

CLAIMS

What Is Claimed Is:

~~1. An anti-cluster of differentiation three (“CD3”) antibody or antibody fragment, wherein said anti-CD3 antibody or antibody fragment comprises:~~

~~(A) a heavy chain variable region (VH) comprising a CDRH1, a CDRH2, and a CDRH3; and~~

~~(B) a light chain variable region (VL) comprising a CDRL1, a CDRL2, and a CDRL3,~~

~~wherein said CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 comprise the amino acid sequences of:~~

~~(i) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab325 as provided in Table 2, or SEQ ID NOS: 5187, 5189, 5191, 5195, 5197, and 5199, respectively;~~

~~(ii) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab326 as provided in Table 2, or SEQ ID NOS: 5203, 5205, 5207, 5211, 5213, and 5215, respectively;~~

~~(iii) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab327 as provided in Table 2, or SEQ ID NOS: 5219, 5221, 5223, 5227, 5229, and 5231, respectively;~~

~~(iv) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab328 as provided in Table 2, or SEQ ID NOS: 5235, 5237, 5239, 5243, 5245, and 5247, respectively;~~

~~(v) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab330 as provided in Table 2, or SEQ ID NOS: 5267, 5269, 5271, 5275, 5277, and 5279, respectively;~~

~~(vi) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab331 as provided in Table 2, or SEQ ID NOS: 5283, 5285, 5287, 5291, 5293, and 5295, respectively;~~

~~(vii) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab332 as provided in Table 2, or SEQ ID NOS: 5299, 5301, 5303, 5307, 5309, and 5311, respectively;~~

~~(viii) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab333 as provided in Table 2, or SEQ ID NOS: 5315, 5317, 5319, 5323, 5325, and 5327, respectively;~~

~~(ix) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab334 as provided in Table 2, or SEQ ID NOS: 5331, 5333, 5335, 5339, 5341, and 5343, respectively;~~

~~(x) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab335 as provided in Table 2, or SEQ ID NOS: 5347, 5349, 5351, 5355, 5357, and 5359, respectively;~~

~~(xi) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab336 as provided in Table 2, or SEQ ID NOS: 5363, 5365, 5367, 5371, 5373, and 5375, respectively;~~

~~(xii) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab337 as provided in Table 2, or SEQ ID NOS: 5379, 5381, 5383, 5387, 5389, and 5391, respectively;~~

~~(xiii) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab338 as provided in Table 2, or SEQ ID NOS: 5395, 5397, 5399, 5403, 5405, and 5407, respectively;~~

~~(xiv) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab339 as provided in Table 2, or SEQ ID NOS: 5411, 5413, 5415, 5419, 5421, and 5423, respectively;~~

~~(xv) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab340 as provided in Table 2, or SEQ ID NOS: 5427, 5429, 5431, 5435, 5437, and 5439, respectively;~~

~~(xvi) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab342 as provided in Table 2, or SEQ ID NOS: 5459, 5461, 5463, 5467, 5469, and 5471, respectively;~~

~~(xvii) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab343 as provided in Table 2, or SEQ ID NOS: 5475, 5477, 5479, 5483, 5485, and 5487, respectively;~~

~~(xviii) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab344 as provided in Table 2, or SEQ ID NOS: 5491, 5493, 5495, 5499, 5501, and 5503, respectively;~~

~~(xix) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab345 as provided in Table 2, or SEQ ID NOS: 5507, 5509, 5511, 5515, 5517, and 5519, respectively;~~

~~(xx) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab347 as provided in Table 2, or SEQ ID NOS: 5539, 5541, 5543, 5547, 5549, and 5551, respectively;~~

~~(xxi) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab348 as provided in Table 2, or SEQ ID NOS: 5555, 5557, 5559, 5563, 5565, and 5567, respectively;~~

~~(xxii) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab350 as provided in Table 2, or SEQ ID NOS: 5587, 5589, 5591, 5595, 5597, and 5599, respectively;~~

~~(xxiii) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab351 as provided in Table 2, or SEQ ID NOS: 5603, 5605, 5607, 5611, 5613, and 5615, respectively;~~

~~(xxiv) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab352 as provided in Table 2, or SEQ ID NOS: 5619, 5621, 5623, 5627, 5629, and 5631, respectively;~~

~~(xxv) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab353 as provided in Table 2, or SEQ ID NOS: 5635, 5637, 5639, 5643, 5645, and 5647, respectively;~~

~~or~~

~~(xxvi) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab354 as provided in Table 2, or SEQ ID NOS: 5651, 5653, 5655, 5659, 5661, and 5663, respectively.~~

2. The antibody or antibody fragment of claim 1, wherein said VH and VL comprise:

- ~~in (i), the amino acid sequences of SEQ ID NOS: 5186 and 5194, respectively, or amino acid sequences with at least 90% or 95% sequence identity to SEQ ID NOS: 5186 and 5194, respectively;~~
- ~~in (ii), the amino acid sequences of SEQ ID NOS: 5202 and 5210, respectively, or amino acid sequences with at least 90% or 95% sequence identity to SEQ ID NOS: 5202 and 5210, respectively;~~
- ~~in (iii), the amino acid sequences of SEQ ID NOS: 5218 and 5226, respectively, or amino acid sequences with at least 90% or 95% sequence identity to SEQ ID NOS: 5218 and 5226, respectively;~~
- ~~in (iv), the amino acid sequences of SEQ ID NOS: 5234 and 5242, respectively, or amino acid sequences with at least 90% or 95% sequence identity to SEQ ID NOS: 5234 and 5242, respectively;~~
- ~~in (v), the amino acid sequences of SEQ ID NOS: 5266 and 5274, respectively, or amino acid sequences with at least 90% or 95% sequence identity to SEQ ID NOS: 5266 and 5274, respectively;~~
- ~~in (vi), the amino acid sequences of SEQ ID NOS: 5282 and 5290, respectively, or amino acid sequences with at least 90% or 95% sequence identity to SEQ ID NOS: 5282 and 5290, respectively;~~
- ~~in (vii), the amino acid sequences of SEQ ID NOS: 5298 and 5306, respectively, or amino acid sequences with at least 90% or 95% sequence identity to SEQ ID NOS: 5298 and 5306, respectively;~~
- ~~in (viii), the amino acid sequences of SEQ ID NOS: 5314 and 5322, respectively, or amino acid sequences with at least 90% or 95% sequence identity to SEQ ID NOS: 5314 and 5322, respectively;~~
- ~~in (ix), the amino acid sequences of SEQ ID NOS: 5330 and 5338, respectively, or amino acid sequences with at least 90% or 95% sequence identity to SEQ ID NOS: 5330 and 5338, respectively;~~
- ~~in (x), the amino acid sequences of SEQ ID NOS: 5346 and 5354, respectively, or amino acid sequences with at least 90% or 95% sequence identity to SEQ ID NOS: 5346 and 5354, respectively;~~

~~in (xi), the amino acid sequences of SEQ ID NOS: 5362 and 5370, respectively, or amino acid sequences with at least 90% or 95% sequence identity to SEQ ID NOS: 5362 and 5370, respectively;~~

~~in (xii), the amino acid sequences of SEQ ID NOS: 5378 and 5386, respectively, or amino acid sequences with at least 90% or 95% sequence identity to SEQ ID NOS: 5378 and 5386, respectively;~~

~~in (xiii), the amino acid sequences of SEQ ID NOS: 5394 and 5402, respectively, or amino acid sequences with at least 90% or 95% sequence identity to SEQ ID NOS: 5394 and 5402, respectively;~~

~~in (xiv), the amino acid sequences of SEQ ID NOS: 5410 and 5418, respectively, or amino acid sequences with at least 90% or 95% sequence identity to SEQ ID NOS: 5410 and 5418, respectively;~~

~~in (xv), the amino acid sequences of SEQ ID NOS: 5426 and 5434, respectively, or amino acid sequences with at least 90% or 95% sequence identity to SEQ ID NOS: 5426 and 5434, respectively;~~

~~in (xvi), the amino acid sequences of SEQ ID NOS: 5458 and 5466, respectively, or amino acid sequences with at least 90% or 95% sequence identity to SEQ ID NOS: 5458 and 5466, respectively;~~

~~in (xvii), the amino acid sequences of SEQ ID NOS: 5474 and 5482, respectively, or amino acid sequences with at least 90% or 95% sequence identity to SEQ ID NOS: 5474 and 5482, respectively;~~

~~in (xviii), the amino acid sequences of SEQ ID NOS: 5490 and 5498, respectively, or amino acid sequences with at least 90% or 95% sequence identity to SEQ ID NOS: 5490 and 5498, respectively;~~

~~in (xix), the amino acid sequences of SEQ ID NOS: 5506 and 5514, respectively, or amino acid sequences with at least 90% or 95% sequence identity to SEQ ID NOS: 5506 and 5514, respectively;~~

~~in (xx), the amino acid sequences of SEQ ID NOS: 5538 and 5546, respectively, or amino acid sequences with at least 90% or 95% sequence identity to SEQ ID NOS: 5538 and 5546, respectively;~~

~~in (xxi), the amino acid sequence of SEQ ID NOS: 5554 and 5562, respectively, or amino acid sequences with at least 90% or 95% sequence identity to SEQ ID NOS: 5554 and 5562, respectively;~~

~~in (xxii), the amino acid sequences of SEQ ID NOS: 5586 and 5594, respectively, or amino acid sequences with at least 90% or 95% sequence identity to SEQ ID NOS: 5586 and 5594, respectively;~~

~~in (xxiii), the amino acid sequences of SEQ ID NOS: 5602 and 5610, respectively, or amino acid sequences with at least 90% or 95% sequence identity to SEQ ID NOS: 5602 and 5610, respectively;~~

~~in (xxiv), the amino acid sequences of SEQ ID NOS: 5618 and 5626, respectively, or amino acid sequences with at least 90% or 95% sequence identity to SEQ ID NOS: 5618 and 5626, respectively;~~

~~in (xxv), the amino acid sequences of SEQ ID NOS: 5634 and 5642, respectively, or amino acid sequences with at least 90% or 95% sequence identity to SEQ ID NOS: 5634 and 5642, respectively; or~~

~~in (xxvi), the amino acid sequences of SEQ ID NOS: 5650 and 5658, respectively, or amino acid sequences with at least 90% or 95% sequence identity to SEQ ID NOS: 5650 and 5658, respectively.~~

31. An anti-cluster of differentiation three (“CD3”)The antibody or ~~antibody-antigen-binding~~ fragment of claim 1thereof, comprising:

- (A) a heavy chain variable region (VH) comprising a CDRH1, a CDRH2, and a CDRH3; and
- (B) a light chain variable region (VL) comprising a CDRL1, a CDRL2, and a CDRL3,

wherein said CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 comprise the amino acid sequences of the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab325 as provided in Table 2 or SEQ ID NOS: 5187, 5189, 5191, 5195, 5197, and 5199, respectively.

~~4. The antibody or antibody fragment of claim 1, wherein said CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3 comprise the amino acid sequences of:~~

(vi) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab330 as provided in Table 2, or SEQ ID NOS: 5267, 5269, 5271, 5275, 5277, and 5279, respectively;

(vii) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab332 as provided in Table 2, or SEQ ID NOS: 5299, 5301, 5303, 5307, 5309, and 5311, respectively;

(viii) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab333 as provided in Table 2, or SEQ ID NOS: 5315, 5317, 5319, 5323, 5325, and 5327, respectively;

(ix) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab334 as provided in Table 2, or SEQ ID NOS: 5331, 5333, 5335, 5339, 5341, and 5343, respectively;

(x) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab335 as provided in Table 2, or SEQ ID NOS: 5347, 5349, 5351, 5355, 5357, and 5359, respectively;

(xi) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab336 as provided in Table 2, or SEQ ID NOS: 5363, 5365, 5367, 5371, 5373, and 5375, respectively;

(xii) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab337 as provided in Table 2, or SEQ ID NOS: 5379, 5381, 5383, 5387, 5389, and 5391, respectively;

(xiii) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab338 as provided in Table 2, or SEQ ID NOS: 5395, 5397, 5399, 5403, 5405, and 5407, respectively;

(xiv) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab339 as provided in Table 2, or SEQ ID NOS: 5411, 5413, 5415, 5419, 5421, and 5423, respectively;

(xv) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab340 as provided in Table 2, or SEQ ID NOS: 5427, 5429, 5431, 5435, 5437, and 5439, respectively;

(xvi) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab342 as provided in Table 2, or SEQ ID NOS: 5459, 5461, 5463, 5467, 5469, and 5471, respectively;

(xvii) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab343 as provided in Table 2, or SEQ ID NOS: 5475, 5477, 5479, 5483, 5485, and 5487, respectively;

(xviii) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab344 as provided in Table 2, or SEQ ID NOS: 5491, 5493, 5495, 5499, 5501, and 5503, respectively;

(xix) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab345 as provided in Table 2, or SEQ ID NOS: 5507, 5509, 5511, 5515, 5517, and 5519, respectively;

(xx) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab347 as provided in Table 2, or SEQ ID NOS: 5539, 5541, 5543, 5547, 5549, and 5551, respectively;

~~(xxi) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab348 as provided in Table 2, or SEQ ID NOS: 5555, 5557, 5559, 5563, 5565, and 5567, respectively;~~
~~(xxii) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab350 as provided in Table 2, or SEQ ID NOS: 5587, 5589, 5591, 5595, 5597, and 5599, respectively;~~
~~(xxiii) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab351 as provided in Table 2, or SEQ ID NOS: 5603, 5605, 5607, 5611, 5613, and 5615, respectively;~~
~~(xxiv) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab352 as provided in Table 2, or SEQ ID NOS: 5619, 5621, 5623, 5627, 5629, and 5631, respectively;~~
~~(xxv) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab353 as provided in Table 2, or SEQ ID NOS: 5635, 5637, 5639, 5643, 5645, and 5647, respectively;~~
~~or~~
~~(xxvi) the CDRH1, CDRH2, CDRH3, CDRL1, CDRL2, and CDRL3, respectively, of Ab354 as provided in Table 2, or SEQ ID NOS: 5651, 5653, 5655, 5659, 5661, and 5663, respectively.~~

2. The anti-CD3 antibody or antigen-binding fragment thereof of claim 1, wherein:

- (A) the VH comprises said CDRH1, said CDRH2, and said CDRH3 and comprises an amino acid sequence with at least 90% identity to the amino acid sequence of SEQ ID NO: 5186; and
(B) the VL comprises said CDRL1, said CDRL2, and said CDRL3 and comprises an amino acid sequence with at least 90% identity to the amino acid sequence of SEQ ID NO: 5194.

3. The anti-CD3 antibody or antigen-binding fragment thereof of claim 1, wherein:

- (A) the VH comprises an amino acid sequence with at least 95% identity to the amino acid sequence of SEQ ID NO: 5186; and
(B) the VL comprises an amino acid sequence with at least 95% identity to the amino acid sequence of SEQ ID NO: 5194.

54. The anti-CD3 antibody or ~~antigen-bindingantibody~~ fragment ~~thereof~~ of claim 1, wherein said VH and VL comprise the amino acid sequences of:

- ~~in (i), SEQ ID NOS: 5186 and 5194, respectively;~~
~~in (vi), SEQ ID NOS: 5282 and 5290, respectively;~~
~~in (vii), SEQ ID NOS: 5298 and 5306, respectively;~~

~~in (xi), SEQ ID NOS: 5362 and 5370, respectively;~~
~~in (xii), SEQ ID NOS: 5378 and 5386, respectively;~~
~~in (xiii), SEQ ID NOS: 5394 and 5402, respectively; or~~
~~in (xxiv), SEQ ID NOS: 5618 and 5626, respectively.~~

~~6. The antibody or antibody fragment of claim 1, wherein said VH and VL comprise the amino acid sequences of:~~

~~in (v), SEQ ID NOS: 5266 and 5274, respectively;~~
~~in (vii), SEQ ID NOS: 5298 and 5306, respectively;~~
~~in (viii), SEQ ID NOS: 5314 and 5322, respectively;~~
~~in (ix), SEQ ID NOS: 5330 and 5338, respectively;~~
~~in (xi), SEQ ID NOS: 5346 and 5354, respectively;~~
~~in (xi), SEQ ID NOS: 5362 and 5370, respectively;~~
~~in (xii), SEQ ID NOS: 5378 and 5386, respectively;~~
~~in (xiii), SEQ ID NOS: 5394 and 5402, respectively;~~
~~in (xiv), SEQ ID NOS: 5410 and 5418, respectively;~~
~~in (xv), SEQ ID NOS: 5426 and 5434, respectively;~~
~~in (xvi), SEQ ID NOS: 5458 and 5466, respectively;~~
~~in (xvii), SEQ ID NOS: 5474 and 5482, respectively;~~
~~in (xviii), SEQ ID NOS: 5490 and 5498, respectively;~~
~~in (xix), SEQ ID NOS: 5506 and 5514, respectively;~~
~~in (xx), SEQ ID NOS: 5538 and 5546, respectively;~~
~~in (xxi), SEQ ID NOS: 5554 and 5562, respectively;~~
~~in (xxii), SEQ ID NOS: 5586 and 5594, respectively;~~
~~in (xxiii), SEQ ID NOS: 5602 and 5610, respectively;~~
~~in (xxiv), SEQ ID NOS: 5618 and 5626, respectively;~~
~~in (xxv), SEQ ID NOS: 5634 and 5642, respectively; or~~
~~in (xxvi), SEQ ID NOS: 5650 and 5658, respectively.~~

5. The anti-CD3 antibody or antigen-binding fragment thereof according to any one of the foregoing claims, which comprises:

(i) a Fc region;

(ii) a wild-type human Fc region;

(iii) a variant of a human IgG1, IgG2, IgG3, or IgG4 Fc region, which comprises glycine or arginine at position 329 according to EU numbering;

(iv) a variant of a human IgG1, IgG2, IgG3, or IgG4 Fc region, which comprises alanine or aspartic acid at position 297 and glycine or arginine at position 329 according to EU numbering;

(v) a variant of a human IgG1, IgG2, IgG3, or IgG4 Fc region, which comprises glycine at position 297 according to EU numbering;

(v) a variant of a human IgG1 Fc region, which comprises glycine or arginine at position 329 according to the EU numbering and further comprises at least one of proline at position 233, alanine at position 234, alanine or glutamic acid at position 235, alanine or aspartic acid at position 297, and serine at position 331 according to EU numbering;

(vi) a variant of a human IgG1 Fc region, which comprises alanine at position 234, alanine at position 235, and glycine position 329 according to EU numbering;

(vii) a variant of a human IgG4 Fc region, which comprises proline at position 228 and glycine position 329 according to EU numbering; and/or

(viii) a variant of a human IgG4 Fc region, which comprises proline at position 228, glutamic acid at position 235, and glycine position 329 according to EU numbering.

~~76.~~ The anti-CD3 antibody or ~~antigen-bindingantibody~~ fragment thereof according to any one of the foregoing claims, which does not form a succinimide intermediate as determined by size exclusion chromatography (SEC) peak breadth.

~~87.~~ The anti-CD3 antibody or ~~antigen-bindingantibody~~ fragment thereof according to any one of the foregoing claims, which comprises a polyspecific reactivity (PSR) score of between about 0.0 and about 0.33 ~~or between about 0.0 and about 0.10~~ as determined by a PSR assay.

8. The anti-CD3 antibody or antigen-binding fragment thereof according to any one of the foregoing claims, which is conjugated to one or more heterologous molecule(s), optionally wherein:

(i) the one or more heterologous molecule(s) comprise a cytotoxic agent, a toxoid, and/or an antibiotic, optionally selected from: auristatin, optionally monomethylauristatin; dolastatin; calicheamicin; anthracycline, optionally daunomycin or doxorubicin; methotrexate; vindesine; taxane, optionally docetaxel, paclitaxel, larotaxel, tesetaxel, or ortataxel; and/or a trichothecene, and/or CC1065;

(ii) the one or more heterologous molecule(s) comprise a toxin, optionally a toxin of bacterial, fungal, plant, or animal origin, further optionally selected from: diphtheria A chain; nonbinding active fragments of diphtheria toxin; *Pseudomonas aeruginosa* exotoxin A chain; ricin A chain; abrin A chain; modeccin A chain; alpha-sarcin; *Aleurites fordii* protein; *dianthin* proteins; *Phytolaca americana* protein PAPI, PAPII, or PAP-S; *Momordica charantia* inhibitor; curcin; crotin; *Saponaia officinalis* inhibitor; gelonin; mitogellin; restrictocin; phenomycin; neomycin; and/or tricothecene;

(iii) the one or more heterologous molecule(s) comprise a non-proteinaceous moiety, optionally a carbone nanotube or a water-soluble polymer, further optionally selected from polyethylene glycol (PEG), ethylene glycol/propylene glycol copolymer, carboxymethylcellulose, dextran, polyvinyl alcohol, polyvinyl pyrrolidone, poly-1,3-dioxolane, poly-1,3,6-trioxane, ethylene/maleic anhydride copolymer, polyaminoacid homopolymer or random copolymer, poly(n-vinyl pyrrolidone)polyethylene glycol, polypropylene glycol homopolymer, polypropylene oxide/ethylene oxide co-polymer, polyoxyethylated polyol, glycerol, polyvinyl alcohol, and/or a mixture thereof;

(iv) the one or more heterologous molecule(s) comprise a radioactive isotope, optionally At211, I131, I125, Y90, Re186, Re188, Sm153, Bi212, P32, H3, Pb212 or a radioactive isotope of Lu, tc99m, iodine-123, iodine-131, indium-111, fluorine-19, carbon-13, nitrogen-15, oxygen-17, gadolinium, manganese, or iron;

(v) the one or more heterologous molecule(s) comprise a label, optionally a fluorescent, chromophoric, electron-dense, chemiluminescent, or radioactive label;

(vi) the one or more heterologous molecule(s) comprise an enzyme or ligand, further optionally selected from luciferase, luciferin, 2,3-dihydrophthalazinedione, horseradish peroxidase (HRP), alkaline phosphatase, β -galactosidase, glucoamylase, lysozyme, saccharide oxidase, glucose oxidase, galactose oxidase, glucose-6-phosphate dehydrogenase, heterocyclic oxidase, uricase, xanthine oxidase, lactoperoxidase, microperoxidase, biotin, and/or avidin; and/or

(vii) the anti-CD3 antibody or antigen-binding fragment thereof comprises:

(vii-1) a variant of a human light chain constant region which comprises cysteine at position V205 according to Kabat numbering;

(vii-2) a variant of a human heavy chain constant region which comprises cysteine at position 118 according to EU numbering; and/or

(vii-3) a variant of a human IgG1, IgG2, IgG3, or IgG4 Fc region, which comprises cysteine at position 400 according to EU numbering,

wherein anti-CD3 antibody or antigen-binding fragment thereof is conjugated to the heterologous molecule via said cysteine(s).

9. The anti-CD3 antibody or antigen-bindingantibody fragment thereof according to any one of the foregoing claims, wherein:

(i) the antibody or antigen-bindingantibody fragment thereof comprises a multispecific antibody or antigen-bindingantibody fragment thereof;

(ii) the antibody or antigen-bindingantibody fragment thereof comprises a bispecific antibody or antigen-bindingantibody fragment thereof;

(iii) the antibody or antigen-bindingantibody fragment thereof comprises at least a second antigen binding domain that specifically binds to an oncology target; ~~an immune-oncology target; a neurodegenerative disease targets;~~ an autoimmune disorder target; an infectious disease target; or a metabolic disease target; ~~a cognitive disorder target; a blood-brain barrier target; or a blood-disease target;~~

the antibody or antigen-bindingantibody fragment thereof comprises at least a second antigen binding domain that specifically binds to an antigen selected from the group consisting of: 17-IA, 4-1BB, 4Dc, 6- keto-PGF1a, 8-iso-PGF2a, 8-oxo-dG, A1 Adenosine Receptor, A33, ACE, ACE-2, Activin, Activin A, Activin AB, Activin B, Activin C, Activin RIA, Activin RIA ALK-2, Activin RIB ALK-4, Activin RIIA, Activin RUB, ADAM, ADAM10, ADAM12, ADAM 15, ADAM 17/T ACE, ADAM8, ADAM9, ADAMTS, ADAMTS4, ADAMTS5, Addressins, aFGF, ALCAM, ALK, ALK-1, ALK-7, alpha-1-antitrypsin, alpha-V/beta-1 antagonist, ANG, Ang, APAF-1, APE, APJ, APP, APRIL, AR, ARC, ART, Artemin, anti-Id, ASPARTIC, Atrial natriuretic factor, av/b3 integrin, Axl, b2M, B7-1, B7-2, B7-H, B-lymphocyte Stimulator (BlyS), BACE, BACE-1, Bad, BAFF, BAFF-R, Bag-1, BAK, Bax, BCA-1, BCAM, Bel, BCMA, BDNF, b-ECGF, bFGF, BID, Bik, BFM, BLC, BL-CAM, BLK, BMP, BMP-2 BMP-2a, BMP-3 Osteogenin, BMP-4 BMP-2b, BMP-5, BMP-6 Vgr-1, BMP-7 (OP-1), BMP-8 (BMP-8a, OP-2), BMPR, BMPR-IA (ALK-3), BMPR-IB (ALK-6), BRK-2, RPK-1, BMPR-II (BRK-3), BMPs, b- NGF, BOK, Bombesin, Bone-derived neurotrophic factor, BPDE, BPDE-DNA, BTC, complement factor 3 (C3), C3a, C4, C5, C5a, CIO, CA125, CAD-8, Calcitonin, cAMP, carcinoembryonic antigen (CEA), carcinoma-associated antigen, Cathepsin A, Cathepsin B, Cathepsin C/DPPI, Cathepsin D, Cathepsin E, Cathepsin H, Cathepsin L, Cathepsin O, Cathepsin S, Cathepsin V, Cathepsin X/Z/P, CBL, CCI, CCK2, CCL, CCL1, CCL11, CCL12, CCL13, CCL 14, CCL15, CCL16, CCL1 7, CCL18, CCL19, CCL2, CCL20, CCL21, CCL22, CCL23, CCL24, CCL25, CCL26, CCL27, CCL28, CCL3, CCL4, CCL5, CCL6, CCL7, CCL8, CCL9/10, CCR, CCR1, CCR10, CCR10, CCR2, CCR3, CCR4, CCR5, CCR6, CCR7, CCR8, CCR9, CD1, CD2, CD4, CD5, CD6, CD7, CD8, CD10, CD11a, CD11b, CD11c, CD13, CD14, CD15, CD16, CD18, CD19, CD20, CD21, CD22, CD23, CD25, CD27L, CD28, CD29, CD30, CD30L, CD32, CD33 (p67 proteins), CD34, CD38, CD40, CD40L, CD44, CD45, CD46, CD49a, CD52, CD54, CD55, CD56, CD61, CD64, CD66e, CD74, CD80 (B7-1), CD89, CD95, CD123, CD137, CD138, CD140a, CD146, CD147, CD148, CD152, CD164, CEACAM5, CFTR, cGMP, CINC, Clostridium botulinum toxin, Clostridium perfringens toxin, CKb8-l, CLC, CMV, CMV UL, CNTF, CNTN-1, COX, C-Ret, CRG-2, CT-1, CTACK, CTGF, CTLA-4, CX3CL1, CX3CR1, CXCL, CXCL1, CXCL2, CXCL3, CXCL4, CXCL5, CXCL6, CXCL7, CXCL8, CXCL9, CXCL10, CXCL11, CXCL12, CXCL13, CXCL14, CXCL15, CXCL16, CXCR, CXCR1, CXCR2, CXCR3, CXCR4, CXCR5, CXCR6, cytokeratin tumor-

associated antigen, DAN, DCC, DcR3, DC-SIGN, Decay accelerating factor, des(1-3)-IGF-I (brain IGF-1), Dhh, digoxin, DNAM-1, Dnase, Dpp, DPPIV/CD26, Dtk, ECAD, EDA, EDA-A1, EDA-A2, EDAR, EGF, EGFR (ErbB-1), EMA, EMMPRIN, EN A, endothelin receptor, Enkephalinase, eNOS, Eot, eotaxinl, EpCAM, Ephrin B2/ EphB4, EPO, ERCC, E-selectin, ET-1, Factor IIa, Factor VII, Factor VIIIc, Factor IX, fibroblast activation protein (FAP), Fas, FcR1, FEN-1, Ferritin, FGF, FGF-19, FGF-2, FGF3, FGF-8, FGFR, FGFR-3, Fibrin, FL, FLIP, Flt-3, Flt-4, Follicle stimulating hormone, Fractalkine, FZD1, FZD2, FZD3, FZD4, FZD5, FZD6, FZD7, FZD8, FZD9, FZD10, G250, Gas 6, GCP-2, GCSF, GD2, GD3, GDF, GDF-1, GDF-3 (Vgr-2), GDF-5 (BMP-14, CDMP- 1), GDF-6 (BMP-13, CDMP-2), GDF-7 (BMP-12, CDMP-3), GDF-8 (Myostatin), GDF-9, GDF- 15 (MIC-1), GDNF, GFAP, GFRa-1, GFR-alpha1, GFR-alpha2, GFR-alpha3, GTR, Glucagon, Glut 4, glycoprotein IIb/IIIa (GP IIb/IIIa), GM-CSF, gp130, gp72, GRO, Growth hormone releasing factor, Hapten (NP-cap or NIP-cap), HB-EGF, HCC, HCMV gB envelope glycoprotein, HCMV) gH envelope glycoprotein, HCMV UL, Hemopoietic growth factor (HGF), Hep B gp120, heparanase, Her2, Her2/neu (ErbB-2), Her3 (ErbB-3), Her4 (ErbB-4), herpes simplex virus (HSV) gB glycoprotein, HSV gD glycoprotein, HGFA, High molecular weight melanoma-associated antigen (HMW-MAA), HIV gp120, HIV IIIB gp 120 V3 loop, HLA, HLA-DR, HM1.24, HMFG PEM, HRG, Hrk, human cardiac myosin, human cytomegalovirus (HCMV), human growth hormone (HGH), HVEM, 1-309, IAP, ICAM, ICAM-1, ICAM-3, ICE, ICOS, IFNg, Ig, IgA receptor, IgE, IGF, IGF binding proteins, IGF-1R, IGFBP, IGF-I, IGF-II, IL, IL-1, IL-1R, IL-2, IL-2R, IL-4, IL-4R, IL-5, IL-5R, IL-6, IL-6R, IL-8, IL- 9, IL-10, IL-12, IL-13, IL-15, IL-18, IL-18R, IL-23, interferon (INF)-alpha, INF-beta, INF- gamma, Inhibin, iNOS, Insulin A-chain, Insulin B-chain, Insulin-like growth factor 1, integrin alpha2, integrin alpha3, integrin alpha4, integrin alpha4/betal, integrin, alpha4/beta7, integrin alpha5 (alphaV), integrin alpha5/betal, integrin alpha5/beta3, integrin alpha6, integrin betal, integrin beta2, interferon gamma, IP- 10, 1-TAC, JE, Kallikrein 2, Kallikrein 5, Kallikrein 6, , Kallikrein 11, Kallikrein 12, Kallikrein 14, Kallikrein 15, Kallikrein LI, Kallikrein L2, Kallikrein L3, Kallikrein L4, KC, KDR, Keratinocyte Growth Factor (KGF), laminin 5, LAMP, LAP, LAP (TGF- 1), Latent TGF-1, Latent TGF-1 bpl, LBP, LDGF, LECT2, Lefty, Lewis-Y antigen, Lewis-Y related antigen, LFA-1, LFA-3, Lfo, LIF, LIGHT, lipoproteins, LIX, LKN, Lptn, L-Selectin, LT-a, LT-b, LTB4, LTBP-1, Lung surfactant, Luteinizing hormone, Lymphotoxin Beta Receptor, Mac-1, MAdCAM, MAG, MAP2, MARC,

MCAM, MCAM, MCK-2, MCP, M-CSF, MDC, Mer, a metalloprotease, MGDF receptor, MGMT, MHC (HLA-DR), MIF, MIG, MIP, MIP-1-alpha, MK, MMAC1, MMP, MMP-1, MMP-10, MMP-11, MMP-12, MMP-13, MMP-14, MMP-15, MMP-2, MMP-24, MMP- 3, MMP-7, MMP-8, MMP-9, MPIF, Mpo, MSK, MSP, mucin (Mucl), MUC18, Muellerian-inhibiting substance, Mug, MuSK, NAIP, NAP, NCAD, N-Cadherin, NCA 90, NCAM, Neprilysin, Neurotrophin-3,-4, or -6, Neurturin, Neuronal growth factor (NGF), NGFR, NGF-beta, nNOS, NO, NOS, Npn, NRG-3, NT, NTN, OB, OGG1, OPG, OPN, OSM, OX40L, OX40R, p150, p95, PADPr, Parathyroid hormone, PARC, PARP, PBR, PBSF, PCAD, P-Cadherin, PCNA, PDGF, PDGF, PDK-1, PECAM, PEM, PF4, PGE, PGF, PGI2, PGJ2, PIN, PLA2, placental alkaline phosphatase (PLAP), PIGF, PLP, PP14, Proinsulin, Prorelaxin, Protein C, PS, PSA, PSCA, prostate specific membrane antigen (PSMA), PTEN, PTHrp, Ptk, PTN, R51, RANK, RANKL, RANTES, Relaxin A-chain, Relaxin B-chain, renin, respiratory syncytial virus (RSV) F, RSV Fgp, Ret, Rheumatoid factors, RLIP76, RPA2, RSK, S100, SCF/KL, SDF-1, SERINE, Serum albumin, sFRP-3, Shh, SIGIRR, SK-1, SLAM, SLPI, SMAC, SMDF, SMOH, SOD, SPARC, Stat, STEAP, STEAP-II, TACE, TACI, TAG-72 (tumor-associated glycoprotein-72), TARC, TCA-3, T-cell receptors (e.g., T-cell receptor alpha/beta), TdT, TECK, TEM1, TEM5, TEM7, TEM8, TERT, testicular PLAP-like alkaline phosphatase, TfR, TGF, TGF-alpha, TGF-beta, TGF-beta Pan Specific, TGF-beta RI (ALK-5), TGF-beta RII, TGF-beta RIIB, TGF-beta RIII, TGF-betal, TGF-beta2, TGF-beta3, TGF-beta4, TGF-beta5, Thrombin, Thymus Ck-1, Thyroid stimulating hormone, Tie, TIMP, TIQ, TMEFF2, Tmpo, TNFRSS2, TNF, TNF-alpha, TNF-alpha beta, TNF-beta2, TNFc, TNF-RI, TNF-RII, TNFRSF10A (TRAIL R1 Apo-2, DR4), TNFRSF10B (TRAIL R2 DR5, KILLER, TRICK-2A, TRICK-B), TNFRSF10C (TRAIL R3 DcR1, LIT, TRID), TNFRSF10D (TRAIL R4 DcR2, TRUND), TNFRSF11A (RANK ODF R, TRANCE R), TNFRSF11B (OPG OCIF, TR1), TNFRSF12 (TWEAK R FN14), TNFRSF13B (TACI), TNFRSF13C (BAFF R), TNFRSF14 (HVEM ATAR, HveA, LIGHT R, TR2), TNFRSF16 (NGFR p75NTR), TNFRSF17 (BCMA), TNFRSF 18 (GITR AITR), TNFRSF19 (TROY TAJ, TRADE), TNFRSF19L (RELT), TNFRSF1A (TNF RI CD120a, p55-60), TNFRSF1B (TNF RII CD120b, p75-80), TNFRSF26 (TNFRH3), TNFRSF3 (LTbR TNF RIII, TNFC R), TNFRSF4 (OX40 ACT35, TXGP1 R), TNFRSF 5 (CD40 p50), TNFRSF6 (Fas Apo-1, APT1, CD95), TNFRSF6B (DcR3 M68, TR6), TNFRSF7 (CD27), TNFRSF8 (CD30), TNFRSF9 (4-1BB CD137, ILA), TNFRSF21 (DR6),

TNFRSF22 (DcTRAIL R2 TNFRH2), TNFRST23 (DcTRAIL RI TNFRH1), TNFRSF25 (DR3 Apo-3, LARD, TR-3, TRAMP, WSL-1), TNFSF10 (TRAIL Apo-2 Ligand, TL2), TNFSF11 (TRANCE/RANK Ligand ODF, OPG Ligand), TNFSF12 (TWEAK Apo-3 Ligand, DR3 Ligand), TNFSF13 (APRIL TALL2), TNFSF13B (BAFF BLYS, TALL1, THANK, TNFSF20), TNFSF14 (LIGHT HVEM Ligand, LTg), TNFSF15 (TLIA/VEGI), TNFSF18 (GITR Ligand AITR Ligand, TL6), TNFSF1A (TNF-a Conectin, DIF, TNFSF2), TNFSF1B (TNF-b LTa, TNFSF1), TNFSF3 (LTb TNFC, p33), TNFSF4 (OX40 Ligand gp34, TXGP1), TNFSF5 (CD40 Ligand CD154, gp39, HIGM1, IMD3, TRAP), TNFSF6 (Fas Ligand Apo-1 Ligand, APT1 Ligand), TNFSF7 (CD27 Ligand CD70), TNFSF8 (CD30 Ligand CD153), TNFSF9 (4-1BB Ligand CD137 Ligand), TP-1, t-PA, Tpo, TRAIL, TRAIL R, TRAIL-R1, TRAIL-R2, TRANCE, transferring receptor, TRF, Trk, TROP-2, TSG, TSLP, tumor-associated antigen CA 125, tumor-associated antigen expressing Lewis Y related carbohydrate, TWEAK, TXB2, Ung, uPAR, uPAR-1, Urokinase, VCAM, VCAM-1, VECAD, VE-Cadherin, VE-cadherin-2, VEGFR-1 (flt-1), VEGF, VEGFR, VEGFR-3 (flt-4), VEGI, VFM, Viral antigens, VLA, VLA-1, VLA-4, VNR integrin, von Willebrand's factor, WIF- 1, WNT1, WNT2, WNT2B/13, WNT3, WNT3A, WNT4, WNT5A, WNT5B, WNT6, WNT7A, WNT7B, WNT8A, WNT8B, WNT9A, WNT9B, WNT10A, WNT10B, WNT11, WNT16, XCL1, XCL2, XCR1, XCR1, XEDAR, XIAP, XPD, CTLA4 (cytotoxic T lymphocyte antigen-4), PD1 (programmed cell death protein 1), PD-L1 (programmed cell death ligand 1), LAG-3 (lymphocyte activation gene-3), TIM-3 (T cell immunoglobulin and mucin protein-3), and hormone receptors ~~and growth factors~~;

(iv) the antibody or ~~antigen-bindingantibody~~ fragment thereof comprises at least a second antigen binding domain that specifically binds to an antigen selected from the group consisting of: BCMA, CTLA4 (cytotoxic T lymphocyte antigen-4), PD1 (programmed cell death protein 1), PD-L1 (programmed cell death ligand 1), LAG-3 (lymphocyte activation gene-3), TIM-3, CD20, CD2, CD19, Her2, EGFR, EpCAM, FcγRIIIa (CD16), FcγRIIIa (CD32a), FcγRIIb (CD32b), FcγRI (CD64), Toll-like receptors (TLRs), TLR4, TLR9, cytokines, IL-2, IL-5, IL-13, IL-6, IL-17, IL-12, IL-23, TNFa, TGFb, cytokine receptors, IL-2R, chemokines, chemokine receptors, growth factors, VEGF, and HGF; and/or

- (v) the antibody or ~~antigen-bindingantibody~~ fragment thereof comprises at least a second antigen binding domain that specifically binds to an antigen, wherein said antibody comprises a multispecific format selected from the group consisting of: Fab-Fc-scFv, "bottle-opener, Mab-scFv, Mab-Fv, Dual scFv, central Fv, central scFv, one-arm central scFv, Fab-Fab, Fab-Fv, mAb-Fv, mAb-Fab, DART, BiTE, common light chain-IgG, TandAb, Cross-Mab, SEED, BEAT, TrioMab, and DuetMab.
10. An isolated or recombinant nucleic acid sequence encoding an anti-CD3 antibody or ~~antigen-bindingantibody~~ fragment thereof according to any one of the foregoing claims.
11. An expression vector comprising an isolated or recombinant nucleic acid sequence according to claim 10.
12. A host cell transfected, transformed, or transduced with a nucleic acid sequence according to claim 10, or ~~a~~ an expression vector according to claim 11, optionally wherein the host cell is:
- (i) a prokaryotic cell, optionally a bacterial cell, further optionally an *E. coli* cell; or
 - (ii) a eukaryotic cell, optionally
 - (ii-1) a cell of a eukaryotic microbe, optionally a filamentous fungus or yeast;
 - (ii-2) an invertebrate cell, optionally a plant or insect cell; or
 - (ii-3) a vertebrate cell, optionally a mammalian cell, further optionally a mammalian cell line, yet further optionally selected from the following: COS-7 cell; human embryonic kidney line 293 cell; baby hamster kidney (BHK) cell; TM4 cell; monkey kidney CV1 cell; African green monkey kidney VERO-76 cell; human cervical carcinoma HELA cell; canine kidney MDCK cell; buffalo rat liver BRL 3A cell; human lung W138 cell; human liver Hep G2 cell; mouse mammary tumor MMT 060562 cell; TRI cell; MRC 5 cell; FS4 cells; Chinese hamster ovary (CHO) cell; DHFR-CHO cell; and/or a myeloma cell line, optionally Y0 cell, NS0 cell, or Sp2/0 cell.
13. A pharmaceutical composition comprising an anti-CD3 antibody or ~~antigen-bindingantibody~~ fragment thereof according to any one of claims 1-9; and a pharmaceutically acceptable carrier and/or excipient.

14. The anti-CD3 antibody or antigen-bindingantibody fragment thereof according to any one of claims 1-9 for use in therapy.
15. Use of the anti-CD3 antibody or antigen-bindingantibody fragment thereof according to any one of claims 1-9 in the manufacture of a medicament for the treatment of a disorder in a mammal, wherein the disorder comprises an oncological disorder, ~~an immune-oncological disorder, a neurological disorder, a neurodegenerative disorder,~~ or an autoimmune disorder.
16. The use according to claim 15, wherein the medicament is to be administered to the mammal in combination with an additional therapeutic agent, optionally wherein:

(i) the additional therapeutic agent is one or more of:

(i-1) an anti-CD20 monoclonal antibody, optionally rituximab, obinituzumab, ofatumumab, ublituximab, or ibritumomab tiuxetan;

(i-2) an alkylating agent, optionally 4-[5-[Bis(2-chloroethyl)amino]-1- methylbenzimidazol-2-yl]butanoic acid or a salt thereof or bendamustine;

(i-3) a BCL-2 inhibitor, optionally 4-(4-{[2-(4-chlorophenyl)-4,4- dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-({3-nitro-4-[(tetrahydro-2H-pyran-4-yl)methyl]amino}phenyl} sulfonyl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide or a salt thereof or venetoclax;

(i-4) a phosphoinositide 3 -kinase (PI3K) inhibitor, optionally a PI3K delta inhibitor or a PI3K alpha and delta inhibitor, further optionally 5-Fluoro-3-phenyl-2- [(1 S)-1-(7H-purin-6-ylamino)propyl]-4(3H)-quinazolinone or a salt thereof, idelalisib, or 2-{3-[2-(1-Isopropyl-3-methyl-1H-1,2,4-triazol-5-yl)-5,6-dihydrobenzo[f]imidazo[1,2-d] [1,4]oxazepin-9-yl]- 1H-pyrazol-1-yl} -2-methylpropanamide or a salt thereof;

(i-5) a Bruton's tyrosine kinase (BTK) inhibitor, optionally 1-[(3R)-3-[4-Amino-3-(4-phenoxyphenyl)- 1H-pyrazolo[3 ,4-d]pyrimidin-1-yl]piperidin-1-yl]prop-2-en-1-one or a salt thereof or ibrutinib;

(i-6) thalidomide or a derivative thereof, optionally (RS)-3-(4-Amino-1-oxo 1,3-dihydro-2H-isoindol-2-yl)piperidine-2,6-dione or a salt thereof or lenalidomide;

- (i-7) an apoptotic agent;
- (i-8) an anti-tubulin agent;
- (i-9) an epidermal growth factor (EGFR) antagonist, optionally erlotinib;
- (i-10) a platelet derived growth factor inhibitor, optionally imatinib mesylate;
- (i-11) a COX-2 inhibitor, optionally celecoxib;
- (i-12) an antibody which binds to ErbB2, ErbB3, ErbB4, PDGFR-beta, BlyS, APRIL, BCMA VEGF, or VEGF receptor(s), TRAIL, Apo2, PD-1, PD-L1, or PD-L2; and/or
- (i-13) one or more of cyclophosphamide, doxorubicin, vincristine, and/or prednisolone);
- (ii) the anti-CD3 antibody or antigen-binding fragment thereof is an anti-CD3 and anti-CD20 bispecific antibody and the additional therapeutic agent is one or more of:
 - (ii-1) an anti-CD20 monoclonal antibody, optionally rituximab, obinituzumab, ofatumumab, ublituximab, or ibritumomab tiuxetan;
 - (ii-2) a chemotherapy agent, optionally one or more of cyclophosphamide, doxorubicin, vincristine, and prednisolone;
 - (ii-3) an antibody-drug conjugate (ADC) selected from: an anti-CD79b ADC, optionally polatuzumab vedotin; an anti-CD19 ADC; an anti-CD22 ADC; an anti-CD45 ADC; and/or an anti-CD32 ADC;
 - (ii-4) a BCL-2 inhibitor, optionally 4-(4-{[2-(4-chlorophenyl)-4,4- dimethylcyclohex-1-en-1-yl]methyl}piperazin-1-yl)-N-({3-nitro-4-[(tetrahydro-2H-pyran-4-yl)methyl]amino}phenyl)sulfonyl)-2-(1H-pyrrolo[2,3-b]pyridin-5-yloxy)benzamide or a salt thereof or venetoclax;
 - (ii-5) lenalidomide;
 - (ii-6) a PI3K-delta inhibitor, optionally a PI3K delta inhibitor or a PI3K alpha and delta inhibitor, further optionally 5-Fluoro-3-phenyl-2- [(1 S)-1-(7H-purin-6-ylamino)propyl]-4(3H)-quinazolinone or a salt thereof, idelalisib, or 2-{3-[2-(1-Isopropyl-3-methyl-1H-1,2,4-triazol-5-

yl)-5,6-dihydrobenzo[f]imidazo[1,2-d][1,4]oxazepin-9-yl)-1H-pyrazol-1-yl}-2-methylpropanamide or a salt thereof

(ii-7) a PD-1 antagonist,

(ii-8) an agonistic antibody against CD40, CD226, CD28, OX40, GITR, CD137, CD27, HVEM, or CD127, optionally urelumab;

(ii-9) an antagonistic antibody against CTLA4, PD-1, TIM-3, BTLA, VISTA, LAG-3, B7-H3, B7-H4, IDO, TIGIT, MICA/B, GITR, or arginase, optionally ipilimumab or tremelimumab;

(ii-10) a TGF beta antagonist, optionally metelimumab or fresolimumab; and/or

(ii-11) a T cell expressing a chimeric antigen receptor or a T cell comprising a dominant-negative TGF receptor; and/or

(iii) the anti-CD3 antibody or antigen-binding fragment thereof is an anti-CD3 and anti-HER2 bispecific antibody and the additional therapeutic agent is one or more of trastuzumab, T-DM1, and/or pertuzumab.

17. The use according to claim 15 or 16, wherein the mammal is a human.

18. Use of the anti-CD3 antibody or antigen-bindingantibody fragment thereof according to any one of claims 1-9 in the manufacture of a medicament for the treatment of hematological cancer, optionally leukemia, lymphoma, or multiple myeloma.

19. The use according to claim 18, wherein the hematological cancer is selected from the group consisting of non-Hodgkin's lymphoma (NHL), small lymphocytic (SL) NHL, germinal-center B-cell-like (GCB) diffuse large B-cell lymphoma (DLBCL), activated B-cell-like (ABC) DLBCL, follicular lymphoma (FL), mantle cell lymphoma (MCL), acute lymphoblastic leukemia (ALL), acute myeloid leukemia (AML), chronic lymphoid leukemia (CLL), chronic myeloblastic leukemia, marginal zone lymphoma (MZL), small lymphocytic leukemia (SLL), lymphoplasmacytic lymphoma (LL), Waldenstrom macroglobulinemia (WM), central nervous system lymphoma (CNSL), and Burkitt's lymphoma (BL), B-cell prolymphocytic leukemia, splenic marginal zone lymphoma, hairy cell leukemia, splenic diffuse red pulp small B-cell lymphoma, 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, pEBV-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, and primary effusion lymphoma.

20. Use of the anti-CD3 antibody or ~~antigen-bindingantibody~~ fragment thereof according to any one of claims 1-9 in the manufacture of a medicament for the treatment of an autoimmune disease selected from the group consisting of arthritis, rheumatoid arthritis, colitis, inflammatory bowel disease, and autoimmune type I diabetes.