ANTI-CD3 ANTIBODIES AND METHODS OF USE

FIELD OF THE INVENTION

The present invention relates to anti-cluster of differentiation 3 (CD3) antibodies and methods of using the same.

BACKGROUND

Cell proliferative disorders, such as cancer, are characterized by the uncontrolled growth of cell subpopulations. They are the leading cause of death in the developed world and the second leading cause of death in developing countries, with over 12 million new cancer cases diagnosed and 7 million cancer deaths occurring each year. The National Cancer Institute estimates that greater than half a million Americans will die of cancer in 2013, accounting for nearly one out of every four deaths in the country. As the elderly population has grown, the incidence of cancer has concurrently risen, as the probability of developing cancer is more than two-fold higher after the age of seventy. Cancer care thus represents a significant and ever-increasing societal burden.

Longstanding approaches to cancer treatment include chemotherapy, radiation therapy, and surgery to remove solid tumors. Recently, bispecific antibody-based immunotherapies have been developed. Such bispecific antibodies are capable of simultaneously binding cell surface antigens on cytotoxic cells and tumor cells, with the intent that the bound cytotoxic cell will destroy the bound tumor cell. Existing bispecific antibodies currently undergoing clinical trials for treating cancer are limited by their short half-lives and/or variable efficacy. Thus, there is an unmet need in the field for the development of effective bispecific antibodies for use in cancer treatment.

SUMMARY

The present disclosure relates to anti-cluster of differentiation 3 (CD3) antibodies and methods of using the same.

In one aspect, the disclosure provides an anti-CD3 antibody which is a bispecific antibody, wherein the bispecific antibody comprises:

an anti-CD3 arm comprising a first binding domain comprising the following six hypervariable regions (HVRs):

(a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 7,
(b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 8,
(c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 9,
(d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 10,
(e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 11, and
(f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 12; and

an anti-LYPD1 arm comprising a second binding domain comprising the following six HVRs:

(a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 175,
(b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 176,
(c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 177,
(d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 178,
(e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 179, and
(f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 180.

In one example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising the following six hypervariable regions (HVRs): (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 1; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 2; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 3; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 4; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 5; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 6. In some examples, the binding domain comprises (a) a heavy chain variable (VH) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 184; (b) a light chain variable (VL) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 185; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 184. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 185. In some examples, the binding domain comprises (a) a heavy chain variable (VH) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID

NO: 186; (b) a light chain variable (VL) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 187; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 186. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 187.

In one example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 7; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 8; (c) an HVR-H3 comprising the amino acid sequence of $X_1X_2YSX_3X_4X_5FDY$, wherein X_1 is selected from the group consisting of D, T, and S; X_2 is selected from the group consisting of G, A, and S; X_3 is R or N; X_4 is Y or A; and X_5 is Y or A (SEQ ID NO: 181); (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 10; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 11; and (f) an HVR-L3 comprising the amino acid sequence of $X_1X_2SX_3X_4LRT$, wherein X_1 is K or T; X_2 is Q or A; X_3 is F or A; and X_4 is I or A (SEQ ID NO: 182). In some examples, the binding domain comprises the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 7; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 8; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 9; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 10; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 11; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 12. In some examples, the binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 188; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 189; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 188. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 189.

In other examples, the binding domain comprises the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 7; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 8; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 13; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 10; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 11; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 12. In some examples, the binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 190; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 191; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 190. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 191.

In other examples, the binding domain comprises the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 7; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 8; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 9; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 10; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 11; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 14. In some examples, the binding domain comprises (a) a VH domain comprising an amino acid

sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 192; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 193; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 192. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 193.

In other examples, the binding domain comprises the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 7; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 8; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 9; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 10; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 11; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 15. In some examples, the binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 194; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 195; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 194. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 195.

In other examples, the binding domain comprises the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 7; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 8; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 9; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 10; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 11; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 16. In some examples, the binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 196; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 197; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 196. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 197.

In other examples, the binding domain comprises the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 7; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 8; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 17; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 10; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 11; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 12. In some examples, the binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 198; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 199; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 198. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 199.

In other examples, the binding domain comprises the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 7; (b) an HVR-H2 comprising the amino acid

sequence of SEQ ID NO: 8; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 18; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 10; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 11; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 12. In some examples, the binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 200; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 201; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 200. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 201.

In other examples, the binding domain comprises the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 7; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 8; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 19; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 10; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 11; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 12. In some examples, the binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 202; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 203; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 202. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 203.

In other examples, the binding domain comprises the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 7; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 8; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 20; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 10; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 11; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 12. In some examples, the binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 204; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 205; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 204. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 205.

In other examples, the binding domain comprises the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 7; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 8; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 21; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 10; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 11; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 22. In some examples, the binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 206; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 207; or (c) a VH domain as in (a) and a VL domain as in (b). In some

examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 206. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 207.

In some examples, the disclosure features an anti-CD3 antibody comprising a binding domain comprising: (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 188 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 189; (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 190 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 191; (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 192 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 193; (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 194 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 195; (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 196 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 197; (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 198 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 199; (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 200 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 201; (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 202 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 203; (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 204 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 205; or (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 206 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 207.

In some examples, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 23; (b) an HVR-H2 comprising the amino acid sequence of LINPYKGVX_1TY$X_2X_3X_4X_5$KX_6, wherein X_1 is S or T; X_2 is N or A; X_3 is Q or D; X_4 is K or S; X_5 is F or V; and X_6 is D or G (SEQ ID NO: 183); (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 25; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 26; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 27; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 28. In some examples, the binding domain comprises the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 23; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 24; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 25; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 26; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 27; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 28. In some examples, the binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 208; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 209; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 208. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 209.

In other examples, the binding domain comprises the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 23; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 29; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 25; (d)

an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 26; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 27; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 28. In some examples, the binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 210; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 211; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 210. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 211.

In other examples, the binding domain comprises the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 23; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 30; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 25; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 26; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 27; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 28. In some examples, the binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 212; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 213; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 212. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 213.

In some examples, the disclosure features an anti-CD3 antibody comprising a binding domain comprising: (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 208 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 209; (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 210 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 211; or (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 212 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 213.

In some examples, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 31; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 32; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 33; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 34; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 35; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 36. In some examples, the binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 214; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 215; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 214. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 215. In some examples, the binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 216; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 217; or (c) a VH

domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 216. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 217.

In some examples, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising: (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 214 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 215, or (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 216 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 217.

In another example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 37; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 38; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 39; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 40; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 41; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 42. In some examples, the binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 218; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 219; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 218. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 219. In some examples, the binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 220; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 221; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 220. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 221.

In some examples, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising: (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 218 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 219, or (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 220 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 221.

In some examples, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 43; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 44; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 45; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 46; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 47; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 48. In some examples, the binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 222; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of

SEQ ID NO: 223; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 222. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 223. In some examples, the binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 224; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 225; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 224. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 225. In some examples, the binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 226; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 227; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 226. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 227.

In some examples, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising: (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 222 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 223; (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 224 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 225; (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 226 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 227.

In some examples, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 49; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 50; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 51; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 52; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 53; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 54. In some examples, the binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 228; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 229; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 228. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 229. In some examples, the binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 230; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 231; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 230. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 231.

In some examples, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising: (a) a VH domain comprising an amino acid sequence of SEQ ID

NO: 228 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 229, or (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 230 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 231.

In another example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 55; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 56; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 57; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 58; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 59; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 60. In some examples, the binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 232; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 233; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 232. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 233.

In another example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising: (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 232 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 233.

In another example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 61; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 62; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 63; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 64; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 65; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 66. In some examples, the binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 234; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 235; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 234. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 235.

In another example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising: (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 234 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 235.

In another example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 67; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 68; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 69; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 70; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 71; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 72. In some examples, the binding domain comprises (a) a VH domain comprising an amino acid sequence

having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 236; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 237; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 236. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 237.

In another example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising: (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 236 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 237.

In another example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 73; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 74; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 75; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 76; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 77; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 78. In some examples, the binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 238; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 239; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 238. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 239.

In another example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising: (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 238 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 239.

In another example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 79; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 80; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 81; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 82; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 83; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 84. In some examples, the binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 240; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 241; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 240. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 241.

In another example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising: (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 240 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 241.

In another example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising the following six HVRs: (a) an HVR-H1 comprising the amino

acid sequence of SEQ ID NO: 85; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 86; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 87; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 88; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 89; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 90. In some examples, the binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 242; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 243; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 242. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 243.

In another example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising: (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 242 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 243.

In another example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 91; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 92; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 93; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 94; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 95; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 96. In some examples, the binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 244; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 245; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 244. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 245.

In another example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising: (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 244 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 245.

In another example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 97; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 98; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 99; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 100; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 101; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 102. In some examples, the binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 246; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 247; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 246. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 247.

In another example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising: (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 246 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 247.

In another example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 103; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 104; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 105; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 106; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 107; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 108. In some examples, the binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 248; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 249; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 248. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 249.

In another example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising: (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 248 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 249.

In another example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 109; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 110; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 111; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 112; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 113; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 114. In some examples, the binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 250; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 251; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 250. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 251.

In another example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising: (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 250 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 251.

In another example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 115; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 116; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 117; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 118; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 119; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 120. In some examples, the binding domain comprises (a) a VH domain comprising an amino acid sequence

having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 252; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 253; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 252. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 253.

In another example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising: (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 252 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 253.

In another example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 121; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 122; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 123; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 124; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 125; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 126. In some examples, the binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 254; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 255; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 254. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 255.

In another example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising: (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 254 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 255.

In another example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 127; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 128; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 129; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 130; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 131; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 132. In some examples, the binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 256; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 257; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 256. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 257.

In another example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising: (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 256 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 257.

In another example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising the following six HVRs: (a) an HVR-H1 comprising the amino

acid sequence of SEQ ID NO: 133; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 134; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 135; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 136; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 137; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 138. In some examples, the binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 258; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 259; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 258. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 259.

In another example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising: (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 258 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 259.

In another example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 139; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 140; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 141; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 142; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 143; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 144. In some examples, the binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 260; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 261; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 260. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 261.

In another example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising: (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 260 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 261.

In another example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 145; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 146; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 147; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 148; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 149; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 150. In some examples, the binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 262; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 263; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 262. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 263.

In another example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising: (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 262 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 263.

In another example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 151; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 152; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 153; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 154; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 155; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 156. In some examples, the binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 264; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 265; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 264. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 265.

In another example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a binding domain comprising: (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 264 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 265.

In another example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody binds to an epitope on CD3 comprising amino acid residue Glu6 of CD3. In certain examples, the disclosure features an anti-CD3 antibody, wherein the epitope further comprises one or more additional amino acid residues selected from the group consisting of Gln1, Asp2, and Met7 of CD3. In a further example, the disclosure features an anti-CD3 antibody, wherein the epitope comprises amino acid residues Gln1, Asp2, and Glu6 of CD3. In certain examples, the disclosure features an anti-CD3 antibody, wherein the epitope comprises amino acid residues Gln1, Asp2, Glu6, and Met7 of CD3. In another example, the disclosure features an anti-CD3 antibody, wherein the epitope does not comprise amino acid residue Glu5 of CD3. In a further example, the disclosure features an anti-CD3 antibody, wherein the epitope does not comprise amino acid residues Gly3 and Glu5 of CD3. In certain examples, the disclosure features an anti-CD3 antibody, wherein the epitope consists of amino acid residues Gln1, Asp2, Glu6, and Met7 of CD3.

In related examples, the disclosure features an anti-CD3 antibody that binds such an epitope and that is a multispecific antibody. In some examples, the multispecific antibody is a bispecific antibody. In some examples, the bispecific antibody comprises a second binding domain that binds to a second biological molecule, wherein the second biological molecule is a cell surface antigen. In some examples, the cell surface antigen is a tumor antigen. In some examples, the tumor antigen is selected from the group consisting of CD20; FcRH5 (Fc Receptor-like 5); HER2; LYPD1; Ly6G6D (lymphocyte antigen 6 complex, locus G61); Ly6-D, MEGT1); PMEL17 (silver homolog; SILV; D12S53E; PMEL17; (SI); (SIL); ME20; gp100); Ly6E (lymphocyte antigen 6 complex, locus E; Ly67, RIG-E, SCA-2, TSA-1); CD19; CD33; CD22 (B-cell receptor CD22-B isoform); CD79a (CD79A, CD79a, immunoglobulin-associated alpha; BMPR1B (bone morphogenetic protein receptor-type IB); CD79b (CD79B, CD79β, 1 Gb (immunoglobulin-associated beta), B29); EDAR (Ectodysplasin A Receptor); GFRA1 (GDNF-Ra1);

VEGF; WT1; XAGE-1b/GAGED2a; and SLC53SLC35D3. In some examples, the tumor antigen is selected from the group consisting of CD20, FcRH5, HER2, LYPD1, LY6G6D, PMEL17, LY6E, CD19, CD33, CD22, CD79A, CD79B, EDAR, GFRA1, MRP4, RET, Steap1, and TenB2. In preferred examples, the tumor antigen is selected from the group consisting of CD20, HER2, FcRH5, and LYPD1.

In some examples, the binding domain of any one of the preceding anti-CD3 antibodies binds to a human CD3 polypeptide or a cynomolgus monkey (cyno) CD3 polypeptide. In some examples, the human CD3 polypeptide or the cyno CD3 polypeptide is a human CD3ε polypeptide or a cyno CD3ε polypeptide, respectively. In some examples, the human CD3 polypeptide or the cyno CD3 polypeptide is a human CD3γ polypeptide or a cyno CD3γ polypeptide, respectively.

In some examples, any one of the preceding anti-CD3 antibodies binds the human CD3ε polypeptide with a Kd of 250 nM or lower. In some examples, the anti-CD3 antibody binds the human CD3ε polypeptide with a Kd of 100 nM or lower. In some examples, the anti-CD3 antibody binds the human CD3ε polypeptide with a Kd of 15 nM or lower. In some examples, the anti-CD3 antibody binds the human CD3ε polypeptide with a Kd of 10 nM or lower. In some examples, the anti-CD3 antibody binds the human CD3ε polypeptide with a Kd of 5 nM or lower.

In some examples, any one of the preceding anti-CD3 antibodies may comprise an aglycosylation site mutation. In some examples, the aglycosylation site mutation is a substitution mutation. In some examples, the substitution mutation is at amino acid residue N297, L234, L235, and/or D265 (EU numbering). In some examples, the substitution mutation is selected from the group consisting of N297G, N297A, L234A, L235A, and D265A. In some examples, the substitution mutation is an N297G mutation. In some examples, the aglycosylation site mutation reduces effector function of the anti-CD3 antibody. In some examples, the aglycosylation site mutation reduces effector function of the anti-CD3 antibody. In some examples, an anti-CD3 antibody comprises a substitution mutation in the Fc region that reduces effector function.

In some examples, any one of the preceding anti-CD3 antibodies can be monoclonal, human, humanized, or chimeric. In some examples, any one of the preceding anti-CD3 antibodies can be an antibody fragment that binds CD3. In some examples, the antibody fragment is selected from the group consisting of Fab, Fab'-SH, Fv, scFv, and $(Fab')_2$ fragments. In other examples, the anti-CD3 antibody is a full-length antibody. In some examples, the anti-CD3 antibody is an IgG antibody (e.g., an IgG1, IgG2, or IgG3 antibody). In some examples, the anti-CD3 antibody is a monospecific antibody. In some examples, the anti-CD3 antibody is a Bispecific T-Cell Engager (BiTE®) antibody).

In some examples, the anti-CD3 antibody is a multispecific antibody. In some examples, the multispecific antibody is a bispecific antibody. In some examples, the bispecific antibody comprises a second binding domain that binds to a second biological molecule, wherein the second biological molecule is a cell surface antigen. In some examples, the cell surface antigen is a tumor antigen. In some examples, the tumor antigen is selected from the group consisting of CD20; FcRH5 (Fc Receptor-like 5); HER2; LYPD1; Ly6G6D (lymphocyte antigen 6 complex, locus G61); Ly6-D, MEGT1); PMEL17 (silver homolog; SILV; D12S53E; PMEL17; (SI); (SIL); ME20; gp100); Ly6E (lymphocyte antigen 6 complex, locus E; Ly67, RIG-E, SCA-2, TSA-1); CD19; CD33; CD22 (B-cell

SNRPD1; SOX10; Sp17; SSX-2; SSX-4; STEAP1; survivin; SYT-SSX1 or -SSX2 fusion protein; TAG-1; TAG-2; Telomerase; TGF-betaRII; TRAG-3; Triosephosphate isomerase; TRP-1 / gp75; TRP-2; TRP2-INT2; tyrosinase; VEGF; WT1; XAGE-1b/GAGED2a; and SLC35D3. In some examples, the tumor antigen is selected from the group consisting of CD20, FcRH5, HER2, LYPD1, LY6G6D, PMEL17, LY6E, CD19, CD33, CD22, CD79A, CD79B, EDAR, GFRA1, MRP4, RET, Steap1, and TenB2.

In some examples, the tumor antigen is CD20 and the second binding domain comprises the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 157; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 158; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 159; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 160; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 161; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 162. In some examples, the second binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 266; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 267; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 266. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 267.

In some examples, the tumor antigen is FcRH5 and the second binding domain comprises the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 163; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 164; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 165; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 166; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 167; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 168. In some examples, the second binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 268; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 269; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 268. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 269.

In some examples, the tumor antigen is HER2 and the second binding domain comprises the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 169; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 170; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 171; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 172; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 173; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 174. In some examples, the second binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 270; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 271; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the

amino acid sequence of SEQ ID NO: 270. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 271.

In some examples, the tumor antigen is HER2 and the second binding domain comprises the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 581; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 582; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 583; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 584; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 585; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 586. In some examples, the second binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 593; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 594; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 593. In some examples the VL domain comprises the amino acid sequence of SEQ ID NO: 594.

In some examples, the tumor antigen is HER2 and the second binding domain comprises the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 587; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 588; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 589; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 590; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 591; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 592. In some examples, the second binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 595; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 596; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 595. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 596.

In some examples, the tumor antigen is RET and the second binding domain comprises the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 613; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 614; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 615; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 616; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 617; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 618. In some examples, the second binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 619; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 620; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 619. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 620.

In some examples, the tumor antigen is LYPD1 and the second binding domain comprises the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 175; (b) an

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HVR-H2 comprising the amino acid sequence of SEQ ID NO: 176; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 177; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 178; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 179; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 180. In some examples, the second binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 272; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 273; or (c) a VH domain as in (a) and a VL domain as in (b). In some examples, the VH domain comprises the amino acid sequence of SEQ ID NO: 272. In some examples, the VL domain comprises the amino acid sequence of SEQ ID NO: 273.

In some examples, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises a second binding domain comprising: (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 266 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 267; (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 268 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 269; (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 270 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 271; (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 272 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 273; (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 593 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 594; (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 595 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 596; or (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 619 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 620.

In another example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises an anti-CD3 arm comprising a first binding domain comprising the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 1; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 2; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 3; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 4; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 5; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 6; and an anti-CD20 arm comprising a second binding domain comprising the following six HVRs: (a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 157; (b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 158; (c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 159; (d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 160; (e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 161; and (f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 162.

In another example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises an anti-CD3 arm comprising a first binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 184 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 185, and an anti-CD20 arm comprising a second binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 266 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 267.

In another example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises an anti-CD3 arm comprising a first binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 184 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 185, and an anti-CD20 arm comprising a second binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 266 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 267, wherein the anti-CD3 antibody comprises an N297G substitution mutation.

In another example, the disclosure features an anti-CD3 antibody, wherein the anti-CD3 antibody comprises an anti-CD3 arm comprising a first binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 184 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 185, and an anti-CD20 arm comprising a second binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 266 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 267, wherein (a) the anti-CD3 arm comprises T366S, L368A, Y407V, and N297G substitution mutations and (b) the anti-CD20 arm comprises T366W and N297G substitution mutations.

In some examples, any one of the preceding anti-CD3 antibodies can comprise one or more heavy chain constant domains, wherein the one or more heavy chain constant domains are selected from a first CH1 ($CH1_1$) domain, a first CH2 ($CH2_1$) domain, a first CH3 ($CH3_1$) domain, a second CH1 ($CH1_2$) domain, second CH2 ($CH2_2$) domain, and a second CH3 ($CH3_2$) domain. In some examples, at least one of the one or more heavy chain constant domains is paired with another heavy chain constant domain. In some examples, the $CH3_1$ and $CH3_2$ domains each comprise a protuberance or cavity, and wherein the protuberance or cavity in the $CH3_1$ domain is positionable in the cavity or protuberance, respectively, in the $CH3_2$ domain. In some examples, the $CH3_1$ and $CH3_2$ domains meet at an interface between said protuberance and cavity. In some examples, the $CH2_1$ and $CH2_2$ domains each comprise a protuberance or cavity, and wherein the protuberance or cavity in the $CH2_1$ domain is positionable in the cavity or protuberance, respectively, in the $CH2_2$ domain. In some examples, the $CH2_1$ and $CH2_2$ domains meet at an interface between said protuberance and cavity.

In some examples, the half-life of any one of the preceding anti-CD3 antibodies may be about 7 days.

In one aspect, the disclosure provides an immunoconjugate comprising the bispecific antibody as disclosed herein and a cytotoxic agent. In some examples, the disclosure features an immunoconjugate comprising any one of the preceding anti-CD3 antibodies conjugated to a cytotoxic agent. In one aspect, the disclosure provides a composition comprising the bispecific antibody as disclosed herein and a pharmaceutically acceptable carrier, excipient, or diluent. Also provided is a composition comprising any one of the preceding anti-CD3 antibodies. In some examples, the composition further comprises a pharmaceutically acceptable carrier, excipient, or diluent. In some examples, the composition is a pharmaceutical composition. In some examples, the composition further comprises a PD-1 axis binding antagonist or an additional therapeutic agent. In one aspect, the disclosure provides an isolated nucleic acid encoding the bispecific antibody as disclosed herein. In another aspect, the disclosure provides a vector comprising the isolated nucleic acid as disclosed herein. In another example, the disclosure features an isolated nucleic acid that encodes any of the anti-CD3 antibodies disclosed herein, comprising a vector (e.g., an expression vector) for expressing the antibody.

In one aspect, the disclosure provides an isolated host cell comprising the vector as disclosed herein. In another example, the disclosure features host cells comprising the preceding nucleic acids and/or vectors. In some examples, the host cell is a mammalian cell (e.g., a Chinese hamster ovary (CHO) cell). In other examples, the host cell is a prokaryotic cell (e.g., an *E. coli* cell). In one aspect, the disclosure provides a method of producing the bispecific antibody as disclosed herein, the method comprising culturing the host cell as disclosed herein in a culture medium and recovering the bispecific antibody from the host cell or the culture medium. A

method of producing any one of the preceding anti-CD3 antibodies is also provided, the method comprising culturing the host cell that produces the anti-CD3 antibody and recovering the anti-CD3 antibody from the host cell or the culture medium.

In one aspect, the disclosure provides the bispecific antibody as disclosed herein for use as a medicament. In some examples, any one of the preceding anti-CD3 antibodies can be for use as a medicament. In one aspect, the disclosure provides the bispecific antibody as disclosed herein for use in (i) treating or delaying progression of a cell proliferative disorder in a subject in need thereof or (ii) enhancing immune function in a subject having a cell proliferative disorder. In some examples, any one of the preceding anti-CD3 antibodies can be for use in treating or delaying progression of a cell proliferative disorder or an autoimmune disorder in a subject in need thereof. In some examples, any one of the preceding anti-CD3 antibodies can be for use in enhancing immune function in a subject having a cell proliferative disorder or an autoimmune disorder.

In one aspect, the present disclosure provides use of the bispecific antibody as disclosed herein in the manufacture of a medicament. In some examples, the disclosure features the use of any one of the preceding anti-CD3 antibodies in the manufacture of a medicament for treating or delaying progression of a cell proliferative disorder or an autoimmune disorder. In some examples, the disclosure features the use of any one of the preceding anti-CD3 antibodies in the manufacture of a medicament for enhancing immune function in a subject having a cell proliferative disorder or an autoimmune disorder.

A further example of the disclosure is a method of treating or delaying the progression of a cell proliferative disorder or an autoimmune disorder in a subject in need thereof, the method comprising administering to the subject an effective amount any one of the preceding anti-CD3 antibodies. In another example, the disclosure features a method of enhancing immune function in a subject having a cell proliferative disorder or an autoimmune disorder, the method comprising administering to the subject any one of the preceding anti-CD3 antibodies. In some examples, the anti-CD3 antibody binds to (a) a CD3 molecule located on an immune effector cell and (b) a second biological molecule located on a target cell other than the immune effector cell. In some examples, the anti-CD3 antibody activates the immune effector cell following binding to (a) and (b). In some examples, the activated immune effector cell is capable of exerting a cytotoxic effect and/or an apoptotic effect on the target cell. In some examples, the anti-CD3 antibody is administered to the subject in a dosage of about 0.01 mg/kg to about 10 mg/kg. In some examples, the anti-CD3 antibody is administered to the subject in a dosage of about 0.1 mg/kg to about 10 mg/kg. In some examples, the anti-CD3 antibody is administered to the subject in a dosage of about 1 mg/kg. In some examples, the anti-CD3 antibody is administered subcutaneously, intravenously, intramuscularly, topically, orally, transdermally, intraperitoneally, intraorbitally, by implantation, by inhalation, intrathecally, intraventricularly, or intranasally. In some examples, the anti-CD3 antibody is administered subcutaneously. In some examples, the anti-CD3 antibody is administered intravenously.

In some examples, the method further comprises administering to the subject a PD-1 axis binding antagonist or an additional therapeutic agent. In some examples, the additional therapeutic agent is administered prior to or subsequent to the administration of the anti-CD3 antibody. In some examples, the additional therapeutic agent is administered concurrently with the anti-CD3 antibody. In some examples, the PD-1 axis binding antagonist is selected from the group consisting of a PD-1 binding antagonist, a PD-L1 binding antagonist, and a PD-L2 binding antagonist. In some examples, the PD-1 axis binding antagonist is a PD-1 binding antagonist. In some examples, the PD-1 binding antagonist is selected from the group consisting of MDX-1106 (nivolumab), MK-3475 (lambrolizumab), CT-011 (pidilizumab), and AMP-224. In other examples, the PD-1 axis binding antagonist is a PD-L1

binding antagonist. In some examples, the PD-L1 binding antagonist is selected from the group consisting of: YW243.55.S70, MPDL3280A, MDX-1105, and MEDI4736. In other examples, the PD-1 axis binding antagonist is a PD-L2 binding antagonist. In some examples, the PD-L2 binding antagonist is an antibody or an immunoadhesin.

In some examples, the disclosure features a method of treating or delaying the progression of a cell proliferative disorder or an autoimmune disorder in a subject in need thereof, the method comprising administering to the subject an anti-CD3 antibody and a PD-1 axis binding antagonist, wherein the anti-CD3 antibody comprises an anti-CD3 arm and an anti-CD20 arm. In some examples, the disclosure features a method of enhancing immune function in a subject having a cell proliferative disorder or an autoimmune disorder, the method comprising administering to the subject an anti-CD3 antibody and a PD-1 axis binding antagonist, wherein the anti-CD3 antibody comprises an anti-CD3 arm and an anti-CD20 arm (i.e., a CD20 TDB). In some examples, (a) the anti-CD3 arm comprises a first binding domain comprising (i) a VH domain comprising an amino acid sequence of SEQ ID NO: 184, and (ii) a VL domain comprising an amino acid sequence of SEQ ID NO: 185; (b) the anti-CD20 arm comprises a second binding domain comprising (i) a VH domain comprising an amino acid sequence of SEQ ID NO: 266, and (ii) a VL domain comprising an amino acid sequence of SEQ ID NO: 267; and/or (c) the PD-1 axis binding antagonist is an anti-PD-L1 antibody.

In some examples, the anti-CD3 antibody comprises an anti-CD20 arm comprising a N297G substitution mutation. In some examples, the anti-CD3 antibody comprises an anti-CD3 arm comprising T366S, L368A, Y407V, and/or N297G substitution mutation(s) and an anti-CD20 arm comprising T366W and/or N297G substitution mutation(s). In some examples, the anti-CD3 antibody comprises an anti-CD3 arm comprising a N297G substitution mutation. In some examples, the anti-CD3 antibody comprises an anti-CD20 arm comprising T366S, L368A, Y407V, and/or N297G substitution mutation(s) and an anti-CD3 arm comprising T366W and/or N297G substitution mutation(s).

In some examples, the anti-CD3 antibody comprises an anti-HER2 arm comprising a N297G substitution mutation. In some examples, the anti-CD3 antibody comprises an anti-CD3 arm comprising T366S, L368A, Y407V, and/or N297G substitution mutation(s) and an anti-HER2 arm comprising N297G, N297A, L234A, L235A, and/or D265A substitution mutation(s). In some examples, the anti-CD3 antibody comprises an anti-CD3 arm comprising a N297G substitution mutation. In some examples, the anti-CD3 antibody comprises an anti-HER2 arm comprising T366S, L368A, Y407V, and/or N297G substitution mutation(s) and an anti-CD3 arm comprising N297G, N297A, L234A, L235A, and/or D265A substitution mutation(s).

In some examples, the method further comprises administering to the subject a glucocorticoid. In some examples, the glucocorticoid is selected from the group consisting of dexamethasone, hydrocortisone, cortisone, prednisolone, prednisone, methylprednisone, triamcinolone, paramethasone, betamethasone, fludrocortisone, and pharmaceutically acceptable esters, salts, and complexes thereof. In some examples, the glucocorticoid is dexamethasone. In some examples, the glucocorticoid is a pharmaceutically acceptable ester, salt, or complex of dexamethasone.

In some examples, the method further comprises administering to the subject rituximab.

In some examples, the method further comprises administering to the subject obinutuzumab.

In some examples, the method further comprises administering to the subject an antibody-drug conjugate (ADC).

In any of the preceding uses or methods, the cell proliferative disorder can be cancer. In some examples, the cancer is selected from the group consisting of breast cancer, colorectal cancer, non-small cell lung cancer, non-Hodgkin's lymphoma (NHL), B cell lymphoma, B cell leukemia, multiple myeloma, renal cancer, prostate cancer, liver cancer, head and neck cancer, melanoma, ovarian cancer, mesothelioma, glioblastoma, germinal-center B-cell-like (GCB) DLBCL, activated B-cell-like (ABC) DLBCL, follicular lymphoma (FL), mantle cell lymphoma (MCL), acute myeloid leukemia (AML), chronic lymphoid leukemia (CLL), marginal zone lymphoma (MZL), small lymphocytic leukemia (SLL), lymphoplasmacytic lymphoma (LL), Waldenstrom macroglobulinemia (WM), central nervous system lymphoma (CNSL), Burkitt's lymphoma (BL), B-cell prolymphocytic leukemia, Splenic marginal zone lymphoma, Hairy cell leukemia, Splenic lymphoma/leukemia, unclassifiable, Splenic diffuse red pulp small B-cell lymphoma, Hairy cell leukemia variant, Waldenström macroglobulinemia, Heavy chain diseases, α Heavy chain disease, γ Heavy chain disease, μ Heavy chain disease, Plasma cell myeloma, Solitary plasmacytoma of bone, Extraosseous plasmacytoma, Extranodal marginal zone lymphoma of mucosa-associated lymphoid tissue (MALT lymphoma), Nodal marginal zone lymphoma, Pediatric nodal marginal zone lymphoma, Pediatric follicular lymphoma, Primary cutaneous follicle centre lymphoma, T-cell/histiocyte rich large B-cell lymphoma, Primary DLBCL of the CNS, Primary cutaneous DLBCL, leg type, EBV-positive DLBCL of the elderly, DLBCL associated with chronic inflammation, Lymphomatoid granulomatosis, Primary mediastinal (thymic) large B-cell lymphoma, Intravascular large B-cell lymphoma, ALK-positive large B-cell lymphoma, Plasmablastic lymphoma, Large B-cell lymphoma arising in HHV8-associated multicentric Castleman disease, Primary effusion lymphoma: B-cell lymphoma, unclassifiable, with features intermediate between diffuse large B-cell lymphoma and Burkitt lymphoma, and B-cell lymphoma, unclassifiable, with features intermediate between diffuse large B-cell lymphoma and classical Hodgkin lymphoma. In some examples, the preferred cancer is germinal-center B-cell-like (GCB) DLBCL, activated B-cell-like (ABC) DLBCL, follicular lymphoma (FL), mantle cell lymphoma (MCL), acute myeloid leukemia (AML), chronic lymphoid leukemia (CLL), marginal zone lymphoma (MZL), small lymphocytic leukemia (SLL), lymphoplasmacytic lymphoma (LL), Waldenstrom macroglobulinemia (WM), central nervous system lymphoma (CNSL), or Burkitt's lymphoma (BL)

In any of the preceding uses or methods, the autoimmune disorder can be selected from the group consisting of rheumatoid arthritis, juvenile rheumatoid arthritis, systemic lupus erythematosus (SLE), Wegener's disease, inflammatory bowel disease, idiopathic thrombocytopenic purpura (ITP), thrombotic thrombocytopenic purpura (TTP), autoimmune thrombocytopenia, multiple sclerosis, psoriasis, IgA nephropathy, IgM polyneuropathies, myasthenia gravis, vasculitis, diabetes mellitus, Reynaud's syndrome, Sjorgen's syndrome, glomerulonephritis, Neuromyelitis Optica (NMO) and IgG neuropathy.

In one aspect, the disclosure provides a kit comprising: (a) the composition as disclosed herein; and (b) a package insert comprising instructions for use of the composition to treat or delay progression of a cell proliferative disorder. In another example, the disclosure features a kit comprising: (a) a composition comprising any one of the preceding anti-CD3 antibodies and (b) a package insert comprising instructions for administering the composition to a subject to treat or delay progression of a cell proliferative disorder.

In any of the preceding uses or methods, the subject can be a human.

WHAT IS CLAIMED IS:

1. An anti-CD3 antibody which is a bispecific antibody, wherein the bispecific antibody comprises:

an anti-CD3 arm comprising a first binding domain comprising the following six hypervariable regions (HVRs):

(a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 7,

(b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 8,

(c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 9,

(d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 10,

(e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 11, and

(f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 12; and

an anti-LYPD1 arm comprising a second binding domain comprising the following six HVRs:

(a) an HVR-H1 comprising the amino acid sequence of SEQ ID NO: 175,

(b) an HVR-H2 comprising the amino acid sequence of SEQ ID NO: 176,

(c) an HVR-H3 comprising the amino acid sequence of SEQ ID NO: 177,

(d) an HVR-L1 comprising the amino acid sequence of SEQ ID NO: 178,

(e) an HVR-L2 comprising the amino acid sequence of SEQ ID NO: 179, and

(f) an HVR-L3 comprising the amino acid sequence of SEQ ID NO: 180.

2. The bispecific antibody of claim 1, wherein the first binding domain comprises (a) a heavy chain variable (VH) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 188; (b) a light chain variable (VL) domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 189; or (c) a VH domain as in (a) and a VL domain as in (b).

3. The bispecific antibody of claim 2, wherein the VH domain of the first binding domain comprises the amino acid sequence of SEQ ID NO: 188 and/or the VL domain comprises the amino acid sequence of SEQ ID NO: 189.

4. The bispecific antibody of any one of claims 1-3, wherein the second binding domain comprises (a) a VH domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 272; (b) a VL domain comprising an amino acid sequence having at least 95% sequence identity to the amino acid sequence of SEQ ID NO: 273; or (c) a VH domain as in (a) and a VL domain as in (b).

5. The bispecific antibody of claim 4, wherein the VH domain of the second binding domain comprises an amino acid sequence of SEQ ID NO: 272 and/or the VL domain comprising an amino acid sequence of SEQ ID NO: 273.

6. The bispecific antibody of any one of claims 1-3, wherein the anti-CD3 arm comprises a first binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 188 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 189, and the anti-LYPD1 arm comprises a second binding domain comprising (a) a VH domain comprising an amino acid sequence of SEQ ID NO: 272 and (b) a VL domain comprising an amino acid sequence of SEQ ID NO: 273.

7. The bispecific antibody of any one of claims 1-6, wherein the first binding domain binds to a human CD3 polypeptide or a cynomolgus monkey (cyno) CD3 polypeptide.

8. The bispecific antibody of claim 7, wherein (a) the human CD3 polypeptide is a human CD3ε polypeptide or a human CD3γ polypeptide; or (b) the cyno CD3 polypeptide is a cyno CD3ε polypeptide or a cyno CD3γ polypeptide.

9. The bispecific antibody of any one of claims 1-8, wherein the bispecific antibody comprises an aglycosylation site mutation.

10. The bispecific antibody of claim 9, wherein the aglycosylation site mutation reduces effector function of the bispecific antibody.

11. The bispecific antibody of claim 9 or 10, wherein the aglycosylation site mutation is a substitution mutation.

12. The bispecific antibody of any one of claims 1-10, wherein the bispecific antibody comprises a substitution mutation in the Fc region that reduces effector function.

13. The bispecific antibody of claim 11 or 12, wherein the substitution mutation is at amino acid residue N297, L234, L235, and/or D265 (EU numbering).

14. The bispecific antibody of claim 13, wherein the substitution mutation is selected from the group consisting of N297G, N297A, L234A, L235A, and D265A.

15. The bispecific antibody of any one of claims 1-14, wherein the bispecific antibody is:
(i) a monoclonal antibody, a humanized antibody, or a chimeric antibody;
(ii) a full-length antibody; and/or
(iii) an IgG antibody.

16. The bispecific antibody of any one of claims 1-15, wherein the bispecific antibody comprises one or more heavy chain constant domains, wherein the one or more heavy chain constant domains are selected from a first CH1 ($CH1_1$) domain, a first CH2 ($CH2_1$) domain, a first CH3 ($CH3_1$) domain, a second CH1 ($CH1_2$) domain, second CH2 ($CH2_2$) domain, and a second CH3 ($CH3_2$) domain.

17. The bispecific antibody of claim 16, wherein at least one of the one or more heavy chain constant domains is paired with another heavy chain constant domain, wherein:

(a) the $CH3_1$ and $CH3_2$ domains each comprise a protuberance or cavity, and wherein the protuberance or cavity in the $CH3_1$ domain is positionable in the cavity or protuberance, respectively, in the $CH3_2$ domain; or

(b) the $CH2_1$ and $CH2_2$ domains each comprise a protuberance or cavity, and wherein the protuberance or cavity in the $CH2_1$ domain is positionable in the cavity or protuberance, respectively, in the $CH2_2$ domain.

18. The bispecific antibody of claim 17, wherein the bispecific antibody comprises the aglycosylation site mutation N297G or N297A, and wherein the anti-CD3 arm comprises the cavity and the anti-LYPD1 arm comprises the protuberance.

19. An isolated nucleic acid encoding the bispecific antibody of any one of claims 1-18.

20. A vector comprising the isolated nucleic acid of claim 19.

21. An isolated host cell comprising the vector of claim 20.

22. A method of producing the bispecific antibody of any one of claims 1-18, the method comprising culturing the host cell of claim 21 in a culture medium and recovering the bispecific antibody from the host cell or the culture medium.

23. An immunoconjugate comprising the bispecific antibody of any one of claims 1-18 and a cytotoxic agent.

24. A composition comprising the bispecific antibody of any one of claims 1-18 and a pharmaceutically acceptable carrier, excipient, or diluent.

25. The composition of claim 24, wherein the composition further comprises a PD-1 axis binding antagonist or an additional therapeutic agent.

26. The bispecific antibody of any one of claims 1-18 for use as a medicament.

27. The bispecific antibody of any one of claims 1-18 for use in (i) treating or delaying progression of a cell proliferative disorder in a subject in need thereof or (ii) enhancing immune function in a subject having a cell proliferative disorder.

28. The bispecific antibody for use of claim 27, wherein the cell proliferative disorder is a cancer.

29. The bispecific antibody for use of claim 28, wherein the cancer is a LYPD1-expressing cancer.

30. The bispecific antibody for use of any one of claims 26-29, wherein the bispecific antibody binds to (a) a CD3 molecule located on an immune effector cell and (b) a LYPD1 molecule located on a target cell other than the immune effector cell.

31. The bispecific antibody for use of claim 30, wherein the bispecific antibody activates the immune effector cell following binding to (a) and (b).

32. The bispecific antibody for use of any one of claims 26-31, wherein the bispecific antibody is formulated for administration at a dosage of about 0.01 mg/kg to about 10 mg/kg, about 0.1 mg/kg to about 10 mg/kg, or about 1 mg/kg.

33. The bispecific antibody for use of any one of claims 26-32, wherein the bispecific antibody is formulated for administration with a PD-1 axis binding antagonist and/or an additional therapeutic agent.

34. The bispecific antibody for use of claim 33, wherein the PD-1 axis binding antagonist is selected from the group consisting of a PD-1 binding antagonist, a PD-L1 binding antagonist, and a PD-L2 binding antagonist.

35. The bispecific antibody for use of claim 34, wherein the PD-1 axis binding antagonist is:

(i) a PD-L1 binding antagonist selected from the group consisting of: MPDL3280A, MDX-1105, and MEDI4736;

(ii) a PD-1 binding antagonist selected from the group consisting of MDX-1106 (nivolumab), MK-3475 (lambrolizumab), and AMP-224; or

(iii) a PD-L2 binding antagonist which is an antibody or an immunoadhesin.

36. The bispecific antibody for use of any one of claims 26-35, wherein the bispecific antibody is formulated for administration in combination with a glucocorticoid or an antibody-drug conjugate (ADC).

37. The bispecific antibody for use of any one of claims 26-36, wherein the bispecific antibody is formulated for administration subcutaneously, intravenously, intramuscularly, topically, orally, transdermally, intraperitoneally, intraorbitally, by implantation, by inhalation, intrathecally, intraventricularly, or intranasally.

38. The bispecific antibody for use of any one of claims 27-37, wherein the subject is a human.

39. Use of the bispecific antibody of any one of claims 1-18 in the manufacture of a medicament.

40. The use of claim 39, wherein the medicament is for (i) treating or delaying progression of a cell proliferative disorder in a subject in need thereof or (ii) enhancing immune function in a subject having a cell proliferative disorder.

41. The use of claim 40, wherein the cell proliferative disorder is a cancer.

42. The use of claim 41, wherein the cancer is a LYPD1-expressing cancer.

43. The use of any one of claims 39-42, wherein the bispecific antibody binds to (a) a CD3 molecule located on an immune effector cell and (b) a LYPD1 molecule located on a target cell other than the immune effector cell.

44. The use of claim 43, wherein the bispecific antibody activates the immune effector cell following binding to (a) and (b).

45. The use of any one of claims 39-44, wherein the bispecific antibody is formulated for administration at a dosage of about 0.01 mg/kg to about 10 mg/kg, about 0.1 mg/kg to about 10 mg/kg, or about 1 mg/kg.

46. The use of any one of claims 39-45, wherein the medicament is formulated for use in combination with a PD-1 axis binding antagonist and/or an additional therapeutic agent.

47. The use of claim 46, wherein the PD-1 axis binding antagonist is selected from the group consisting of a PD-1 binding antagonist, a PD-L1 binding antagonist, and a PD-L2 binding antagonist.

48. The use of claim 47, wherein the PD-1 axis binding antagonist is:

(i) a PD-L1 binding antagonist selected from the group consisting of: MPDL3280A, MDX-1105, and MEDI4736;

(ii) a PD-1 binding antagonist selected from the group consisting of MDX-1106 (nivolumab), MK-3475 (lambrolizumab), and AMP-224; or

(iii) a PD-L2 binding antagonist which is an antibody or an immunoadhesin.

49. The use of any one of claims 39-48, wherein the medicament is formulated for use in combination with a glucocorticoid or an antibody-drug conjugate (ADC).

50. The use of any one of claims 39-49, wherein the medicament is formulated for administration to a subject subcutaneously, intravenously, intramuscularly, topically, orally, transdermally, intraperitoneally, intraorbitally, by implantation, by inhalation, intrathecally, intraventricularly, or intranasally.

51. The use of any one of claims 40-50, wherein the subject is a human.

52. A kit comprising:

(a) the composition of claim 24 or 25; and

(b) a package insert comprising instructions for use of the composition to treat or delay progression of a cell proliferative disorder.

53. The kit of claim 52, wherein the cell proliferative disorder is a cancer.

54. The kit of claim 53, wherein the cancer is a LYPD1-expressing cancer.