) activity compared to the parent antibody.
28. The antibody or antigen binding fragment thereof of any one of claims 1-27, wherein the antibody or antigen binding fragment thereof is a human or humanized antibody or fragment thereof.
29. A nucleic acid or set of nucleic acids encoding the antibody or antigen binding fragment thereof of any one of claims 1-28.
30. A vector comprising the nucleic acid or set of nucleic acids of claim 29.
31. The vector of claim 30, wherein the vector is selected from a DNA vector, a RNA vector, a plasmid, a cosmid, or a viral vector.
32. The vector of claim 31, wherein the vector is a viral vector based on any one of the following viruses: lentivirus, adenovirus, adeno-associated virus (AAV), Herpes Simplex Virus (HSV), parvovirus, retrovirus, vaccinia virus, Sinbis virus, influenza virus, reovirus, Newcastle disease virus (NDV), measles virus, vesicular stomatitis virus (VSV), poliovirus, poxvirus, Seneca Valley virus, coxsackievirus, enterovirus, myxoma virus, or maraba virus.
33. The vector of claim 32, wherein the vector is an AAV vector.
34. The vector of claim 31, wherein the vector is a lentiviral vector.

35. The vector of any one of claims 30-34, further comprising a promoter.
36. The vector of any one of claims 30-35, further comprising a detectable marker.
37. A cell comprising the nucleic acid or set of nucleic acids of claim 29 or the vector of any one of claims 30-36.
38. A method of producing an antibody or antigen binding fragment thereof, the method comprising culturing the cell of claim 37 and collecting the antibody or antigen-binding fragment thereof from the culture medium.
39. A pharmaceutical composition comprising the antibody or antigen binding fragment thereof of any one of claims 1-28, the nucleic acid or set of nucleic acids of claim 29, the vector of any one of claims 30-36, or the cell of claim 37, and a pharmaceutically acceptable carrier.
40. The antibody or antigen binding fragment thereof of any one of claims 1-28, the nucleic acid or set of nucleic acids of claim 29, the vector of any one of claims 30-36, the cell of claim 37, or the pharmaceutical composition of claim 39, for use as a medicament.
41. The antibody or antigen binding fragment thereof of any one of claims 1-28, the nucleic acid of claim 29, the vector of any one of claims 30-36, the cell of claim 37, or the pharmaceutical composition of claim 39, for use in the treatment of a cancer.
42. Use of the antibody or antigen binding fragment thereof of any one of claims 1-28, the nucleic acid of claim 29, the vector of any one of claims 30-36, the cell of claim 37, or the pharmaceutical composition of claim 39, in the manufacture of a medicament for treatment of a cancer.
43. The antibody for use according to claim 41, or the use according to claim 42, wherein the cancer is an ENTPD2+ cancer.
44. The antibody for use according to claim 41, or the use according to claim 42, wherein the cancer is colorectal cancer (CRC), gastric cancer (e.g., stomach adenocarcinoma, gastric carcinoma), esophageal cancer (e.g. esophageal squamous cell carcinoma (ESCC)), pancreatic cancer, cholangiocarcinoma, lung cancer (e.g., small cell lung cancer), breast cancer (e.g., breast adenocarcinoma), or ovarian cancer.

45. The antibody for use according to claim 41, or the use according to claim 42, wherein the antibody or antigen binding fragment thereof, the nucleic acid or set of nucleic acids, the vector, the cell, or the pharmaceutical composition, is administered to the subject through an intravenous, intratumoral or subcutaneous route.

46. The antibody for use according to claim 41, or the use according to claim 42, wherein the antibody molecule is administered in combination with at least one additional therapeutic agent or procedure.

47. The antibody for use according to claim 46, or the use according to claim 46, wherein the at least one additional therapeutic agent or procedure is selected from one or more of chemotherapy, a targeted anti-cancer therapy, an oncolytic drug, a cytotoxic agent, an immune-based therapy, a cytokine, surgical procedure, a radiation procedure, an activator of a costimulatory molecule, an inhibitor of an inhibitory molecule, a vaccine, or a cell therapy.

48. The antibody for use according to claim 46 or the use according to claim 46, wherein the at least one additional therapeutic agent is a PD-1 inhibitor, e.g., a PD-1 antibody.

49. The antibody for use according to claim 48 or the use according to claim 48, wherein the PD-1 inhibitor is selected from PDR001, Nivolumab, Pembrolizumab, Pidilizumab, MEDI0680, REGN2810, TSR-042, PF-06801591, or AMP-224.

50. The antibody for use according to claim 46, or the use according to claim 46, wherein the at least one additional therapeutic agent is a PD-L1 inhibitor, e.g., a PD-L1 antibody.

51. The antibody for use according to claim 50 or the use according to claim 50, wherein the PD-L1 inhibitor is selected from FAZ053, Atezolizumab, Avelumab, Durvalumab, or BMS-936559.

52. The antibody for use according to claim 46-51, or the use according to claim 46-51, wherein the at least one additional therapeutic agent is an A2AR antagonist, wherein the A2AR antagonist is selected from:

- i. an anti-CD73 antibody molecule, or antigen-binding fragment thereof, optionally wherein the anti-CD73 antibody is selected from:
 - a. an anti-CD73 antibody molecule comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 295 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 296, or an amino acid sequence at least 85%, 90%, 95% identical or higher to SEQ ID NO: 295 or 296.;
 - b. an anti-CD73 antibody molecule comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 299 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 300, or an amino acid sequence at least 85%, 90%, 95% identical or higher to SEQ ID NO: 299 or 300;
 - c. an anti-CD73 antibody molecule comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 302 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 303, or an amino acid sequence at least 85%, 90%, 95% identical or higher to SEQ ID NO: 302 or 303;
 - d. an anti-CD73 antibody molecule comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 304 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 305, or an amino acid sequence at least 85%, 90%, 95% identical or higher to SEQ ID NO: 304 or 305;
 - e. an anti-CD73 antibody molecule comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 306 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 307, or an amino acid sequence at least 85%, 90%, 95% identical or higher to SEQ ID NO: 306 or 307;
 or
 - f. an anti-CD73 antibody molecule comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 308 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 309, or an amino acid sequence at least 85%, 90%, 95% identical or higher to SEQ ID NO: 308 or 309;
 or
- ii. PBF509/NIR178, CPI444/V81444, AZD4635/HTL-1071, Vipadenant, GBV-2034, AB928, Theophylline, Istradefylline, Tozadenant/SYN-115, KW-6356, ST-4206, and Preladenant/SCH 420814; or
- iii. 5-bromo-2,6-di-(1H-pyrazol-1-yl)pyrimidine-4-amine, or a pharmaceutically acceptable salt thereof; (S)-7-(5-methylfuran-2-yl)-3-(((6-(((tetrahydrofuran-3-yl)oxy)methyl)pyridin-2-yl)methyl)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-5-amine, or a

pharmaceutically acceptable salt thereof; (R)-7-(5-methylfuran-2-yl)-3-((6-(((tetrahydrofuran-3-yl)oxy)methyl)pyridin-2-yl)methyl)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-5-amine, or racemate thereof, or a pharmaceutically acceptable salt thereof; 7-(5-methylfuran-2-yl)-3-((6-(((tetrahydrofuran-3-yl)oxy)methyl)pyridin-2-yl)methyl)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-5-amine, or a pharmaceutically acceptable salt thereof; and 6-(2-chloro-6-methylpyridin-4-yl)-5-(4-fluorophenyl)-1,2,4-triazin-3-amine, or a pharmaceutically acceptable salt thereof.

53. The antibody for use according to claim 46, or the use according to claim 46, wherein the at least one additional therapeutic agent is selected from:

- i. a CTLA-4 inhibitor, optionally wherein the CTLA-4 inhibitor is selected from Ipilimumab or Tremelimumab;
- ii. a TIM-3 inhibitor, optionally wherein the TIM-3 inhibitor is selected from MBG453, TSR-022, or LY3321367;
- iii. a LAG-3 inhibitor, optionally wherein the LAG-3 inhibitor is selected from LAG525, BMS-986016, TSR-033, MK-4280 or REGN3767;
- iv. a GITR agonist, optionally wherein the GITR agonist is selected from GWN323, BMS-986156, MK-4166, MK-1248, TRX518, INCAGN1876, AMG 228, or INBRX-110;
- v. an anti-CD3 multispecific antibody molecule, optionally wherein the anti-CD3 multispecific antibody molecule is an anti-CD3 x anti-CD123 bispecific antibody molecule (e.g., XENP14045), or an anti-CD3 x anti-CD20 bispecific antibody molecule (e.g., XENP13676);
- vi. a cytokine molecule, optionally wherein the cytokine molecule is IL-15 complexed with a soluble form of IL-15 receptor alpha (IL-15Ra);
- vii. a macrophage colony-stimulating factor (M-CSF) inhibitor, optionally wherein the M-CSF inhibitor is MCS110;
- viii. a CSF-1R inhibitor, optionally wherein the CSF-1R inhibitor is BLZ945;
- ix. an inhibitor of indoleamine 2,3-dioxygenase (IDO) and/or tryptophan 2,3-dioxygenase (TDO);
- x. a TGF- β inhibitor;
- xi. an oncolytic virus;
- xii. a chimeric antigen receptor (CAR) T-cell therapy.

54. The antibody for use according to claim 46, or the use according to claim 46, wherein the at least one additional therapeutic agent is selected from: 1) a protein kinase C (PKC) inhibitor; 2) a heat shock protein 90 (HSP90) inhibitor; 3) an inhibitor of a phosphoinositide 3-kinase (PI3K) and/or target of rapamycin (mTOR); 4) an inhibitor of cytochrome P450 (e.g., a CYP17 inhibitor or a 17 α -Hydroxylase/C17-20 Lyase inhibitor); 5) an iron chelating agent; 6) an aromatase inhibitor; 7) an inhibitor of p53, e.g., an inhibitor of a p53/Mdm2 interaction; 8) an apoptosis inducer; 9) an angiogenesis inhibitor; 10) an aldosterone synthase inhibitor; 11) a smoothened (SMO) receptor inhibitor; 12) a prolactin receptor (PRLR) inhibitor; 13) a Wnt signaling inhibitor; 14) a CDK4/6 inhibitor; 15) a fibroblast growth factor receptor 2 (FGFR2)/fibroblast growth factor receptor 4 (FGFR4) inhibitor; 16) an inhibitor of macrophage colony-stimulating factor (M-CSF); 17) an inhibitor of one or more of c-KIT, histamine release, Flt3 (e.g., FLK2/STK1) or PKC; 18) an inhibitor of one or more of VEGFR-2 (e.g., FLK-1/KDR), PDGFRbeta, c-KIT or Raf kinase C; 19) a somatostatin agonist and/or a growth hormone release inhibitor; 20) an anaplastic lymphoma kinase (ALK) inhibitor; 21) an insulin-like growth factor 1 receptor (IGF-1R) inhibitor; 22) a P-Glycoprotein 1 inhibitor; 23) a vascular endothelial growth factor receptor (VEGFR) inhibitor; 24) a BCR-ABL kinase inhibitor; 25) an FGFR inhibitor; 26) an inhibitor of CYP11B2; 27) a HDM2 inhibitor, e.g., an inhibitor of the HDM2-p53 interaction; 28) an inhibitor of a tyrosine kinase; 29) an inhibitor of c-MET; 30) an inhibitor of JAK; 31) an inhibitor of DAC; 32) an inhibitor of 11 β -hydroxylase; 33) an inhibitor of IAP; 34) an inhibitor of PIM kinase; 35) an inhibitor of Porcupine; 36) an inhibitor of BRAF, e.g., BRAF V600E or wild-type BRAF; 37) an inhibitor of HER3; 38) an inhibitor of MEK; 39) an inhibitor of a lipid kinase; or one or more agents as provided in Table 16.

55. A method of treating cancer in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of the antibody or antigen binding fragment of any one of claims 1-28, the nucleic acid of claim 29, the vector of any one of claims 30-36, the cell of claim 37, or the pharmaceutical composition of claim 39.

56. The method of claim 55, wherein the cancer is an ENTPD2+ cancer.

57. The method of claim 55, wherein the cancer is colorectal cancer (CRC), gastric cancer (e.g., stomach adenocarcinoma, gastric carcinoma), esophageal cancer (e.g. esophageal squamous cell carcinoma (ESCC)), pancreatic cancer, cholangiocarcinoma, lung

cancer (e.g., small cell lung cancer), breast cancer (e.g., breast adenocarcinoma), or ovarian cancer.

58. The method of any one of claims 55-57, wherein the antibody or antigen binding fragment thereof, the nucleic acid or set of nucleic acids, the vector, the cell, or the pharmaceutical composition, is administered to the subject through an intravenous, intratumoral or subcutaneous route.

59. A method of stimulating an immune response in a subject, the method comprising administering to the subject the antibody or antigen binding fragment of any one of claims 1-28, the nucleic acid or set of nucleic acids of claim 29, the vector of any one of claims 30-36, the cell of claim 37, or the pharmaceutical composition of claim 39, in an amount effective to stimulate the immune response.

60. The method of any one of claims 55-59, further comprising administering to the subject at least one additional therapeutic agent or procedure.

61. The method of claim 60, wherein the at least one additional therapeutic agent or procedure is selected from one or more of chemotherapy, a targeted anti-cancer therapy, an oncolytic drug, a cytotoxic agent, an immune-based therapy, a cytokine, surgical procedure, a radiation procedure, an activator of a costimulatory molecule, an inhibitor of an inhibitory molecule, a vaccine, or a cell therapy.

62. The method of claim 60, wherein the at least one additional therapeutic agent is a PD-1 inhibitor, e.g., a PD-1 antibody.

63. The method of claim 62, wherein the PD-1 inhibitor is selected from PDR001, Nivolumab, Pembrolizumab, Pidilizumab, MEDI0680, REGN2810, TSR-042, PF-06801591, or AMP-224.

64. The method of claim 60, wherein the at least one additional therapeutic agent is a PD-L1 inhibitor, e.g., a PD-L1 antibody.

65. The method of claim 64, wherein the PD-L1 inhibitor is selected from FAZ053, Atezolizumab, Avelumab, Durvalumab, or BMS-936559.

66. The method of claim 60, wherein the at least one additional therapeutic agent is an A2AR antagonist, wherein the A2AR antagonist is selected from:

i. an anti-CD73 antibody molecule, or antigen-binding fragment thereof, optionally wherein the anti-CD73 antibody is selected from:

a. an anti-CD73 antibody molecule comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 295 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 296, or an amino acid sequence at least 85%, 90%, 95% identical or higher to SEQ ID NO: 295 or 296.;

b. an anti-CD73 antibody molecule comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 299 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 300, or an amino acid sequence at least 85%, 90%, 95% identical or higher to SEQ ID NO: 299 or 300;

c. an anti-CD73 antibody molecule comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 302 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 303, or an amino acid sequence at least 85%, 90%, 95% identical or higher to SEQ ID NO: 302 or 303;

d. an anti-CD73 antibody molecule comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 304 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 305, or an amino acid sequence at least 85%, 90%, 95% identical or higher to SEQ ID NO: 304 or 305;

e. an anti-CD73 antibody molecule comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 306 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 307, or an amino acid sequence at least 85%, 90%, 95% identical or higher to SEQ ID NO: 306 or 307; or

f. an anti-CD73 antibody molecule comprising a heavy chain variable region comprising the amino acid sequence of SEQ ID NO: 308 and a light chain variable region comprising the amino acid sequence of SEQ ID NO: 309, or an amino acid sequence at least 85%, 90%, 95% identical or higher to SEQ ID NO: 308 or 309; or

ii. PBF509/NIR178, CPI444/V81444, AZD4635/HTL-1071, Vipadenant, GBV-2034, AB928, Theophylline, Istradefylline, Tozadenant/SYN-115, KW-6356, ST-4206, and Preladenant/SCH 420814; or

iii. 5-bromo-2,6-di-(1H-pyrazol-1-yl)pyrimidine-4-amine, or a pharmaceutically acceptable salt thereof; (S)-7-(5-methylfuran-2-yl)-3-((6-(((tetrahydrofuran-3-yl)oxy)methyl)pyridin-2-yl)methyl)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-5-amine, or a pharmaceutically acceptable salt thereof; (R)-7-(5-methylfuran-2-yl)-3-((6-(((tetrahydrofuran-3-yl)oxy)methyl)pyridin-2-yl)methyl)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-5-amine, or racemate thereof, or a pharmaceutically acceptable salt thereof; 7-(5-methylfuran-2-yl)-3-((6-(((tetrahydrofuran-3-yl)oxy)methyl)pyridin-2-yl)methyl)-3H-[1,2,3]triazolo[4,5-d]pyrimidin-5-amine, or a pharmaceutically acceptable salt thereof; and 6-(2-chloro-6-methylpyridin-4-yl)-5-(4-fluorophenyl)-1,2,4-triazin-3-amine, or a pharmaceutically acceptable salt thereof.

67. The method of claim 60, wherein the at least one additional therapeutic agent is selected from:

- i. a CTLA-4 inhibitor, optionally wherein the CTLA-4 inhibitor is selected from Ipilimumab or Tremelimumab;
- ii. a TIM-3 inhibitor, optionally wherein the TIM-3 inhibitor is selected from MBG453, TSR-022, or LY3321367;
- iii. a LAG-3 inhibitor, optionally wherein the LAG-3 inhibitor is selected from LAG525, BMS-986016, TSR-033, MK-4280 or REGN3767;
- iv. a GITR agonist, optionally wherein the GITR agonist is selected from GWN323, BMS-986156, MK-4166, MK-1248, TRX518, INCAGN1876, AMG 228, or INBRX-110;
- v. an anti-CD3 multispecific antibody molecule, optionally wherein the anti-CD3 multispecific antibody molecule is an anti-CD3 x anti-CD123 bispecific antibody molecule (e.g., XENP14045), or an anti-CD3 x anti-CD20 bispecific antibody molecule (e.g., XENP13676);
- vi. a cytokine molecule, optionally wherein the cytokine molecule is IL-15 complexed with a soluble form of IL-15 receptor alpha (IL-15Ra);
- vii. a macrophage colony-stimulating factor (M-CSF) inhibitor, optionally wherein the M-CSF inhibitor is MCS110;
- viii. a CSF-1R inhibitor, optionally wherein the CSF-1R inhibitor is BLZ945;
- ix. an inhibitor of indoleamine 2,3-dioxygenase (IDO) and/or tryptophan 2,3-dioxygenase (TDO);
- x. a TGF- β inhibitor;

- xi. an oncolytic virus;
- xii. a chimeric antigen receptor (CAR) T-cell therapy.

68. The method of claim 60, wherein the at least one additional therapeutic agent is selected from: 1) a protein kinase C (PKC) inhibitor; 2) a heat shock protein 90 (HSP90) inhibitor; 3) an inhibitor of a phosphoinositide 3-kinase (PI3K) and/or target of rapamycin (mTOR); 4) an inhibitor of cytochrome P450 (e.g., a CYP17 inhibitor or a 17 α -Hydroxylase/C17-20 Lyase inhibitor); 5) an iron chelating agent; 6) an aromatase inhibitor; 7) an inhibitor of p53, e.g., an inhibitor of a p53/Mdm2 interaction; 8) an apoptosis inducer; 9) an angiogenesis inhibitor; 10) an aldosterone synthase inhibitor; 11) a smoothened (SMO) receptor inhibitor; 12) a prolactin receptor (PRLR) inhibitor; 13) a Wnt signaling inhibitor; 14) a CDK4/6 inhibitor; 15) a fibroblast growth factor receptor 2 (FGFR2)/fibroblast growth factor receptor 4 (FGFR4) inhibitor; 16) an inhibitor of macrophage colony-stimulating factor (M-CSF); 17) an inhibitor of one or more of c-KIT, histamine release, Flt3 (e.g., FLK2/STK1) or PKC; 18) an inhibitor of one or more of VEGFR-2 (e.g., FLK-1/KDR), PDGFR β , c-KIT or Raf kinase C; 19) a somatostatin agonist and/or a growth hormone release inhibitor; 20) an anaplastic lymphoma kinase (ALK) inhibitor; 21) an insulin-like growth factor 1 receptor (IGF-1R) inhibitor; 22) a P-Glycoprotein 1 inhibitor; 23) a vascular endothelial growth factor receptor (VEGFR) inhibitor; 24) a BCR-ABL kinase inhibitor; 25) an FGFR inhibitor; 26) an inhibitor of CYP11B2; 27) a HDM2 inhibitor, e.g., an inhibitor of the HDM2-p53 interaction; 28) an inhibitor of a tyrosine kinase; 29) an inhibitor of c-MET; 30) an inhibitor of JAK; 31) an inhibitor of DAC; 32) an inhibitor of 11 β -hydroxylase; 33) an inhibitor of IAP; 34) an inhibitor of PIM kinase; 35) an inhibitor of Porcupine; 36) an inhibitor of BRAF, e.g., BRAF V600E or wild-type BRAF; 37) an inhibitor of HER3; 38) an inhibitor of MEK; 39) an inhibitor of a lipid kinase; or one or more agents as provided in Table 16.

69. The method of claim 60, wherein the antibody or antigen binding fragment of any one of claims 1-24, the nucleic acid or set of nucleic acids of claim 25, the vector of any one of claims 26-32, the cell of claim 33, or the pharmaceutical composition of claim 35 is administered concurrently with, prior to, or subsequent to, the at least one additional therapeutic agent.

70. The method of any of claims 55-69, wherein administering the antibody or antigen binding fragment thereof, the nucleic acid or set of nucleic acids, the vector, the cell, or the pharmaceutical composition has one or more of the following effects:

- (a) increased number of CD45+ CD4- CD8+ CD69+ CD25+ cells in a tumor or lesion site in the subject;
- (b) increased number of CD45+ CD8- CD4+ FOXP3- CD69+ CD25+ cells in a tumor or lesion site in the subject;
- (c) decreased plasma MCP1 or IL-1 β level in the subject; or
- (d) increased MCP1 level in a tumor or lesion site in the subject.

71. A method of treating cancer in a subject in need thereof, the method comprising administering to the subject a therapeutically effective amount of the antibody or antigen binding fragment of any one of claims 1-28, in combination with a second therapeutic agent selected from a PD-1 inhibitor or a PD-L1 inhibitor.

72. A method of stimulating an immune response in a subject, the method comprising administering to the subject the antibody or antigen binding fragment of any one of claims 1-28, in combination with a second therapeutic agent selected from a PD-1 inhibitor or a PD-L1 inhibitor.

73. A composition comprising the antibody or antigen binding fragment of any one of claims 1-28 for use, in combination with a second therapeutic agent selected from a PD-1 inhibitor or a PD-L1 inhibitor, in the treatment of cancer in a subject.

74. A composition for use in the treatment of cancer in a subject, wherein the composition comprises the antibody or antigen binding fragment of any one of claims 1-28, in combination with a second therapeutic agent selected from a PD-1 inhibitor or a PD-L1 inhibitor.

75. The method of claim 71 or 72, or the composition of claim 73 or 74, wherein the second therapeutic agent is a PD-1 inhibitor.

76. The method of claim 71 or 72, or the composition of claim 73 or 74, wherein the PD-1 inhibitor is a PD-1 antibody.

77. The method of claim 71 or 72, or the composition of claim 73 or 74, wherein the PD-1 inhibitor is selected from PDR001, Nivolumab, Pembrolizumab, Pidilizumab, MEDI0680, REGN2810, TSR-042, PF-06801591, or AMP-224.

78. The method of claim 71 or 72, or the composition of claim 73 or 74, wherein the second therapeutic agent is a PD-L1 inhibitor.

79. The method of claim 71 or 72, or the composition of claim 73 or 74, wherein the PD-L1 inhibitor is a PD-L1 antibody.

80. The method of claim 71 or 72, or the composition of claim 73 or 74, wherein the PD-L1 inhibitor is selected from FAZ053, Atezolizumab, Avelumab, Durvalumab, or BMS-936559.

81. The method of claim 71, or the composition of claim 73 or 74, wherein the cancer is an ENTPD2+ cancer.

82. The method of claim 71, or the composition of claim 73 or 74, wherein the cancer is colorectal cancer (CRC), gastric cancer (e.g., stomach adenocarcinoma, gastric carcinoma), esophageal cancer (e.g. esophageal squamous cell carcinoma (ESCC)), pancreatic cancer, cholangiocarcinoma, lung cancer (e.g., small cell lung cancer), breast cancer (e.g., breast adenocarcinoma), or ovarian cancer.

FIG. 1A

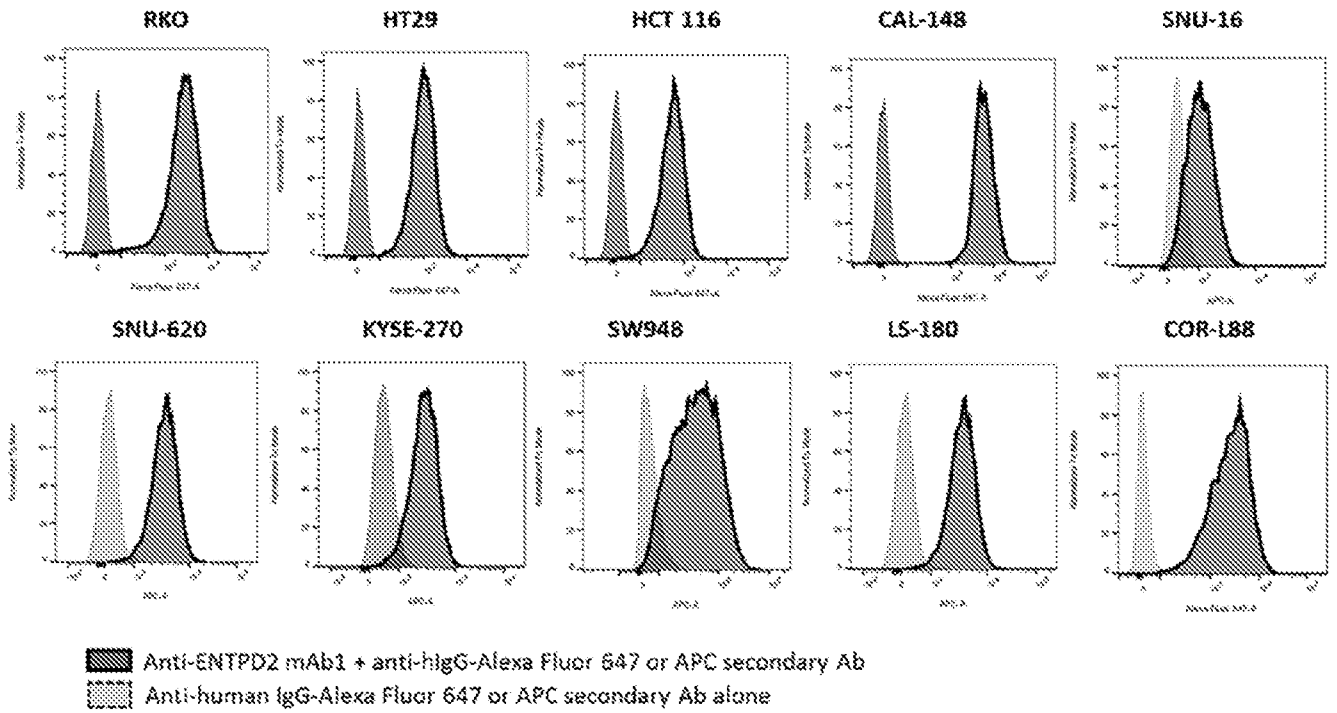


FIG. 1B

Table 20: ENTPD2 expression density across representative cancer cell lines

Cell Line	Source	Indication	Receptor Density
CAL-148	DSMZ (Germany)	Breast Adenocarcinoma	111,726
COR-L88	ECACC (UK)	Small Cell Lung Cancer	90,000
RKO	ATCC (Manassas, VA)	Colorectal Cancer	51,203
LS-180	ATCC (Manassas, VA)	Colorectal Cancer	44,708
SW948	ATCC (Manassas, VA)	Colorectal Cancer	41,576
HT29	ATCC (Manassas, VA)	Colorectal Cancer	28,337
KYSE-270	DSMZ (Germany)	Esophageal Cancer	28,273
SNU-620	KCLB (South Korea)	Stomach Adenocarcinoma	19,646
HCT 116	ATCC (Manassas, VA)	Colorectal Cancer	18,697
SNU-16	ATCC (Manassas, VA)	Gastic Carcinoma	12,763

FIG. 2

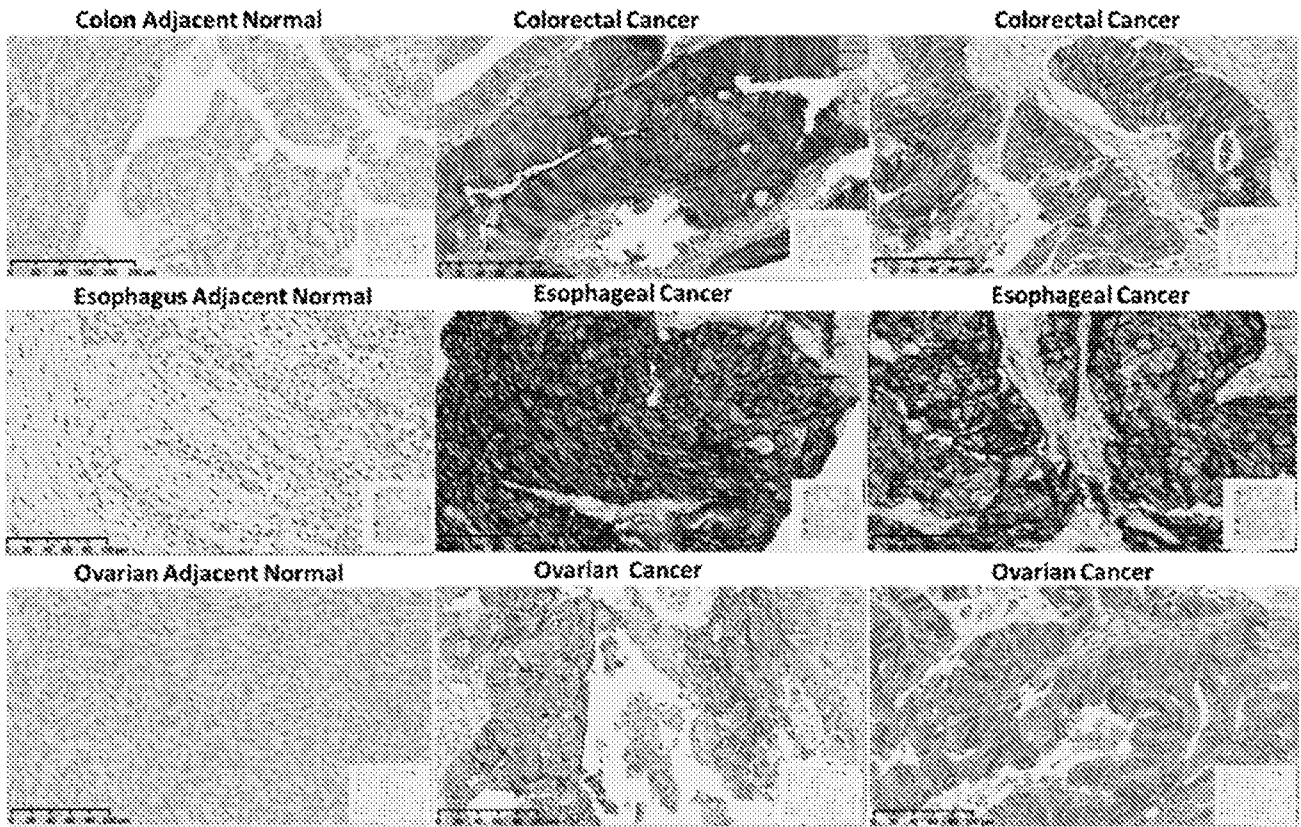


FIG. 3A

Heavy chain amino acid sequence of anti-human ENTPD2 FAb22 (SEQ ID NO: 330)

```

EVKLEQSGPGLVKPSQSLSLTCSVTGYSITSGYYWNWIRQFPGNKLEWMSYISYDGDNNYNPSLKNRISITROTSKNQFF
*          *      ****          ** *
LKLSSVTTEDTATYYCAGGYRYGLSYYYVMDYWGQGTSVTVSAASTKGPSVFERLPSSKSTSGGTAALGCLVKDYFPEP
          **** ** **
VTVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSC

```

Light chain amino acid sequence of anti-human ENTPD2 FAb22 (SEQ ID NO: 334)

```

DIKMTQSPASLAVSLGQRATISCKASQSVDDYDGNSYMNWYQQKPGQPPKLLIYAASNLESIGIPARFSGSGSGTDFTLNH
          *** *          ***
PVEEEDAATYYCQGSNEDPPTFGGGTKLELKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPREAKVQWKVDNALQS
          ** *
GNSQESVTEQDSKDSYSLSSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

```


FIG. 3B

Heavy chain amino acid sequence of anti-human ENTPD2 FAb23 (SEQ ID NO: 336)

EVQLQQFGAELVKGASVKISCKASGYTFTDYNMDWVKQSHGKSLEWIGDINPKYDISTYNQQFKGKATLTVDKSSSTAY
 * * * *
 MELRSLTSEDITAVYYCAERGEFLYYGINYYYYFDVWGAGTTVTVSSASTKGPSVFELAPSSKSTSGGTAALGCLVKDYFPEEPTVSW
 * * * *
 NSGALTSGVHTFPAVLQSSGLYSLSSVTVTPSSSLGTQTYICNVNHKPSNTKVDKRVEPKSC

Light chain amino acid sequence of anti-human ENTPD2 FAb23 (SEQ ID NO: 239)

QIVLTQSPAIMASASLGEEITLTCSSASSSVSYIHWYQQKSGTSPITLLIYSTSNLASGVFSPRFGSGSGSTFYSLTISSEAE
 * * * * *
 DAADYYCHQWSSYPWTFGGCTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNFYPPEAKVQWKVDNALQSGNSQE
 * * * * *
 SVTEQDSKDSSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

FIG. 3C

Heavy chain amino acid sequence of anti-murine ENTPD2 FAb24 (SEQ ID NO: 338)

QVQLVQSGAELKQPGQSVKISCKASGYTFTHYGMNWVKQAPGQGLKWMGWINTDTGNPTYADDFKGR FVFSLDTSVSTAY
 * * * * * * * * * *
 LQISNLKNEDTATFYCVRYYGTLYSGYGFFDSWQGQTLVTVSSASTKGPSVFEPLAPSSSESTSGGTAALGCLVKDYFPEPV
 * * * * * *
 TVSWNSGALTSGVHTFPAVLQSSGLYSLSSVTVPSSSLGTQTYICNVNHKPSNTKVDKRVPEKSC

Light chain amino acid sequence of anti-murine ENTPD FAb24 (SEQ ID NO: 340)

DIMMTQSPSSLSVSAGEKATITCKSSQSLFNSNTNKNYLNWYLQKPGQSPKLLFYYASTRHTGVFPDRFIGSGSGTDFTLT
 * * *
 ITSVQDEDLADYYCQOWYSYPWTFGPGTKLEIKRTVAAPSVFIFPPSDEQLKSGTASVVCLLNNEYFPREAKVQWKVDNAL
 *
 QSGNSQESVTEQPSKDSSTYLSSTLTLSKADYEKHKVYACEVTHQGLSSPVTKSFNRGEC

FIG. 4A



FIG. 4B

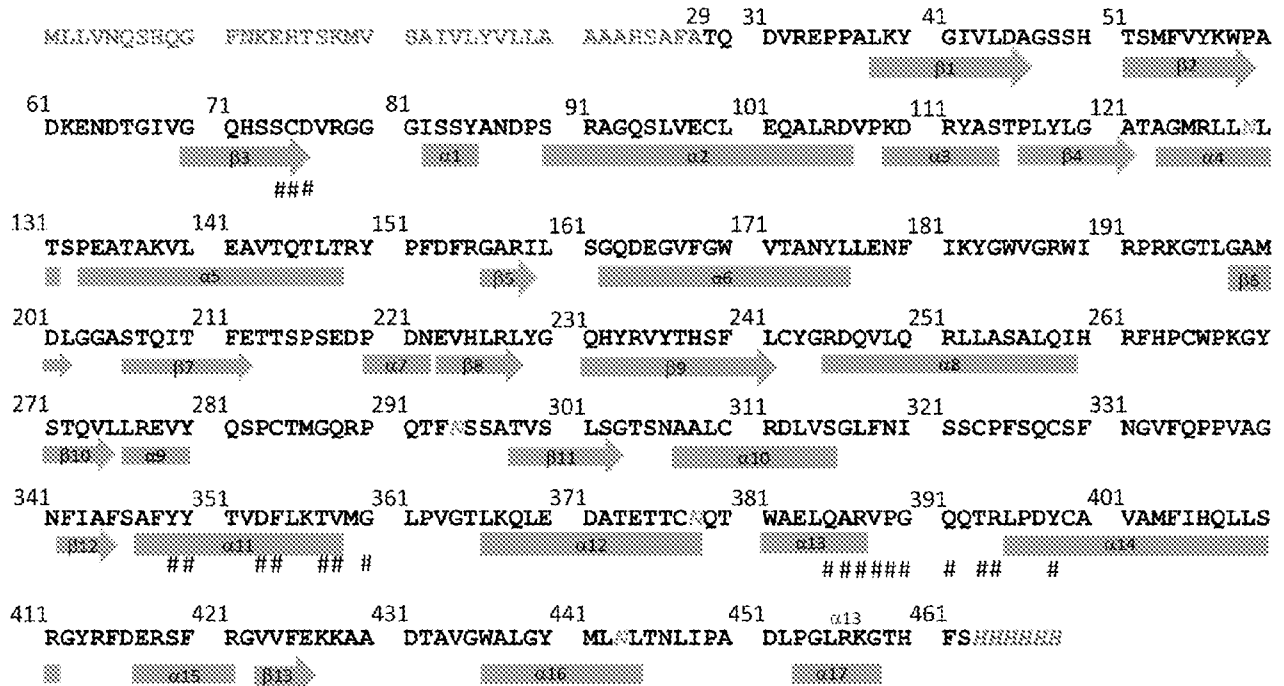


FIG. 5A

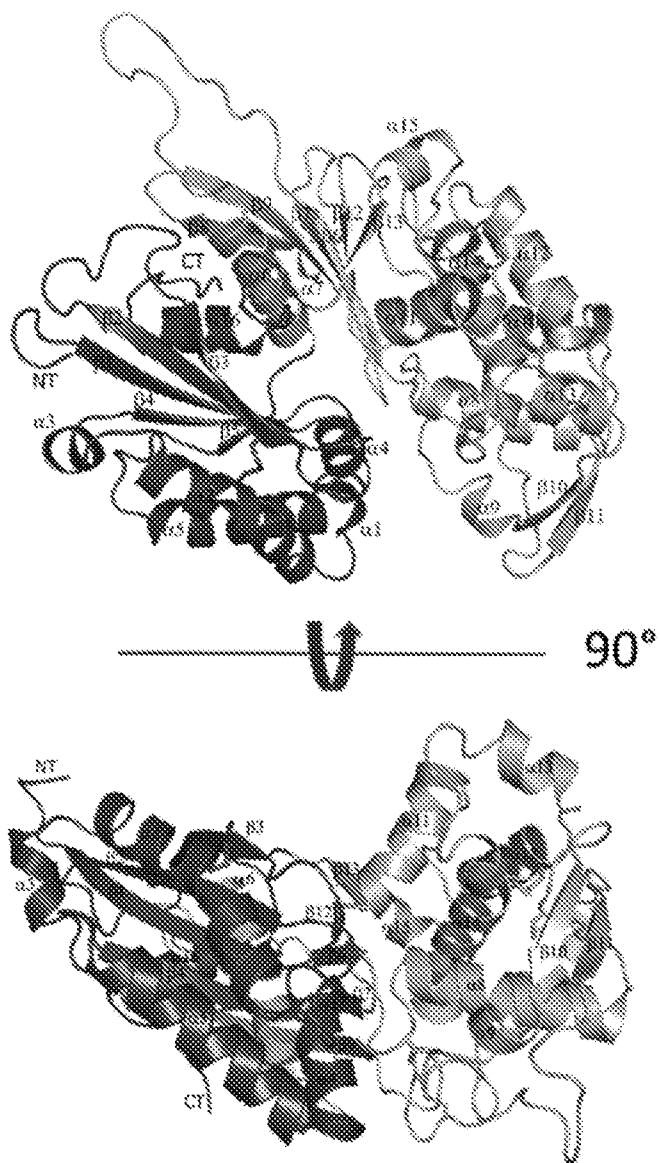


FIG. 5B



FIG. 6

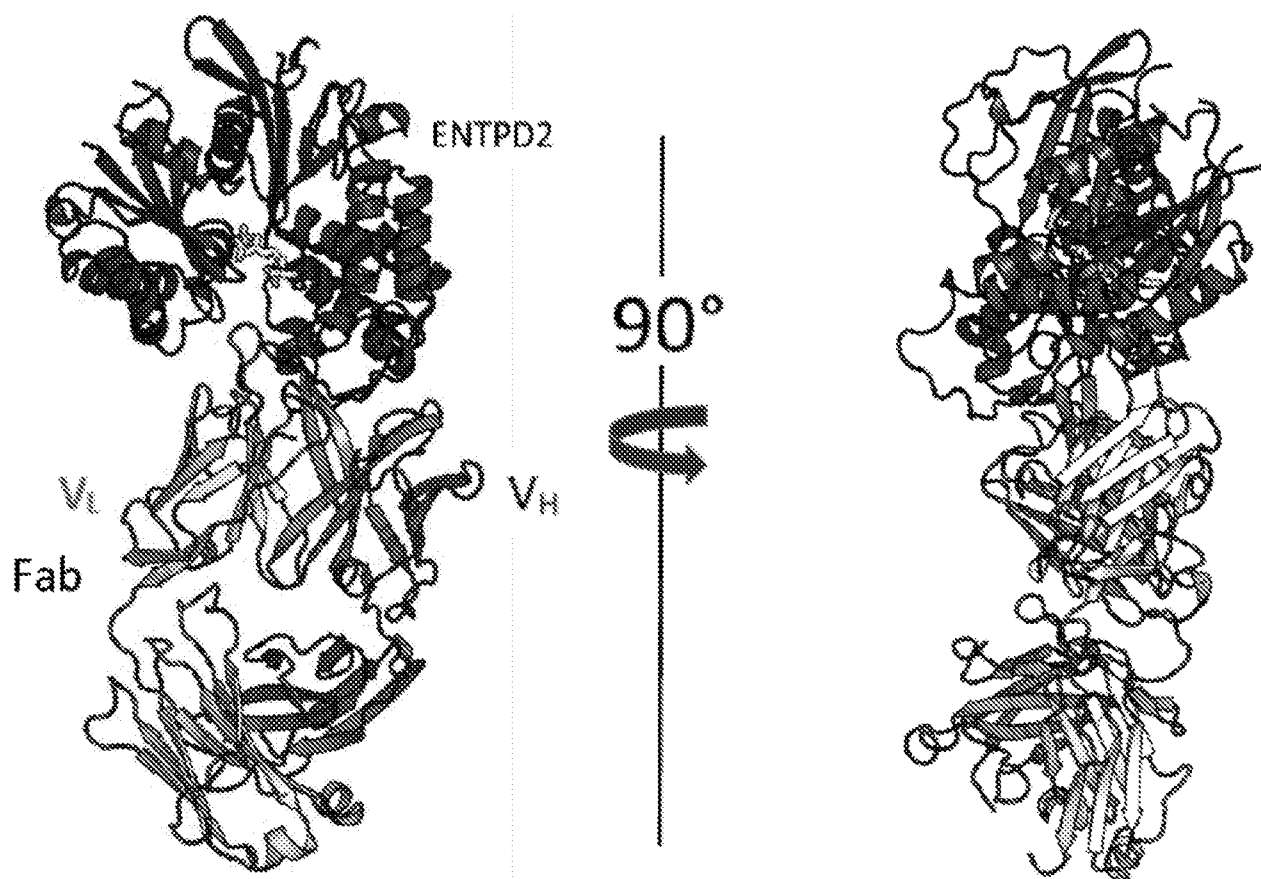


FIG. 7

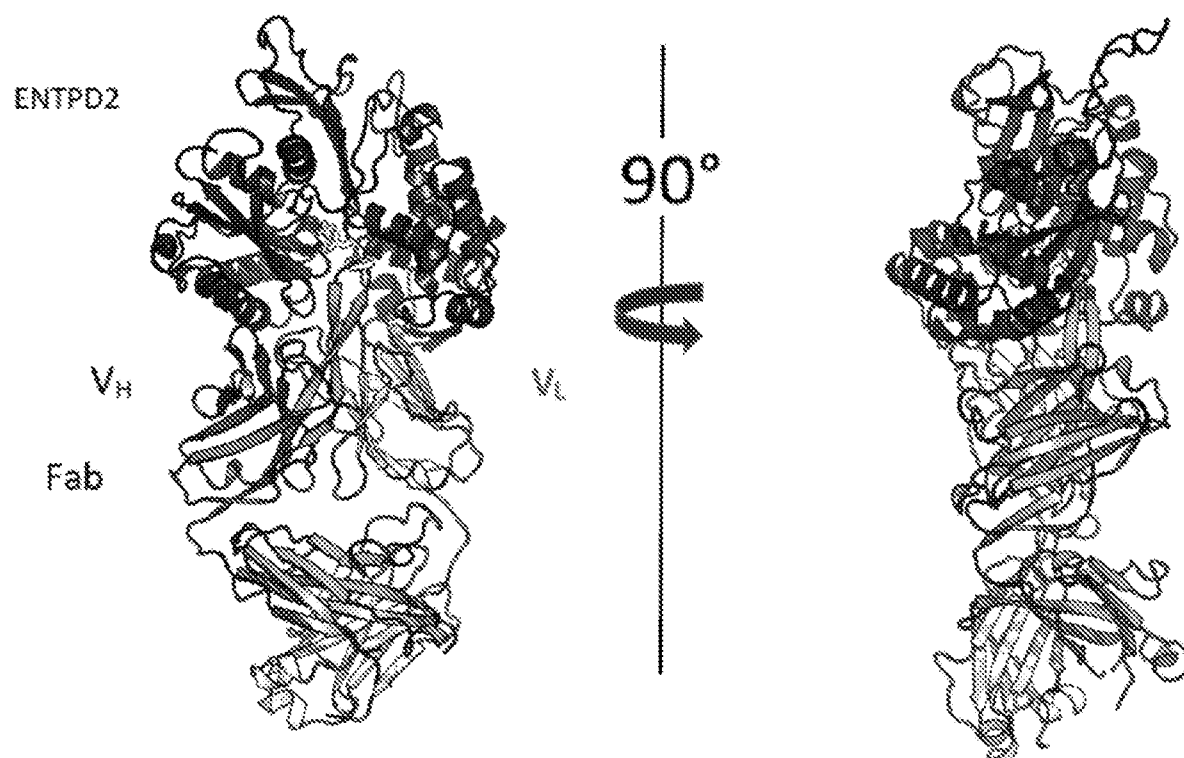


FIG. 8

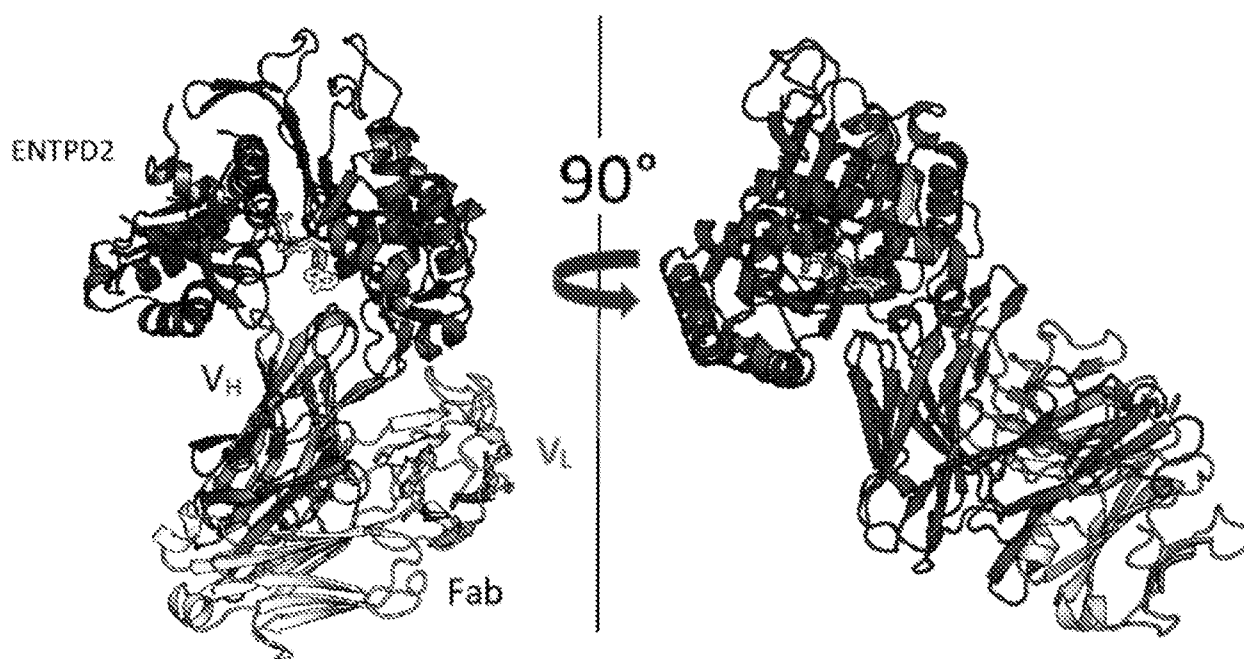


FIG. 9

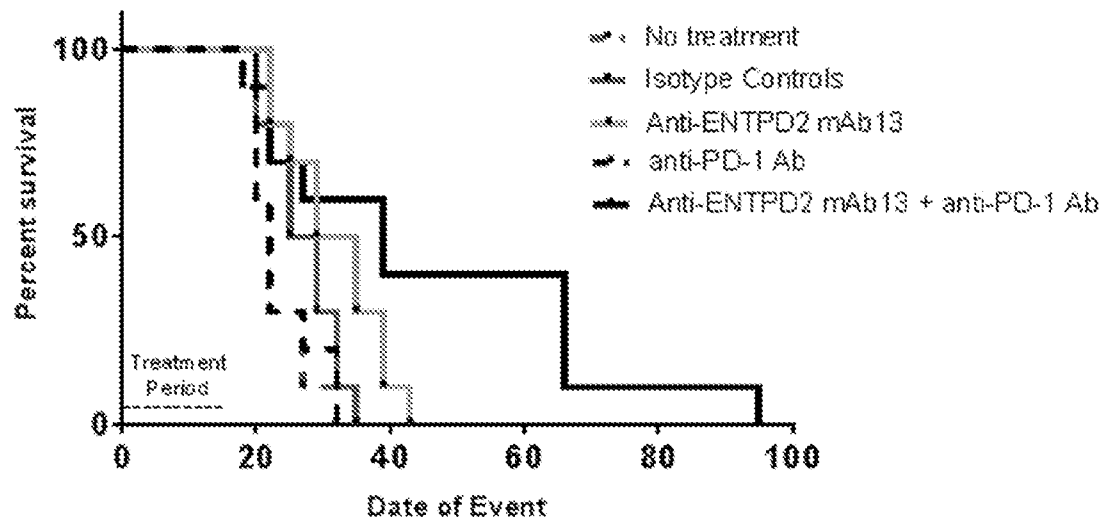


FIG. 10A

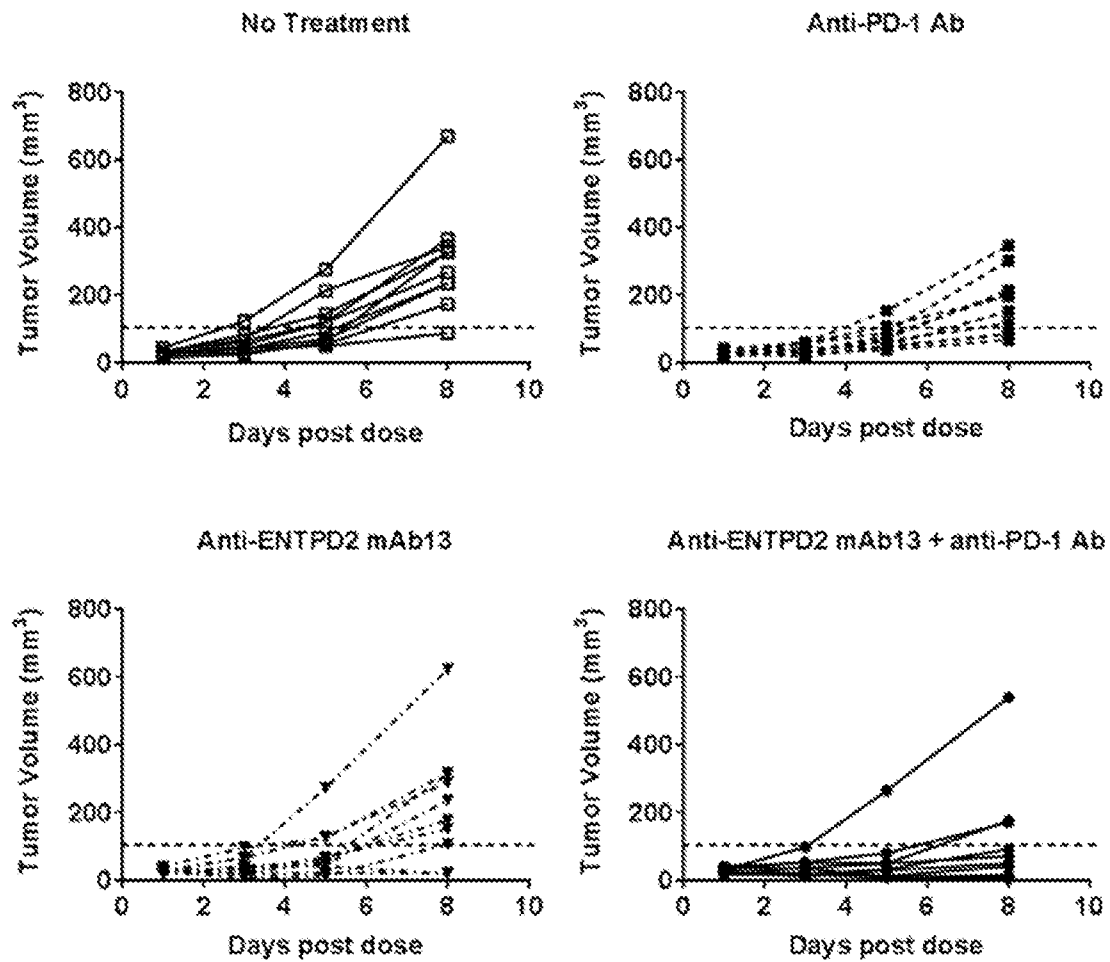


FIG. 10B

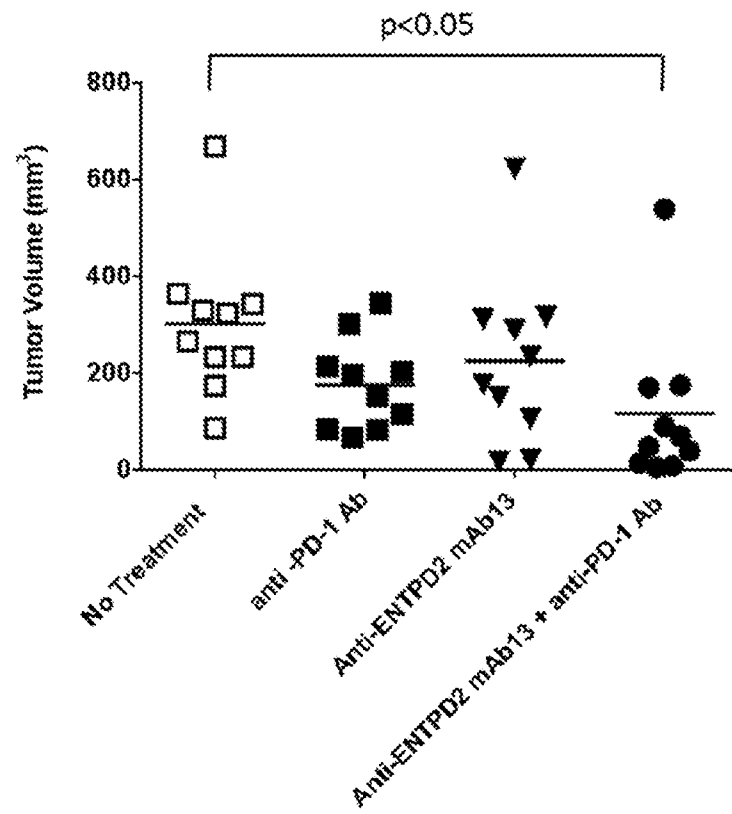


FIG. 10C

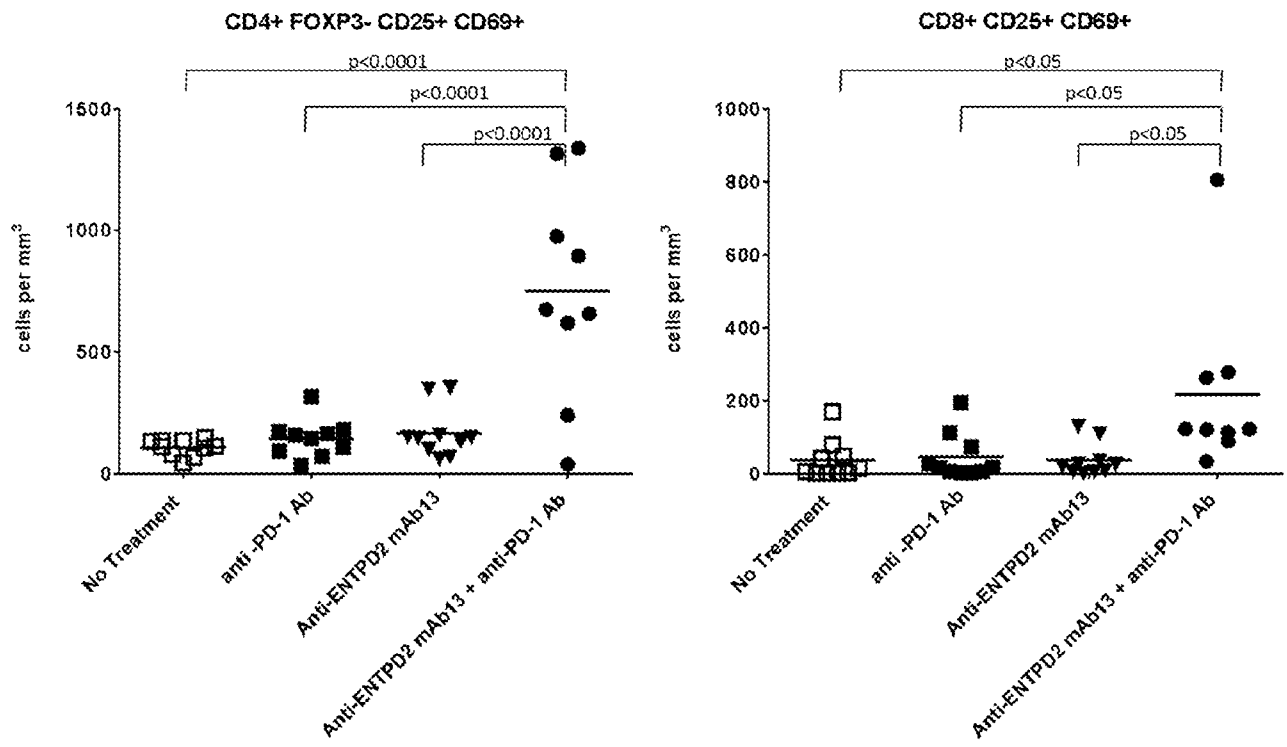


FIG. 11A

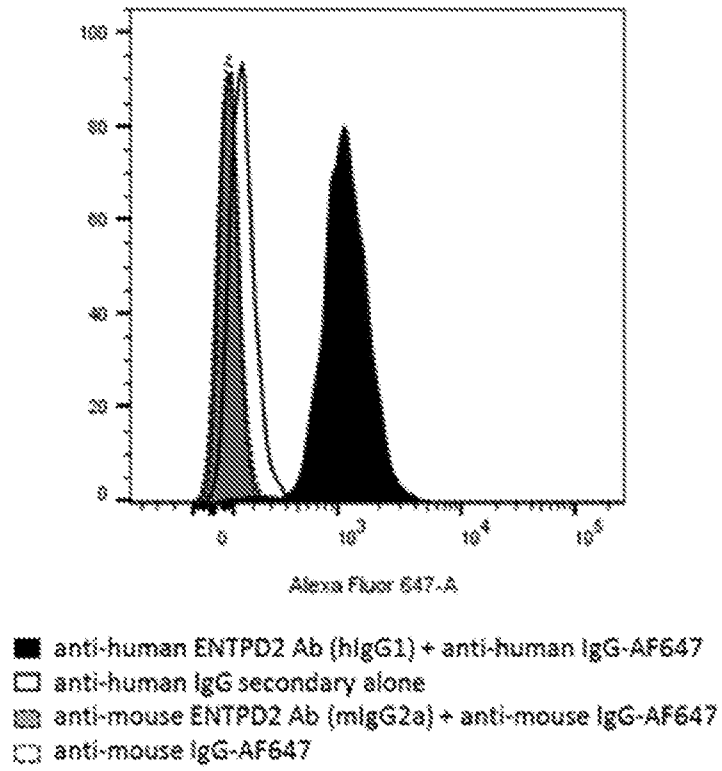


FIG. 11B

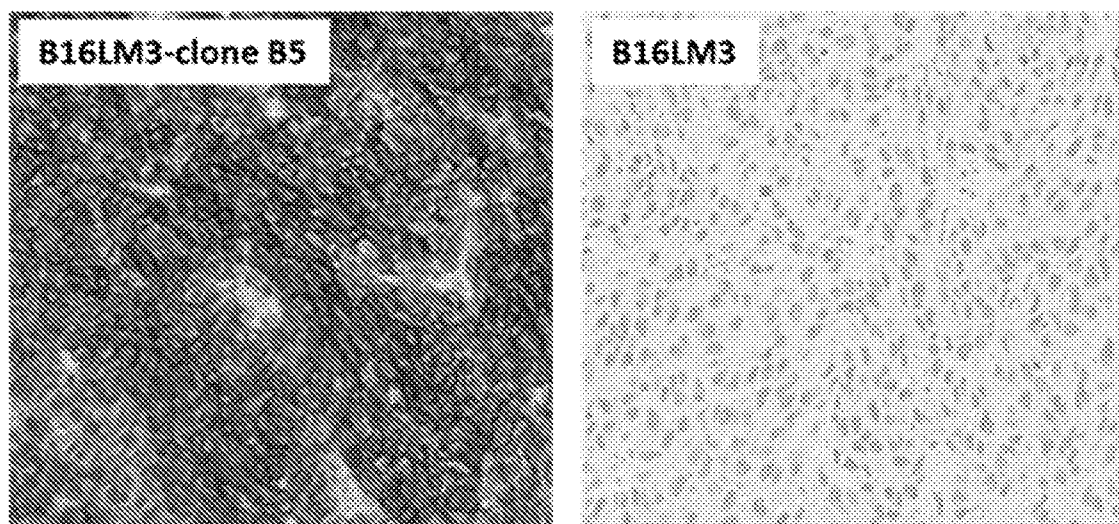


FIG. 12A

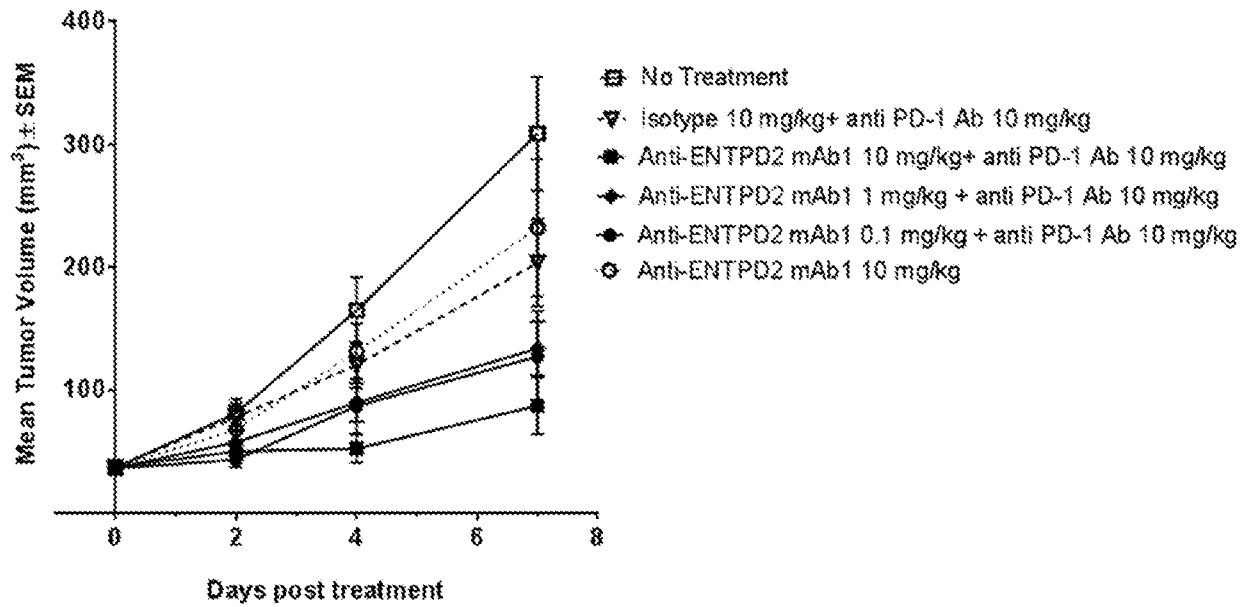


FIG. 12B

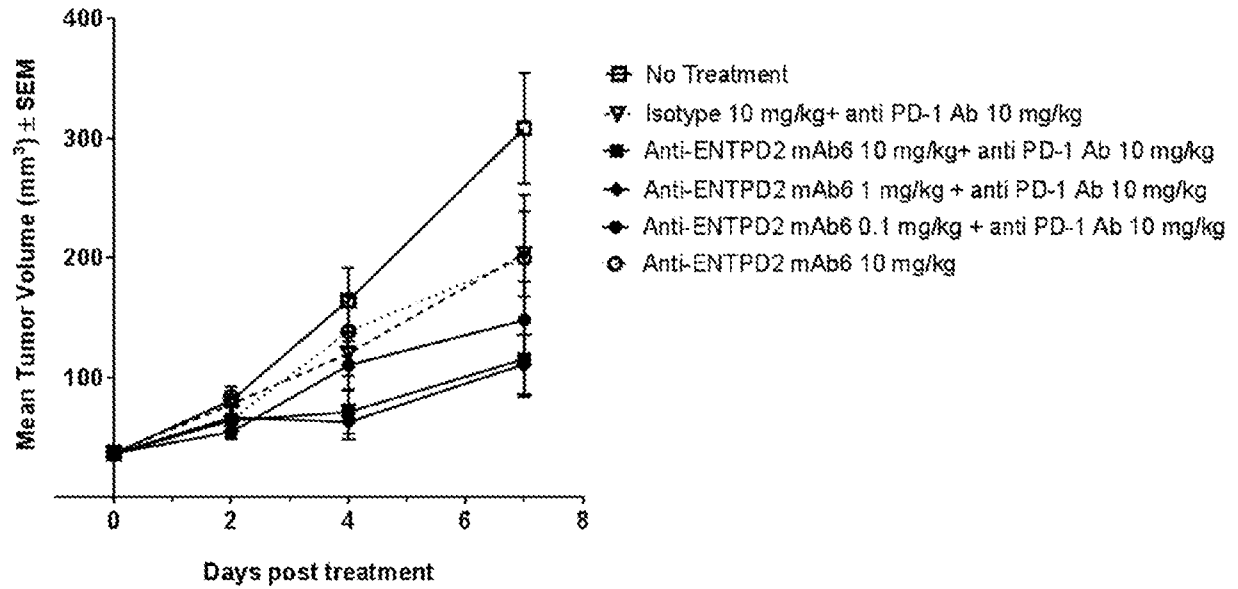


FIG. 13A

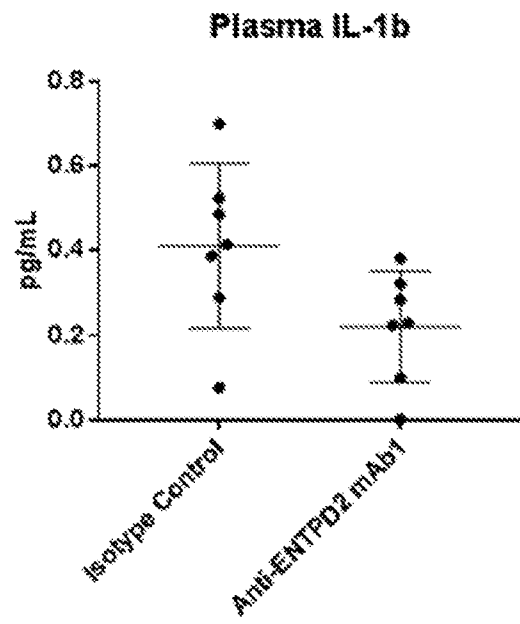


FIG. 13B

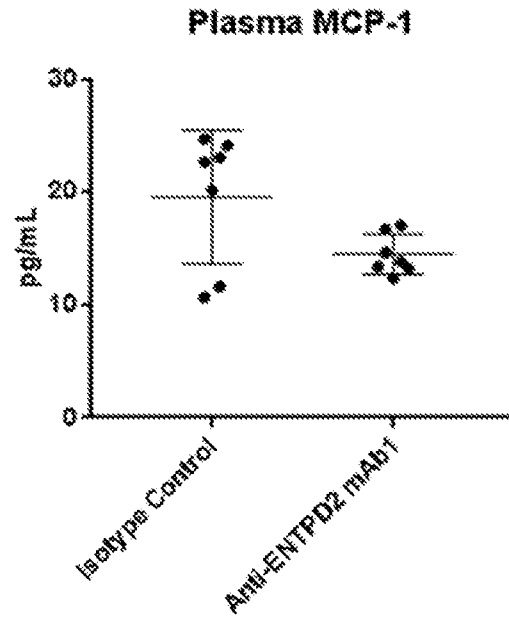


FIG. 13C

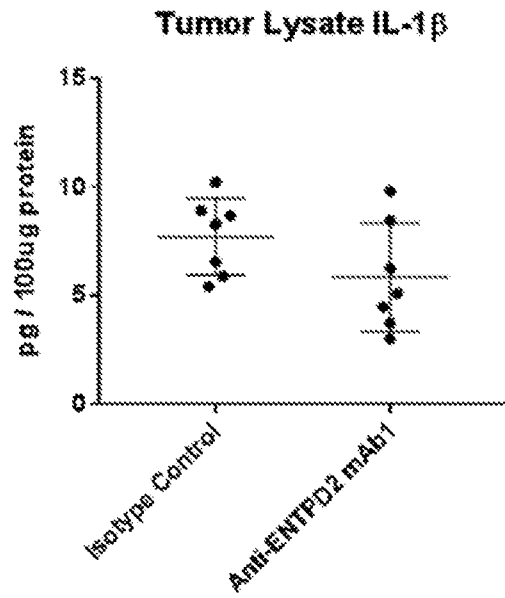


FIG. 13D

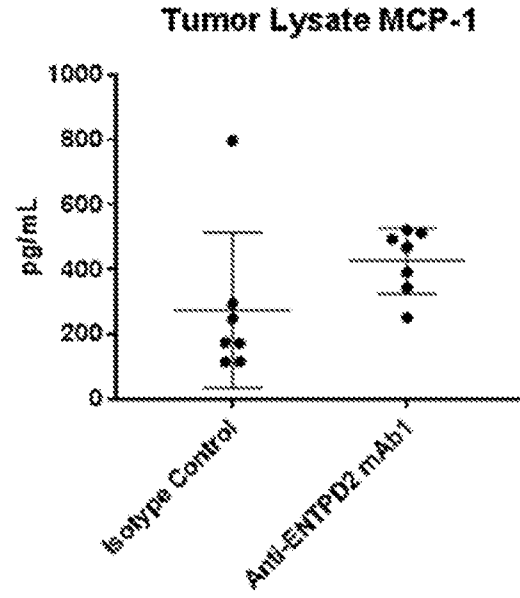


FIG. 14

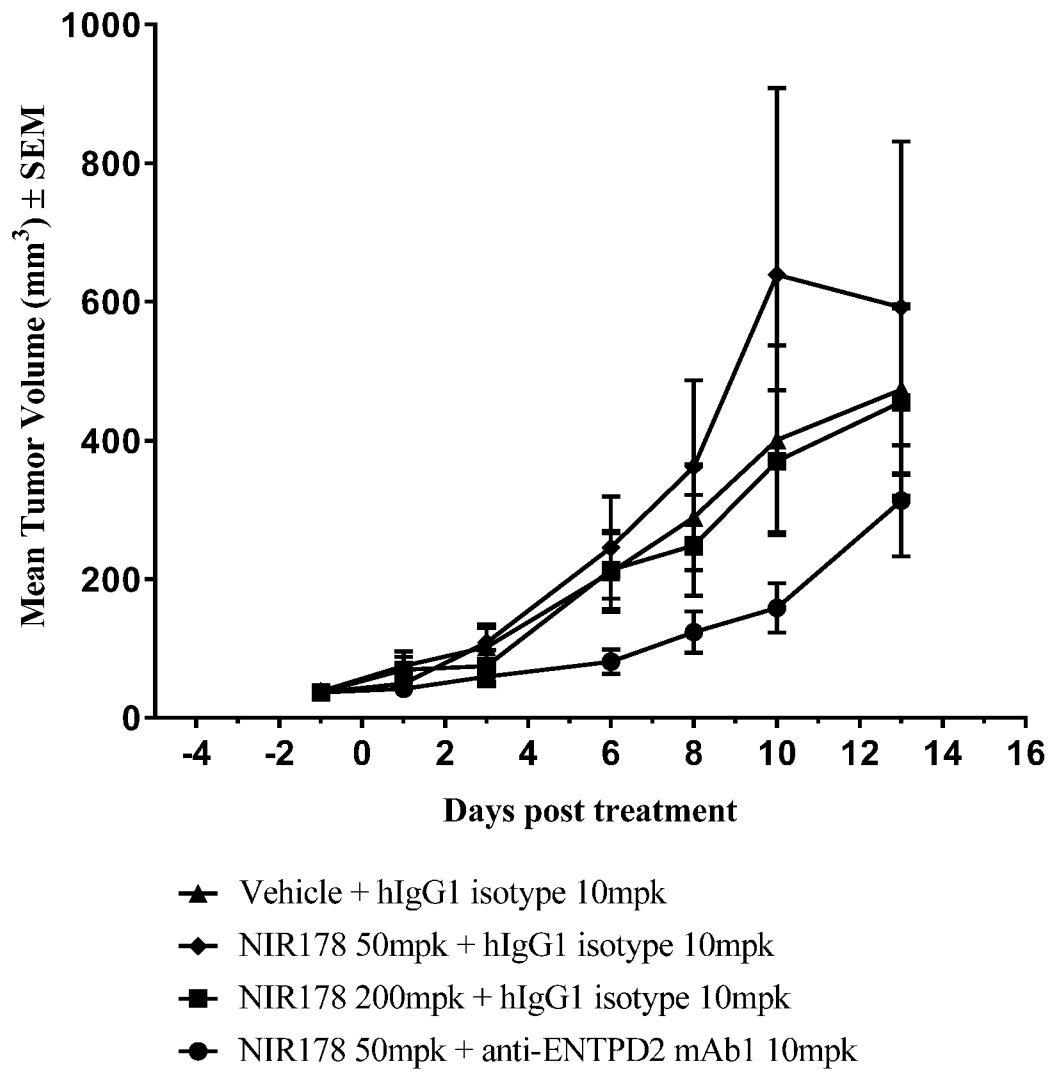


FIG. 15

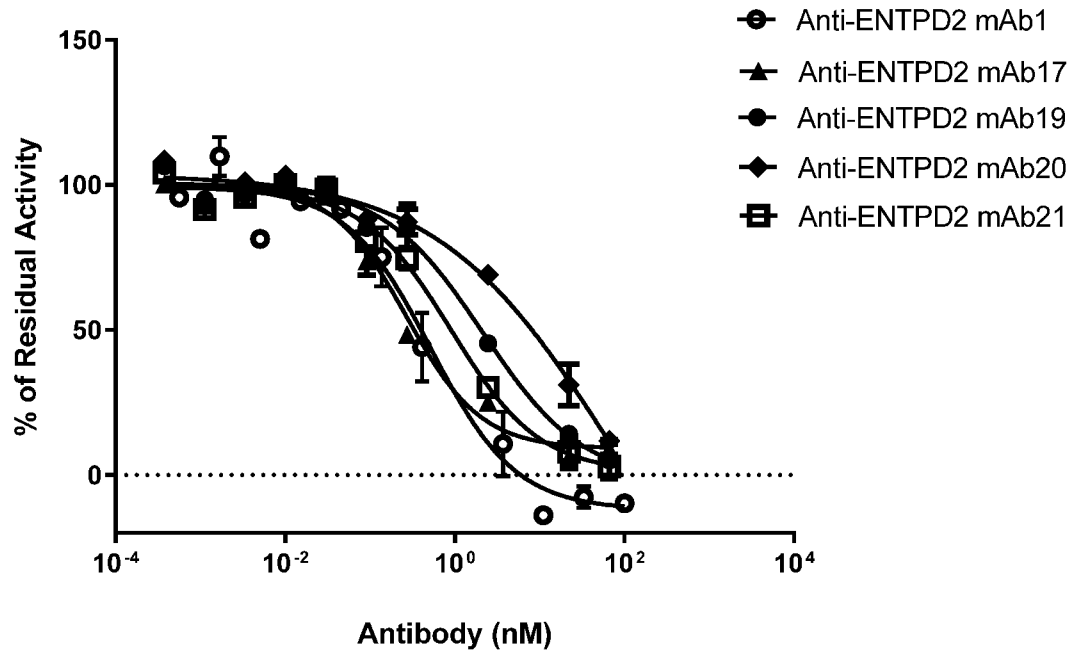


FIG. 16A

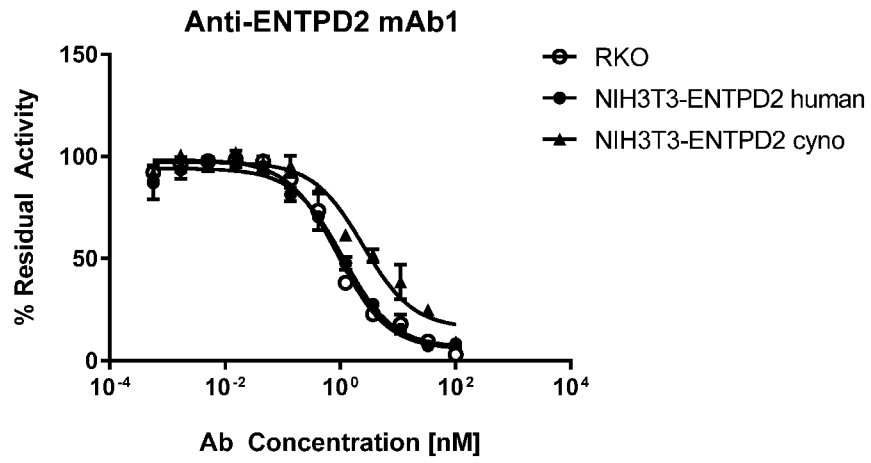


FIG. 16B

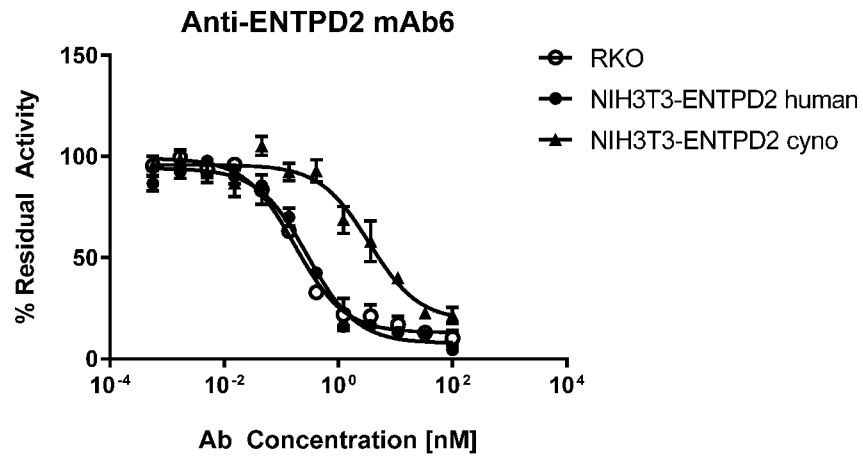


FIG. 17

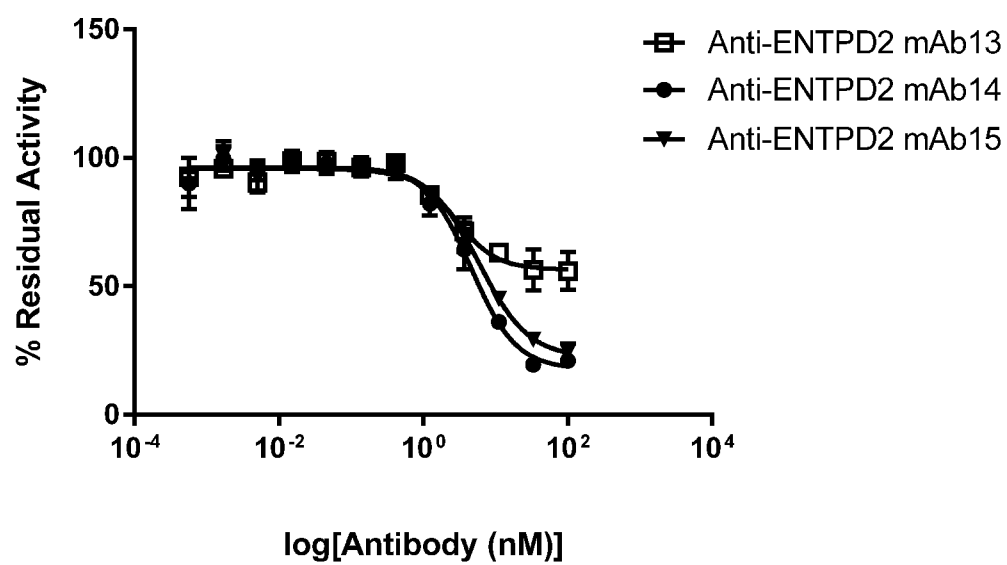


FIG. 1A

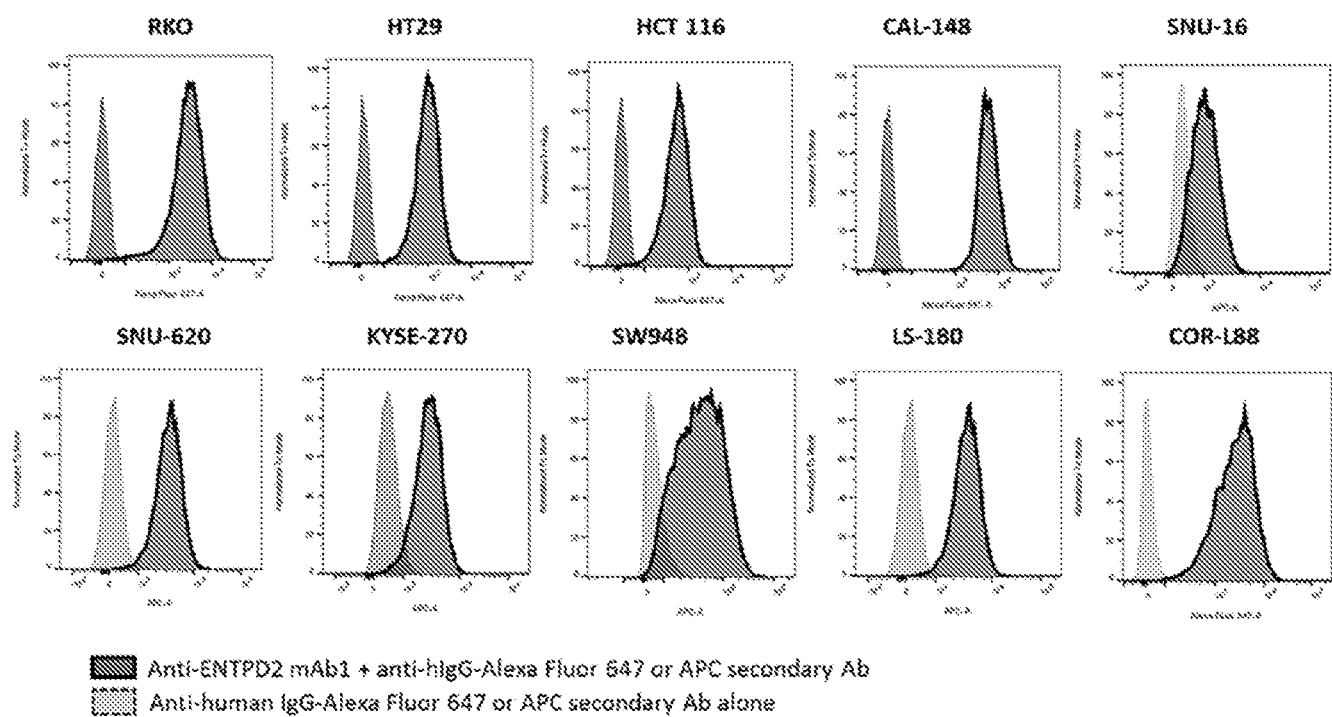


FIG. 1B

Table 20: ENTPD2 expression density across representative cancer cell lines

Cell Line	Source	Indication	Receptor Density
CAL-148	DSMZ (Germany)	Breast Adenocarcinoma	111,726
COR-L88	ECACC (UK)	Small Cell Lung Cancer	90,000
RKO	ATCC (Manassas, VA)	Colorectal Cancer	51,203
LS-180	ATCC (Manassas, VA)	Colorectal Cancer	44,708
SW948	ATCC (Manassas, VA)	Colorectal Cancer	41,576
HT29	ATCC (Manassas, VA)	Colorectal Cancer	28,337
KYSE-270	DSMZ (Germany)	Esophageal Cancer	28,273
SNU-620	KCLB (South Korea)	Stomach Adenocarcinoma	19,646
HCT 116	ATCC (Manassas, VA)	Colorectal Cancer	18,697
SNU-16	ATCC (Manassas, VA)	Gastic Carcinoma	12,763