ANTI-PROGRAMMED DEATH-LIGAND 1 (PD-L1) ANTIBODY MOLECULES, ENCODING POLYNUCLEOTIDES, AND METHODS OF USE

Related Applications

[0001] This application claims priority from U.S. Provisional Application No. US 63/311,924, filed February 18, 2022, entitled "ANTI-PROGRAMMED DEATH-LIGAND 1 (PD-L1) ANTIBODY MOLECULES, ENCODING POLYNUCLEOTIDES, AND METHODS OF USE," the contents of which are incorporated by reference in their entirety.

Incorporation By Reference of Sequence Listing

[0002] The content of the electronic Sequence Listing (file name: 751702002740SeqList.xml, date created: February 7, 2023, size: 418,493 bytes) is herein incorporated by reference in its entirety.

Field

[0003] The present disclosure relates to Programmed Death-Ligand (PD-L1) binding molecules, in particular, to anti-PD-L1 antibodies, including antibody fragments and compositions, combinations, methods, and uses thereof. The present disclosure further relates to conjugates containing such antibodies and compositions, combinations, methods, and uses for such conjugates. The disclosure is further related to nucleic acid molecules encoding the PD-L1 antibodies and fragments described herein.

Background

[0004] Programmed death-ligand 1 (PD-L1), also known as cluster of differentiation 247 (CD247) or B7-H1, is a protein receptor that functions as an immune checkpoint and downregulates immune responses. While therapies involving inhibitors of the PD-1:PD-L1 pathway and have been used in the treatment of cancers, challenges remain. Improved compositions and methods are still urgently needed to address the clinical challenges. Provided are embodiments that meet such needs.

Summary

[0005] Provided herein is an antibody or antigen-binding fragment that specifically binds a Programmed Death-Ligand (PD-L1) protein. In some of any of the examples, the PD-L1 binding antibody or antigen-binding fragment comprises a heavy chain variable (VH) region

comprising a heavy chain complementarity determining region 1 (CDR-H1), a CDR-H2, and a CDR-H3, respectively, comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, contained within the VH region sequence set forth in SEQ ID NO:1; and a light chain variable (VL) region comprising a light chain complementarity determining region 1 (CDR-L1), a CDR-L2, and a CDR-L3, respectively, comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, contained within the VL region sequence set forth in SEQ ID NO:17. In some of any of the examples, the PD-L1 binding antibody or antigen-binding fragment comprises a VH region comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, contained within the VH region sequence set forth in SEQ ID NO:2; and a VL region comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, contained within the VL region sequence set forth in SEQ ID NO:18. In some of any of the examples, the PD-L1 binding antibody or antigen-binding fragment comprises a VH region comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, contained within the VH region sequence set forth in SEQ ID NO:3; and a VL region comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, contained within the VL region sequence set forth in SEQ ID NO:19. In some of any of the examples, the PD-L1 binding antibody or antigen-binding fragment comprises a VH region comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, contained within the VH region sequence set forth in SEQ ID NO:4; and a VL region comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, contained within the VL region sequence set forth in SEQ ID NO:19. In some of any of the examples, the PD-L1 binding antibody or antigen-binding fragment comprises a VH region comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, contained within the VH region sequence set forth in SEQ ID NO:5; and a VL region comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, contained within the VL region sequence set forth in SEQ ID NO:20. In some of any of the examples, the PD-L1 binding antibody or antigen-binding fragment comprises a VH region comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, contained within the VH region sequence set forth in SEQ ID NO:1; and a VL region comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, comprising a CDR-

L1, a CDR-L2, and a CDR-L3, respectively, contained within the VL region sequence set forth in SEQ ID NO:21. In some of any of the examples, the PD-L1 binding antibody or antigen-binding fragment comprises a VH region comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, contained within the VH region sequence set forth in SEQ ID NO:2; and a VL region comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, contained within the VL region sequence set forth in SEQ ID NO:22. In some of any of the examples, the PD-L1 binding antibody or antigen-binding fragment comprises a VH region comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, contained within the VH region sequence set forth in SEQ ID NO:6; and a VL region comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, contained within the VL region sequence set forth in SEQ ID NO:238. In some of any of the examples, the PD-L1 binding antibody or antigen-binding fragment comprises a VH region comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, contained within the VH region sequence set forth in SEQ ID NO:7; and a VL region comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, contained within the VL region sequence set forth in SEQ ID NO:24. In some of any of the examples, the PD-L1 binding antibody or antigen-binding fragment comprises a VH region comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, contained within the VH region sequence set forth in SEQ ID NO:8; and a VL region comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, contained within the VL region sequence set forth in SEQ ID NO:25. In some of any of the examples, the PD-L1 binding antibody or antigen-binding fragment comprises a VH region comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, contained within the VH region sequence set forth in SEQ ID NO:9; and a VL region comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, contained within the VL region sequence set forth in SEQ ID NO:26. In some of any of the examples, the PD-L1 binding antibody or antigen-binding fragment comprises a VH region comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, contained within the VH region sequence set forth in SEQ ID NO:10;

and a VL region comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, contained within the VL region sequence set forth in SEQ ID NO:27. In some of any of the examples, the PD-L1 binding antibody or antigen-binding fragment comprises a VH region comprising a CDR-H1 a CDR-H2, and a CDR-H3, respectively, comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, contained within the VH region sequence set forth in SEQ ID NO:11; and a VL region comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, contained within the VL region sequence set forth in SEQ ID NO:28. In some of any of the examples, the PD-L1 binding antibody or antigen-binding fragment comprises a VH region comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, contained within the VH region sequence set forth in SEQ ID NO:12; and a VL region comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, contained within the VL region sequence set forth in SEQ ID NO:29. In some of any of the examples, the PD-L1 binding antibody or antigen-binding fragment comprises a VH region comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, contained within the VH region sequence set forth in SEQ ID NO:13; and a VL region comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, contained within the VL region sequence set forth in SEQ ID NO:30. In some of any of the examples, the PD-L1 binding antibody or antigen-binding fragment comprises a VH region comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, contained within the VH region sequence set forth in SEQ ID NO:14; and a VL region comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, contained within the VL region sequence set forth in SEQ ID NO:31. In some of any of the examples, the PD-L1 binding antibody or antigen-binding fragment comprises a VH region comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, contained within the VH region sequence set forth in SEQ ID NO:15; and a VL region comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, contained within the VL region sequence set forth in SEQ ID NO:32. In some of any of the examples, the PD-L1 binding antibody or antigen-binding fragment comprises a VH region comprising a CDR-H1, a CDR-H2, and a CDR-H3,

respectively, comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, contained within the VH region sequence set forth in SEQ ID NO:12; and a VL region comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, contained within the VL region sequence set forth in SEQ ID NO:33. In some of any of the examples, the PD-L1 binding antibody or antigen-binding fragment comprises a VH region comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, contained within the VH region sequence set forth in SEQ ID NO:16; and a VL region comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, contained within the VL region sequence set forth in SEQ ID NO:34. In one aspect, the present disclosure refers to an antibody or antigen-binding fragment that specifically binds a Programmed Death-Ligand (PD-L1) protein, wherein the antibody or antigen-binding fragment comprises:

(a) a heavy chain variable (VH) region comprising a heavy chain complementarity determining region 1 (CDR-H1), a CDR-H2, and a CDR-H3, respectively, comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, contained within the VH region amino acid sequence set forth in SEQ ID NO:6; and a light chain variable (VL) region comprising a light chain complementarity determining region 1 (CDR-L1), a CDR-L2, and a CDR-L3, respectively, comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, contained within the VL region amino acid sequence set forth in SEQ ID NO:23;

(b) a VH region comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, contained within the VH region amino acid sequence set forth in SEQ ID NO:1; and a VL region comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, contained within the VL region amino acid sequence set forth in SEQ ID NO:17;

(c) a VH region comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, contained within the VH region amino acid sequence set forth in SEQ ID NO:2; and a VL region comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, contained within the VL region amino acid sequence set forth in SEQ ID NO:18;

(d) a VH region comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, contained within the VH region amino acid sequence set forth in SEQ ID NO:3; and a VL region comprising a CDR-L1,

a CDR-L2, and a CDR-L3, respectively, comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, contained within the VL region amino acid sequence set forth in SEQ ID NO:19;

(e) a VH region comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, contained within the VH region amino acid sequence set forth in SEQ ID NO:4; and a VL region comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, contained within the VL region amino acid sequence set forth in SEQ ID NO:19;

(f) a VH region comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, contained within the VH region amino acid sequence set forth in SEQ ID NO:5; and a VL region comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, contained within the VL region amino acid sequence set forth in SEQ ID NO:20;

(g) a VH region comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, contained within the VH region amino acid sequence set forth in SEQ ID NO:1; and a VL region comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, contained within the VL region amino acid sequence set forth in SEQ ID NO:21;

(h) a VH region comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, contained within the VH region amino acid sequence set forth in SEQ ID NO:2; and a VL region comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, contained within the VL region amino acid sequence set forth in SEQ ID NO:22;

(i) a VH region comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, contained within the VH region amino acid sequence set forth in SEQ ID NO:7; and a VL region comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, contained within the VL region amino acid sequence set forth in SEQ ID NO:24;

(j) a VH region comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, contained within the VH region amino acid sequence set forth in SEQ ID NO:8; and a VL region comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, contained within the VL region amino acid sequence set forth in SEQ ID NO:25;

(k) a VH region comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, contained within the VH region amino acid sequence set forth in SEQ ID NO:9; and a VL region comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, contained within the VL region amino acid sequence set forth in SEQ ID NO:26;

(l) a VH region comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, contained within the VH region amino acid sequence set forth in SEQ ID NO:10; and a VL region comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, contained within the VL region amino acid sequence set forth in SEQ ID NO:27;

(m) a VH region comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, contained within the VH region amino acid sequence set forth in SEQ ID NO:11; and a VL region comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, contained within the VL region amino acid sequence set forth in SEQ ID NO:28;

(n) a VH region comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, contained within the VH region amino acid sequence set forth in SEQ ID NO:12; and a VL region comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, contained within the VL region amino acid sequence set forth in SEQ ID NO:29;

(o) a VH region comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, contained within the VH region amino acid sequence set forth in SEQ ID NO:13; and a VL region comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, contained within the VL region amino acid sequence set forth in SEQ ID NO:30;

(p) a VH region comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, contained within the VH region amino acid sequence set forth in SEQ ID NO:14; and a VL region comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, contained within the VL region amino acid sequence set forth in SEQ ID NO:31;

(q) a VH region comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, contained within the VH region amino acid sequence set forth in SEQ ID NO:15; and a VL region comprising a CDR-L1,

a CDR-L2, and a CDR-L3, respectively, comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, contained within the VL region amino acid sequence set forth in SEQ ID NO:32;

(r) a VH region comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, contained within the VH region amino acid sequence set forth in SEQ ID NO:12; and a VL region comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, contained within the VL region amino acid sequence set forth in SEQ ID NO:33; or

(s) a VH region comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, comprising a CDR-H1, a CDR-H2, and a CDR-H3, respectively, contained within the VH region amino acid sequence set forth in SEQ ID NO:16; and a VL region comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, comprising a CDR-L1, a CDR-L2, and a CDR-L3, respectively, contained within the VL region amino acid sequence set forth in SEQ ID NO:34.

[0006] In some of any of the examples, the VH region comprises a CDR-H1 comprising SEQ ID NO:35, a CDR-H2 comprising SEQ ID NO:36, and a CDR-H3 comprising SEQ ID NO:37; and the VL region comprises a CDR-L1 comprising SEQ ID NO:210, a CDR-L2 comprises SEQ ID NO:211, and a CDR-L3 comprising SEQ ID NO:212. In some of any of the examples, the VH region comprises a CDR-H1 comprising SEQ ID NO:48, a CDR-H2 comprising SEQ ID NO:49, and a CDR-H3 comprising SEQ ID NO:37; and the VL region comprises a CDR-L1 comprising SEQ ID NO:218, a CDR-L2 comprises SEQ ID NO:211, and a CDR-L3 comprising SEQ ID NO:212. In some of any of the examples, the VH region comprises a CDR-H1 comprising SEQ ID NO:58, a CDR-H2 comprising SEQ ID NO:59, and a CDR-H3 comprising SEQ ID NO:60; and the VL region comprises a CDR-L1 comprising SEQ ID NO:221, a CDR-L2 comprises SEQ ID NO:222, and a CDR-L3 comprising SEQ ID NO:223. In some of any of the examples, the VH region comprises a CDR-H1 comprising SEQ ID NO:71, a CDR-H2 comprising SEQ ID NO:72, and a CDR-H3 comprising SEQ ID NO:60; and the VL region comprises a CDR-L1 comprising SEQ ID NO:229, a CDR-L2 comprises SEQ ID NO:222, and a CDR-L3 comprising SEQ ID NO:223. In some of any of the examples, the VH region comprises a CDR-H1 comprising SEQ ID NO:35, a CDR-H2 comprising SEQ ID NO:36, and a CDR-H3 comprising SEQ ID NO:37; and the VL region comprises a CDR-L1 comprising SEQ ID NO:233, a CDR-L2 comprises SEQ ID NO:234, and a CDR-L3 comprising SEQ ID NO:235. In some of any of the examples, the VH region comprises a CDR-H1 comprising SEQ ID NO:48, a CDR-H2 comprising SEQ ID NO:49, and a CDR-H3 comprising SEQ ID NO:37; and the VL region comprises a CDR-L1 comprising SEQ ID NO:241, a CDR-L2 comprises SEQ ID NO:234, and a CDR-L3 comprising SEQ ID NO:242. In some of any of the examples, the VH region comprises a CDR-H1 comprising SEQ ID NO:82, a CDR-H2

comprising SEQ ID NO:83, and a CDR-H3 comprising SEQ ID NO:84; and the VL region comprises a CDR-L1 comprising SEQ ID NO:246, a CDR-L2 comprises SEQ ID NO:247, and a CDR-L3 comprising SEQ ID NO:248. In some of any of the examples, the VH region comprises a CDR-H1 comprising SEQ ID NO:48, a CDR-H2 comprising SEQ ID NO:95, and a CDR-H3 comprising SEQ ID NO:84; and the VL region comprises a CDR-L1 comprising SEQ ID NO:246, a CDR-L2 comprises SEQ ID NO:254, and a CDR-L3 comprising SEQ ID NO:255. In some of any of the examples, the VH region comprises a CDR-H1 comprising SEQ ID NO:48, a CDR-H2 comprising SEQ ID NO:104, and a CDR-H3 comprising SEQ ID NO:105; and the VL region comprises a CDR-L1 comprising SEQ ID NO:258, a CDR-L2 comprises SEQ ID NO:259, and a CDR-L3 comprising SEQ ID NO:260. In some of any of the examples, the VH region comprises a CDR-H1 comprising SEQ ID NO:116, a CDR-H2 comprising SEQ ID NO:117, and a CDR-H3 comprising SEQ ID NO:118; and the VL region comprises a CDR-L1 comprising SEQ ID NO:265, a CDR-L2 comprises SEQ ID NO:266, and a CDR-L3 comprising SEQ ID NO:267. In some of any of the examples, the VH region comprises a CDR-H1 comprising SEQ ID NO:129, a CDR-H2 comprising SEQ ID NO:130, and a CDR-H3 comprising SEQ ID NO:131; and the VL region comprises a CDR-L1 comprising SEQ ID NO:246, a CDR-L2 comprises SEQ ID NO:273, and a CDR-L3 comprising SEQ ID NO:274. In some of any of the examples, the VH region comprises a CDR-H1 comprising SEQ ID NO:142, a CDR-H2 comprising SEQ ID NO:143, and a CDR-H3 comprising SEQ ID NO:144; and the VL region comprises a CDR-L1 comprising SEQ ID NO:278, a CDR-L2 comprises SEQ ID NO:279, and a CDR-L3 comprising SEQ ID NO:280. In some of any of the examples, the VH region comprises a CDR-H1 comprising SEQ ID NO:155, a CDR-H2 comprising SEQ ID NO:156, and a CDR-H3 comprising SEQ ID NO:157; and the VL region comprises a CDR-L1 comprising SEQ ID NO:286, a CDR-L2 comprises SEQ ID NO:287, and a CDR-L3 comprising SEQ ID NO:288. In some of any of the examples, the VH region comprises a CDR-H1 comprising SEQ ID NO:168, a CDR-H2 comprising SEQ ID NO:169, and a CDR-H3 comprising SEQ ID NO:170; and the VL region comprises a CDR-L1 comprising SEQ ID NO:294, a CDR-L2 comprises SEQ ID NO:234, and a CDR-L3 comprising SEQ ID NO:295. In some of any of the examples, the VH region comprises a CDR-H1 comprising SEQ ID NO:35, a CDR-H2 comprising SEQ ID NO:181, and a CDR-H3 comprising SEQ ID NO:182; and the VL region comprises a CDR-L1 comprising SEQ ID NO:299, a CDR-L2 comprises SEQ ID NO:300, and a CDR-L3 comprising SEQ ID NO:301. In some of any of the examples, the VH region comprises a CDR-H1 comprising SEQ ID NO:168, a CDR-H2

comprising SEQ ID NO:169, and a CDR-H3 comprising SEQ ID NO:193; and the VL region comprises a CDR-L1 comprising SEQ ID NO:306, a CDR-L2 comprises SEQ ID NO:234, and a CDR-L3 comprising SEQ ID NO:307. In some of any of the examples, the VH region comprises a CDR-H1 comprising SEQ ID NO:155, a CDR-H2 comprising SEQ ID NO:156, and a CDR-H3 comprising SEQ ID NO:157; and the VL region comprises a CDR-L1 comprising SEQ ID NO:311, a CDR-L2 comprises SEQ ID NO:312, and a CDR-L3 comprising SEQ ID NO:313. In some of any of the examples, the VH region comprises a CDR-H1 comprising SEQ ID NO:197, a CDR-H2 comprising SEQ ID NO:198, and a CDR-H3 comprising SEQ ID NO:199; and the VL region comprises a CDR-L1 comprising SEQ ID NO:319, a CDR-L2 comprises SEQ ID NO:320, and a CDR-L3 comprising SEQ ID NO:321.

[0007] In some of any of the examples, the VH region comprises a CDR-H1 comprising SEQ ID NO:40, a CDR-H2 comprising SEQ ID NO:41, and a CDR-H3 comprising SEQ ID NO:37; and the VL region comprises a CDR-L1 comprising SEQ ID NO:210, a CDR-L2 comprises SEQ ID NO:211, and a CDR-L3 comprising SEQ ID NO:212. In some of any of the examples, the VH region comprises a CDR-H1 comprising SEQ ID NO:52, a CDR-H2 comprising SEQ ID NO:53, and a CDR-H3 comprising SEQ ID NO:37; and the VL region comprises a CDR-L1 comprising SEQ ID NO:218, a CDR-L2 comprises SEQ ID NO:211, and a CDR-L3 comprising SEQ ID NO:212. In some of any of the examples, the VH region comprises a CDR-H1 comprising SEQ ID NO:63, a CDR-H2 comprising SEQ ID NO:64, and a CDR-H3 comprising SEQ ID NO:60; and the VL region comprises a CDR-L1 comprising SEQ ID NO:221, a CDR-L2 comprises SEQ ID NO:222, and a CDR-L3 comprising SEQ ID NO:223. In some of any of the examples, the VH region comprises a CDR-H1 comprising SEQ ID NO:75, a CDR-H2 comprising SEQ ID NO:76, and a CDR-H3 comprising SEQ ID NO:60; and the VL region comprises a CDR-L1 comprising SEQ ID NO:229, a CDR-L2 comprises SEQ ID NO:222, and a CDR-L3 comprising SEQ ID NO:223. In some of any of the examples, the VH region comprises a CDR-H1 comprising SEQ ID NO:40, a CDR-H2 comprising SEQ ID NO:41, and a CDR-H3 comprising SEQ ID NO:37; and the VL region comprises a CDR-L1 comprising SEQ ID NO:233, a CDR-L2 comprises SEQ ID NO:234, and a CDR-L3 comprising SEQ ID NO:235. In some of any of the examples, the VH region comprises a CDR-H1 comprising SEQ ID NO:52, a CDR-H2 comprising SEQ ID NO:53, and a CDR-H3 comprising SEQ ID NO:37; and the VL region comprises a CDR-L1 comprising SEQ ID NO:241, a CDR-L2 comprises SEQ ID NO:234, and a CDR-L3 comprising SEQ ID NO:242. In some of any of the examples, the VH region comprises a CDR-H1 comprising SEQ ID NO:87, a CDR-H2

comprising SEQ ID NO:88, and a CDR-H3 comprising SEQ ID NO:84; and the VL region comprises a CDR-L1 comprising SEQ ID NO:246, a CDR-L2 comprises SEQ ID NO:247, and a CDR-L3 comprising SEQ ID NO:248. In some of any of the examples, the VH region comprises a CDR-H1 comprising SEQ ID NO:98, a CDR-H2 comprising SEQ ID NO:99, and a CDR-H3 comprising SEQ ID NO:84; and the VL region comprises a CDR-L1 comprising SEQ ID NO:246, a CDR-L2 comprises SEQ ID NO:254, and a CDR-L3 comprising SEQ ID NO:255. In some of any of the examples, the VH region comprises a CDR-H1 comprising SEQ ID NO:108, a CDR-H2 comprising SEQ ID NO:109, and a CDR-H3 comprising SEQ ID NO:105; and the VL region comprises a CDR-L1 comprising SEQ ID NO:258, a CDR-L2 comprises SEQ ID NO:259, and a CDR-L3 comprising SEQ ID NO:260. In some of any of the examples, the VH region comprises a CDR-H1 comprising SEQ ID NO:121, a CDR-H2 comprising SEQ ID NO:122, and a CDR-H3 comprising SEQ ID NO:118; and the VL region comprises a CDR-L1 comprising SEQ ID NO:265, a CDR-L2 comprises SEQ ID NO:266, and a CDR-L3 comprising SEQ ID NO:267. In some of any of the examples, the VH region comprises a CDR-H1 comprising SEQ ID NO:134, a CDR-H2 comprising SEQ ID NO:135, and a CDR-H3 comprising SEQ ID NO:131; and the VL region comprises a CDR-L1 comprising SEQ ID NO:246, a CDR-L2 comprises SEQ ID NO:273, and a CDR-L3 comprising SEQ ID NO:274. In some of any of the examples, the VH region comprises a CDR-H1 comprising SEQ ID NO:147, a CDR-H2 comprising SEQ ID NO:148, and a CDR-H3 comprising SEQ ID NO:144; and the VL region comprises a CDR-L1 comprising SEQ ID NO:278, a CDR-L2 comprises SEQ ID NO:279, and a CDR-L3 comprising SEQ ID NO:280. In some of any of the examples, the VH region comprises a CDR-H1 comprising SEQ ID NO:160, a CDR-H2 comprising SEQ ID NO:161, and a CDR-H3 comprising SEQ ID NO:157; and the VL region comprises a CDR-L1 comprising SEQ ID NO:286, a CDR-L2 comprises SEQ ID NO:287, and a CDR-L3 comprising SEQ ID NO:288. In some of any of the examples, the VH region comprises a CDR-H1 comprising SEQ ID NO:173, a CDR-H2 comprising SEQ ID NO:174, and a CDR-H3 comprising SEQ ID NO:170; and the VL region comprises a CDR-L1 comprising SEQ ID NO:294, a CDR-L2 comprises SEQ ID NO:234, and a CDR-L3 comprising SEQ ID NO:295. In some of any of the examples, the VH region comprises a CDR-H1 comprising SEQ ID NO:185, a CDR-H2 comprising SEQ ID NO:186, and a CDR-H3 comprising SEQ ID NO:182; and the VL region comprises a CDR-L1 comprising SEQ ID NO:299, a CDR-L2 comprises SEQ ID NO:300, and a CDR-L3 comprising SEQ ID NO:301. In some of any of the examples, the VH region comprises a CDR-H1 comprising SEQ ID NO:173, a CDR-H2

comprising SEQ ID NO:174, and a CDR-H3 comprising SEQ ID NO:193; and the VL region comprises a CDR-L1 comprising SEQ ID NO:306, a CDR-L2 comprises SEQ ID NO:234, and a CDR-L3 comprising SEQ ID NO:307. In some of any of the examples, the VH region comprises a CDR-H1 comprising SEQ ID NO:160, a CDR-H2 comprising SEQ ID NO:161, and a CDR-H3 comprising SEQ ID NO:157; and the VL region comprises a CDR-L1 comprising SEQ ID NO:311, a CDR-L2 comprises SEQ ID NO:312, and a CDR-L3 comprising SEQ ID NO:313. In some of any of the examples, the VH region comprises a CDR-H1 comprising SEQ ID NO:202, a CDR-H2 comprising SEQ ID NO:203, and a CDR-H3 comprising SEQ ID NO:199; and the VL region comprises a CDR-L1 comprising SEQ ID NO:319, a CDR-L2 comprises SEQ ID NO:320, and a CDR-L3 comprising SEQ ID NO:321.

[0008] In some of any of the examples, the VH region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:1; and the VL region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:17. In some of any of the examples, the VH region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:2; and the VL region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:18. In some of any of the examples, the VH region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:3; and the VL region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:19. In some of any of the examples, the VH region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:4; and the VL region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:19. In some of any of the examples, the VH region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:5; and the VL region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:20. In some of any of the examples, the VH region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:1; and the VL region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:21. In some of any of the examples, the VH region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:21; and the VL region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:22. In some of any of the examples, the VH region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:6; and the VL region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:23. In some of any of the examples, the VH region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:7; and the VL region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:24. In some of any of the examples, the VH region

comprises a sequence that has at least 95% sequence identity to SEQ ID NO:8; and the VL region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:25. In some of any of the examples, the VH region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:9; and the VL region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:26. In some of any of the examples, the VH region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:10; and the VL region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:27. In some of any of the examples, the VH region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:11; and the VL region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:28. In some of any of the examples, the VH region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:12; and the VL region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:29. In some of any of the examples, the VH region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:13; and the VL region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:30. In some of any of the examples, the VH region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:14; and the VL region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:31. In some of any of the examples, the VH region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:15; and the VL region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:32. In some of any of the examples, the VH region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:12; and the VL region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:33. In some of any of the examples, the VH region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:16; and the VL region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:34.

[0009] In some of any of the examples, the VH region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:330; and the VL region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:335. In some of any of the examples, the VH region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:331; and the VL region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:336. In some of any of the examples, the VH region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:332; and the VL region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:337. In some of any of the examples, the VH region

comprises a sequence that has at least 95% sequence identity to SEQ ID NO:333; and the VL region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:338. In some of any of the examples, the VH region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:330; and the VL region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:339. In some of any of the examples, the VH region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:334; and the VL region comprises a sequence that has at least 95% sequence identity to SEQ ID NO:340.

[0010] In some of any of the examples, the VH region comprises SEQ ID NO:1; and the VL region comprises SEQ ID NO:17. In some of any of the examples, the VH region comprises SEQ ID NO:2; and the VL region comprises SEQ ID NO:18. In some of any of the examples, the VH region comprises SEQ ID NO:3; and the VL region comprises SEQ ID NO:19. In some of any of the examples, the VH region comprises SEQ ID NO:4; and the VL region comprises SEQ ID NO:19. In some of any of the examples, the VH region comprises SEQ ID NO:5; and the VL region comprises SEQ ID NO:20. In some of any of the examples, the VH region comprises SEQ ID NO:1; and the VL region comprises SEQ ID NO:21. In some of any of the examples, the VH region comprises SEQ ID NO:21; and the VL region comprises SEQ ID NO:22. In some of any of the examples, the VH region comprises SEQ ID NO:6; and the VL region comprises SEQ ID NO:23. In some of any of the examples, the VH region comprises SEQ ID NO:7; and the VL region comprises SEQ ID NO:24. In some of any of the examples, the VH region comprises SEQ ID NO:8; and the VL region comprises SEQ ID NO:25. In some of any of the examples, the VH region comprises SEQ ID NO:9; and the VL region comprises SEQ ID NO:26. In some of any of the examples, the VH region comprises SEQ ID NO:10; and the VL region comprises SEQ ID NO:27. In some of any of the examples, the VH region comprises SEQ ID NO:11; and the VL region comprises SEQ ID NO:28. In some of any of the examples, the VH region comprises SEQ ID NO:12; and the VL region comprises SEQ ID NO:29. In some of any of the examples, the VH region comprises SEQ ID NO:13; and the VL region comprises SEQ ID NO:30. In some of any of the examples, the VH region comprises SEQ ID NO:14; and the VL region comprises SEQ ID NO:31. In some of any of the examples, the VH region comprises SEQ ID NO:15; and the VL region comprises SEQ ID NO:32. In some of any of the examples, the VH region comprises SEQ ID NO:12; and the VL region comprises SEQ ID NO:33. In some of any of the examples, the VH region comprises SEQ ID NO:16; and the VL region comprises SEQ ID NO:34.

[0011] . In some of any of the examples, the VH region comprises SEQ ID NO:330; and the VL region comprises SEQ ID NO:335. In some of any of the examples, the VH region comprises SEQ ID NO:331; and the VL region comprises SEQ ID NO:336. In some of any of the examples, the VH region comprises SEQ ID NO:332; and the VL region comprises SEQ ID NO:337. In some of any of the examples, the VH region comprises SEQ ID NO:333; and the VL region comprises SEQ ID NO:338. In some of any of the examples, the VH region comprises SEQ ID NO:330; and the VL region comprises SEQ ID NO:339. In some of any of the examples, the VH region comprises SEQ ID NO:334; and the VL region comprises SEQ ID NO:340.

[0012] In some of any of the examples, the PD-L1 protein is a human PD-L1 protein.

[0013] In some of any of the examples, the antibody or antigen-binding fragment is recombinant. In some of any of the examples, the antibody or antigen-binding fragment is monoclonal. In some of any of the examples, the antibody or antigen-binding fragment is a human, chimeric, or humanized antibody or antigen-binding fragment.

[0014] In some of any of the examples, the antibody or antigen binding fragment comprises an Fc region of a human immunoglobulin and/or human antibody framework regions.

[0015] In some of any of the examples, the antibody or antigen-binding fragment is that is a single chain antibody fragment. In some of any of the examples, the antibody fragment comprises a single chain Fv (scFv).

[0016] In some of any of the examples, the antibody is a whole or intact antibody.

[0017] In some of any of the examples, the antibody or antigen-binding fragment is a bispecific antibody that further specifically binds to a second antigen. In some of any of the examples, the second antigen is an antigen expressed on a tumor cell or an immune cell. In some of any of the examples, the second antigen is an antigen expressed on an immune cell that is a T cell and the antigen is CD25.

[0018] In some of any of the examples, the antibody or antigen-binding fragment thereof comprises an Fc region that exhibits one or more Fc-mediated effector function(s). In some of any of the examples, the antibody or antigen-binding fragment thereof an Fc region that lacks Fc-mediated effector function(s), exhibits substantially reduced Fc-mediated effector function(s) or does not exhibit substantial Fc-mediated effector function(s). In some of any of the examples, the antibody or antigen-binding fragment thereof comprises an Fc region that exhibits enhanced Fc-mediated effector function(s). In some of any of the examples, the Fc-mediated effector function is selected from one or more of an antibody-dependent cellular

cytotoxicity (ADCC), antibody-dependent cellular phagocytosis (ADCP) or complement-dependent cytotoxicity (CDC).

[0019] In some of any of the examples, the antibody or antigen binding fragment comprises an IgG1 Fc region or an IgG1 isotype, an IgG2 Fc region or an IgG2 isotype, IgG3 Fc region or an IgG3 isotype, or an IgG4 Fc region or an IgG4 isotype.

[0020] Also provided is a conjugate, comprising any of the provided antibody or antigen-binding fragment and a heterologous molecule or moiety. In one aspect, the present disclosure refers to a conjugate, comprising the antibody or antigen-binding fragment as disclosed herein and a heterologous molecule or moiety. In some of any of the examples, the heterologous molecule or moiety is a protein, peptide, nucleic acid, dye, or small molecule. In some of any of the examples, the heterologous molecule or moiety is a cytotoxic agent, a toxin, a radioisotope, a chemotherapeutic agent, a lytic peptide, a cytokine, or a photoactivatable dye.

[0020a] In another aspect, the present disclosure refers to a conjugate, comprising:

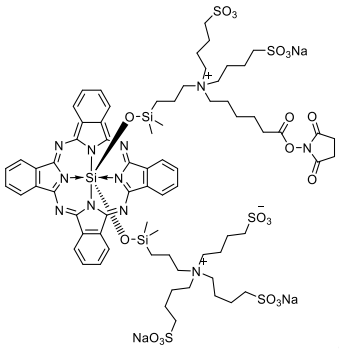
a) an antibody or antigen-binding fragment that specifically binds a Programmed Death-Ligand (PD-L1) protein, wherein the antibody or antigen-binding fragment comprises:
    i) a VH region comprising a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO:87, a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO:88, and a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO:84; and
    ii) a VL region comprising a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO:246, a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO:247, and a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO:248; and

b) a heterologous molecule or moiety that is a Si-phthalocyanine dye.

[0021] In some of any of the examples, the photoactivatable dye is a phthalocyanine dye. In some of any of the examples, the phthalocyanine dye is a Si-phthalocyanine dye.

[0022] In some of any of the examples, the phthalocyanine dye is IR700.

[0023] In some of any of the examples, the phthalocyanine dye has the structure of Formula (I):



, or is a salt, stereoisomer, or tautomer thereof.

[0024] In some of any of the examples, the conjugate is activated by illumination at a wavelength between at or at about 600 nm and at or about 850 nm to effect cell killing.

[0025] In some of any of the examples, the activated conjugate effects tumor growth inhibition or killing at a higher level, activity, or potency than the unconjugated antibody.

[0026] In some of any of the examples, the antibody or antigen-binding fragment and the moiety are linked directly or indirectly via a linker.

[0027] In some of any of the examples, the antibody or antigen-binding fragment is covalently attached to the heterologous molecule or moiety.

[0028] In some of any of the examples, when contacted with a cell expressing a PD-L1 protein, the conjugate exhibits increased internalization compared to an unconjugated antibody or antigen-binding fragment, or a conjugate comprising a reference antibody. In some of any of the examples, when contacted with a cell expressing a PD-L1 protein, the conjugate exhibits reduced internalization compared to an unconjugated antibody or antigen-binding fragment, or a conjugate comprising a reference antibody. In some of any of the examples, the reference antibody is avelumab.

[0029] In some of any of the examples, the conjugate does not exhibit substantially reduced binding affinity to a PD-L1 protein compared to the unconjugated antibody, or exhibits at least 50%, at least 60%, at least 70%, at least 80%, at least 90%, at least 95%, at least 96%, at least 97%, at least 98%, or at least 99% of the binding affinity of the unconjugated antibody to the PD-L1 protein. In some of any of the examples, the conjugate exhibits similar binding to a PD-L1 protein compared to the unconjugated antibody.

[0030] Also provided is a polynucleotide encoding any of the provided antibody or antigen-binding fragment. In one aspect, the present disclosure refers to a polynucleotide encoding the antibody or antigen-binding fragment as disclosed herein or the antibody or antigen-binding fragment of the conjugate as disclosed herein.

[0031] Also provided is a vector, comprising any of the provided polynucleotide. In some of any of the examples, the vector is an expression vector. In one aspect, the present disclosure refers to a vector, comprising the polynucleotide as disclosed herein.

[0032] In one aspect, also provided is an engineered cell comprising any of the provided vectors.

[0033] Also provided is an engineered cell expressing any of the provided antibody or antigen-binding fragment. In one aspect, the present disclosure refers to an engineered cell expressing the antibody or antigen binding fragment as disclosed herein or comprising the conjugate as disclosed herein.

[0034] Also provided is a composition comprising any of the provided antibody or antigen-binding fragments, or the any of the provided conjugates. In some of any of the examples, the composition also comprises a pharmaceutically acceptable excipient. In one aspect, the present disclosure refers to a composition comprising the antibody or antigen-binding fragment thereof as disclosed herein, or the conjugate as disclosed herein, optionally further comprising a pharmaceutically acceptable excipient.

[0035] Also provided is a method of treatment of a disease or disorder. Also provided are any of the provided antibody or antigen-binding fragment, any of the provided conjugates or any of the provided compositions for use in any of such methods. Also provided are uses of any of the provided antibody or antigen-binding fragment, any of the provided conjugates or any of the provided compositions in the manufacture of a medicament for the treatment of a disease or disorder. In some of any of the examples, the method involves administering any of the provided antibody or antigen-binding fragment, any of the provided conjugates or any of the provided compositions, to a subject having a disease or disorder. In one aspect, the present disclosure refers to an antibody or antigen-binding fragment thereof of as disclosed herein, a conjugate as disclosed herein, or a composition as disclosed herein, for use as a medicament.

[0036] Also provided is a method of treatment, comprising administering any of the provided compositions to a subject having a disease or disorder. In some of any of the examples, the disease or disorder is a tumor or a cancer. In one aspect, the present disclosure refers to use of the antibody or antigen-binding fragment thereof as disclosed herein, or the conjugate as disclosed herein, or the composition as disclosed herein in the manufacture of a medicament for treatment of a tumor or a cancer.

[0037] Also provided is a method of treating a tumor or a lesion in a subject. In some of any of the examples, the method involves administering to the subject the any of the provided conjugates or any of the provided compositions; and illuminating a target area within the subject with a wavelength of between at or about 600 nm and at or about 850 nm, and at a dose of from at or about 25 J/cm^2 to at or about 400 J/cm^2 or from at or about 2 J/cm fiber length to at or about 500 J/cm fiber length, thereby activating the conjugate; whereby the growth, volume or dimensions of the tumor or the lesion is reduced or inhibited. In one aspect, the present disclosure refers to use of the conjugate as disclosed herein or the composition as disclosed herein in the manufacture of a medicament for treating a tumor or a lesion in a subject, wherein:

a) the conjugate or the composition is to be administered to the subject; and

b) a target area within the subject is to be illuminated with a wavelength of between at or about 600 nm and at or about 850 nm, and at a dose of from at or about 25 J/cm^2 to at or about 400 J/cm^2 or from at or about 2 J/cm fiber length to at or about 500 J/cm fiber length, thereby activating the conjugate;

whereby the growth, volume or dimensions of the tumor or the lesion is to be reduced or inhibited.

[0038] Also provided is a method of treating a tumor or lesion. In some of any of the examples, the method involves administering to the subject any of the provided conjugates or any of the provided compositions to a subject having a tumor or lesion that has had a low response to, was unresponsive to, was resistant to, was refractory to, had failed to respond to or has relapsed after, a prior immunotherapy; and illuminating a target area where the tumor or lesion is located, at a wavelength of at or about 600 nm to at or about 850 nm and at a dose of from at or about 25 J/cm^2 to at or about 400 J/cm^2 or from at or about 2 J/cm fiber length to at or about 500 J/cm fiber length; wherein the method results in the killing of a PD-L1 expressing cell in the target area.

[0039] In some of any of the examples, the prior immunotherapy is a treatment with an immune checkpoint inhibitor.

[0040] In some of any of the examples, the subject has primary resistance or acquired resistance to a prior immunotherapy that comprises a PD-1/PD-L1 blockade therapy.

[0041] Also provided is a method of treating a tumor or lesion. In some of any of the examples, the method involves administering to the subject any of the provided conjugates or any of the provided compositions to a subject that is treatment-naïve for an immune checkpoint inhibitor or that has not previously received a treatment with an immune checkpoint inhibitor; and illuminating a target area where a tumor or lesion is located in the subject at a wavelength of at or about 600 nm to at or about 850 nm and at a dose of from at or about 25 J/cm^2 to at or about 400 J/cm^2 or from at or about 2 J/cm fiber length to at or about 500 J/cm fiber length; wherein after the illumination, the growth, size or viability of the tumor or lesion is reduced or inhibited.

[0042] In some of any of the examples, the subject is administered the conjugate to treat, inhibit the growth of and/or reduce the size of a first tumor or lesion; and the method inhibits, delays or prevents the appearance, growth or establishment of one or more second tumors or lesions, located distally to the first tumor or lesion.

[0043] Also provided is a method of immunizing a subject having a first tumor or lesion. In some of any of the examples, the method involves administering to the subject any of the provided conjugates to a subject having a tumor or lesion; and illuminating a target area within the first tumor or lesion at a wavelength of at or about 600 nm to at or about 850 nm and at a dose of from at or about 25 J/cm^2 to at or about 400 J/cm^2 or from at or about 2 J/cm fiber length to at or about 500 J/cm fiber length; wherein the first tumor or lesion is inhibited in growth and/or reduced in size; and the appearance, growth or establishment of one or more second tumors or lesions, located distally to the treated first tumor or lesion, is inhibited, delayed or prevented. In one aspect, the present disclosure refers to use of the conjugate as disclosed herein or the composition as disclosed herein in the manufacture of a medicament for immunizing a subject having a first tumor or lesion, wherein:

(a) the conjugate or the composition is to be administered to the subject having a tumor or lesion; and

(b) a target area within the first tumor or lesion is to be illuminated at a wavelength of at or about 600 nm to at or about 850 nm and at a dose of from at or about 25 J/cm^2 to at or about 400 J/cm^2 or from at or about 2 J/cm fiber length to at or about 500 J/cm fiber length; wherein the first tumor or lesion is to be inhibited in growth and/or reduced in size; and the appearance, growth or establishment of one or more second tumors or lesions, located distally to the treated first tumor or lesion, is to be inhibited, delayed or prevented.

[0044] In some of any of the examples, the second tumor or lesion is a metastasis of the first tumor or lesion. In some of any of the examples, the method results in killing of a PD-L1-expressing cell in the vicinity of the first tumor or lesion and/or activates an immune cell response, thereby inhibiting, delaying or preventing the appearance, growth or establishment of the second tumor or lesion. In some of any of the examples, the second tumor or lesion is phenotypically and/or genotypically the same as the first tumor or lesion. In some of any of the examples, the second tumor or lesion is phenotypically and/or genotypically different from the first tumor or lesion.

[0045] In some of any of the examples, the second tumor or lesion is not derived from a metastasis of the first tumor or lesion. In some of any of the examples, the method results in the killing of the PD-L1-expressing cell or the PD-L1-expressing immune cell. In some of any of the examples, the tumor or lesion comprises a tumor cell, and the tumor cell does not express or has a reduced expression of an immune checkpoint protein. In some of any of the examples, the immune checkpoint protein is selected from among PD-L1, PD-1, and CTLA-4.

[0046] In some of any of the examples, the tumor cell does not express PD-L1 in response to an inflammatory stimulus. In some of any of the examples, the inflammatory stimulus is interferon.

[0047] In some of any of the examples, the tumor cell is not specifically recognized by an anti-PD-L1 antibody. In some of any of the examples, the tumor or lesion comprises PD-

L1 negative tumor cells. In some of any of the examples, at least or at least about 40%, 50%, 60%, 70%, 80%, 90% or 95% of the tumor cells in the tumor or lesion are PD-L1 negative tumor cells.

[0048] In some of any of the examples, the treatment delays regrowth of the tumor or lesion, prevents a relapse of a cancer associated with the tumor or lesion or prolongs the duration of remission of a cancer associated with the tumor or lesion. In some of any of the examples, the inhibition of the growth of the tumor or lesion and/or killing of the PD-L1-expressing cell is dependent on the presence of CD8+ T cells.

[0049] In some of any of the examples, the subject is naïve to treatment with an immune checkpoint inhibitor or has not previously received treatment with an immune checkpoint inhibitor. In some of any of the examples, the subject has been previously treated with an immune checkpoint inhibitor. In some of any of the examples, the subject has had a low response to, was unresponsive to, was resistant to, was refractory to, had failed to respond to or has relapsed after the previous treatment with the immune checkpoint inhibitor. In some of any of the examples, the inhibition of the growth, size or viability of the tumor or lesion resulting from carrying out the method is greater compared to the inhibition resulting from the previous treatment with the immune checkpoint inhibitor.

[0050] In some of any of the examples, the immune checkpoint inhibitor is an inhibitor of PD-L1, PD-1 or CTLA-4. In some of any of the examples, immune checkpoint inhibitor is a PD-1 inhibitor. In some of any of the examples, the PD-1 inhibitor is an anti-PD-1 antibody. In some of any of the examples, the PD-1 inhibitor is an anti-CTLA-4 antibody. In some of any of the examples, the immune checkpoint inhibitor is PD-L1 inhibitor. In some of any of the examples, the PD-L1 inhibitor is an anti-PD-L1 antibody.

[0051] In some of any of the examples, the method increases the number or activity of immune cells in the tumor or lesion and/or in the microenvironment of the tumor or lesion.

[0052] In some of any of the examples, the target area comprises immune cells expressing PD-L1. In some of any of the examples, the PD-L1 expressing cell is an immune cell. In some of any of the examples, the immune cell is a monocyte, a macrophage, a dendritic cell (DC), or a myeloid-derived suppressor cell (MDSC). In some of any of the examples, the immune cell is selected from the group consisting of monocytes, macrophages, such as M1 macrophages, M2 macrophages and/or M2 tumor associated macrophages (M2 TAM), dendritic cells (DC), tolerogenic dendritic cells (tDC) and myeloid derived suppressor cells (MDSC). In some of any of the examples, the immune cell is a

monocyte. In some of any of the examples, the immune cell is a macrophage. In some of any of the examples, the immune cell is an M1 macrophage. In some of any of the examples, the immune cell is an M2 macrophage. In some of any of the examples, the immune cell is an M2 tumor associated macrophages (M2 TAM). In some of any of the examples, the immune cell is a dendritic cell (DC). In some of any of the examples, the immune cell is a tolerogenic dendritic cell (tDC). In some of any of the examples, the immune cell is a myeloid derived suppressor cell (MDSC). In some of any of the examples, the immune cell is located in the tumor, the tumor microenvironment or a lymph node.

[0053] In some of any of the examples, prior to administering the conjugate, the subject has a tumor or lesion having a low number or level of CD8+ T cell infiltration. In some of any of the examples, the number, level or activity of immune cells is increased in the tumor or lesion or in the microenvironment of the tumor or lesion after the administering and the illuminating. In some of any of the examples, the number or level of CD8+ T cell infiltration in the tumor or lesion is increased after the administering and the illuminating. In some of any of the examples, the number or level of memory T cells in the vicinity of the tumor or lesion is increased after the administering and the illuminating. In some of any of the examples, the targeting molecule is or comprises an antibody, an antigen-binding antibody fragment or antibody-like molecule that binds PD-L1. In some of any of the examples, the targeting molecule is or comprises an anti-PD-L1 antibody or antigen-binding fragment thereof. In some of any of the examples, the target area is a lymph node or in the vicinity of a lymph node. In some of any of the examples, the subject exhibits a durable response, prolonged progression-free survival, a reduced chance of relapse, and/or a reduced chance of metastasis, after the administering and the illuminating.

[0054] In some of any of the examples, the illuminating is carried out between 30 minutes and 96 hours after administering the conjugate. In some of any of the examples, the illuminating is carried out 24 hours ± 4 hours after administering the conjugate. In some of any of the examples, the target area is illuminated at a wavelength of 690 ± 40 nm. In some of any of the examples, the target area is illuminated at a wavelength of 670 ± 50 nm. In some of any of the examples, the target area is illuminated at a dose of at or about of 50 J/cm^2 or at or about 100 J/cm of fiber length.

[0054a] In one aspect, the present disclosure refers to a conjugate comprising:

a) an antibody or antigen-binding fragment that specifically binds a Programmed Death-Ligand (PD-L1) protein, wherein the antibody or antigen-binding fragment comprises:

(i) a VH region comprising a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO:87, a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO:88, and a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO:84; and

ii) a VL region comprising a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO:246, a CDR-L2 comprising the amino acid sequence set forth in SEQ ID

NO:247, and a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO:248; and

b) a Si-phthalocyanine dye that is IR700,

for use as a medicament.

[0054b] In another aspect, the present disclosure refers to use of a conjugate in the manufacture of a medicament for killing a PD-L1 expressing cell in a subject, wherein:

1) a conjugate is to be administered to the subject, wherein the conjugate comprises:

a) an antibody or antigen-binding fragment that specifically binds a Programmed Death-Ligand (PD-L1) protein, wherein the antibody or antigen-binding fragment comprises:

(i) a VH region comprising a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO:87, a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO:88, and a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO:84; and

(ii) a VL region comprising a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO:246, a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO:247, and a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO:248; and

b) a Si-phthalocyanine dye that is IR700; and

2) a target area, comprising the PD-L1-expressing cell to be killed, within the subject is to be illuminated with a wavelength of 690 ± 40 nm, to activate the conjugate;

whereby a PD-L1-expressing cell is killed.

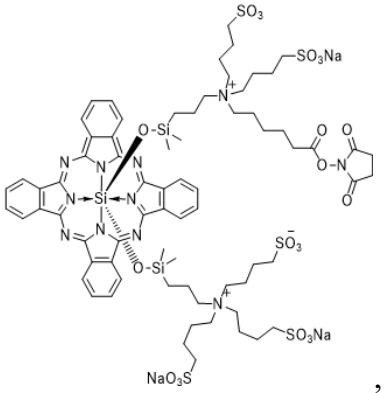
[0054c] In one aspect, the present disclosure refers to a conjugate comprising:

a) an antibody or antigen-binding fragment that specifically binds a Programmed Death-Ligand (PD-L1) protein, wherein the antibody or antigen-binding fragment comprises:

(i) a VH region comprising a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO:87, a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO:88, and a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO:84; and

(ii) a VL region comprising a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO:246, a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO:247, and a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO:248; and

b) a Si-phthalocyanine dye that has the structure of Formula (I):



, or is a salt, stereoisomer, or tautomer thereof,

for use as a medicament.

[0054d] In one aspect the present disclosure refers to a use of a conjugate in the manufacture of a medicament for killing a PD-L1 expressing cell in a subject, wherein:

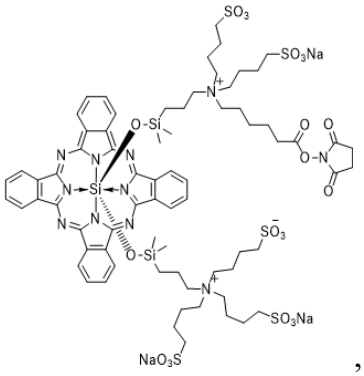
1) a conjugate is to be administered to the subject, the conjugate comprising:

a) an antibody or antigen-binding fragment that specifically binds a Programmed Death-Ligand (PD-L1) protein, wherein the antibody or antigen-binding fragment comprises:

(i) a VH region comprising a CDR-H1 comprising the amino acid sequence set forth in SEQ ID NO:87, a CDR-H2 comprising the amino acid sequence set forth in SEQ ID NO:88, and a CDR-H3 comprising the amino acid sequence set forth in SEQ ID NO:84; and

(ii) a VL region comprising a CDR-L1 comprising the amino acid sequence set forth in SEQ ID NO:246, a CDR-L2 comprising the amino acid sequence set forth in SEQ ID NO:247, and a CDR-L3 comprising the amino acid sequence set forth in SEQ ID NO:248; and

b) a Si-phthalocyanine dye that has the structure of Formula (I):



, or is a salt, stereoisomer, or tautomer thereof; and

2) a target area, comprising the PD-L1-expressing cell to be killed, within the subject is to be illuminated with a wavelength of 670 ± 50 nm, to activate the conjugate;

whereby a PD-L1 expressing cell is killed.

[0055] In some of any of the examples, the tumor, lesion or cancer is associated with a cancer selected from the group consisting of colon cancer, colorectal cancer, pancreatic cancer, breast cancer, skin cancer, lung cancer, non-small cell lung carcinoma, renal cell carcinoma,

thyroid cancer, prostate cancer, head and neck cancer, gastrointestinal cancer, stomach cancer, cancer of the small intestine, spindle cell neoplasm, hepatic carcinoma, liver cancer, cancer of peripheral nerve, brain cancer, cancer of skeletal muscle, cancer of smooth muscle, bone cancer, cancer of adipose tissue, cervical cancer, uterine cancer, cancer of genitals, lymphoma, and multiple myeloma.

[0056] In some of any of the examples, one or more of steps of the method are repeated. In some of any of the examples, the administration of the antibody or antigen-binding fragment, the conjugate or the composition is repeated one or more times. In some of any of the examples, after each repeated administration of the conjugate or the composition, the illuminating step is repeated.

[0057] In some of any of the examples, the method further involves administering an additional therapeutic agent or anti-cancer treatment.

Brief Description of the Drawings

[0058] **FIGS. 1A-1F** show the binding of exemplary anti-PD-L1 antibodies to human PD-L1 (**FIGS. 1A**, **1C**, and **1E**) and cynomolgus PD-L1 (**FIGS. 1B**, **1D**, and **1F**) determined by ELISA.

[0059] **FIG. 1G** shows the binding specificity of an exemplary anti-PD-L1 antibody, 1P4, for PD-L1 compared to other B7 ligands, determined by ELISA. **FIG. 1H** shows the binding specificity of an exemplary anti-PD-L1 antibody, 1P9, for PD-L1 compared to other B7 ligands, determined by ELISA.

[0060] **FIG. 2A** shows the binding of exemplary anti-PD-L1 antibodies, containing a wild-type Fc or an effector knock-out Fc region, to human PD-L1 expressed on the surface of CHO cells engineered to express human PD-L1. **FIG. 2B** shows the binding of exemplary anti-PD-L1 antibodies, containing a wild-type Fc or an effector knock-out Fc region, to wild-type CHO cells.

[0061] **FIG. 3** shows the binding of exemplary anti-PD-L1 antibodies to PD-L1-expressing A431 cancer cells.

[0062] **FIGS. 4A-4B** show the ADCC activity of exemplary anti-PD-L1 antibodies containing a wild-type Fc region (**FIG. 4A**) or an effector knock-out Fc region (**FIG. 4B**).

[0063] **FIGS. 5A-5B** show the binding of exemplary anti-PD-L1-IR700 conjugates to human PD-L1 (**FIG. 5A**) and cynomolgus PD-L1 (**FIG. 5B**).